Parallel Session

Cell and Intra-Cell Dynamics V

INCOMPRESSIBLE LIMIT OF A CONTINUUM MODEL OF TISSUE GROWTH WITH SEGREGATION FOR TWO CELL POPULATIONS

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Joint work with Pierre Degond (ICL) and Jean-Paul Vincent (Francis Crick Insitute).

Keywords: Tissue growth, Two cell populations, Gradient flow, Incompressible limit, Free boundary problem.

In developmental biology, the mechanisms by which an organ knows when it has reached its adult size and shape and stops growing are still poorly understand. Among a lot of explanations, the role of mechanical feedback has emerged. In some tissue, mechanical forces such as stretching and compression may arise during the development due to segregation of different type of cell. We proposes a model for two interacting populations of cells which avoid mixing. The dynamics is driven by pressure and cohesion forces on the one hand and proliferation on the other hand. Following earlier works on the single population case, we show that the model approximates a free boundary Hele Shaw type model that we characterise using both analytical and numerical arguments.

Parallel Session

Cell and Intra-Cell Dynamics V

ON A THEORY OF CELL DECISION-MAKING IN MULTICELLULAR SYSTEMS: THE LEAST MICROENVIRONMENTAL UNCERTAINTY PRINCIPLE

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Keywords: Cell decision-making, Variational principle, Entropy, Statistical mechanics.

Cell decision-making is the cellular process of responding to microenvironmental cues. This can be regarded as the regulation of cell's intrinsic states to extrinsic stimuli. Currently, little is known about the principles dictating cell decision-making in the context of multicellular systems. Regarding cells as Bayesian decision-makers under energetic constraints, I postulate the principle of least microenvironmental uncertainty (LEUP). This is translated into a free-energy principle and I develop a theory cell decision making in multicellular systems. Initially, I show that LEUP is compatible with the intrinsic state entropy minimization for differentiating cells. Finally, I will provide examples of LEUP in the context of tissue development and cancer growth.

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Parallel Session

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INSIGHT INTO A NONLOCAL PDE MODEL OF CELLULAR ADHESION BY MICROSCALE SPACE-JUMP PROCESS MODELLING

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Joint work with Andreas Buttenschön (UBC, Canada), Thomas Hillen (U Alberta, Canada), and Kevin J. Painter (Heriot-Watt University, UK).

Keywords: Integro partial differential equations, Discrete-continuous coupling, Numerical simulation, Tissue growth, Cancer invasion.

Cellular adhesion provides one of the fundamental forms of biological interaction between cells and their surroundings. The integro-partial differential equation model of Armstrong, Painter, and Sherratt [1] initiated a stream of research in that area with applications in morphogenesis, tumour growth, and tissue engineering. In this talk we give an overview of a framework, see [2], in which we derive such a nonlocal continuous model from a space-jump process, thus connecting the micro- with the macroscale. This framework, in fact, also provides for models different or more general than the original one and these are investigated and compared numerically.

References

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Parallel Session

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POROELASTIC TWO-PHASE MODEL FOR MOVING DROPLETS OF PHYSARUM POLYCEPHALUM WITH FREE BOUNDARIES

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Keywords: Physarum polycephalum, Modelling cell motility.

Motivated by recent experiments, we model the flow-driven amoeboid motility that is exhibited by protoplasmic droplets of Physarum [1]. Here, a feedback loop between a chemical regulator, active mechanical deformations, and induced flows give rise to spatio-temporal contraction patterns that result in directed motion. Our model describes the droplet's cytoskeleton as an active viscoelastic solid phase that is permeated by a passive viscous fluid representing the cytosol. The active tension in the solid phase depends on the concentration of a regulating agent that is advected by the fluid phase. Previously, it was shown that under rigid boundary conditions that impose a fixed shape, this model reproduces a large variety of mechano-chemical patterns such as antiphase oscillations and rotating spirals [2]. This in line with experimental observations of contraction patterns in these droplets. Here, we present an approach that includes free boundary conditions, nonlinear friction between droplet and substrate and a nonlinear reaction kinetic for the regulator to model the movement of these droplets. We find deformations of the droplet boundary as well as oscillatory changes in the droplets position with a net motion in each cycle.

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ON A MECHANOCHEMICAL MODEL FOR CELL POLARIZATION

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Keywords: Cell migration, Polarization, Mechanochemical model.

Directed migration of eukaryotic cells is caused by a polarization of the actomyosin cytoskeleton (AMC). Throughout many cell types the polar alignment of the AMC is i.a. initiated by the activation of the Rho GTPases Rac and RhoA. In response to an external chemical gradient active Rac accumulates and determines the cell front, while active RhoA predominantly accumulates at the rear of the cell. Current experimental evidence indicates that in neutrophils mechanical tension of the plasma membrane confines Rac activity patterns to the leading edge. The patterning mechanism behind the Rho-based polarization process of eukaryotic cells has interested mathematical modellers over the last decades. While elaborated concepts for purely biochemical and purely mechanical patterning processes are available, the basics of mechanochemical patterning with respect to cell polarization are not well understood yet. In accordance to the aforementioned experimental findings, we suggest a mechanochemical model for cell polarization, including Rho GTPase mediated AMC dynamics and changes in membrane tension as upstream controller of Rho GTP, in which active Rac patterns are locally confined to the cell front by membrane tension. Rho proteins can become activated or inactivated due to complex formation with specific effector proteins. In the model active Rac and active RhoA mediate actin polymerization and the generation of myosin-dependent contractile force, respectively. The model cell is considered as a two dimensional layer adhering to a flat substrate, wherein the embedded AMC is modelled as a viscous active gel. Morphological changes of the AMC induce changes in membrane tension. Rho based chemical signalling is modelled by reaction-diffusion equations. Chemical signalling induces a mechanical response of the actomyosin cytoskeleton. Actomyosin mechanics are modelled by a Stokes-related equation. The spatial change of the domain is determined by the solution of a free-boundary problem. We numerically show that the model exhibits key features of neutrophil polarization and shape generation. The model accounts for a minimal mechanochemical circuit capable of generating robust polarity patterns and demonstrates how cell mechanics could serve as a long range signal transmitter in Rho based cell polarization.

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STRUCTURED CELL POPULATION DYNAMICS: APPLICATION TO THE MORPHOGENESIS OF OVARIAN FOLLICLES

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Keywords: Multi-type age dependent branching processes, Renewal equations, McKendrick-VonFoerster model, Long-time behavior, Data calibration.

We present a multi-type age dependent model in both a deterministic and stochastic framework dedicated to the study of the development of ovarian follicles in mammals Inspired by the model introduced in [1], we derive a linear age-structured version that represents the changes in the distribution of follicular cells into successive layers surrounding the oocyte. We study the large-time behavior and derive explicit analytical formulas characterizing an exponential growth of the population (Malthus parameter, asymptotic cell number moments and stable age distribution). We compare the theoretical and numerical outputs of our model with experimental biological data informing on the follicle morphology (follicle and oocyte diameters, layer number and total cell number). In the case of age independent division rates, we prove the structural parameter identifiability of our model, and estimate the parameter values to fit the cell numbers in each layer during the early stages of follicle development.

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