

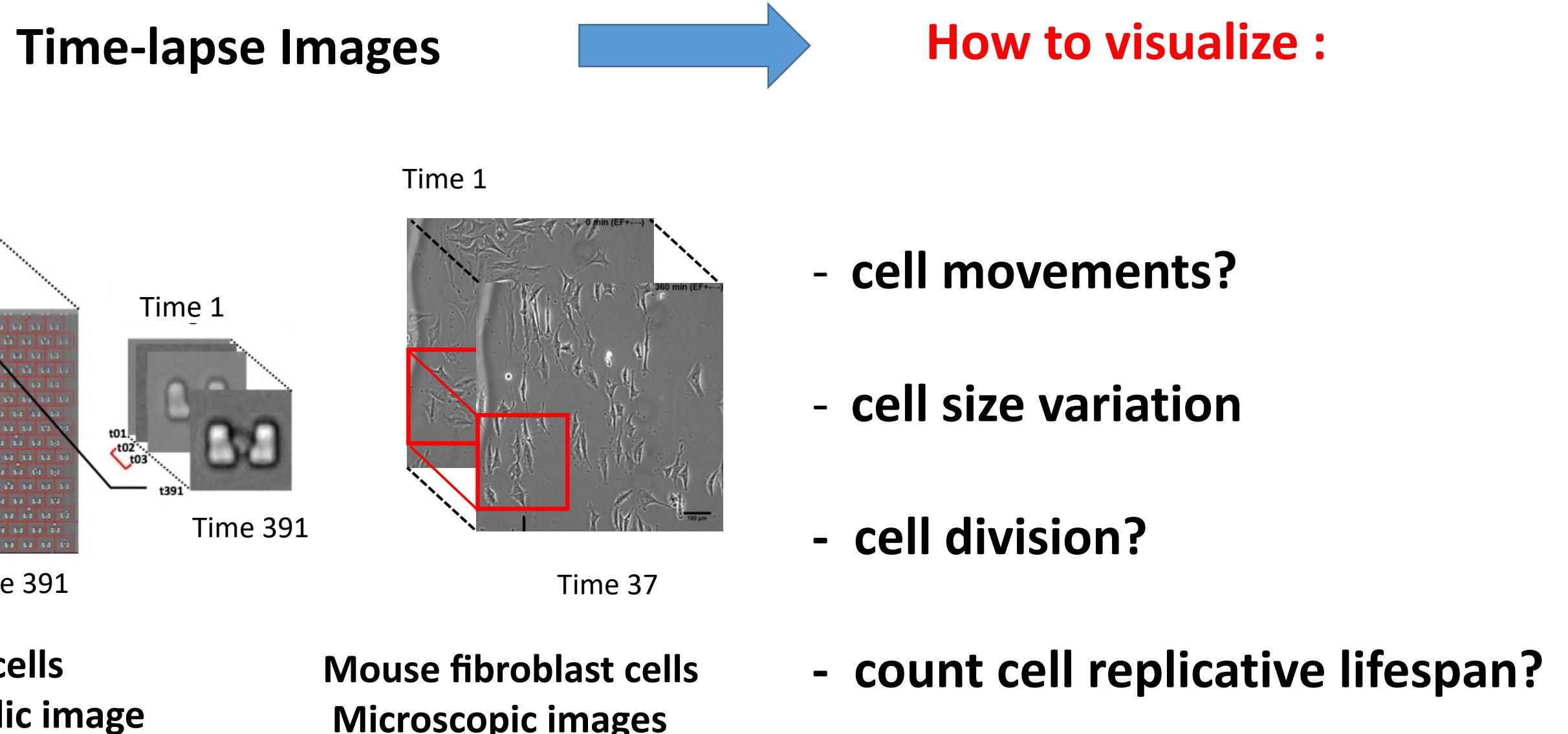
μ Polar : An Interactive 2D Visualization Tool for Microscopic Time-series Images



