

Week of 9/11 Deliverables

Claritrons team

Last week's goals

- Committed
 - ✓ Literature review - [Link to detailed summaries](#)
 - ✓ Tractography (Vikram)
 - DoD: Bibliography with list of relevant papers + summary (1 paragraph)
 - ✓ Cell Counting/Detection (Srivathsa)
 - DoD: Bibliography with list of relevant papers + summary (1 paragraph)
 - ✓ Connectomics (Jason)
 - DoD: Bibliography with list of relevant papers + summary (1 paragraph)

Tractography

- [Neuron Tracing in Perspective](#) (2010)
 - Long review paper and good resource to find other papers on the topic
 - Numerous methods for performing each step in workflow
 - Tree segmentation
 - Global
 - Local
 - Provides list of software for performing segmentation

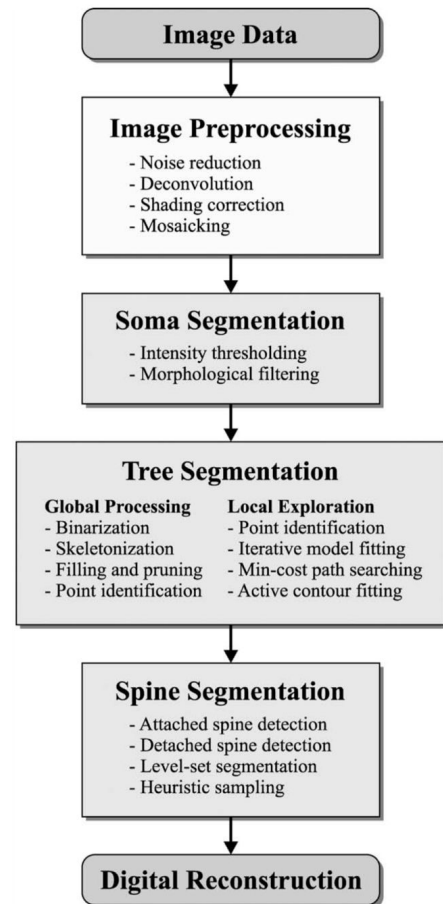
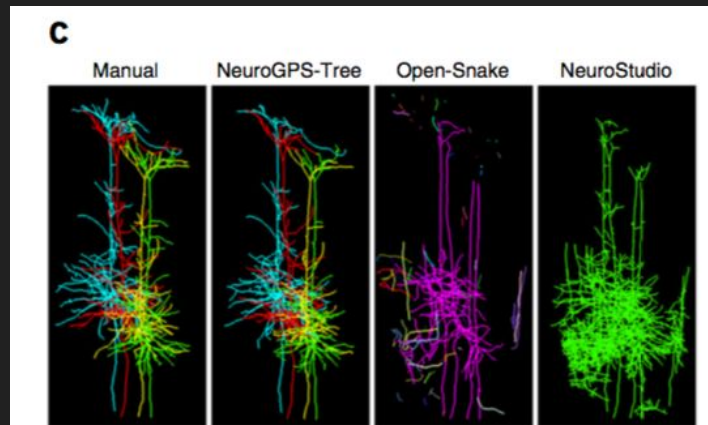


Figure 2. Flow diagram sketching the key processing steps to obtain digital neuronal reconstructions starting from the raw image data. As discussed in more detail in the main text, these include image preprocessing, soma segmentation, tree segmentation, and finally spine segmentation. The box (rectangle) corresponding to each of these main processing steps also lists the most frequently used approaches for performing that step.

Tractography

- NeuroGPS-Tree: automatic reconstruction of large-scale neuronal populations with dense neurites (2016)
 - Software to perform automated analysis on sparse and dense neuronal trees
 - Algorithm based on constrained principal curves for initial identification
 - Spurious links pruned and disconnected branches joined next
 - Use of constrained principal curves and rayburst sampling method allows effective reconstruction of:
 - Crossing processes
 - Parallel processes
 - Sharp direction change of processes

