Topological Analysis of Neural Circuitry

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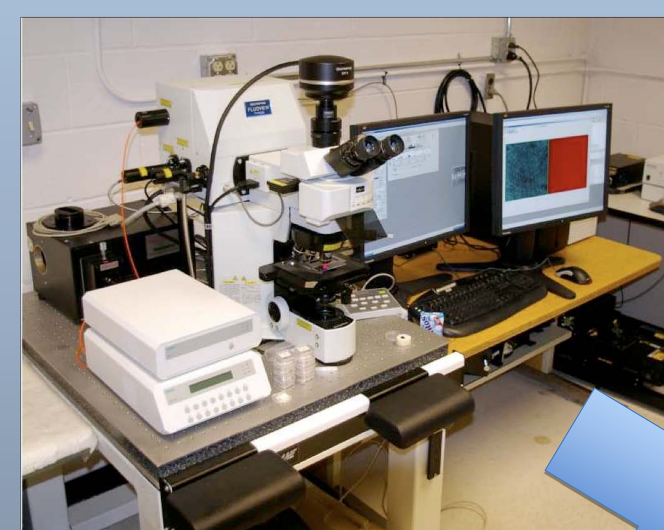
Investigating the Cerebral Cortex

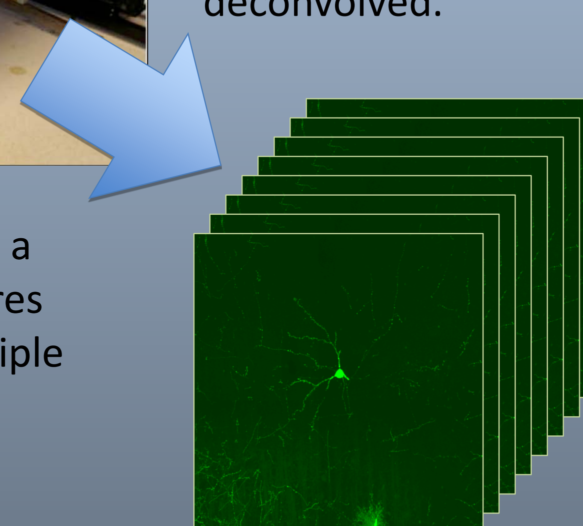
A Need for Automation

The mammalian cerebral cortex consists of billions of neurons, organized as thousands of different cell types connected into circuits. Sensory perception results from the activity of specific neural circuits. Despite over a century of neuroanatomical studies, little is known about organizing principles of cortical circuits and their role in cortical computations, due to the complexity of cortical circuits and the lack of methodologies that could reveal the fine-scale connectivity of specific cell types. The lack of wiring diagrams for most cortical circuits is perhaps the biggest impediment to understanding cortical networks and their function. A major challenge in systems neuroscience is to understand general organizing principles for these circuits that determine how they compute the cortical neuron responses underlying perception.

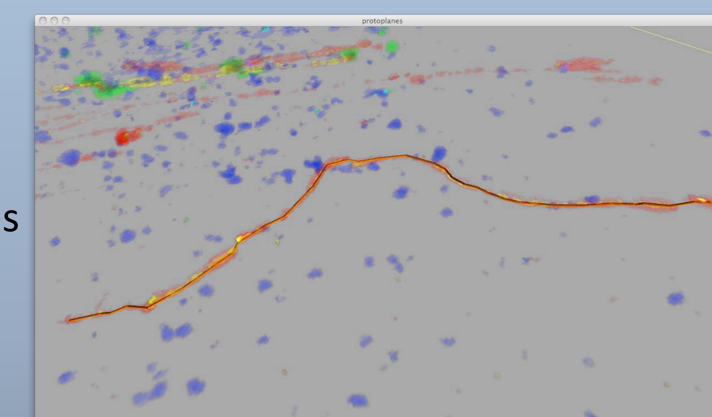
Imaging and Processing



Imaging.
After a sample is prepared, a confocal microscope acquires images of a sample at multiple depths.



