Segmentation, Tracking and Lineaging of Proliferating Cells from 2-D to 5-D

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Modern microscopes are able to capture huge quantities of multidimensional time-lapse image data. Multichannel 3-D time-lapse (5-D) microscopy allows cell dynamics to be captured in the intact micro-environment (Figure 1). Long term phase contrast imaging incorporates multiple fluorescence channels to interrogate cell state throughout clonal development (Figure 2). We have developed a set of computational tools called LEVER (lineage editing and validation) for measuring the developmental properties of cells and clones imaged with 2-D and 3-D multidimensional time-lapse microscopy[1-3]. LEVER combines visualization with automated image analysis techniques, allowing humans to explore the high dimensional imaging data together with the automatic measurements of cell and clone dynamic development.

Measuring the development of cells that are proliferating, or dividing, from live cell microscopy image data requires accurate segmentation, tracking and lineaging. Automated algorithms for segmentation, tracking and lineaging continue to improve in accuracy, but will never be perfect. LEVER incorporates visualization to allow humans to inspect the image data together with the analysis results, allowing any errors to be more easily detected and quickly corrected.

The LEVER program combines high performance DirectX 3-D graphics acceleration and a C language based cell tracker all scripted and controlled from the MATLAB programming environment. This talk will describe newly developed hardware accelerated 3-D image processing and multimodal fluorescence analysis tools recently added to LEVER. The software is available free and open source from http://bioimage.coe.drexel.edu.

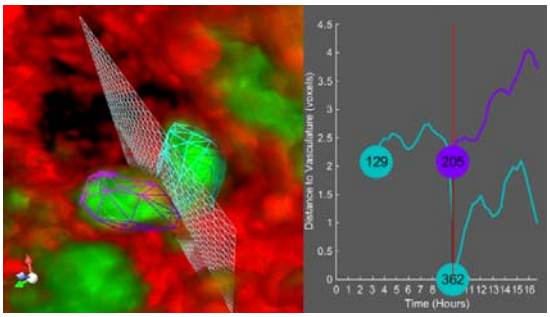

Figure 1. LEVER captures the spatial relationships between dividing stem cells and their intact environment in live tissue. 5-D image sequence (left) shows stem cells (green) dividing in the vascular niche. The lineage tree (right) shows division timing along with distance between each cell and the nearest vessel.

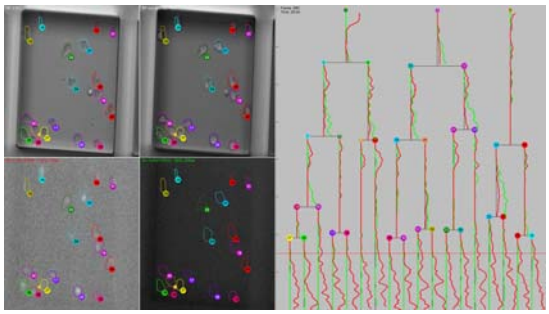

Figure 2. LEVER processes 2-D multimodal image data, segmenting and tracking brightfield images (top), and incorporating FUCCI fluorescence markers that indicate cell cycle state (bottom). The FUCCI intensity curves for each cell is encoded on the lineage tree (right).

References

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2. Wait, E. *et al.* Visualization and Correction of Automated Segmentation, Tracking and Lineaging from 5-D Stem Cell Image Sequences. *BMC Bioinformatics* **15**, 328, doi:10.1186/1471-2105-15-328 (2014).
3. Winter, M. *et al.* Vertebrate Neural Stem Cell Segmentation, Tracking and Lineaging with Validation and Editing. *Nature Protocols* **6**, 1942-1952, doi:10.1038/nprot.2011.422 (2011).