A MULTI-SEED 3D LOCAL GRAPH MATCHING MODEL FOR TRACKING OF DENSELY PACKED CELLS

*Min Liu *, Yalan Liu, and Weili Qian*

College of Electrical and Information Engineering, Hunan University, Changsha 410082, China

ABSTRACT

Automated tracking of cells in time-lapse live-imaging datasets of developing multicellular tissues is required for high throughput spatio-temporal quantitative measurements of a range of cell behaviors. The tracking of shoot apical meristems (SAM) cells in large-scale microscopy image sequences is challenging, because plant cells are densely packed within a specific honeycomb structure and share very similar physical features. In this paper, we propose a 3D local graph matching model to track the plant SAM cells, by exploiting the cells' tight spatial and temporal contextual information. The proposed 3D local graph matching model is further combined with a multi-seed based majority voting scheme to rectify possible matching errors in the cell correspondence growing process. Compared with the existing 2D local graph matching model, the experimental results show that the proposed method can greatly improve the tracking accuracy for plant cells.

Index Terms— Cell tracking, honeycomb structure, 3D local graph matching, multi-seed

1. INTRODUCTION

A local spatiotemporal coordination of cell growth and cell division plays a critical role in morphogenesis of both the plant and the animal tissues. The subject of this study, the shoot apical meristems, is the most important part of the plant body because it supplies cells for all the above ground plant parts such as leaves, branches and stem. For high-throughput analysis of plant cell image data acquired by confocal laser scanning microscopy at different time instances and different spatial slices (as shown in Fig. 1.), the development of fully automated image analysis pipelines is becoming a necessity.

There has been some work on automated tracking of animal cells and other common objects in time-lapse images [1-3]. However, those methods are difficult to track the plant cells within a special honeycomb structure in microscopic image stacks, where the plant cells are in close contact with each other and share very similar physical features.

In the earlier studies, a 2D local graph matching method was proposed in [4-6] to track plant SAM cells. In such framework, every cell is represented by a vertex in the graph and the neighboring vertices are connected by an edge. The local graph structure automatically includes the relative position information of the cells, such as the distance between two neighboring cells and edge orientation. It successfully exploits the cells neighborhood structure (geometry structure) and spatiotemporal context to match the plant cells, and the experimental results have confirmed the effectiveness of the local graph matching approach.

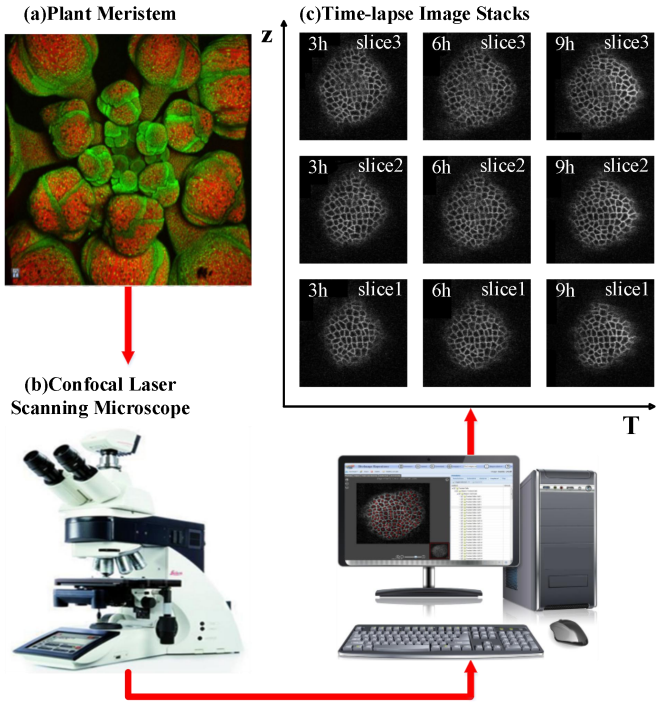

Fig. 1. (a) Plant meristem; (b) Confocal laser scanning microscope; (c) Time-lapse microscopic plant cell image stacks.

