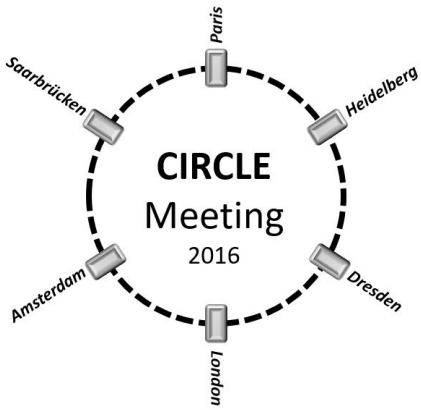

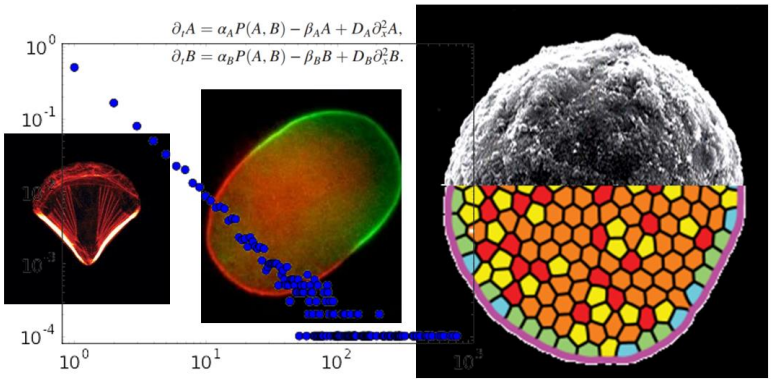

CIRLCE MEETING 2016

May 9th & 10th

PARIS

Program at a glance

Sunday, May 8th

20:00-22:00 *Welcome drink at the WOS Bar, 184 Rue Saint Jacques 75005 Paris*

Monday, May 9th

IPGG conference room

8:30 *start of the registration*

8:30-9:20 *Welcome coffee*

9:20-9:30 *Opening of the meeting*

9:30-10:30 **Keynote Lecture from Jean-François Joanny**

10:30-11:00 *coffee break*

Morphogenesis - chair SCHOLICH Andre

11:00-11:20 1. ***Understanding the physical basis of complex tissue spreading during Zebrafish gastrulation***
GRIGOLON Silvia The Francis Crick Institute, London

11:20-11:40 2. ***Emergent cell and tissue shapes: Active matter in complex and deforming geometries***
MIETKE Alexander Max Planck Institute for the Physics of Complex Systems, Dresden

11:40-12:00 3. ***Mechanics of blastocyst morphogenesis***
MAÎTRE Jean-Léon EMBL, Heidelberg

12:00-12:20 4. ***3D physical modeling of the early mouse embryo morphogenesis***
TURLIER Hervé EMBL, Heidelberg

12:30-13:50 *lunch at the IPGG*

Multicellularity - chair GRIGOLON Silvia

14:00-14:20 5. ***Modeling pili-mediated colony formation of N. gonorrhoeae***
POENISCH Wolfram Max Planck Institute for the Physics of Complex Systems, Dresden

14:20-14:40 6. ***A quantitative study of growth and cell turnover in flatworms***
WERNER Steffen MPI for the Physics of Complex Systems, Dresden

14:40-15:00 7. ***Biaxial nematic order in liver tissue***
SCHOLICH Andre MPI-PKS, Dresden

15:00-15:30 *coffee break*

Mechanics - chair MULLA Yuval

15:30-15:50 8. ***Mechanical forces and Stem Cell asymmetric division***
CHAIGNE Agathe LMCB, UCL, London

15:50-16:10 9. ***Pulling and patching single fibrin fibers using optical tweezers combined with fluorescence microscopy***
VOS Bart Amolf, Amsterdam

Cytoskeleton

16:10-16:30 10. ***Cell motility driven by spontaneous actin waves***
ECKER Nicolas Saarland University, Saarbrucken

16:30-16:50 11. ***Recruitment of ezrin in filopodia-like protrusions***
TSAI Feng-Ching curie institute, Paris

IPGG hall, Poster session with social drinks

17:00-18:30 **even numbers**

18:30-20:00 **odd numbers**

Institut Curie "Chez Marie"

20:00-23:00 *Cocktail and drinks*

Tuesday, May 10th

IPGG conference room

9:00-9:30 *Welcome coffee*

Out of equilibrium - chair CHAIGNE Agathe

9:30-9:50 12. ***Biological materials that last forever***
MULLA Yuval AMOLF, Amsterdam

9:50-10:10 13. ***Principles of a biomimetic kidney-on-a-chip for advanced nanofiltration***
MARBACH Sophie Ecole Normale Supérieure de Paris, Paris

10:10-10:30 14. ***Spatially Inhomogeneous Search Strategies for Intracellular Transport: A Random Velocity Model***
HAFNER Anne Theoretical Physics, Saarland University, Saarbrucken

Regulation of gene expression

10:30-10:50 15. ***Expression regulation by a methyl-CpG binding domain in an E. coli based, cell-free TX-TL system***
FINKLER Marc Universität des Saarlandes, Saarbrucken

11:00-11:30 *coffee break*

Information - chair VAGNE Quentin

11:30-11-50 16. ***Learning causal networks from multivariate information in genomic data***
SELLA Nadir Institut Curie, Paris

11:50-12:10 17. ***Entrainment and synchronization of circadian clocks***
MONTI Michele Amolf, Amsterdam

12:10-12:30 18. ***Diversity of immune strategies explained by adaptation to pathogen statistics***
MAYER Andreas ENS PARIS, Paris

12:30-13:50 *lunch at the IPGG terrace*

Stochasticity and fluctuations - chair MONTI Michele

13:50-14:10 19. ***Stochastic model of Golgi organization***
VAGNE Quentin Institut Curie, Paris

14:10-14:30 20. ***Intrinsic noise profoundly alters the dynamics and steady state of morphogen-controlled bistable genetic switches***
PEREZ-CARRASCO Ruben UCL - The Francis Crick Institute, London

14:30-14:50 21. ***Quantitative Analysis of Stochastic Gene Expression Dynamics During the AC/VU Cell Fate Decision in Caenorhabditis elegans***
KIENLE Simone FOM Institute AMOLF, Amsterdam

14:50-15:10 22. ***Fluctuating fitness shapes the clone size distribution of immune repertoires***
DESPONDS Jonathan ENS PARIS, Paris

15:10-15:40 *coffee break*

16:00 *end of the meeting and departure*

TALKS

1. ***Understanding the physical basis of complex tissue spreading during Zebrafish gastrulation***

   GRIGOLON Silvia
   The Francis Crick Institute, London

   Tissue spreading is fundamental to many developmental and disease-related processes, such as gastrulation and wound healing. Radial cell intercalations are commonly thought to mediate tissue spreading by simultaneously narrowing the tissue along its height (radial extend) and expanding it along its plane. Yet, whether radial cell intercalations drive tissue spreading or represent the response of the tissue to exogenous spreading forces remains unclear.

   In this talk, we use a combination of theory and experiments to dissect the fundamental force-generating processes underlying the initial spreading of the blastoderm over the yolk cell at early zebrafish gastrulation, an exemplary case of tissue spreading involving radial cell intercalations. Unexpectedly, we found that active radial cell intercalations are dispensable for blastoderm spreading per se and that, instead, this process is driven by epithelial surface cells autonomously reducing their surface tension and thus actively expanding.