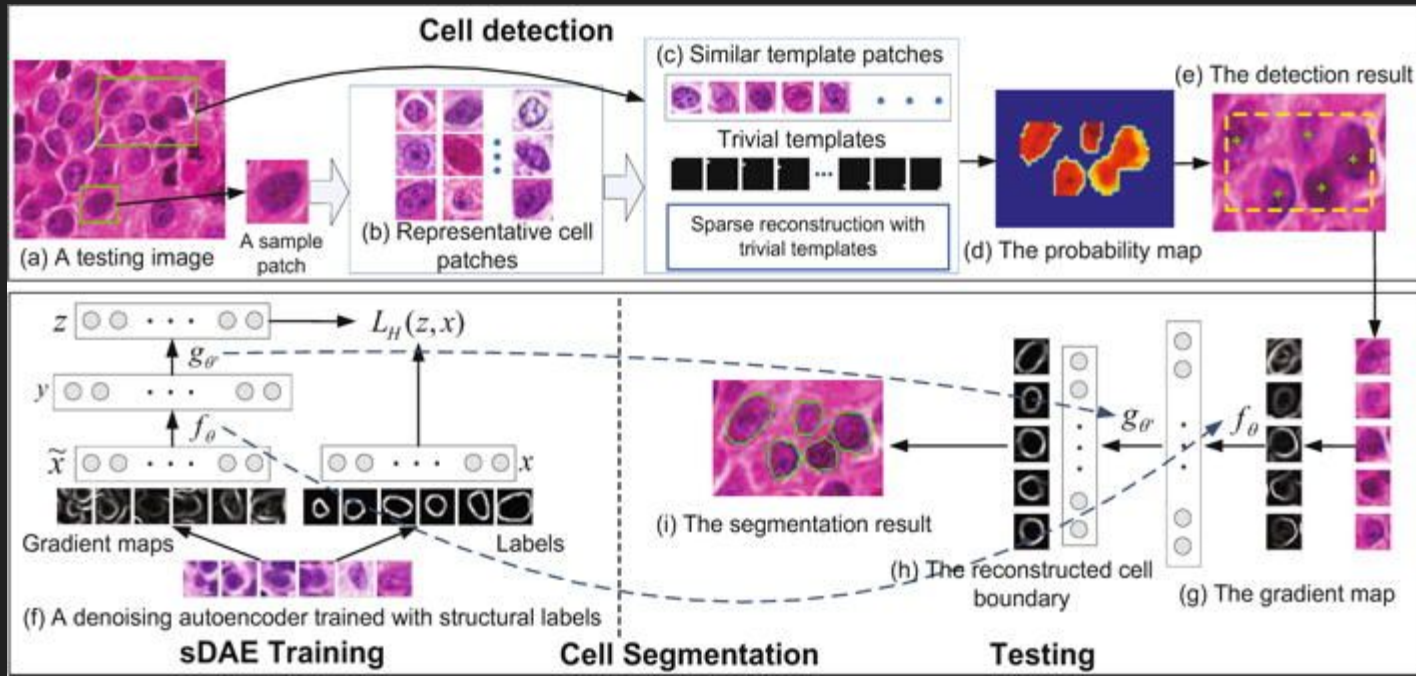


Cell detection

1. *Robust Cell Detection and Segmentation in Histopathological images using sparse reconstruction and stacked denoising autoencoders*
 - a. **Single Line Summary:** Sparse reconstruction with trivial templates and stacked Denoising Auto-Encoders (sDAE)
2. *3D segmentation of neuronal nuclei from confocal microscope image stacks*
 - a. **Single Line Summary:** Proposes 3D reconstruction algorithm that can be used with an array of different 2D segmentation algorithms

Paper 1

- Robust Cell Detection and Segmentation in Histopathological images using sparse reconstruction and stacked denoising autoencoders*



Paper 1 (cont...)

- A compact cell dictionary is learned by applying K-Selection to a cell-patch repository containing single centered cells.
- In the testing, a sample patch from the input image is used as a query to obtain similar patches from the learned dictionary.
- *Trivial templates* are used to generate a probability map of possible locations of cells by sparse reconstruction.

