Angiogenic Factors produced by Hypoxic Cells drive Anastomosis in Sprouting Angiogenesis

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Cancer is among the leading causes of death worldwide. Sprouting angiogenesis, the process by which new blood vessels grow from existing ones, is crucial in the growth of solid tumors, and it is also present in over seventy different pathologies [1]. In response to a chemotactic stimulus (Vascular Endothelial Growth Factor), endothelial cells of the vessel sprout can adopt either a migratory or a proliferating phenotype [2]. In this work we use a multi-scale phase field model of vessel growth [3] in 2D and in 3D coupled with blood flow hydrodynamics. We use this model to discuss the role of irrigation, endothelial cells' chemotactic response and proliferation rate as key factors in determining the morphology of vascular networks. The computation of blood flow was introduced into the model as the main quantitative element in the hypoxia regulation mechanism, allowing to determine the deactivation of VEGF production by the tissue cells as a function of tissue irrigation. Preliminary results show a significant influence in the morphology of 2D vascular networks for the case where the blood flow is taken into account in hypoxia regulation. Surprisingly in the 3D model we did not observe such influence, obtaining similar morphologies with both approaches, with and without computing the tissue irrigation. This result is unexpected and raises questions about the role of mechanical forces exerted by cells on the formation of anastomosis in 3D. Overall, these results indicate that blood flow has an important role in angiogenesis, but the active work of cells such as macrophages could be determinant in the morphology of the new capillary network.

FIGURE 1. Vessel network resulting from sprouting angiogenesis.

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