CELL-BASED MODELING OF BIOMECHANICS IN BIOLOGICAL DEVELOPMENT

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Background

To form the patterns and behaviors that we observe in multicellular development, cells must carefully coordinate their behavior through biophysical and biochemical cues. Numerical modeling and theory are essential for analyzing the mechanism of such coordinated, collective cell behavior. To do so, single-cell models must be sufficiently detailed so they correctly capture essential aspects of individual cells and do not oversimplify. At the same time, single-cell models must be sufficiently simple and computationally efficient so they can be upscaled to multicellular systems. My team analyzes single cell behavior and multicellular development using a combination of mathematical, computational and experimental approaches. Our central tool is the cellular Potts model (CPM), a widely-used, lattice-based framework for modeling cell behavior. For most applications we couple the CPM with simulation models of the cellular microenvironment and relevant intracellular dynamics, a technique known as the hybrid CPM.

Recent Advances

I will present a series of our recent hybrid CPMs for modeling individual cell behavior, and show how these can be used to study the coordinated cell behavior that is seen in biological development. I will first discuss a series of models used to analyze observations such as anomalous cell migration patterns of immune cells [1], the effect of extracellular matrix stiffness on cell shape ([2] and Fig, 1A), cellular force transduction in fibrous ECMs ([3] and Fig. 1B), and models of anisotropic force generation [4]. I will then discuss how insights from single cell models translate to understanding of multicellular development [5,6] (Fig. 1C-D).

Future directions

In our ongoing work, we are developing strategies for experimental falsification and iterative correction of multicellular models of angiogenesis. Recent versions of our cell-ECM interaction models focus on how our descriptions of focal adhesions, the mechanosensitive 'feet' of cells by which they hold on the extracellular matrix, must be improved to analyze mechanical cell-ECM interactions. Also we invest in computational improvements to advance towards more detailed multicellular models. Altogether, I will resent the use of cell-based modeling in analyzing how local cell-microenvironment interactions coordinate cell behavior during multicellular patterning.

Roeland Merks is Professor of Mathematical Biology at the Faculty of Science of Leiden University. He leads an interdisciplinary team at the intersection of experimental biology, mathematics, and physics. Merks has developed novel mathematical and computational approaches to modeling the biomechanical and chemical interactions between cells and the extracellular matrix that guide the development of multicellular systems, which he has applied to studies of angiogenesis and related problems. His current research is funded by an NWO Vici, an NWO-XL, and by private funding. He is an author of 62 publications in peer-reviewed journals, 14 book chapters and more than 100 invited lectures.

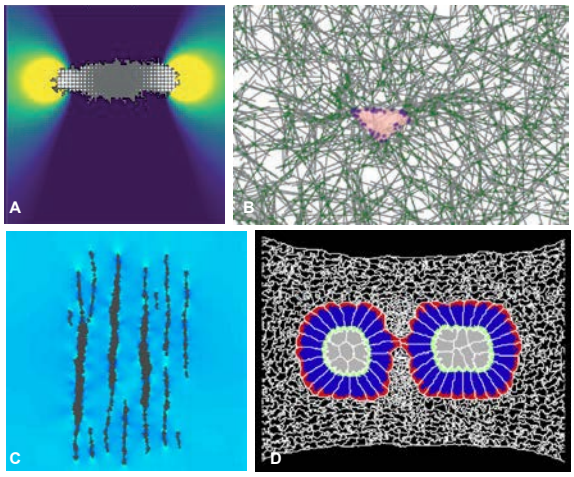

Figure 1: Cell-based models of biomechanics in development. (A,B) cell-ECM interactions [2,3]; (C) cell alignment to static strain [5]; somite splitting in strained chick embryos [6].

References

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