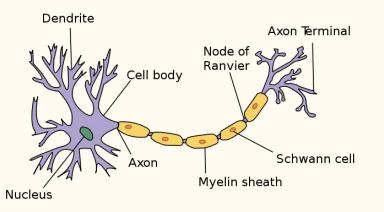
Metrics for Comparing 3D Neuron Segmentations in Expansion Microscopy Connectomics

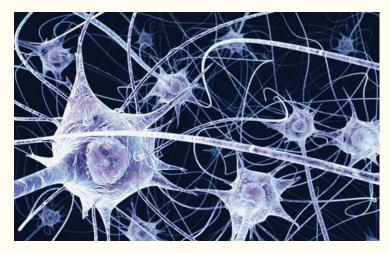
By Albert Gerovitch Mentors: Adam Marblestone, Daniel Goodwin (Boyden Lab)

Background Information

Neurons

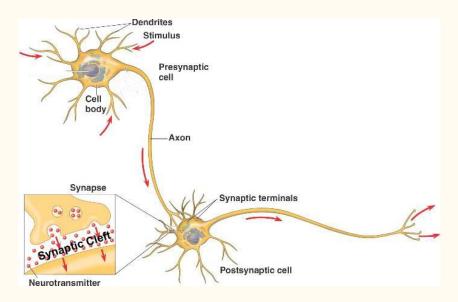
- Functional unit (cell) of the nervous system
 - \circ Convey information in the brain
 - \circ Electrical and chemical signals
- Provide foundation for brain function
 - $\circ \quad \text{Understanding the brain} \\$





Synapses

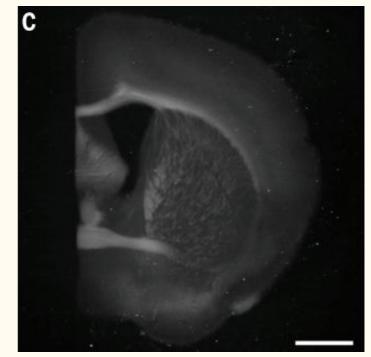
- Connections between neurons
 - Signals transferred
- Knowing shape of neuron would help track signals
- Looking at individual neurons for now
 - $\circ \quad \ \ {\rm Multi-cell\ connected\ networks\ later}$



Expansion Microscopy Connectomics

- Study of comprehensive maps of connections in the nervous system
- Traditional light microscopy up to 300nm
- Expansion microscopy works by physically expanding tissue
 - \circ Allows large 3D images at high resolutions
 - \circ Color
 - \circ 5x can see down to 60nm

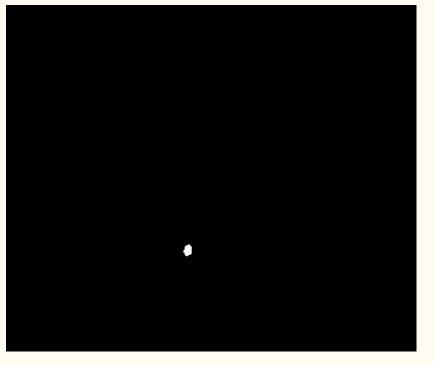




(Chen, Tillberg, Boyden 2014)

Segmentation

- Finding and isolating shape of individual neuron(s)
- Laborious for humans, computers would accelerate process
- Difficulties with misleading background "noise," isolating individual neuron

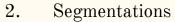


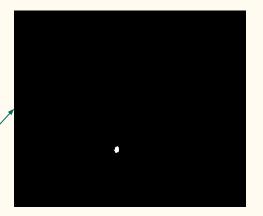
Goal

- Implement metrics to evaluate the performance of a computer algorithm at segmenting neurons in 3D
- Ultimately find the best segmentation algorithm

Raw Data 1.







MATLAB

3. Adjusted

0

imclose, ımfıll

Obtaining Segmentations

Metrics of Segmentation Performance

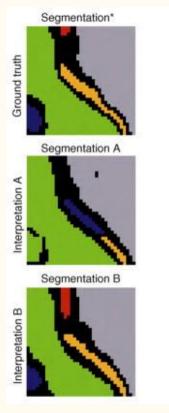
Metrics of Segmentation Performance

- Compare segmentation from computer vs. human ("ground truth")
- Error types: deletion, split (incorrect boundary), merger (incorrect gap)
- Ideal metric: tolerate minor differences, strongly penalize splits/mergers (topological disagreements)

Evaluation metrics:

- *Pixel error* count number of pixels where computer disagrees with human

 Misleading, fails to notice intuitive disagreements
- *Rand error* fraction of pixels pairs that belong to same region in one segmentation but not other
- *Warping error* count of topologically-relevant boundary labeling errors



(Jain, Seung, Turaga)

