New eScience Tools for *in silico* Craniofacial Development

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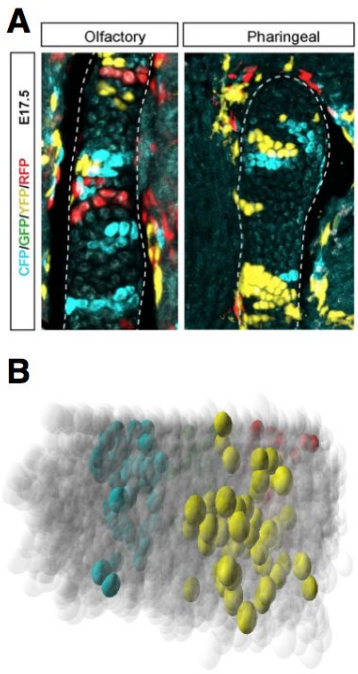
Project

In this project we seek to develop eScience simulation methods and software to be used together with advanced imaging-techniques based on genetic labeling in developmental biology (Fig 1). The potential for simulations to probe intricate cellular coordination processes is large [1], but currently there are no eScience methods available to bridge the large scale differences between the microscopic, cellular level organization and the macroscopic shape transitions that define the developmental processes. In this project we aim to develop new multiscale methods that capture both mechanical and molecular interactions between individual cells. We will use the methods to study how they give rise to rapid and reliable scaling of structures in the facial region of embryonic mice. The project has the dual objective to serve as a driving example for a cloud-based virtual laboratory for collaborative modeling in biology.



In the Adameyko lab, the spatial and temporal organization of the cellular composition in developing embryonic structures is approached with an experimental model based on genetic labeling (Fig 1:A). In simple terms, stem cells are labeled (by genetic manipulation) with colors that are passed on through generations. This type of data opens up unique opportunities for quantitative mathematical modeling. Not only is it possible to observe the distribution of cells on a fine spatial scale, but also to trace the evolution of clones of cells originating from the same ancestor stem cell after many generations of cell divisions (since they show up with the same color).

Soft, thin cartilage forms in the developing face, and provides the scaffold for bone formation at later developmental stages. These cartilage sheets are then scaled up by proliferative growth and in the resulting macroscale structure, the thickness is significantly smaller than the lateral dimensions. Eventually, these thin cartilage sheets formed in the early embryonic stages undergo shape transitions, likely driven by variation in sheet thickness and density. This variation arises due to the cellular configurations and due to localized zones of increased cellular growth and causes the sheets to bend, fold and combine into the more complex structures that will harden and become skeletal scaffolds in the later stages of the embryonic development. This project aims at developing models and simulation methods to study how the scaling is regulated. Contact one of the the PIs for more information.

Our current approach for studying the processes uses a lattice-based stochastic rule-based model that in the language of the recent review [2] falls in the category of a cellular automaton type A. This simple model is suitable for the questions we study in [1] and it is computationally efficient and scales to large number of cells (millions) [2]. However, in its current form it is not suitable for studying the complex scaling mechanisms of the cartilage since the biomechanics of cell-cell contact, deformations of cells, and molecular regulatory mechanisms are not appropriately captured.

Collaboration

The postdoc will be situated in the Hellander lab at UU and will mainly work towards new computational methods to model the developmental processes. He or she will also be expected to spend significant time at KI to develop appropriate knowledge of the experimental system and to interact with the Adameyko team for modeling.

Competency of the candidate

The successful candidate will have a PhD in computational/mathematical biology, applied mathematics, scientific computing (or for the project relevant field) with high-quality publications as principal author in international peer-reviewed journals or conferences. Previous experience with one or more modeling frameworks for multicellular dynamics (such as cellular automata, center-based model, vertex-based models or cellular Potts) is required as is strong programming skills and excellent oral and written communication in English. Previous experience of cloud computing is considered a merit, but not a prerequisite.

References

[1] M. Kaucka, E. Ivashkin, D. Gyllborg, T. Zikmund, M. Tesarova, J. Kaiser, M. Xie, J. Petersen, V. Pachnis, S. K. Nicolis , T. Yu, P. Sharpe, E. Arenas, H. Brismar, H. Blom, H. Clevers , U. Suter, A. S. Chagin, K. Fried, **A. Hellander** and **I. Adameyko**, (2016) Analysis of neural crest-derived clones reveals novel aspects of facial development, *Science Advances 2(8).*

[2] P. Van Liedekerke, M. M. Palm, N. Jagiella, and D. Drasdo. Simulating tissue mechanics with agent-based models: concepts, perspectives and some novel results. *Computational Particle Mechanics*, 2(4):401–444, 2015.