However, the spatial contextual information across different image slices along the z-direction is ignored in the existing 2D local graph matching model [7-9]. In this paper, we extend the 2D local graph matching model to build a 3D plant cell matching framework using a 3D local graph matching model, by exploiting the cells' 3D neighborhood structure and spatiotemporal context. Compared to the 2D

Corresponding author's e-mail: liu_min@hnu.edu.cn

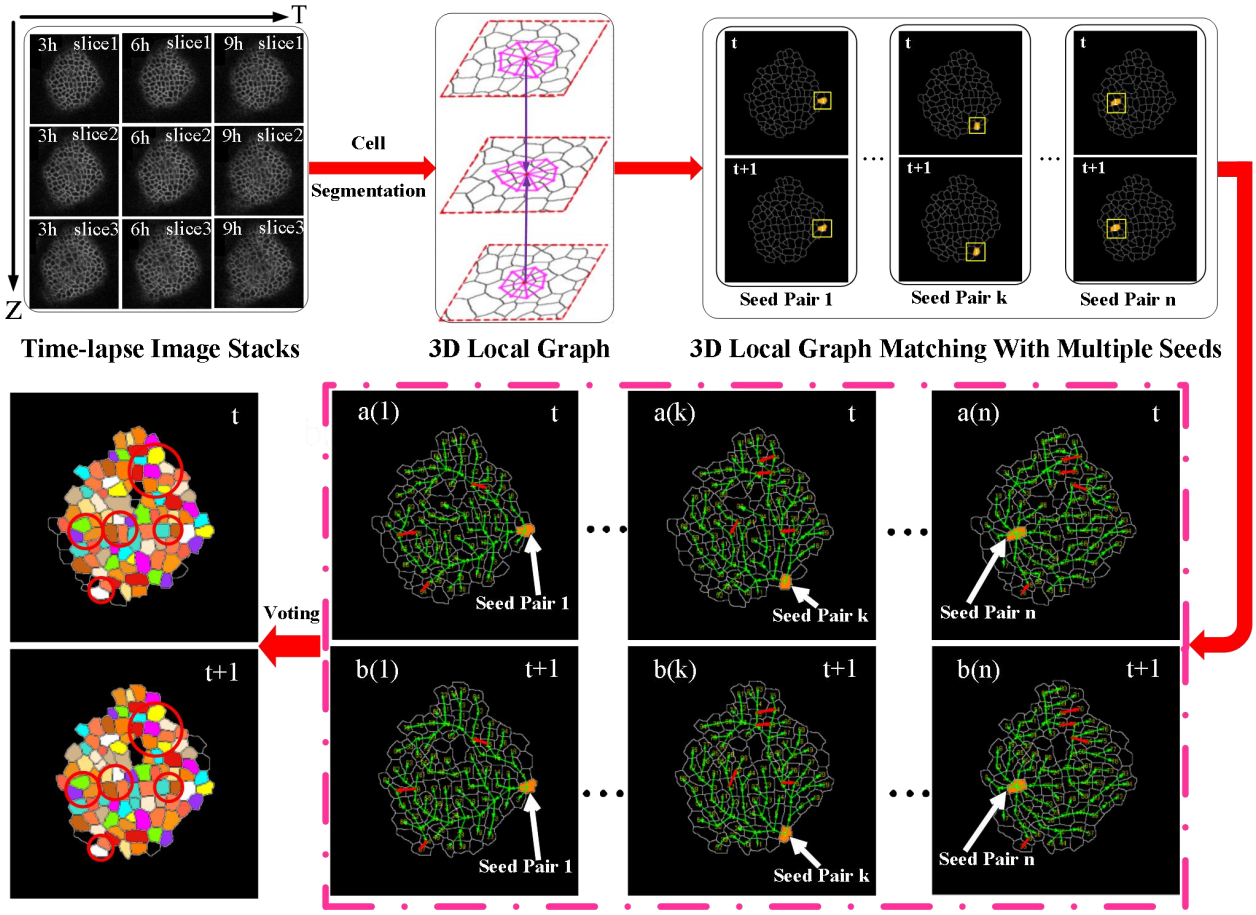

Fig. 2. The diagram of the proposed 3D local graph matching model with multiple seeds.

local graph matching model, the 3D local graph matching model is able to track the "3D plant cells".