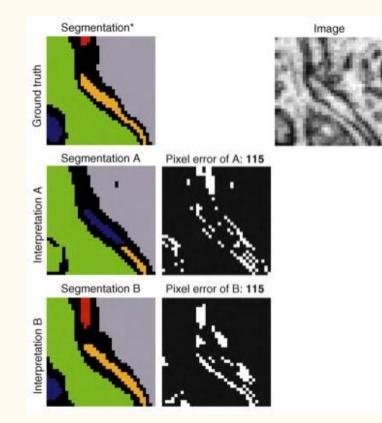
Visual comparison of evaluation metrics

Image

• Human interpretation

• Contains deletion, split, and merger

• Contains no serious errors



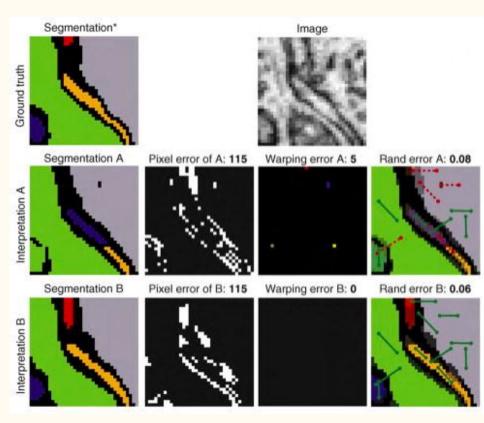
(Jain, Seung, Turaga)

Visual comparison of evaluation metrics

• Human interpretation

- Contains deletion, split, and merger
- *Pixel error* misleading

• Contains no serious errors



(Jain, Seung, Turaga)

Visual comparison of evaluation metrics

• Human interpretation

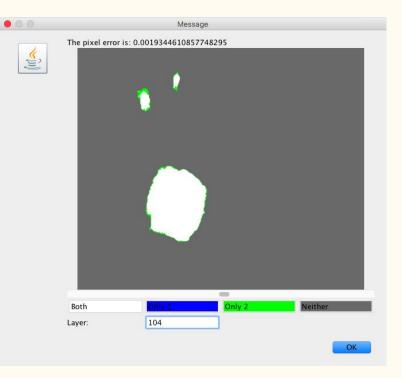
- Contains deletion, split, and merger
- *Pixel error* misleading

- Contains no serious errors
- *Warping error* and *Rand error* much better representation

Developing an Application

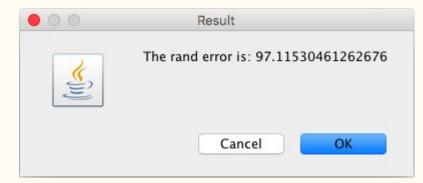
Working with Pixel Error

- *Pixel error* count number of pixels where computer disagrees with human
- Wrote program in Java
- Able to:
 - Give score as decimal
 - \circ Visualize error
 - See where segmentations differ
 - Provide feedback for developers of algorithms
 - Export result as TIFF



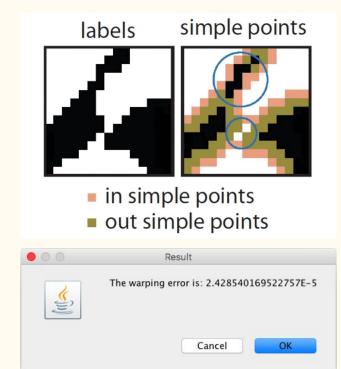
Working with Rand Error

- *Rand error* fraction of pixels pairs that belong to same region (connected component) in one segmentation but not other
- Able to:
 - Give score as decimal
- Improvements:
 - Solve accuracy issues
 - Generate visualization



Working with Warping Error

- *Warping error* fraction of topologically-relevant boundary labeling errors
- Able to:
 - $\circ \quad \ \ {\rm Give \ accurate \ score \ as \ decimal}$
- Improvements:
 - Generate visualization
 - Improve speed (currently ~ 10 min to run)



Conclusions

Results

- Wrote program able to compare two segmentations with pixel, rand, and warping error
 - $\circ ~~ Visualize/export ~pixel ~error$
- Applied application to expansion microscopy data
 - \circ Converted segmentations to common format (TIFF image)
- Ongoing: Collaborating with Boyden Lab researchers to provide feedback for algorithms

Future Plans

- Visualize results of Rand and Warping error
 - $\circ \quad \ \ {\rm Provide \ better \ feedback \ for \ algorithm \ developers}$
- Add capability to evaluate multi-cell segmentations
- Automate scoring and improving algorithms



Multi-cell segmentation courtesy of Nick Barry (Boyden Lab)

Sources

- <u>http://expansionmicroscopy.org/15.01.chen.FULL.pdf</u>
- <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2975605/#S7title</u>
- <u>imagej.net/Topology_preserving_warping_error</u>
- https://www.sfn.org/~/media/SfN/Documents/Short%20Courses/2011%20S
 hort%20Course%20II/2011_SC2_Seung.ashx

Acknowledgements

- Dr. Adam Marblestone and Daniel Goodwin, my mentors, for suggesting the project and guiding me through the process
- MIT PRIMES program, and in particular Dr. Slava Gerovitch and Dr. Pavel Etingof, for making this experience possible and Slava for being a wonderful dad
- Prof. Ed Boyden, Nick Barry, Grace Huynh, and the entire Synthetic Neurobiology group, for giving me the opportunity and resources to work on this amazing research









