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ITMO Cell biology, development and evolution

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Modeling in Cell and Developmental Biology

http://modeling.sciencesconf.org

December, 1st 2015

ABSTRACTS BOOK LIVRET DES RÉSUMÉS

Création graphique: Myriem BELKACEM. Photos: Emmanuel FAURE, Danielle MONNIAUX, Guillaume PEZERON, Marie BREAU, Danielle MONNIAUX, Marie BREAU

- Organizers of the event : ITMO BCDE and Scientific organizers
- Scientific program
- Speakers contact
- Speakers Abstracts
- Poster listing
- Participants contact

An additional booklet is provided containing the poster summary

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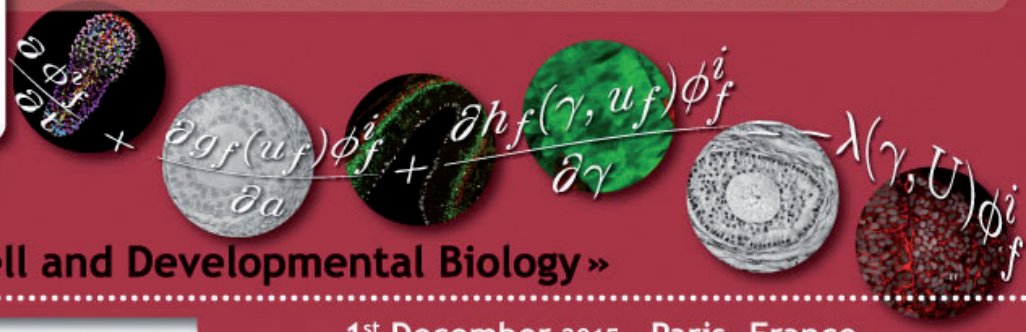

Workshop « Modeling in Cell and Developmental Biology »

1st December 2015 - Paris, France

MODELING IN CELL AND DEVELOPMENTAL BIOLOGY

Program

8:30 - 9:20 AM — Arrival of the Participants & Poster Hang-up

9:20 - 9:30 AM — Welcome Address

Session I: Biophysical modeling of intracellular processes
Chair: *Laurent Héliot*

- 9:30 - 10:10 AM — Integrated models of cytoskeleton-driven morphogenetic processes
  François Nedelec, EMBL Heidelberg, Germany
- 10:10 - 10:50 AM — From active gel models of cell mechanics to cell trajectories
  Raphaël Voituriez, *Université Pierre et Marie Curie*, Paris, France
- 10:50 - 11:10 AM — Coffee Break

Session II: Cell dynamics and tissue differentiation
Chair: *Frédérique Clément*

- 11:10 - 11:50 AM — Multistability in cell fate specification during development
  Geneviève Dupont, *Université Libre de Bruxelles,* Belgium
- 11:50 - 12:30 AM — Multiscale modeling of ovarian follicular development
  Danielle Monniaux, INRA Tours, France
- 12:30 AM - 2:45 PM — Buffet lunch and poster session

Session III: Modeling plant morphogenesis
Chair: *Sylvie Schneider-Maunoury*

- 2:45 - 3:25 PM — Swarms and Traffic-jams in Development
  Veronica Grieneisen, John Innes Centre, Norwich, United-Kingdom
- 3:25 - 4:05 PM — Unraveling the biophysical mechanisms behind plant morphogenesis
  Arezki Boudaoud, *Ecole Normale Supérieure Lyon*, France
- 4:05 - 4:25 PM — Coffee Break

Session IV: Modeling animal morphogenesis and morphological evolution
Chair: *Nadine Peyriéras*

- 4:25 - 5:05 PM — Building a body: towards a multi-scale image-driven dynamical model of limb development
  James Sharpe, CRG, Barcelona, Spain
- 5:05 - 5:45 PM — Models of embryonic development and morphological evolution
  Isaac Salazar-Ciudad, University of Helsinki, Finland
- 5:45 - 6:00 PM — Concluding remarks
  Franck Varenne, Gemass, Paris Sorbonne Université, France

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François Nedelec,
EMBL Heidelberg, Germany

Integrated models of cytoskeleton driven morphogenetic processes

Francois Nedelec and Serge Dmitrieff,
Cell Biology and Biophysics, EMBL Heidelberg, Germany

The actin cytoskeleton drives many essential processes in vivo, such as the extension of filopodia and lamellipodia, or endocytosis in yeast. The direction and amplitude of the forces that an actin network can produce depend on its composition and on the organization of the components in space. Molecular motors and actin assembly itself are important force generators. We will focus on how forces due to actin polymerization are harvested, depending on the geometry of the system. We discuss configurations associated with mechanical amplification, whereby the force generated by the network is greater than the sum of the polymerisation forces. We will apply these ideas to endocytosis in yeast, discussing how actin polymerisation may extend the nascent invagination leading to the internalization of a vesicle.

