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Ying Chen
Rensselaer Polytechnic Institute

Gang Lin
Rensselaer Polytechnic Institute

William A. Mohler
Rensselaer Polytechnic Institute

Omar Al-Kofahi
University of Connecticut

Badrinath Roysam
Rensselaer Polytechnic Institute

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Automated Extraction of Cell Lineages and Spatial Migration Paths in Live *C. elegans* Embryos from 4D Fluorescence Microscopy Image Sequences

Ying Chen [1], Gang Lin [1], William A. Mohler [2], Omar Al-Kofahi [1], and Badrinath Roysam [1]
Dept. of ECSE, Rensselaer Polytechnic Institute [1],
Genetics & Developmental Biology, Univ. of Connecticut Health Center [2]

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Abstract

This work presents automatic methods for analyzing time-lapse 3D confocal image sequences of fluorescently tagged *C.elegans* worm embryos to extract the lineage, as well as 3D spatial migration paths of cells.

Significance

Cell lineage of *C. elegans* is a family-tree representation of cell division pattern, ancestor-descendant relationship, and marker events (e.g. cell death) timeline in embryogenesis. It is essential to genetic, behavioral, and structural analysis of multi-cellular organism development [1].

Challenge

- Automation with tolerable error rate
- User-friendly GUI for human expert edition
- Multiple cell measurements for practical analysis [4]

State-of-the-art

- 3D Time-lapse Microscopy Imaging: Fluorescence [2]
- 3D Cell Nuclei Segmentation: Watershed Algorithm [3]
- Cell Nuclei Tracking: MHT [4]

Technical approach

1. System overview

Step 1: Time-lapse 3D Fluorescence Microscopy Imaging
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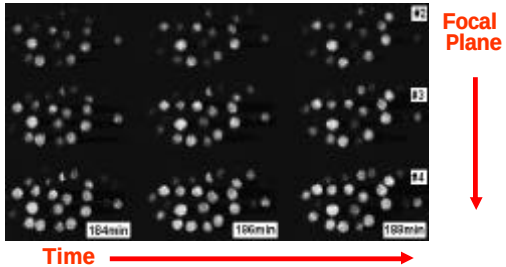
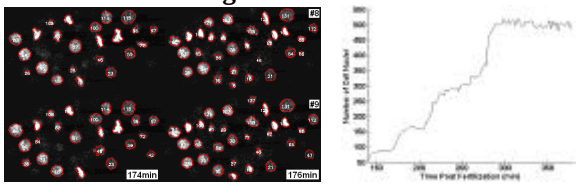
Step 2: Automated 3D Segmentation & Morphometry of Cell Nuclei
↓
Step 3A: Feature-Based Nuclear Similarity Measurement
↓
Step 3B: Track nuclei by MxN Rectangular Assignment
↓
Step 3C: Analyze Unassigned Objects & Refine Assignment
↓
Step 4: Cell Lineage Construction & Cell Migration Paths

2. Time-lapse Fluorescence Microscopy Imaging

- Two-photon microscopy: excitation at 900nm
- High GFP signal from fluorescence-tagged cell nuclei
- Low level of auto-fluorescence from unlabeled components
- Tolerable photo-bleaching and photo-toxicity.
- Temporal Interval: 2 minutes between successive image stacks
- Image Resolution:
  - ❖ 6 pixels/µm (X-Y plane), 63 planes/image stack (Z axis)



3. 3D Watershed Segmentation of Cell Nuclei

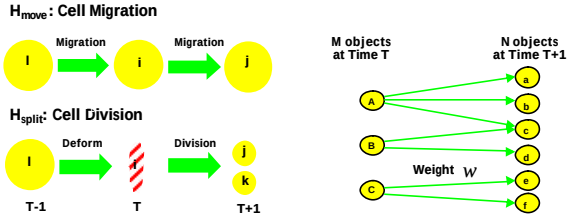


4. Automated Multiple-Cell-Tracking

4.1 ***Morphometry Analysis for Similarity Measurement***

Feature	Definition	Feature	Definition
Centroid	3D coordinates of nucleus centroid	Perimeter	# of boundary pixels for a nucleus
Size	3D volume of a nucleus	Convexity	Ratio of convex hull to nucleus size
Intensity	Avg. gray-scale value of a nucleus	Shape	Circularity measure of a nucleus
Texture	Std. deviation of intensity gradient	Eccentricity	Ratio of major axis to minor axis

4.2 ***Multiple Hypothesis Tracking (MHT) Framework***



4.3 ***Rectangular Assignment Problem***

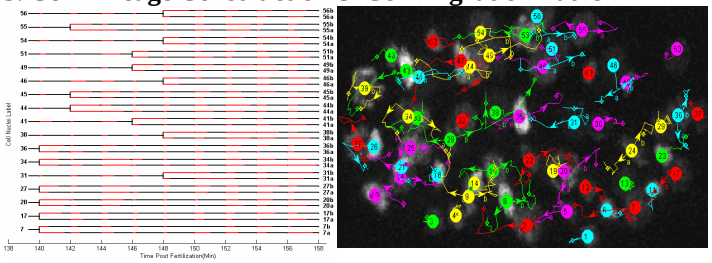
Determine optimal matches between *M* nuclei detected at *t* and *N* nuclei at *t+1*.

$$\min_x \left(\sum_i w_i x_i \right) \quad x_i = \begin{cases} 1 & \text{if the hypothesis is selected} \\ 0 & \text{if the hypothesis is ignored} \end{cases}$$

4.4 ***Refinement***

- Ground truth: a cell can have at most 2 successors and only 1 ancestor
- Forbidden Cell Behaviors
  - ❖ Disappearance without cell death
  - ❖ Emerge without cell division
- Cell Division Cycle: 28 ~ 30 mins (14 ~ 15 time points)

5. Cell Lineage Construction & Cell Migration Paths



6. Result

The automated procedure achieved a 97% accuracy (33 out of 34 cell division events were detected correctly) for a lineage of *C. elegans* from 56-90 cell stages, covering a span of 140~170mins post fertilization.

7. Technology Transfer

Our automated methods can be integrated into a common MHT core for a diversity of problems, e.g. changing detection, multiple objects tracking, etc.

References

1. Sulston, J. E., et al., *The Embryonic Cell Lineage of the Nematode Caenorhabditis elegans*, Developmental biology, 100(1), 1983.
2. Mohler, William A., et al., *Imaging in Neuroscience and Development: A Laboratory Manual*, Cold Spring Harbor Laboratory Press. 2005.
3. Lin, Gang, et al., Cytometry Part A, 63A, 2005.
4. Al-Kofahi, Omar, et al., Cell Cycle, 5: 3, 2006.

Contact info.

Badrinath Roysam , Professor
Dept. of Electrical, Computer, and Systems Engineering
Rensselaer Polytechnic Institute, 110 8th Street, Troy, NY 12180
Phone: (518)276-8067; Fax: 518-276-8715; Email: roysam@ecse.rpi.edu