Mathematical Methods and Algorithms for Identification, Tracking, and Quantitative Analysis in Cellular Bioimaging

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Automated cell segmentation and tracking enables the quantification of static and dynamic cell characteristics and is very important for biomedical research. I present my work on development of a fully automated system for cell segmentation and tracking. In the cell segmentation part, we propose a PDE-based formulation of spatio-temporal motion diffusion to detect temporal cell discontinuities in the joint spatio-temporal domain. We introduce an intensity standardization technique to address intensity variability complicating frame-to-frame analysis in differential techniques using statistical learning. To refine cell delineation accuracy, we propose to use an energy minimization technique based on an implicit active contour that assumes a piece-wise constant image region model and temporal linking of the region-based level sets for faster convergence and to resolve non-convexity that is typical in image analysis inverse problems. In the cell tracking part of this work we apply a variational method for joint local-global optical flow to estimate cell motion. For cell matching, we propose to use the predicted cell motion in a probabilistic Maximum Likelihood decision strategy assuming Markov dependency. We formulate cell tracking as a partitioning problem in the domain of cell tracks with temporal constraints. To perform track linking and to identify the cell states in the time-lapse sequence we find a solution that minimizes a global cost function defined over the set of all cell tracks by a heuristic approach. We represent cell tracks by an acyclic oriented graph that we use to visualize the cell lineage trees and cell trajectories. Finally, we compute morphological, motility, diffusivity, and velocity cell measures. We validated the cell segmentation and tracking stages both individually and as a joint system against reference standards over 12 time-lapse image sequences obtained from a publicly available database.