Moreover, the existing 2D local graph matching model matches the plant cells in a sequential way, by growing the cell correspondence from the most similar cell pair ("Seed Pair"), it tends to accumulate matching errors. For example, one certain matching error caused by improper segmentation in noisy region will result in a series of incorrect matches during the cell correspondence growing process. In order to correct such possible wrong matches, we propose a multi-seed local graph matching framework, in which the final matching results are the voting output of the matching results produced by multiple seeds. Therefore, possible matching errors caused by one single seed can be rectified by majority voting of the matching results produced by other seeds. The diagram of the proposed multi-seed 3D local graph matching model is shown in Fig. 2.

2. DETAILED METHODOLOGY

2.1. 3D Local Graph

The plant cell boundaries are segmented by the watershed transformation method [10]. As described in the 2D local graph model [5, 10], for the k_{th} slice $S_{k,t}$ within an image stack at time point t, plant cells are related to one another via a 2D neighboring system, as shown in Fig. 3 (a). Let us define $\mathcal{N}_i$ as the neighboring cell set of a central cell, its neighbor set is $\mathcal{N}_i = \{j_1, j_2, ..., j_8\}$. Similarly, the neighbor set of a given cell u in slice $S_{k,t+1}$ is $\mathcal{N}_u = \{v_1, v_2, ..., v_8\}$. The number of neighbors depends on the cells' physical neighborhood.

Based on the 2D local graph model above, we build the 3D local graph framework, where the plant cells are related to one another via a 3D neighboring system within image stacks. For a given cell i in the k_{th} slice $S_{k,t}$ within an image stack at time point t, its neighbor set consists of the 2D neighboring cells and the 3D neighboring cells across the adjacent slices $S_{k-1,t}$ and $S_{k+1,t}$ within the image stack. As shown in Fig. 3 (b), the 3D neighbor set of the given cell i in the 3D local graph G_i can be denoted by $\mathcal{N}_i = \{j_1, j_2, ..., j_8, j_9, j_{10}, ..., j_{25}\}$. It includes the 2D neighboring cells $\{j_1, j_2, ..., j_8\}$ and the 3D neighboring cells $\{j_9, j_{10}, ..., j_{25}\}$ in the adjacent slices $S_{k-1,t}$ and $S_{k+1,t}$. The 3D neighboring cells are obtained through the 2D local graph matching model [5].

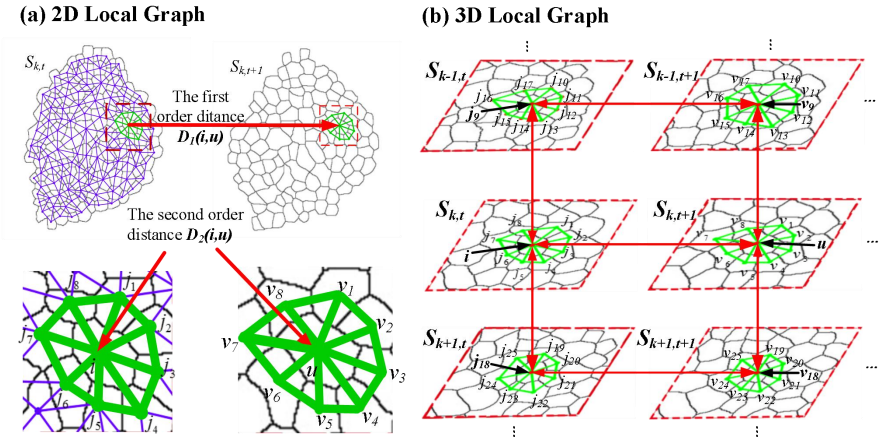

Fig. 3. 2D and 3D local graphs. The first order distance $D_1(i,u)$ and the second order distance $D_2(i,u)$ are illustrated in the 2D local graphs.

2.2. 3D Local Graph Distance Functions

Based on the definitions above, we construct the distance function $D(i,u)$ for any two 3D local graphs G_i and G_u, which are related to their central cell pairs (i,u). $D(i,u)$ is composed of the first order distance function $D_1(i,u)$ between central cells, and the second order distance function $D_2(i,u)$ defined on edges connecting pairs of neighboring cells.

