(3) The CellOrganizer Project: An Open Source System to Learn Image-derived Models of Subcellular Organization over Time and Space

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Abstract

The CellOrganizer project (http://cellorganizer.org) provides open source tools for learning generative models of cell organization directly from images and for synthesizing cell images (or other representations) from one or more of those models. Model learning captures variation among cells in a collection of images. Images used for model learning and instances synthesized from models can be two- or three-dimensional static images or movies. Current components of CellOrganizer can learn models of cell shape, nuclear shape, chromatin texture, vesicular organelle number, size, shape and position, and microtubule distribution. These models can be conditional upon each other: for example, for a given synthesized cell instance, organelle position will be dependent upon the cell and nuclear shape of that instance. The models can be parametric, in which a choice is made about an explicit form to represent a particular structure, or non-parametric, in which distributions are learned empirically. One of the main uses of the system is in support of cell simulations: models learned from separate experiments can be combined into one or more synthetic cell instances that are output in a form compatible with cell simulation engines such as MCell, Virtual Cell and Smoldyn. Another important application of the system is in comparison of target patterns and perturbagen effects in high content screening and analysis. This is currently done using numerical features, but these are difficult to compare across different microscope systems or cell types since features can be affected by changes in more than one aspect of cell organization. More robust comparisons can be made using generative model parameters, since these can distinguish effects on cell size or shape from effects on organelle pattern. Ultimately, it is anticipated that collaborative efforts by many groups will enable creation of image-derived generative models that permit accurate modeling of cell behaviors, and that can be used to drive experimentation to improve them through active learning.

Biography

Robert F. Murphy is the Ray and Stephanie Lane Professor of Computational Biology and Professor of Biological Sciences, Biomedical Engineering, and Machine Learning at Carnegie Mellon University, and Director (Department Head) of the Lane Center for Computational Biology in the School of Computer Science. He is also Honorary Professor of Biology at the Albert Ludwig University of Freiburg, Germany, a Fellow of the American Institute for Medical and Biological Engineering, and the recipient of an Alexander von Humboldt Foundation Senior Research Award. He is Past-President of the International Society for Advancement of Cytometry, and is a member of the National Advisory General Medical Sciences Council and the NIH Council of Councils. He has published over 190 research papers in the areas of cell and computational biology.

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Dr. Murphy's career has centered on combining fluorescence-based cell measurement methods with quantitative and computational methods. In the mid 1990's, his group pioneered the application of machine learning methods to high-resolution fluorescence microscope images depicting subcellular location patterns. His current research interests include image-derived models of cell organization and active machine learning approaches to experimental biology.