

A Survey of Visualization and Analysis in High-Resolution Connectomics

Johanna Beyer*, Jakob Troidl*, Saeed Boorboor,

Markus Hadwiger, Arie Kaufman, and Hanspeter Pfister

(*) indicates equal contribution



HARVARD
School of Engineering
and Applied Sciences

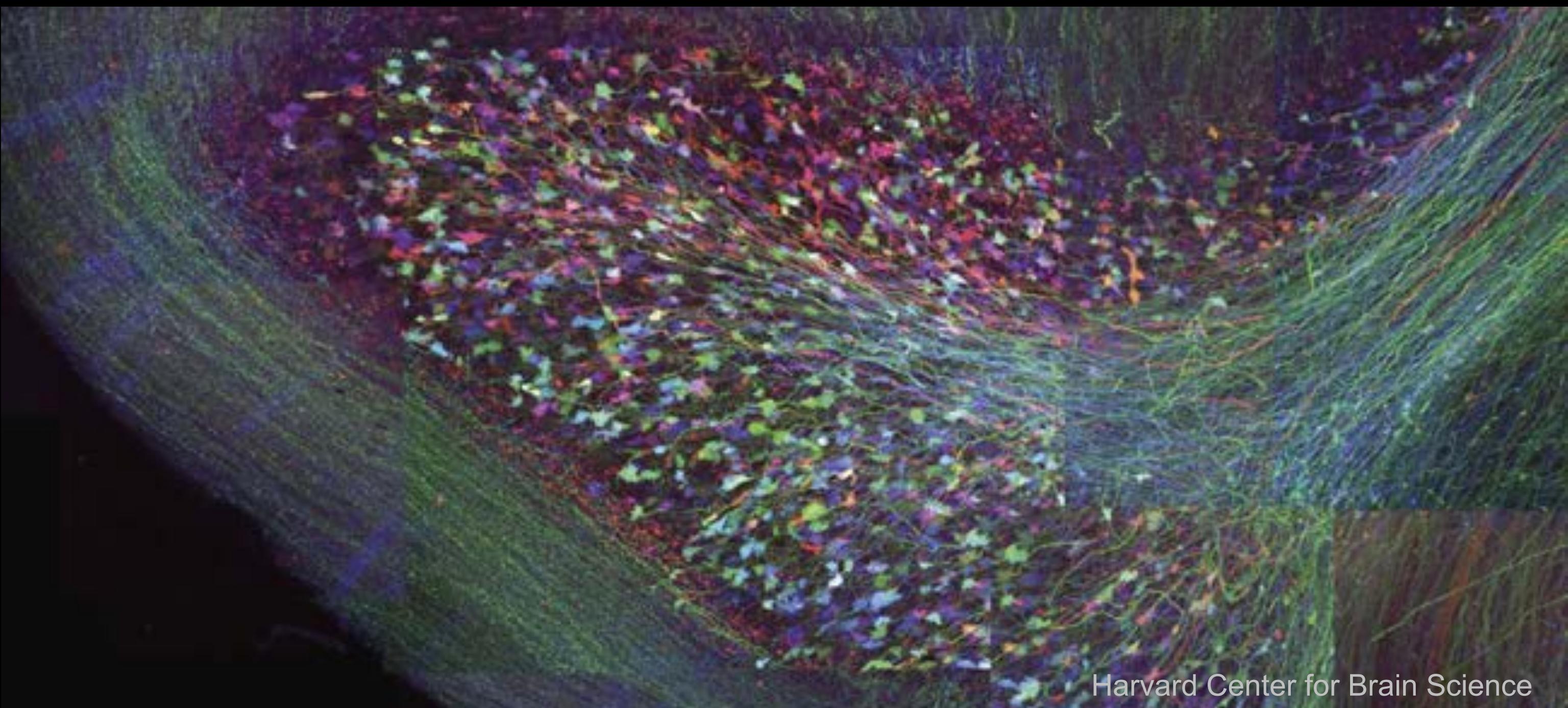


KAUST

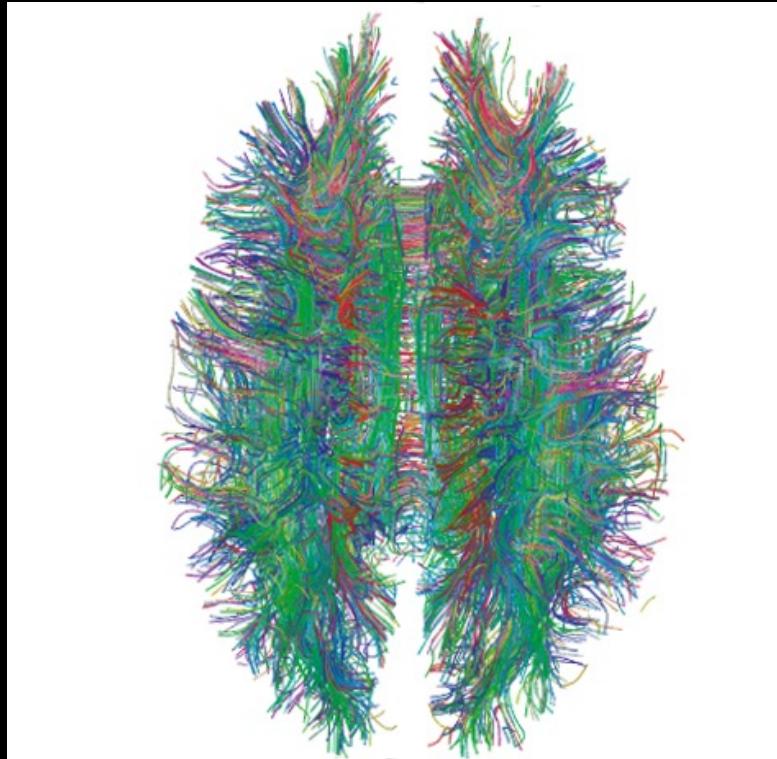


Stony Brook
University

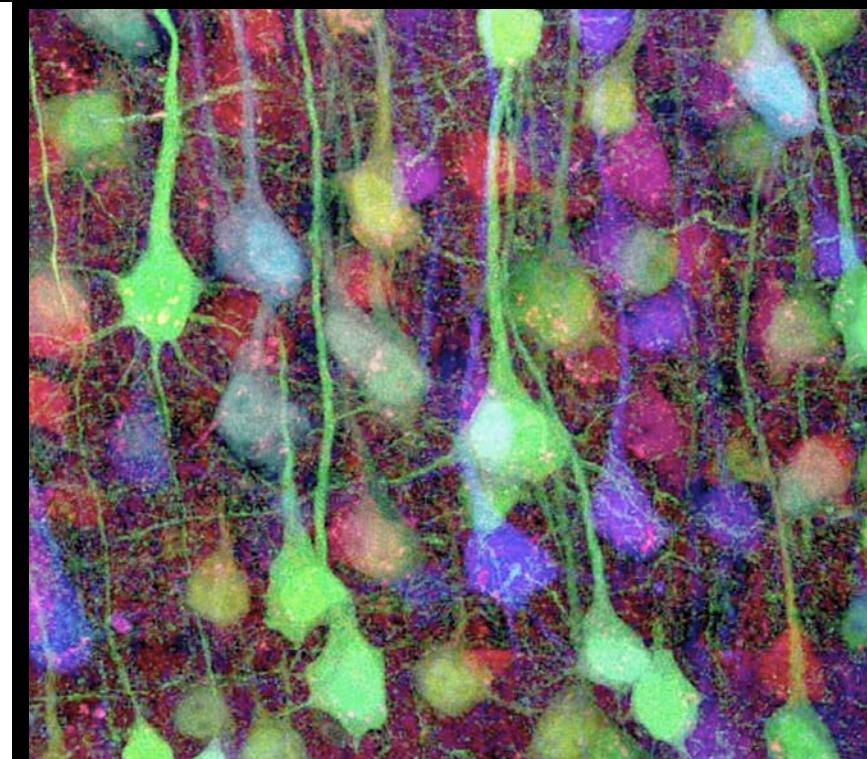
The Connectome – Discovering the Wiring Diagram of the Brain



Neuroscience

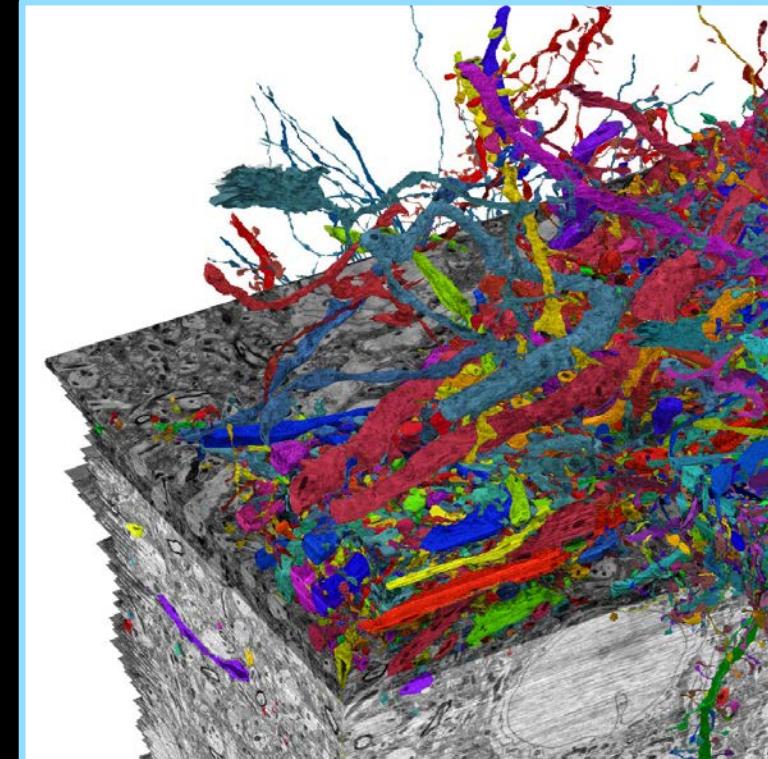


Macro



Meso

Micrometer



Nano

Nanometer

~2 Petabyte / 1mm³

Resolution:

