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Tracking of multiple cells with ant pheromone field evolution

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ABSTRACT

Tracking of biological cells is necessary to improve the understanding of their growth and behavior. Most methods used in cell tracking are time consuming and inaccurate for large population density or closely interacting cells. In this paper, a fast and accurate ant-inspired estimating algorithm for tracking multiple cells is proposed that uses a dual prediction mechanism and a pheromone updating strategy. The dual prediction mechanism is novel and uses ant individual state prediction for a given colony as well as the corresponding pheromone field prediction from the previous frame to the current frame. Ant state prediction aims to guide ant clustering around cells of interest, while pheromone field prediction helps to accelerate the pheromone formation of the current frame using the Gaussian mixture model (GMM) approximation technique. To handle the problem of tracking closely interacting cells, we design a novel ant decision-making model based on the pheromone gradient information and heuristic function with two forms. The pheromone updating strategy is also a novel pheromone diffusion and deposit model to obtain the expected pheromone field for extracting cell states in collision and cohesion. We provide quantitative validation of the method using two challenging datasets characterized by cohesion and collision by comparing them with the results from recently reported approaches.

1. Introduction

Studying the behavior of cells plays an essential role in understanding biological processes, such as abnormality identification and classification, immune response, embryonic development, and early cancer detection. Cellular image sequences usually contain large numbers of objects which may be densely packed. In addition, the behavior of cells may be diverse, including division, varying size and shape, random movement, leaving/entering the field of view (FOV) and death. Taken together, the estimation of the state of cells becomes a very difficult task. Although a number of segmentation and tracking methods have been reported in the literature, most methods used to analyze motion of cells are time consuming, error prone and for a specific cell dataset. Manual cell tracking is a tedious process that requires a lot of skill and training. An effective and accurate automated tracking method for eliminating the bias is desirable.

Current literature on cell tracking can be organized into three general methodologies (Ray et al., 2002; Fuhai et al., 2010; Huh et al., 2012; Liu et al., 2011). The first type of approach is detection based on tracking methods. In this category, cells in each frame are segmented first. Then the features, such as cell centroid, intensity and area are detected. Finally, cells between consecutive frames are associated by a given assignment strategy. The second type of approach is the module evolution method. Different from the detection based tracking method, the module evolution method handles cell segmentation and tracking simultaneously, and mean-shift (Debeir et al., 2005; Haynor, 2010), active contours (Huo et al., 2017; Zhou et al., 2016), and level set (Mukherjee et al., 2004; Maska et al., 2013; Nanthakumar et al., 2017; Ghasemi et al., 2017; Nanthakumar et al., 2016) belong to this category. These methods work well in the case of smooth cell motion and clear cell contour, but are not effective for fast moving cells. The third type of approach is the stochastic filtering method (Hoseinnezhad et al., 2012; Smal et al., 2008; Ramesh and Tasdizen, 2014; Smal et al., 2012). The stochastic filtering method optimally performs cell segmentation and association in a Bayesian framework, which exploits the spatiotemporal information directly from the image sequence. One benefit of using such a method is that it is more robust to low resolution and low signal-to-noise (SNR) scenarios than other tracking methods.

Ant colony optimization (ACO), originally proposed by Dorigo (Dorigo et al., 1996; Dorigo and Gambardella, 1997), is a nature inspired algorithm for solving continuous or discrete optimization problems. One major advantage of this approach is that a simple communicating agent of the system is capable of solving complex problems, and it has proven to be a powerful tool in the traveling salesman problem

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(TSP) (Ur and Aydin, 2009; Zhou, 2009; Liu and Wang, 2007), vehicle routing (Khouadjia et al., 2013), clustering (Ji et al., 2013) and image processing (Kuo, 2016; Yin et al., 2016). Intuitively, the advantages of a self-organizing and cooperative ant system could provide an accurate way of capturing individual objects for state estimation, and some initial attempts have been made in Lu et al. (2017, 2014). However, in contrast to (Xu et al., 2014; Xu and Lu, 2014), the tracking performance could be further improved by a well-defined pheromone updating and propagation strategy to aid ant colony decision to move towards potential regions.

In this paper, we aim to develop a fast and accurate ant estimating algorithm for tracking multiple cells in the presence of cell collision or cell adjacency. Firstly, to guide ant colony movement towards cells of interest, ant colony state prediction is conducted to generate the initial distribution of the ant colony in the current frame. Secondly, to speed up the pheromone formation in the current frame, pheromone field prediction is also performed using the Gaussian mixture models (GMM) approximation technique. Thirdly, both the ant decision-making mode using pheromone gradient information and the deposit model using the pheromone divergence are developed for extracting effectively cell states on collision or cell adjacency. These three approaches are novel additions to the ACO method. Finally, the experimental results of our method are compared with recently reported approaches.

The rest of this paper is organized as follows. In Section 2, we review related work on cell tracking. In Section 3, we briefly describe the basic ACO algorithm. In Section 4, we present our method in detail. In Section 5, we show the experimental results with performance comparisons and some remarks. Finally, a summary and directions for future work are provided in Section 6.

