SEGMENTATION AND TRACKING ALGORITHMS FOR MONITORING CELLULAR MOTION AND FUNCTION

By

Dirk Ryan Padfield

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Examining Committee:

Prof. Badrinath Roysam, Thesis Adviser

Prof. Charles Stewart, Member

Prof. George Nagy, Member

Prof. Peter Kramer, Member

Dr. Igor Roninson, Member

Dr. Jens Rittscher, Member

Rensselaer Polytechnic Institute
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ABSTRACT

Automated cell phase analysis of live cells over extended time periods requires both novel assays and automated image analysis algorithms. Among other applications, this is necessary for studying the effect of inhibitor compounds that block the replication of cancerous cells in any of the four phases of the cell cycle: G1, S, G2, and M. More generally, a growing number of screening applications require the automated monitoring of cell populations in a high-throughput, high-content environment. These applications depend on accurate segmentation and tracking of individual cells in images with low contrast-to-noise and occasional microscope defocusing and stage shift.

In the first part of this work, we introduce a set of image analysis tools for measuring time-lapse datasets of a novel non-toxic cell cycle phase marker that distinguishes the four phases of the cell cycle. We approach the tracking problem as a spatio-temporal volume segmentation task, where the 2D slices are stacked into a volume.Our main contribution in this approach is the design of a speed function connected with a fast marching path planning approach for tracking cells across the phases based on the appearance change of the nuclei. We also designed a model-based shape/size constraint to control the evolution of level sets for segmentation. We demonstrate the ability of these algorithms to measure the effect of cell cycle inhibitors.

In the second part of this work, we present a generalized framework for cell segmentation, tracking, and analysis. We introduce an algorithm that we call "coupled minimum-cost flow" that solves the global matching problem using explicit models of cell behaviors such as mitosis, occlusion, rapid movement, and moving in and out of the field-of-view. For the denoising and segmentation step, we introduce a wavelet-based approach that is able to accurately segment cells even in images with very low contrast-to-noise. In addition, the framework is able to measure and correct for the microscope defocusing and stage shift. Taken as a whole, this framework enables quantitative and accurate analysis of cell events and provides a valuable tool for high-throughout, high-content biological studies.