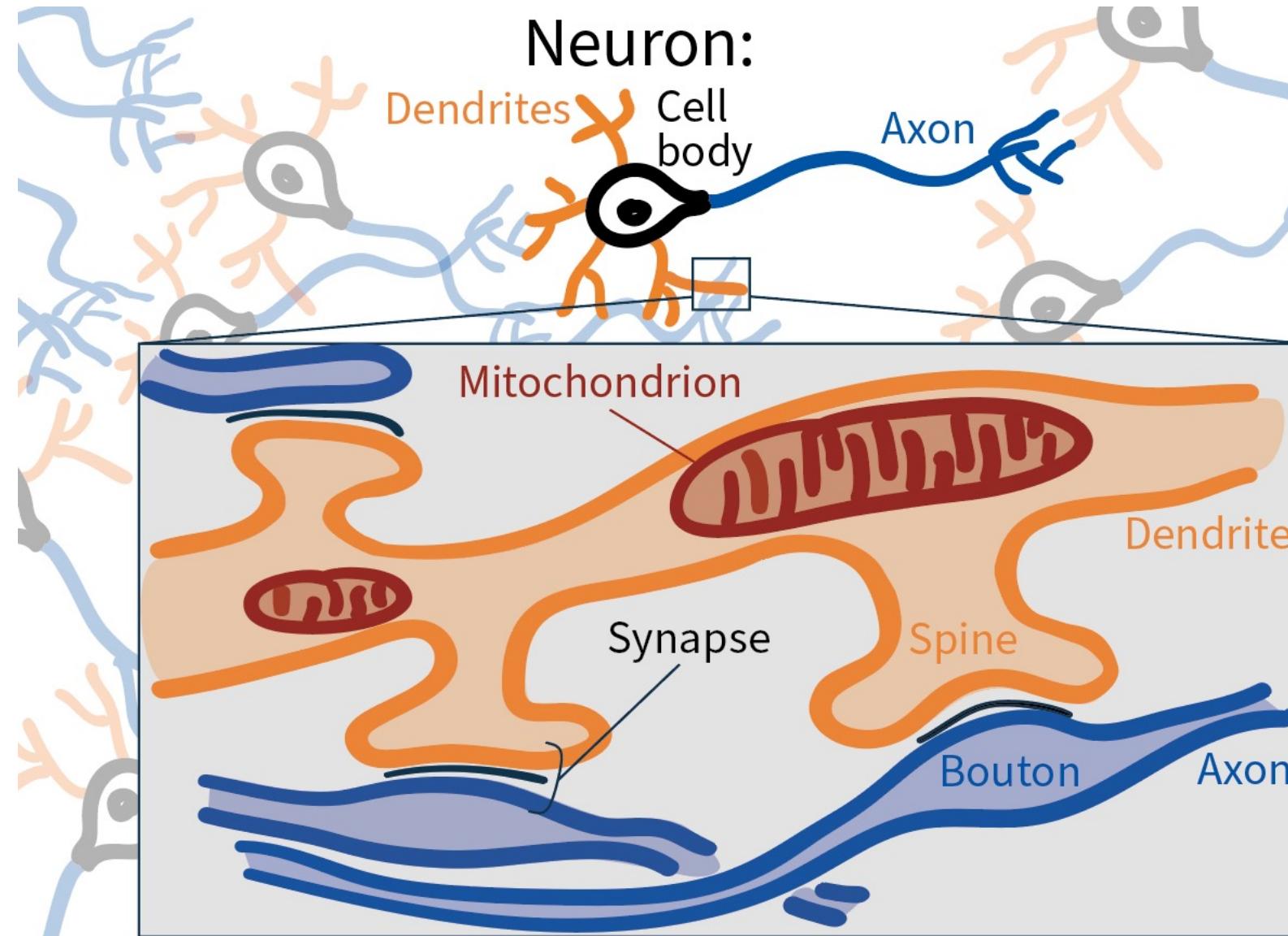
Millimeter

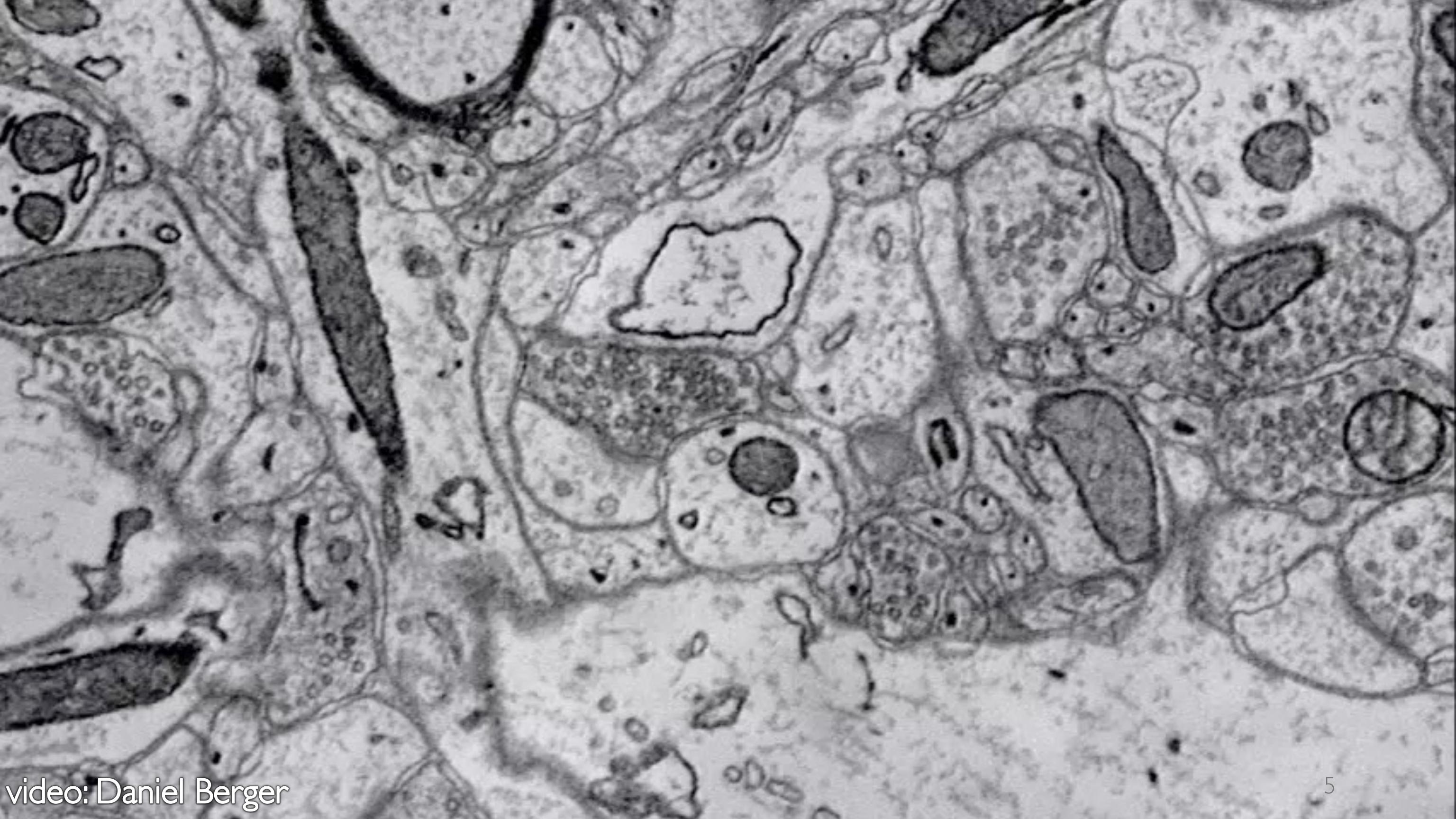
Data Size:

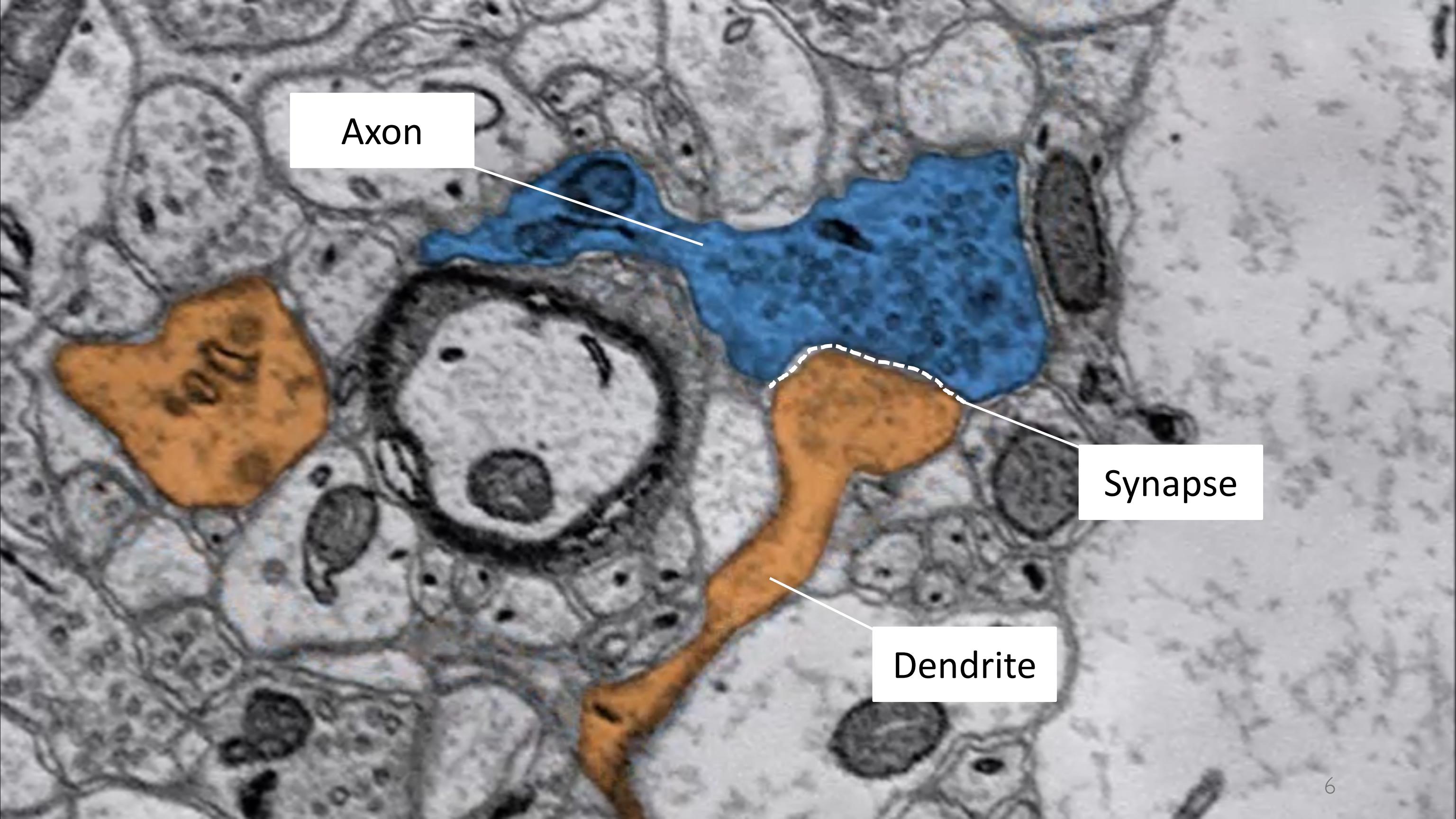
1 Byte / 1mm³

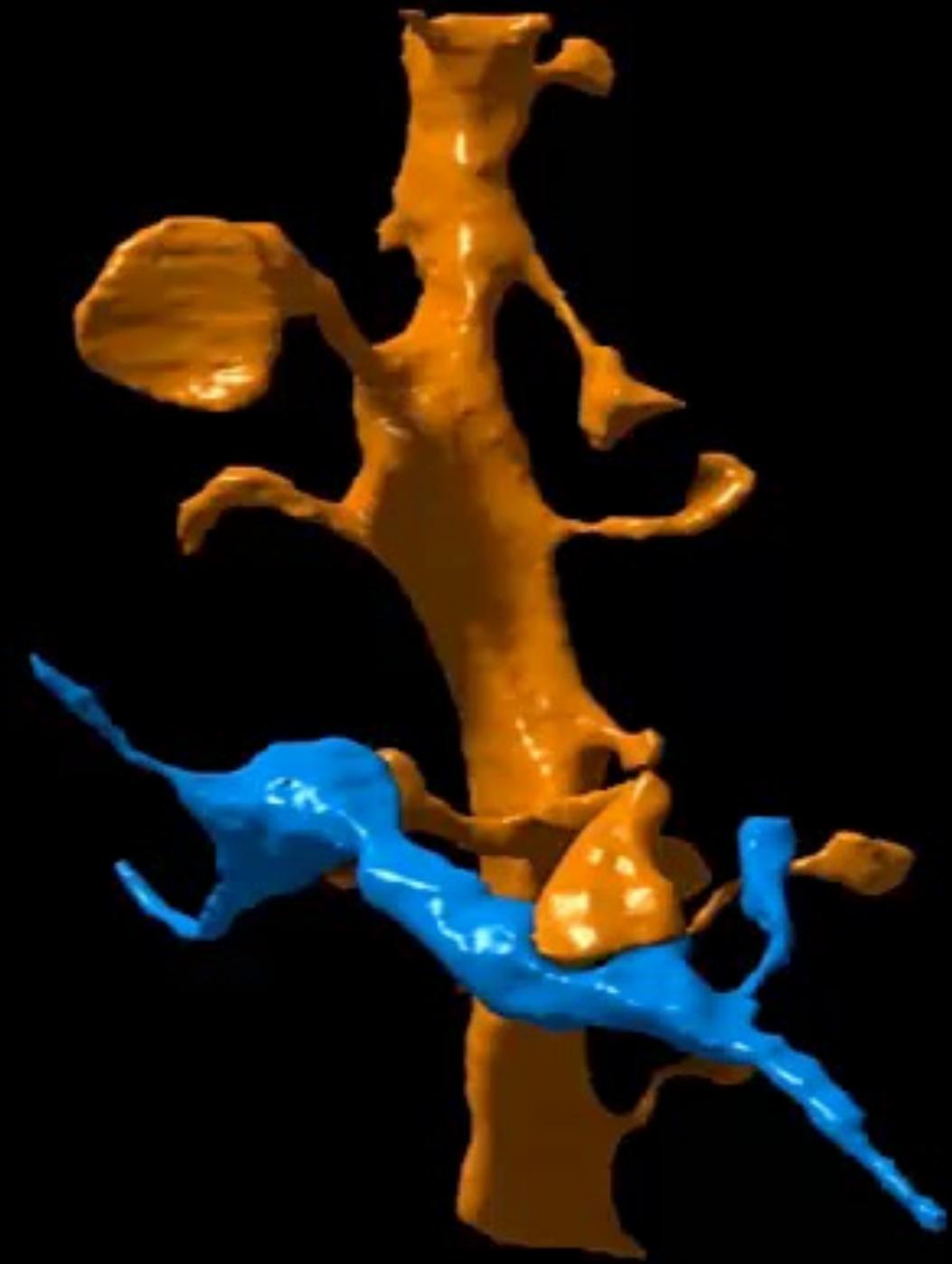
1 Gigabyte / 1mm³

Terminology









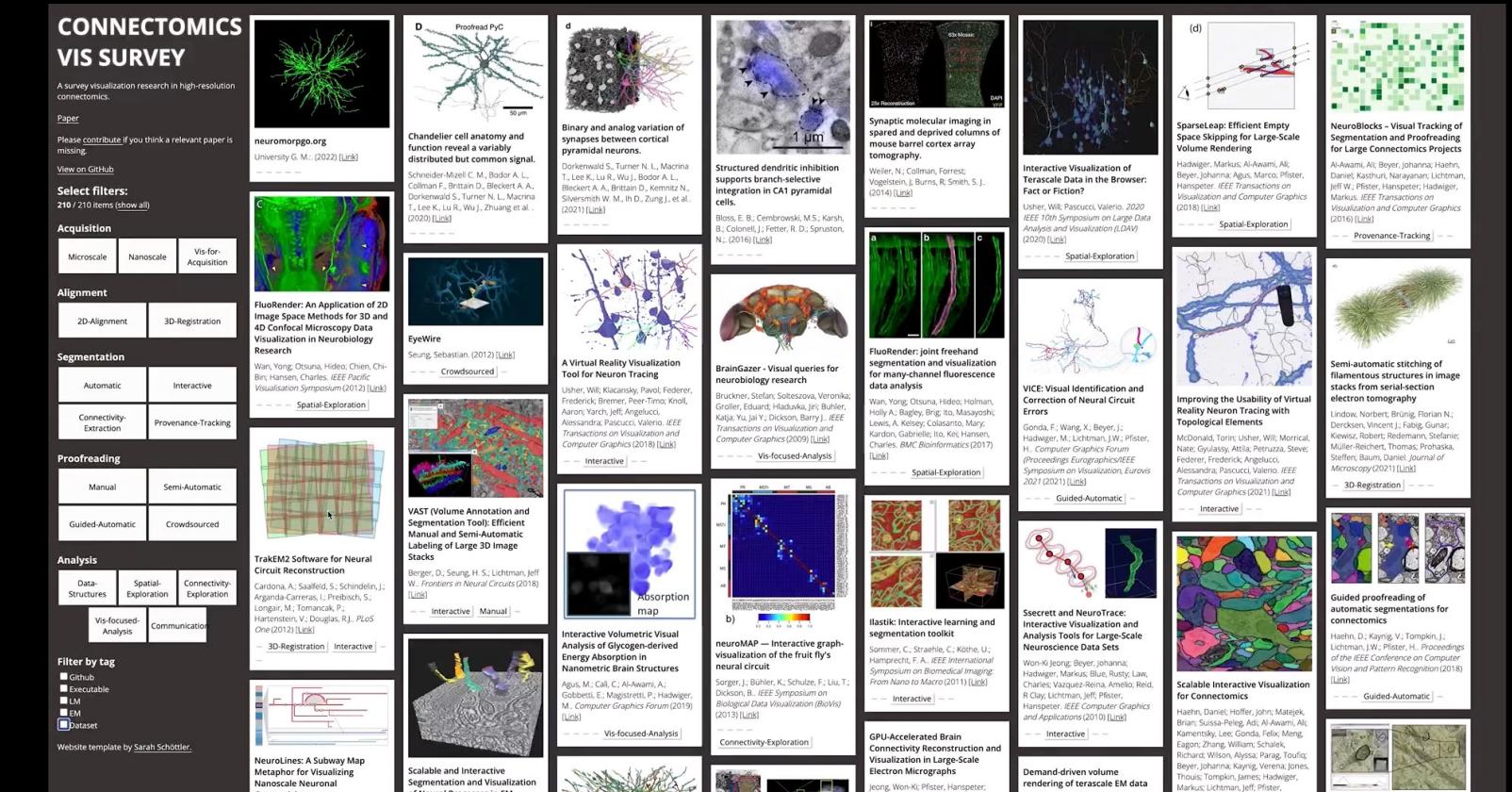
Connectomics Workflow



This STAR

- Our Focus:
Visualization approaches for every step along
the **high-resolution connectomics pipeline**