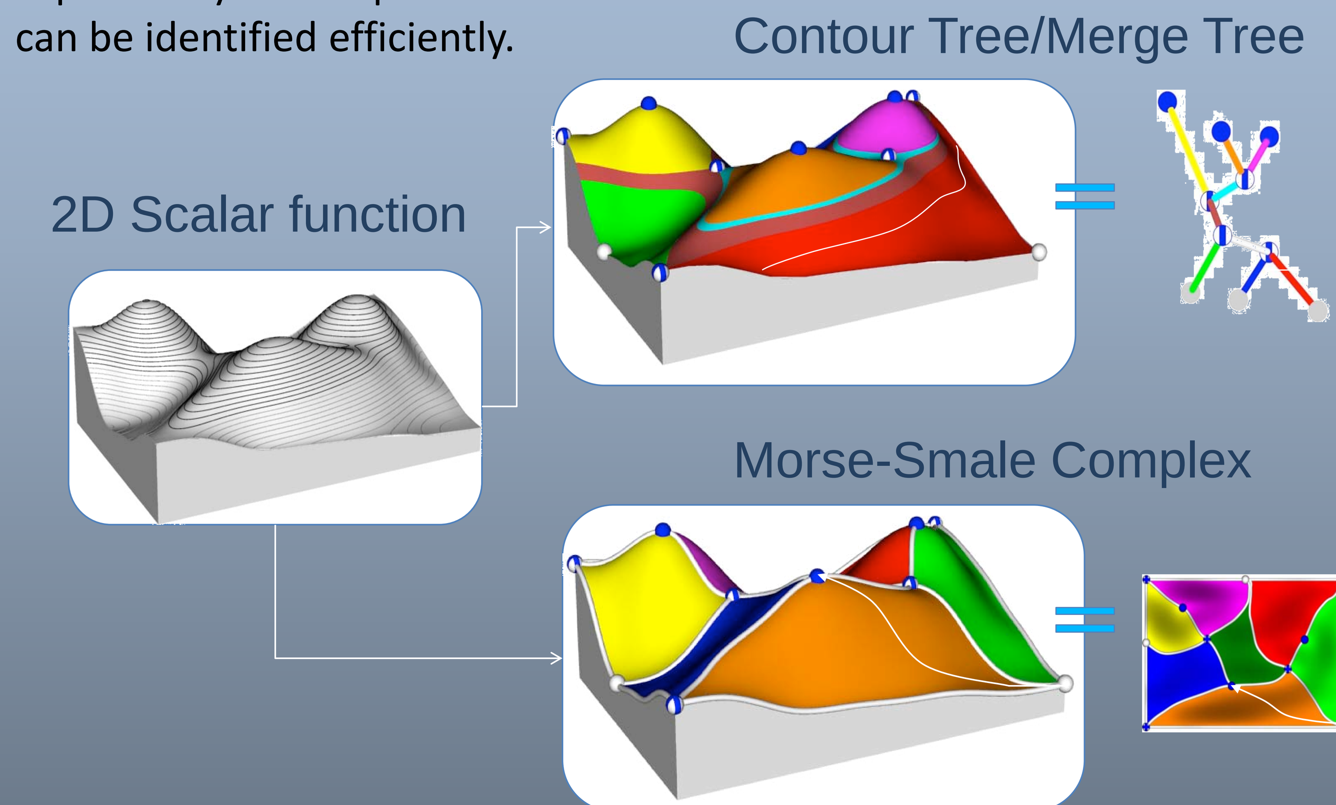
Alignment and Processing.
A sample may require several tiles, and several image stacks of adjacent tiles (both horizontally and vertically) are aligned and deconvolved.



Tracing Neuronal Processes.
Traditionally, neuronal processes are traced by hand, a time-consuming and error-prone process. A single sample may take days to trace by hand, and the scales necessary for understanding large-scale connectivity are intractable.

