Mechanics of Sprouting Angiogenesis in Tumors

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ABSTRACT

The formation of a functional blood vessel network is essential for drug delivery in tumors. Sprouting angiogenesis, where new blood vessels grow from pre-existing ones, is a complex process where biochemical and mechanical signals regulate endothelial cell proliferation and movement. In this work, we introduce the first phase-field model of sprouting angiogenesis capable of predicting sprout morphology as a function of the elastic properties of the tissues and the traction forces exerted by the cells. The model is compact, only consisting of three coupled partial differential equations, and has the clear advantage of a reduced number of parameters. This model allows us to describe sprout growth as a function of the cell-cell adhesion forces and the traction force exerted by the sprout tip cell. In the absence of proliferation, we observe that the sprout either achieves a maximum length or, when the traction and adhesion are very large, it breaks. We explore how different types of endothelial cell proliferation regulation are able to determine the shape of the growing sprout. The largest region in parameter space with well formed long and straight sprouts is obtained always when the proliferation is triggered by endothelial cell strain and its rate grows with angiogenic factor concentration. We conclude that in this scenario the tip cell has the role of creating a tension in the cells that follow its lead. On those first stalk cells, this tension produces strain and/or empty spaces, inevitably triggering cell proliferation. The new cells occupy the space behind the tip, the tension decreases, and the process restarts.