- We discuss:
 - > 200 papers
 - Open source tools
 - Public datasets

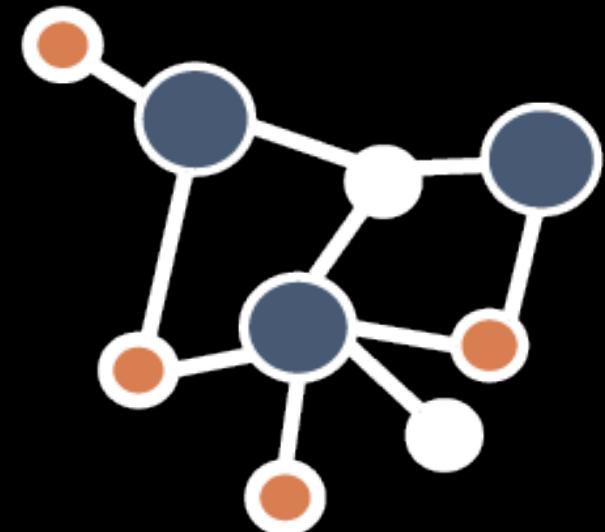
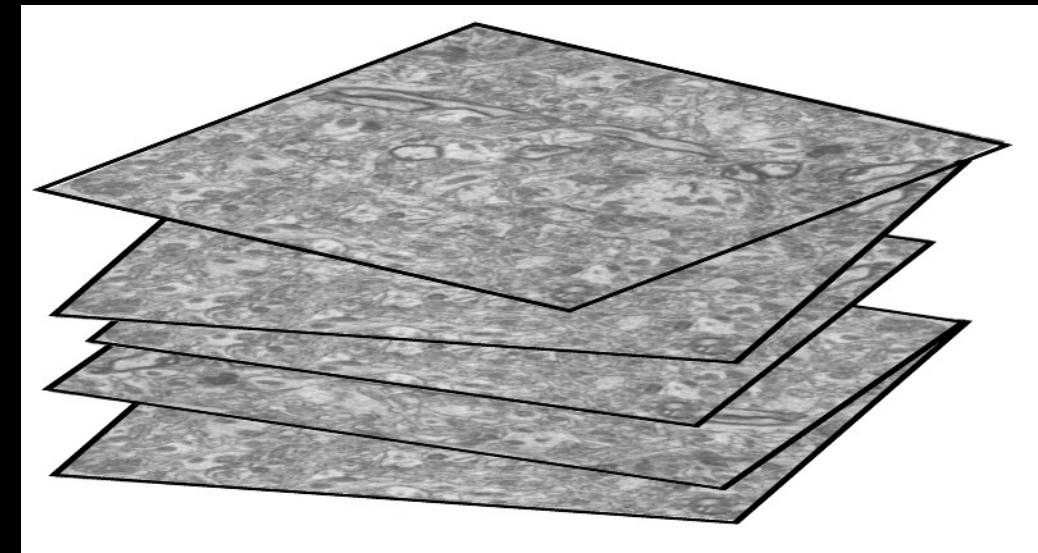


connectomics-vis-survey.github.io

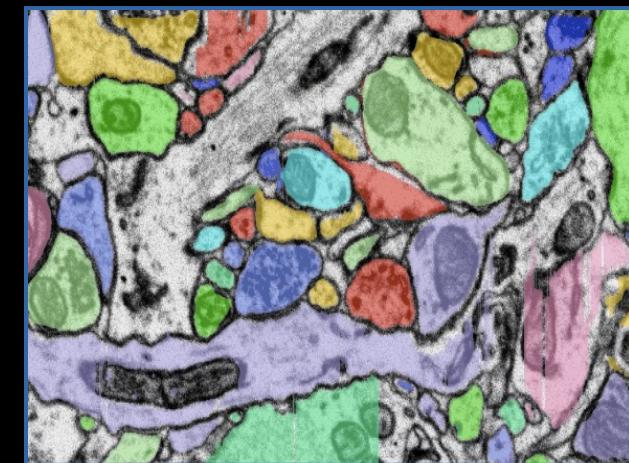
Website template: @Sarah Schoettler

Connectomics Data

- Large image stacks
- Segmentation image stacks
- Connectivity data
- Meta data



	col 1	...	col n
1	x	.	0.2
2	y	.	0.5
3	x	.	1.3
4	z	.	
5	p	.	0.7

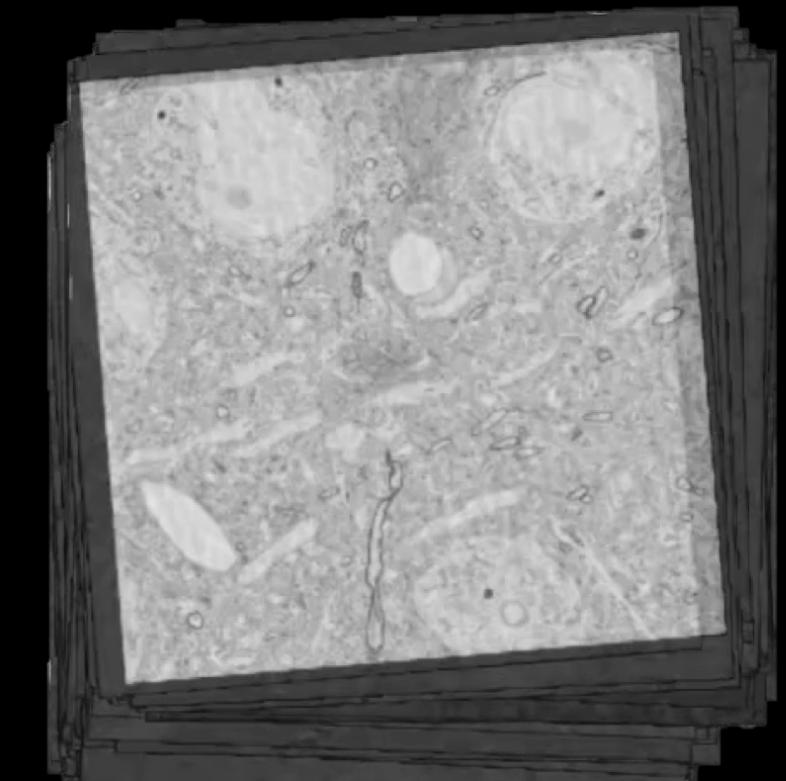
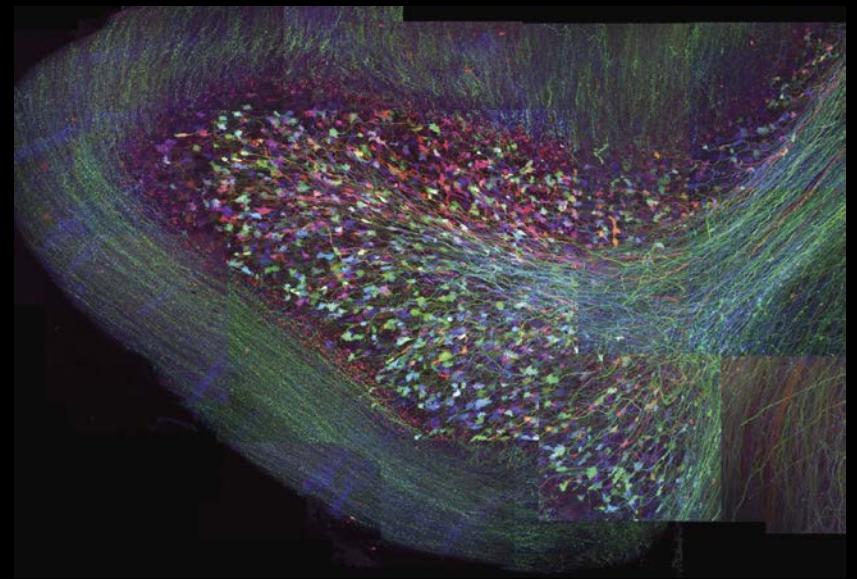


Connectomics Workflow



Micro- and Nanoscale Brain Imaging

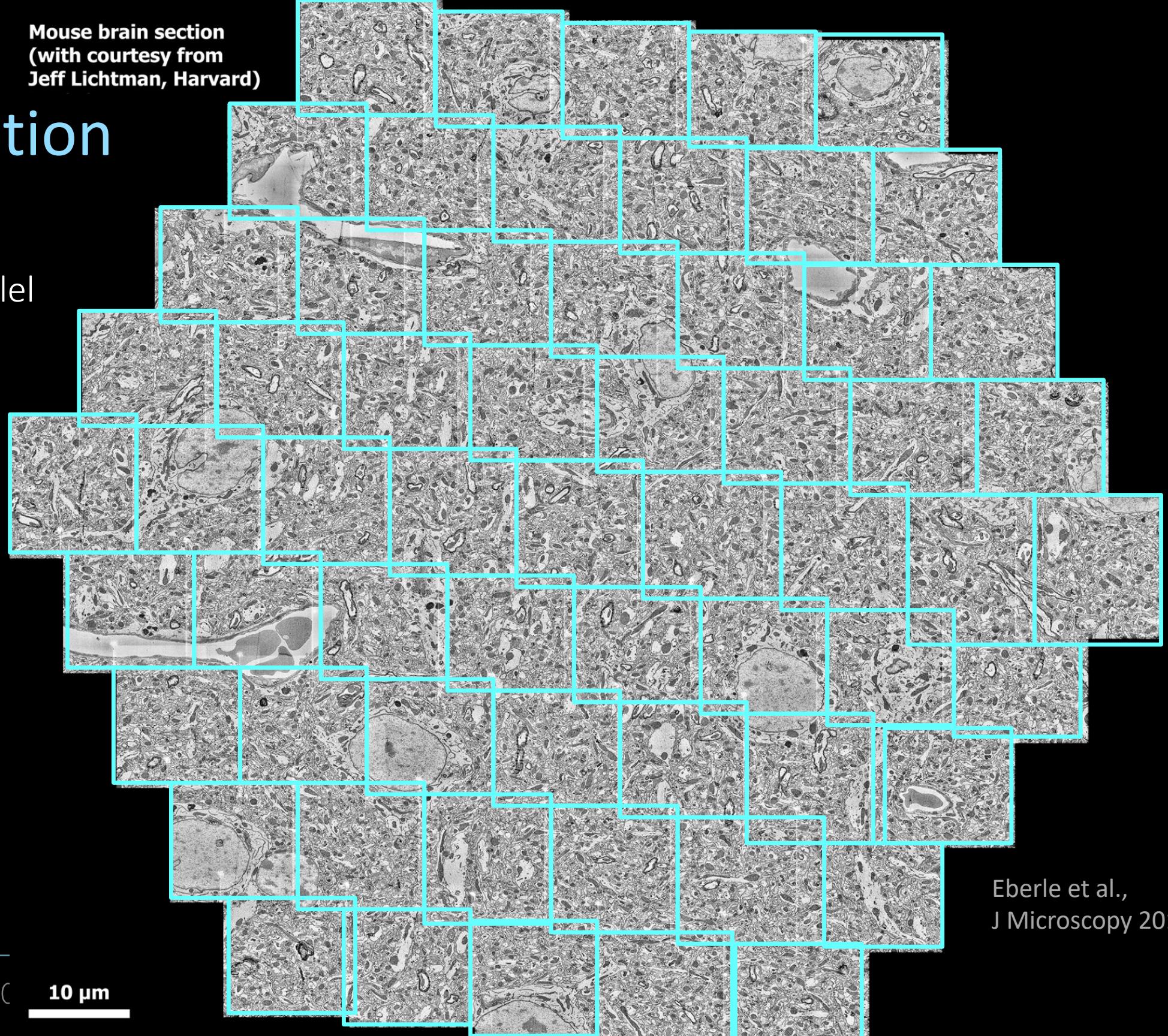
- Light Microscopy
 - **Resolves entire neurons**
 - Resolution: x/y: 200 nm, z: 600 nm
- Electron Microscopy
 - **Resolves cell organelles and synapses**
 - Resolution: x/y 3-5 nm, z: 30-50 nm



Mouse brain section
(with courtesy from
Jeff Lichtman, Harvard)

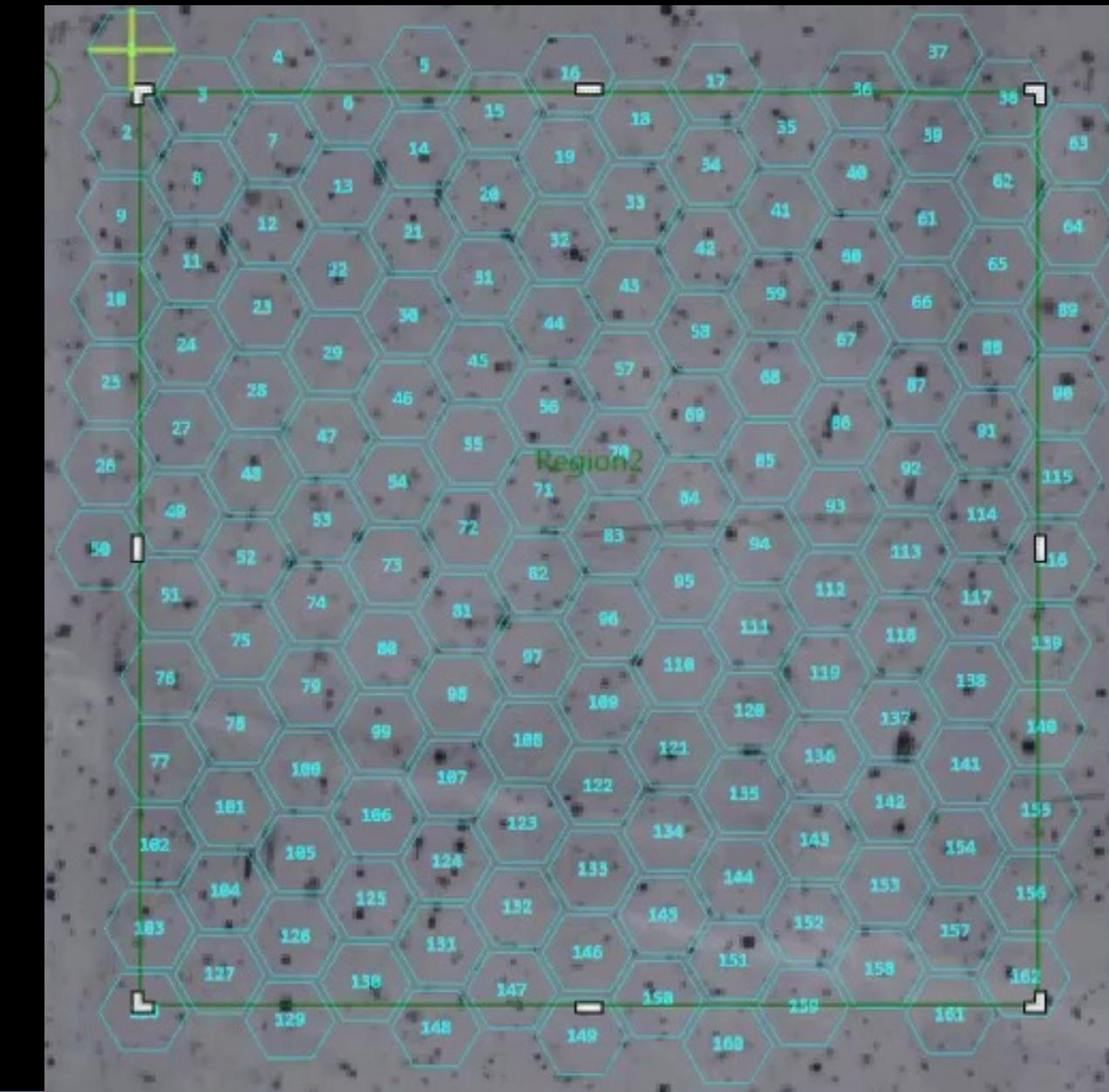
Multi-Beam Acquisition

- Takes multiple images in parallel
- Here:
- 61 images
- Tissue size: $108 \times 108 \mu\text{m}$
- Data size: 495 MB



