

## Angiogenesis and Blood Flow: The Role of Blood Flow in Proliferation and Migration of Endothelial Cells

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**Abstract :** Angiogenesis is formation of new blood vessels from existing vessels. Due to flow of blood in vessels, during angiogenesis, blood flow plays an important role in regulating the angiogenesis process. Multiple mathematical models of angiogenesis have been proposed to simulate the formation of the complicated network of capillaries around a tumor. In this work, a multi-scale model of angiogenesis is developed to show the effect of blood flow on capillaries and network formation. This model spans multiple temporal and spatial scales, i.e. intracellular (molecular), cellular, and extracellular (tissue) scales. In intracellular or molecular scale, the signaling cascade of endothelial cells is obtained. Two main stages in development of a vessel are considered. In the first stage, single sprouts are extended toward the tumor. In this stage, the main regulator of endothelial cells behavior is the signals from extracellular matrix. After anastomosis and formation of closed loops, blood flow starts in the capillaries. In this stage, blood flow induced signals regulate endothelial cells behaviors. In cellular scale, growth and migration of endothelial cells is modeled with a discrete lattice Monte Carlo method called cellular Potts model (CPM). In extracellular (tissue) scale, diffusion of tumor angiogenic factors in the extracellular matrix, formation of closed loops (anastomosis), and shear stress induced by blood flow is considered. The model is able to simulate the formation of a closed loop and its extension. The results are validated against experimental data. The results show that, without blood flow, the capillaries are not able to maintain their integrity.

**Keywords :** angiogenesis, endothelial cells, multi-scale model, cellular Potts model, signaling cascade

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