

CellOrganizer@MMBioS: Image-derived models of cell structure and organization

Robert F. Murphy

National Center for Multiscale Modeling of Biological Systems  
and Computational Biology Department, Carnegie Mellon University

Developing and improving technologies for creating accurate and predictive cell simulations is a major focus within MMBioS. These technologies include BioNetGen, for creating rule-based models of complex biochemical reaction pathways, CellOrganizer, for creating statistically-accurate cell geometries, CellBlender, for creating complete specifications for cell simulations, and MCell, for performing particle-based simulations. Most previous cell simulation studies used either compartmental models without a spatially-realistic geometry or used a geometry constructed by hand from single images. Such geometries are difficult to generate and do not capture cell-to-cell variation. CellOrganizer learns *generative* models of cell organization directly from microscope images of many cells. These models capture general aspects such as cell and nuclear size and shape, and highly-specific aspects such as the relationships between the positions of organelles and microtubules. We have established collaborations with a number of laboratories collecting large image collections, and used our tools to (1) demonstrate a relationship between cell and nuclear shape and identified proteins and drugs involved in this relationship, (2) identify spatiotemporal dynamics of signaling molecules during T cell costimulation, (3) construct continuous models of differentiation from static images, and (4) demonstrate heterogeneity in signal transduction kinetics due to variation in cell organization. Potential areas of collaboration with other P41 centers include creation of generative models combining electron and light microscopy, development of new standards for exchanging heterogeneous geometries for simulations, and use of our tools for characterizing cell shape and organization in other projects.