Module 3
Graph Theoretic Segmentation

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Neuroscience will be the main application of information theory as we transition from the century of physics to the century of biology.

-- Toby Berger, November 2011

This lecture

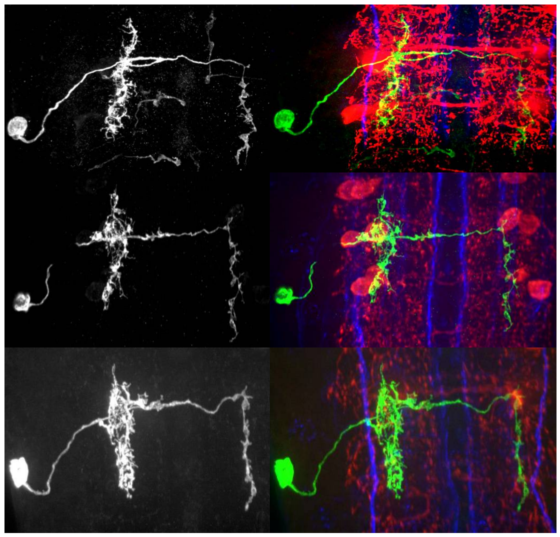
- Will address
  - (*In detail*) Graph Theoretic Segmentation and matching of filamentous objects – e.g., neurons
    - Tree2Tree Segmentation
    - Path2Path Neuron Matching
  - (*Briefly*) Graph Cut segmentation
- Will not address the entirety of graph theoretic segmentation methods for biology

The NEUROME

- Idea: create an atlas of neurons for a given organism
  - **Shape**: determines **function** and **connectivity**
  - **Is shape important?** YES!
  - Useful for determining the function/circuit of the animal
  - Useful for measuring changes in neuron morphology as targeted by a drug
- Our work: fruit fly (*Drosophila*) central nervous system neurons

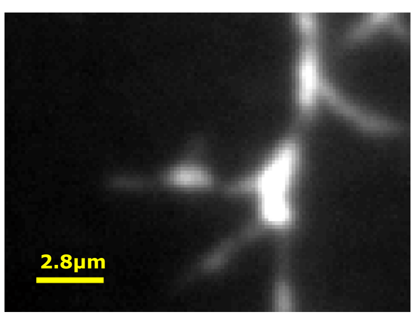
(images acquired by Barry Condron lab)

NEUROME



Challenges in Image Analysis

- Images have very low contrast, filament discontinuity and poorly defined boundaries
- Difficult to have a reliable ground truth
- Edge-finding or seed growing algorithms perform poorly because of lack of contrast and inconsistent thickness in dendritic trees.



Stages of Image Analysis in NEUROME

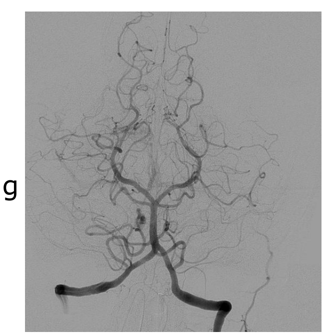
- First Stage:
  - Automatic segmentation/tracing of a single neuron
- Second Stage:
  - Use segmented neurons to build a neuron database
  - Classify neurons as same type/function
  - Use query neurons to retrieve similar neurons

To Accomplish Comparison

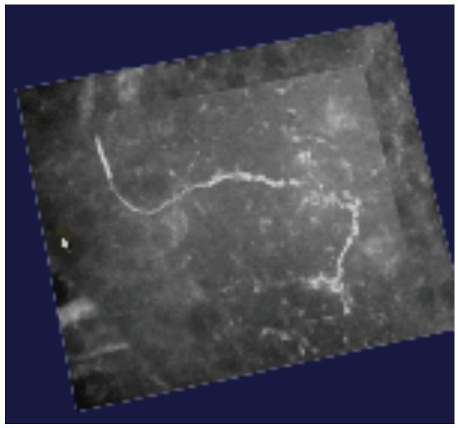
1. Segmentation (tracing): Tree2Tree
2. Neuron Matching: Path2Path

Both use basic graph theory…

Methods here can be applied to other segmentation problems in biology involving objects such as angiography



Example 3D Neuron



Hessian

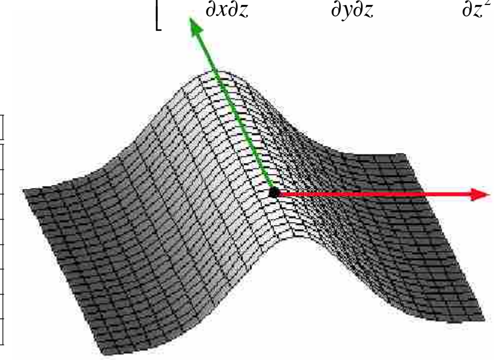
$$\begin{bmatrix} \frac{\partial^2 I(x,y,z)}{\partial x^2} & \frac{\partial^2 I(x,y,z)}{\partial x \partial y} & \frac{\partial^2 I(x,y,z)}{\partial x \partial z} \\ \frac{\partial^2 I(x,y,z)}{\partial x \partial y} & \frac{\partial^2 I(x,y,z)}{\partial y^2} & \frac{\partial^2 I(x,y,z)}{\partial y \partial z} \\ \frac{\partial^2 I(x,y,z)}{\partial x \partial z} & \frac{\partial^2 I(x,y,z)}{\partial y \partial z} & \frac{\partial^2 I(x,y,z)}{\partial z^2} \end{bmatrix}$$

