Mechanotaxis in the Cellular Potts Model

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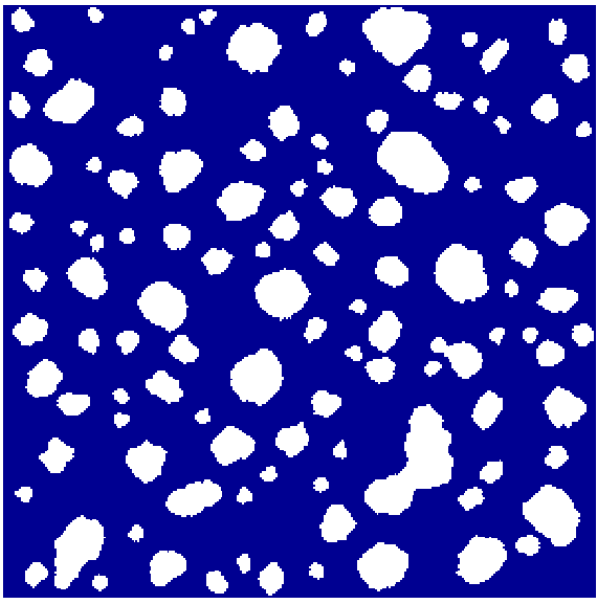
Blood vessel growth is essential for many biological processes such as embryonic development, wound healing, and tumor growth. The Cellular Potts Model (CPM) has been used to study various possible mechanisms for vasculogenesis, including cell-cell adhesion, cell elongation, chemotaxis, and contact inhibition [1]. Another known factor in blood vessel growth is mechanotaxis, the guidance of cell migration by mechanical cues such as substrate stretch [2]. Therefore, we are currently developing a CPM that includes mechanotaxis.
We integrated the CPM grid with a finite element (FE) mesh, so substrate stretch can be determined. Then we added a strain-term to the CPM algorithm, which increases the probability for cell extensions along the principal strain axis once strain is high enough. As a result, cells align to the loading direction in a stretched substrate (second figure). The next step was to have cells generate forces themselves. This was implemented by treating the FE nodes along the cell boundary as focal adhesions. Each of these pulls on the other nodes along the cell surface, and the contractile forces thus generated create stretch in the surrounding tissue. This results in 'stretch highways' between nearby groups of cells, which in turn cause the cells to migrate and connect over these highways (lower figure), simular to what has been observed in experimental studies [2].

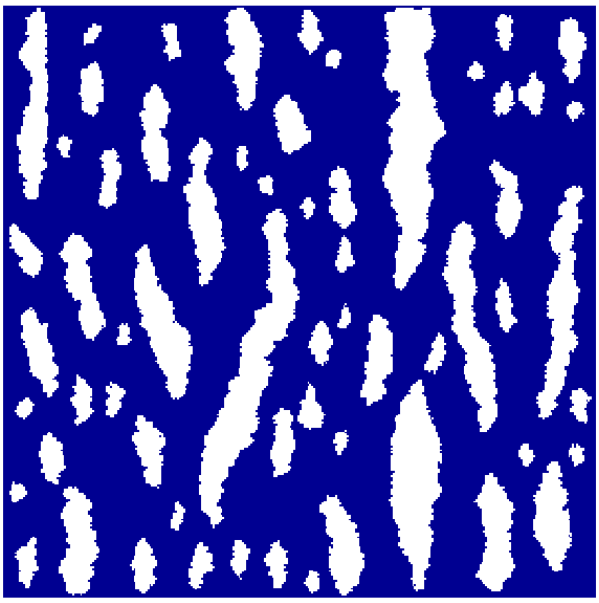
References:

[1] Merks RMH, Glazier JA. Dynamic mechanisms of blood vessel growth. Nonlinearity 2006;19:C1-C10.
[2] Califano JP, Reinhart-King CA. Exogenous and endogenous force regulation of endothelial cell behavior. J Biomech 2010;43:79-86.

cell-cell adhesion only
(cells in white, medium in blue)



mechanotaxis to external load
(stretch in vertical direction)



mechanotaxis to self-generated load
(contractile forces by cells)

'stretch highways' between
cells direct mechanotaxis