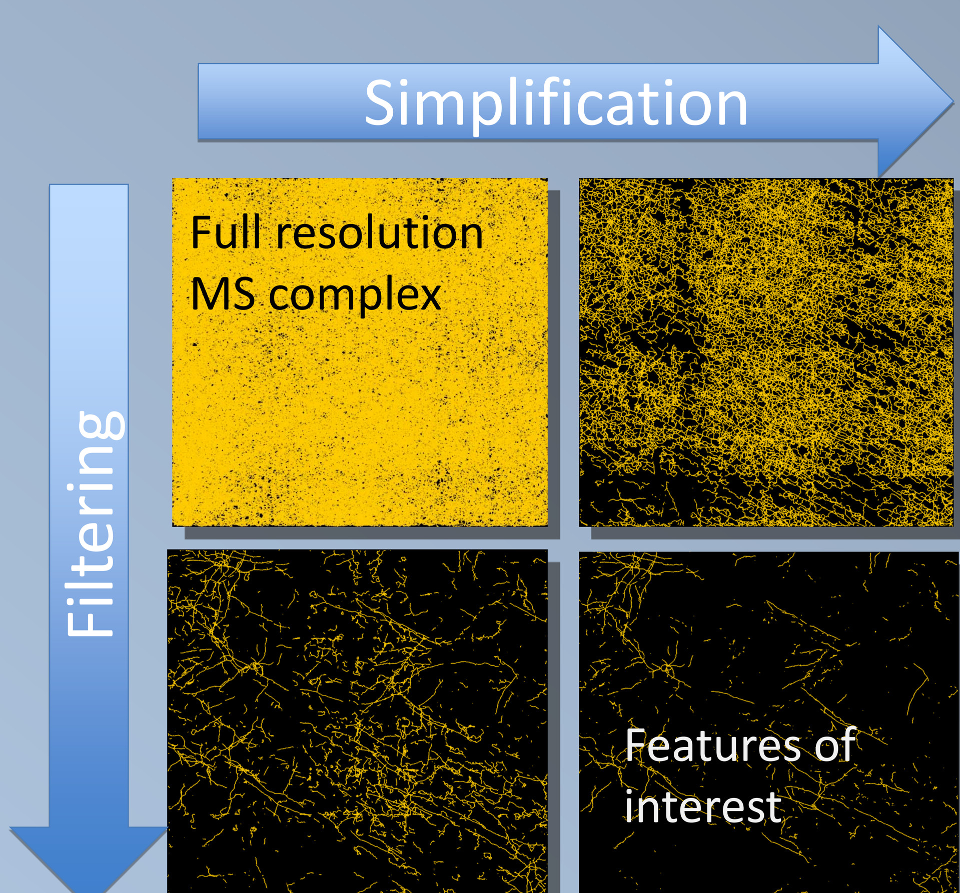
Topological Abstractions

Topological structures such as contour trees and Morse-Smale complexes represent families of features at multiple scales. Any class of feature captured by such representations can be identified efficiently.

