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## Poster 1

# Agarose-based microwells to study transport and efficacy of polymeric nanoprobes within 3D Colorectal tumour spheroids.

Juliette Codevelle*[1]

[1]iLM - Biophysique – Institut Lumière Matière [Villeurbanne] – France

**Abstract**

Juliette Codevelle1 , E. Bastien1 , A. Tillement2 , O. Tillement1 , F. Lux1 , Clair Poignard3 , Charlotte Rivière1,4,5
1Univ Lyon, Université Claude Bernard Lyon 1, CNRS, Institut Lumière Matière, UMR 5306, Villeurbanne, France 2 Nano-H SAS, France 3 INRIA Bordeaux, France 4 Institut Universitaire de France (IUF), France 5 Institut Convergence PLAsCAN, Centre de Cancérologie de Lyon, INSERM U1052-CNRS UMR5286, Univ Lyon, Université Claude Bernard Lyon 1, ntre Léon Bérard, Lyon, France
Colorectal cancer is the third most common type of cancer worldwide, with almost 2 million cases diagnosed in 2020. Despite a growing number of innovative anti-cancerous therapeutic strategies, the vast majority of drug candidates, including nanotherapies, fail in clinical trials. This failure is largely attributed to the difficulty of modeling and predicting the in-vivo transport and therapeutic efficacy to the target site. In this context, the development of an integrated 3D multicellular spheroids in vitro platform offers a promising approach to predict patient responses to treatment. We used human colon cancer cell lines (HCT116 and HT29) to initiate spheroids that mimic avascular tumor features (hypoxia, metabolic constraints). Based on a multi-microwell agarose mold, our experimental set-up allows easy high-content drug screening and spheroid growth monitoring. First, spheroid growth was quantified using a combination of microscopy and mathematical modeling to predict cell proliferation states. Our results demonstrate that our set-up can be used to study the impact of environmental metabolic constraints on spheroid growth. Next, the transport and internalization properties of chitosan-based nanoparticles (MexCD1@Dotaga) were analyzed, and appear to demonstrate cellular uptake by endocytosis and efficient diffusion into spheroids. Overall, this study integrates experimental and modeling approaches to advance the understanding of nanoparticle transport and therapeutic outcomes in 3D model recapitulating key features of tumour environment.

*Speaker

## Poster 2

# An image-based workflow to study whether mechanical rules guide the trek of pollen tubes in the stigma

Jonathas Pereira Das Graças*[1], Ingrid Revel[1], Guillaume Cerutti[1], Jonathan Legrand[1], Christophe Godin[1], and Isabelle Fobis-Loisy†[1]

[1]Reproduction et développement des plantes – Ecole Normale Supérieure de Lyon, Université Claude Bernard Lyon 1, Centre National de la Recherche Scientifique, Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement – France

**Abstract**

In the flowering plant *Arabidopsis thaliana*, the pollen tube navigates through the female organ to deliver the immobile sperm cells to the ovules for fertilization. The pollen tube first penetrates the cell wall (CW) of the female epidermal stigmatic cell (papilla) and progresses inside the CW, constrained to follow a trajectory towards the papilla basis. Our team recently proposed that the guidance of pollen tube trek in this first step of sexual reproduction obeys mechanical cues pre-existent in the papillae. To date, little is known about papilla guiding factors, and neither whether the pollen tube obeys major rules while it navigates in the papilla, *e.g.,* geometrical rules. It is necessary now to provide accurate experimental data to minutely examine this interaction between the pollen tube and the papilla and find new clues to decipher this complex guidance process. Data will be extracted from in vivo high-resolution imaging describing the tube growth pattern in the papilla curved surface, to next identify features relevant to the mechanical behavior of the pollen tube path. For this purpose, we are establishing a complete workflow, linking targeted pollination in the papilla to the acquisition of high-resolution confocal images of pollen tube-papilla interaction, followed by image segmentation and 3D reconstruction of the interaction partners with a computational platform developed in our lab (GNOMON) devoted to analyzing the development of living forms in 3D. Thus, using this workflow we want to address mechanical questions regarding the pollen tube trek on the stigma: its natural receptive female platform.

*Speaker
†Corresponding author: isabelle.fobis-loisy@ens-lyon.fr

sciencesconf.org:mecanobio-grenoble:515900

## Poster 3

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# Cell&Soft: The Innovative Soft Culture Plates

Camille Migdal*[1]

[1]CellSoft – French Southern Territories

**Abstract**

Cell&Soft is a DeepTech company with value proposition in the development, production, and sale of soft and bio-mimetic solutions for *in vitro* cell culture and cell-based assays. Cell&Soft develops a complete range of soft-bottom Petri dishes, elaborate with innovative matrices, which reproduce the chemo-mechanical features of natural and diseased organs. Cell&Soft matrices mimic the natural environment on which each cell evolves *in vivo* and offer a new and physiologic way to culture cells *in vitro*, far away for plastic culture dishes. Cell&Soft offers different products and services:

-Catalogue products: range MecaChips®, choice among 11 stiffnesses, 6 coatings available in 6 formats and range MecaTract, with fluorescent beads for mechanical force studies by Traction Force Microscopy (TFM).

- Custom products: range $\mu$pattern MecaChips® with stiffness $\mu$-pattern (geometrical shapes, dual stiffness, stiffness gradient) from tissue scale to sub-cellular scale. We design the $\mu$-pattern(s) and stiffness(es) on demand.

- Custom development solutions and support services: entirely customized development of soft supports to meet your specific needs (in terms of stiffness, special coating, for "atypical" cells), which may lead to exclusive operating licenses. For TFM force measurements, we can analyze and process your images, or provide you with training to enable you to make your own use of the results.

All our products are delivered ready-to-use, dehydrated and aseptic, with batch number and certificate of analysis.
Cell&Soft products and services will be the tomorrow's tools that will reinvent in vitro cell culture by drastically improving the relevance of the overall in vitro cell based assays, and thus offer to researchers the possibly to make revolutionary discoveries.

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*Speaker

## Poster 4

# Decreasing size in 2D microplatforms for optimizing magnetic hyperthermia in vitro

Daniela Iglesias Rojas*[1,2], Ainara Castellanos-Rubio[3], Jon Mentxaka[4], Robert Morel[2], Bernard Dieny[2], Maite Insausti[1], Luis Lezama[1], and Idoia Castellanos-Rubio[1]

[1]Dept. Organic and Inorganic Chemistry, Faculty of Science and Technology, University of the Basque Country UPV/EHU, 48940 Leioa – Spain

[2]SPINtronique et TEchnologie des Composants – Centre National de la Recherche Scientifique, Institut de Recherche Interdisciplinaire de Grenoble, Université Grenoble Alpes – France

[3]Dpto. de Genética, Antropología Física y Fisiología Animal, UPV/EHU, 48940 Leioa – Spain

[4]Dpto. de Bioquímica y Biología Molecular, UPV/EHU, 48940 Leioa – Spain

**Abstract**

In the past few years, the research on magnetic nanoparticles (MNP) in biomedicine has increased due to their potential as anticancer agents, as they can be used in minimally invasive therapies, such as magnetic hyperthermia (1). However, the incorporation of MNPs into a biological environment has two significant limitations: MNPs tend to agglomerate, reducing their magneto-thermal capacity (2), and they are prematurely eliminated by endocytic mechanisms (3), limiting the efficacy of the therapy. For overcoming these two drawbacks, the fabrication of hybrid microdiscs (MDs) (polymeric-inorganic) as platforms to support the MNPs is presented. These MDs are formed by depositing an inorganic film (Au), a polymeric multilayer and a monolayer of magnetite (Fe3O4) NPs onto a sacrificial photolithographic template.

