PHYSICS OF LIVING MATTER: EXPERIMENTS AND THEORETICAL MODELS

The main goal of this first symposium “Physics of living matter: experiments and theoretical models” is to promote interactions between physicists, biologists and mathematicians at the University of Nice Sophia Antipolis. We aim to bring together scientists with interests at the interface of these fields creating a forum, which facilitates informal discussion, identifies common interests and potential collaborations as well as presenting interdisciplinary projects currently underway at the UNS. With this symposium, we propose to launch a new interdisciplinary axis entitled "Physique du vivant : expériences et modèles théoriques".

We have planned a combination of short talks, including brief reviews and “how to” presentations, a poster session and ample time for discussion. Without being exhaustive, this mini-symposium will touch on diverse problems, which cover a range of different levels from molecules to collective phenomena between organisms.

Organizers:

M Argentina *(INLN)*
R Arkowitz *(iBV)*
F Brau *(IPMC)*
L Counillon *(LP2M)*
X Noblin *(LPMC)*
M Ribot *(LJAD)*
A Seminara *(LPMC)*

Website

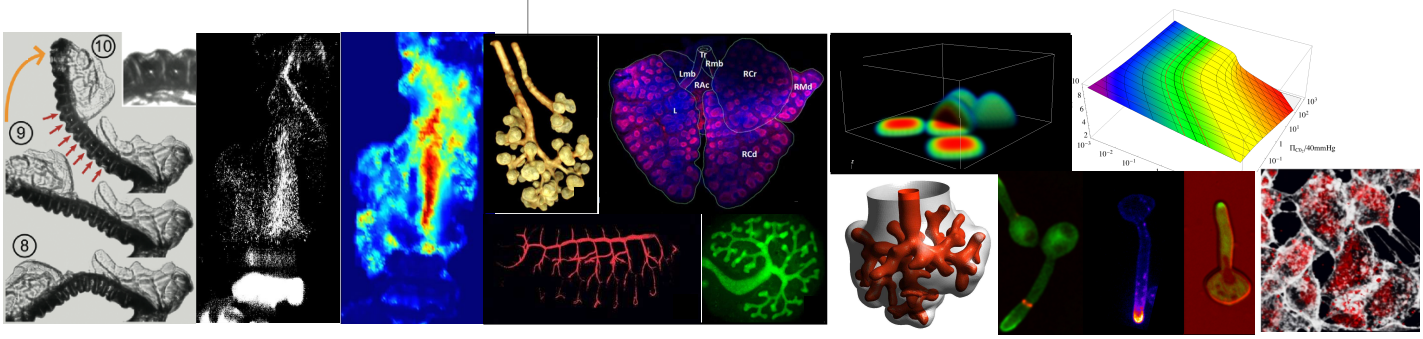
phylivmat.weebly.com
Register by Dec 8th
Admission : free

Venue

Théatre du Grand Château
Parc Valrose
28 avenue de Valrose
Nice

SPEAKERS:

Médéric Argentina (INLN)
Frédéric Brau (IPMC)
Laurent Counillon (LP2M)
Guillaume Drin (IPMC)
Gian Luca Lippi (INLN)
Francis Mairet (INRIA)
Benjamin Mauroy (LJAD)
Xavier Noblin (LPMC)
Fernando Peruani (LJAD)
Sabrina Pisano (IRCAN)
Magali Ribot (LJAD)
Sebastien Schaub (iBV)
Agnese Seminara (LPMC)
Darren Thomson (iBV)