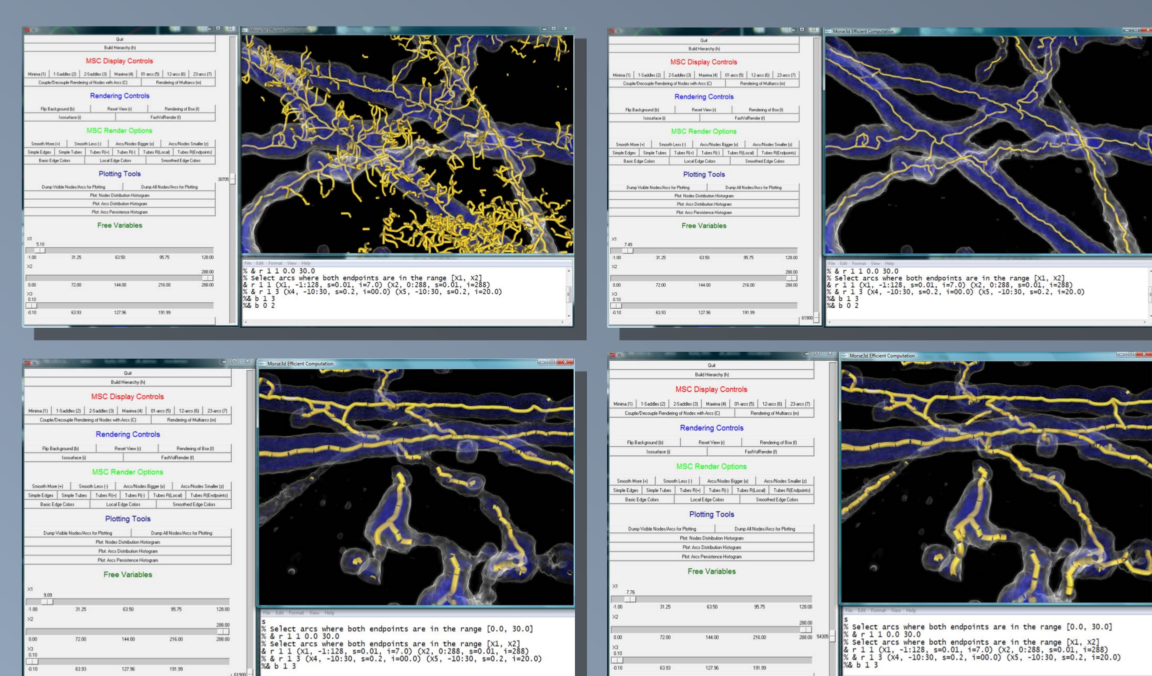


MSCEER

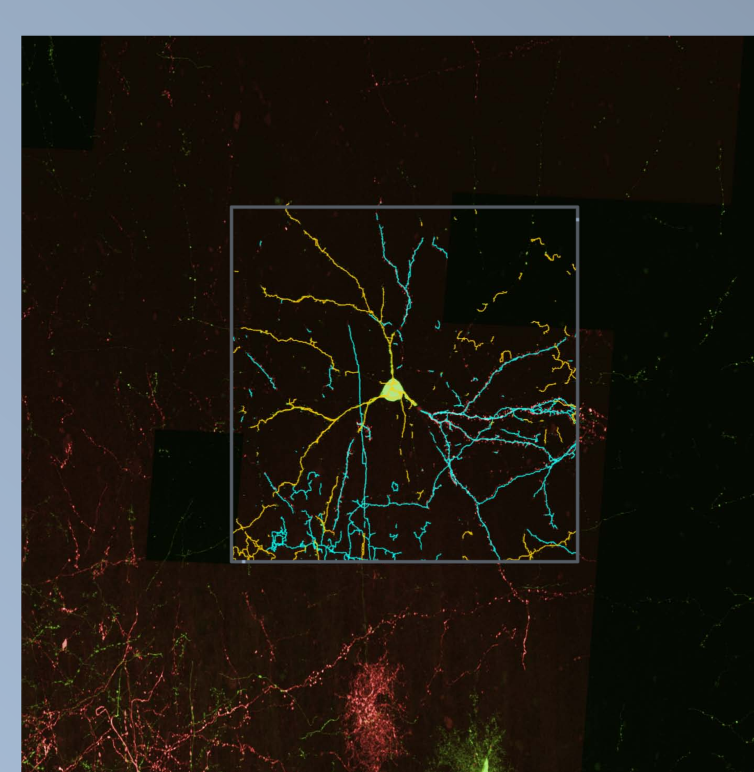
Morse-Smale complexes track features that are based on gradient flow, and therefore are well suited to find ridge-like features such as axons and dendrites. The MSCEER tool computes a full Morse-Smale complex for each image stack, and combines topological simplification with user-specified queries to identify which arcs correspond to features of interest.



Although topological persistence and range queries are standard operations to identify features of interest, more sophisticated queries are possible. In fact, any sub-graph algorithm can operate on the combinatorial structure of the Morse-Smale complex.



Interface for Exploration.
Sliders are used to set parameter values, and the 3D visualization is updated interactively. A basic scripting language allows for more complex filters, or fine-tuning a selection.



Aligning Sections.
Automatically extracted axons and dendritic processes can be used to align two segments. These are image stacks that are spatial neighbors in the Z axis. The same filters are used for the blue and yellow features.

L. Hogrebe et al, Serial section registration of axonal confocal microscopy datasets for long-range neural circuit reconstruction, Journal of Neuroscience Methods, Volume 207, Issue 2, 15 June 2012

