Bouton Detection Using Three Dimensional Models

18-795 Bioimage Informatics Course Project

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What Are Boutons?

- A vital component for understanding of the developmental dynamics of the visual cortex.
- Basically a swelling on an axon containing cellular machinery for neurotransmitter release.

What Are Boutons?

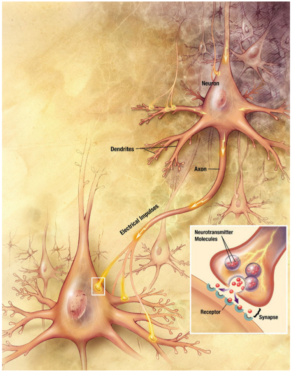

Figure: What Are Boutons?

Use Of Boutons

- Presence of boutons is indicative of one or more synapses.
- In still images, boutons indicate where a neuron sends its information.
- In live tissue work, bouton stability and change can be measure of synaptic change in the brain.

Example Image

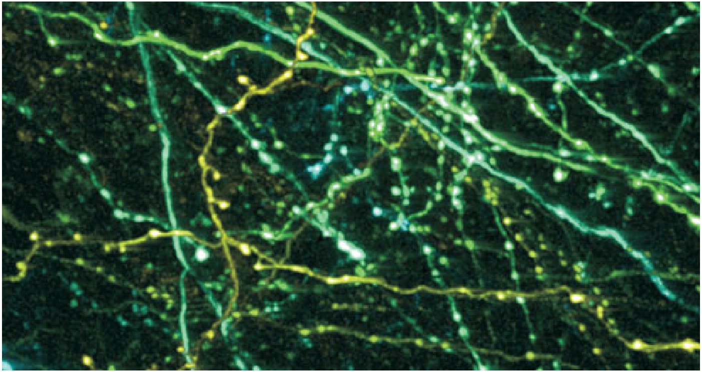

Figure: Fluorescence Microscopy Image of Axons and Boutons in a Monkey Brain

The Problem

- Bouton location and distribution are dependent variables in a variety of studies in systems neuroscience.
- The human brain has about 10^{15} synapses, and the number of images collected is vast.
- Manual bouton detection is inefficient and error-prone.

Previous Work

- Hallock et al proposed axonal bouton modeling and automated detection in a previous paper.
- The method uses simple geometric models for axonal boutons with variations in size, position, rotation and curvature.
- However, the algorithm processes volumetric data accrued from bright-field microscopy slice-by-slice as different 2D images.
- Since the data is inherently 3D, it is reasonable to assume that more information can be extracted from the data by processing it as such.

The Goal

- The goal of the project is to use similar techniques as used by Hallock et al, to model and identify boutons in a 3D field.
- The key idea is to process all the slices together as one 3D images, instead of as seperate slices.

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The Goal

1. Propose a 3D mathematical model for the bouton which exhibits variations in size, position, rotation and curvature.
2. Change the input parameters and variables to account for the new model.
3. Extend the routines and functions to handle data in 3D format.

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The Original Model

- The original model of the bouton was enclosed in a square.
- The bouton was a circle, the radius of which can be changed
- The axon was a variable thickness quadratic curve passing through the center of the bouton, with a limited curvature.
- The entire mode (axon + bouton) can be rotated by arbitrary (though discretely quantified) angle about the center of the bouton.
- Terminal boutons have only an incoming axon.

Examples

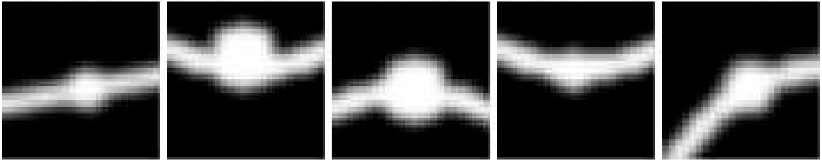

Figure: Examples Of 2D Axon-Bouton Model

The Proposed Model

- Logically extending, the new model is enclosed in a cube instead of a square.
- The new bouton is a sphere, with variable radius
- The new axon is a variable thickness *cubic* curve passing through the center of the bouton.
- The model rotation has been replaced by a different way of generating different models.

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The Proposed Model

- Rotation in three dimensions is a computationally intensive and a cumbersome process.
- Rotation is in two directions, and the angles do not add vectorally.
- Thus model rotation is not the best way of ensuring all possible orientations without significant double countings.

The Proposed Model

- We first assume equally spaced points on each face of the cube.
- Two points are chosen, and a curve passing through these points and the center of the bouton is calculated.
- This curve is assumed to be the center line, and a cylinder is generated around it using a rotating vector.
- Terminal boutons can be generated by using first one and then the other half of the axon.

The Proposed Model

$$t \in [-1, 1]$$

$$\begin{pmatrix} x(t) \\ y(t) \\ z(t) \end{pmatrix} = \begin{pmatrix} d_x & c_x & b_x & a_x \\ d_y & c_y & b_y & a_y \\ d_z & c_z & b_z & a_z \end{pmatrix} \begin{pmatrix} 1 \\ t \\ t^2 \\ t^3 \end{pmatrix}$$

$$a_x = a_y = a_z = 0$$

$$x(0) = y(0) = z(0) = 0$$

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The Proposed Model

$$t \in [-1, 1]$$

$$\begin{pmatrix} x(t) \\ y(t) \\ z(t) \end{pmatrix} = \begin{pmatrix} c_x & b_x \\ c_y & b_y \\ c_z & b_z \end{pmatrix} \begin{pmatrix} t \\ t^2 \end{pmatrix}$$

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The Proposed Model

- Rotations are taken care of.
- The limit of curvature is varied by varying the spacing of the possible end points.
- The cubic coefficients need to be set by hand, they are currently set to zero.

