"Delineating Mechanisms of BMP-mediated Patterning and Organization During Development Through Integrative Experiment and Simulation"

Virtual Seminar
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Abstract

The emergence of coordinated cellular, tissue, and organismal responses rely on complex biological networks. While the connectivity of the networks is increasingly defined, understanding the dynamics of the system and the emergence of coordinated responses at multiple spatial and temporal scales is an unsolved problem in many systems. This is a challenge addressed by all living systems that utilize highly conserved chemical reaction networks that coordinate single cell behavior into tissues and into organisms. To study the coordination, we rely on the back and forth between simulation and experiments. Specifically, we developed and applied integrative simulations reaction-advection-diffusion partial differential equation models to discern the mechanism of Bone Morphogenetic Protein (BMP) signaling along the dorsal/ventral (DV) axis in zebrafish embryos, and in the mouse developing organ or Corti. In each of these systems, gradients of BMP signaling form through the interplay of BMP ligands interacting with other secreted factors that shape the gradient. We developed methods to quantify inputs and outputs of BMP signaling activity, developed AI tools to segment every cell in a developing embryo, and used the data to build and test mathematical models of different biological hypotheses of gradient formation and differentiation. In zebrafish embryonic development, we found that a source-sink mechanism is most consistent with formation of the ventral-to-dorsal gradient of BMP signaling; and in the developing organ of Corti in mouse, we found that the BMP gradient forms an information-maximizing linear profile sufficient for multiple boundary specification along the developing organ. These systems highlight how the back and forth between experiment and simulation drives an integrative understanding of developmental systems.

Bio

David M. Umulis is a Professor and Associate Head for Research in the Weldon School of Biomedical Engineering and Professor of Biological Engineering in the Department of Agricultural and Biological Engineering at Purdue University. Dr. Umulis obtained his Ph.D. in Chemical Engineering at the University of Minnesota in 2007, and a BSE in Chemical Engineering at the University of Michigan, 2002. Dr. Umulis' group couples quantitative imaging, developmental biology, mathematical modeling, and large-scale computation to identify mechanisms of cellular regulation by Bone Morphogenetic Proteins and other cytokines during embryonic development and in cancer. A pillar of the Umulis lab is the integration of data in the design and optimization of mathematical models. Their work merging optimization metrics from the social sciences with quantitative optimization methods in engineering has provided a dramatic increase in the ability to use biological data to predict outcomes in embryonic development and cancer. Dr. Umulis' research has been published in leading journals, including eLife, Development, Developmental Cell, Cell, PNAS, and the NIH and NSF currently fund his work. He was the 2012 recipient of the Richard L. Kohls Early Career Award through the College of Agriculture at Purdue University.

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