First Order Distance

$D_1(i,u)$ is the distance between the central cells i and u in 3D local graphs G_i and G_u. It is composed of the shape histogram distance and the cell area difference, as below

$$D_1(i,u) = \omega_1 KLD(h_i, h_u) + \omega_2 \frac{\|A_i - A_u\|}{A_i} \quad (1)$$

Let the shape histogram associated with cell i in image slice $S_{k,t}$ at time t be h_i, and that with cell u in the next image slice $S_{k,t+1}$ at time $t+1$ be h_u, we compute the K-L divergence (KLD) between h_i and h_u [11] as $KLD(h_i, h_u)$. A_i, A_u are the cell area sizes of cells i and u. The normalization parameters ω_1 and ω_2 are learned from a training dataset.

Second Order Distance

$D_2(i,u)$ is defined on edges connecting pairs of neighboring nodes. Its computation relies on the fact that if cell i is matched to u, then the relative position of i with respect to its neighboring cell j should be very similar to that of u with respect to its neighboring cell v. Let's define the cell i in slice $S_{k,t}$ with its 3D neighboring cells $\mathcal{N}_i = \{j_1, j_2, \cdots j_m\}$, and another cell u in the next slice $S_{k,t+1}$ with its neighboring cells $\mathcal{N}_u = \{v_1, v_2, \cdots v_n\}$. m and n are the number of neighbors for cells i and u respectively. If $m \neq n$, that means i and u are not the corresponding cell pair, so we assign a large value to the second order distance. Otherwise, the second order distance can be computed as below,

$$D_2(i,u) = \lambda_1 \sum_{k=1}^{m} \left| \frac{\theta_i^{j_k} - \theta_u^{v_k}}{\theta_i^k} \right| + \lambda_2 \sum_{k=1}^{m} \left\| (c_i - c_{j_k}) \right\| - \left\| (c_u - c_{v_k}) \right\| \quad (2)$$

Here the first component is the edges' orientation differences in 3D local graphs G_i and G_u, $\theta_i^{j_k}$ is the orientation angle of the edge between the central cell i and its neighboring cell j_k, measured relative to a horizontal axis; $\theta_u^{v_k}$ is the orientation angle of the edge between cell u and its neighboring cell v_k. The second order component is the differences between the corresponding edges' lengths, where c_i and c_u are the centroid positions of cell i and u respectively, and c_{j_1}, c_{j_2} … c_{j_m} are the centroid positions of the neighbors of cell i, c_{v_1}, c_{v_2} … c_{v_n} are the centroid positions of the neighbors of cell u. The normalization parameters λ_1 and λ_2 are learned from a training dataset.

2.3. 3D Local Graph Matching

Given two central cells i and u in 3D local graphs G_i and G_u across two time instances respectively, the 3D local graph distance between G_i and G_u can be expressed as

$$D(i,u) = D_1(i,u) + D_2(i,u) \quad (3)$$

In the existing 2D local graph matching model, the cell pair with the least distance will be regarded as the seed pair, from which we grow the cell correspondence sequentially to find all possible cell matches, the details is illustrated in [4]. In this paper, we find the top few most similar cell pairs as the seed cell pairs instead, which can be used in our proposed multi-seed 3D local graph matching framework.

2.4. Multi-seed 3D Local Graph Matching

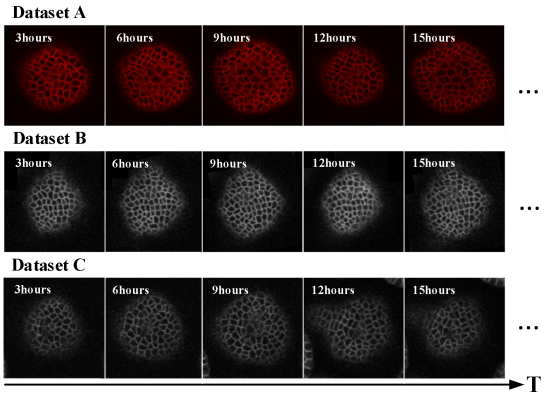

Fig. 4. Different plant cell datasets.