Automated Acquisition of 1mm² Section

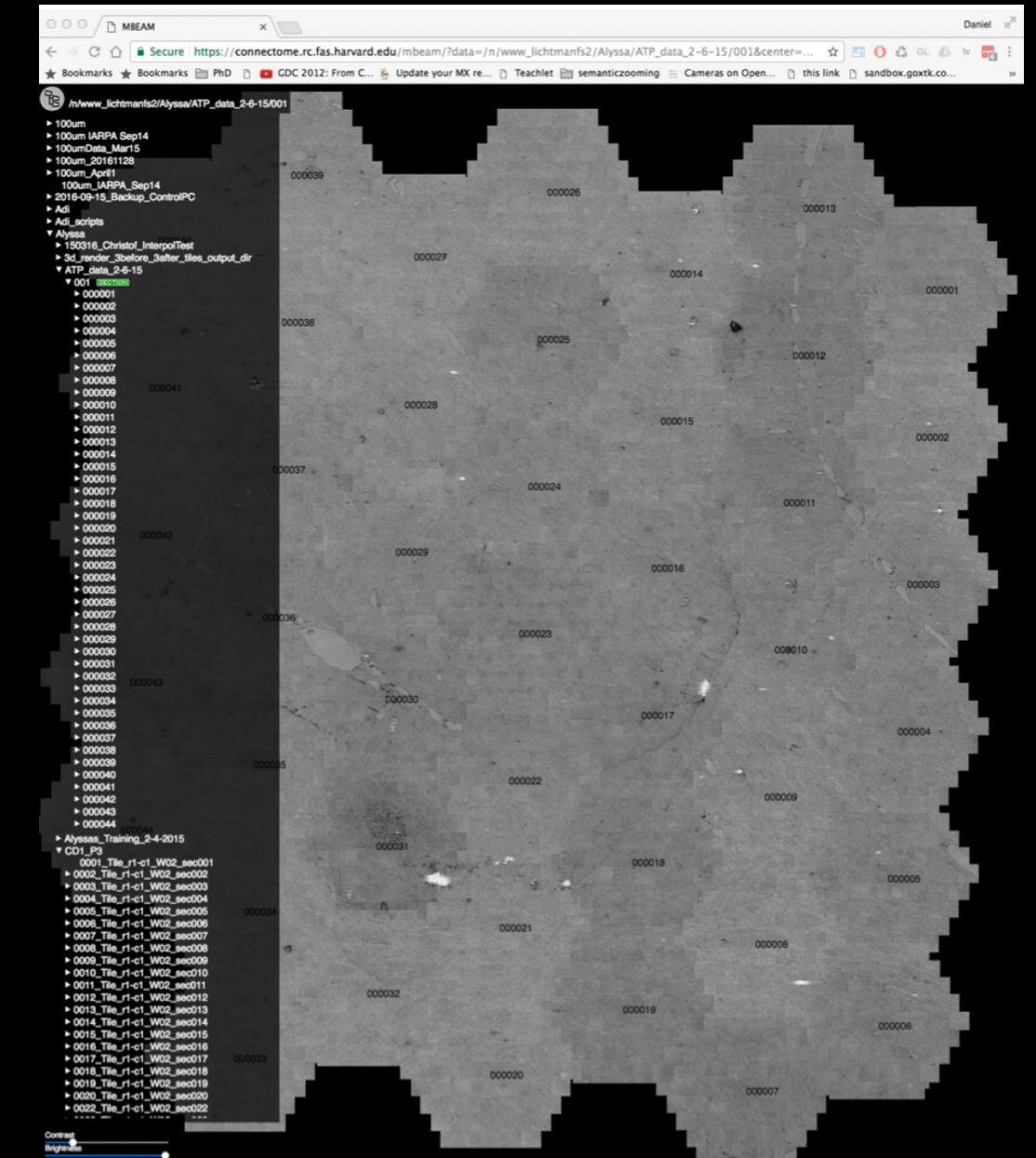
- 1mm²: Previously 5 hours, now less than 5 minutes



Richard Schalek

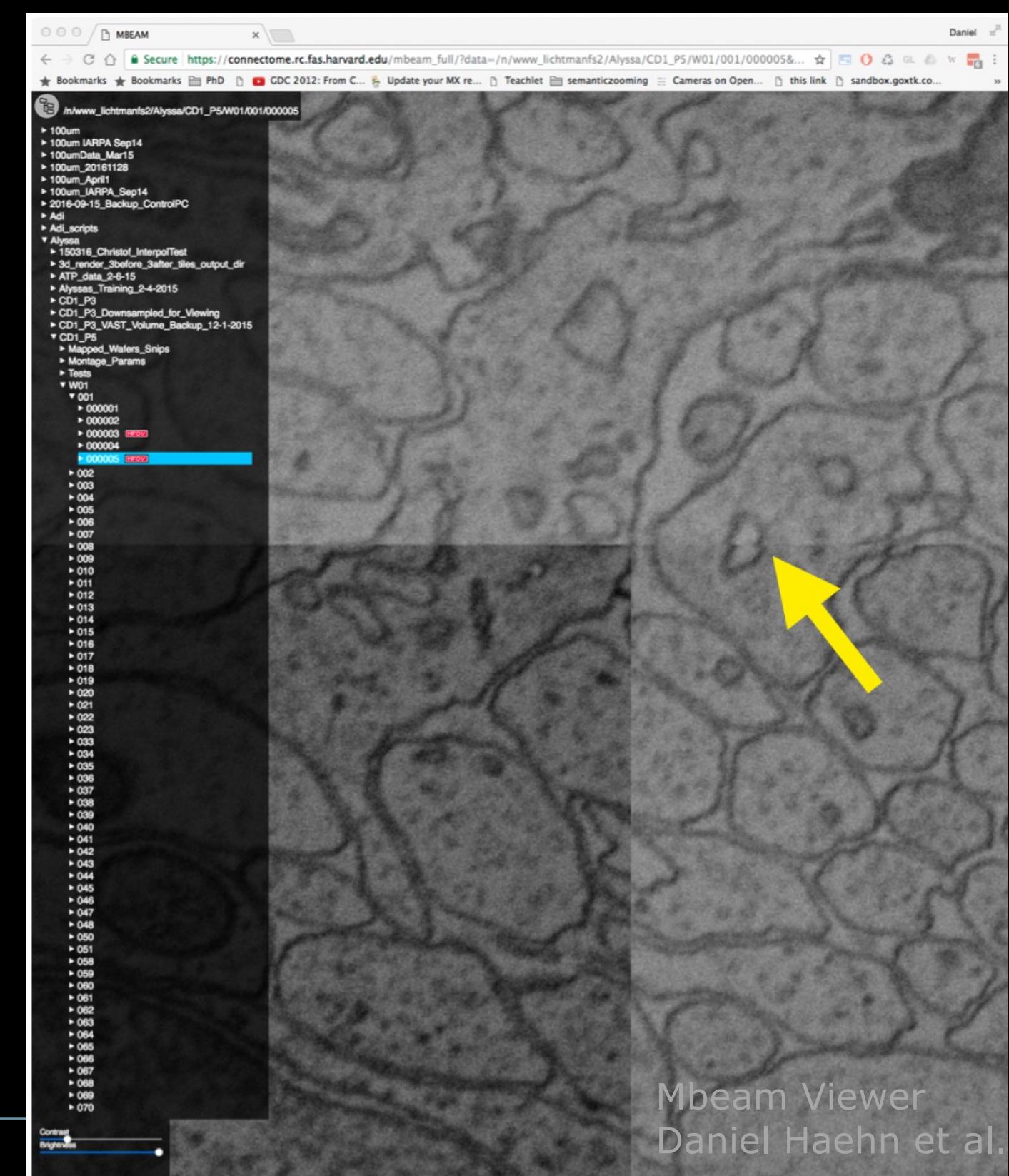
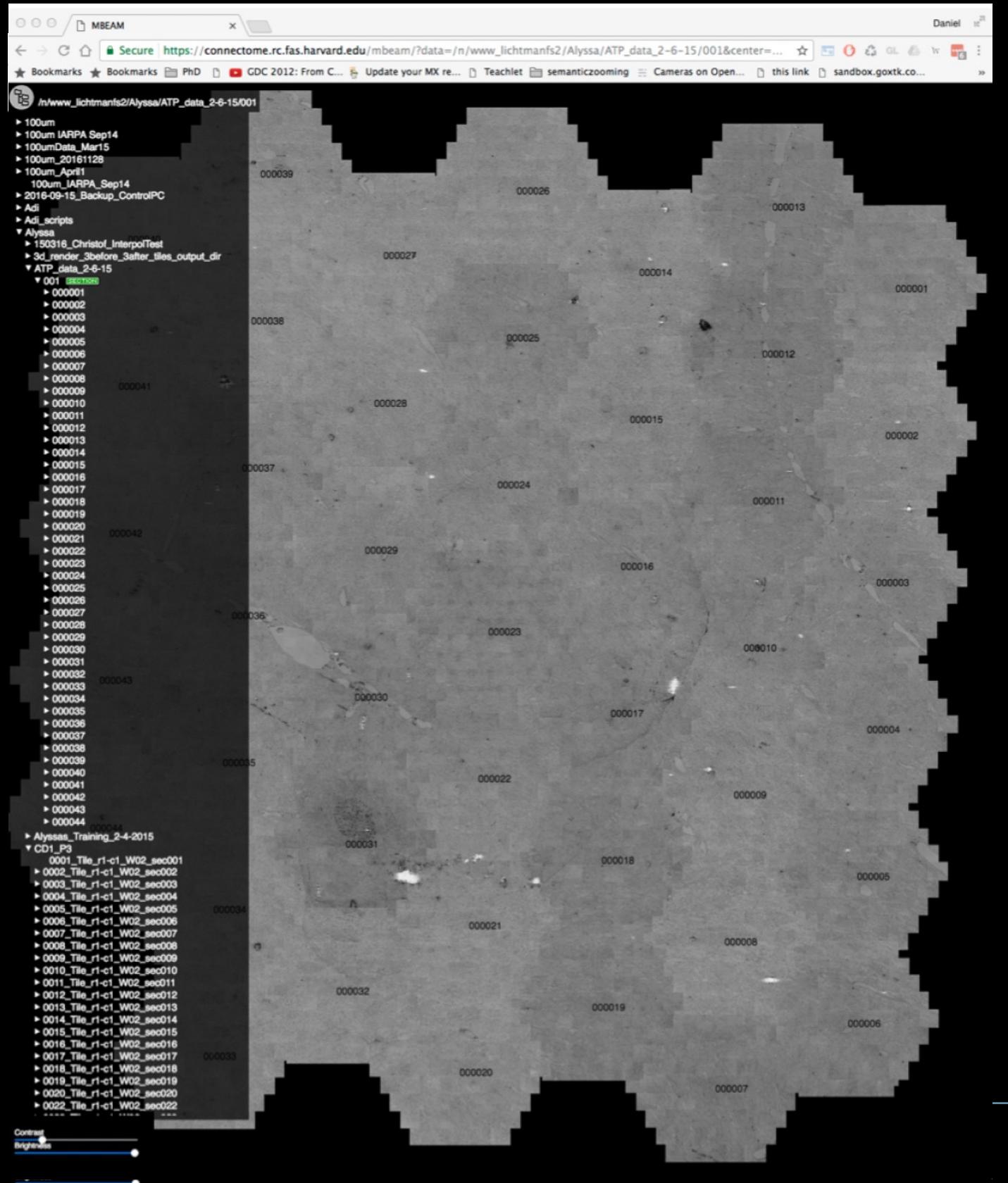
Visualization for Image Acquisition

- Goal:
 - Quick sanity check of data
 - Detecting acquisition errors
 - Unfocused regions
 - Dirt
 - Non-uniform contrast
 - Beam alignment



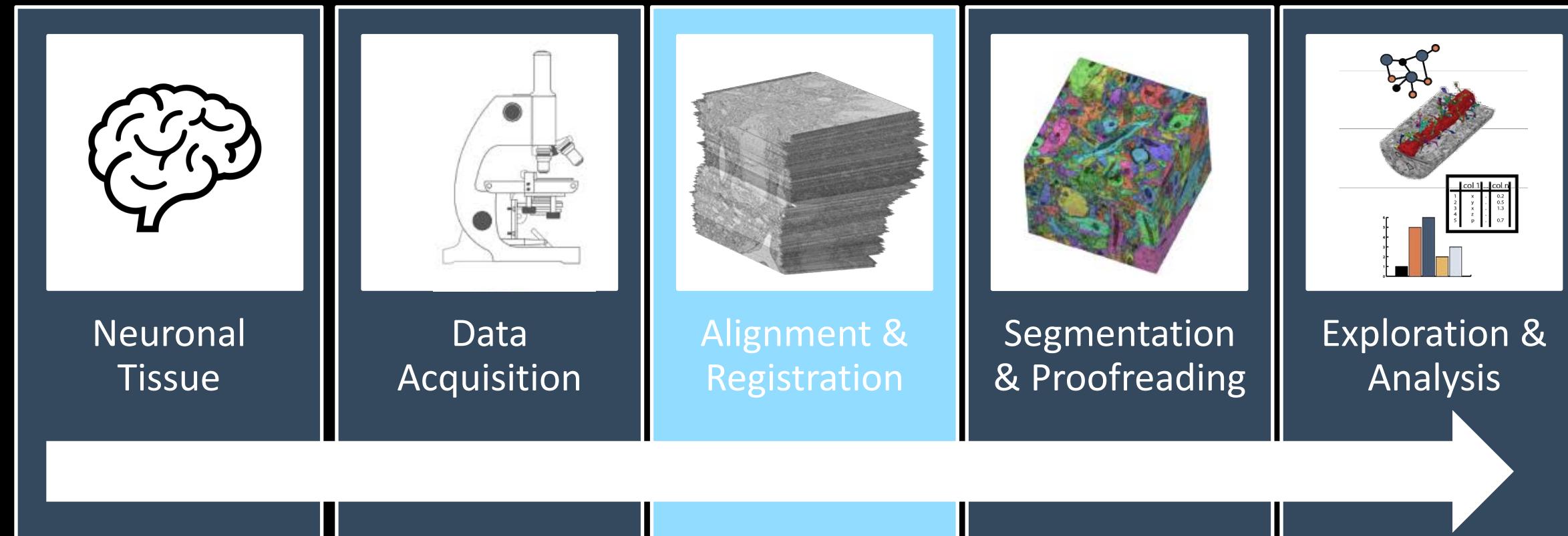
Mbeam Viewer

Daniel Haehn



Mbeam Viewer
Daniel Haehn et al.

