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An accurate multi-cell parameter estimate algorithm with heuristically restrictive ant system

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ABSTRACT

To reliably analyze multi-cell motion in a series of low-contrast image sequences, we present a novel heuristically restrictive ant system, which operates in a non-optimization way, to adaptively estimate multiple parameters of multiple cells. First, the local intensity variation measure on each pixel of image is defined to generate ant colony initial distribution positions, which are further treated as boundary markers to restrict ant searching behavior. Afterwards, to speed up the ant searching process, both location and contour ant decision behaviors are modeled appropriately to acquire cell position and edge estimates on their individual pheromone fields, which are formed by restrictive pheromone deposits but operate independently and in parallel. Finally, the stability of our proposed pheromone control mechanism is proven to guarantee reliable multi-parameter extraction. Experiment results show that our algorithm could automatically and accurately track numerous cells in various scenarios, and it shows considerable robustness against other popular tracking methods.

1. Introduction

Motion analysis of cancer cells' cycle progression is crucial in understanding drug effects on cancer cells. The quantitative analysis of cancer cell behaviors, such as the moving velocity and the density of cell population, is used to characterize disease development process. Fortunately, recent development of time-lapse microscopy provides a direct tool to observe and measure the cell-cycle progression of individual cells in a large population. However, cellular motion analysis poses many challenges to those existing techniques due to poor image quality (low contrast and high noise levels), irregular cell migration, the varying density of cell populations, and changes of cellular morphology. Large volumes of image data make manual analysis time consuming and tedious. Sometimes, it becomes impossible for an expert to accurately follow many different events over a long sequence, especially when it requires tracking a large number of cells during long period of time in order to obtain robust results. Therefore, automatic techniques to analyze cell-cycle progression have become a major research direction for easily understanding the full potential of time-lapse microscopy in biological research or drug discovery.

Up to now, there exist three categories of automated or half-automated cell tracking techniques, i.e., deterministic detect-before-track method, model evolution method, and probabilistic method. The deterministic detect-before-track approach usually treats the tracking problem as frame-by-frame detection followed by correspondence (linking) between consecutive frames, and it could produce good results for high image quality and low cell density [1–3]. The obvious advantage of such approach is computational efficiency with respect to detection, but it encounters problems during the temporal data association stage especially in high cell density. The model evolution

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approach, also termed as integrated detection and tracking method, handles the detection and tracking simultaneously, such as active contours, mean-shift, and level set [4–7]. From the perspective of computation cost, model evolution approach is expensive and time-consuming. The probabilistic approach based on particle filtering (PF) [8–12] has been shown to yield superior robustness and accuracy even though each cell exhibits strong nonlinear dynamics in poor original or detection image data. With the combination of spatiotemporal information and appropriate posterior proposal density function assumption, it is expected that the probabilistic method with PF could accomplish all cell tracking tasks. Recently, various random finite sets (RFS) based probabilistic approaches are proposed in a multi-object Bayesian framework to recursively estimate multi-object state in an analytic form [13–19]. Specifically, among these approaches, the "track-before-detect" techniques could by-pass the detection module and exploit the spatiotemporal information directly from poor image sequences, and finally lead to favorable performance in various occasions [15,17,19] including cell tracking [19].

Among the gamut of technologies aiming at multi-cell tracking, advantages of self-organizing and cooperative ant system are expected to offer an adaptive and accurate way to capture individual cell parameter at each frame. In this paper, we present a novel heuristically restrictive ant system from the perspective of non-optimization to estimate multiple cell parameters, such as cell location and contour. The local region intensity variation measure with respect to each pixel of image is utilized to generate ant colony initial positions distribution, which are further treated as potential boundary markers to confine ant searching range. During the construction process of state pheromone field, to accurately capture the center of each cell, we employ the gradient of pheromone and model ant's sensory capacity to sense pheromone decreases at high concentrations. Meanwhile, in the contour-oriented pheromone field, the ant orientation change is added into decision model with the purpose of improving the quality of ant tour. Finally, we give the stability proof of our proposed pheromone control mechanism, which could guarantee the reliable cell parameter extraction.

This paper is organized as follows. We first present an overview of related efforts on cell tracking in Section 2. Then, the generic ant colony system is introduced in Section 3. Next, our method with heuristically restrictive ant system is described in Section 4. In Section 5, the experiment results on real cell data and discussions are detailed. Finally, the conclusions are summarized in Section 6.

2. Related efforts

The interest in cell tracking has been attracting many researchers over the last decades, and significant progress has been made as indicated in the survey literature [20]. In this section, we will focus on recently developed tracking methods and its potential to be used in this area.

The deterministic detect-before-track method consists of separated two steps, i.e., detecting all cells in a whole image sequence and establishing linking between detected cells frame-by-frame based on distance, shape and other criteria. A colliding cell tracking algorithm is proposed by Nguyen et al. [1], in which a supervised learning approach is first trained to classify each pixel as a cell or background in image segmentation, and then the Kalman filter incorporated with colliding hypothesis is employed for tracking the detected cells. Chen et al. [2] propose an integration detection method, which consists of Ostu, watershed and KNN classifier, to obtain accurate segmentation of cell nuclei, and a matching process is performed through an association matrix to set up the frame-by-frame correspondence between nuclei. Yang et al. [3] propose a mathematical morphology based marker-controlled watershed and context information among neighboring frames to segment under-segmented cells or to merge over-segmented cells, then a tracking method, a combination of mean-shift and Kalman filter, is designed to achieve a more robust cell nuclei tracking. The main characteristic of the above approaches is its computational efficiency with respect to segmentation, but it often encounters data association problem, which is NP-hard one for a large number of cells.

The model evolution method parameterizes and optimizes the shape of the cells so as to fit the cells to the targeted objects, therefore each object being tracked preserves its identity. Active contours [7], level set [5,6], and mean shift [4] are categorized in such method. Ray et al. [7] propose an active contour approach with shape and size constraints by energy functional. Mukherjee et al. [6] propose a level set analysis that can automatically identify and track multiple cells by exploiting the shape and intensity characteristics of the cells. Debeir et al. [4] introduce an adaptive combination of several kernels to establish migrating cell trajectories. It can be observed that active contours can capture object boundary, but it requires cells to be partially overlapping in adjacent frames; level set is able to tackle object topology changes, but it will merge two contacting contours into a single one and it also requires cells to be partially overlapping in different frames; mean shift algorithms give a fast solution for object tracking in video sequences, but usually do not give object contours. They have a common characteristic that the model parameters obtained from the former frame are used to initiate the process of the current frame.

The probabilistic method could overcome the drawbacks of the above two approaches by improved interaction between cell detection and correspondence, and it combines spatiotemporal information and appropriate posterior proposal density function assumption to estimate cell dynamic parameters. Cui et al. [8] propose a robust Monte Carlo tracker for automatically tracking a single rolling leukocyte in vivo even if rolling leukocyte is in contact with the vessel wall. Smal et al. [11] first propose a fully automated PF-based method, built within a Bayesian probabilistic framework, for robust and accurate tracking of multiple cells. Another work of Smal et al. [9] focuses on a variable-rate particle filtering method based on a transformation of the 2-D image sequences into kymographs, and such method results in more accurate extraction of the spatiotemporal structures. Juang et al. [18] first use the Gaussian mixture PHD filter to track cells. On the basis of this, Hoseinnezhad et al. [19] propose a novel Bayesian method, called multi-Bernoulli filtering, to