Stochastic modeling of blood vessel growth

Luis L. Bonilla[1], Manuel Carretero[1], Filippo Terragni[1], Rui Travasso[2], Rocío Vega[1]

Affiliations: [1]Universidad Carlos III de Madrid, Department of Materials Science and Engineering and G. Millan Institute for Fluid Dynamics, Nanoscience and Industrial Mathematics; Avenida de la Universidad 30, 28911 Leganés, Spain. [2]CFisUC, Department of Physics, University of Coimbra, R. Larga, 3004-516 Coimbra, Portugal.

ABSTRACT

Angiogenesis is the multiscale process of blood vessel formation and growth that brings oxygen and nutrients to hypoxic cells in tissues. While angiogenesis is fundamental in healthy organ growth and repair, its imbalance is behind many diseases, including cancer or forms of age-related macular degeneration. We describe two-dimensional multi-scale stochastic models of early-stage angiogenesis. The first and simpler model [1] represents cells at the tips of new blood vessels as active particles whose trajectories are the blood vessels themselves. Vessel tips are subject to chemotaxis and haptotaxis forces in Langevin equations and branch stochastically producing new tips. When one active tip meets a preexisting vessel (trajectory of another tip) joins it and ceases to be active, a process called anastomosis. The same occurs when it arrives at the hypoxic region. Thus, anastomosis is a killing point process that depends on the past history of the given realization. We have derived a deterministic equation for the density of active vessel tips containing source terms with memory characterizing anastomosis and branching. For simple geometries, the density of active tips evolves to a soliton-like wave whose shape and velocity follow simple differential equations [2]. Numerical simulations of the stochastic process confirm our findings, which could be helpful for angiogenesis control. The second model is a cellular Potts model in which pixels may belong to cells, or to the extracellular matrix. Tip cells move by chemotaxis, haptotaxis and durotaxis, following chemical, adhesion and stiffness gradients. The concentration of vessel endothelial growth factor satisfies a reaction-diffusion equation and the deformation of the substrate due to interaction with the cells is described by linear elasticity. Stalk cells proliferate and build the sprouting vessels. Notch signaling dynamics coupled to mechanics and chemistry determine the character of cells and branching of new sprouts from existing vessels. This more detailed model illustrates the role of mechanical, chemical and biological cues in the early stages of angiogenesis, before blood circulation reshapes the network of blood vessels [3].

[1] F. Terragni, M. Carretero, V. Capasso, L. L. Bonilla, Stochastic Model of Tumor-induced Angiogenesis: Ensemble Averages and Deterministic Equations, Physical Review E **93,** 022413 (2016).

[2] L.L. Bonilla, M. Carretero, and F. Terragni, Solitonlike attractor for blood vessel tip density in angiogenesis, Physical Review E **94**, 062415 (2016).

[3] R. Vega, M. Carretero, R. D. M. Travasso, L. L. Bonilla, in preparation (2018).

This is an invited talk for the AMMSA Special Session *(Code 2)* at Coupled Problems 2019