# Commentary: Tracking Biological Cells in Time-Lapse Microscopy

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## Introduction

In recent years, the automation of cell tracking has become an essential method for describing biological processes and diagnosing diseases. At the same time, in the area of human analysis, it can also improve the efficiency when a large number of cells need to be processed and tracked to obtain valid data. Although automated tracking is a popular technique and have a big effect on recent research, there are still many challenges which have to be faced and addressed. This paper aims to solve some challenges in the automation of cell tracking. There are three types of problems that author hopes to solve. The first type of problem is some problems caused by the image acquisition techniques and labelling which will lead to the images with low quality and low signal to noise ratio. The second one is the topological challenges, various events will change the cell topology over time, which will increase the complexity of detection. The last type of problems is caused by the uneven motion of the cells. These three different types of problems can affect and interfere with cell detection and tracking to some extent, thus affecting accuracy and results. Therefore, it is important to solve these problems in the automation of cell tracking because solving these problems will lead to a higher accuracy of automated tracking and analysis, thus achieving a better cell detection and tracking performance. At the same time, it will also reduce a part of workload of some researchers, thus improving the efficiency of some biological experiments. If these problems can be solved, some biological and medical researchers will make great breakthroughs in research related to the automation of cell tracking, which is beneficial for diagnosing disease, development of vaccine and development of biological research, and also contribute to physical rehabilitation and treatment of patients.

## **Methods**

The method of automated cell tracking totally contain three main parts, respectively detection, tracking and trajectory recovery.

Since the accuracy of cell detection will directly affect the performance of cell tracking, therefore, there are three main steps in the detection part to ensure the accuracy. As for illumination correction, the author mainly mentioned that using top-hat filter and do the subtraction to the inverted image of the input image in order to achieve the purpose of illumination correction and noise removal because there are shading artifact and noise in the phase-contrast microscopy in the process of image acquisition, which will have the interference on the cell detection. In addition, the use of hmaxima transformation can also achieve a good cell segmentation performance. As for segmentation of Nuclei, the author mainly mentioned that although the threshold method can separate the cells and background of the image, it still remain unsegmented region because of the touching, therefore, the Gaussian filtering followed by h-maxima transformation has been used to make cells have an unique intensity maximum, which can decrease the complexity of the cell tracking and localization of the cell.

In the tracking part, a single feature is hard to find the correct correspondence between cells in consecutive frames because of the migration, mitosis or occlusion of the cell. Therefore, the author decided to use several parameters together as the criterion for cell matching to increase the accuracy. Then, using these parameters together to compute the cost between different cells in consecutive frames based on the weighted bipartite matching.

In the trajectory recovery part, since there may be several broken trajectories in the process of cell tracking, therefore, a template-matching-based tracking method has been used to make the broken trajectories of the cell connected in order to recovery a complete trajectory.

As far as I am concerned, the method mentioned in this article does a good job in cell detection and cell tracking, the strength of this method is that for different types of the sequence, this method not only have a good performance on cell segmentation and detection, but also achieve a high accuracy in cell tracking. However, it still exists some weaknesses of this method, for example, it is hard to make sure weights of different parameters that mentioned in tracking part, which will affect the accuracy of tracking. As for possible alternative methods, deep learning method can be considered to improve the performance but finding training dataset and labelling is also a hard work.

#### Results

In the evaluation, the author mainly evaluates the performance of the detection and tracking when using the proposed method.

In the detection part, it contains two parts, respectively evaluation by comparing with other method and a quantitative evaluation. The evaluation strategy in the first part is mainly based on the comparison. The author discovered that the proposed method would separate cell successfully and have a high accuracy of cell segmentation. In addition, it can also overcome a series of problems, such as cell clustering, touching and so on. Simultaneously, in order to show robustness of the proposed method, the author also found it can perform better than the watershed segmentation method in challenging conditions. As for quantitative evaluation, in addition to comparing with other methods, the author presented two parameters, one is the ratio of the number of true detection of the cells to the total number of detected cells which is used to measure the precision of the cell detection, the other one is the ratio of the number of true detection of cells to the total number of cells which is used to measure the completeness. After computing these two parameters and comparing with other three methods, it can discover that the proposed method has a best performance and highest accuracy among all the methods. In tracking part, the main evaluation strategy is mainly based on a quantitative evaluation. To evaluate the performance of the cell tracking, the author also presented a parameter which is a ratio of the number of detected valid track segments to the total number of actual track segments. In order to achieve a better evaluation results, the author also use several sequences which contain different ranges of motion, cell migration, mitosis and so on to test performance and accuracy. According to the comparison, the proposed method can also show the best performance when comparing with other methods.

As far as I am concerned, these findings can effectively attract potential users to adopt this method, although the computation speed of this method is not faster than other methods, the performance of detection and accuracy of cell tracking are the most important points in the automation tracking and analysis because these two points will directly affect the results of experiment. Therefore, it is better to choose a method which has the highest accuracy and good performance for the potential users. In order to make this method to be more convincing, more sequences could be tested and observing the performance to evaluate. In addition, this proposed method can be combined with deep learning when appropriate.

### **Conclusions**

The automatic method for cell detection and tracking mentioned in this article can address many challenges in detection and tracking, but it still exists some disadvantages. In the detection part, the strength I believe is that the problem of shading artifact and noise can be solved very well by using top-hat filtering followed by an h-maxima transformation. In addition, the use of Gaussian filtering followed by h-maxima transformation can achieve a better cell segmentation performance, which could make cell tracking more properly. One of the most attractive strength is that this method focuses on the segmentation of the nucleus instead of on the entire cellular structure, which can avoid interference of cell morphologies. As for tracking part, the method combines several parameters to compute the cost between different cells, which is sufficient to increase the accuracy in the process of cell tracking. The weakness of this method may be the computation time, but it is possible to affect the performance of the method if we just focus on the computation time.

There are still some problems which does not mentioned in introduction. For example, in some image sequences which may contain many transparent cells, there are many substances in the cytoplasm of the cells, it is hard to do the cell segmentation and perform cell detection because these substances will have an interference with the detection and increase the complexity of detecting the nucleus of the cell, which also increase the difficulty of cell tracking.

As for the future research, there are some recommendations of mine, with the development and application of deep learning, we can choose to use deep learning with this method together to train a model which can handle some complex images and increase the computation time, compensating the weakness of the method mentioned in the article.