2. ***Emergent cell and tissue shapes: Active matter in complex and deforming geometries***

   MIETKE Alexander
   Max Planck Institute for the Physics of Complex Systems, Dresden

   Morphogenesis, the dynamic process of shaping cells and tissue during developmental processes, is a complex, emergent phenomenon. Self-organization arises from feedback loops in which active forces, by inducing deformations and material flows, indirectly affect their own mechano-chemical regulation. In recent years, the existence of mechano-chemical patterning mechanisms in simple, fixed geometries has been demonstrated. However, a quantitative link between these processes and the actual deformations and shapes they generate is still missing so far. Here we use the theory of active gels in complex geometries, and we develop analytical and numerical tools to capture the geometry of dynamically evolving surfaces. Additionally, diffusive and advective transport processes can redistribute molecules responsible for local stress generation within those surfaces. This description resembles the interplay between active forces, the shape changes they imply and the effects this has on their regulation. The deforming domains that our approach describes can for example represent the cortex of animal cells or tissue layers that undergo folding and invagination processes. This work provides novel opportunities to explore different scenarios of mechano-chemical self-organization and could help better understand the role of geometry and shape as a regulating element in morphogenetic processes.

3. ***Mechanics of blastocyst morphogenesis***

   MAÎTRE Jean-Léon
   EMBL, Heidelberg

   During pre-implantation development, the mammalian embryo self-organizes into the blastocyst consisting of an epithelial layer encapsulating the inner-cell mass (ICM), which gives rise to all embryonic tissues. In mice, oriented cell division, apico-basal polarity and acto-myosin contractility are thought to contribute to the formation of the ICM. However, how these processes work in concert remains unclear. Here, we show that asymmetric

segregation of the apical domain generates blastomeres with different contractility, which triggers their sorting into inner and outer positions. 3D physical modeling of embryo morphogenesis reveals that cells internalize only when differences in surface contractility exceed a predictable threshold. We validate this prediction using biophysical measurements and successfully re-direct cell sorting within the developing blastocyst using maternal myosin (Myh9) knockouts. We propose that this ensures the robust self-organization of blastomeres into the blastocyst, which confers remarkable regulative capacities to mammalian embryos.

4. ***3D physical modeling of the early mouse embryo morphogenesis***

TURLIER Hervé
EMBL, Heidelberg

During mammalian pre-implantation development, the fate of cells is specified according to their position within the embryo. Combining theory and experiments we describe the physical process of cell positioning in the early mouse embryo. Morphogenesis starts with compaction, where blastomeres increase their contact area to round up the 8-cell embryo. At the next round of divisions, a few cells are internalized to form the inner-cell mass. We show that these two processes can be explained physically by differences in the surface tensions both within cells and between cells. Using doublets of blastomeres as a minimal system, we first derive an analytical model for its quasi-static evolution upon tension changes. We find that its shape is determined by three dimensionless parameters only: a compaction parameter, a tension asymmetry and a volume asymmetry. We show that above a well-defined tension asymmetry, one cell is fully internalized in the other one, mimicking the process of entosis. Generalizing this physical description to multi-cellular systems in using 3D numerical simulations, we can reproduce both compaction and cell internalization in mouse embryos very realistically. Our results lay the groundwork for an integrated 3D biophysics model of early mammalian development in toto.

5. ***Modeling pili-mediated colony formation of N. gonorrhoeae***

POENISCH Wolfram
Max Planck Institute for the Physics of Complex Systems, Dresden

N. gonorrhoeae is the causative agent of gonorrhea, the second most common sexually transmitted disease. An important step during the infection process is the formation of microcolonies, agglomerates of up to thousands of cells [1]. The attractive cell-to-cell interactions driving the agglomeration of colonies are caused by type IV pili, µm-long and thin filaments that emerge from the cell membrane [2]. Additionally, the pili are involved in the motility of single cells and colonies over a substrate.

In my talk I will present a theoretical simulation model of individual cells interacting via multiple pili with each other or a surface. This model allows us simulate a wide range of processes: from the motility of single cells over a substrate to collective processes involving multiple colonies.

I will compare the results of the simulation to experimental data and focus on the coalescence of two equally-sized microcolonies and the motility of cells within a colony. These experiments show that cells on the surface of a colony are highly motile, while cells within a colony show a strongly reduced motility. Our simulation model will give us a deeper understanding of this observation.

[1] Higashi et al., Microbiology 155(12), 4084-4092 (2011)
[2] Taktikos et al., Plos One 10(9), e0137661 (2015)

6. ***A quantitative study of growth and cell turnover in flatworms***

WERNER Steffen
MPI for the Physics of Complex Systems, Dresden

How do organisms regulate cell division and cell death, to control growth at the organism scale? We address this general question in the model system of flatworms, by combining theory and experiment.
Flatworms have a high cell turnover rate in the order of weeks and they are able to reversibly grow by a factor of 20 in length depending on feeding conditions. We analyzed the growth dynamics and investigated mechanisms for size control by metabolic energy balances. Thereby, we aim to explain the macroscopic growth behavior in terms of microscopic cell turnover dynamics. Our theory makes testable predictions for ongoing experiments in the group of our collaboration partners Jochen Rink at the MPI CBG.

7. ***Biaxial nematic order in liver tissue***

SCHOLICH Andre
MPI-PKS, Dresden

Tissue cells typically exhibit an anisotropic distribution of membrane proteins that characterizes a structural polarity of the cell. This cell polarity is linked to function, such as directed transport. In cellular monolayers and various epithelial tissues, cells are known to exhibit a vectorial cell polarity with distinct domains of apical and basal membrane proteins at opposite sides of the cell that face the two boundary surfaces of the flat tissue. Here, we analyze cell polarity in a bulk tissue, namely the mouse liver. We propose a concept of nematic cell polarity to describe the distinct cell polarity of hepatocyte liver cells. Analyzing high-resolution two-photon microscopy images of mouse liver, we find spatial patterns of aligned cell polarity axes at the tissue scale. These spatial patterns characterize liver tissue as a biological nematic liquid crystal. Spatial patterns are well-accounted for by a curvilinear reference system set by structural landmarks of large veins within the liver tissue. We discuss minimal mechanisms of cell-scale interactions that can account for the emergence of tissue-scale patterns.

8. ***Mechanical forces and Stem Cell asymmetric division***

CHAIGNE Agathe
LMCB, UCL, London

9. ***Pulling and patching single fibrin fibers using optical tweezers combined with fluorescence microscopy***

VOS Bart
Amolf, Amsterdam

The mechanical properties of fibrin are crucial for determining the biological function of blood clots in hemostasis and wound healing as well as the application of fibrin networks in tissue engineering. Accordingly, there is a long history on characterizing the mechanics of fibrin, ranging from bulk measurements with rheology in the early days to more recent nanoscale measurements on single fibrin molecules with AFM. However, the relation between fibrin structure and mechanics across the scales from molecular, to fiber, to the whole clot still remains elusive.
Here, I will present a new biophysical approach to bridge these scales based on measurements of the elasticity and plasticity of single fibrin fibers by optical tweezers

manipulation in combination with fluorescence microscopy. Using a dedicated setup equipped with a multichannel microfluidic flow cell, we are able to grab individual fibrin fibers between micron-sized beads and apply controlled forces reaching up to 1nN.
We discovered that the fibers strongly stiffen upon straining and remodel their internal structure depending on the applied force and loading rate. With a similar setup, we are also able to grab two filaments and measure the interactions between them under a controlled angle. We demonstrate that fibrin fibers spontaneously adhere when brought into contact, explaining observations of shear- and compression induced network remodeling observed by rheometry. The combined tweezer-fluorescence method provides a powerful new approach to dissect the molecular basis of fiber mechanics.