Connectomics Workflow



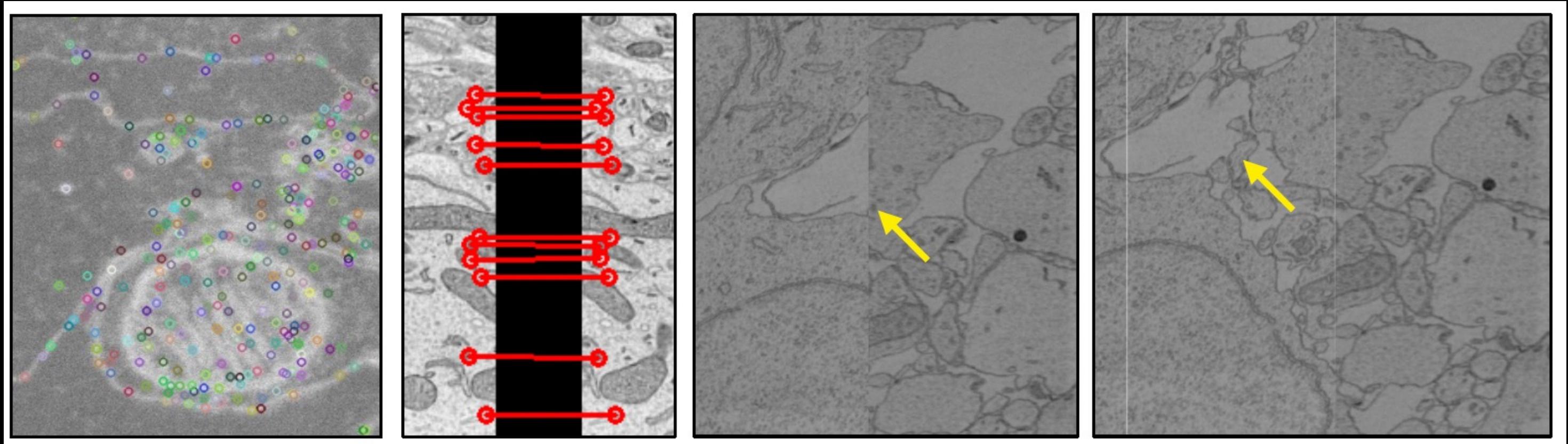
Alignment & Registration

- 2D Alignment
 - Align and stitch individual image tiles in xy plane
- 3D Registration
 - Register slices along z direction

Visualization for Alignment & Registration

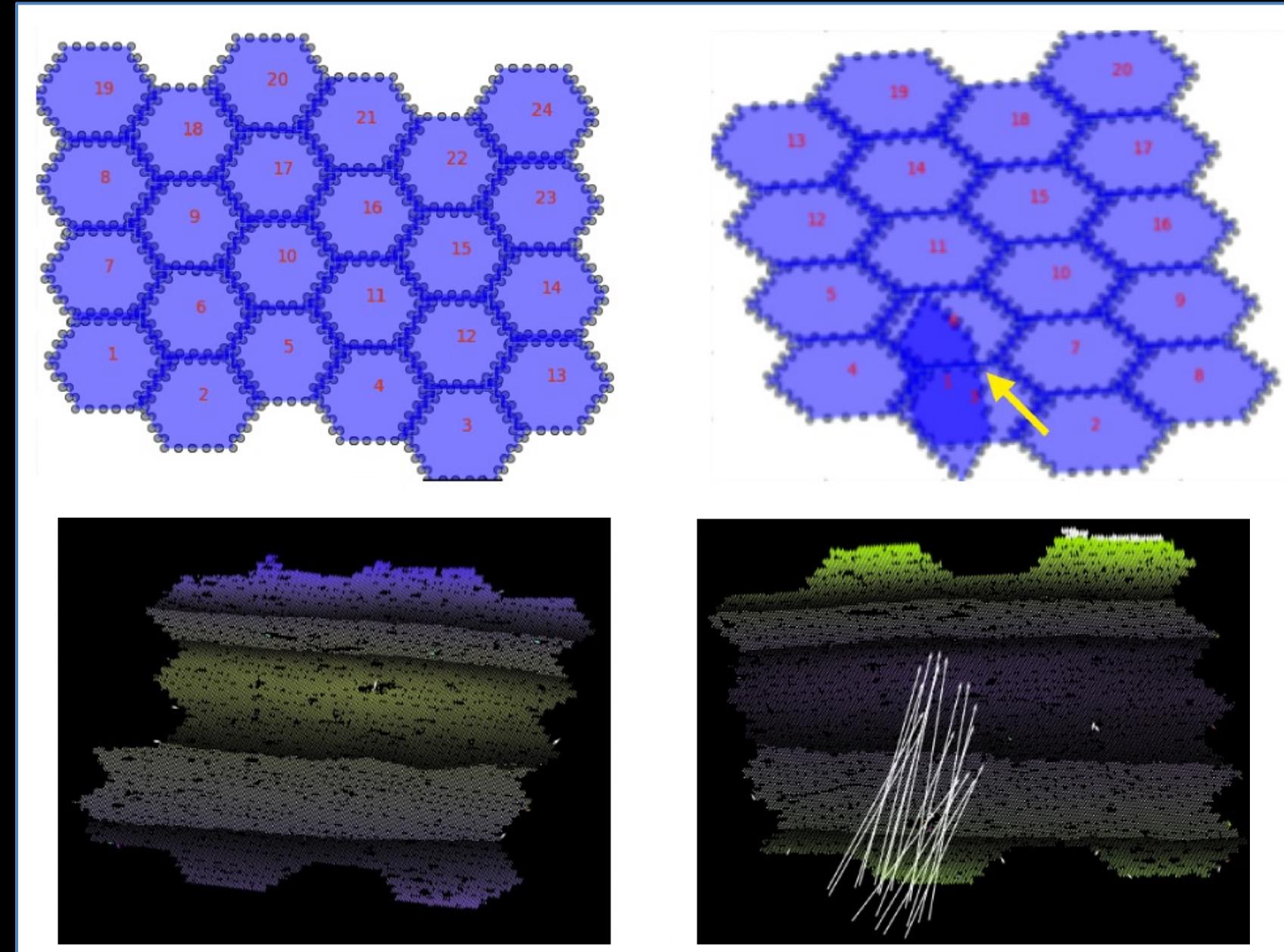
- Goal:
 - Show alignment/registration progress to identify errors
 - Highlight identified image features (allow modification)
 - Show result

Registration & Alignment



RHAligner
Haehn et al.

Registration & Alignment



RHAligner
Haehn et al.

Connectomics Workflow



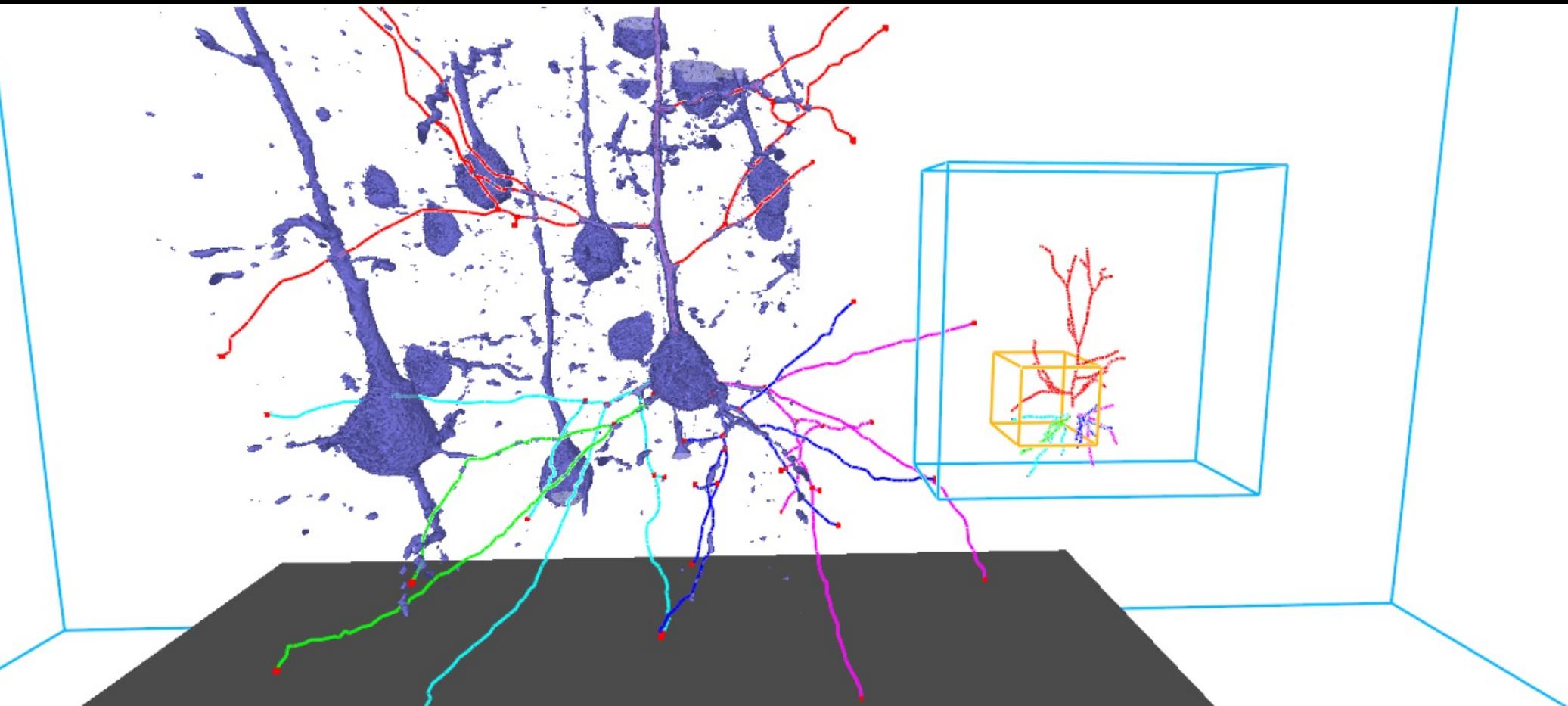
Segmentation

- Labeling of individual structures in neuronal tissue
- Synapse annotation
- Connectivity extraction
- Automatic, semi-automatic, and manual approaches

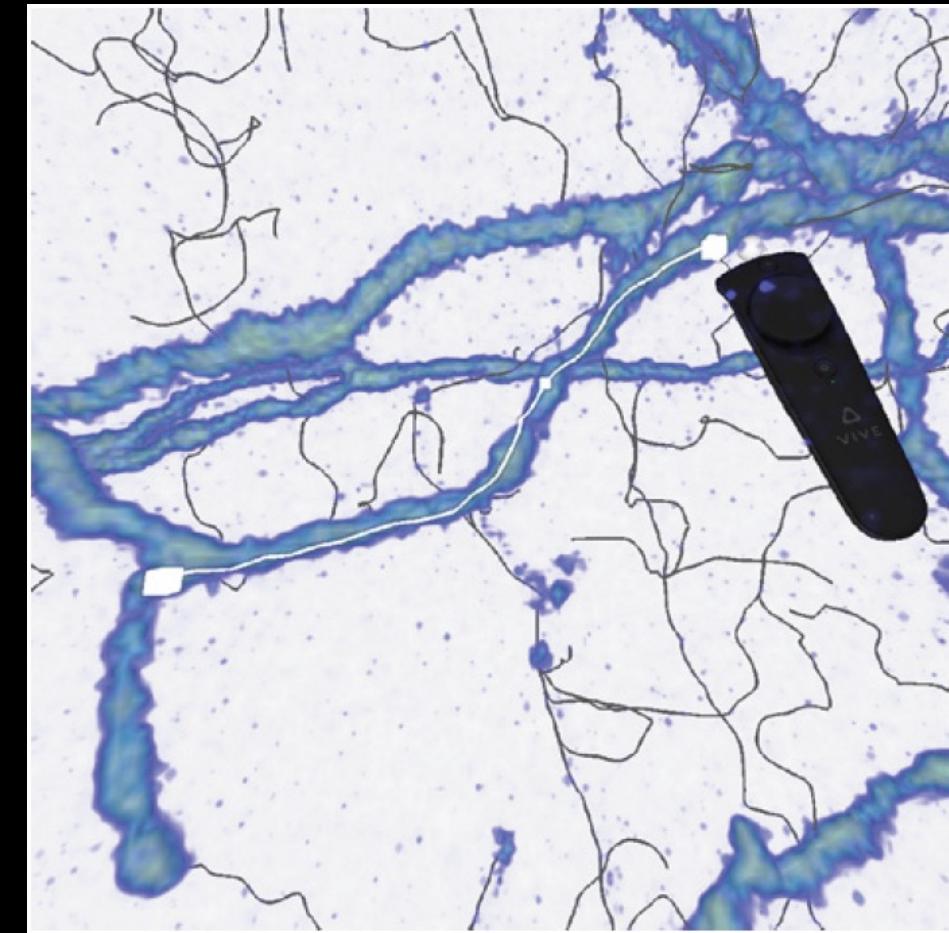
Visualization for Segmentation

- Goal:
 - Verify and correct segmentation results
 - Manage large segmentation project
- Approaches:
 1. Visualize segmentation result or ongoing segmentation
 2. Visual proofreading
 3. Visualize segmentation provenance or progress

Neuron Tracing in VR

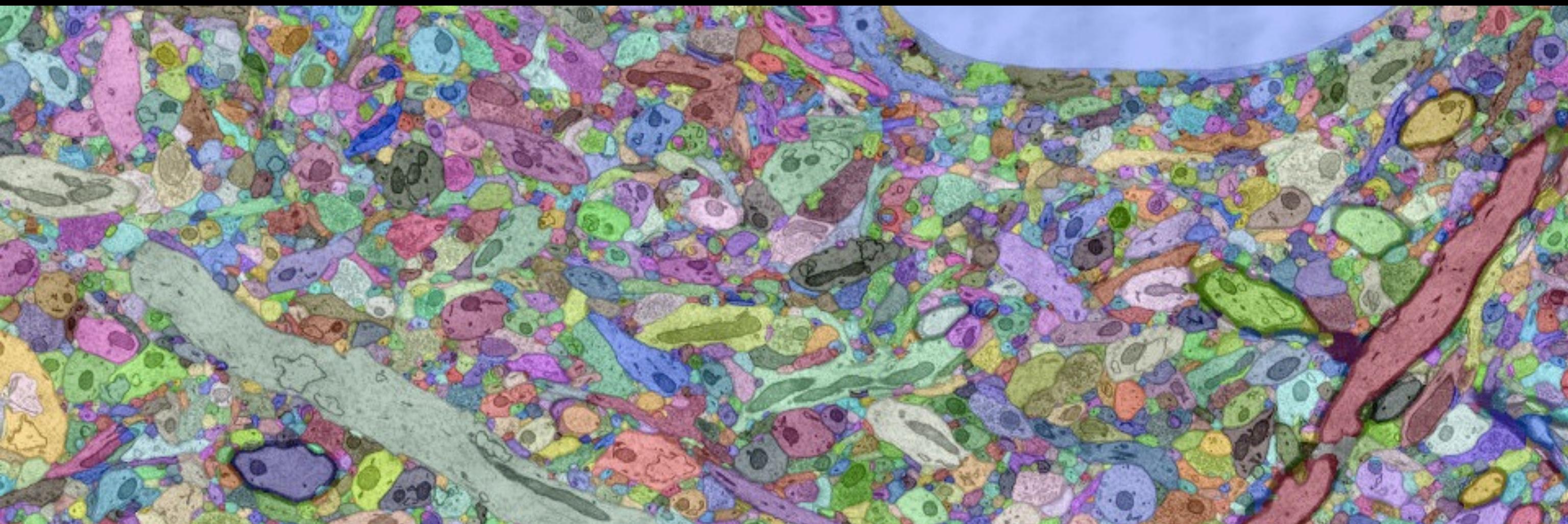


[Usher et al., IEEE Vis 2017]