Raphaël Voituriez,
Université Pierre et Marie Curie, Paris, France

From active gel models of cell mechanics to cell trajectories

Eukaryotic cell movement has essential functions (in development, immunity or cancer) and so far very diverse cell migration patterns have been reported, but no general rule has emerged. We will show on the basis of experimental data in vitro and in vivo that in fact cell persistence, which quantifies the straightness of trajectories, is robustly coupled to cell migration speed. We suggest that this "universal" coupling constitutes a generic law of cell migration, which originates in the advection of polarity cues by an actin cytoskeleton undergoing flows at the cellular scale. The analysis relies on a theoretical model that yields a generic phase diagram of cellular trajectories, which recapitulates the range of observed migration patterns.

Geneviève Dupont,
Université Libre de Bruxelles, Belgium

Multistability in cell fate specification during development

Geneviève Dupont[1], Didier Gonze[1], Laurane De Mot[1], Albert Goldbeter[1], Sylvain Bessonnard[2], Claire Chazaud[3]

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During development, interactions between transcription factors control the specification of different cell fates. The regulatory networks of genetic interactions often exhibit multiple stable steady states; such multistability provides a common dynamical basis for differentiation. During early murine embryogenesis, cells from the inner cell mass (ICM) can be specified in epiblast (Epi) or primitive endoderm (PrE). Two antagonistic transcription factors control the differentiation of the ICM into Epi and PrE: Nanog is required for the differentiation into Epi cells whereas Gata6 is necessary to produce the PrE epithelium. Besides the intracellular gene regulatory network, specification is also controlled by intercellular interactions involving Erk signaling through extracellular Fgf4. We propose a model that describes the gene regulatory network and its interaction with Erk signaling in ICM cells. The model displays tristability in a range of Fgf4 concentration and accounts for the self-organized specification process observed *in vivo*. Results of simulations of a population of 25 cells under various conditions compare well with the outcome of mutant embryos and of embryos submitted to exogenous treatments interfering with Fgf signaling. Finally, the model predicts that heterogeneities in extracellular Fgf4 concentration play a primary role in the observed spatial arrangement of the Epi/PrE cells in a 'salt-and-pepper' pattern.

Bessonnard S. *et al.* Gata6, Nanog and Erk signaling control cell fate in the inner cel mass through a tristable regulatory network. Development (2014) 141, 3637.

De Mot L. *et al*. Cell fate specification in the inner cell mass of mouse blastocysts: Analysis of a model based on tristability. *Submitted.*

Danielle Monniaux,
INRA Tours, France

Multiscale modeling of ovarian follicular development
From follicular morphogenesis to selection for ovulation

Danielle Monniaux[*], Philippe Michel[†], Marie Postel[‡§] and Frédérique Clément[§]
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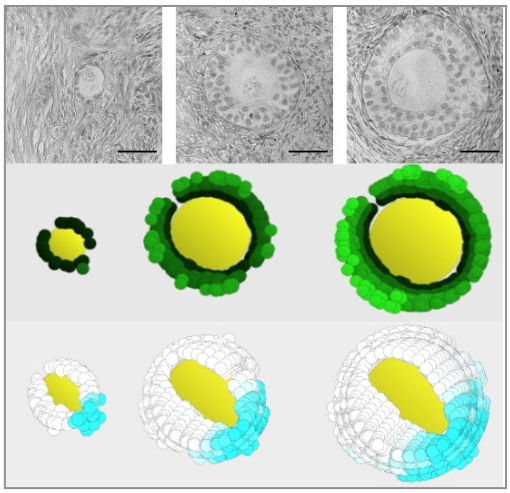
The presentation will be devoted to multiscale mathematical models of ovarian follicular development that are based on the embedding of physiological mechanisms into the cell scale. During basal follicular development, follicular growth operates through an increase in the oocyte size concomitant with the proliferation of its surrounding granulosa cells. We have developed a spatio-temporal model of follicular morphogenesis explaining how the interactions between the oocyte and granulosa cells need to be properly balanced to shape the follicle. During terminal follicular development, the ovulatory follicle is selected among a cohort of simultaneously growing follicles. To address this process of follicle selection, we have developed a model giving a continuous and deterministic description of follicle development, adapted to high numbers of cells and based on the dynamical and hormonally-regulated repartition of granulosa cells into different cell states, namely proliferation, differentiation and apoptosis. This model takes into account the hormonal feedback loop involving the growing ovarian follicles and the pituitary gland, and enables the exploration of mechanisms regulating the number of ovulations at each ovarian cycle. Both models are useful for addressing ovarian physiopathological situations. Moreover, they can be proposed as generic modeling environments to study various developmental processes and cell interaction mechanisms.