Initially, the fabrication of the mushroom-shaped photolithographic templates with different diameters (20 and 10 $\mu$m) were optimized to properly assembly and lift off the MDs with a monolayer of MNPs with minimal agglomeration (4). In order to demonstrate the suitability of the fabricated microplatforms for biomedical applications, in vitro experiments were performed on colon cancer-derived cell line (HCT116), demonstrating the high resistance of the MDs to endocytosis and their good biocompatibility in the cell medium. In vitro magnetic hyperthermia experiments were also carried out, using 1-2 MDs/cell being a lower concentration of MNPs than usually is used, but no statistically significant cell death was achieved. With the aim of improving the efficiency of the magnetic hyperthermia treatment in vitro, microdiscs of a considerably smaller size (1-2 $\mu$m) were manufactured to increase the MDs/cell rate and enhance the number of MDs in contact with the cell surface to make the hyperthermia treatment more efficient. The photolithographic templates for the fabrication of the smaller MDs, were obtained using the deep ultraviolet (DUV) lithography technique and the step of the process where the assembly of the polymeric multilayers and monolayer of MNPs is performed has been optimized to obtain an efficient lift off.

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*Speaker

## Poster 5

# Development of a biomimetic high throughput essay to study neuroblastoma cell differentiation.

Nathan Thibieroz*[1], João Lopes[1], Paul Machillot[1], Fabrice Cordelieres[2], Elisa Migliorini[1], and Catherine Picart[1]

[1]BioSanté – Institut National de la Santé et de la Recherche Médicale, Institut de Recherche Interdisciplinaire de Grenoble, Université Grenoble Alpes – France

[2]Bordeaux Imaging Center – Université de Bordeaux, Institut François Magendie, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France

**Abstract**

Neuroblastoma (NB) is one of the most common cancer for children, from 7 to 10% of all pediatric cancers. Because of its heterogeneity, no specific treatments are available. Extracellular matrix composition and stiffness was found to have an impact on the proliferation and differentiation of NB. What could be the combined effect of those two parameters?
Proliferation and differentiation of NeuroBlastoma (NB) are affected by the extracellular matrix composition and stiffness. New treatments are needed to address the high-risk situations and heterogeneity of neuroblastoma. We want to mimic some aspects of NB using biomaterials to investigate the roles of matrix stiffness and bioactivity on NB differentiation, in a high throughput manner.

For that, we use two types of biomaterials. First, Streptavidin (SAv) biomimetic platform with well-defined surface functionalization on a PDMS base of controlled stiffness. Second, Layer by Layer (LbL) films to test the role of Retinoic Acid RA and Transforming Growth Factors (TGF) when bound to the film or added in solution (soluble) on NB behavior. NB differentiation is assessed via cell morphology and neurite formation.

Tests are performed with Neuro2A and SH-SY5Y neuroblastoma cell lines.

The biomaterials were automatically prepared using a pipetting robot. To match this high throughput production, data were obtained with high content living cell imaging to quantify cell proliferation and high content immuno-fluorescence microscopy to visualize specific markers. Images were analyzed using an array of high content analysis software, notably a high content FijiJ macro. We aim to analyze a wide range of parameter (shape of cell, neurite length and number, size of cell) in a high throughput manner, on support going from simple glass, to biomimetic platforms and films.

Softer substrates, LbL films, and grow factor presentation seem to enhance cellular differentiation. However, we still need to optimize the conditions, increase the number of experiments, and acquire more data. High content images acquisition is settled up, but the analysis could require improvement.

*Speaker

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## Poster 6

# Evaluation of cancer cells mechanical phenotype associated with the resistance to treatment in myeloid leukemia

Camila Martin Cardozo*[1,2], Sylvain Lefort[2], and Magalie Faivre[1]

[1]INL - Dispositifs pour la Santé et l'Environnement – Institut des Nanotechnologies de Lyon, Université Claude Bernard - Lyon I, CPE LYON, Centre National de la Recherche Scientifique - CNRS, Ecole Centrale de Lyon, INSA Lyon, France – France

[2]Centre de Recherche en Cancérologie de Lyon – Centre Léon Bérard [Lyon], Université Claude Bernard Lyon 1, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France

**Abstract**

Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the abnormal proliferation of leukemia cells (or blasts) that build up in the bone marrow and the blood. These blasts interfere with normal blood cell production due to their inability to differentiate into mature cells. Despite the recent progress in therapies, which consist essentially, despite the emergence of new targeted therapies, in intensive cycles of chemotherapy, most of the AML patients do not recover, having a five-year survival rate of 20%. Preliminary results show different mechanical profile associated with cells that are sensitive and resistant to different types of treatment, these results suggest that there is a correlation between resistance to treatment and cell stiffness.
One of the simplest and widely utilized methods in literature for measuring cellular mechanical properties involves passive microfluidic techniques with high throughput is the monitoring of cell deformations as they flow through microfluidic constricted channels (1). Here we propose an original readout traducing the way the cell perturbs the pressure distribution in the device when flowing through the constriction (2).

This project seeks to evaluate and characterize the mechanical properties of AML cells, aiming to establish a correlation between cell stiffness and their resistance to treatment. In the long term, the goal of this study is to utilize cell stiffness as a predictive factor in determining the likelihood of disease relapse for AML patients, offering valuable insights for personalized treatment strategies.

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*Speaker

## Poster 7

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# Folding oneself into shape: Apical actomyosin buckles an embryonic epithelium

Julien Fierling , Jocelyn Etienne*[1], Philippe Marmottant , Catherine Quilliet , and Matteo Rauzi

[1]Laboratoire Interdisciplinaire de Physique – Centre National de la Recherche Scientifique : UMR5588, Université Grenoble Alpes, Université Grenoble Alpes : UMR5588 – France

**Abstract**

Cell apical constriction driven by actomyosin contraction forces is a conserved mechanism during tissue folding in embryo development. While much is now understood of the molecular mechanism responsible for apical constriction and of the tissue-scale integration of the ensuing in-plane deformations, it is still not clear if apical actomyosin contraction forces are necessary or sufficient per se to drive tissue folding.

To tackle this question, we use the Drosophila embryo model system that forms a furrow on the ventral side, initiating mesoderm internalization. Past computational models support the idea that cell apical contraction forces may not be sufficient and that active or passive cell apico-basal forces may be necessary to drive cell wedging leading to tissue furrowing. By using 3D computational modelling and in toto embryo image analysis and manipulation, we now challenge this idea and show that embryo-scale force balance at the tissue surface, rather than cell-autonomous shape changes, is necessary and sufficient to drive a buckling of the epithelial surface forming a furrow which propagates and initiates embryo gastrulation.

*Speaker

sciencesconf.org:mecanobio-grenoble:509694

## Poster 8

# Intestinal epithelial cells under variable curved substrates

Thibault Mercier*†[1], Valentin Chalut[2], Anne-Laure Deman-Him[3], and Caterina Tomba[1]

[1]INL - Dispositifs pour la Santé et l'Environnement – Univ Lyon, CNRS, INSA Lyon, ECL, UCBL, CPE Lyon, INL, UMR5270, 69622 Villeurbanne, France – France
[2]INL - Dispositifs pour la Santé et l'Environnement – Univ Lyon, CNRS, INSA Lyon, ECL, UCBL, CPE Lyon, INL, UMR5270, 69622 Villeurbanne, France – France
[3]INL - Dispositifs pour la Santé et l'Environnement – Univ Lyon, CNRS, INSA Lyon, ECL, UCBL, CPE Lyon, INL, UMR5270, 69622 Villeurbanne, France – France

**Abstract**

The intestinal epithelium is made from small (0.5–1 mm), repetitive, compartmentalized structures called crypt-villus units. Intestinal cells grow on curved surfaces, with highly organized stem cells (crypts) and differentiated cell compartments (villi) residing in concave and convex regions, respectively. Recent studies have highlighted the importance of curvature as a crucial physical cue influencing cellular behaviour. Cells demonstrate the ability to perceive local curvature, leading to changes among others in focal adhesion organization and dynamics, nuclear shape, gene expression, and differentiation behaviour. In the context of intestinal tissues, folding occurs through a series of biochemical signals triggering changes in cell shape, ultimately resulting in spatial phenotypic patterning. To differentiate the consequences of these cell shape alterations from the effects of the pathways initiating them, it is necessary to replicate such curvature in in vitro models of the intestine. Despite the growing interest in understanding the impact of substrate curvature on the intestinal epithelium, challenges persist in fabricating substrates with precisely dynamically controllable microscale curvatures, along with defined mechanical stiffness and biochemical composition. To address these challenges, we developed magnetic polymer membranes to grow intestinal epithelial cells under curved, reversible and controlled deformations. This approach would allow creation of substrates with dynamically controlled curvature and give some insights on the role of curvature of intestinal tissue composition and organisation. With this aim, we firstly investigated cell viability on such membranes, under static and varying magnetic fields.