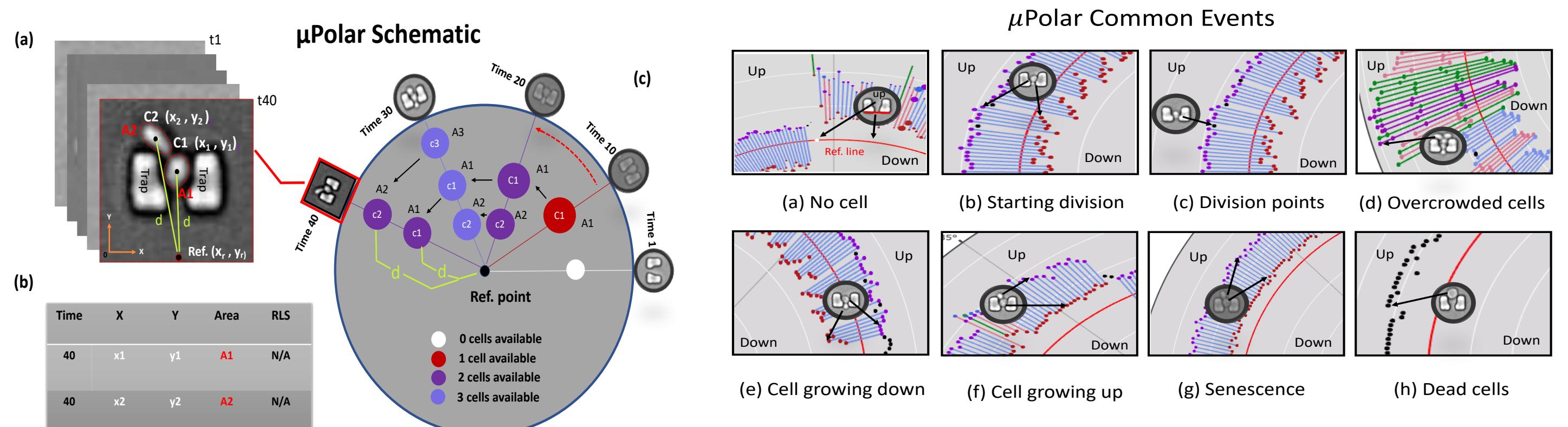
Summary

Time-lapse microscopy is an effective research tool to monitor cell behavior and cell divisions. Recent advances in microfluidics have accelerated the adoption of time-lapse microscopy in research. However, it is challenging to visualize and interpret the time-series data gathered through time-lapse microscopy. We have developed a circular plotting software tool, μ Polar, to visualize the trends and patterns of the cell movements and cell division events in a time-series. μ Polar is interactive and easy to use. We demonstrate the utility of μ Polar by visualizing the events of dividing yeast cells where cell divisions lead to oscillating plotting patterns, and in migrating mouse fibroblasts where cell shapes change during the migration. μ Polar potentially could be applied to other types of time-series of microscopic images.