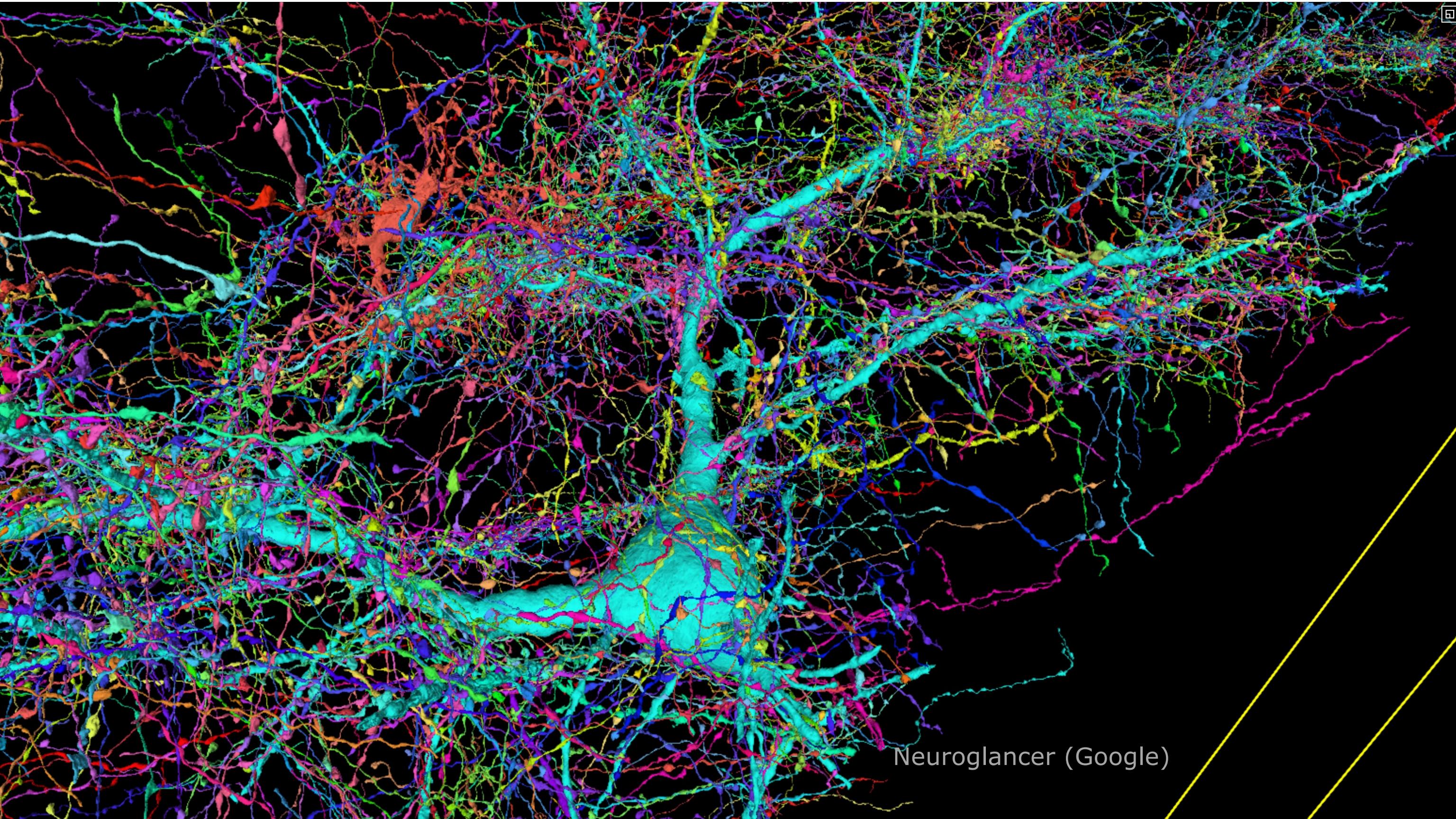


[McDonald et al., IEEE Vis 2020]

Visualize Segmentation Result

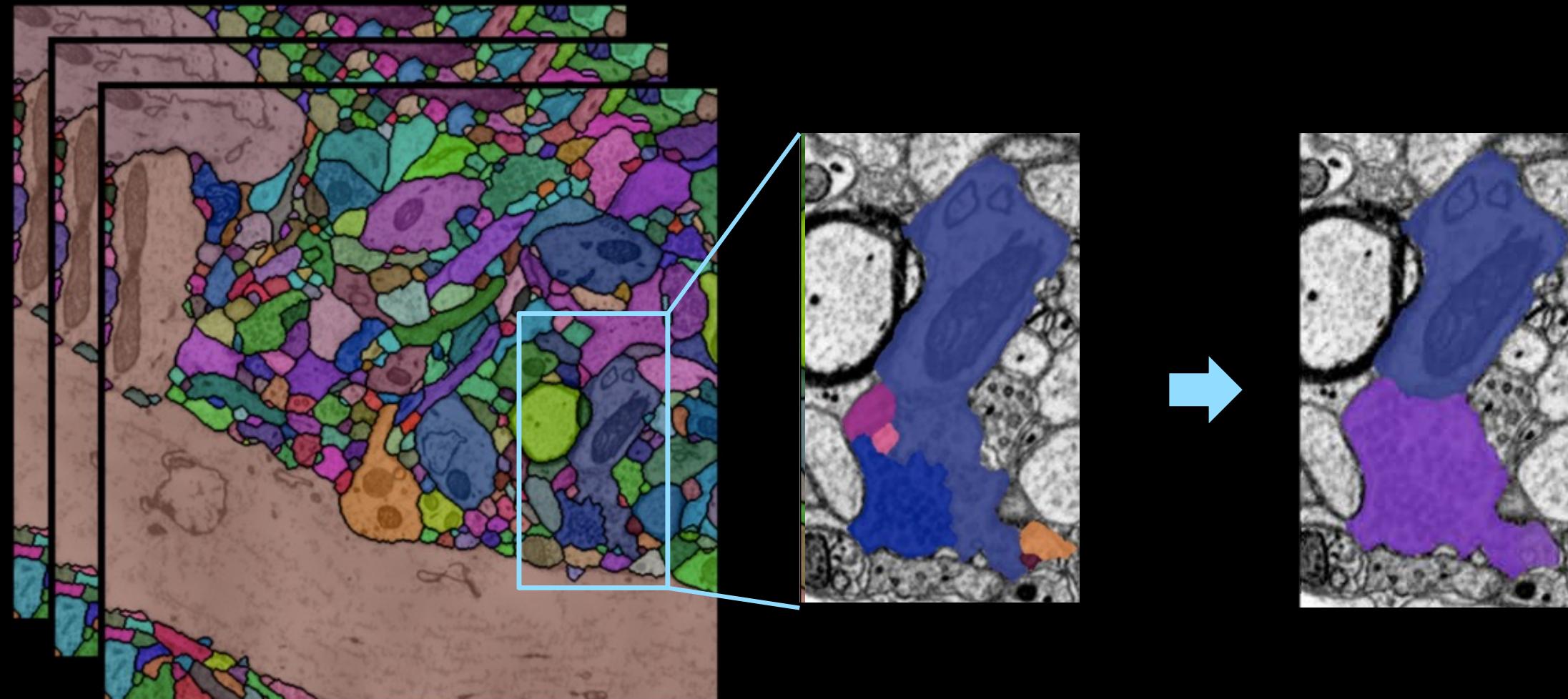


rhoana.org/dojo/



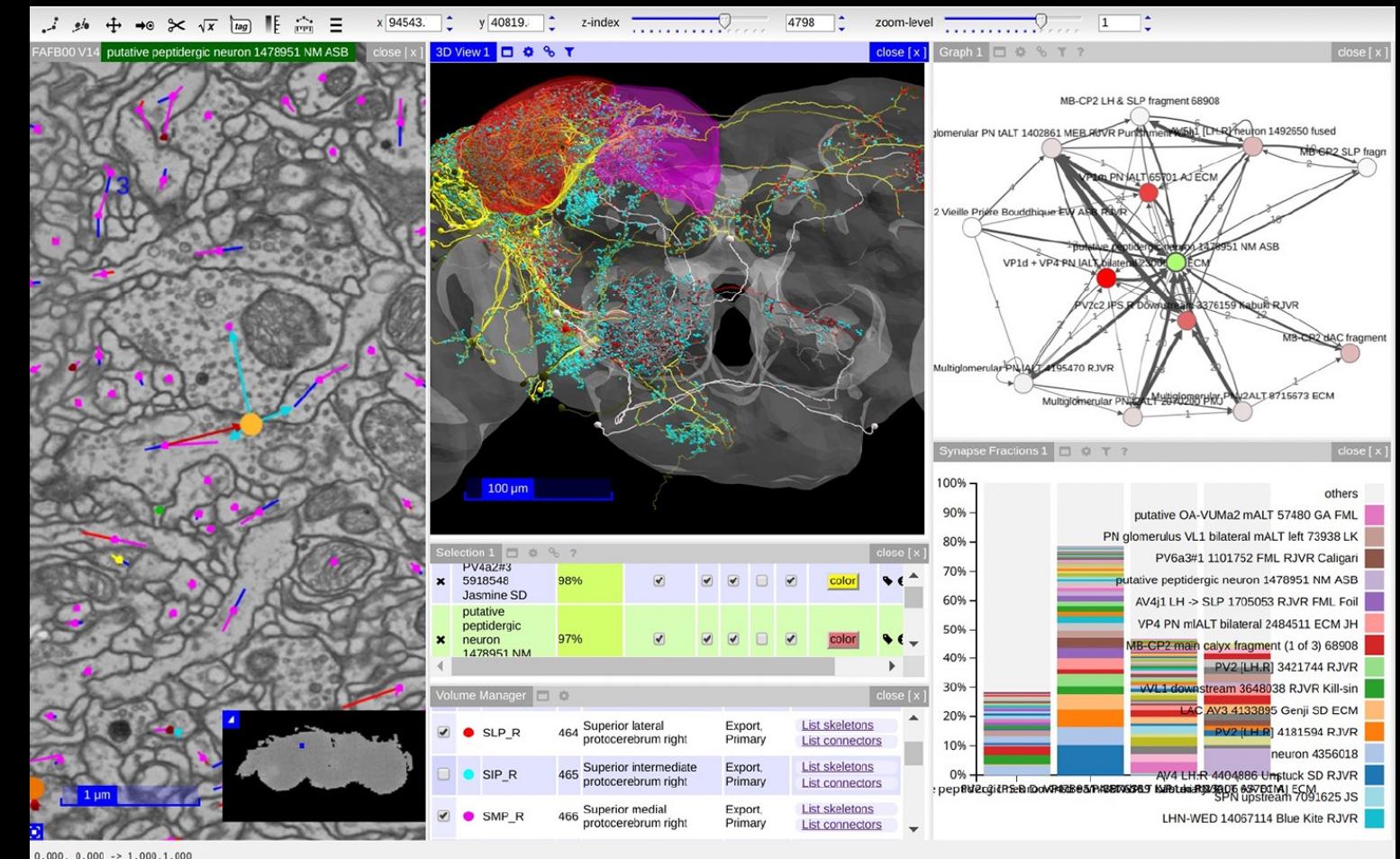
Neuroglancer (Google)

Visual Proofreading



Manual Proofreading

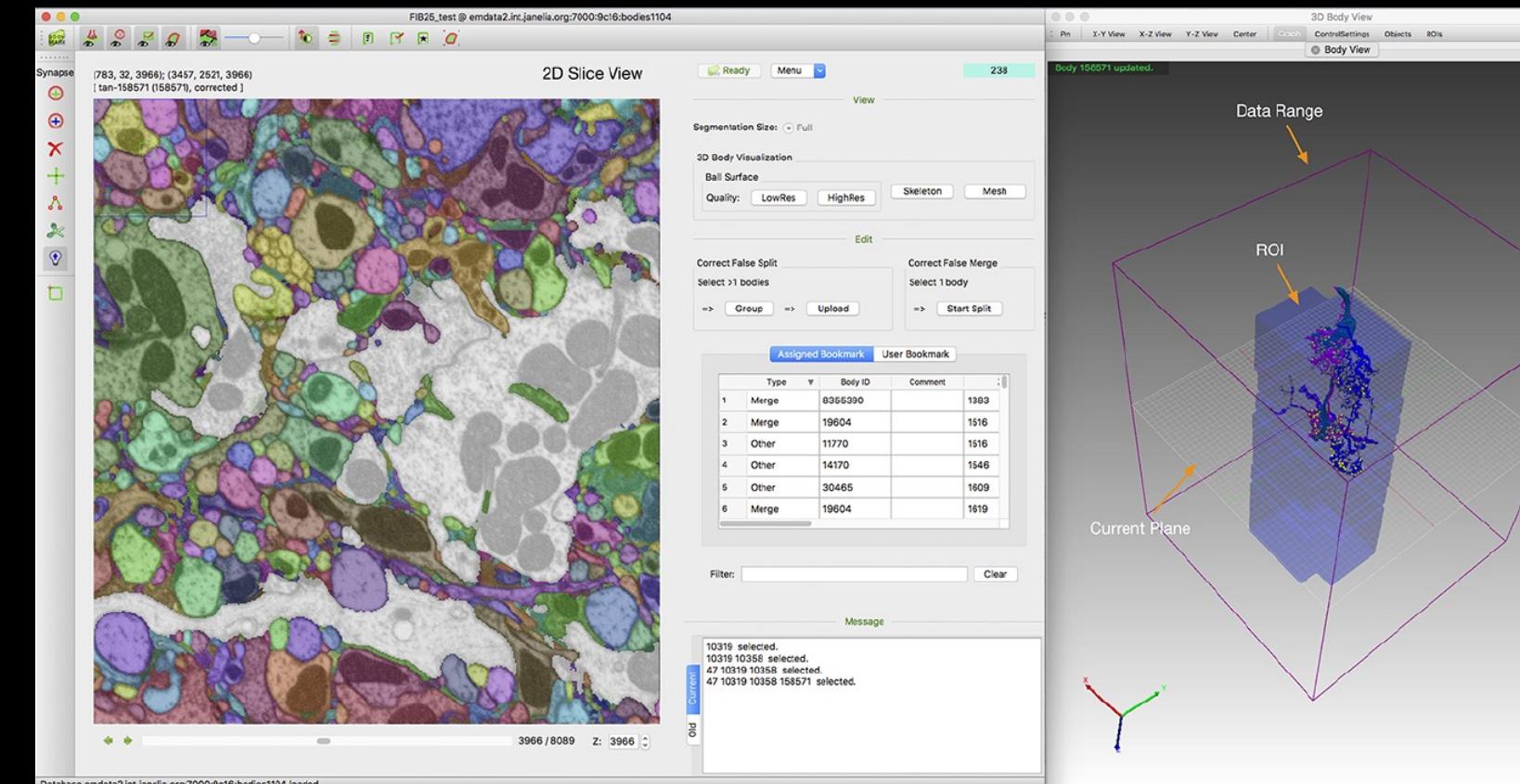
- Users can manually change incorrect segmentations
- Example tools:
 - Catmaid
 - Viking Viewer
 - WebKnossos
 - VAST