*Speaker
†Corresponding author: thibault.mercier@hotmail.com

sciencesconf.org:mecanobio-grenoble:513626

## Poster 9

# Investigating the dynamic response of nucleolus to mechanical compression

Yuthika Shetty*[1] and Monika Dolega†

[1]Institute for Advanced Biosciences / Institut pour l'Avancée des Biosciences (Grenoble) – Université Grenoble Alpes – France

**Abstract**

Cellular microenvironment is crucial in determining cell fate and function. Cells have the ability to perceive and respond to various extracellular chemical and mechanical stimuli. These stimuli trigger complex intracellular signaling pathways that have evolved to help maintain cellular homeostasis. Nucleolus, a prominent sub-nuclear organelle, has been established as a hub that coordinates cellular stress response pathways. Due to its dynamic properties, the nucleolus has been shown to rapidly respond to various extracellular stressors. A previous study within our team revealed that static mechanical compression of epithelial monolayer triggers changes in the regulation of genes encoding ribosomal proteins, suggesting a potential mechanical regulation of the ribosome biogenesis process. Here, we investigate the nucleolar state when exposed to a static compressive force. Live cell imaging was performed to observe the dynamic changes in the nucleolar composition during mechanical stress response and the possible biomechanical triggers involved. Functional consequences were investigated by performing Click-IT RNA Imaging Assay and Immunofluorescence which revealed changes in the rate of transcription of rDNA and associated histone modifications. We conclude that external biomechanical stress triggers dynamic changes in the nucleolar composition and function which may be significant in the mechanical stress response pathway.

*Speaker

†Corresponding author: monika.dolega@univ-grenoble-alpes.fr

sciencesconf.org:mecanobio-grenoble:516404

## Poster 10

# MEASURING RIGIDITY OF CELLULAR INTERRIROR OF NORMAL AND KELOID FIBROBLAST WITH MICRO-BRILLOUIN LIGHT SCATTERING (mBLS) TECHNIQUE

Fehima Ugarak*†[1], Yasmin El Mahi[2], Gwenaël Rolin[2,3], Céline Elie-Caille[1], Alexis Mosset[1], and Vincent Laude[1]

[1]Université de Franche-Comté – Institut FEMTO-ST CNRS – France
[2]Université de Franche-Comté – EFS, INSERM, UMR RIGHT – France
[3]INSERM CIC-1431 – CHU Besançon – France

**Abstract**

**INTRODUCTION**

Brillouin Light Scattering (BLS) implies an inelastic scattering of light by spontaneous thermal fluctuations in a material. Viscoelastic properties are afterward accessible from the frequency shift and Full Width at Half Maximum of the peak. Traditional techniques for the characterization of biomaterials such as magnetic bead twisting, deformation microscopy, micro-rheology, or atomic force microscopy (AFM) either require contact, are destructive, or do not provide sufficient resolution. In contrast, Brillouin imaging offers an alternative approach. It is non-contact, label-free, and non-destructive, making it well-suited for investigating biological samples at the GHz/micron scale. Moreover, it holds significant promise for enhancing clinical diagnostic capabilities. The idea of our project is to compare stiffness of normal and keloid fibroblast cells, by obtaining their Brillouin maps, with the goal of detecting the cause and possible therapeutic treatment of keloid disease.

**MATERIALS AND METHODS**

Non-contact mechanical and chemical analysis of a single living cell was obtained by Mattana et al (1) where it has been shown the successful ability of the BLS spectroscopic technique to characterize subcellular compartments and distinguish cell status. In our project, we aim to examine keloid disease, its cause and possible treatment. Keloids are characterized by excessive collagen production at the dermis level and overgrowth beyond initial wound due to abnormal wound healing (2), often triggered by skin injuries like surgery or burns. Keloids are considered as a chronic inflammatory disease which shares similarities with cancer (3). At a cellular level, fibroblasts play a crucial role in the development of keloids, those cells are sensitive to their biological and mechanical microenvironment (2). Keloid fibroblasts are in close contact with immune cells which release inflammatory signals, activating fibroblasts into myofibroblasts, which overproduce collagen (4). This excess collagen stiffens tissue, perpetuating a feedback loop. Fibroblasts migrate toward stiffness, deposit more collagen, and

*Speaker
†Corresponding author: ugarakfehima@outlook.com

trigger further activation and growth factor release (2).

## RESULTS AND DISCUSSION

Understanding how mechanical signals and inflammation collaborate in keloid formation is a current research focus (5). This synergy is essential in this part of the project, aiming to unravel keloid development mechanisms for potential therapeutic insights. Using the BLS technique, we would be able to access the stiffness and losses of normal and keloid fibroblast cells, knowing their refractive index and mass density. Combination of the mBLS setup with fluorescent microscope represents a big advantage as it helps us assign different cell parts during the scan by obtaining Brillouin maps from which we can deduce the mechanical properties at every point across the cell.

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## Poster 11

# Mechanical characterization of regenerating Hydra tissue spheres

Thomas Perros*[1], Anaïs Biquet-Bisquert[2], Zacchari Ben Meriem[3], Morgan Delarue[3], Pierre Joseph[3], Philippe Marcq[4], and Olivier Cochet-Escartin[1]

[1]Institut Lumière Matière [Villeurbanne] – Université Claude Bernard Lyon 1, Centre National de la Recherche Scientifique – France

[2]Centre de Biologie Structurale [Montpellier] – Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Université de Montpellier – France

[3]Laboratory for Analysis and Architecture of Systems [Toulouse] – Institut National des Sciences Appliquées de Toulouse, Université Toulouse III - Paul Sabatier, Université Toulouse-Jean-Jaurès, Institut National Polytechnique de Toulouse, Institut des Sciences de l'Ingénierie et des Systèmes, Centre National de la Recherche Scientifique - CNRS – France

[4]Ecole Superieure de Physique et de Chimie Industrielles de la Ville de Paris – Université Paris sciences et lettres – France

**Abstract**

*Hydra Vulgaris* is a fresh water polyp known for its regenerative capabilities. Each piece excised from its body can reform, in a few days, a new complete and functional *Hydra*. The observed influence of tissue mechanics on their regeneration suggests that there is a mechano-biological coupling at play. However, the study of such coupling has suffered from a lack of knowledge of the mechanical properties of regenerating *Hydra* samples. Here, we used a novel parallel micro-aspiration setup and numerical simulations to fill this gap. We demonstrated that the rheology of *Hydra* tissue spheres displays three different regimes depending on the applied stress: elastic, visco-elastic and finally tissue rupture. Using models of deformable spherical shells, we were able to determine the Young modulus and viscosity associated with the elastic and viscous phases as well as the stresses required to switch between these different responses, including the critical stress inducing tissue rupture. This full mechanical characterization therefore offers a first step for the future elaboration of new models of *Hydra* patterning based on experimental results and including both the mechanical and biochemical levels.