Graphical abstract
We present two multiscale mathematical models of ovarian follicular development based on the embedding of physiological mechanisms into the cell scale. One studies the process of basal follicular morphogenesis, while the other investigates the terminal selection for ovulation among a cohort of simultaneously growing follicles. These mechanistic and spatio-temporal models are built on current biological hypotheses and concepts. They can be proposed as generic modeling environments to study various developmental processes and cell interaction mechanisms.

Veronica Grieneisen,
John Innes Centre, Norwich, UK

Swarms and Traffic-jams in Development

There is much movement within plants. During this talk, I will discuss how computational modelling efforts have helped capture some of these internal dynamics, by dissecting the flow of hormones through plant tissue. In the root, models have helped us understand the formation of morphogen gradients that guide growth. Coupled with genetic regulatory networks, gradients of hormones and proteins can further specify important stem cell decisions, which impact the very layout of the tissue itself. And the dynamic nature of root growth, imposes constraints on transition points to be regulated. I will discuss some of the current results we have gained in how gradients move and are warped within the dynamically growing root. Moreover, the complexity of root development is even further increased when one realizes that roots do not grow in isolation: they interact with their environment, from which they take up essential nutrients, such as Boron. Through a collaborative effort between UK (Marée Lab) and Japan (Fujiwara Lab), we establish important parallels between Boron transport mechanisms with those of endogenous auxin transport. We have found that dynamic regulation of transporters, mediated through transcription and translation, is key to maintain stable internal fluxes. Lastly, I will briefly highlight how our Systems Biology approach to biological development is allowing us to extrapolate important developmental processes to swarms of locally interacting robots, which we currently use as a framework to test our ideas of emergent pattern formation and morphogenesis.

Arezki Boudaoud,
ENS Lyon, France

“Stochasticity and robustness in growth and morphogenesis”

How do organisms cope with natural variability to achieve well-defined morphologies and architectures? We addressed this question by combining experiments with live plants and analyses of stochastic models that integrate cell-cell communication and tissue mechanics. This led us to counterintuitive results on the role of noise in development, whereby noise is either filtered or enhanced according to the level at which it is acting.

James Sharpe,
CRG, Barcelona, Spain

Building a body: Towards a multi-scale image-driven dynamical model of limb development

The goal of our group is to bring together an interdisciplinary team of scientists to focus on the research of a particular complex system – development of the vertebrate limb. We aim to understand it both at the level of gene regulatory networks, and at the level of the physical interactions between cells and tissues.
To achieve this the group includes embryologists, computer scientists, imaging specialists and engineers. We thus aim to capture the whole process of understanding, from novel approaches for data-capture (live time-lapse OPT imaging) to finite-element simulations of the growing 3D structure and computer models of the gene networks responsible for pattern formation across the organ.
This combination of approaches is allowing us to address the following questions: What kinds of cellular movements are responsible for creating to correct 3D shape of the limb? How are these behaviours coordinated? How is the correct spatial pattern of gene expression controlled? What topology of gene regulatory network may be responsible for this complex phenomenon?

Green, Jeremy B. A., Sharpe, James. Positional information and reaction-diffusion: two big ideas in developmental biology combine. Development 142:1203-1211. 01/04/2015. F.I.: 6.273. [doi:10.1242/dev.114991]

Isaac Salazar-Ciudad,
University of Helskinki, Finland

Models of embryonic development and morphological evolution

Senior researcher on the mechanisms of evolution.
My focus is on morphological evolution and to this end I have been developing theories about the interdependence between the dynamics of development and the dynamics of evolution. This has brought me to study the mechanisms of pattern formation in development that are responsible for the generation of phenotypic variation in populations. Thus, my aim is to understand the multiple types of relationships between genetic (and environmental) variation and morphological variation in different animal species and their effects on evolution. In practice my work involves integrating experimental data in developmental biology into mathematical models of development and evolution.

Franck Varenne,
Gemass, Paris Sorbonne Université, France

Multi-scale modelling is the future, but what about the challenge?