10. ***Cell motility driven by spontaneous actin waves***
    ECKER Nicolas
    Saarland University, Saarbrucken
    A cell's ability to move is one of its greatest merits. It enables the cell to efficiently search for nutrients and drives complex processes in tissues. Cell motility is often driven by the actin cytoskeleton. Although many important factors involved in actin-driven cell crawling have been identified and characterized in amazing detail, it is still poorly understood how the actin filament network is organized in this process. Spontaneous actin waves have been observed in a large number of different cell types. They present an attractive concept to understand actin-network organization during crawling. We introduce a mean-field description for actin assembly by nucleating promoting factors, negative feedback of actin filaments on the nucleators' activity, and active stress generation by molecular motors. The system can spontaneously generate traveling waves. We study confinement of this system to a cellular domain by means of a phase field and calculate the corresponding phase diagram. In particular, we find erratic motion due to the formation of spiral waves.

11. ***Recruitment of ezrin in filopodia-like protrusions***
    TSAI Feng-Ching
    curie institute, Paris

12. ***Biological materials that last forever***
    MULLA Yuval
    AMOLF, Amsterdam
    Hold a piece of paper with two hands. Start pulling on it. After a while you will tear it apart. More than a decade ago, a novel type of bond was discovered in bacteria, called catch bonds. Catch bonds are noncovalent bonds which increase(!) binding upon force. This surprising force-dependence turns out to be wide-spread in protein-protein interactions.
    These molecules are intensively studied on the single molecule level - but what happens when you make a material out of it? We show catch bonds have emergent behaviour, leading to unprecedented robustness again stress. This can explain why the catch bonds are so widely present in biology. Furthermore, this robustness can be a source of inspiration for novel smart materials.

13. ***Principles of a biomimetic kidney-on-a-chip for advanced nanofiltration***

MARBACH Sophie
Ecole Normale Supérieure de Paris, Paris

The clear need in fresh water is one of the main challenges now faced by humanity. While water desalination and water recycling involve costly separation processes in terms of energy, the domain has been boosted over the last decades by the progresses made in membrane technology for water purification, such as reverse osmosis or nanofiltration, and more recently by the possibilities offered by nanoscale materials. In this paper we investigate the physical mechanisms underlying one of the most efficient filtration devices: the kidney. Building on a minimal model of the Henle Loop - the central part of the kidney filtration -, we investigate theoretically the detailed out-of-equilibrium fluxes in this separation process in order to obtain theoretical bounds for its efficiency in terms of separation ability and energy consumption. A key discovery is that this separation device operates at a remarkably small energy cost as compared to traditional sieving processes, while working at much smaller pressures. This unique energetic efficiency originates in the serpentine geometry of the nephron, which operates as an active osmotic exchanger. The principles for such a ""kidney on a chip"" could be readily mimicked based on existing technologies to build compact and low-energy artificial dialytic devices. They also point to new avenues for advanced water recycling, in particular during sea-water pretreatment for decontamination and hardness reduction.

14. ***Spatially Inhomogeneous Search Strategies for Intracellular Transport: A Random Velocity Model***

HAFNER Anne
Theoretical Physics, Saarland University, Saarbrucken

15. ***Expression regulation by a methyl-CpG binding domain in an E. coli based, cell-free TX-TL system***

FINKLER Marc
Universität des Saarlandes, Saarbrucken

Cytosine methylation plays an important role in the epigenetic regulation of eukaryotic gene-expression. The methyl-CpG binding domain (MBD) is common to a family of eukaryotic transcriptional regulators. How MBD, a stretch of about 80 amino acids, recognizes CpGs in a methylation dependent manner, and as a function of sequence, is only partly understood. Here we show, using an E. coli cell-free expression system, that MBD from the human transcriptional regulator MeCP2 performs as a specific, methylation-dependent repressor in conjunction with the BDNF (Brain-Derived neurotrophic factor) promoter sequence. Mutation of either base flanking the central CpG pair changes the expression level of the target gene. However, the relative degree of repression as a function of MBD concentration remains unaltered. Two mutations within a distant AT stretch of the promoter make MBD act as a weak activator on a reduced expression level. Molecular dynamics simulations that address the DNA B fiber ratio and the handedness reveal cooperative transitions in the promoter DNA upon MBD binding that correlate well with our experimental observations. We suggest that not only steric hindrance, but also conformational changes of the BDNF promoter as a result of MBD binding are required for MBD to act as a specific inhibitory element. Our work demonstrates that the prokaryotic transcription machinery can reproduce features of epigenetic mammalian transcriptional regulatory elements.

16. ***Learning causal networks from multivariate information in genomic data***

SELLA Nadir
Institut Curie, Paris

Learning causal networks from large-scale genomic data remains difficult in absence of time series or systematic perturbation data. We have developed and implemented an information theoretic method, that circumvents the robustness and complexity issues of existing methods, in particular, in the presence of latent variables. Starting from a complete graph, it iteratively removes dispensable edges by partitioning their mutual information into significant contributions from indirect paths and orient the remaining edges based on the signature of causality in observational data. This information theoretic approach outperforms earlier methods on a broad range of benchmark networks with or without latent variables and is applied to reconstruct different causal networks from gene expression data in single cells, genomic alterations in tumors or co-evolving residues in protein structures.

17. ***Entrainment and synchronization of circadian clocks***

MONTI Michele
Amolf, Amsterdam

Circadian clocks are the central timekeepers of life, allowing cells to anticipate changes between day and night. Experiments in recent years have revealed that circadian clocks can be highly stable. These clocks can maintain stable rhythms for months or even years in the absence of any daily signal from the environment, such as light/dark or temperature cycles. This raises the question: how reliably they can be entrained by external cues?
In this project we describe analytically and numerically the entrain-ability of the clock with respect to the daily cycle. We describe the behavior of the clock with a phase variable that diffuses with a drift. Using well known techniques of the Phase Response Curve, we are able to connect experimental measurements with a Fokker Planck description of the phase behavior. In this context we insert the external interaction introducing a time and space periodic potential. The key quantity that we are going to compute is the Mutual Information that interplays between the phase of the clock and time. This observable allows us to quantify how many time states, so how many different functional decision, the cell is able to make during the day. Moreover, in this context it can be used to estimate the stability of the clock.
We aim to explain why biology evolved different strategies in different organisms to be entrained by the light. What are they optimizing? Why is there such a huge variability among the Phase Response Curves? Using information theory we can predict the parameters that allow the clock to optimally follow the external signals. Moreover, in this context, we use the mutual information that flows between time and phase in order to quantify the stability and regularity of the clock. Our predictions can reproduce and explain a wide range of biological observations.
The final goal is to understand the optimal strategies that the cells have developed in order to be synchronized with the day-night rhythm.
Using this new approach of inferring the data we hope to bring a new and useful contribution to the field and to offer nice suggestion for future experiments.

18. ***Diversity of immune strategies explained by adaptation to pathogen statistics***
MAYER Andreas
ENS PARIS, Paris
Biological organisms have evolved a wide range of immune mechanisms to defend themselves against pathogens. Beyond molecular details, these mechanisms differ in how protection is acquired, processed and passed on to subsequent generations. These differences may be essential to long-term survival and thus drive the evolution of different immune strategies. Here, we introduce a mathematical framework to compare the long-term adaptation of populations to the environmental pathogen statistics. We find that the two key determinants of an optimal immune strategy are the frequency and the characteristic timescale of the pathogens. Depending on these two parameters, our framework identifies distinct optimal modes of immunity, including adaptive, innate, bet-hedging and CRISPR-like immunities recapitulating the diversity of natural immune systems.