Compared to the 2D local graph matching model, the 3D local graph matching model will be more robust to find the cells' correspondence by incorporating the cells' 2D neighborhood information and 3D spatial context [12, 13] across the adjacent image slices. Besides, the 2D local graph matching model is employing a cell correspondence growing scheme starting from a seed pair, so it tends to accumulate errors, especially in noisy images. Different from such iterative searching strategy used in the 2D local graph matching method, a multi-seed based majority voting scheme is proposed to rectify such possible matching errors. The final matching results are the majority voting output from the 3D local graph matching results generated by multiple seeds. Therefore, the possible matching errors caused by one single seed can be rectified by the voting of matching results from other seeds.

3. EXPERIMENTAL RESULTS

The confocal laser scanning microscopy based live-imaging is set up to acquire time-lapse plant cell image stacks [14-16]. Each 3D image stack, taken at every 3 hours, consists of a series of images of optical cross-section SAMs that are separated by approximately 1.5 uM, as shown in Fig. 1 and Fig. 3. We have tested our proposed multi-seed 3D local graph tracking approach on multiple SAM datasets, as shown in Fig. 4. The algorithm is implemented using MATLAB on a PC with 3.3 GHz CPU and 4 GB memory.

Fig. 5 illustrates the comparison of the matching results between the existing 2D local graph matching method (a1, a2), 3D local graph matching method (b1, b2), and our proposed multi-seed based 3D local graph matching algorithm (c1, c2), in two consecutive image frames. The cells in the same color across different time points represent the same cells. As denoted by the red box, it is seen that the 3D local graph matching model outperforms the 2D local graph matching model, and the 3D local graph matching model with multiple seeds achieves even better tracking results.

In order to demonstrate the strength of the proposed multi-seed based 3D local graph tracking approach, we first compared the tracking performance of the 3D local graph matching model and the 2D local graph matching model in

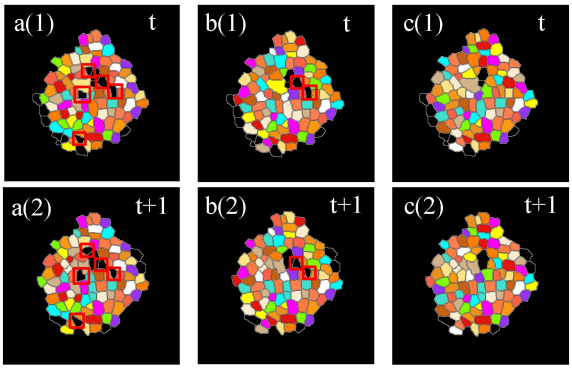

Fig. 5. Cell tracking results by different methods. The cells in the same color across different time points represent the same cells.

TABLE 1
TRACKING ACCURACY COMPARISON

Dataset	2D local graph matching	3D local graph matching	Multiple seeds +3D local graph matching
A	80.37%	89.09%	96.95%
B	84.21%	90.71%	98.44%
C	77.50%	87.97%	95.26%

Table 1, from which we can clearly see that the proposed 3D local graph matching model achieves much higher matching accuracy in all datasets. Furthermore, we compared the tracking accuracy of the proposed multi-seed based 3D local graph tracking approach with the 3D local graph matching model with one seed (as used in the existing 2D local graph matching model), it is seen that the proposed matching approach achieves much higher tracking accuracy than the 3D local graph matching model with one seed only.

4. CONCLUSIONS

In this paper, a 3D local graph matching model with multiple seeds is proposed to track the plant cells in a densely packed structure, by exploiting the tight 3D contextual information. The combination of 2D local graph information and the spatial information across different image slices within the 3D image stacks greatly improves the plant cell tracking accuracy. Furthermore, a multi-seed voting scheme is proposed to automatically rectify possible matching errors caused by one seed only. The effectiveness of the proposed method is evidenced by the experimental results.

ACKNOWLEDGEMENTS

The authors would like to thank Prof. Amit Roy-Chowdhury and Prof. Venugopala Reddy from the University of California, Riverside for offering insightful suggestions on building the proposed plant cell tracking framework. This work was supported by the National Natural Science Foundation of China under Grant Nos. 61771189 and 61301254.