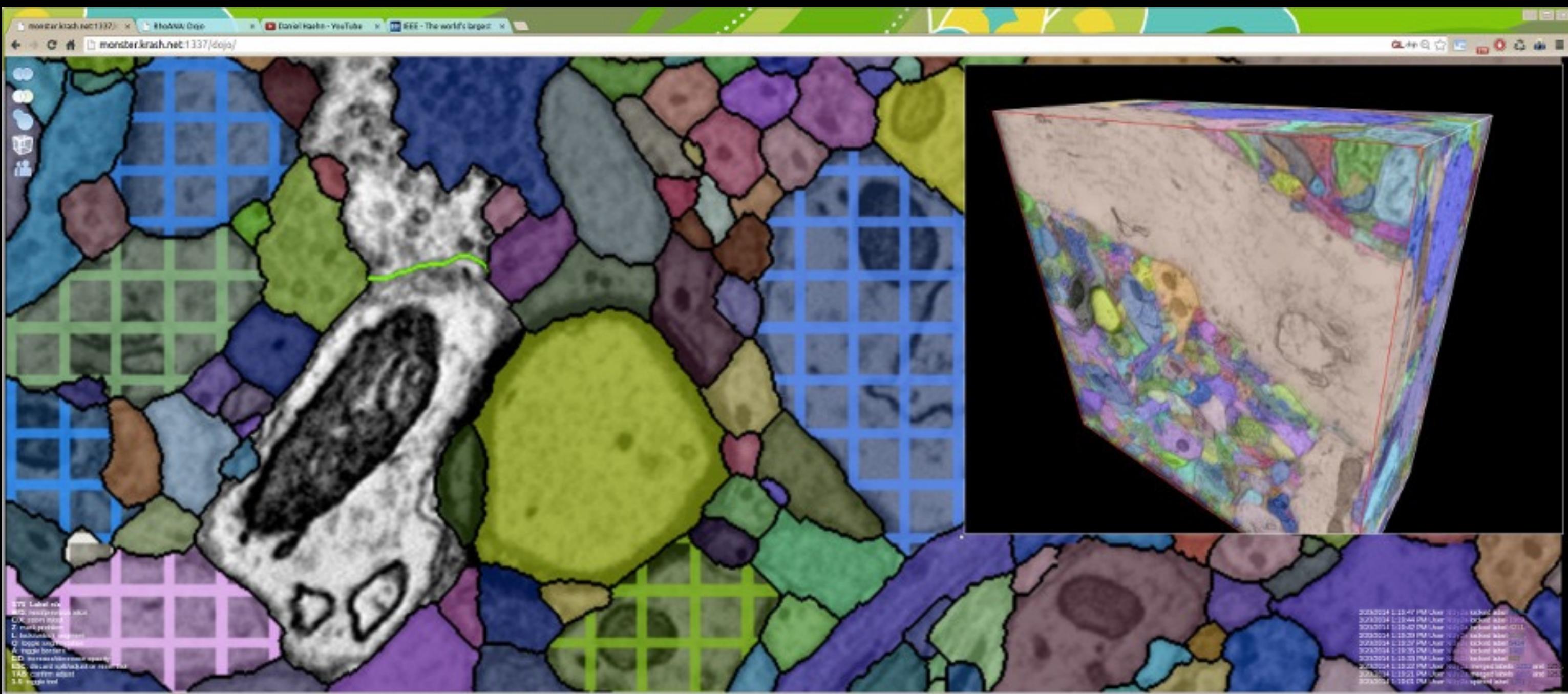
[Sallfeld et al., Bioinformatics 2009 - Catmaid]

(Semi-)Automatic Proofreading

- Minimizes required user input
- Speeds up and simplifies proofreading
- Example tools:
 - NeuTu
 - Dojo
 - WebKnossos



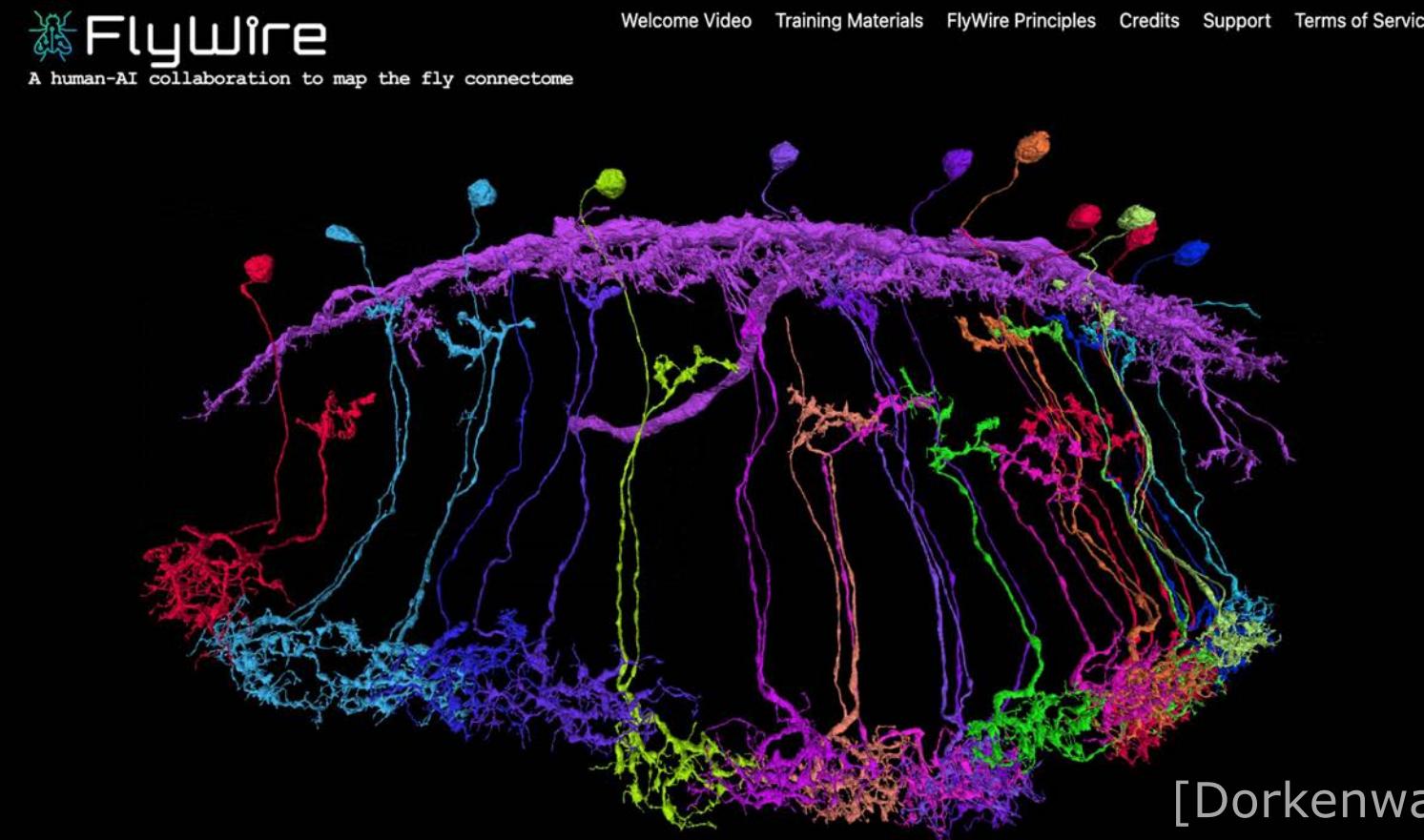
[Zhao et al., Front. in Neural Circuits 2018 - NeuTu]



[Haehn et al., IEEE Vis 2014 - Dojo]

Crowdsourced Proofreading

- Mobilize gamers and citizen scientists to help in proofreading
- Users improve existing (automatic) segmentation



[Dorkenwald et al., Nature Methods 2022]

Connectomics Workflow

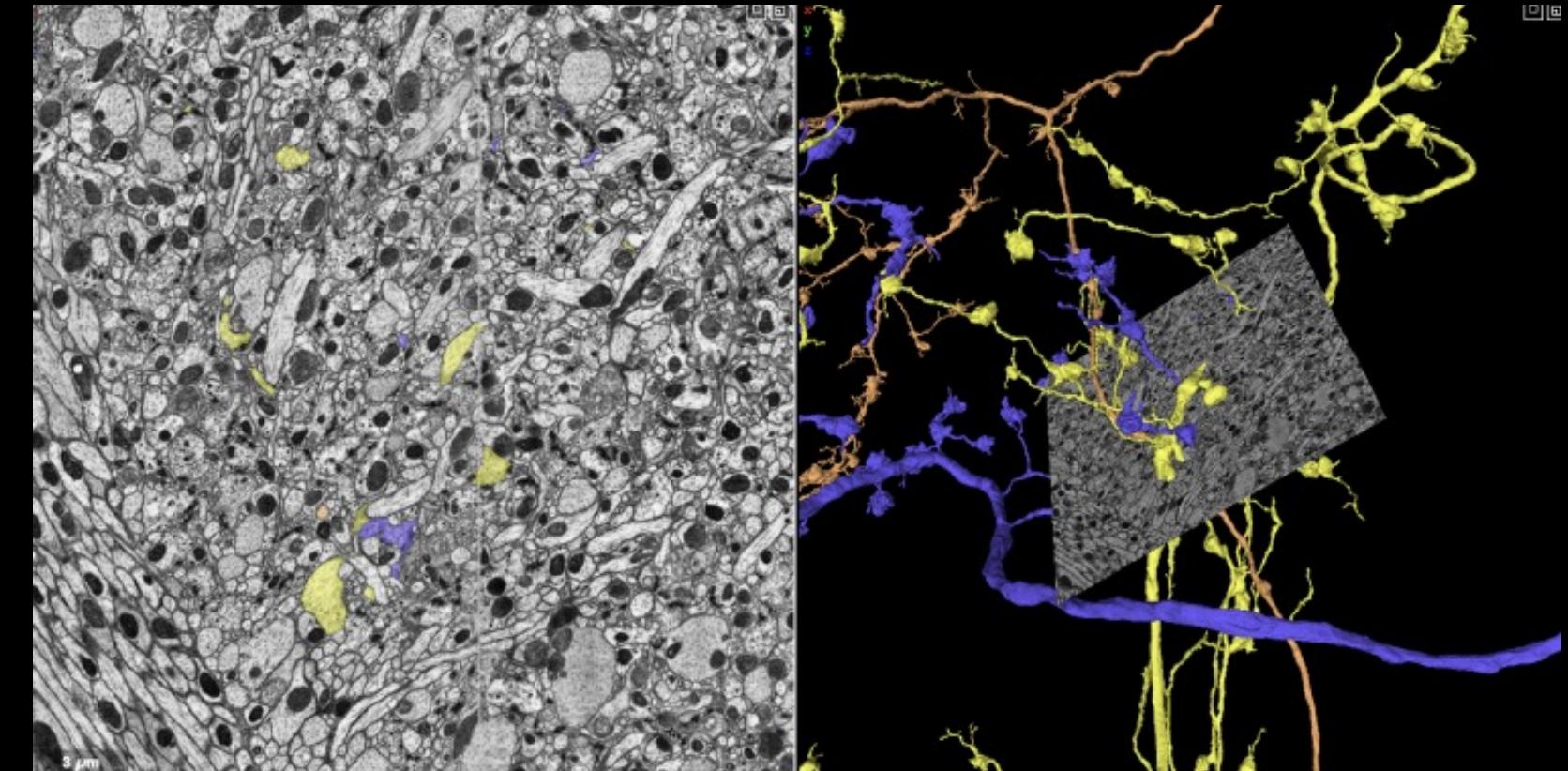


Visualization for Exploration & Analysis

- Goal:
 - Visual exploration of connectomics data
 - Quantitative analysis
 - Connectivity analysis
 - Hypotheses Testing
- Approaches:
 1. Spatial Exploration
 2. Connectivity Exploration
 3. Visualization-focused Analysis

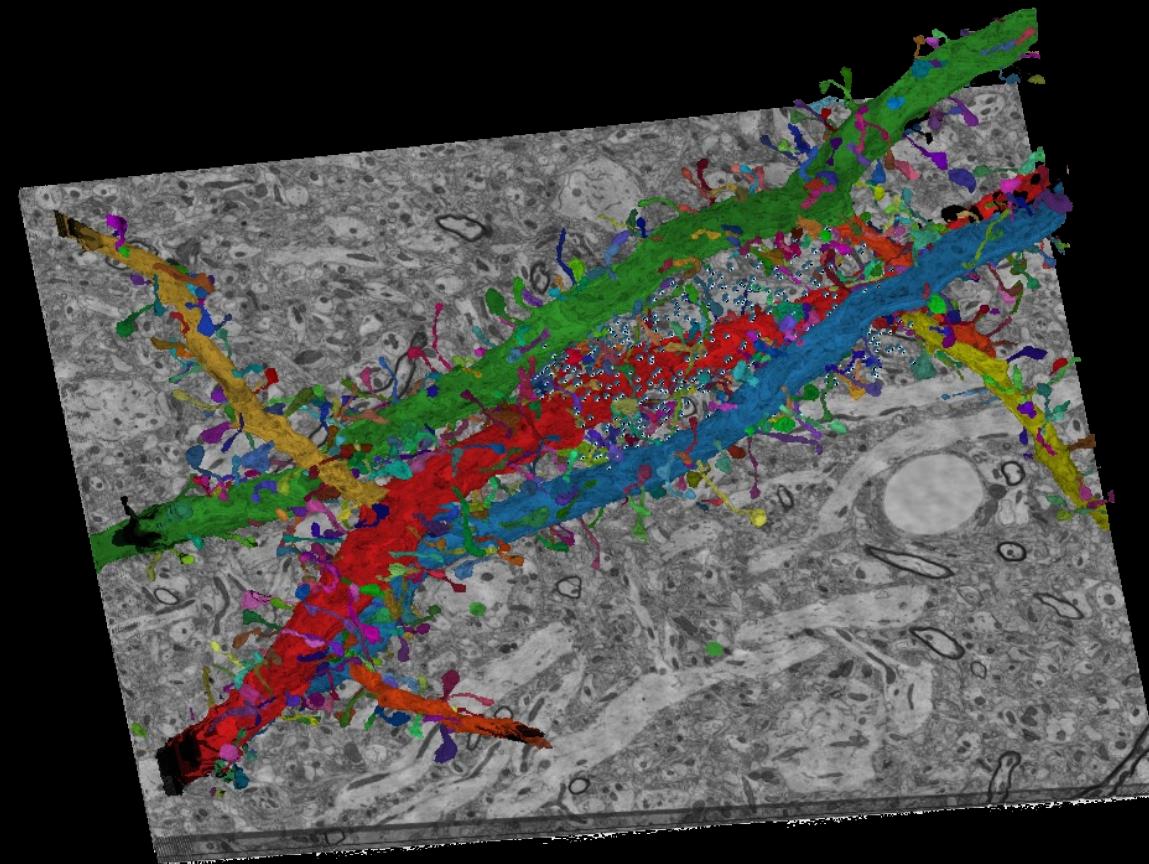
Spatial Exploration

- Unsegmented/Segmented Data
- Approaches:
 - Slice Views
 - Volume Rendering
 - Surface Rendering

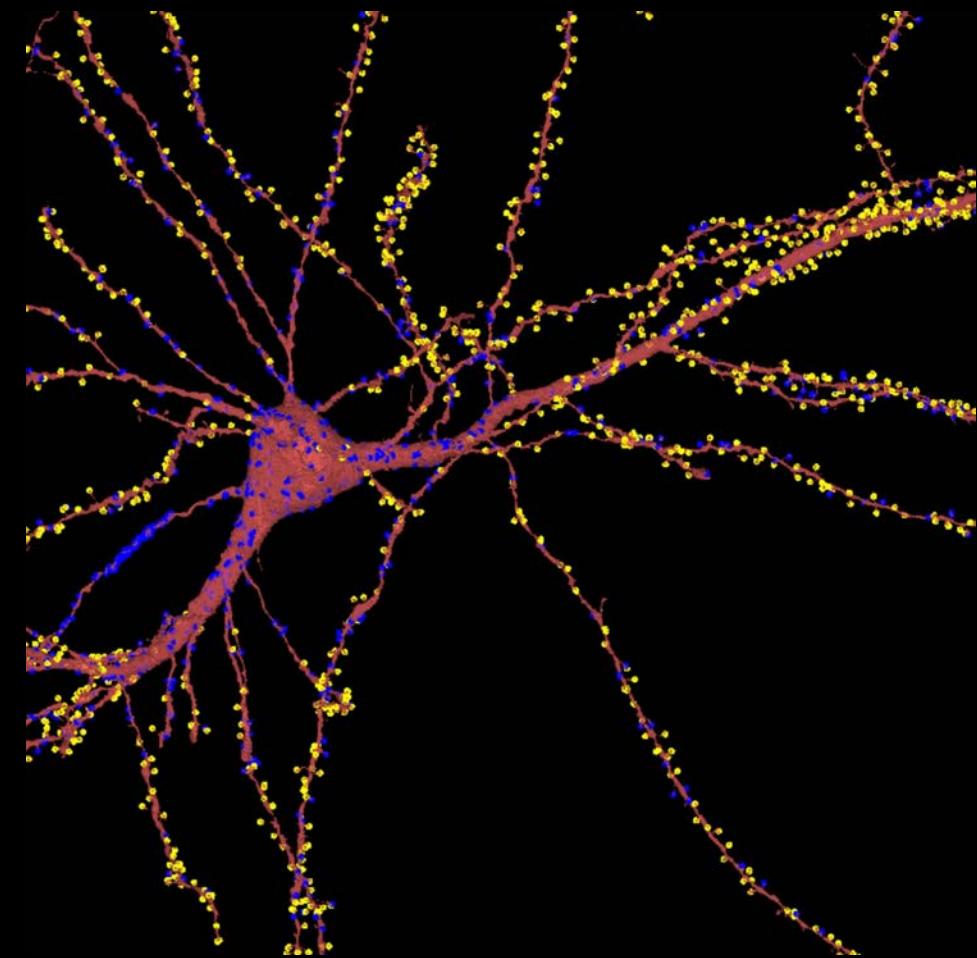


[Google Inc. - Neuroglancer]