Basic idea:

- Evaluate eigenvalues of Hessian

$$\mathbf{Tx} = \lambda \mathbf{x}$$

2D		3D			orientation pattern
λ_1	λ_2	λ_1	λ_2	λ_3	
N	N	N	N	N	noisy, no preferred direction
		L	L	H-	plate-like structure (bright)
		L	L	H+	plate-like structure (dark)
L	H-	L	H-	H-	tubular structure (bright)
L	H+	L	H+	H+	tubular structure (dark)
H-	H-	H-	H-	H-	blob-like structure (bright)
H+	H+	H+	H+	H+	blob-like structure (dark)



Credit: Frangi et al.

Hessian Based Directional Enhancing

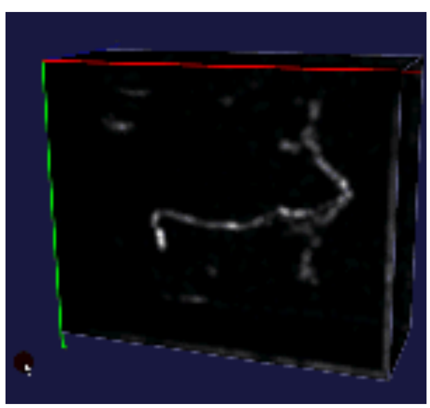
$$H(x,y,z) = \text{Hessian of 3D image } I(x,y,z) = \begin{bmatrix} \frac{\partial^2 I(x,y,z)}{\partial x^2} & \frac{\partial^2 I(x,y,z)}{\partial x \partial y} & \frac{\partial^2 I(x,y,z)}{\partial x \partial z} \\ \frac{\partial^2 I(x,y,z)}{\partial x \partial y} & \frac{\partial^2 I(x,y,z)}{\partial y^2} & \frac{\partial^2 I(x,y,z)}{\partial y \partial z} \\ \frac{\partial^2 I(x,y,z)}{\partial x \partial z} & \frac{\partial^2 I(x,y,z)}{\partial y \partial z} & \frac{\partial^2 I(x,y,z)}{\partial z^2} \end{bmatrix}$$

$\lambda_1(x,y,z), \lambda_2(x,y,z)$ and $\lambda_3(x,y,z)$ are eigenvalues of $H(x,y,z)$ such that

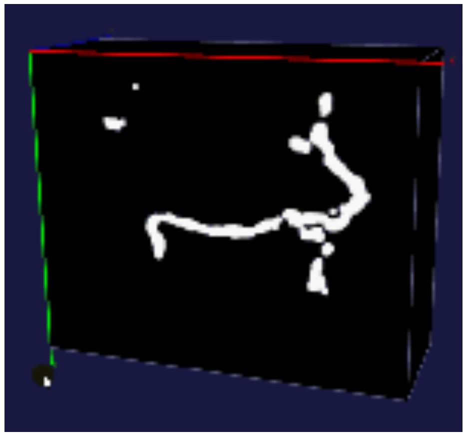
$$|\lambda_1(x,y,z)| \le |\lambda_2(x,y,z)| \le |\lambda_3(x,y,z)|$$

$$\text{Enhanced pixel } E(x,y,z) = \begin{cases} \dfrac{(|\lambda_1| - |\lambda_2|)^2}{|\lambda_1|(|\lambda_2| - |\lambda_3|)} & \text{when } \lambda_2 < 0 \text{ and } \lambda_3 < 0 \\ 0 & \text{otherwise} \end{cases}$$