An Example

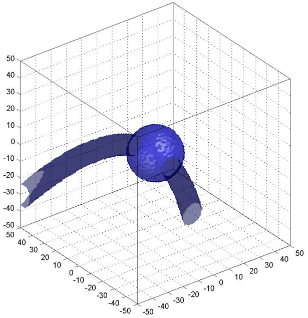

Figure: An Example Of 3D Axon-Bouton Model

Overview

- First all possible models which fit the given parameters are generated.
- Bouton locations in the image are found using normalized cross-correlation γ, between the image f and the model t at (u, v, w).

$$\gamma = \frac{\sum \left[f(x,y,z) - \bar{f}_{u,v,w}\right]\left[t(x-u, y-v, z-w) - t\right]}{\sqrt{\sum \left[f(x,y,z) - \bar{f}_{u,v,w}\right]^2 \sum \left[t(x-u, y-v, z-w) - t\right]^2}}$$

- The locations whose correlation coefficients are greater than that of a global threshold parameter T are extracted.

Flow Chart

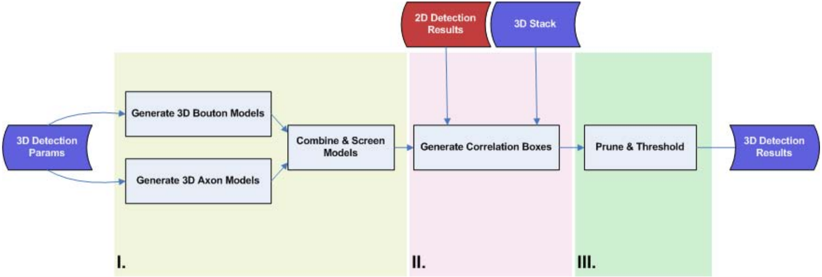

Figure: Flow Chart of the Bouton Detection Algorithm

The Algorithm

1. Set the parameters, such as ranges for radius, thickness, resolutions, and other search specific settings.
2. Generate axon and bouton models, combine them and use a blurring filter.
3. Use the output of the 2D detector to find possible locations and correlate.
4. Prune the output, use a global thresholding to weed out partial matches.

Issues

- A 3D normalized correlation takes $\mathcal{O}\left(N^3 \log N\right)$ operations for a cube of side N.
- Processing the entire image can take a long time, especially if the number of possible models is large.
- The solution is to first use the 2D code to find possible boutons in the slices, and then do the correlations only for a small space surrounding the possible boutons.

Inhomogenous Resolutions

- The resolution in Z direction is very low compared to that in X and Y directions.
- In pixel form, this translates to the 3D model being *flattened*, e.g., the boutons are no longer spheres but ellipsoids.
- Interpolation of data was considered, but since the factor between the resolutions is high (10), it was not practical.

Time And Storage Complexity

- Time complexity is still a major issue, even after using data from 2D detection.
- There is no easy way to get around this problem, we are limited by the computational complexity of the Fast Fourier Transform.

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Results

- As mentioned before, time complexity is a major issue.
- The execution time depends on the number of false alarms in the output, which can be controlled by the threshold set for the 2D boutons.
- At current settings, for bouton detection to be processed completely it can require as much as 2 days.
- As of now a few executions of our program are still running on different machines.

Input

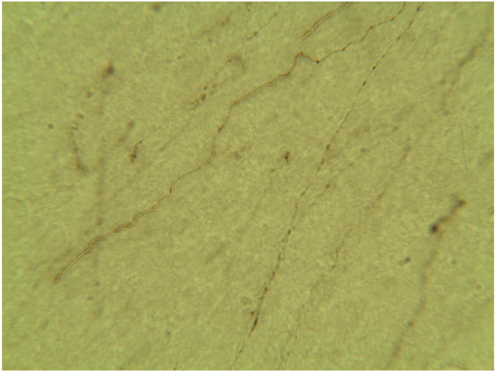

Figure: Input to the Detector, One Slice

Output

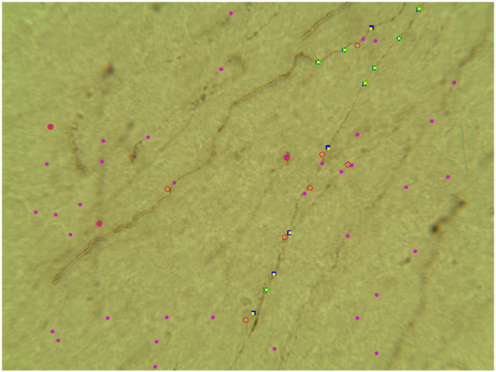

Figure: Output of the Detector, with Marked Boutons

Final Conclusion

- A new model for boutons and axons was proposed and explained.
- The 2D detection algorithm was successfully converted to work in three dimensions.
- The current algorithm is very time consuming. The complexity needs to be reduced for a practical application.

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References

Hallock, C. A., Özgüneş, I., Bhagavatula, R., Rohde, G. K., Crowley, J. C., Onorato, C. E., Mavalankar, A., Chebira, A., Chuen Hwa Tan, Püschel, M., Kovačević, J.,
Axonal bouton modeling, detection and distribution analysis for the study of neural circuit organization and plasticity
Biomedical Imaging: From Nano to Macro, 2008. ISBI 2008. 5th IEEE International Symposium on, **165-168**, May 2008.

Fast 3D normalized Cross Correlation (MATLAB Function)
`normxcorr3.m` by *Daniel Eaton*
http://www.cs.ubc.ca/~deaton/tut/normxcorr3.html

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