Balancing Stochastic and Deterministic Behaviors in an Agent-based Model of Sprouting Angiogenesis

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In recent years, innovations in microscopy have produced techniques such as confocal microscopy and multi-photon imaging that have become mainstream for imaging dynamic processes in living tissues and ex vivo organotypic model systems. Thanks to these imaging approaches, data-rich movies that capture the behaviors of cells as they move around tissues to form multicellular structures, like blood vessel networks during angiogenesis, are now prevalent particularly in the fields of developmental biology, cancer biology, neuroimmunology, and regenerative medicine. When viewing these types of movies, it is only natural to wonder: are these cell behaviors random, or are they determined by biological cues in the local environment that the cells are sensing? With these types of movies/data becoming more abundant, the curious mind is all the more provoked to want to understand the control systems that govern dynamic cell behaviors. And if one wants to simulate these behaviors in an attempt to better understand what mechanisms control them, an obvious first question to pose is: can a model based on random chance adequately predict what I see, or are there underpinning mechanistic "rules" that direct cell behaviors, which are specific to (or irrespective of) the cells' local environments? Inherent in this question is the consideration of the spatial scale at which the experimental observations are made. At 600x magnification, cell behaviors within a tissue may appear random, like the extension and retraction of endothelial filopodia at the end of a single capillary sprout during angiogenesis, for example. At a different level of scale, 100x magnification for example, these same cell behaviors may appear more deterministic. For example, a network of blood vessels may be undergoing angiogenesis only in a localized region of a retina along the leading edge of a vascular plexus at the tissue periphery. In this sense, the spatial scale at which the biological phenomena are observed is inextricably linked to the types assumptions that one might make about the role of deterministic vs. stochastic behaviors in the system. Moreover, the types of computational modeling approaches that one would be inclined to deploy at different levels of scale (in an effort to understand fundamental biological mechanisms) might be biased toward these assumptions in ways that haven't fully been assessed. Our work aims to explore how deterministic and stochastic models deployed at different levels of spatial scale during angiogenesis can have different predictive powers and be leveraged together to yield accurate new biological understanding. This poster will present our agent-based computational models of angiogenesis and new Monte Carlo simulations of sprouting angiogenesis and describe how we have compared their abilities to offer new insights at different levels of spatial scale within the vasculature.