*Speaker

sciencesconf.org:mecanobio-grenoble:513599

## Poster 12

# Mechanical Stability of Multicellular Assemblies

Daniel Selma*[1], Vladimir Misiak*[1], Simon De Beco[2], Giovanni Cappello[1], Thomas Boudou[1], and Martial Balland[1]

[1]Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – Centre National de la Recherche Scientifique, Université Grenoble Alpes, Centre National de la Recherche Scientifique : UMR5588 – France

[2]Institut Jacques Monod – Centre National de la Recherche Scientifique, Université Paris Cité, Centre National de la Recherche Scientifique : $UMR_7592 - -France$

**Abstract**

Cell intercalation –or T1 transition– is a crucial event in morphogenetic processus where cells exchange positions by remodeling their cell-cell and cellsubstrate adhesions. It allows a dynamic spatial redistribution of cells while keeping their integrity and collective cohesiveness as a tissue. Most of the experiments performed to assess this process are done in vivo where mechanical readouts are indirectly retrieved from image analysis. Therefore, a complete understanding of cell intercalation is still lacking. To address this gap, we designed a novel in vitro assay to simplify the system by making a compromise: reducing the biological relevance but allowing the imaging of specific molecular pathways and the quantitative measurement of forces involved. Practically, assemblies of four cells –cell quadruplets– were arranged in vitro to mimic the "minimal tissue pavement" that exists in vivo, i.e. the most basic structure that makes possible the T1 transition. To this end, a variety of extracellular matrix (ECM) architectures were micropatterned on treated glass coverslips. Subsequently, those patterns were seeded with Madin-Darby Canine Kidney (MDCK) cells, which self-organized into cell quadruplets, owing to the optimization of the geometrical boundary conditions of the patterns. With such minimalistic system, in vitro cell intercalation events were recorded in two different patterns, although with a rare frequency. Thus, this approach allows the morphological characterization and the mechanical assessment of cell quadruplets' dynamics on different micropatterns, over their lifetime and during the T1 transition.

*Speaker

sciencesconf.org:mecanobio-grenoble:516254

## Poster 13

# Modeling and Simulation of RBCs Aggregation in Cardiovascular Networks

Fouzia Imharken[*†1,2], Misbah Chaouqi[‡1], and Hamid Ez-Zahraouy[2]

[1]Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – Centre National de la Recherche Scientifique, Université Grenoble Alpes, Centre National de la Recherche Scientifique : UMR5588 – France

[2]Faculté des sciences de Rabat – Morocco

**Abstract**

Cardiovascular dysfunctions due to undesirable adhesion among blood elements (like red blood cells-RBcs) are the main causes of mortality in the world. In our study, we intend to develop simple models to better understand the perfusion of blood in microcirculation by considering a complex geometry under several conditions (shear, confinement, pressure, etc.) in the presence of adhesion among RBCs using an immersed boundary-lattice Boltzmann method. Our primary results show that the aggregation of RBCs and their mechanical properties has a strong impact on their distribution in the network. For stiff RBCs (due to a disease) a weak adhesion leads to super diffusion instead of ballistic transport, as compared to the case without adhesion.

[*]Speaker

[†]Corresponding author: fouzia46imharkan@gmail.com

[‡]Corresponding author: chaouqi.misbah@univ-grenoble-alpes.fr

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## Poster 14

# Modelling the positioning of the cell division plane in brown algal cells

Tanguy Dufourt*[1], Bénédicte Charrier[1], and Bernard Billoud†[2]

[1]Morphogenesis of brown algae - CNRS – Institut de Génomique Fonctionnelle De Lyon (IGFL), École Normale Supérieure de Lyon, CNRS - Université Claude Bernard, France, Centre National de la Recherche Scientifique - CNRS – France

[2]Morphogenesis of brown algae - SU – Institut de Génomique Fonctionnelle De Lyon (IGFL), Sorbonne Université UPMC Paris VI – France

**Abstract**

Cytokinesis involves a variety of mechanisms, depending on the taxon studied. In animal cells, cytokinesis takes place through the formation of a furrow perpendicular to the mitotic spindle (D'Avino et al., 2015) 1, while in plant cells, the phragmoplast develops from position memory cues deposited before mitosis (Rasmussen & Bellinger, 2018) 2. In brown algae, which are phylogenetically distant from these two taxa, very little is known about the mechanisms controlling the positioning and orientation of the cell division plane.
Detailed cytology observations during the cell cycles of several brown algae have led to a canonic model, in which 1) the cytokinetic plane lies perpendicular to the axis established by the two centrosomes, usually relatively long after the end of the telophase (Nagasato & Motomura, 2002) 3 and 2) during most of the cell cycle, the nucleus is surrounded by two centrosomes. Thus, it should be possible to predict the position of the cytokinetic plane by monitoring or predicting the displacement of the two centrosomes during the cell cycle, and this, independently of the position and orientation of the mitotic spindle.

It is difficult to observe the dynamics of the cytoskeleton in brown algae. Therefore, while appropriate and relevant cell biology and imaging tools are currently being developed in the lab, my PhD project began with *in silico* modelling.

So far, I have aimed to simulate the displacement of two centrosomes in the two brown algae *Saccharina* and *Sphacelaria*. Using the Cytosim software (Nedelec & Foethke, 2007) 4, we implemented a cortical pushing model, in which growing microtubules initiate a reactive force on centrosomes. Using this model, we have shown how several cellular geometric features impact the centring and alignment of centrosomes, and consequently, the position and orientation of the cell division plane.

Cell size is predicted to have a strong impact while cell shape has a moderate impact. In addition, preliminary results have shown that the presence or absence of organelles like chloroplasts or vacuoles, which are abundant in algal cells, have a limited effect on centrosome positioning.

*Speaker
†Corresponding author: bernard.billoud@ens-lyon.fr

sciencesconf.org:mecanobio-grenoble:515116

These initial results establish a base from which more complex cellular mechanisms, such as cortical or cytoplasmic pulling, can be elaborated together with data from wet experiments, in order to account for the mechanisms underlying the position and orientation of centrosomes in other brown algal cells. This also requires Cytosim to be adapted to our needs, for example so that it is able to simulate the movement of centrosomes in growing cells.

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3 Nagasato & Motomura, 2002, Influence of the centrosome in cytokinesis of brown algae: polyspermic zygotes of *Scytosiphon lomentaria* (Scytosiphonales,Phaeophyceae), Journal of Cell Science, vol. 115, num. 12, 2541-2548, DOI : 10.1242/jcs.115.12.2541

4 Nedelec & Foethke, 2007, Collective Langevin dynamics of flexible cytoskeletal fibers, New Journal of Physics, vol. 9, num. 11, 427, DOI : 10.1088/1367-2630/9/11/427

## Poster 15

# Morphomechanical characterization of Extracellular Vesicles subpopulation

Geetika Raizada*[1], Eric Lesniewska[2], Wilfrid Boireau[3], and Céline Elie-Caille[3]

[1]Femto-ST – CNRS UMR 6174, CNRS : UMR6174 – France
[2]Laboratoire Interdisciplinaire Carnot de Bourgogne – Université de Technologie de Belfort-Montbeliard, Université de Bourgogne, Université Bourgogne Franche-Comté [COMUE], Centre National de la Recherche Scientifique – France
[3]Franche-Comté Électronique Mécanique, Thermique et Optique - Sciences et Technologies (UMR 6174) – Université de Franche-Comté, Centre National de la Recherche Scientifique, Ecole Nationale Supérieure de Mécanique et des Microtechniques, Université de Technologie de Belfort-Montbeliard, Centre National de la Recherche Scientifique : UMR6174, Université de Technologie de Belfort-Montbeliard : UMR6174 – France

**Abstract**

Extracellular vesicles (EVs) are nano objects which are released from all types of cells. Once thought to be garbage of the living cells, in the last decade they have been used in many applications in the medical field (1), due to their role in cell to cell communication. They are being explored as biomarkers for several pathological conditions for the diagnostic purposes. Many researchers have been exploring their cargo for the therapeutic benefits and as drug delivery vehicles. However despite having these potentials, they are still not being used in medical applications as the mainstream solution. The reason for this arises from their complexities in the isolation and characterization due to their size range and diverse biogenesis pathways. Their overlapping physical properties such as size and density with other elements like lipoproteins, viruses, etc. makes the isolation and characterization methods very challenging.

