Keynote Abstract

Building Models of Cell Organization Directly from Microscope Images: New Tools for Comparison and Simulation of Cell Behavior

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Abstract

Given the complexity of biological systems, machine learning methods are critically needed for building systems models of cell and tissue behavior and for studying their perturbations. Such models require accurate information about the subcellular distributions of proteins, RNAs and other macromolecules in order to be able to capture and simulate their spatiotemporal dynamics. Microscope images provide the best source of this information, and we have developed tools to build *generative* models of cell organization directly from such images. Generative models are capable of producing new instances of a pattern that are expected to be drawn from the same underlying distribution as those it was trained with. Our open source system, CellOrganizer (http://CellOrganizer.org), currently contains components that can build probabilistic generative models of cell, nuclear and organelle shape, organelle position, and microtubule distribution. Our current work is focused on methods for learning the dependency of organelle patterns upon each other, so that high dimensional models of many components can be created. All of the generative models created by our system capture heterogeneity within cell populations, and their parameters can be used as a highly interpretable basis for analyzing perturbations (e.g., induced by drug addition). Further, generative models of cell organization can be used as a basis for cell simulations to identify mechanisms underlying cell behavior. To this end, we have developed an automated pipeline for carrying out simulations of cellular biochemistry within different cell geometries without the need for manual processing of images or drawing of hypothetical compartments. We have used this approach to show that kinetics of cell signaling can be affected by cell shape and organelle distribution.

Bio

Robert F. Murphy is the Ray and Stephanie Lane Professor of Computational Biology and Director (Department Head) of the Ray and Stephanie Lane Center for Computational Biology in the School of Computer Science at Carnegie Mellon University. He also is Professor of Biological Sciences, Biomedical Engineering, and Machine Learning, and was a founding director (with Ivet Bahar) of the Joint Carnegie Mellon University-University of Pittsburgh Ph.D. Program in Computational Biology. He is also Honorary Professor of Biology at the Albert Ludwig University of Freiburg, Germany, and a Fellow of the American Institute for Medical and Biological Engineering. He has served as President of the International Society for Advancement of Cytometry and as a member of the National Advisory General Medical Sciences Council, and the NIH Council of Councils. Dr. Murphy's career has centered on combining fluorescence-based cell measurement methods with quantitative and computational methods. His group at

Carnegie Mellon has pioneered a number of machine learning methods for analyzing and modeling various aspects of cell organization. He is a Founder of Quantitative Medicine LLC, a startup biomedical analytics and computational biology company offering a novel drug discovery platform that dramatically reduces the time, cost and risk of discovering new therapeutic drugs.