2. Related work

The main challenges of cell tracking fall under the categories of cell interaction with one another, cell collision or cell adjacency. To overcome these difficulties, some attempts have been described in the literature.

Balomenos et al. (2015) proposed a method based on the dynamic neighborhood formation and matching approach to solve effectively the tracking problem in overcrowded bacterial colonies, in which the lineage tree is required to identify and correct segmentation errors. Dufour et al. (2005) presented an automated method based on the active contours algorithm to track cells when they merge together then separate. The main advantages of their method are robustness in low signal noise ratios and ability to track multiple cells in cases where cells interact with one another. However, since these methods still rely on the existence of an image background, they cannot be adapted to cluster cells in tissues. Massoudi et al. (2012) proposed an automatic cell tracking algorithm. Tracking with a network flow algorithm is used for detecting cell mitosis, entering or exiting. It does not rely on a perfect segmentation module. The algorithm can track cells that enter or leave the FOV and can also handle cell division. However, when occlusion happens at a node in the graph, the algorithm cannot distinguish between occluded cells. Nguyen et al. (2011) proposed a method to automatically track multiple collisions of cells by modeling the appearance and motion for each collision state and testing collision hypotheses of possible transitions between states. First, a supervised learning approach is used for cell detecting. Then, the track segment is linked to the observation using a greedy method. Finally, cell states are updated using the Kalman filter. Harvey et al. (2011) proposed a dynamic cell curvature analysis algorithm using a cell-based three-dimensional computational model to track cells that change their shape during collisions. However, when tracking cell collisions in high density conditions, these methods are not adequate. Zhang et al. (2015) proposed a novel system for adhesive cell detection and tracking by processing a sequence of images with non-rigid objects changing position and shape. The system first detects and localizes cells, followed by a feature extraction step in the image sequence. Then, an improved mean shift algorithm is used for inactive cells and dynamic local prediction (DLP) and gray prediction (GP) algorithms are used for active cells. Unfortunately, this method requires very good detection in almost all frames because low performance in cell detection may heavily affect the tracking results. Zou and Tomasi (2016) presented a novel algorithm based on a deformable graph for tracking cells that are connected through a visible network of membrane junctions. This method may be a major tool especially in developmental organisms by helping to characterize these general biological features from the tissue to the sub-cellular level. However, the method is inefficient and requires a variety of graph topology changes to handle biological events such as cell divisions. Magnusson et al. (2015) developed a global track linking algorithm to handle mitosis, apoptosis, migration in and out of the imaged area, and can also deal with missed detections and clusters of jointly segmented cells.

Although the aforementioned algorithms have been verified in many cells tracking applications, there is a strong need for a higher efficiency algorithm. This is because these methods are mostly applied to a specific practical cell dataset and also suffer from their relatively high computational complexity. The objective of this paper is to develop a technique for an effective and accurate cell tracking algorithm to solve the cell collision or cell adjacency tracking problems.

3. Basic ACO

ACO algorithms are based on the behavior of an ant colony foraging by the shortest path. Initially, each ant randomly selects a path to reach the food source. When ants find a food source, they will deposit pheromone on the trail. The deposited pheromones evaporate with time and their concentration decreases with the trail length. The amount of the pheromone indicates the degree of attraction of other ants to the food source. This indirect cooperation among ants enables them to find the shortest path between their nest and the food source.

In the ant colony optimization algorithm for cell state extraction, discovery of the cells is looked upon as an ant colony foraging problem. A directed graph, denoted by G, is constructed to generate the solution space and the heuristic information for cell state extraction. Each node in G corresponds to a pixel in the cell image. Suppose that ant a (located at pixel i) decides the next pixel j to visit, according to the transition probability

$$p_{i,j}^{a} = \begin{cases} \dfrac{[\tau_{ij}]^{\alpha}[\eta_{ij}]^{\beta}}{\sum_{a \in \Psi_a}[\tau_{ia}]^{\alpha}[\eta_{ia}]^{\beta}}, & if\ j \in \Psi_a \\ 0, & otherwise \end{cases} \tag{1}$$

where $\tau_{i,j}$ represents pheromone on edge (i, j), Ψ_a denotes the set of unvisited cities of ant a. $\eta_{i,j} = \frac{1}{d_{i,j}}$ is heuristic function, where $d_{i,j}$ is the Euclidean distance between pixel i and j. α and β control the relative importance of pheromone $\tau_{i,j}$ and the heuristic function $\eta_{i,j}$.

If all ants have completed moving, the pheromone level update according to

$$\tau_{ij} \leftarrow \xi\tau_{ij} + \Delta\tau_{ij} \tag{2}$$

where $\xi(0 < \xi < 1)$ is the pheromone persistence coefficient, the term $\Delta\tau_{i,j}$ is the pheromone amount that ant deposit on the edge (i, j).

The algorithm stops when the iterations number increases to the maximum number.

4. Method

In this section, we will discuss our algorithm in detail. Based on the framework of the basic ACO, the proposed algorithm is designed with several attractive features for enhancing the accuracy and efficiency. These new features include ant colony state prediction, pheromone