19. ***Stochastic model of Golgi organization***
VAGNE Quentin
Institut Curie, Paris
We model the organization and dynamics of membrane exchanges between cellular organelles and more particularly in the context of the Golgi apparatus. We aim at finding the governing physical mechanisms underlying the generation, maintenance and functionality of these highly dynamics structures through which high fluxes of proteins are transported, matured and sorted.

20. ***Intrinsic noise profoundly alters the dynamics and steady state of morphogen-controlled bistable genetic switches***
PEREZ-CARRASCO Ruben
UCL - The Francis Crick Institute, London
Bistable switches are a common regulatory motif in biological processes. In developing tissues, they are often controlled by gradients of secreted signalling molecules - morphogens -, providing a mechanism to convert a signalling gradient into stripes of gene expression that determine the arrangement of distinct cell types. In this talk I will analyze the temporal response of such a system focusing on the role of intrinsic fluctuations that result from the stochastic nature of gene expression. To tackle this problem I will make use of different approximations, using Gillespie simulations, Langevin equations and Minimum Action Path theory. The results reveal that noise induces a switching wave that propels the stripe boundary away from the morphogen source, eventually settling at a steady state different from the deterministic description.

21. ***Quantitative Analysis of Stochastic Gene Expression Dynamics During the AC/VU Cell Fate Decision in Caenorhabditis elegans***
KIENLE Simone
FOM Institute AMOLF, Amsterdam
Cells in developing organisms have to robustly assume the correct fate in order to fulfill their specific function. However, some cell fate decisions are made in a stochastic manner, with cells randomly choosing one cell fate out of a repertoire of different possible ones. It is thought that stochastic cell fate decisions exploit random molecular fluctuations, so-called molecular noise, by using positive feedback loops in the signaling network to convert this

noise into discrete cell fates. Yet, how a cell uses such a stochastic process to reliably drive cell fate decisions is an open question. We address this question by novel quantitative approaches, focusing on one of the genetically best-understood stochastic cell fate decision: the AC/VU decision in C. elegans gonad development. During the AC/VU decision two initially equivalent cells, Z1.ppp and Z4.aaa, interact, so that one cell becomes the anchor cell (AC) and the other cell a ventral uterine precursor cell (VU). It is thought that small stochastic differences in gene expression are amplified by lateral Notch signaling, leading to one cell expressing only the Notch receptor lin-12 (VU) and the other cell only its ligand lag-2 (AC). However, it is currently not known what noise sources drive this decision and how proper cell fates are guaranteed within the (short) given time. To answer this, we use two complementary methods: 1.) single molecule FISH to quantify expression of lag-2 and lin-12 with single mRNA resolution in fixed animals at different stages of the decision process and 2.) a novel timelapse technique to follow expression dynamics of both genes in individual live animals over the first 30 hours of larval development. Surprisingly, our results reveal lag-2 being the main driver of the decision process with strong stochastic, Notch-independent expression of lag-2 in the mother cells Z1.pp and Z4.aa. Our results suggest that the transmission of variable lag-2 levels from the mother cells to Z1.ppp and Z4.aaa facilitate a rapid and robust cell fate decision.

22. ***Fluctuating fitness shapes the clone size distribution of immune repertoires***

DESPONDS Jonathan
ENS PARIS, Paris

The adaptive immune system relies on the diversity of receptors ex- pressed on the surface of B and T-cells to protect the organism from a vast amount of pathogenic threats. The proliferation and degradation dynamics of different cell types (B cells, T cells, naive, memory) is governed by a variety of antigenic and environmental signals, yet the observed clone sizes follow a universal power law distribution. Guided by this reproducibility we propose effective models of somatic evolution where cell fate depends on an effective fitness. This fitness is determined by growth factors acting either on clones of cells with the same receptor responding to specific antigens, or directly on single cells with no regard for clones. We identify fluctuations in the fitness acting specifically on clones as the essential ingredient leading to the observed distributions. Combining our models with experiments we characterize the scale of fluctuations in antigenic environments and we provide tools to identify the relevant growth signals in different tissues and organisms. Our results generalize to any evolving population in a fluctuating environment.

POSTERS

1. ***mRNA promotes liquid-liquid phase separation of PGL-3.***
   ADAME ARANA Omar
   Max Planck Institute for the Physics of Complex Systems, Dresden
   We show that the presence of mRNA promotes liquid-liquid phase separation in a solution of PGL-3 in physiological buffer for lower concentrations of PGL-3 compared to the same solution in the absence of mRNA.
   In order to study this system, we use a Flory-Huggins free energy model and construct the phase diagram to assess the concentrations of the different phases. Additionally, using experimental data we fit the Flory-Huggins interaction parameter and the molecular volumes of the different components in order to explain the behavior observed experimentally of the difference between concentrations in both phases.

2. ***Quantitative analysis of macrophage cell dynamics during brain surveillance***
   ALBERT Marvin
   EMBL, Heidelberg
   For motile cells, an intrinsic link exists between cell shape changes and cell function. Microglia in the developing brain exhibit highly dynamic behaviours as they scan their surroundings, engulf dying neurons and relocate to find new targets. While probing the environment, multiple cellular branches are continuously extended and retracted from the cell body, forming transient contacts with neighbouring cells. During these cycles, a given branch can become stabilized, which in turn leads to the retraction of the other processes. As the outcome of this competition, cell polarity is established along the direction of a single branch, which then mediates neuronal engulfment or cell migration. Using highly spatially and temporally resolved in vivo light sheet microscopy in the transparent zebrafish brain together with structural cell segmentation and tracking in 3D, we aim to quantitatively describe the link between branching dynamics and cell behaviour in these cells.

3. ***Fluidized bed***
   ALEXANDRE Lucile
   Institut Curie-Recherche-UMR168, Paris

4. ***In vitro study on microtubule-actin coordination***
   ALKEMADE Celine
   AMOLF, Amsterdam

5. ***Force Microscopy of Three-Phase Phospholipid Bilayers***
   AUFDERHORST-ROBERTS Anders
   FOM Institute AMOLF, Amsterdam
   Lipid ternary mixtures are useful model system for understanding phase separation in the membrane bilayer. Studies of ternary mixtures have informed our understanding of transmembrane protein function, antimicrobial peptide activity and, more broadly, have allowed us to predict phase separation under a range of different conditions.
   Ternary systems are well understood, however there are still open questions, particularly relating to a proposed state of 3-phase coexistence. Measuring 3 phases simultaneously is

challenging as the liquid ordered and gel phases cannot be distinguished by fluorescent microscopy and are of similar height, making imaging with AFM difficult.
To overcome this, we use a novel AFM mode known as peak force tapping to finely control the force applied by the AFM tip. This can cause domains to be compressed according to their packing density, clearly identifying 3 distinct phases by height and by mechanical properties such as deformability and adhesion.
We present, to our knowledge, the first images of 3 coexisting lipid phases and propose the boundaries of a 3-phase region in the phase diagram. In this region, clear evidence of a tree-ring growth process in the ordered gel phase domains is presented. We also show that this gel phase has an unusually low structural integrity. This finding supports the hypothesis of a ""disrupted gel"" state that has been proposed from NMR studies of similar systems, where the addition of small amounts of cholesterol was shown to disrupt the regular packing of the gel state.

