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# Characterizing Endothelial Cell Behavior and Adaptation During Brain Capillary Regeneration by Rule Oriented Modeling

Cell-cell communication defines how blood vessels regenerate through a process called angiogenesis. Growth factors like vascular endothelial growth factor (VEGF) and brain-derived growth factor (BDNF) guide angiogenic sprouting in the brain, in conditions of hypoxia, such as during a stroke or in brain cancer. Here, we present a computational strategy to characterize the sequence and magnitude of cell-cell interactions, allowing us to quantify how each endothelial cell behavior inhibits or augments each other. We introduce a novel rule-oriented agent-based programming method to allow rapid testing and comparison of multiple hypotheses in silico to in vitro angiogenic experiments. Results show the interaction of tip and stalk endothelial cells, and predict how migration, proliferation, branching, elongation and quiescence states inhibit or enhance one another to form capillary structures within an in vitro 3D matrix, leading to distinct capillary phenotypes in the presence of VEGF and BDNF. This quantitative understanding of how cells move as a function of molecular stimuli, and form vessels, will be used to help guide small molecule drugs and tissue engineering therapies targeting the brain microvasculature.