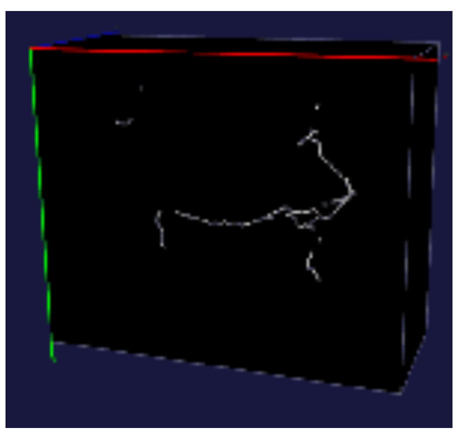
Hessian Based Directional Enhancing



Binary Clustering of Enhanced Image



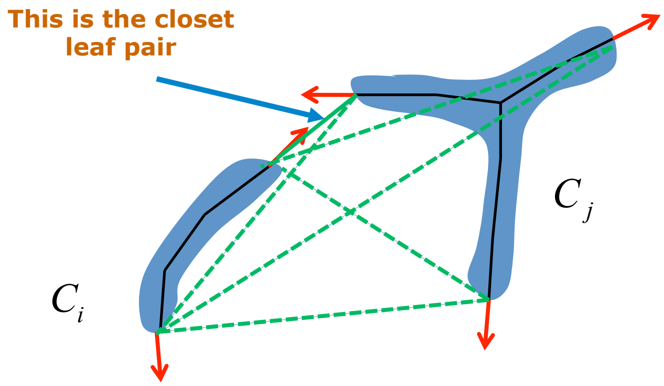
Broken Components



3D Medial Tree of Each Connected Component

Tree2Tree

- **Linking Components**

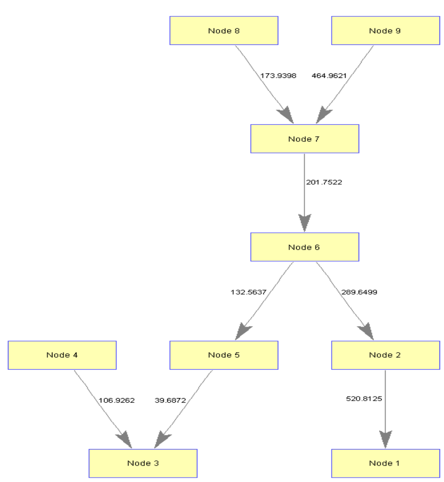


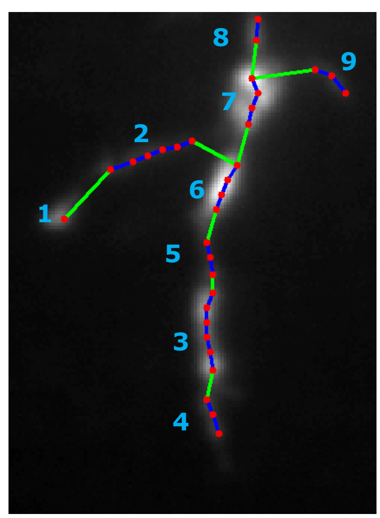
$$d_{ij} = \lambda(\text{euclidean distance}) + (1 - \lambda)(\text{leaf tangent orientation difference})$$

Basu, Aksel, Condron, Acton, 2010

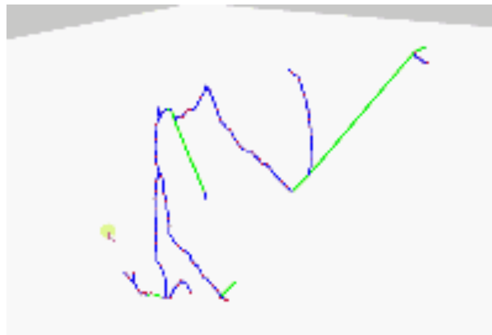
Tree2Tree

- **Step 4**: Find the minimum spanning tree of the *k*-NN graph



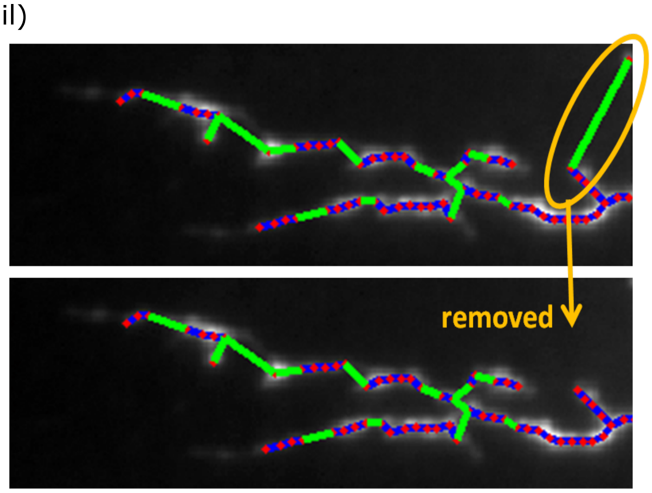


Linking Components Through Tree2Tree

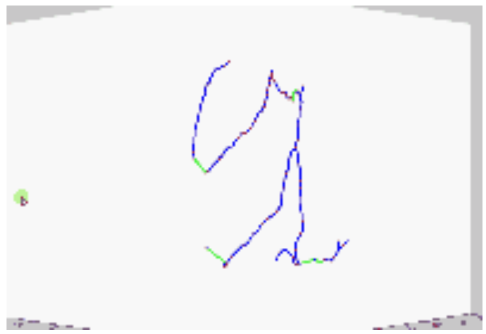


Tree2Tree

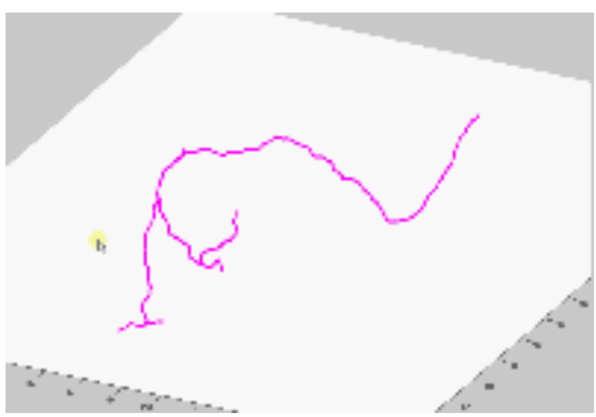
- Alpha-Beta prunes less likely nodes contributing to high edge weight - removal of cluttering artifacts (see appendix for more detail)