In this study, we combined fluorescent microscopy and Atomic Force Microscopy (AFM) to study the metrology of large EVs (lEVs) subsets coming from different cell conditions. We performed nanomechanical mapping by using Quantitative Imaging (QI) mode of fluorescent and non fluorescent tagged lEVs, adsorbed on positively charged mica substrate.

We measured Young's modulus of approximately 100 lEVs from each cell culture condition. Through Young's modulus map generated and also with the help of size profiling of lEVs, we identified several sub-populations of lEVs. We also observed the variation in the elasticity across a single vesicle.

This information can explain the effect of different cell culture conditions on the EV. Also by combining this information with other methods like vibrational spectroscopy, we can attribute the presence of different molecules as well as shed light to their biogenesis.

*Speaker

sciencesconf.org:mecanobio-grenoble:516418

## Poster 16

# Nuclear deformation and cell fate

Ben O'gormann , Marvin Brun-Cosme-Bruny , Omar Aldarawish* , Lydia Pernet , Monika Dolega , and Sandrine Fraboulet†[1]

[1]IAB – Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Université Grenoble Alpes, UGA – France

**Abstract**

Cells in a tissue are subjected to different mechanical forces and it is now known that the mechanical properties of cellular microenvironment greatly influence many fundamental aspects of their physiology including their differentiation, growth, and migration. For a long time, cell surface adhesions were considered to be the main transducers of mechanical stress. Recent studies indicate that the nuclear envelope itself may also play a role in mechanotransduction regulating chromatin organization and signalling pathways that will have a profound impact on cell behaviour and fate.
In this context, we have studied the long-term consequences of a lack of contractility in fibroblasts and characterized the induced phenotype. The relaxed cells enter a senescent state associated with DNA damage and telomere dysfunction.
We have shown that DNA damage is a late component and does not seem to initiate the senescent phenotype. Surprisingly, we also show that the molecular complex LINC connecting the nuclear envelope and the cytoskeleton is not necessary to induce the senescent phenotype. We have dissected the molecular changes preceding the induction of the senescent phenotype. Lamin A/C changes, pre-lamin A processing and the consequences on nuclear deformation using confocal imaging is dissected. Understanding these mechanisms may potentially lead to the identification of new pharmacological targets influencing cell cycle and cell fate and is therefore useful for anti-cancer therapy.

*Speaker
†Corresponding author: sandrine.fraboulet@univ-grenoble-alpes.fr

sciencesconf.org:mecanobio-grenoble:513175

## Poster 17

# Quantitative analysis of the mechanical properties of healthy and cancer lung tissue for the design of mechano-mimetic culture substrates

Alice Nicolas*[1], Fabien Delebosse[2,3], David Fuard[2], Sebastien Soulan[2], Corine Perrin[4], Lara Chalabreysse[4], and Camille Migdal[3]

[1]Laboratoire des Technologies de la Microelectronique – University Grenoble Alpes, CNRS, CEA – France

[2]Laboratoire des Technologies de la Microelectronique – University Grenoble Alpes, CNRS, CEA – France

[3]CellSoft – Cell and Soft – France

[4]Hospices Civils de Lyon – Department of Pathology, Groupement Hospitalier Est, HCL, Lyon, Université de Lyon, Université Lyon 1 – France

**Abstract**

Mechanical properties of tissues are increasingly recognized as crucial in disease progression. Here we investigate the mechanical properties of normal and adenocarcinoma lung tissues from 18 patients using indentation-type atomic force microscopy. We show that these tissues exhibit a predominant linear elastic behavior. Microscale tissue stiffness and shape descriptors of stiffness texture are extracted from maps of the Young's modulus. Furthermore, a correlation between tissue composition and stiffness is performed. Combining these parameters with photolithography, stiffness-textured polyacrylamide hydrogels are engineered, resulting in culture substrates that mimic the tumor tissue's stiffness distribution. By culturing A549 cells on these hydrogels, the influence of substrate stiffness texture on cellular behavior is evaluated. The development of this versatile mechanomimetic platform reveals its potential applicability to other human tissues and is envisioned as an in vitro model to improve the predictability of drug screening.

*Speaker

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## Poster 18

# Study of cell sensitivity to stiffness in 3D environment with controlled geometry

Aida Gabriela Fernandez Contreras*[1], Alice Nicolas[1], and Jean-Hervé Tortai[2]

[1]LTM – Universite Grenoble Alpes, CNRS, LTM, 38054 Grenoble, France, Université Grenoble Alpes, CNRS, LTM, 38054 Grenoble, France – France
[2]LTM – Universite Grenoble Alpes, CNRS, LTM, 38054 Grenoble, France, Université Grenoble Alpes, CNRS, LTM, 38054 Grenoble, France – France

**Abstract**

**Aída G. Fernández Contreras 1,*, Jean-Hervé Tortai 1 and Alice Nicolas 1**
1 Université Grenoble Alpes, CNRS, LTM, 38054, Grenoble, France

*Correspondence: aida-gabriela.fernandezcontreras@cea.fr

Cell culture is an important tool that enables the study of physiological and pathological cell activity in vitro with applications in fields such as cell biology, drug discovery, cancer research, tissue engineering, and stem cell studies (Serban et al., 2008). In traditional cell culture, cells adhere to rigid two-dimensional (2D) surfaces, typically made of polystyrene or glass. However, cells in the body are usually supported by a complex three-dimensional (3D) extracellular matrix (ECM) (Langhans, 2018).

There is a complex feedback relationship between cells and this matrix, as cells exert mechanical forces to remodel the extracellular matrix according to their requirements. In turn, mechanical signals from the extracellular matrix, like stiffness, create stimuli that cells can sense and transduce to regulate cellular behavior including adhesion, growth, migration, proliferation and differentiation (Wang et al., 2019). Since this dynamic environment cannot be accurately represented by the static nature of traditional 2D cell culture surfaces, data obtained from in vitro studies with these models can be non-predictive of in vivo behavior, often resulting in disparities with animal and clinical tests (Prestwich, 2007).

Given the high impact of the extra cellular matrix on cell behavior, several attempts have been made to better recreate its properties in vitro by creating artificial extra cellular matrix models. However, most current models are in 2D, including hydrogels with patterned material properties like protein composition and stiffness. Although these models represent a step forward by providing a more dynamic and relevant microenvironment that can influence aspects like cell polarity and spatial distribution, they still fall short in recreating the full dimensionality of many in vivo systems (Wang et al., 2019)

In consequence, there has been a transition towards the creation of 3D scaffolds. Various classical techniques such as solvent casting, salt leaching, freeze-drying, and phase separation, have been used for the fabrication of 3D scaffolds with high porosity and large surface

*Speaker

area that stimulate cell adhesion. However, precise control over the scaffold architecture is limited, and there can be high variability from sample to sample (Bourdon et al., 2018).

New 3D printing or additive manufacturing (AM) techniques have been developed, that allow the production of structures with controllable and complex architecture based directly on Computer Aided Design (CAD) models, achieving higher repeatability. A particularly promising technique for the fabrication of 3D scaffolds with high resolution is two-photon polymerization (TPP), as it enables the control of features down to the submicrometer scale (Tayalia et al., 2008).

The objective of this project is, therefore, to develop 3D scaffolds with defined mechanical properties in the $\mu$m scale, employing the high-resolution capability of two-photon polymerization, to customize the cell environment and investigate the effect of specific mechanical cues such as scaffold stiffness and pore size in cell behavior.

These properties are highly dependent on the fabrication parameters and material selection. For this reason, first, a commercial photoresist called OrmoComp that is compatible with cell culture and has been highly reported in literature (Bonabi et al., 2019), was used to determine the attainable resolution as well as to understand and optimize the key fabrication parameters that allow to control scaffold mechanical properties.