PROGRAM

8.45 - 9.00	Reception	
9.00 - 9.30	Welcome, presentation of aims. S Mellet, P Chossat, X Noblin, A Seminara	
9.30 - 9.55	A Seminara (LPMC)	*The physics of cooperation in microbial systems*
9.55 - 10.20	F Peruani (LJAD)	*Bacteria as self-propelled liquid crystals*
10.20 - 10.50	L Counillon (LP2M) + M Argentina (INLN)	*Capturing pH dynamics by coupling its molecular mechanisms within a fully-tractable mathematical model*
10.50 - 11.20	Coffee break + Posters	
11.20 - 11.45	S Pisano (IRCAN)	*Atomic force microscopy: a tool for nanoscale imaging and quantitative nanomechanical properties of biological samples*
11.45 - 12.10	D Thomson (iBV)	*Invasive Forces of Pathogenic Fungal Filaments*
12.10 - 14.00	Lunch break + Posters	
14.00 - 14.25	S Schaub (iBV)	*Highlights on two PRISM imaging facility developments: Total Internal Reflexion Fluorescence and Non Linear microscopies*
14.25 - 14.55	F Brau (IPMC) + GL Lippi (INLN)	*Lightsheet and optical manipulation as optical techniques in biology*
14.55 - 15.20	X Noblin (LPMC)	*Microfluidics for biology: a review*
15.20 - 15.50	Coffee break + Posters	
15.50 - 16.15	G Drin (IPMC)	*A general PI(4)P-driven exchange mechanism to create lipid gradients between cellular membrane*
16.15 - 16.40	M Ribot (LJAD) + F Mairet (INRIA)	*Modeling of micro-algae biofilms*
16.40 - 17.05	B Mauroy (LJAD)	*From guinea pigs to lung: a cliff-edge story*
17.05 - 18.00	Discussion	

ABSTRACTS

8.45 - 9.00 : Reception

9.00 - 9.30 : Welcome

Sylvie Mellet

Vice-présidente de la Commission de Recherche de l'UNS

Pascal Chossat

Directeur de la Fédération W Doeblin

Xavier Noblin

Presentation of the axis

Agnese Seminara

Presentation of the day

9.30 - 10.50 : First session. Chair person : Magali Ribot

9.30 - 9.55

Speaker: Agnese Seminara

Laboratoire de physique de la matière condensée

"The physics of cooperation in microbial systems"

The evolution of living organisms is shaped by the physical environment where they live. Because of their small size, microbial system cannot count on large inertial forces. In turn, bacteria and fungal spores cooperate to actively manipulate their surrounding flows and elude the physical constraints on locomotion of individual cells. I will discuss how cooperation can be understood borrowing ideas and tools from the physics of fluid motion and the behavior of soft matter out of equilibrium, combined with high speed imaging, rheology and microfluidics. I will show how a quantitative understanding of the biomechanics of bacterial biofilms and fungal spore dispersal contributes to elucidate the dynamics of collective motility in these systems. Finally, I will discuss how the physics of these complex systems may be under biological control, closing the loop: from biology, to physics, back to biology.

9.55 - 10.20

Speaker: Fernando Peruani

Laboratoire JA Dieudonné

"Bacteria as self-propelled liquid crystals"

Bacteria exhibit fascinating collective phenomena such as collective motion, vortex formation, and aggregation. It is usually believed that such kind of collective effects require cells to coordinate their motion via (diffusive) chemotactic signaling. Despite of this common belief, I will show that in experiments with myxobacteria such collective effects emerge in absence of biochemical regulation and even hydrodynamic interactions. This finding strongly suggests the existence of a pattern formation mechanism based on simple physical interactions. As proof of principle, I will show that collective phenomena such as collective motion and aggregation, naturally emerge in models of simple self-propelled rods that interact by volume exclusion. Combining experiments and theoretical models, we will explain that the interplay of bacterial self-propulsion and steric interactions among the elongated (rod-like) bacteria leads to an effective (nematic) velocity alignment mechanism. Such an effective velocity alignment allows cells to display a non-equilibrium clustering transition that marks the onset of bacterial collective motion. I will argue that even though the symmetry of the resulting velocity alignment mechanism is clearly nematic, it induces, counterintuitively, polar order. Finally, I will show that by increasing the cell density, or alternatively the aspect ratio of bacteria, above a given threshold, collective motion patterns become unstable, and cells self-organize into aggregation patterns with neither polar nor nematic order. In short, our results indicate that for (gliding) bacteria moving on surfaces, the cell shape plays a crucial role in the bacterial self-organization process. By thinking of

bacteria as self-propelled liquid crystals, we can explain complex behaviors such as collective motion and aggregation. Such physical approach to bacterial self-organization has proved to be useful to interpret and understand experiments, as well as to make new predictions that I will present in the talk.

