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Physique multi-échelle de la morphogénèse / *Multiscale physics of morphogenesis*

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PHYSIQUE MULTI-ÉCHELLE DE LA MORPHOGÉNÈSE / *MULTISCALE PHYSICS OF MORPHOGENESIS*

Responsables : Hervé TURLIER

RECHERCHE

Page web : https://www.college-de-france.fr/site/en-cirb/Turlier.htm.

Introduction

Invaluable progress has been made last decades in the molecular, genetic and cellular characterization of morphogenetic processes. Yet, the precise physical processes governing the shape and dynamics of cells remain poorly characterized.

The laboratory is developing theoretical models of morphogenesis, combining physics, mechanics and advanced numerical simulations. To understand how morphology controls biological functions, and, ultimately, how multicellular systems self-organize, we aim at integrating molecular, cellular and multicellular levels of description into a new and versatile simulation framework for embryo morphogenesis: Virtual Embryo.

From molecular to mesoscopic models of the actomyosin cortex

As elegantly illustrated by D'Arcy Thompson back in 1917, cells in suspension or in tissues adopt spatial configurations remarkably similar to soap bubbles, an analogy which can be drawn from the physical concept of surface tension. In animal cells, the surface tension is mainly provided by the contractile forces generated by molecular motors within the actin-myosin (or actomyosin) cortex, a thin layer of polymeric filaments, which lies under the plasma membrane. In contrast to passive objects like bubbles, cortical tension is actively regulated in space and time by several biochemical pathways – such as the RhoA signaling cascade – and strongly depends on the deformations of the layer. From a biological perspective, the tools available to perturb the cortex operate at the molecular level (chemical drugs, genetic engineering and environmental cues). Characterizing quantitatively how the self-organization and regulation of molecular players in the cortex (actin filaments, myosin motors, crosslinkers...) control its coarse-grained physical properties (elasticity, fluidity, contractility...) represents therefore a critical step to directly relate experiments to quantitative models.

At the cellular scale, the recent active-gel hydrodynamic theories have proven their efficiency in capturing the essential physics of various actomyosin based dynamical cell processes (Turlier *et al.*, 2014). However their relation to microscopic properties of actomyosin networks remains unclear, and no generic tool is available to simulate the mechanics of active surfaces in 3 dimensions. Combining physics and numerical simulations, we aim at filling these gaps in the next years in close collaboration with experimental groups.

From cellular to multicellular models of morphogenesis

At the multicellular level, morphogenesis is furthermore regulated by mechanical interaction and biochemical communication between cells, and by external mechanical constraints. In particular, the interplay between cell contractility, cell-cell adhesion, molecular expression and fate specification remains poorly understood in early embryos and small tissues. To identify and understand the minimal self-organization principles driving multicellular morphogenetic processes, it is essential to develop realistic 4-dimensional models of interacting cells, offering general and accurate description of cell surface mechanics but also complemented by versatile options to model surface signaling dynamics and simple gene networks regulation.

The morphogenesis of early embryos is the main biological focus and guideline for developing new theoretical tools in the laboratory. In mammalian species, early embryos develop over several days, which leads to a decoupling between morphogenetic timescales (several hours) and typical viscous relaxation timescales (a few minutes). Dynamics is limited in this case first by the slow regulation of surface

tensions, and morphogenesis is well captured by a quasi-static mechanical description, as we recently proposed for compaction and for the formation of the inner-cell mass in the mouse embryo (Maître, Turlier *et al.*, 2016). At the opposite, most non-mammalian embryo types, such as marine animals or insects, develop on much shorter timescales, of the order of a few hours. In this case, viscous dissipation becomes essential to consider again as it constitutes a main factor limiting cell shape dynamics (Turlier *et al.*, 2014). On such timescales, the biophysical characterization and precise modeling of cell divisions and its mechanical coupling to the rest of the embryo is an essential point that we aim to integrate into realistic simulations of embryo morphogenesis.

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DYNAMIQUE ET PHYSIOPATHOLOGIE DES RÉSEAUX NEURONAUX / *DYNAMICS AND PHYSIOPATHOLOGY OF NEURONAL NETWORKS*

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RECHERCHE

Page web : https://www.college-de-france.fr/site/en-cirb/venance.htm.

Our main interest is how neural networks of the brain support its cognitive capacities. We aim at providing rational mechanistic explanations of adaptative control of behavior. Procedural learning corresponds to the acquisition of skills through repeated performance and practice of a behavior in response to external cues, such as biking or playing an instrument. Basal ganglia, a set of subcortical nuclei, participate in the detection of environmental cues and in the selection of appropriate actions based on motivation and reward, thanks to their reciprocal connections to the cerebral cortex and limbic system. Cortex-basal ganglia loops are involved in the adaptive control of behavior and are the main substrate for procedural learning. We therefore focus our work on dissecting the processing of information in cortico-basal ganglia circuits, from sub-cellular to neural network levels. The key roles of basal ganglia are highlighted by motor and cognitive disorders observed in pathologies such as Parkinson diseases, for which no fully satisfying treatments are available yet.

Our main focus is about the role of the striatum, the primary input nucleus of basal ganglia, which is a strategic gate extracting pertinent information and a major site of memory formation. Indeed, striatum acts as a coincidence detector of distributed patterns of cortical and thalamic activity and is in charge to extract pertinent information from background noise at a t time in a given situation, which will give