This process resulted in the fabrication of two mesh structures with the same fiber thickness (10 $\mu$m), but different cavity sizes (20 and 40 $\mu$m), that were used in preliminary cell culture studies with adenocarcinoma (A549) cells to asses the effect of pore size on cell behavior. Fluorescence microscopy images showed that both models displayed 3D cell distribution and cell proliferation. Differences in cell morphology and distribution were observed in function of the pore size, as cells appeared to adhere to the edges and surround the cavity in the model with a larger cavity size, while they showed a tendency to stretch out across the cavities in the case of smaller cavity size.

To further advance this technology and create models with tunable stiffness in addition to tunable pore size, initial experiments were conducted using an acrylamide-based photoresist formulation. This hydrogel, in contrast to OrmoComp, has high-swelling capabilities that allow tuning the scaffold stiffness in the range of biological tissues. However, the high solvent content poses a challenge for the creation of structures with high definition and mechanical stability (Zaari et al., 2004). Nevertheless, a proof of concept on the fabrication of 3D scaffolds was achieved.

The results from this study collectively show that two-photon polymerization combined with material technology provides a promising path for the creation of artificial 3D scaffold models that better emulate in vitro the intricate natural environment of cells within the body, towards the advancement in basic cell behavior understanding as well as application in tissue engineering and drug development.

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## Poster 19

# Symmetry breaking in biological tissues using bioelectricity

Niloofar Pishkari*[1]

[1]Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – Centre National de la Recherche Scientifique, Université Grenoble Alpes, Centre National de la Recherche Scientifique : UMR5588 – France

**Abstract**

Directed cell migration plays an important role in fundamental multicellular processes such as morphogenesis, healing, and cancer progression. Understanding the details of migratory system in cells would provide us with a huge potential for further investigations. In such phenomena, we observe collective cell migration with electrotactic bias, highlighting the importance of cell–cell junctions. We take advantage of a specialized bioreactor with computer-controlled electrodes to investigate electrotaxis, guiding cells along electric field gradients. While biochemical cues offer insights into electric field sensing, a clear physical portrait of collective cell response remains elusive. Notably, a distinctive electric field-induced reorientation of cell bodies perpendicular to the field is observed across diverse cell types. Our research extends to explore intercellular stresses under electrotaxis, unraveling the intricate dynamics of collective cell migration within a concise framework. These findings promise valuable contributions to our understanding of motility machinery role in morphogenesis and wound healing.

*Speaker

sciencesconf.org:mecanobio-grenoble:516035

## Poster 20

# Unveiling microtubule fracture dynamics: A comprehensive examination of the influence of lattice defects on the breakage process of microtubules

Amir Zablotsky*†[1] and Karin John[1]

[1]Université Grenoble Alpes / CNRS, LIPhy – Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – France

**Abstract**

Microtubules (MTs), crucial to many cellular functions, are tube-like structures formed by a quasi-crystalline arrangement of $\alpha\beta$–tubulin heterodimers.
Two parameters that are major determinants for MT stability and dynamics are the lattice binding energy and anisotropy (defined as the ratio between the longitudinal and lateral binding energies).

Despite considerable effort on comprehending the dynamics of the MT tip, in particular the so called dynamic instability, the dynamics within the "bulk" MT lattice have received little attention.

Recent experimental findings revealed that MTs often present dimer and monomer sized vacancies along their shaft, resulting in structural defects that compromise their shaft integrity and may interfere with the dynamic instability at the tip.

Here we employ kinetic Monte Carlo simulations, as well as analytical approaches, to study the defects dynamics in the MT shaft and their effects on MT breakage in the absence of free tubulin dimers.
Our findings highlight the significant role of initial defects in the fracture propagation dynamics. Furthermore, comparison with experiments allows us to identify lattice binding energies and anisotropies that accurately reproduce experimental observations of fracture times and lengths.

*Speaker
†Corresponding author: amir.zablotsky@univ-grenoble-alpes.fr

sciencesconf.org:mecanobio-grenoble:513493

## Poster 21

# Cellular Interaction with Low-Frequency-Vibrating Magnetic Nanoparticles in Bio-Mimetic Mechanical Environment

Andrea Visona*[1,2], Bernard Dieny[2], Robert Morel[2], Sebastien Soulan[1], Hélène Joisten[2], and Alice Nicolas[1]

[1]Laboratoire des technologies de la microélectronique – Commissariat à l'énergie atomique et aux énergies alternatives, Centre National de la Recherche Scientifique, Université Grenoble Alpes – France
[2]SPINtronique et TEchnologie des Composants – Centre National de la Recherche Scientifique, Institut de Recherche Interdisciplinaire de Grenoble, Université Grenoble Alpes – France

**Abstract**

Nanotechnologies have the potential of reshaping the biomedical scene, opening the doors to novel approaches
for therapies and detection techniques. Among these, magnetic nanoparticles (MNPs) have already shown great promise thanks to their ability of being controlled remotely through magnetic fields. Indeed, applications which span all domains of biomedical fields have risen in the past years, such as disease treatment, imaging contrast agent, drug delivery and regenerative medicine. In particular, vibrating MNPs can be used to exert very local forces and transfer mechanical energy at cellular scale. They can be exploited to target mechanosensitive proteins and trigger their associated mechanotransduction processes, influencing therefore cellular life. For instance, it was shown that low frequency vibrating particles (few Hz range) can induce apoptosis in cancer cells (1), (2) or increase insulin release in pancreatic cells (3). Indeed, in the past decades more and more knowledge has been provided about the mechanosensitivity of cells with respect of the surrounding environment. A constant exchange of forces between the cell and the extracellular matrix (ECM) or between neighbouring cells is responsible of different cellular functions such as motility, proliferation, shape modifications and even gene and protein expression (4). For this reason, it has become clear that studying cell behaviour on traditional culture substrate, such as plastic and glass, could mislead the preliminary in vitro tests, due to the huge difference in mechanical properties compared to almost all physiological environments (Stiffness of GPa instead of kPa). Very viable options to mimic mechanical properties of the ECM are the use of hydrogels as culture supports; in particular Polyacrylamide gels (PAAG) allow different level of polymerisation for a fine tuning of the Young's modulus and easy protein coating. (5)

We present a study of the interaction of cells with MNPs, either static or vibrating, as a function of substrate stiffness the cells are grown on. The cell type studied is U87 Glioblastoma human cancer. This cancer represent a great challenge for current therapies and an effective cure has yet to be found. This is thought to be attributed to its heterogeneity and the difficulty to reproduce its very complex mechanical and chemical native environment. The cells are exposed to Vortex Micro-disks MNP. These particles with a flake geometry

*Speaker

sciencesconf.org:mecanobio-grenoble:511035

are fabricated by a "top-down approach" (lithography/metal deposition/lift-off) for a fine shape and size control. Their design maximizes the transferable mechanical energy under vibration, their biocompatibility and dispersion (1).

In this work, we show that the interaction of cell with magnetic nanoparticles in absence of field depends on the substrate stiffness. In particular, it was shown that cellular functions like proliferation and MNPs uptake are altered differently when varying the mechanical properties of substrates. Field application also results in different cell outcome. Based on previous studies (6), amplitude, duration and frequency of the field were chosen such that both large effects (like cell death) and more subtle ones (like force rearrangement, difference in motility) could be achieved and evaluated. Dose of MNPs, and therefore the amount of mechanical energy transferred, appears to be crucial in defining whether cells can survive or not in the following hours after the treatment; whereas the frequency allows a finer tuning of the outcome, preventing cells to recover normal cellular functions more or less effectively.

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## Poster 22

# Living Droplets: Cell Spreading as a Wetting Problem

Ali Alhadi Wahhod*[1]

[1]Phitem E – University of Grenoble Alpes, CNRS, LIPhy, F-38000 Grenoble, France – France

**Abstract**

The shape taken by cells is intrinsically linked to the mechanics of their cytoskeleton, particularly the actomyosin cortex, a gel which organizes as a thin sheet localized beneath the cell membrane. Within this cortex, the myosin generates a mechanical tension that can be modeled as a surface tension. However, the 3D mechanical balance at the surface of cells, either isolated or in tissue, is not fully understood. As a cell spreads on a flat substrate, it resembles a water droplet, except that the surface concavity reverses from convex to concave near the triple line formed with the substrate. The change in curvature is a key indicator of the mechanical balance governing cell shape, indicating the presence of additional phenomena that modify cell balance. Fluorescence microscopy images reveal the presence of a structure of intermediate filament proteins (vimentin), forming a cortex beneath the actomyosin one, which appears to influence the morphology.