10.20 - 10.50

Speakers: Médéric Argentina[1], Laurent Counillon[2]

[1]Institut non linéaire de Nice, [2]Laboratoire de physiomédecine moléculaire
With Y. Bouret, Laboratoire de physique de la matière condensée

"Capturing Intracellular pH Dynamics by Coupling Its Molecular Mechanisms within a Fully Tractable Mathematical Model"

We will present the construction of a fully tractable mathematical model for intracellular pH. This work is based on coupling the kinetic equations depicting the molecular mechanisms for pumps, transporters and chemical reactions, which determine this parameter in eukaryotic cells. Such a model required the development of a novel algebraic method that couples differential equations for slow relaxation processes to steady-state equations for fast chemical reactions. Compared to classical heuristic approaches based on fitted curves and ad hoc constants, this yields significant improvements. This model is mathematically self consistent and allows for the first time to establish analytical solutions for steady-state pH and a reduced differential equation for pH regulation. Because it integrates kinetic equations for pumps and transporters that play a role in proton homeostasis, our system also calculates the membrane potential and the cytosolic ionic composition. Because of its modular structure, it can integrate any additional mechanism that may directly or indirectly affect pH. In addition, it provides mathematical clarifications for widely observed biological phenomena such as overshooting in regulatory loops. Finally, we will show that our numerical calculations are also extremely consistent with intracellular pH experimental measurements gathered by different groups in different cellular systems. The expansion of this mathematical approach to cell clusters and different external microenvironments is at present under way and will be discussed

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–> 10.50 - 11.20 : Coffee and Posters

11.20 - 12.10 : Second session. Chair person : Laurent Counillon, Médéric Argentina

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11.20 -11.45

Speaker: Sabrina Pisano

Institute for research on cancer and ageing

"Atomic force microscopy: a tool for nanoscale imaging and quantitative nanomechanical properties of biological samples"

abstract Atomic force microscopy (AFM) is a scanning probe technique based on a specific mechanical interaction between a physical probe and the sample surface. This interaction is due to both attractive and repulsive forces existing between the probe and the sample as a function of their distance. The power of this technique lies not only on the achievement of three dimensional topographic images at nano-metric resolution, but also on the possibility to study the local mechanical properties, such as stiffness or adhesion at the nano-scale. AFM is a very versatile technique in terms of applications, experimental conditions and sample size. Actually it can be used to study almost any surface in any environment (vacuum, air or liquids).
The possibility of working in physiological condition makes the AFM a very outstanding tool to study biological samples (ranging in size from proteins and DNA to cells and tissues) and to obtain new insights about their structure and function.

11.45 - 12.10

Speaker: Darren Thomson

Institut de biologie de Valrose

"Invasive Forces of Pathogenic Fungal Filaments"

abstract Physical forces have been relatively understudied during filamentous fungal growth, where only non-pathogenic yeasts have been characterized. *Candida albicans* is the leading fungal pathogen that resides in humans, causing superficial and systemic infection. Filamentous (hyphal) growth is critical for its pathogenicity and ability to invade solid surfaces such

as medical plastics and most human cell layers. This collaborative project between the iBV and LPMC institutes aims to fill a large gap in the understanding of this pathogen by characterizing the mechanical forces involved in *C. albicans* hyphal invasion. PDMS micro-well arrays have been fabricated to act as force sensors. Elastic PDMS deformations and filamentous growth will be quantified under live-cell conditions to calculate the applied forces and pressures exerted by hyphal tips. Further, for the first time, live-cell hyphal invasion has been visualized in surfaces close to the Young's Modulus of human tissue. This talk will outline the biophysical approaches taken to obtain the mechanical properties of invasive pathogenic hyphae. Future approaches will also be discussed that identify biological components that facilitate normal mechanical properties in the cell.