Motivation

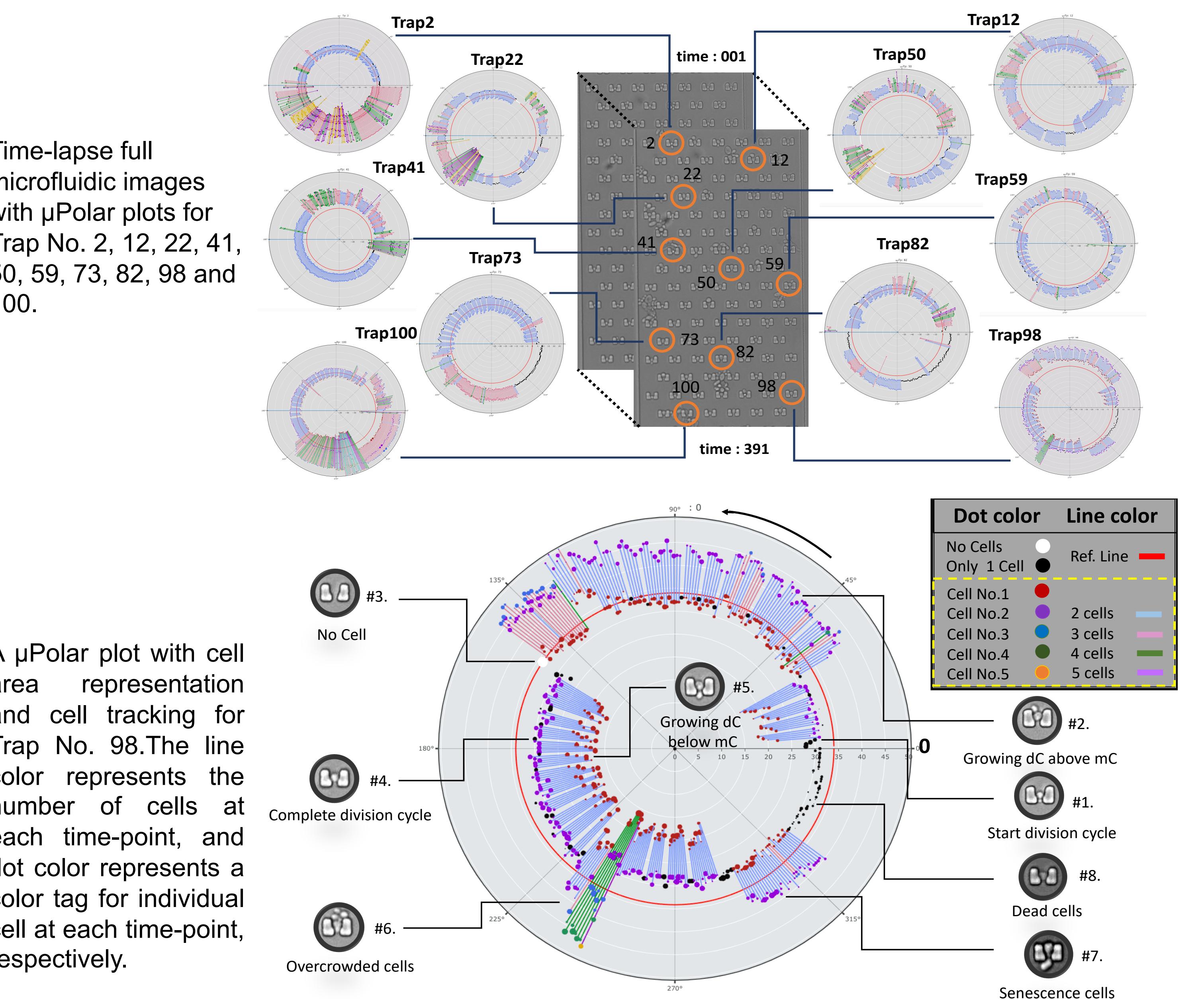


Methods & Materials

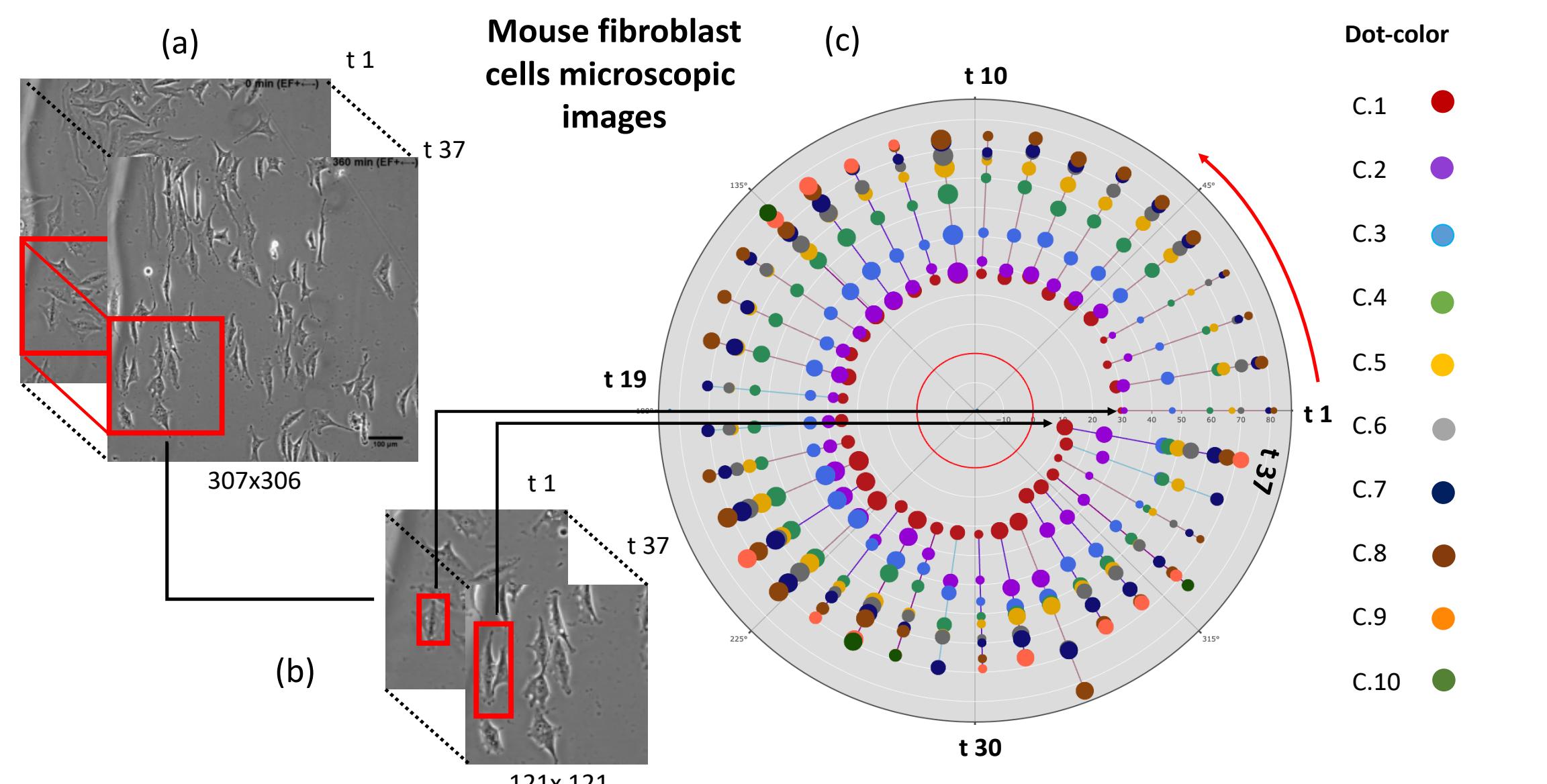


- There is no cell at the presented time-point (white dot)
- The two cells represented by dark red dots and purple dots are close to each other, and division already happened
- The black dots represent a division after the cell completed its separation cycle
- Indication of overcrowded cell events
- Representation of steady cells in the up region (purple color) and developing cells in the down region (dark red color)
- Representation of steady cells in the up region (dark red color) and developing cells in the up region (purple color)
- Two cells are in a steady situation for some time, an indication of senescent cells
- The representation of a cell that has been dead for some time