Paper 2

- *3D segmentation of neuronal nuclei from confocal microscope image stacks*

Algorithm 1

3D Reconstruction Algorithm.

```
1:  for every 3D connected component do
2:      Obtain the 3D Bounding Box of the connected component.
3:      Initialize a set of cells with the 2D information of the first slice ( $S_0$ ). Slices are numbered in increasing order and they are processed from top to bottom. If this
        first slice contains  $k$  2D cells, each of the 3D cells will be numbered accordingly ( $C_1$  to  $C_k$ ).
4:      for each remaining slice ( $S_i$ ) do
5:          Compute the overlapping of each 2D cell ( $c_{i,j}$ ) in current slice ( $S_i$ ) with the bottom-most slice of each of the currently identified cells ( $C_j$ ) (provided that the
            bottom-most slice of that cell is at position  $i - 1$ , i.e., both slices are directly touching; if they are not touching, the overlap is zero).
6:          If cell  $c_{i,j}$  overlaps similarly with several bottom-most slices ( $c_{i-1,l}, c_{i-1,m}$ ) of several cells ( $C_l, C_m$ ), cell  $c_{i,j}$  is divided into multiple parts. To
            consider two or more overlappings of similar size, the difference between them can not exceed a given threshold ( $\delta_1$ ).
7:          For the remaining cells, assign each 2D cell ( $c_{i,j}$ ) of current slice ( $S_i$ ) to the 3D cell it overlaps the most, given that this overlapping is over a minimum
            threshold ( $\delta_2$ ).
8:          Cells not satisfying the minimum overlapping threshold  $\delta_2$  are assigned to a new 3D cell ( $C_{k+1}$ ).
9:      end for
10: end for
```

Paper 2 (cont...)

- A robust 3D reconstruction algorithm irrespective of the 2D segmentation method used
- Addresses the problems of under and over-segmentation, during the reconstruction phase
- Results for various 2D segmentation variants like Two-step binarization, Watershed, Clump-splitting, Level set methods etc are analyzed

Connectomics

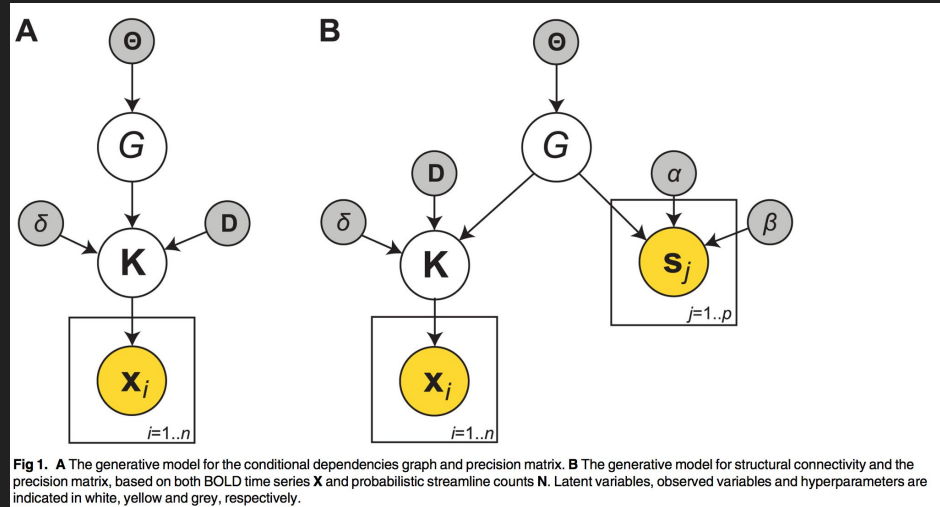
Long summaries: <http://bit.ly/2wR1Qvx>

Papers read:

- Title: Connectomic Analysis of Brain Networks: Novel Techniques and Future Direction
 - A survey of the different technologies and techniques used in connectomics along with the current major challenges and future developments in the field. Parts relevant to us are:
 - CLARITY is a promising avenue of pursuing connectomics as it is the best tissue clearing method and allows for brain-wide mapping while maintaining fine cellular resolution.
 - Data analysis pipelines is the biggest challenge in connectomics.
- Title: CLARITY for mapping the nervous system
 - The inventors of CLARITY explain the opportunities of CLARITY in connectomics research and how it's global-local resolution can allow for advances in the field.
 - The ability of CLARITY to be used in conjunction with multiple different immunolabeling, phenotyping, imaging methods makes it a powerful supplement to existing methods.

