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Intracellular events regulate tissue scale phenomena in sprouting angiogenesis, A mathematical model

During sprouting angiogenesis, endothelial cells (EC) grow and migrate in extracellular matrix (ECM) to build new capillaries for delivery of oxygen and nutrients to the tumor. When sprouts start to grow from parent vessel, biochemical and biomechanical signals in the ECM regulate EC behavior; however, after anastomosis of sprouts and formation of a loop, blood flow induced shear stress is the main regulator of EC behavior. In this work, a multiscale mathematical model is developed to show endothelial cells collective behavior in a single sprout or a loop. Results show that when the loop forms, its hemostasis and elongation strongly depend on the intracellular events. Activation of different signaling cascades due to shear stress on ECs changes the cell behavior and also the behavior of ECs as a whole in the loop. This is the main reason that in the presence of blood flow, the loop keeps its integrity and elongates while in the absence of blood flow, the loop collapses.