6. ***Tackling fundamental processes of polarization and migration in living cells with magnetogenetic combined with light or a chemically induced dimeriz***er

BALLOUL Elie
Institut Curie, Paris

Axial polarity is an important feature needed for cell behaviors such as migration or differentiation. The polarity is defined by an asymmetric repartition of specific signaling molecules inside cells. Thus studying this mechanism requires a tool allowing fine spatio-temporal control of the intra-cellular localization of signals. Here, we propose to use magnetogenetics to remotely control these signals in mammalian cells. Magnetogenetics is based on biofunctionalized magnetic nanoparticles that can be controlled by a magnetic device. We have two kinds of nanoparticles at our disposal. (1) We use chemically synthesized nanoparticles made of a magnetic core embedded in a silica shell of 20 to 50 nm diameter and (2) we use biosynthesized ferritin nanoparticles of roughly 20 nm. Nanoparticles are targeted by bioengineered fusion proteins upon internalization inside the cell. This allows us to have nanoparticles presenting signaling molecules that we can manipulate inside the cytoplasm. For the long term project, we want to use this method to decipher how input information is treated by cells to generate the correct output during axial polarization and migration, but for now we are optimizing our capabilities to manipulate signals using magnetogenetics. At the moment, we want to decouple the displacement of the particles with the recruitment of the signaling proteins. To achieve this, internalized particles are targeted by a first class of targeting proteins fused with a dimerizing protein, either being part of an optogenetic couple (CRY2/CIB1) or a chemically induced dimerizer (FKBP/FRB). We then move the magnetic nanoparticles at desired locations inside cells with our magnetic device before triggering dimerization to recruit the second class of fusion proteins made of the dimerizing partner and the signaling protein itself. We hypothesize that this can help provide a more efficient way to position signals inside cells. Additionally, using the homodimerizer CRY2olig we could trigger both a larger recruitment of signaling molecules on nanoparticles and create bigger complexes of nanoparticles that can be moved with higher forces. In conclusion, we plan to combine these multiple techniques to have high precision control of intra-cellular signals.

7. ***Molecular control of adhesion-free migration***

BODOR Dani
UCL-LMCB, London

Cell migration in vivo does not always follow the canonical model of protrusion-adhesion-retraction cycles. For example, under confinement many cell types can efficiently migrate in the absence of integrin-based focal adhesion. Instead, it was recently discovered that cells can use non-specific friction to generate propelling forces on their substrate. My goal is to identify the molecular mechanisms governing this friction. As I have only recently started working on this project, I will present an overview of what my goals are rather than what I have done so far.

8. ***Artificial neuronal networks***

COHEN Floriane
Institut Curie - Recherche - UMR168, Paris

9. ***Diffusion of rigid filaments as the basis for a model of microtubule systems***

DALTON Benjamin
Max Planck Institute for the Physics of Complex Systems, Dresden

The bipolar spindle is comprised of a myriad of actively interacting microtubule filaments. The microtubule filaments interact via motor proteins and cross linker proteins, as well as via steric interactions. Microtubules undergo active transport due to motor activity and passive transport due to the filament diffusion. As a foundation for the development of a simulation of interacting microtubules we will here consider the passive processes involved, namely diffusion and steric interaction. We will treat the microtubules as rigid filaments that undergo translational and rotation diffusion. We will also include filament length dynamics as a stochastic process representing the dynamic instability of polymerization and depolymerization. With the passive mechanics of the rigid filament representation of microtubules in place the way is open to simulate the full active system with an aim for understanding the self-organization of bipolar spindle structures.

10. ***Robust patterning of multicellular organisms by noisy signals***

FILINA Olga
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The mechanism of asymmetric cell division is widely used by developing organisms to establish cellular diversity. One example - asymmetric divisions of epithelial seam cells - occurs during postembryonic development of the nematode worm C. elegans. These cells divide in a stem cell-like fashion, where anterior cell most often becomes a hypodermal cell, while posterior cell retains its seam cell identity.

The asymmetry is thought to be established in the seam cells prior to their division in response to the gradients of Wnt signalling molecules. This asymmetry then propagates through a signalling network (Wnt/beta-catenin asymmetry pathway) and results in the daughter cells acquiring different fates.

We investigate how signal processing is performed in the seam cells and how a potentially noisy input signal results in a robust cell fate specification. In particular, an interesting possibility would be that the signal is improved by a cell as it propagates through the network.

We use high-resolution time-lapse fluorescence microscopy to measure the spatial distribution of various components of the Wnt/beta-catenin asymmetry pathway in living worms. Quantitative comparison of the spatial distributions of these proteins will allow us to infer the signal processing mechanisms.

11. ***Sagittal Contraction Mechanism for Ventral Furrow Formation in Drosophila***
    GANGULY Poulami Somanya
    The Francis Crick Institute, London

12. ***Shaping of veins in Drosophila melanogaster pupal wing***
    GEISLER Laura
    Max Planck Institute for the Physics of Complex Systems, Dresden

13. ***Organ on chip***
    GEREMIE Lauriane
    Institut Curie - Recherche-UMR168, Paris

14. ***Optimal nutrient uptake by non-spherical cells.***
    GORDILHO FERNANDES Felicio
    AMOLF / University of Amsterdam, Amsterdam

15. ***Towards a model of growth and patterning in the vertebrate neural tube.***
    GUERRERO Pilar
    UCL/ CRICK, London
    In the context of development, it is important to understand the mechanisms that coordinate growth and patterning of tissues. These processes occur as a result of cell adhesion, migration, division, differentiation and death, and involve multiple processes acting at the cellular and molecular level. We are working in modelling the spatial patterning of the neural tube in the vertebrate embryo. In order to describe three-dimensionally packed cells in the vertebrate neural tube tissue both mathematically and physically, we have been developed novel geometrical model using vertex model where we introduce the inter-kinetic movement as a new interpretation of target area and developing new tools for model validation.

16. ***Coordinated control of Notch-Delta signalling and cell cycle progression drives lateral inhibition mediated tissue patterning***
    HADJIVASILIOU Zena
    UCL, London
    Coordinating cell differentiation with cell growth and division is critical for the successful development, homeostasis, and regeneration of multicellular tissues. Here we use bristle patterning in the fly notum as a model system to explore the regulatory and functional coupling of cell cycle progression and cell fate decision-making. The pattern of bristles and intervening epithelial cells (ECs) becomes established through Notch-mediated lateral inhibition during G2-phase of the cell cycle, as neighbouring cells physically interact with each other via lateral contacts and/or basal protrusions. Since Notch signalling controls cell division timing downstream of Cdc25, ECs in lateral contact with a Delta-expressing cell experience higher levels of Notch signalling and divide first, followed by more distant

neighbours, and lastly Delta-expressing cells. Conversely, mitotic entry and cell division makes ECs refractory to lateral inhibition signalling, fixing their fate. Using a combination of experiments and computational modeling, we show that this reciprocal relationship between Notch signalling and cell cycle progression acts like a developmental clock, providing a delimited window of time during which cells decide their fate, ensuring efficient and orderly bristle patterning.

17. ***Robustness against anatomical variability in C. elegans organ development***

HUELSZ PRINCE Guizela
AMOLF, Amsterdam

Development is highly robust, resulting in the same outcome despite genetic, external or intrinsic variability. How such robustness is achieved remains a fundamental question. An example of robust development is C. elegans vulva induction, where a spatially graded EGF signal from the anchor cell (AC) induces an invariant 2°-1°-2° cell fate pattern in the vulva precursor cells (VPCs). It is thought that the pattern results from the AC being positioned directly adjacent to the VPC that becomes 1° cell. However, we found that at the start of induction cell positions are highly variable, with the AC often positioned equidistant to two VCPs. Yet, induction always resulted in the same VPC fate pattern, with the AC adjacent to the 1° cell. To understand how this was achieved, we quantified 1° fate induction as a function of AC position using smFISH to measure gene expression. We found that if the AC was positioned equidistant to two VPCs, both received equal levels of EGF signal. Subsequent EGF-induced Notch signaling between VPCs randomly restricted 1° fate to a single cell, which later moved towards the AC. Our experiments, combined with mathematical modeling, showed that both Notch signaling and VPC migration are needed to reach the desired VPC fate pattern for all initial AC positions. Our results show that vulva induction is canalized, meaning that the underlying signaling network is optimized to reach the same final configuration despite variability in initial conditions.

