Quantifying and simulating spatial organization in iPSC-derived tissues

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Engineering multicellular systems is enhanced by understanding how collective organization arises during developmental processes through mechanical, biochemical and electrical communication. Which aspects of these processes can be circumvented, accelerated or modified according to specification to yield robust, reproducible organoids? Computational models that simulate the growth, division, and differentiation of pluripotent cells into emergent structures could accelerate experimental design, yet currently lag in their ability to inform organoid culture protocols. I will discuss my lab's computational results from developing agent-based models that capture heterogeneity and stochasticity within colonies and aggregates to both i) formulate hypotheses of intercellular communication during stem cell differentiation and ii) design new organoid structures using synthetic biology components. To address the challenges of agent-based model optimization, we have pursued new methods for analyzing microscopy images and simulation results by topological data analysis. Through a tight iteration between computation and experimentation, we have established a critical role of intercellular transport, adhesion, and cell cycle asynchrony in the propagation of dynamic patterning in engineered iPSC systems.