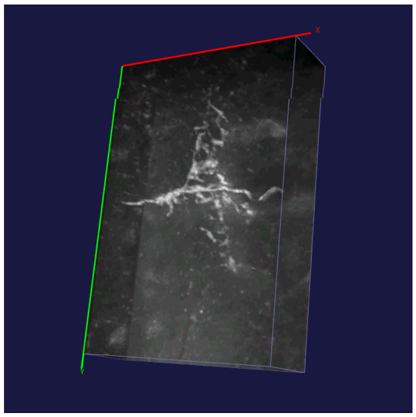


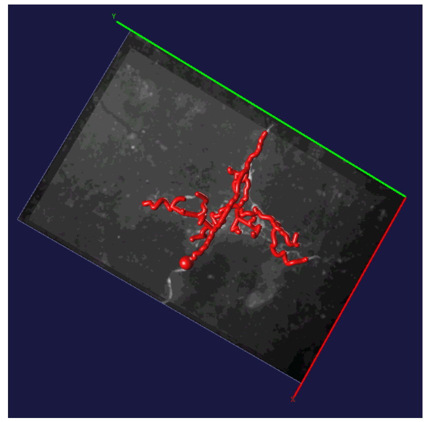
Pruning Unlikely Branches



Spline Fitting

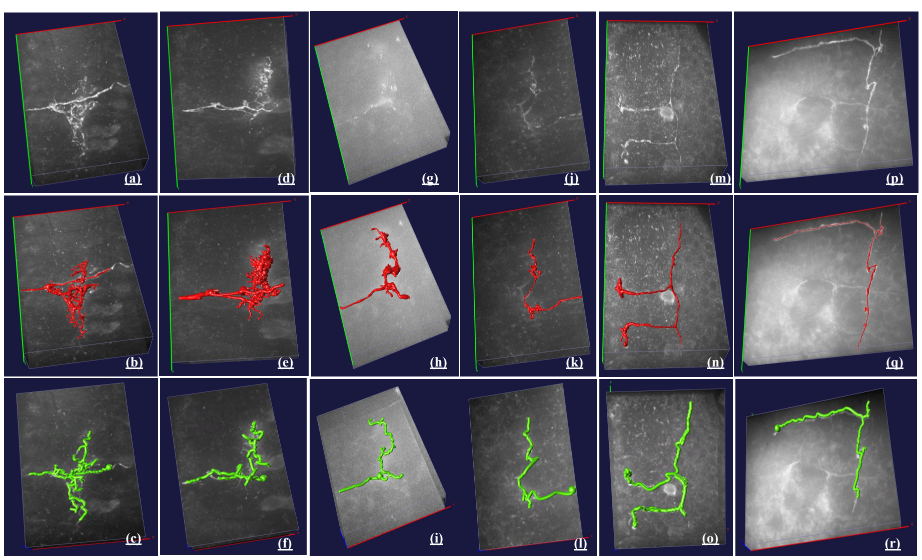






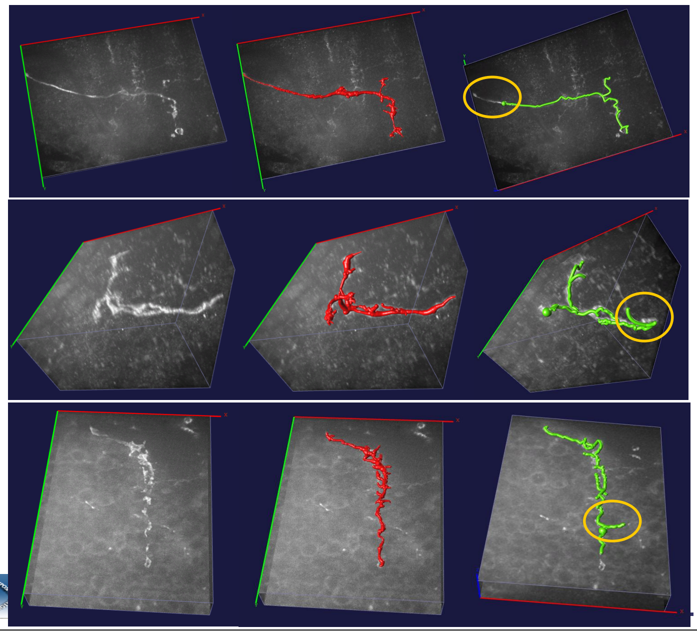
Red: Tree2Tree

Red: Truth; Green: Tree2Tree



*example in Neuron

Where does it break?