18. ***Physical basis of microtubule aster growth***

ISHIHARA Keisuke
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Microtubule asters - radial arrays of microtubules organized by centrosomes - play a fundamental role in the spatial coordination of animal cells. By spanning the entire cytoplasm, asters shape cell morphology, act as tracks for intracellular cargo transport and position the cleavage furrow during cell division. The standard model of aster growth assumes radial elongation of a fixed number of microtubules originating from the centrosomes. This model faces spatial scaling problems in large egg cells, and we recently found evidence for nucleation of new microtubules away from centrosomes in egg extract. Here, we develop a biophysical model that describes aster growth in terms of microtubule plus end polymerization dynamics and autocatalytic nucleation. The model predicts a critical transition from an aster with steady-state radius to one that expands continuously as a travelling wave. The transition is characterized by a minimum velocity for aster growth, which we term the gap velocity. We test our theory with biochemical perturbations in egg extract and find qualitative agreement with theory, including evidence for a gap velocity. Combining theory and experiments, we propose that large aster growth is an emergent property of short microtubules with autocatalytic nucleation.

19. ***Spatial Regulation of Phase Separation***

KRÜGER Samuel
Max Planck Institute for the Physics of Complex Systems, Dresden

Cells contain chemical components that are not separated from the cytoplasm by a membrane. An example are P-granules in the C. elegans embryo. They are liquid-like structures, that form droplets. They consist of RNA and proteins that are segregated spontaneously from the cytoplasm and are known to play a role in the specification of germ cells. During asymmetric cell division, P granules are segregated to one side of the cell. This segregation is guided by a spatial concentration gradient of the protein Mex-5. We simplify the multicomponent nature of the cytoplasm with a ternary model: The P granule material, the solvent (cytoplasm), and a regulator corresponding to Mex-5. Using this model we aim to understand the physical principles controlling the droplet position in a simplified scenario, where an external potential establishes the regulator gradient. We use the Flory-Huggins mean field theory and calculate the equilibrium solutions by minimizing the free energy functional. There are two equilibrium states. Droplets either localize at high external potential or low external potential. Changing the interaction between the regulator and the solvent we find that the free energy exhibits a kink indicating that the transition between both states being a discontinuous phase transition.

20. ***Bringing Filament Dynamics and Reaction Networks in Silico***

LI Yao
FOM Institute AMOLF, Amsterdam

21. ***How cells can measure so precisely time-varying external signals?***

MALAGUTI Giulia
AMOLF, Amsterdam

In order to survive, living cells need to sense the stimuli of the environment, process information and take decisions. In particular, cells can sense external chemical ligand concentrations via receptors on their surface that transmit information to the interior of the cell, driving the activation of chemical reactions constituting the cell biochemical signalling network. The major limitation to the accuracy of sensing is represented by noise, which arises from the ligand diffusion, the ligand-receptor binding and the stochastic chemical reactions of the signalling network. However, the accuracy of cell sensing is surprising and it is relevant to understand what sets the fundamental limits to it.

It is known that, for a constant ligand concentration and for the widespread push-pull network class of sensing systems, three classes of resources are required for sensing: receptors and their integration time, copies of downstream molecules in the cell and energy (fuel turnover). Each class imposes a limit, and it is the limiting class that imposes the fundamental limit on sensing precision.

However, cells are in general exposed to time-varying environments and it becomes crucial to extend the analysis to this more realistic scenario. We consider the simplest case of a time-varying ligand signal described by a birth-death process, and we compute the instantaneous mutual information between the input ligand molecules and the activated downstream molecules to measure of the quality of sensing. Maximizing the mutual information reveals a trade-off between the need to average the input signal over time to filter the receptor-ligand binding noise and the need to track the fluctuations in time of the input signal to properly respond to them. The emergence of an optimal integration time yields to identify also the integration time as a new resource that independently

fundamentally limits the sensing precision and revisit the principles of an optimally designed sensing system.

22. ***Role of cytoskeleton in morphological changes of blood platelets***

MATHUR Aastha
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Platelets are 2-3µm sized discoid cell fragments that help maintain homeostasis. Activation of platelets, caused by chemical factors released upon injury, results in drastic morphological changes brought about by a repertoire of cytoskeletal proteins. During the first step of platelet activation, a microtubule marginal band that runs along platelet periphery undergoes coiling while the platelet changes from a disc to a sphere shape. Both actin and microtubules are implicated in this process but its mechanics are not well understood.
We use a combination of experimental and quantitative analysis techniques to assess mechanical properties of this system by direct measurement of the marginal band morphology. The structure of the band was analyzed using electron tomography, which provided information on individual microtubules. The dynamics of coiling process was observed with live cell fluorescence microscopy in conjunction with a microfluidic system. This enabled visualization of marginal band shape change in response to platelet agonists or cytoskeletal perturbations. A large population of platelets was analyzed to infer the intrinsic variations in properties of the marginal band. Additionally, we simulated the coiling process with the software Cytosim.
Our approach enabled us to get novel insight into the mechanics of marginal band coiling. With our data, we can infer that the marginal band behaves like a visco-elastic ring upon activation with ADP. This response was found to be actin dependent. Furthermore, analysis of platelet population indicated an unusual scaling of their tubulin content implying possible enrichment of the protein. Finally, our data suggests that platelets with longer marginal bands have a higher propensity to coil. We provide a framework that enables analysis of platelet cytoskeleton morphology with an aim to understand the mechanics of platelet activation in healthy and disease states.

23. ***Cell competition in controlled micro-environments***

MOITRIER Sarah
Institut Curie - CNRS, Paris

At the early stages of carcinogenesis, one or several cells undergo irreversible genetic mutations. These transformed cells are then surrounded with normal cells. It is well accepted that interactions between transformed cells and their environment (including the normal neighbouring cells) play an important role in the early stages of the development of a tumor. In order to understand the mechanisms that control tumor invasion, we focus on cell dynamics at the interface between normal and transformed cells.
We study cell monolayers in well–controlled micro-environments (geometry and density). Our strategy consists in studying the dynamical evolution of well-defined coexisting populations of transformed and non-transformed cells. In particular, we map the force and velocity fields and characterize the extrusion events in relation with oncogene activity and mechanical state.

24. ***Control of single cell somitogenesis***

NEGRETE JR Jose
Max Planck institute for the Physics of Complex Systems, Dresden

Embryo somitogenesis is preceded by the spatiotemporal evolution of a kinematic wave of cyclic genes such as her1. It is conjectured that this wave is at the same time modulated by the presence signaling gradients. In this work we have developed a theoretical formalism for analyzing the dynamics of her1 at the single cell level. Remarkably these cells show an oscillatory transient when they are disassociated from the embryo and positioned far from each other, suggesting that autonomous dynamics play an important role in somitogenesis. We have been able to identify the key parameters that are modulated during the evolution of her1 and from these we developed predictions that can be tested in experiment. In particular the parameters of the reaction rates of her1 are non-stationary suggesting that these are controlled by the signaling system.

