Development of a System for Automatic Construction of Cell-Lineage of *C. elegans* from Nomarski DIC Microscope Images

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1 Introduction

The development of a multi-cellular organism starts from a single cell, which consecutively divides to be an adult. The whole relationship of parent cells and their daughter cells is called the *cell lineage*, which can be described as a tree structure. The analysis of the cell lineage is important for understanding the development of multi-cellular organisms [3]. It is also important for studying gene functions. When certain genes are disrupted, the cell lineage may change from that of wild types [1, 2]. Such information is very useful for studying the function of the disrupted genes.

By using a Nomarski DIC microscope system, we can record images of a *C. elegans* embryo at multiple focal planes and multiple time-points. However, manual construction of the cell lineage is very time conuming and laborious, and a method which automates this procedure will greatly increase the productivity of cell lineage construction. We have developed and verified a system for this purpose [4].

2 Method and Results

Our system consists of four components: (1) Detection of nuclei from each 2D image included in a 4D image (image processing), (2) Removal of false positive nuclei by hand, (3) Unification of a single nucleus detected in multiple 2D images, and (4) Construction of a cell lineage. Since there are differences in the appearances of the nuclei, our nucleus detector employs multiple image processing algorithms and combines the outputs of them. Currently, we have developed three algorithms. The output of our nucleus detector contains lots of false positives, which are removed manually with a GUI tool developed to facilitate this task. A single nucleus will be detected in multiple time points and in multiple focal planes. Our system unifies them into one. Finally, a hypothetical cell lineage based on the detected nuclei is constructed.

We tested our algorithm using a 4D-image of *C. elegans* embryo up to the 7-cell stage for our data set (Fig. 1). The result is given in Fig 2. The hypothetical cell lineage created by our system was

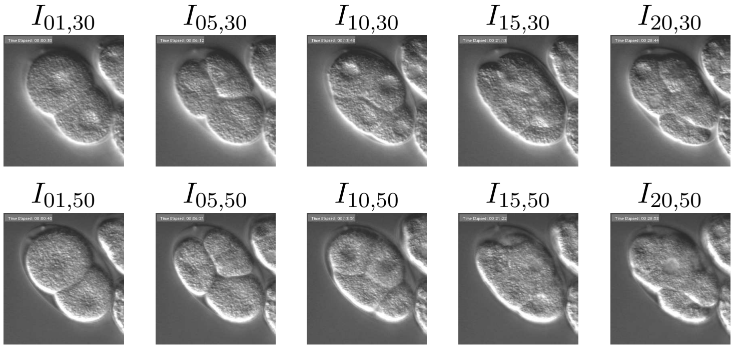

Figure 1: Part of the data set. Images from the 30th and 50th focal planes, at 1st,5th,10th,15th,20th time-points. The notation '$I_{t,f}$' means the image at time-point t and at focal plane f.

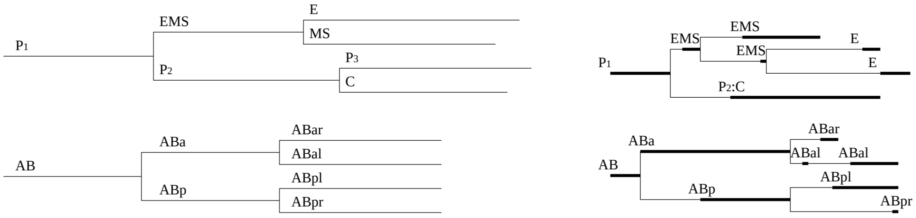

Figure 2: The left tree is the true cell lineage [3]. Here, forking points show the time-points of cell division. The right tree is the cell lineage constructed by our system. Here, each thick line represents a detected nucleus. Each end of the thick line represents the time-point when the corresponding nucleus emerges or disappears. P_2 and C was recognized as a single nucleus, written as P_2:C in this figure.

close to the true lineage for the AB descendants. However, for the P_1 descendants, EMS and E were split into multiple nuclei, and P_2 and C were incorrectly recognized as a single nucleus. To overcome these problems, we should mainly improve the nucleus detection step of our system.

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