Red: Truth; Green: Tree2Tree

Need for Quantitative Comparison

- Given segmentation, we would like to compare two neurons
- Difference in morphology can provide insight into structure and function
- Morphological variation inside the same functional class reveals effects genetics or environment on specialized function

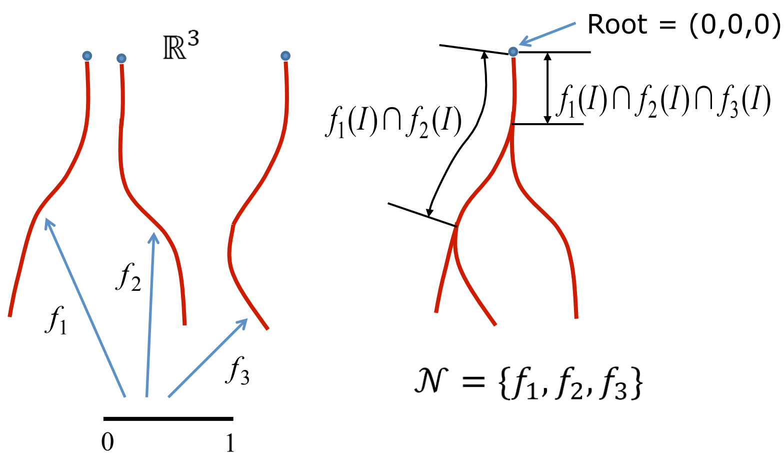
Neuron Comparison

- Based on discussion with biological collaborators
- We want to compare neuron morphology based on
  - Structure (number of branches, sub-branches, etc.)
  - Position (deviation in 3-space)
  - Hierarchy (with the notion that differences in leaves are less significant than in base branches)

Path2Path

- Paradigm shift – view neuronal tree as collection of continuous paths in 3D space that overlap along their length

A Neuron Model



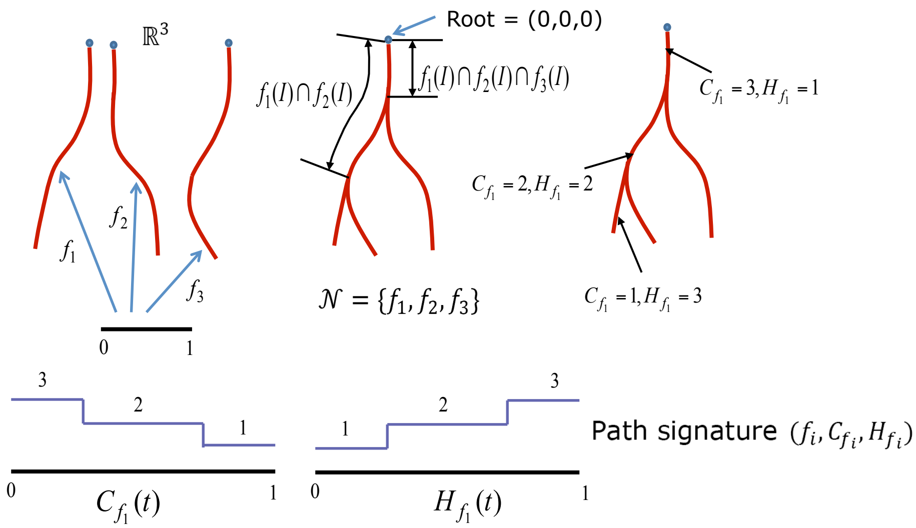
$$\mathcal{N} = \{f_1, f_2, f_3\}$$

Path Concurrence and Path Hierarchy

- **Concurrence** function of a path C_{fi} – number of times a point in a path is shared by other paths. Measure of membership and structure

- **Hierarchy** function of a path H_{fi} – number of bifurcations above a given point in a given path (plus 1).

Concurrence and Hierarchy Example



Path Deformation Cost

- For a path pair from 2 neurons

$$\mathcal{N} = \{f_1, f_2, \ldots, f_n\} \text{ and } \mathcal{M} = \{g_1, g_2, \ldots, g_m\}$$

$$f_i \in \mathcal{N} \text{ and } g_j \in \mathcal{M}$$

- Path deformation cost

$$P_{f_i, g_j} = \int_0^1 \frac{\gamma_1(C_{f_i}(t), C_{g_j}(t))\gamma_2(f_i(t), g_j(t))}{\lambda + \gamma_3} dt$$

  - One possible cost function:

$$P_{f_i, g_j} = \int_0^1 \frac{|C_{f_i}(t) - C_{g_j}(t)||f_i(t) - g_j(t)|}{\lambda + \sqrt{H_{f_i}(t) H_{g_j}(t)}} dt$$

Overall Match

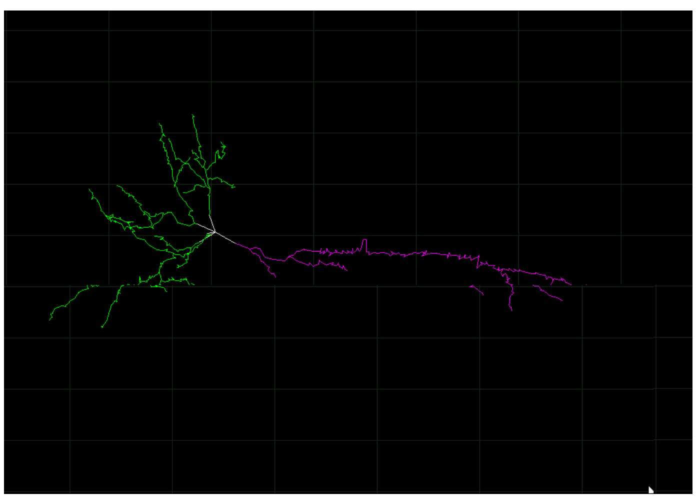
- The sum of minimum path deformation costs for each path in the query neuron $\mathcal{N}$

$$\mathcal{N} = \{f_1, f_2, \ldots, f_n\} \text{ and } \mathcal{M} = \{g_1, g_2, \ldots, g_m\}$$