25. ***Infimum Theorem and First-Passage-Time Fluctuation Theorem for Entropy Production***

NERI Izaak
Max Planck Institute for the Physics of Complex Systems, Dresden

We derive an infimum law and a first-passage-time fluctuation theorem for entropy production of stochastic processes at steady state. We show that the ratio between the probability densities of the first-passage time to produce S of entropy and of the first-passage time to produce ?S of entropy equals exp(S)/k, with k Boltzmann's constant. This first-passage-time fluctuation relation is valid for processes with one or higher order passages. In addition, we derive universal bounds for the infimum statistics of entropy production. We show that the mean value of the entropy-production infimum is larger or equal than minus the Boltzmann constant. Our results imply thermodynamic constraints on the dynamics of biological processes at the mesoscopic scale, e.g. of enzymatic reactions.

26. ***Shaping, clustering and sorting of BmrA, a multi-drug membrane transporter with specific lipids***

PAIK Su-Jin
Institut Curie - Recherche-UMR168, Paris

ABC (ATP-binding cassette) transporters are membrane proteins that hydrolyze ATP for the efflux of various types of substrates including lipids, peptides, hormones, drugs, antibiotics... Several human ABC transporters are involved in a cellular multi-drug resistance (MDR) phenotype against e.g. anticancer agents. Some models of mechanism of drug transport are proposed but it is far to be understood. Our previous structural data have shown that a large conformational change of membrane domains is associated to the drug transport by BmrA, a bacterial ABC MDR transporter, highly homologous to the human PgP. We hypothesized that the coupling of ABCs transporters and the surrounding membrane could be an important modulator of the function. We combine structural biology, biomimetic systems and membrane biophysics to study this coupling. We aim to determine according to ATP concentration, lipid composition and membrane curvature : the 3D structures of BmrA by cryo-electron microscopy, the formation of lipid/protein domains and the sorting of protein after reconstituting into GUVs and the dynamic of BmrA by single-molecule FRET measurements.

27. ***Monitoring secreted Listeria monocytogenes virulence factors in real time with a novel fluorescence tag***

PERON CANE Caroline
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Upon invasion of a mammalian host, Listeria monocytogenes switches on virulence genes that allow colonization and subversion of host functions to the bacterial benefit. Intracellular stages of Listeria monocytogenes virulence are highly constrained by the adequate timing and localization of the activity of these virulence factors, for diffusible factors as well as for those anchored to the bacterial surface. However, insights into the spatiotemporal organization of secreted virulence factors are missing, due to a lack of tools allowing their detection in real time. Indeed, the active form of most currently available fluorescent protein tags, the prototype of which is represented by GFP, cannot undergo secretion through the general bacterial Sec pathway. In case they are exported under a premature form, the extracellular environment is not suitable for the maturation of their core fluorophore. In addition, fluorophore maturation is a long and oxygen-dependent process, incompatible with the monitoring of rapid switches in virulence factor production, or with microaeroby conditions.

The development a novel fluorescence tag, Y-FAST, where the fluorophore is provided in trans as a soluble cofactor, now allows us to overcome this limitation (Plamont et al. 2016). The 14-kDa Y-FAST fused to a virulence factor can be efficiently secreted, and folds into an active state with rapid kinetics.

We have taken advantage of this novel tool to explore the chronology of molecular events that lead to the rupture of the listeria-containing vacuole after entry into host cell or cell-to-cell spread. To this end, we have analyzed the export of the pore-forming toxin listeriolysin O (LLO) in infected cells, and investigated its accessibility to host membranes or to the cytoplasm.

In addition to providing dynamic information about the fate of secreted LLO, Y-FAST should enable us to monitor a wide array of secreted virulence factors and analyze their changes in location during infection. More generally, the system could be adapted to other bacterial secretion systems from various bacteria, and allow the monitoring of virulence factors in real time, including for anaerobes.

28. ***Torque generation by actomyosin cytoskeleton for chiral symmetry breaking in cell division.***

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Most animals are left-right asymmetric, and the molecular and physical mechanism that drive LR symmetry breaking are largely unexplored. In C.elegans the primary determinant for symmetry breaking event to define LR polarity is thought to be linked to the cytoskeleton. Recently, Naganathan et al, showed that the actomyosin cortex generates active chiral torques in a single cell embryo leading to chiral morphogenetic events that are subsequently involved in establishing the LR axis at the 6-cell stage. We speculate that chiral movements are much more prevalent in development, driving cellular rearrangements and axis repositioning than previously known. I plan to explore these chiral morphogenetic features in a quantitative manner in early stages of the worm development, and determine the extent of chiral cortical flows and chiral morphogenesis in the first few division of the nematode. Using RNAi mediated perturbations for myosin regulators, I plan to modulate chiral flows and monitor its effect on axis establishment and cellular rearrangement until the 6-cell stage.

Finally using thin film active chiral fluid theory with experimental data, I plan to deliver a physical description of how torques are generated in the actomyosin cortex and how these events lead to morphogenetic changes in development.

29. ***Active particle positioning by myosin assemblies in a geometrically-controlled actin networks.***
POCHITALOFF Marie
Institut Curie - CNRS, Paris
I am beginning a PhD on the behavior of an assembly of molecular motors on actin-filament network with an vitro system enabling the control of both the chemistry and the network architecture to get a better understanding of transport issues in the cell on the cytoskeleton.

30. ***Optomechanical control of myosin motor proteins in C. elegans***
POLIC Dora
Grill lab, Biotec, TU Dresden, Paris
Morphogenesis is one of the fundamental processes for organism development. The forces that operate during morphogenesis are generated by the actomyosin cortex. We are interested in studying biophysical forces and stresses during morphogenesis, using the single cell C. elegans embryo as a model system. Identifying how large-scale mechanical parameters of the cortex originate from nanoscale molecular force generation by myosin motors is crucial for understanding cellular and tissue morphogenesis in all animal cells. To solve this problem, one would like to perform controlled molecular scale perturbations of force generation and investigate the systems' response at larger scales. However, current tools to manipulate myosin function lack spatiotemporal control. Recent technological advances (Bryant lab, Stanford) enable optically-controlled changes of myosin to "remote-control" by light its stepping and force generation behavior. During my PhD I will develop this approach for use in the C. elegans zygote. In order to understand how NMY-2 force generation sets active tensions and torques that drive cortical flow we are going to generate NMY-2 mutants that allow for a light-based regulation of motor function and introduce it into C. elegans embryos. Using spinning disc confocal fluorescence microscopy coupled with laser nano-dissection I will characterize forces, flows and rotations in the active cortex during cytokinesis. I aim to provide a theoretical description of cortical mechanics in the C. elegans embryo. To summarize, the aim of this proposal is to characterize the mechanisms by which molecular scale force and torque generation drive large-scale morphogenetic processes.

31. ***Correlation analysis of microtubule growth and cap fluctuations validates a simple chemical kinetic model of the systems dynamics***
RICKMAN Jamie
The Francis Crick Institute, London
Microtubule growth is highly stochastic and intrinsic fluctuations contain rich information about the system dynamics. With fluorescence microscopy one can monitor fluctuations in microtubule growth and in its stabilizing cap simultaneously (using the +TIP EB1 as a reporter). Since the cap is linked to stability characterizing cap fluctuations in conjunction with growth fluctuations could increase our understanding of the underlying mechanisms. The formation and removal of cap sites can be modelled as a simple biochemical reaction network. Using correlation analysis one can relate the amplitudes and timescales of fluctuations to kinetic rate constants. Quantitative comparison of the rates derived from

correlation analysis and independent methods using mean growth properties shows good agreement, validating the model. Cross-correlation of growth and cap site fluctuations captures the theoretical picture growth is driven by fast and random addition and loss of subunits at the tip the resulting ‘noise’ is then filtered by the tubulin maturation process giving rise to exponentially correlated fluctuations in cap sites. The model makes simple but powerful statements about the stochastic processes at work that have potentially significant implications for microtubule dynamic instability.