In this work, an approach is explored to calculate the shape of cell while spreading, treating it as a solution to the Young-Laplace equation, similar to problem of wetting of water droplets and capillary bridges.

Our methodology views the interfaces within the cells, shaped by the actomyosin and vimentin cortices, as portions of surfaces of revolution of constant mean curvature (such as unduloids and nodoids).

Then, using pointwise experimental geometric data, such as the contact radius with the substrate, radius at the inflection point, and the cell height, we solve an inverse problem that leads to the determination of pressures and tensions. As a result, a comprehensive reconstruction of the cell 3D-geometry is achieved, which corresponds well with the observations.

The findings from this work open up new possibilities in understanding how cell compartment volumes might be influenced by osmotic processes within the cell. While this study provides significant insights into the static case, it also sets the stage for the explorations into the dynamics of cell shape.

This contributes to a broader perspective on the changes of cell shape and its mechanical equilibrium, laying the groundwork for future investigations into the mechanical functions of cell cortices.

*Speaker

sciencesconf.org:mecanobio-grenoble:510428

## Poster 23

# Role of contractility in the chiral swirling of endothelial cells

Ghina Badih[1], Benoit Vianay[1], Manuel Thery[2], Laurent Blanchoin[3], and Laetitia Kurzawa*†[1]

[1]Physiologie cellulaire et végétale – Institut de Recherche Interdisciplinaire de Grenoble – France
[2]Institut Pierre-Gilles de Gennes pour la Microfluidique – ESPCI Université PSL – France
[3]Physiologie cellulaire et végétale – Centre National de la Recherche Scientifique – France

**Abstract**

Chirality, defined as the property of an object not being superimposable to its mirror image, is a conserved feature, with critical implications in biology, including physiological processes such as tissue morphogenesis and embryonic development. Recently, both individual cells and cell collectives have been shown to exhibit spontaneous chiral symmetry break when constrained on confined surfaces or when migrating. Despite the lack of a clear molecular mechanism explaining the manifestation of this intrinsic property, several studies point at a key role of the actin cytoskeleton in this phenomenon. In particular, actomyosin network contractility appears as a key determinant of chiral cell alignment and cell rotation. However, the exact contribution of contractile forces to the emergence and maintenance of cellular chirality remains to be elucidated.

Our project thus focuses on the role of contractility in establishing chirality among endothelial cell pairs. By confining cells on disk-shaped micropatterns of different sizes, we first show that cell doublets undergo spontaneous and persistent chiral swirling. We additionally demonstrate that both the rotation and the expression of this chiral phenotype are strongly dependent on the contractile forces produced by the actin cytoskeleton and their transmission to the underlying substrate. In particular, our results demonstrate that an optimal amount of forces and focal adhesion strength is required to maintain the persistent rotation of the cell doublets. We also show that any deviation from this optimum impairs not only the rotation of the doublets but also its bias, resulting in, either its enhancement or complete reversion.

Taken together, these results suggest that the balance of forces exerted within the cell doublet and their transmission to the substrate could represent important regulators of the emergence and maintenance of cellular chirality.

*Speaker
†Corresponding author: Laetitia.Kurzawa@cea.fr

sciencesconf.org:mecanobio-grenoble:499031

## Poster 24

# Study of the mechanical stability of a minimalist in vitro model of epithelial tissue

Vladimir Misiak*[1,2]

[1]Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – Centre National de la Recherche Scientifique, Université Grenoble Alpes, Centre National de la Recherche Scientifique : UMR5588 – France

[2]Université Grenoble Alpes – Univ. Grenoble Alpes, CNRS, LIPhy, 38000 Grenoble – France

**Abstract**

Morphogenesis is a complex process requiring subtle adjustments to tissue properties. At the heart of tissue dynamics lies the ability of cells to stabilize or remodel their cell-cell contacts, which respectively inhibit or promote cellular movement and tissue reorganization, while maintaining stability. This duality between mechanical stability and reorganization is crucial to the development of organisms.
In this thesis, we take a bottom-up approach to studying this mechanical stability at the microscopic level. We use cellular micro-modeling to create a quadruplet of cells, thus reproducing the basic paving unit of living tissue. By observing this elementary epithelial model and combining tensile force microscopy, we unravel the underlying distribution of stresses responsible for the epithelium's mechanical stability. To understand the role of intercellular junctions in this stability, we use optogenetics to modulate their adhesion.

Our project aims to answer a crucial, hitherto unanswered question: how are stresses distributed within epithelial architecture, and how are these forces dynamically regulated to ensure cellular reorganization during morphogenesis while preserving tissue integrity?
We aim to illustrate how a bottom-up approach with a simplified model can provide essential insights into the mechanical stability of epithelia during morphogenesis.This knowledge can lay the foundations for future advances in understanding the mechanisms underlying complex tissue reorganizations such as cell intercalation (also known as T1 transition).

*Speaker

sciencesconf.org:mecanobio-grenoble:513195

## Poster 25

# Effect of the composition and viscoelasticity of the ECM in cell behavior

Pablo Saez*†[1]

[1]Universitat Politècnica de Catalunya [Barcelona] – Spain

**Abstract**

The extracellular matrix (ECM) is a fundamental regulator of the cell adhesion behavior, which is essential for the most fundamental processes in life, such as embryonic development, wound healing, and tumor invasion. Here, we present a computational model, based on the clutch model (1,2) and a 1D active gel model (3), to describe the response of cells to the ECM composition and viscoelasticity. First, we analyze how matrices with different composition establish differential mechanical linkages between the ECM and the keratin and the actin cytoskeleton. The differences in the ECM composition further control YAP nuclear localization (4). Then, we use the model to address how ECMs with different elasticity and viscosity gradients induce a directed cell migration which, depending on the strength and direction of the elastic and viscous gradients may induce positive or negative viscoelastotaxis (5). We also show how elastic and viscous gradients compete with each other to enhance, arrest or shift directional cell migration. In summary, our model provides a useful tool to design the composition and mechanical properties of the ECM, which may allow us to, e.g., engineer better regenerative therapies or arrest tumor invasion. 1. A. Elosegui-Artola, et al. Nat. Cell Biol., 18, 540 (2016).
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*Speaker
†Corresponding author: pablo.saez@upc.edu

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## Poster 26

# Initial steps of bacterial surface motility studied by with optical microscopy and microfluidics

Yeraldinne Carrasco*†[1], Sigolène Lecuyer[2], Lionel Bureau[3], and Delphine Débarre[1]

[1]Mécanique des Cellules en Milieu Complexe – Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – France

[2]Département de Physique [ENS Lyon] – Ecole Normale Supérieure de Lyon, Université de Lyon – France

[3]Matière molle, Organisation, Dynamique et Interfaces – Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – France

**Abstract**

Bacterial adhesion is the first step of forming biofilms or tissue infection, and it is essential for both processes. In particular, antibiotic-resistant biofilms cause chronic and recurring diseases. This study aims to understand better the mechanisms of the surface motility of Pseudomonas Aeruginosa, an opportunist pathogen that colonizes solid/liquid interfaces. Surface motility in P. aeruginosa is called twitching and refers to the surface displacement mediated by appendices called type IV pili. We have previously modelled the twitching efficiency as a balance between the pulling force caused by pilus retraction and the friction force between the bacterial body and the surface (Gomez et al., 2023). To validate this model and gain further insight into the critical parameters controlling the strength of bacterial adhesion, we have developed a protocol of adhesion force measurement that combines microfluidics and in situ, cell tracking using optical microscopy. By combining surface colonization assays at low shear rates with orientation and detachment assays at higher shear rates, we can determine the relative adhesion strengths of the cell body and the pili and relate them to the twitching velocity of the bacteria. By varying the chemical functionalization of the surface, we show that this balance can be modulated to test our theoretical model of bacterial motility.