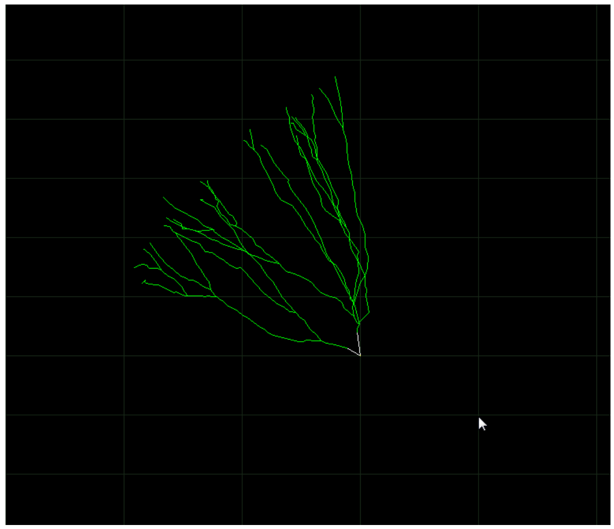
$$f_i \in \mathcal{N} \text{ and } g_j \in \mathcal{M}$$

$$P_{\mathcal{N}\mathcal{M}} = \min_{\sigma} \frac{1}{n} \sum_{1}^{n} P_{f_i, \sigma(f_i)}$$

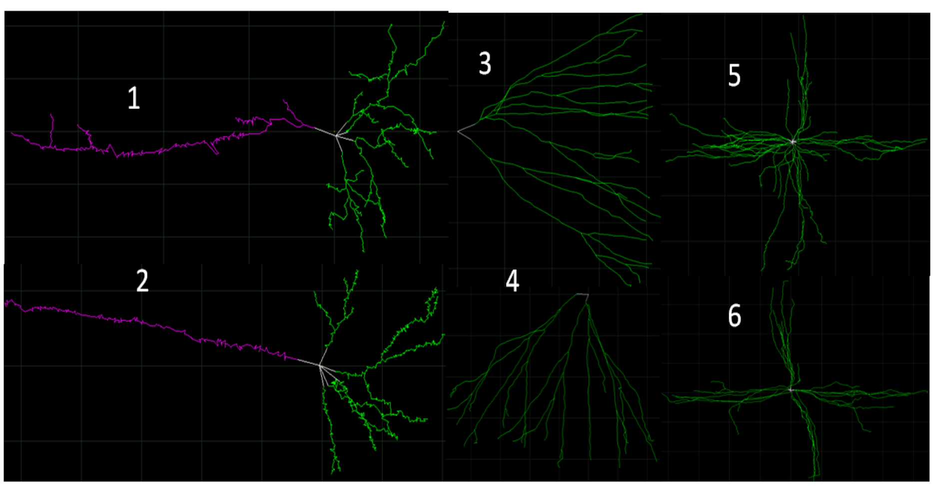
Neuron 3D view



Neuron 3D view

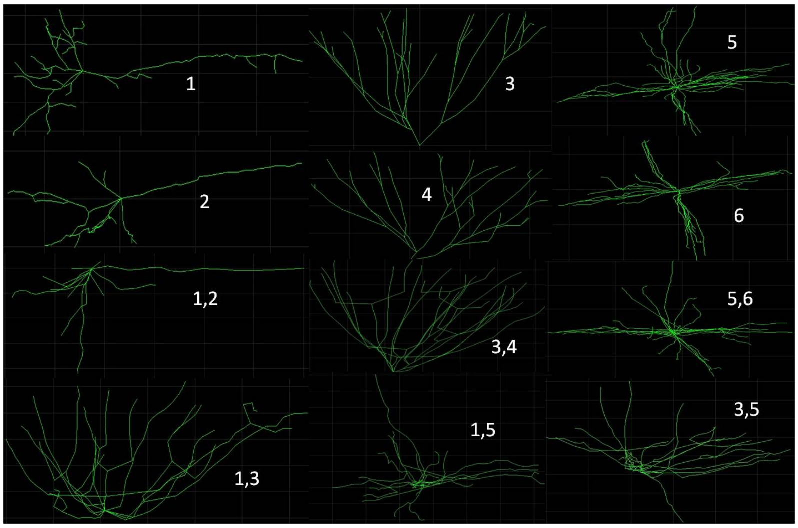


Three matching pairs of Neurons



Three examples of matching pairs (1,2), (3,4), (5,6)