Connectomics

- Title: Bayesian Estimation of Conditional Independence Graphs Improves Functional Connectivity Estimates
 - A bayesian approach to mapping functional connectivity in different regions of brain using resting BOLD fMRI data.
 - Graphical representation of model to right:
 - Model A is the simple one for computing the partial correlation.
 - Model B is a extension that uses structural connectivity to add more expressibility.
 - G is the graph prior, \mathbf{x}_i are the brain regions, K is the covariance matrix, \mathbf{s}_j is structural connectivity data from tractography.



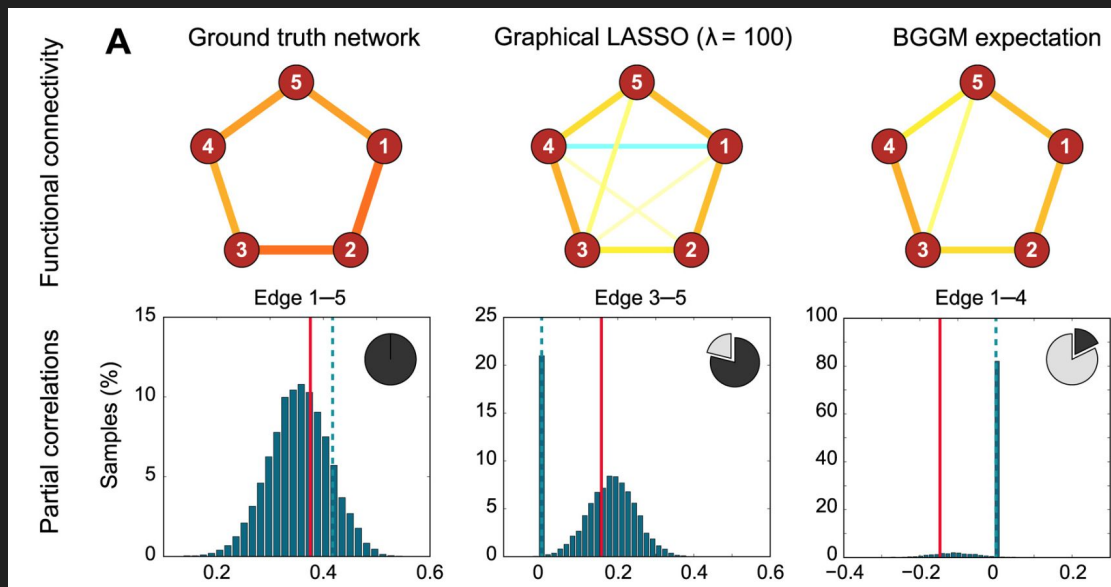
$$P(G, \mathbf{K} \mid \mathbf{X}) \propto P(\mathbf{X} \mid \mathbf{K})P(\mathbf{K} \mid G)P(G)$$

The equation for Model A

- For those interested in methodology, they used MCMC to approximate the graph posterior, took its MAP, and then transformed the precision (inverse covariance) matrix into the partial correlation matrix. The partial correlation matrix was then used to build the connectivity graph with the values indicating connection strength.

Connectomics

- Using simulations and with actual fMRI data they achieve promising results that show the bayesian approach improves upon previous point-estimation LASSO/MLE approaches
- A simple result of the bayesian analysis on simulated data is shown to the side
- The nodes represent regions and edges are connectivity calculated for ground truth, graphical lasso, and bayesian GGM (gaussian graphical model)



In the graphs, the solid blue is the posterior distribution, the red is the point-estimation of LASSO, the dotted line is the ground truth value. As you see the mode is closer to the ground truth in 2 of the 3 graphs and also tell us how certain each estimate is based on the distribution.



Connectomics summary

- Connectomics would be awesome to explore with CLARITY data.
- The graphical model approach seems to be the most popular in terms of functional connectivity modeling (see bibliography).
- I did want to note that I am an organizer (director) of Hophacks and the event is this weekend (9/15-9/17) so I'm going to be busy running it.

Next week

- Cell detection software survey (Srivathsa)
 - DoD: List of software tools with functionality and brief description (<1 paragraph)
- Draft of project proposal (Vikram and Jason)
 - DoD: draft of proposal
- Become more familiar with the Boss (Jason and Srivathsa)
 - DoD: Download a subvolume of a given dataset