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Combined Experimental And Agent-Based Modeling Approach For Studying Tissue Patterning Processes

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To date, the main focus of Systems Biology has been on developing computational simulations of biological phenomena within single cells, and these approaches have generated new understanding of how intracellular systems function that was not achievable using experimental approaches alone. However, equally important in biological processes, and especially central to how biological tissues grow and adapt in response to physiological and pathological stimuli, are the multi-cell interactions—cells interacting with other cells and responding to their dynamic and heterogeneous tissue environment. Therefore, it is necessary to develop and employ new computational tools that effectively span spatial and temporal scales and encompass multi-cell, tissue level phenomena. Agent-based modeling (ABM), a technique that has been used widely in ecology and the social sciences, is used to study spatially- and temporally-dynamic multi-cell tissue patterning events during physiological and pathological adaptations. We pair simulations with experiments to generate new understanding of how these complex systems are regulated and to probe new targets for protein- and cell-based therapies. We have developed an array of models to investigate microvascular tissue adaptations (e.g. angiogenesis and arteriogenesis) in the face of ischemia, which underpin such complex diseases as diabetes, cancer, and heart disease. We have also applied this combined approach to study morphogenetic tissue patterning processes in the Xenopus embryo, such as epithelial and mesendoderm migration in the blastocoel roof.