Neuronal Averages

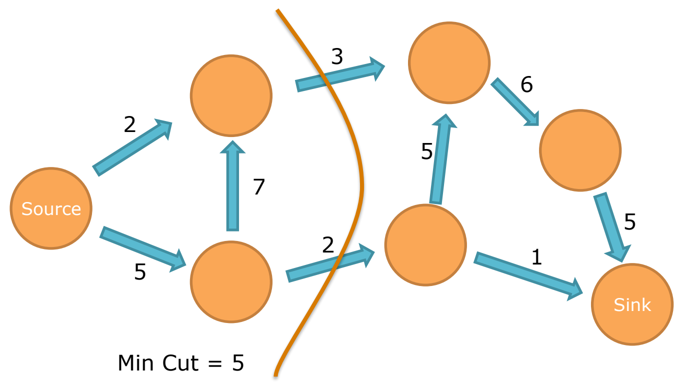


And now…

- On to graph cuts

Graph Cuts

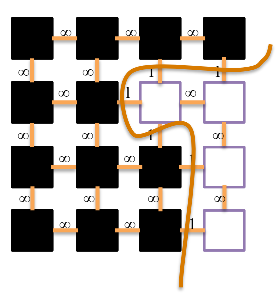
- Basic Approach: partition source, sink with minimum-energy cut



Min-Cut Applied to Images

- Weight edges between pixels
- Minimize $E_{cut} = \sum_{u \in A, v \in B} w(u, v)$

- Simple weight:
  $w(u, v) = |I(u) - I(v)|^{-1}$

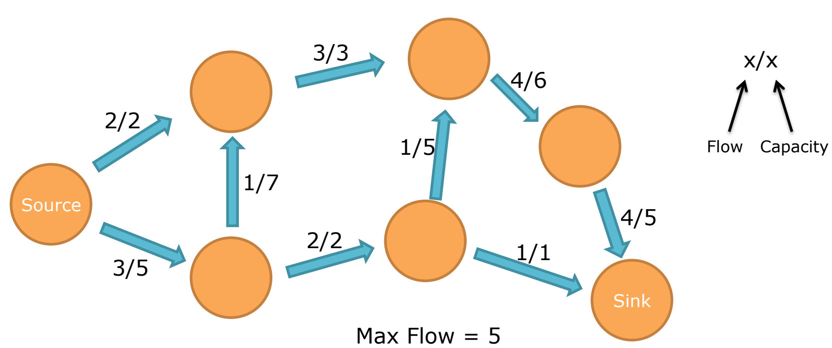


Alternatively…

- Min-Cut implementations exist, but far more effective to approach graph cuts from a different angle…
- Can optimize a general energy functional via max-flow, the dual of min-cut
  - Much more powerful and efficient!

Max-Flow

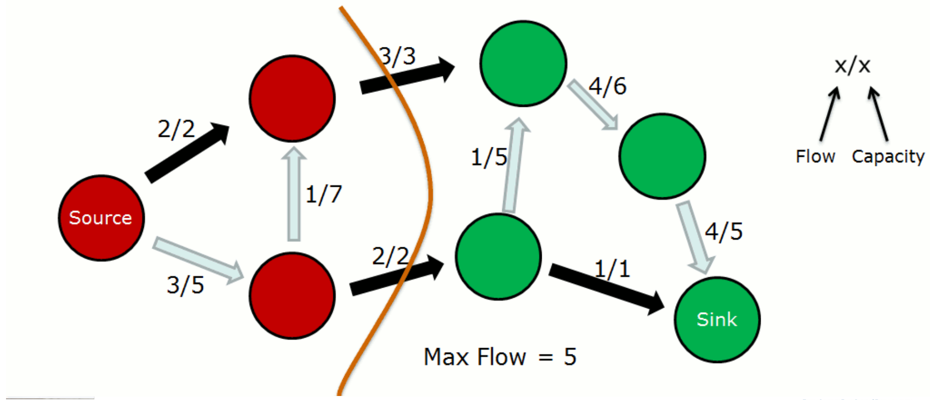
- Maximize 'flow' from source to sink
- Weights=capacities for flow
- Flow into node = flow out of node



Max-Flow/Min-Cut Duality

- With proper algorithm (search tree propagation), max-flow determines same min-cut partition

All paths saturated and no more viable nodes to adopt -- done



Max-Flow Applied to Images

$$E(L) = \lambda \underbrace{\sum_{p\in P} D_p(L_p)}_{\text{Data Term}} + \underbrace{\sum_{\{p,q\}\in N} V_{\{p,q\}}(L_p, L_q)}_{\text{Region Term}}$$

Label Matrix

Weighting Factor

- Minimize *E* (non-convex)
  - The max-flow partition corresponds to optimal label matrix
- *E* can be tailored to address various image analysis problems

Data Term

$$E(L) = \lambda \sum_{p \in P} D_p(L_p) + \sum_{\{p,q\} \in N} V_{\{p,q\}}(L_p, L_q)$$

- Penalty function based on intensity of current pixel *p*

Data Term (cont'd)

$$E(L) = \lambda \sum_{p \in P} D_p(L_p) + \sum_{\{p,q\} \in N} V_{\{p,q\}}(L_p, L_q)$$

- Example penalty function

$$D_p(L_p) = -\log(\Pr(L_p))$$

- Example *Pr*: cluster image intensities, define *Pr*() as normalized distance from intensity of pixel *p* to center of cluster *I*

