Do Endothelial Cells Dream of Eclectic Shape?

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Endothelial cells (ECs), which line our blood vessels, exhibit dramatic plasticity and diversity of form/behavior at the individual and collective cell level. They reorganize themselves in space and time to extend new blood vessel networks during development and during a huge array of diseases including cancer. Here we will describe, using examples from our integrated *in silico/in vitro/in vivo* research program, how the Artificial Life (ALife) perspective and approaches have been paramount in driving entirely new experimental biology understanding of the vasculature by capitalizing on the emergent, predictive capacity and testable nature of agent-based models in close combination with *in vitro* and *in vivo* experiments.

Our agent-based simulations explicitly consider the role of individual EC embodiment, active perception, heterogeneous vs homogeneous collective dynamics, pattern formation and counter-intuitive emergence from feedback in "controller" networks and many more Alife centric concepts. We recently identified *in silico* that the time it takes ECs to collectively decide who should move and who should stay during blood vessel branching morphogenesis can be varied by altering tissue environment conditions, including some changes found in tumors. By proceeding to validate these predictions *in vitro* and *in vivo* by integrating the studies in the wetlab we have been able to provide a solid new mechanism to explain the diversity of vascular network structures found across tissues and the malformations arising in disease.

There is a bright future with untapped potential for the Alife community to further contribute to understanding of animals, including humans, at the cell and tissue level, where many organizational principles of the systems behavior are still lacking. If we take care to be rigorous in how we calibrate our models to biological data and make clear experimentally testable predictions, we will show we can make real change in a experimental cell biology field, traditionally segregated from in silico research. Learning from the plight of the insightful, but ostracized, Androids in Philip K Dicks novel, overcoming our cultural differences and integrating better between the artificial and natural living systems research communities could lead to huge advantages in achieving our common goals to "understand life as it is".