IRis

Northeastern University

Research Thrust R2 Publications

CenSSIS Research Thrust R2: Physics Based Signal Processing and Image Understanding

January 01, 2007

4-D Image Analysis of Cell Migration and Cell-Cell Interaction

Ying Chen
Rensselaer Polytechnic Institute

Ena Ladi
University of California - Berkeley

Ellen Robey
University of California - Berkeley

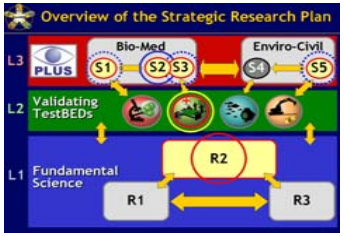
Omar Al-Kofahi
Rensselaer Polytechnic Institute

Badrinath Roysam
Rensselaer Polytechnic Institute

Recommended Citation

Chen, Ying; Ladi, Ena; Robey, Ellen; Al-Kofahi, Omar; and Roysam, Badrinath, "4-D Image Analysis of Cell Migration and Cell-Cell Interaction" (2007). *Research Thrust R2 Publications.* Paper 1. http://hdl.handle.net/2047/d10008986

This work is available open access, hosted by Northeastern University.



4-D Image Analysis of Cell Migration and Cell-Cell Interaction

Ying Chen [1], Ena Ladi [2], Ellen Robey [2], Omar Al-Kofahi [1], and Badrinath Roysam [1]
Department of ECSE, Rensselaer Polytechnic Institute [1],
Department of Molecular & Cell Biology , University of California, Berkeley [2]

This work was supported in part by CenSSIS, the Center for Subsurface Sensing and Imaging Systems, under the Engineering Research Centers Program of the National Science Foundation (Award Number EEC-9986821).

Abstract

This work presents automatic methods to analyze 4D images of thymocytes (T-cells) and dendritic cells (DCs) from Two-Photon Laser Scanning microscopy, characterize patterns of cell migration, and quantitate the interactions between T-cells and DCs.

Significance

Via visual inspection of the T-cell and DC contacts, biologists noted that T-cells expressing P14 TCR or CCR7 were in association with DCs more frequently than wild type T-cells. Our work aims to provide biologists an automated method to confirm and quantitate their manual observations.

State-of-the-art

- Cell Segmentation: Mean-shift Algorithm [1]
- Multiple-Hypothesis Tracking (MHT) [2]
- Hypothesis Testing on Distribution [3]

Technical approach

1. Two-Photon Microscopy Imaging

- Green channel: High GFP signal from T-cells
- Red channel: High YFP signal from host dendritic cells

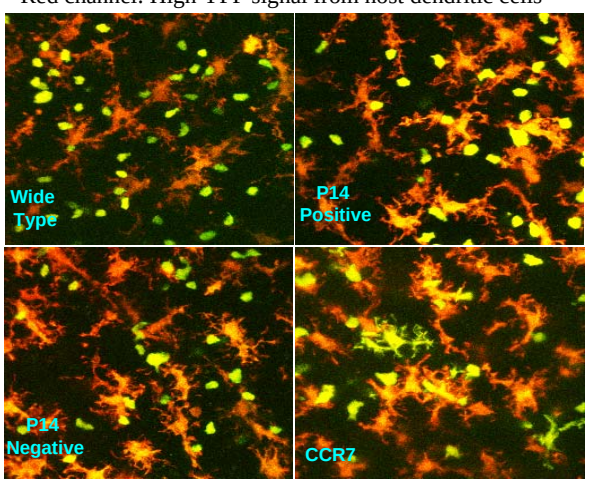


Figure 1. Two-channel images of DCs in red and different types of T-cells in green (wide type, P14 positive, P14 negative, and CCR7)