32. ***Linking phenotypic heterogeneity and population demography in Pseudomonas fluorescent switching strains***
    ROMANO Orso M
    IBENS, Paris
    Phenotypic heterogeneity is a common, complex property of microbial populations: it bridges genetics, the organism's response to the environment, and evolutionary concepts such as bet-hedging. Pseudomonas fluorescent switching strains, evolved in Paul Rainey's lab to perform an ON/OFF phenotypic switch at higher rates than the wild type, are a model system to study microbial phenotypic heterogeneity. At the population level, one can observe the frequencies of the two cellular states, and their change through time. Under stationary conditions, such frequencies are expected to be at an equilibrium underpinned by the genetic background. However, frequencies were observed to vary substantially over time depending on culture conditions, hinting to a possible dependence of the switching rates on the population demography. We developed a mathematical model where such rates depend on population's growth state. The model reproduces qualitatively the kinetics of the frequency of the two phenotypes in the population. The dependence of such a dynamics on the demographic history of the population stresses how trans-generational ``memory'' could be a simple consequence of coupling gene regulation to cell metabolism.

33. ***Hardening of protein droplets***
    SAHA Suropriya
    Max Planck Institute for the Physics of Complex Systems, Dresden

34. ***A role for mechanics in somitogenesis***
    SCHULZE Ulrike
    The Francis Crick Institute, London

35. ***Modelling poroelastic behaviour of a living cell***
    SRIVASTAVA Pragya
    The Francis Crick Institute, London

36. ***Modulating septin organization on biomimetic lipid membranes***
    SZUBA Agata
    AMOLF, Amsterdam

37. ***Self-assembly characterization of Saccharomyces Cerevisiae and Drosophila Melanogaster septins by cryo-electron microscopy and tomography***

TAVENEAU Cynthia
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Septins are a highly conserved1 family of proteins in eukaryotes required for cell division. These proteins are recognized as the fourth component of the cytoskeleton. They promote membrane remodelling by a specific phosphoinositide binding2. Consequently, septins are multi-tasking proteins and have prominent role in cytokinesis3, establishing diffusion barriers for membrane-bound proteins4, neuron morphogenesis5 and contribute to the development of neurodegenerative diseases (Alzheimer, Parkinson6) as well as tumor formation. Thus, recent years have seen renewed for the study of septins.

Septins are GTPases proteins which are bound to the inner cell membrane. As opposed to other cytoskeletal proteins, they polymerize in a non-polar fashion into paired filaments2,7. They display a remarkable plasticity, both in term of binding partners (several proteins, membranes) and self-assembly organizations. Indeed, the filaments have a potential to self-assemble into higher-order structures including rods, filaments, rings and gauzes2,7,8.

We focus our interest in understanding how septins self-assembly in distinct ultra-structures. To this end, we are using cryo-electron microscopy and tomography. Thus, we are now characterizing (i) liposome remodelling by septins (ii) septins organizations in the different ultra-structures (iii) physico-chemical conditions required for the formations of the ultra-structures and their functions (type of lipid, membrane curvature…). So far, we concentrate our study on Saccaharomyces Cerevisiae septins and recently on Drosophila Melanogaster ones, which is one of the first septins ultra-structure characterization in higher eukaryotes.

38. ***Quantifying the migration: optogenetic control of intracellular gradients of RhoGTPases***

VAIDZIULYTE Kotryna
Institut Curie, Paris

The migration of a mammalian cell in a complex tissue requires the detection and processing of numerous chemical and physical signals distributed in the environment. In order to navigate correctly, a cell needs to amplify some signals, to filter out other ones, or to take a decision based on a combination of them. To get a quantitative understanding of the intracellular processes in charge of such tasks, we are developing tools allowing the control of the cell microenvironment and allowing the perturbation of intracellular biochemical activities. The present project is centered on setting up simplified experimental schemes to quantify the migration process. We are studying the sensitivity of cells when initiating migration and use a controlled microenvironment in order to initially deprive cells of any directional cue. Then we perform optogenetic perturbations to induce intracellular signaling gradients, hereby imposing a favored direction. For the time being, we are focused on small RhoGTPases, especially Rac1 and Cdc42, which are known to exhibit coordinated spatiotemporal programs of activities directing the architecture of the cell during cell polarization and migration.

39. ***TBA***

WASNIK Vaibhav
Saarland University, Saarbrucken

40. ***Stuttering of Min oscillations is induced by stochastic effects***

WETTMANN Lukas
Saarland University, Saarbrucken
The site of cell division in wild type E. coli bacteria is determined through pole-to-pole oscillations of the Min proteins. Although the oscillations are fairly stable across a wide variety of cell shapes and protein concentrations the emerging patterns are subject to molecular noise, due to the small copy number of proteins in a single cell. This causes the oscillations to sometimes ”stutter” and remain in the same polar configuration. We use a simple, generic model of protein interactions which shows similar behaviour as the Min-system and analyze the stochastic dynamics in the limit of weak noise to understand the underlying effects.

41. ***Building a cortex – 2-dimensional contractile actomyosin networks***

WOLLRAB Viktoria
Amolf, Amsterdam
Actin filaments and myosin motors form a dense network below the cell membrane, the cell cortex. This structure is relevant in numerous cell phenomena, such as cell polarization and cortical flows, as well as cell shape transformations including blebbing, cell rounding and cell division. Cell membrane and cortex show a complex composition. In vitro they are difficult to image with light or electron microscopy and manipulation of single parameters is impossible. Therefore, we chose an in vitro approach, where we rebuild the cell cortex with a minimal system containing actin, myosin and regulating proteins and a biomimetic lipid membrane. This allows us to fully control protein and lipid composition and at the same time provides maximal freedom concerning the imaging methods. We generate quasi 2-dimensional, membrane associated actomyosin networks. By systematically probing the influence of the protein composition and concentration, as well as membrane attachment, we can deceiver their respective influences on network architecture and contractility.

42. ***Increasing complexity of linear, prevailing, autocatalytical molecules***

ZIMMER Philipp
Universität des Saarlandes, Saarbrucken
Two common concepts of Darwinian evolution are mutation and selection. In natural evolution, these processes have permanently generated increasingly complex species. Nevertheless evolution has maintained to avoid dead ends such that a further development is proceeding. This process is not well understood. Performing stochastic simulations as well as experiments with DNA, we find that our system evolves reproducibly towards consecutive states of increasing complexity, if the autocatalytic activity exceeds a critical value.

43. ***Membrane organization and diffusion***

MULLA Yuval
Amolf, Amsterdam

44. ***Equilibrium physics breakdown reveals the active nature of red blood cell flickering***

TURLIER Hervé
Heidelberg, EMBL

Red blood cells, or erythrocytes, are seen to flicker under optical microscopy, a phenomenon initially described as thermal fluctuations of the cell membrane. But recent studies have suggested the involvement of non-equilibrium processes, without definitively ruling out equilibrium interpretations. Using active and passive microrheology to directly compare the membrane response and fluctuations on single erythrocytes, we report here a violation of the fluctuation–dissipation relation, which is a direct demonstration of the non-equilibrium nature of flickering. With an analytical model of the composite erythrocyte membrane and realistic stochastic simulations, we show that several molecular mechanisms may explain the active fluctuations, and we predict their kinetics. We demonstrate that tangential metabolic activity in the network formed by spectrin, a cytoskeletal protein, can generate curvature-mediated active membrane motions. We also show that other active membrane processes represented by direct normal force dipoles may explain the observed membrane activity. Our findings provide solid experimental and theoretical frameworks for future investigations of the origin and function of active motion in cells.