–> 12.10 - 14.00 : Lunch and Posters

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14 - 15.20: Third session. Chair person : Robert Arkowitz

14.00 - 14.25

Speaker: Sebastien Schaub

Institut de biologie de Valrose

"Highlights on two PRISM imaging facility developments: Total Internal Reflexion Fluorescence (TIRF) and Non Linear microscopies"

PRISM microscopy platform is a common facility providing access to commercial setup. But we also develop methodological and instrumental approaches. Here we'll present the technique of Variable-Angle TIRF based on a home-made instrument and some applications based on non-linear optic microscope. TIRF is a well-known method having an excellent resolution in the vicinity of a diopter. This is particularly useful to study processes close to the cell membrane. With a fast switch between different illuminations, we can vary the penetration of the evanescent wave and then we could improve the resolution with respect to standard TIRF.
Another example of techniques is based on the confocal microscopy coupled with both continuous visible laser and a pulsed NIR laser. Due to the versatility of the sources, we'll illustrate combinations of multi-photon imaging, Second Harmonic Generation and laser-surgery.

14.25 - 14.55

Speaker: Frédéric Brau[1], Gian Luca Lippi[2]

[1]Institut de pharmacologie moléculaire et cellulaire, [2]Institut non linéaire de Nice

"Light sheet and optical manipulation as optical techniques in biology"

(1) The principle of illumination with a light sheet in microscopy had been introduced since the beginning of the XXth century. This technology became more attractive since 10 years in biology after its use on living and transparent organisms and plants. In that talk we will discuss the major approaches and applications used in the past and nowadays in fluorescence microscopy. We will present the technological choices done on the MICA facility and the results obtained with these tools.
(2) Based on the early work of Arthur Ashkin and coworkers, who in the late 1970's began handling microsized dielectric objects, a new field of micromanipulation has emerged. Slowly, the technology -- now known under the name *optical tweezers* -- has evolved into a sturdy, flexible and reliable tool which nowadays finds very numerous applications in the manipulation of living cells. The second part of the talk will be devoted to a brief introduction to this field, to its basic principles and to an illustration of the main features currently available for biologists.

14.55 - 15.20

Speaker: Xavier Noblin

Laboratoire de physique de la matière condensée

"Microfluidics for Biology: a Review"

In this talk, I will review recent advances in microfluidics (manipulation of fluids at the micron scale) and microfabrication technologies for biology. Miniaturization, high-throughput experiments, precise spatio-temporal control of cells/tissues microenvironment are a few characteristics of microfluidic devices. 15 years ago, the introduction of soft-lithography using molding of polymer enables the fabrication of cheap microfluidic devices which have additional advantages due to the physical characteristics of those polymers such as transparency, mechanical properties, permeability to gas... Operations

such as proteins crystallization, PCR and DNA sequencing, protein expression of single cells and cell sorting, development studies, cells culture, medical diagnosis, mechanobiology experiments are now common.
I will first present the technical and physical principles used in designing microfluidic devices (microfabrication, flow control, measurements and sensing). I will then show several examples of applications at various scales. I will conclude by showing the current and future possibilities of the microfabrication platform in LPMC and the interest in developing these new versatile techniques.

