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Modeling the Angiogenic Switch: A Multi-Scale Approach to Solid Tumor Progression

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Abstract
The transition from a localized avascular tumor to an aggressive, vascularized state is a critical yet poorly understood phase in cancer progression. While existing mathematical models often focus solely on avascular growth, they fail to capture the dynamics of this crucial "angiogenic switch," where the tumor stimulates the creation of its own blood supply. In this work, we bridge this gap by introducing a novel multi-scale mathematical model that integrates the avascular and vascular stages.

The framework couple's ordinary deferential equations for tumor cell densities (proliferating, quiescent, necrotic) with a dynamic equation for vascular endothelial growth factor (VEGF) concentration and sub- sequent blood vessel density. This allows the nutrient supply to evolve from a constant to a variable controlled by the tumor's own signaling. We perform a complete stability analysis to identify the conditions that trigger the angiogenic switch and employ global sensitivity analysis to pinpoint the model parameters with the greatest influence on tumor fate. Our results provide a mechanistic understanding of a key threshold in cancer development and establish a computational tool for identifying potential therapeutic targets aimed at suppressing the transition to vascularization.

This model ores a more holistic and clinically relevant perspective on solid tumor evolution.