NeuroTracker

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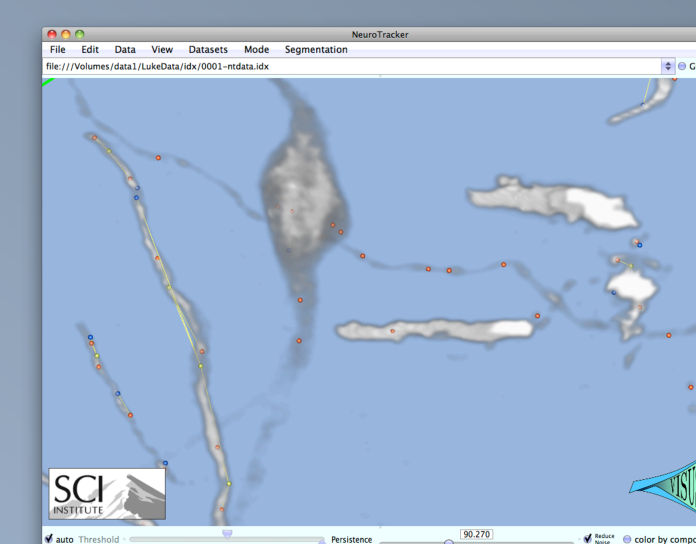
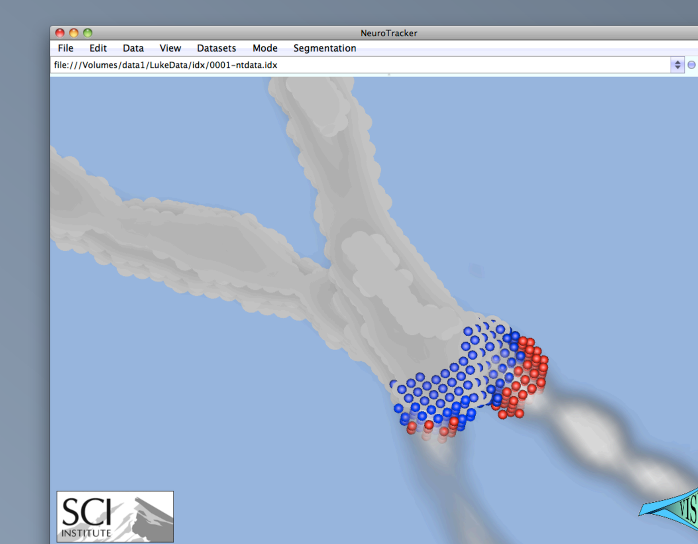
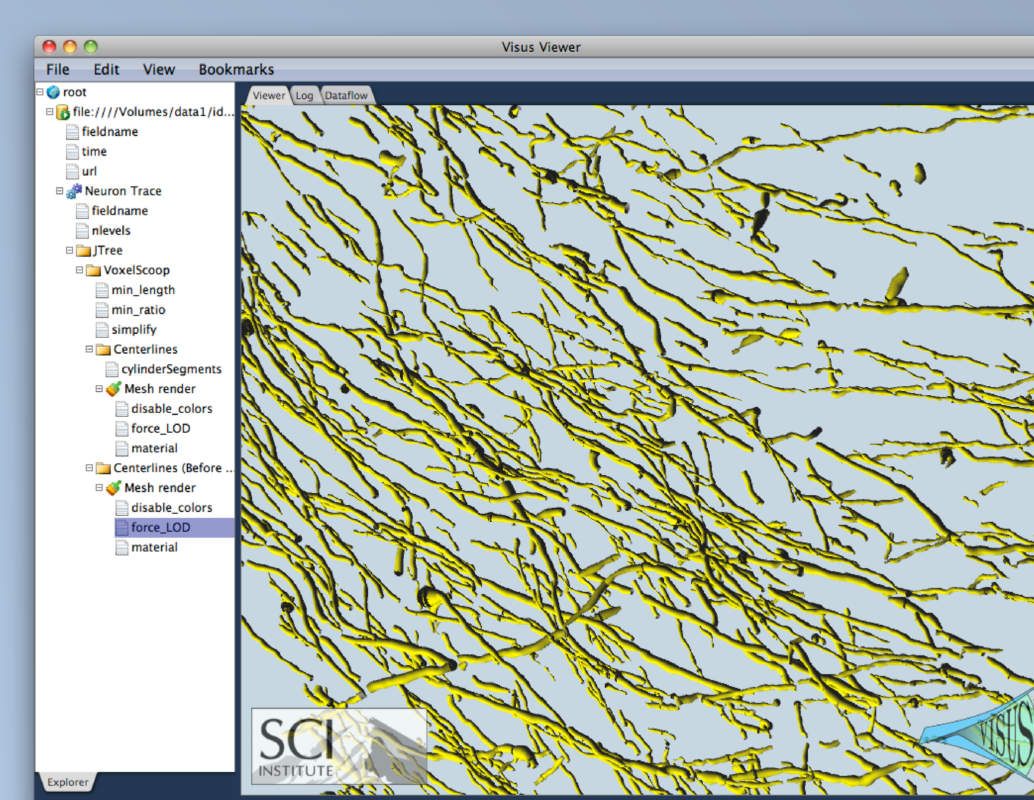
Topological information can also guide more traditional approaches to automatic tracing. For example, NeuroTracker finds and filters maxima in a contour tree, using them as seeds for voxel scooping. The segmentation produced represents the interior of axons and dendrites, and can be easily skeletonized.

