Virtual angiogenesis : mathematical and multiphysics approach for directed tissue engineering

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Background

Adding a blood vessel network to cultured tissues is an essential step for clinical application. A physiological organization of these networks is important for the functioning of the blood vessels. Endothelial cells seeded in a hydrogel can give rise to microvascular networks. In reaction to external chemical (growth factor gradients) and mechanical forces (matrix stiffness, interstitial fluid flow), the networks grow into adjacent empty matrix [1,3]. A range of cell-cell interactions leading to microvascular network formation have been proposed [2,4]. However, the cell-based models (cellular potts model) studying these mechanisms, often fail to include factors as opposed by the environment.

Objective

We developed a framework for studying the effect of extracellular regulating factors such as chemical gradients, matrix stiffness, interstitial flow, coupled with cellular component in a single model for predicting the evolution of microvascular network in a given geometry.

Methods

An hybrid cellular potts – partial differential equation (CPM-PDE) model is presented to study the microvascular network formation. This hybrid model consisting of a CPM component for cellular representation, and a PDE component solving mathematical equations for the distribution of chemicals. Individual cells are represented in a 2D discrete space. The cells secrete and react to chemicals in their environment, which diffuse and decay in the ECM.

Results and Discussion

The model in this study is based upon the previous work of the lab of Roeland Merks.We modeled the network formation in a microfluidic device setting as shown in figure. From the cells seeded in the hydrogel matrix and their local interactions, network structures emerge. The shapes of arising structures are studied and correlated to calculated properties and parameter values. New boundary conditions were set-up as to be comparable to experimental data and an external Vascular Endothelial Growth Factor (VEGF) source was added.

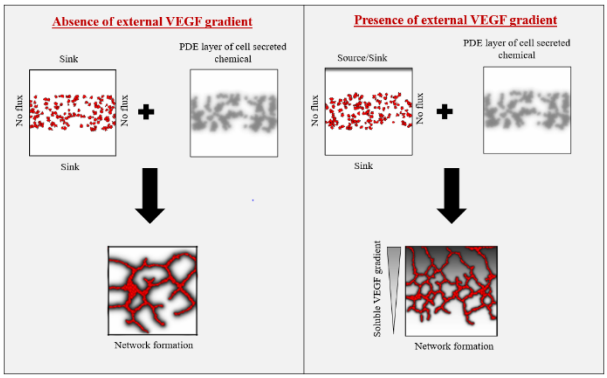

Figure. Modeling chemotaxis of microvascular angiogenesis

Future plans

We anticipate our model framework to be a starting point for more sophisticated experimental driven (microfluidic-based) insilico testing tool for tissue engineering applications. For example, the possible addition of aptamer binding kinetics coupled to the mechano-chemical parameters could be used to study the network organization within a spatiotemporal controlled growth factor release system. This would help us to predict the emerging network types within the tissue constructs of specific extracellular regulating parameter values. Furthermore, it would be used to design the quantitative assay for in vitro testing.

References

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