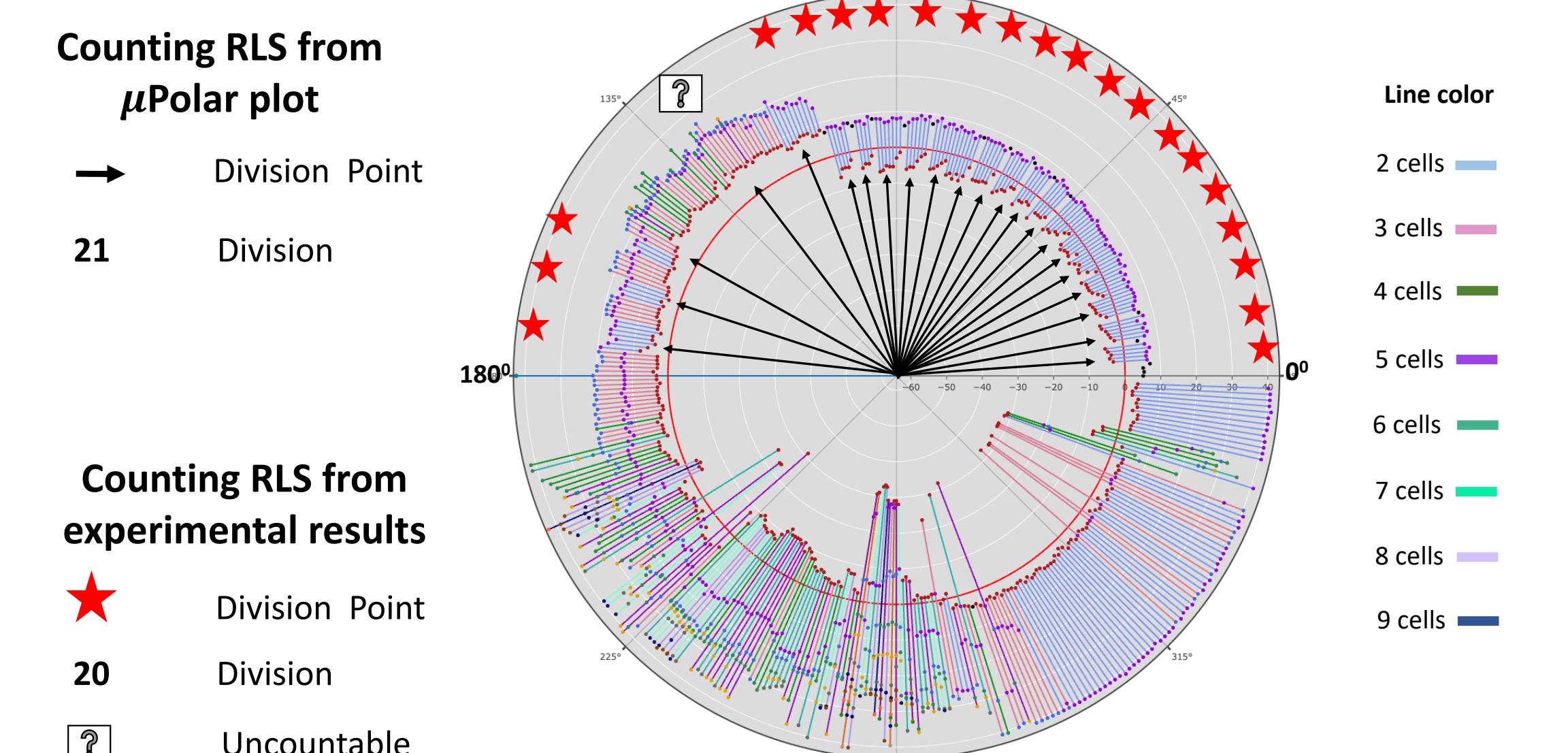
Results



A μ Polar plot with cell area representation and cell tracking for Trap No. 98. The line color represents the number of cells at each time-point, and dot color represents a color tag for individual cell at each time-point, respectively.



Identifying RLS measurements from μ Polar plot for Trap No. 1. The black arrows indicate the potential number of yeast cell division time-points from μ Polar plot estimating 22 divisions. The red stars indicate the 21 cell division events identified from the experimental results.



Discussion

Overall, μ Polar is a useful tool for visualizing cell migration, cell monitoring, and estimating cell division events from time-lapse microscopic images. The μ Polar interpretation of cell division at each time-point can facilitate lifespan estimation in aging studies. The comparison between yeast cell time-lapse microfluidics images and mouse fibroblast cell time-lapse microscopic images demonstrates that μ Polar can be a general tool for visualizing time-lapse images. Visualizing cell division events can offer biological insights. For instance, in the microfluidic images, when yeast cells become older, interestingly, the cell division cycle becomes longer. It can also be seen that there is a relationship between cell size and cell division time-length. Similarly, visualizing and tracking mouse fibroblast cells show how cell sizes change during their migration.

Conclusion

- We developed an R package based on a circular plotting method, μ Polar, to visualize cell movements and cellular division events at hundreds of time points.
- Our method is 2D, interactive and easy to use.
- We demonstrated the utility of our method to describe the events of dividing yeast cells and migrating mouse fibroblast cells.

Overall, μ Polar visualization tool could be applied to other types of microfluidic devices and time-lapse microscopic imaging experiments.

Acknowledgements

The work is partially supported by NSF CAREER award #1453078 (transferred to #1720215), NSF award #1761839, a start-up fund, internal awards from the University of Tennessee at Chattanooga (Tennessee of Higher Education funds via the Center of Excellence in Applied Computational Science and Engineering)

References

- Carpenter E. Image-based chemical screening. *Nature Chemical Biology* 3, 8 (2007), 461–465
- Wollma R, Stuurman N. High throughput microscopy: From raw images to discoveries. *Journal of Cell Science* 120, 21 (2007), 3715–3722
- Oates, A. C. et al., Quantitative approaches in developmental biology. *Nat. Rev. Genet.* 10, 517–530 (2009)
- Mavrakis M, Rikhy R, Lilly M, Lippincott-Schwartz J. Fluorescence imaging techniques for studying Drosophila embryo development. *Cell Biol.* 39, 4, 18.1–4.18.43 (2008)
- Amat, F. et al., Fast, accurate reconstruction of cell lineages from large-scale fluorescence microscopy data. *Nat. Methods* 11, 951–958 (2014)
- Elcic KW, Berthold MR, Goldberg IG, Ibañez L, Manjunath BS, Martone ME, et al. Biologi-cal imaging software tools. *Nat. Methods*. 2012; 9: 697–710. <https://doi.org/10.1038/nmeth.2084PMID: 22743775>
- McQuin C, Goodman A, Chernyshov V, Kamentsky L, Cimini BA, et al. CellPro-filer 3.0: Next-generation image processing for biology. *PLOS Biology* 16(7), 2008, <https://doi.org/10.1371/journal.pbio.2005970>
- Ghafari, M. et al. Complementary Performances of Convolutional and Capsule Neural Networks on Classifying Microfluidic Images of Dividing Yeast Cells. *PLOS ONE*, 2021, bioRxiv 852566; doi: <https://doi.org/10.1101/852566>
- Farokhi H, Ghayesh MH (2018) Nonlinear mechanics of electrically actuated microplates. *Inter-national Journal of Engineering Science*, 123: 197–213
- Jensen EC., Overview of live-cell imaging: Requirements and methods used, *The Anatomical Record* 296, 1 (2013), 1–8