Gomez, S., Bureau, L., John, K., Chêne, E. N., Débarre, D., & Lecuyer, S. (2023). Substrate stiffness impacts early biofilm formation by modulating Pseudomonas aeruginosa twitching motility. Elife, 12, e81112.

*Speaker

†Corresponding author: yeraldinne.carrasco-salas@univ-grenoble-alpes.fr

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## Poster 27

# Modèle physique apportant un nouvel éclairage sur les interactions complexes entre les molécules membranaires

Mohammed Adel Djibaoui*[1]

[1]Université de Picardie Jules Verne – Université de Picardie Jules Verne, Chemin du Thil, 80000 Amiens – Chemin du Thil - 80000 Amiens, France

**Abstract**

Du fait de leur organisation et des fonctions multiples qui leur sont conférées par leur structure complexe (2), les membranes cellulaires présentent un intérêt à la fois fondamental et applicatif mais leur approche nécessite souvent une approche interdisciplinaire combinant outils mathématiques et physiques et connaissances biologiques. Reflet de cette complexité, l'élucidation de la relation entre leurs structures et leurs fonctions multiples se heurte à des obstacles majeurs. D'origine structurale et fonctionnelle, la complexité des membranes biologiques résultant d'un vaste ensemble d'interactions moléculaires s'exprime dans les processus biologiques mais aussi de l'exploitation de couplages naturels entre divers mécanismes physico-chimiques. De nombreux modèles pertinents de la Biophysique visent une description mécanique et thermodynamique de ces membranes s'appuyant sur la fameuse fonctionnelle (énergie) de Canham-Helfrisch (3, 5, 20), prenant en compte la forme, c'est-à- dire la géométrie et la topologie des membranes et permettant la détermination des configurations d'équilibre des membranes. Du point de vue mécanique, ces membranes présentent les caractéristiques combinées de solides et de fluides (écoulement interne à la membrane comme évoqué dans le vieux modèle de la mosaïque fluide (3)). L'étude présentée ici concerne un modèle mécanique simple de membranes cellulaires planes ou courbées et permettant de décrire les interactions induites entre protéines incluses dans celle-ci (14, 15). Basé sur une extension simple de la fonctionnelle de Helfrisch, le modèle décrit d'abord la dynamique déterministe des déplacements normaux de membranes élastiques homogènes et isotropes (1, 6, 16). Le spectre des excitations de basse énergie (ondes de courbure) est discuté dans le cas de membranes de haute symétrie telles les vésicules sphériques ainsi que la forme générale de la conformité de celles-ci (7, 8, 9). Dans une seconde étape, la théorie générale des fluctuations thermiques (4) de la membrane est présentée ainsi que ses effets sur les interactions résiduelles entre protéines incluses, de nature entropique (13, 17, 18). La forme du potentiel d'interaction correspondant est calculée numériquement dans le cas de membranes planes. Le rôle potentiel de ces interactions sur l'organisation des protéines au sein de la membrane est discuté.
Mots clefs : Membrane cellulaire ; Helfrich ; Courbure ; Fluctuations thermiques ; mouvement aléatoire

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*Speaker

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## Poster 28

# Self-sustained velocity waves and pattern emergence in tissues

Genesis Marquez*[1]

[1]Laboratoire Interdisciplinaire de Physique [Saint Martin d'Hères] – Centre National de la Recherche Scientifique, Université Grenoble Alpes, Centre National de la Recherche Scientifique : UMR5588 – France

**Abstract**

Supra-cellular organization is crucial for establishing and maintaining the structure, function, and homeostasis of biological tissues. Several recent studies have reported the spontaneous emergence of wave-like patterns in colonies of epithelial cells. Strikingly, supra-cellular waves exhibit precise wavelengths and periods. My main question is to investigate whether supra-cellular waves induce transcriptomic divergence between the cells located in the wave nodes and those in the antinodes.

*Speaker

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## Poster 29

# Vibrating magnetic particles as a tool for new therapies

Robert Morel*[1], Andrea Visonà[1,2], Cecile Naud[1,3], Caroline Thebault[1], Svetlana Ponomareva[1], Daniela Iglesias-Rojas[1,4], Hélène Joisten[1], François Berger[3], Marie Carriere[5], Yanxia Hou[5], Alice Nicolas[2], and Bernard Dieny[1]

[1]SPINtronique et TEchnologie des Composants – Centre National de la Recherche Scientifique, Institut de Recherche Interdisciplinaire de Grenoble, Université Grenoble Alpes – France

[2]Laboratoire des technologies de la microélectronique – Commissariat à l'énergie atomique et aux énergies alternatives, Centre National de la Recherche Scientifique, Université Grenoble Alpes – France

[3]BrainTech Laboratory [CHU Grenoble Alpes - Inserm U1205] – CHU Grenoble, Institut National de la Santé et de la Recherche Médicale, Université Grenoble Alpes – France

[4]Dept. Organic and Inorganic Chemistry, Faculty of Science and Technology, University of the Basque Country UPV/EHU, 48940 Leioa, Spain – Spain

[5]SYstèmes Moléculaires et nanoMatériaux pour l'Energie et la Santé – Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique, Institut de Recherche Interdisciplinaire de Grenoble, Université Grenoble Alpes – France

**Abstract**

The mechanical vibration of magnetic particles under low frequency magnetic field allows for the application of mechanical stress at the cell level. This mechanical stress induces a large variety of physiological reactions from the cells depending on their nature and on the intensity of the magneto-mechanical stimulation. It has for instance a strong influence on the cells cytoskeleton that triggers a variety of cell physiological reactions. Using U87 glioma brain cancer cells, we observed that a weak stimulation induces already a disorganization of the cell cytoskeleton resulting in a cell contraction, a loss of motility and a temporary stops of the mitosis. A stronger stimulation can induce the apoptotic cell death (1, 2), which can lead to a new approach towards cancer treatment.
Studies on cancer cells were conducted *in-vitro* as well as *in-vivo* revealing quite different results for a variety of reasons. Ongoing studies are carried out on spheroids of cells embedded in 3D gels, which represent *in-vitro* models much closer to *in-vivo* situations.

Experiments were also conducted on INS1 pancreatic cells where it has been demonstrated that the magnetically induced mechanical stimulation allows enhancing insulin release, which can also open a new route towards innovative diabetes treatment (3).

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*Speaker

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## Poster 30

# Force-associated changes in nuclear tension together with calcium waves orchestrate mechanical-stress dissipation at the tissue-scale level

Marvin Brun-Cosme-Bruny , Kenny Elias* , Orsi Guillermo , and Monika Dolega*[1]

[1]Institute for Advanced Biosciences / Institut pour l'Avancée des Biosciences (Grenoble) – Centre Hospitalier Universitaire [Grenoble], Centre National de la Recherche Scientifique, Université Grenoble Alpes – France

**Abstract**

It is for long accepted that biochemical signals and mechanical cues regulate cell fate and function. Cells are equipped with specific protein complexes to perceive mechanical stimuli at the cell-ECM and cell-cell junctions, and also at the nuclear envelope. Using these receptors tissues sense global changes in tension and through various mechanisms including cell intercalation, proliferation and apoptosis, actively respond to maintain tissue tensional-homeostasis. The exact molecular mechanisms, and specifically the role of calcium signaling in orchestrating tissue response to mechanical stress are only being uncovered. In our work, we used microfluidic system that enables local epithelial stretching and we precisely investigated the role of the triggered calcium waves in the regulation of the tissue response to mechanical stimulation. We showed, that local increase in tissue tension triggers calcium waves that together with the increase in nuclear envelope tension and activation of the cPLA2 phospholipase, orchestrate cellular contractility to actively and rapidly dissipate mechanical stress. We support our *in vitro* model, with the in vivo observations in drosophila and cricket's embryos.

*Speaker

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