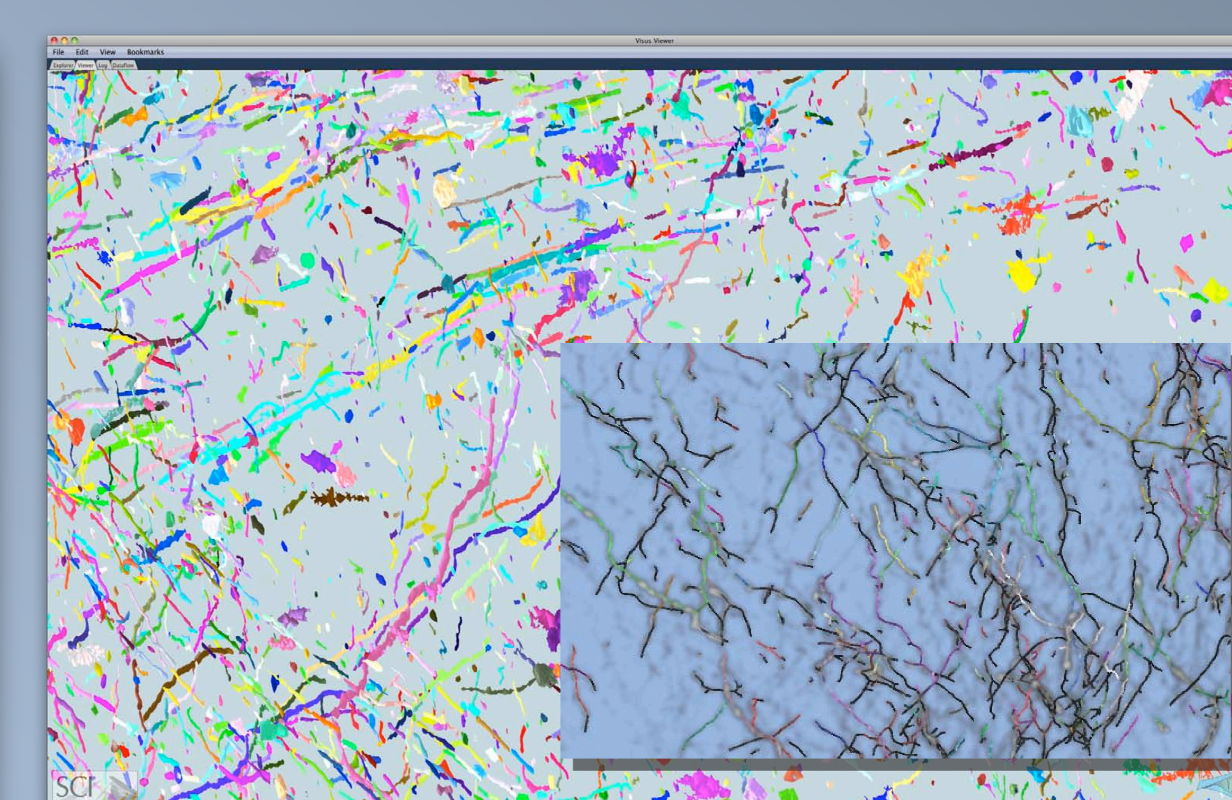


Seed Locations at Local Extrema.



Iterative Voxel Scooping.





NeuroTracker is built on top of the ViSUS platform, and is capable of visualizing and processing terabytes of data interactively.

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