2. Segmentation of T-cells via Mean Shift Clustering

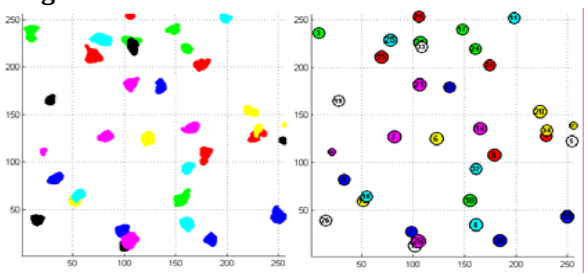
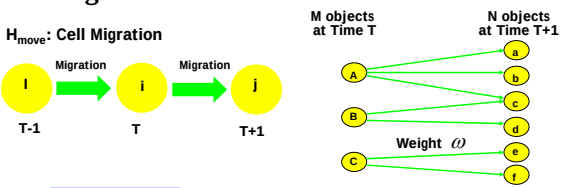


Figure 2. Color-coded (left) and numerical-labeled (right) segmentation results of T-cells generated by mean shift clustering algorithm

4. Tracking of T-cells via MHT



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

Figure 3. Multiple-Hypothesis Tracking (MHT) framework

5. Characterization of T-cell Migration Pattern

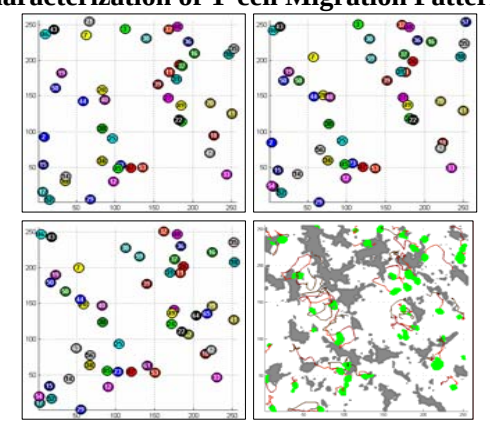


Figure 4. Color-coded and numerical-labeled tracking of T-cells over time (upper two and bottom left) and their migration paths (bottom right)

6. Quantitation of Cell-Cell Association

	Manual Inspection		Automated Analysis	
Sample	Avg. Distance (um)	% tp in contact	Avg. Distance (um)	% tp in contact
P14 type 040805m1b	10.5	34.2%	12.81	21.33%
P14 type 040805m1c	9.46	45.02%	9.98	26.53%
Wild type 022105m5b	12	17.03%	14.47	15.75%
Wild type 022105m2wt	12.7	11.03%	12.43	17.74%

7. Hypothesis Testing

- Null Hypothesis H_0 :
  T-cells expressing P14 and wild type T-cells have the same underlying distribution of distance measurement.
- Alternative Hypothesis H_1 :
  T-cells expressing P14 have more frequent contact with DCs than wide type.

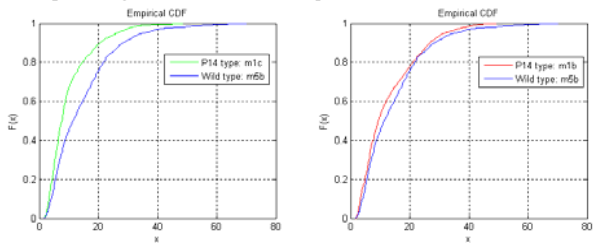


Figure 5. Empirical Cumulative Distribution Function (CDF) of Cell-Cell distance

- Kolmogorov-Smirnov Test for Distribution Testing

Test	P14 m1b v.s. Wild Type	P14 m1c v.s. Wild Type
Significance Level	0.05	0.05
Test Statistic	0.0843	0.2218
Null Hypothesis	Rejected	Rejected
Alternative Hypothesis	-	-

References

1. Comaniciu, Dorin, et al., PAMI, 24:5, pp.603-619, 2002.
2. Al-Kofahi, Omar, et al., Cell Cycle, 5: 3, 2006.
3. Martinez, Wendy, et al., Computational Statistics Handbook with Matlab, 2002.

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