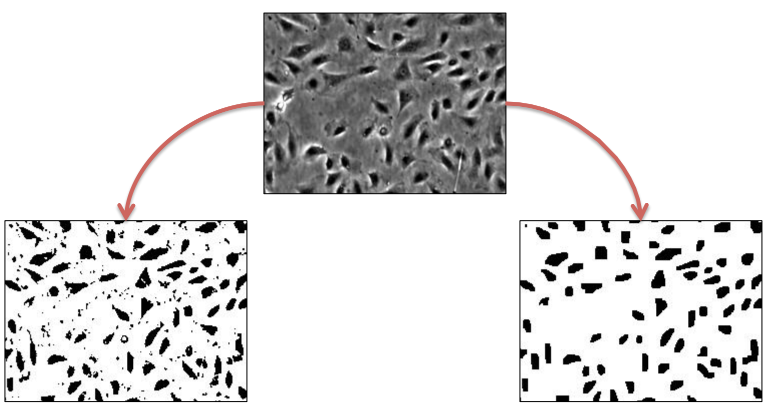
Region Term

$$E(L) = \lambda \sum_{p \in P} D_p(L_p) + \sum_{\{p,q\} \in N} V_{\{p,q\}}(L_p, L_q)$$

- Enforces spatial coherence
- Given a neighborhood N around pixel p, $V_{\{p,q\}}(L_p,L_q)$ penalizes dissimilarity between pixels p and q if they are assigned the same label
- Example V: Sobel magnitude

Why not just use clustering labels?

- Spatial coherence



k-means clustering, k=3 (darkest cluster shown)

Minimization E_{cut} with D_p based on k-means

*example in GrCuts

Optimizing *E*

See:

- "An Experimental Comparison of Min-Cut/Max-Flow Algorithms for Energy Minimization in Vision," Yuri Boykov and Vladimir Kolmogorov. In IEEE Transactions on Pattern Analysis and Machine Intelligence (PAMI), vol. 26, no. 9, September 2004, pp. 1124-1137.
- "Efficient Approximate Energy Minimization via Graph Cuts," Yuri Boykov, Olga Veksler, Ramin Zabih, IEEE transactions on PAMI, vol. 20, no. 12, p. 1222-1239, November 2001.

- We recommend: http://www.csd.uwo.ca/~olga/code.html

END

- The graph theoretic approach:
  - Neuron segmentation by **Tree2Tree**
  - Neuron matching using **Path2Path**

- Graph cuts provide a nice framework for biological segmentation

Appendix: Alpha-Beta Graph Pruning

For connected components C_i and C_j

d_{ij} = distance metric between C_i and C_j

$W(C_i)$ = weight of node C_i = Length of medial tree of C_i

Original Tree = M_o

Pruned Tree = M_p

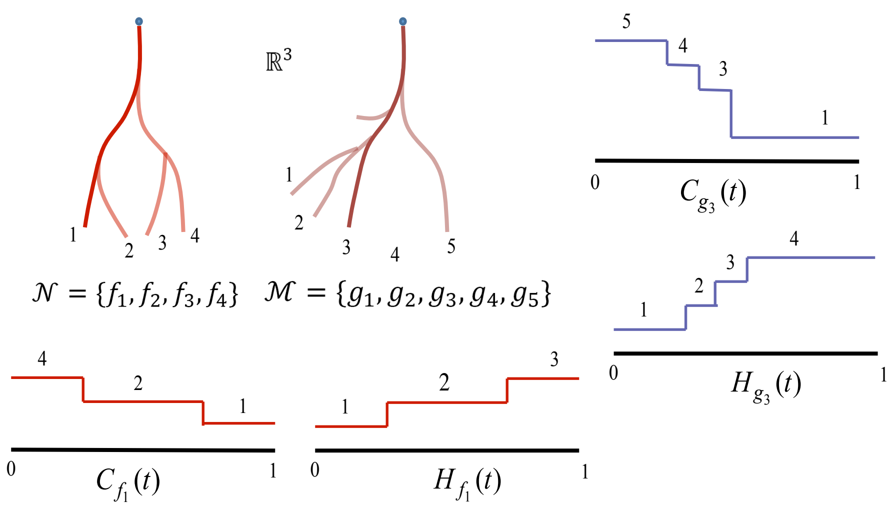
M_p = Largest subtree of M_o such that

$$\frac{\sum_{C_k \in M_p} W(C_k)}{\sum_{C_i \in M_o} W(C_i)} \geq \alpha \quad \text{and} \quad \frac{\sum_{d_{kl} \in M_p} (d_{kl})}{\sum_{d_{ij} \in M_o} (d_{ij})} \leq \beta$$

Alpha: determined by percentage of clutter

Beta: determined by maximum linking distance

Match Path 1, Neuron *N* to Path 3, Neuron *M*



Early Results

Neuron#	1	2	3	4	5	6
1	0	**64.11**	174.92	120.68	162.74	245.58
2		0	149.67	145.90	159.17	189.72
3			0	**61.41**	190.99	348.04
4				0	257.97	385.88
5					0	**96.36**
6						0

Dataset for Initial Prototype

Neuron	Archive	Animal	Brain Region	Cell Type
1	Allman	Human	Cerebral Cortex	Pyramidal
2	Allman	Human	Cerebral Cortex	Pyramidal
3	Claiborne	Rat	Hippocampus	Granule
4	Claiborne	Rat	Hippocampus	Granule
5	Cameron	Cat	Spinal Cord	Motor
6	Cameron	Cat	Spinal Cord	Motor