Network formation in tissues with two cell types

MSc Thesis with Lisanne Rens

contact: e.g.rens@tudelft.nl

Biological background

The formation of new blood-vessels occurs during health and disease. In wound healing, vessel growth is benificial, as it allows oxygen to flow into the tissue, aiding the repair. However, in tumours, blood-vessel formation is harmful, as it allows the tumour to grow. A proper understanding of the mechanisms and environmental conditions that regulate bloodvessel formation is required for the development of medicine and artificial tissues. With mathematical modeling, we aim to understand the role of distinct mechanisms and how they are connected in network formation.

Project description

Typical lab experiments that are used to study blood vessel formation are endothelial network assays. Endothelial cells, the cells that line up your blood vessels, when initially randomly distributed, actively migrate to form a network. In this project, we will focus on the role of the extracellular matrix (ECM), a network of proteins that supports tissues and guides cell migration. Experimental observations have shown that the stiffness (flexibility) of the ECM regulates network formation. This is mimicked using a computational model. In real-life tissues, the endothelial cells are co-existing and interacting with other cell types, such as fibroblasts (skin) or muscle cells. In this project, you will study how the presence of other cell types affects network formation.

Mathematical modeling

You will build up-on an existing computational model [1], written in C++. This model combines several mathematical techniques. The cells are modelled using the cellular Potts model (a kind of cellular automata, or agent-based model). The ECM is modeled using a finite element method. You will become familiar with these approaches and reproduce existing results. To analyse the simulated images, you will use and extend codes in Matlab and/or Python. Then, you will expand the model by introducing two different cell types and study the effect of different cell behavior and the relative density of the two types. More extensions, such as the role of chemical signaling between cells (partial differential equations) are possible, if there is enough time. You are also free and encouraged to come up with other biologically questions yourself.

References

[1] R. F. M. van Oers, E. G. Rens, D. J. LaValley, C. A. Reinhart-King, and R. M. H. Merks. Mechanical cell-matrix feedback explains pairwise and collective endothelial cell behavior in vitro. *PLoS Computational Biology*, 10(8):e1003774, 2014.

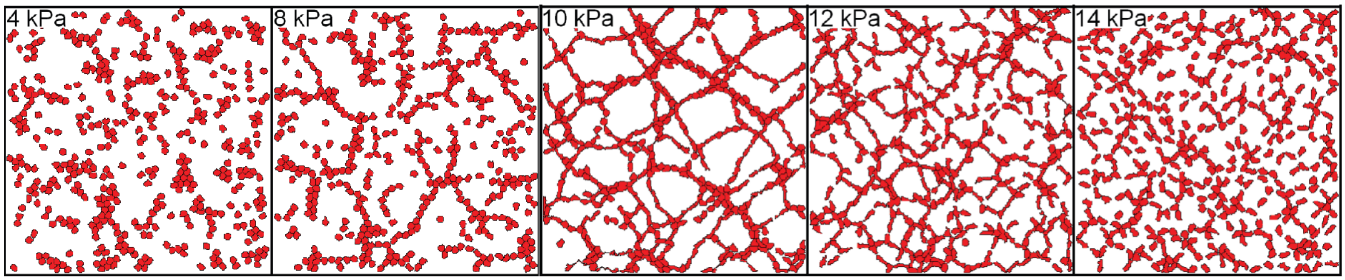

Figure 1: Simulated network formation on matrices of increasing stiffness.