We undoubtedly are entering the era of multi-scale modelling in biology, especially in developmental biology. The challenges are numerous and great (Hasenauer et al., 2015). One of them relies on what appeared to be a necessary questioning for all modeling project: what comes first? What are the building-blocks of the model? Are these building-blocks concepts or data? This talk will focus on this specific challenge. Based on examples taken from the literature but also on the conferences presented in this colloquium, I will suggest that in the new context of multi-scale modelling, this preliminary question becomes spurious when taken from a too global hence binary standpoint. That is: Multi-scale modelling not only has to simultaneously focus on *different scales* but it also has to simultaneously implement different *types of sources of knowledge*, i.e. concepts *and* data. Most of the times, a multi-scale modelling project has to go back and forth between concepts and data, so as to cautiously intertwine data-driven and concept-driven models at different scales. Moreover, seen from the viewpoint of scales, concepts in concept-driven models are twofold. *Ontological*-concept-driven models are based on the ontology of the elements of the scale whereas *theoretical*-concept-driven models are based on available theories belonging to the discipline which is the best known or the most successful at this scale. Facing this duality, the questions related to the status of data (are they measures or *ad hoc* paremetrizations? are they biologically meaningful or not?, etc.), e.g., cannot uniformly be solved for all the submodels of the same multi-scale-model. As a consequence, we need to develop, test and teach a more explicit and self-aware methodology of this controlled alternation of concepts (be they ontologically or theoretically grounded) and data if we want to enhance and promote this rapidly growing interdisciplinary domain of multi-scale modelling.

LISTING POSTERS Workshop "Modeling in Cell and Developemental Biology"
1er décembre 2015, Biopark, Paris

NAME, Surname	MAIL	TITLE
CORSON Francis	corson@lps.ens.fr	**Dynamic Notch signaling organizes bristle patterns in the Drosophila thorax**
DOURSAT René	rene.doursat@iscpif.fr	**Zebrafish epiboly and formation of compartments in 3D tissues: coupling mechanical behavior and gene regulation**
FERNANDEZ-GARCIA Soledad	soledad.fernandez-garcia@inria.fr	**Modeling ionic and secretory rhythms in adult and embryonic neural networks with multiple time scale dynamical systems.**
GERVASI Nicolas	nicolas.gervasi@inserm.fr	**Neuronal geometry shapes neuronal cAMP signalling to the nucleus.**
GONZALEZ CURTO Gloria	gloria.curto@ijm.fr	**Reconstruction and modelling of Pax3 and Pax7 linked transcriptional network underpinning spinal development**
HERNANDEZ Celine	celine.hernandez@ens.fr	**Logical modelling of the regulatory network governing dorsal-ventral axis specification in the sea urchin P. lividus**
HUE Isabelle	isabelle.hue@jouy.inra.fr	**Towards the modelling of conceptus morphogenesis in ruminants**
KOKSAL ERSOZ Elif	elif.koksal@inria.fr	**Complex oscillatory rhythms in neurohormone secretion : the instance of the GnRH neurosecretory system**
LOPEZ-MENENDEZ Horacio	horacio.lopez.menendez@gmail.com	**Microstructural model for cyclic hardening in F-actin networks cross-linked by alpha-actinin**
		Cell extrusion as a mechanical instability
MOLINA DELGADO Angie	angie-patricia.molina-delgado@univ-tlse3.com	**Analyzing the cell cycle in neural stem cells using quantitative real time imaging in an integrated system**
PEYRIERAS Nadine	nadine.peyrieras@iscpif.fr	**A workflow to process 3D+time microscopy images of developing organisms and reconstruct their cell lineage**
POSTEL Marie & KARAM Alice	postel@ann.jussieu.fr alice.karam@upmc.fr>	**Designing a mathematical model of the dynamics of progenitor cell populations in the mouse cerebral cortex**
RAUSCH Adeline	rausch@inaf.cnrs-gif.fr	**Calculating a prototypic model of Ascidian embryonic development**
RAZETTI Agustina	arazetti@unice.fr	**Statistical characterization, modelling and classification of morphological changes in imp mutant Drosophila gamma neurons**
ROUX Pierre-François	pierre-francois.roux@pasteur.fr	**Dynamic multidimensional profiling defines the oncogene-induced senescence (OIS) gene expression programme**
WACQUIER Benjamin	bwacquie@ulb.ac.be	**The role of the IpgD protein on calcium signalling during Shigella invasion: a modelling approach**
YVINEC Romain	romain.yvinec@tours.inra.fr	**Accurate parameter optimisation leads to predictive dynamical models for systems biology**

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