–> 15.20 - 15.50 : Coffee and Posters

15.50 - 17.05: Fourth session. Chair person : Frédéric Brau

15.50 - 16.15

Speaker: Guillaume Drin

Institut de pharmacologie moléculaire et cellulaire

"A general PI(4)P-driven exchange mechanism to create lipid gradients between cellular membranes"

In eukaryotic cells, various lipid gradients exist between the early (ER, *cis*-Golgi) and late membranes (*trans*-Golgi, plasma membrane) of the secretory pathway. The creation of some lipid gradients, important for defining organelles identity, relies on non-vesicular transport mechanisms mediated by specialized carriers. We have found that some members of the Oxysterol-binding protein related-proteins (ORP)/Oxysterol-binding homology (Osh) family are sterol/phosphatidylinositol-4-phosphate (PI(4)P) exchangers. Moreover, we have recently demonstrated by biochemical and biophysical approaches that Osh4p, by lipid exchange, can dissipate a PI(4)P gradient between two membranes to actively transport sterol against its concentration gradient. Thus, Osh4p would be able to create and maintain sterol gradients between cell compartments. Interestingly, other recent studies suggest that all ORP/Osh proteins bind PI(4)P but recognize a second lipid that is not necessarily sterol. Consequently, we suggest that the use of PI(4)P gradient by ORP/Osh proteins might be a general mechanism to generate and maintain various lipid gradients within the cell.

16.15 - 16.40

Speaker: Magali Ribot

Laboratoire JA Dieudonné

"Modeling of micro-algae biofilms and a little bit more..."

The main concern of this talk is the modeling of collective behaviors of organisms for biology and medecine. The first (and main) part deals with the modeling of micro-algae biofilms, in order to control and optimize the amount of lipids for the production of biofuel. This work is a collaboration between LJAD - INRIA team COFFEE and INRIA team BIOCORE - LOV. Then, we will present quickly two other works in progress : the modeling of fibers degradation by the human gut microbiota (in collaboration with INRA Jouy en Josas) and the modeling of adipocytes growth and its role in obesity (in collaboration with C3M-INSERM).

16.40 -17.05

Speaker: Benjamin Mauroy

Laboratoire JA Dieudonné

"From guinea pigs to lung: a cliff-edge story"

These experimental results gave rise to the "cliff-edge theory": if the fitness (function that measures the reproductive success) related to a trait of an organism is asymmetrical near its maximum, and if this trait is submitted to unpredictable noise, then the best trait is not anymore the one that maximizes the fitness. In this talk, I will develop a model for cliff-edge theory and show how this theory may explain some features relating lung geometry and its inner fluid dynamics. This work is a collaboration between the Laboratory JA Dieudonné, INRA Sophia Antipolis and the Department of Biology in Lund University (Sweden) [2,3].

[1] Mountford. J Anim Ecol 37: 363 (1968); [2] Vercken,Wellenreuther, Svensson, Mauroy. PLoS ONE 7:e34889, 2012; [3] Mauroy, Bokov. Phys Biol 7 016007, 2010

–> 17.05 - 18.00 : Discussion

Posters:

Serge Antonczak
Institut de chimie de Nice
"Modeling of a Multienzymatic Complex : Theoretical Insights"

Etienne Boulter
Institut de recherche sur le cancer et le vieillissement, Nice
"Regulation of Mechanotransduction and Rigidity Sensing by CD98hc"

Simona Catozzi
Institut non linéaire de Nice
"Direct and Retro Signaling in Intracellular Signaling Cascades"

Fabien Fontaine-Vive
Institut de chimie de Nice
"Providing relevant biological information with molecular modeling methods"

Julian Hennicker
Laboratoire JA Dieudonné
"Hybrid dimensional modelling of multiphase Darcy flows in fractured porous media"

Emmanuel Lemichez
Centre Méditerranéen de Médecine Moléculaire
"Transendothelial cell tunnel dynamic : A system model for studying actomyosin organization at newly curved plasma membrane"

Iuliia Myrgorodska
Institut de chimie de Nice
"Multidimensional enantioselective analysis of amino acids in meteorites"

Jeremie Roux
Institut de recherche sur le cancer et le vieillissement, Nice
"Cell-fate decision in response to cancer therapies arises from cell-to-cell variability in death receptor-dynamics near a caspase activity threshold"

Pierre Vandenbussche
Coastal Marine Ecosystems and Response to Stress
"Fish stress and fluctuating asymmetry"

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