5. REFERENCES

[1] K. E. G. Magnusson, J. Jaldén, P. M. Gilbert, and H. M. Blau, "Global linking of cell tracks using the Viterbi algorithm," *IEEE Trans. Med. Imag.*, vol. 34, no. 4, pp. 911-929, 2015.

[2] L. Chen, Z. Zhao, and H. Yan, "A probabilistic relaxation labeling (PRL) based method for C. elegans cell tracking in microscopic image sequences," *IEEE J. Sel. Topics Signal Process*, vol. 10, no. 1, pp. 185-192, 2016.

[3] O. Dzyubachyk, W. A. Van Cappellen, J. Essers, W. J. Niessen, and E. Meijering, "Advanced level-set-based cell tracking in time-lapse fluorescence microscopy," *IEEE Trans. Med. Imag.*, vol. 29, no. 3, pp. 852-867, 2010.

[4] M. Liu, A. Chakraborty, D. Singh, R. K. Yadav et al, "Adaptive cell segmentation and tracking for volumetric confocal microscopy images of a developing plant meristem," *Mol. Plant*, vol. 4, no. 5, pp. 922-931, 2011.

[5] M. Liu, P. Xiang, and G. Liu, "Robust plant cell tracking using local spatial-temporal context," *Neurocomputing*, vol. 208, no. 10, pp. 309-314, 2016.

[6] M. Liu, Y. He, Y. Wei, and P. Xiang, "Plant cell tracking using Kalman filter based local graph matching," *Image Vis. Comput.*, vol. 60, pp. 154-161, 2017.

[7] R. S. Zou and C. Tomasi, "Deformable graph model for tracking epithelial cell sheets in fluorescence microscopy," *IEEE Trans. Med. Imag.*, vol. 35, no. 7, pp. 1625-1635, 2016.

[8] H. Chui and A. Rangarajan, "A new algorithm for non-rigid point matching," in *Proc. IEEE Conf. Comput. Vis. Pattern Recognit. (CVPR)*, 2000, pp. 44-51.

[9] M. Schiegg, P. Hanslovsky, C. Haubold et al, "Graphical model for joint segmentation and tracking of multiple dividing cells," *Bioinformatics*, vol. 31, no. 6, pp. 948-956, 2015.

[10] K. Mkrtchyan, D. Singh, M. Liu, G. V. Reddy, A. K. Roy Chowdhury, and M. Gopi, "Efficient cell segmentation and tracking of developing plant meristem," in *IEEE Int. Conf. Imag. Process. (ICIP)*, 2011, pp. 2165-2168.

[11] M. Ankerst, G. Kastenmüller, H. P. Kriegel, and T. Seidl, "3d shape histograms for similarity search and classification in spatial databases," in *Int. Sym. Spat. Dat. (SSD)*, 1999, pp. 207-226.

[12] M. Liu, R. K. Yadav, A. Roy-Chowdhury, and G. V. Reddy, "Automated tracking of stem cell lineages of arabidopsis shoot apex using local graph matching," *Plant J.*, vol. 62, no. 1, pp. 135-147, 2010.

[13] K. Li, M. Chen, T. Kanade, E. Miller, L. Weiss, and P. Campbell, "Cell population tracking and lineage construction with spatiotemporal context," *Med. Imag. Anal.*, vol. 12, no. 5, pp. 546-566, 2008.

[14] R. Fernandez, P. Das, V. Mirabet, E. Moscardi, J. Traas, J. L. Verdeil, G. Malandain, and C. Godin, "Imaging plant growth in 4D: robust tissue reconstruction and lineaging at cell resolution," *Nat. Methods*, vol. 7, no. 7, pp. 547-553, 2010.

[15] M Liu, R Gong, W Chen, H Peng, "3D neuron tip detection in volumetric microscopy images using an adaptive ray-shooting model," *Pattern Recognition*, vol. 75, pp. 263-271, 2018.

[16] J Hu, J Lu, and YP Tan, "Deep metric learning for visual tracking," *IEEE Transactions on Circuits and Systems for Video Technology*, vol. 26, no. 11, 2056-2068, 2016.