Scalable EM Volume Visualization

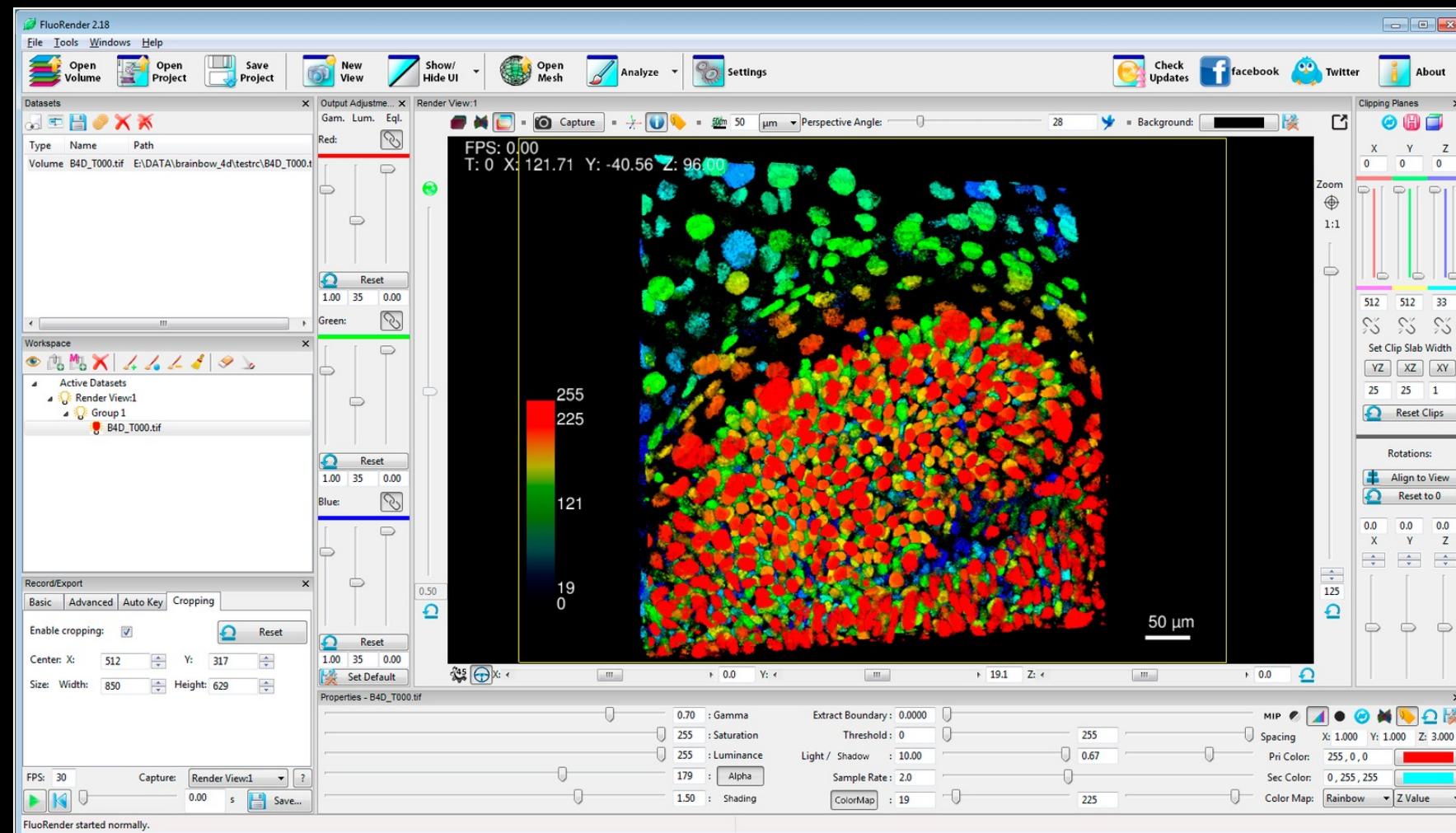


[Hadwiger et al., IEEE Vis 2012]



[Google Inc. - Neuroglancer]

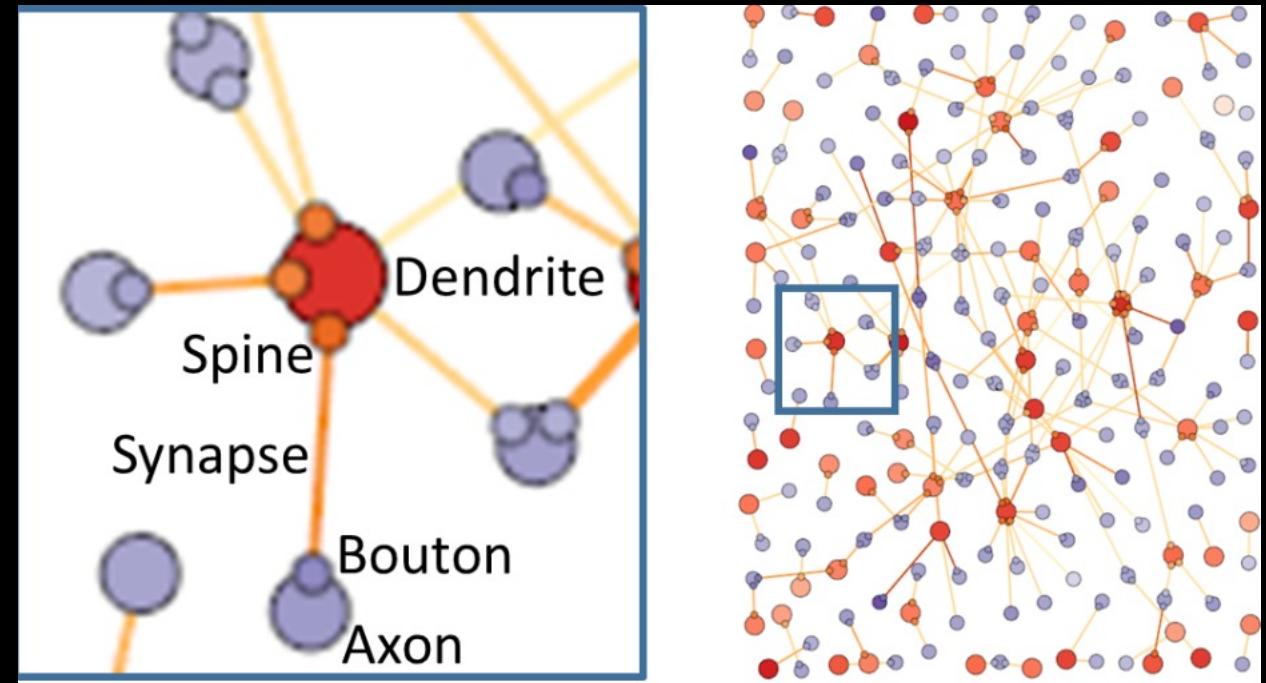
Confocal Microscopy Visualization



[Wan et al., Pacific Vis 2012 - FluoRender]

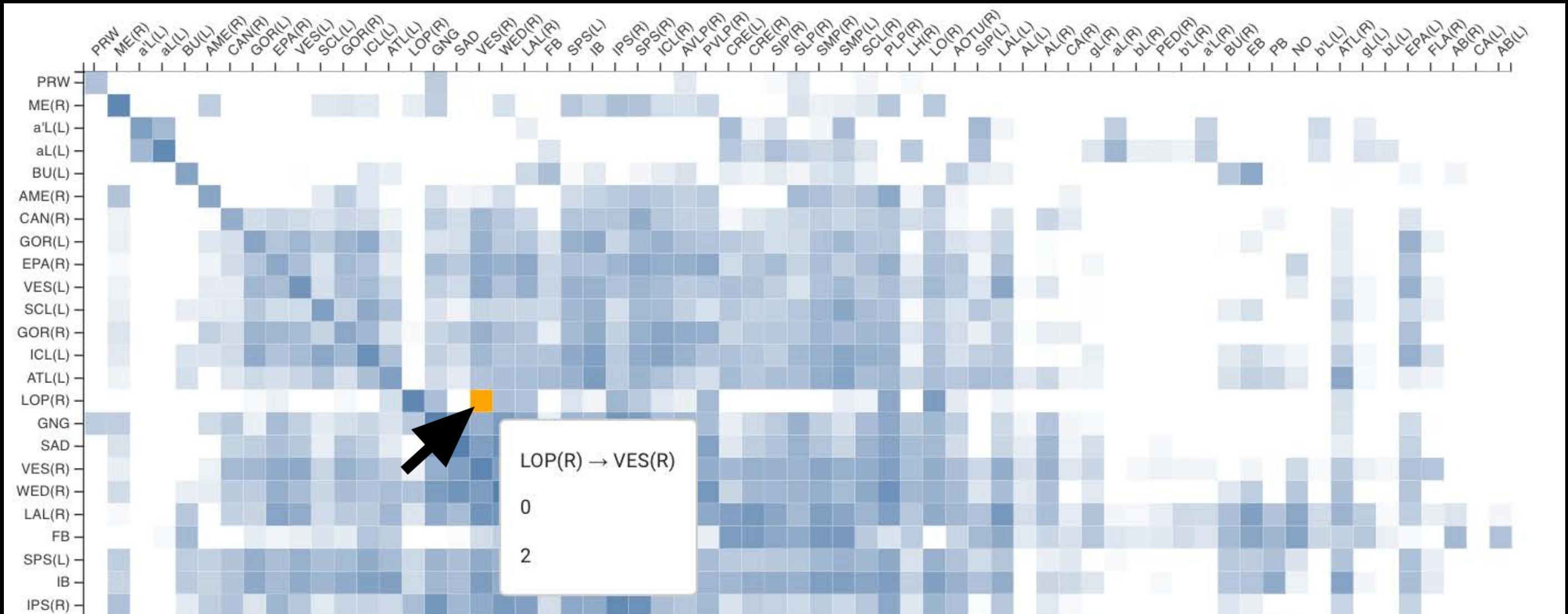
Connectivity Exploration

- Study connectivity in data (at multiple levels)
- Abstract complex 3D morphology
- Approaches:
 - Node-Link views
 - Matrix views
 - Abstract connectivity views



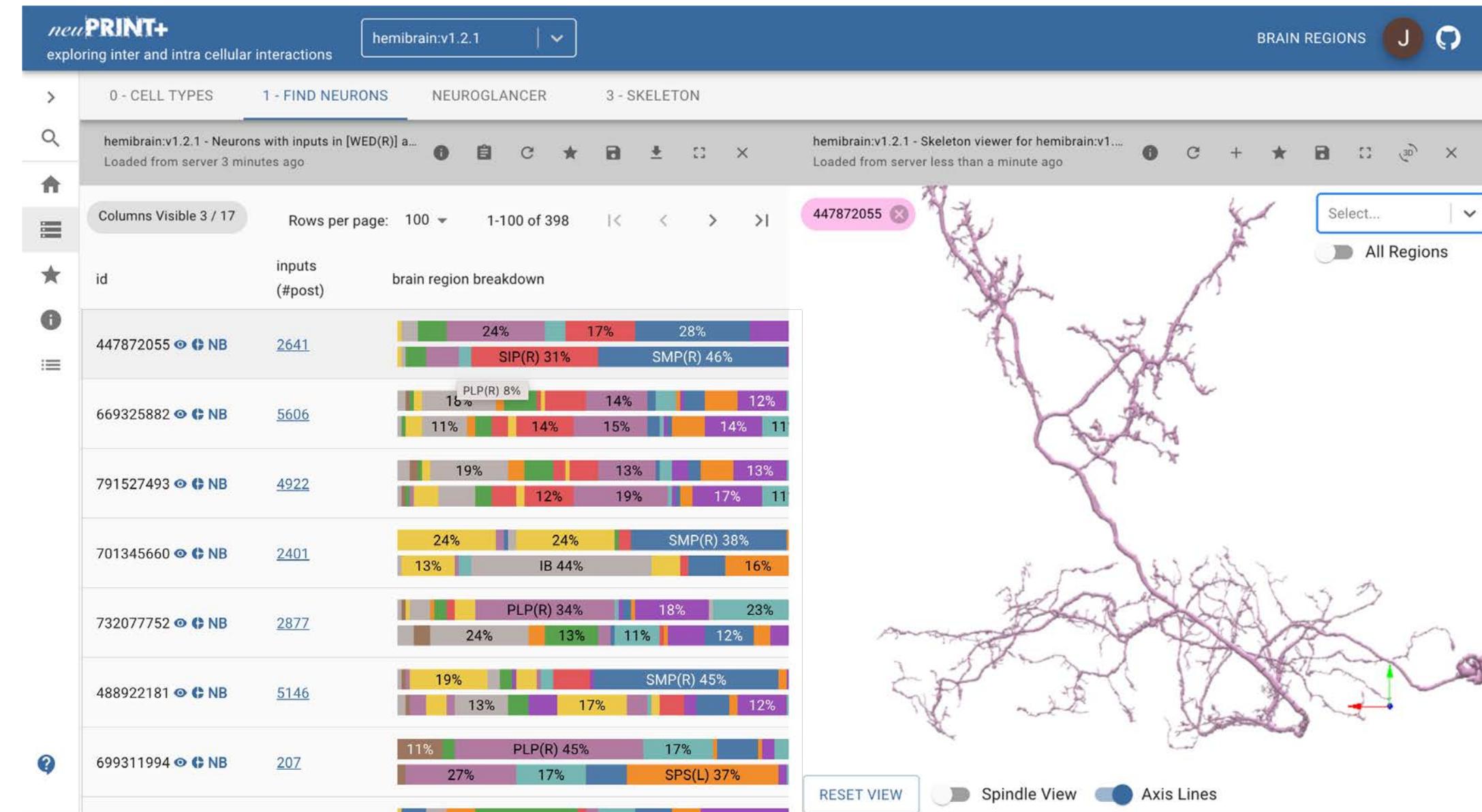
[Agus et al., Eurovis 2019]

Connectivity Exploration

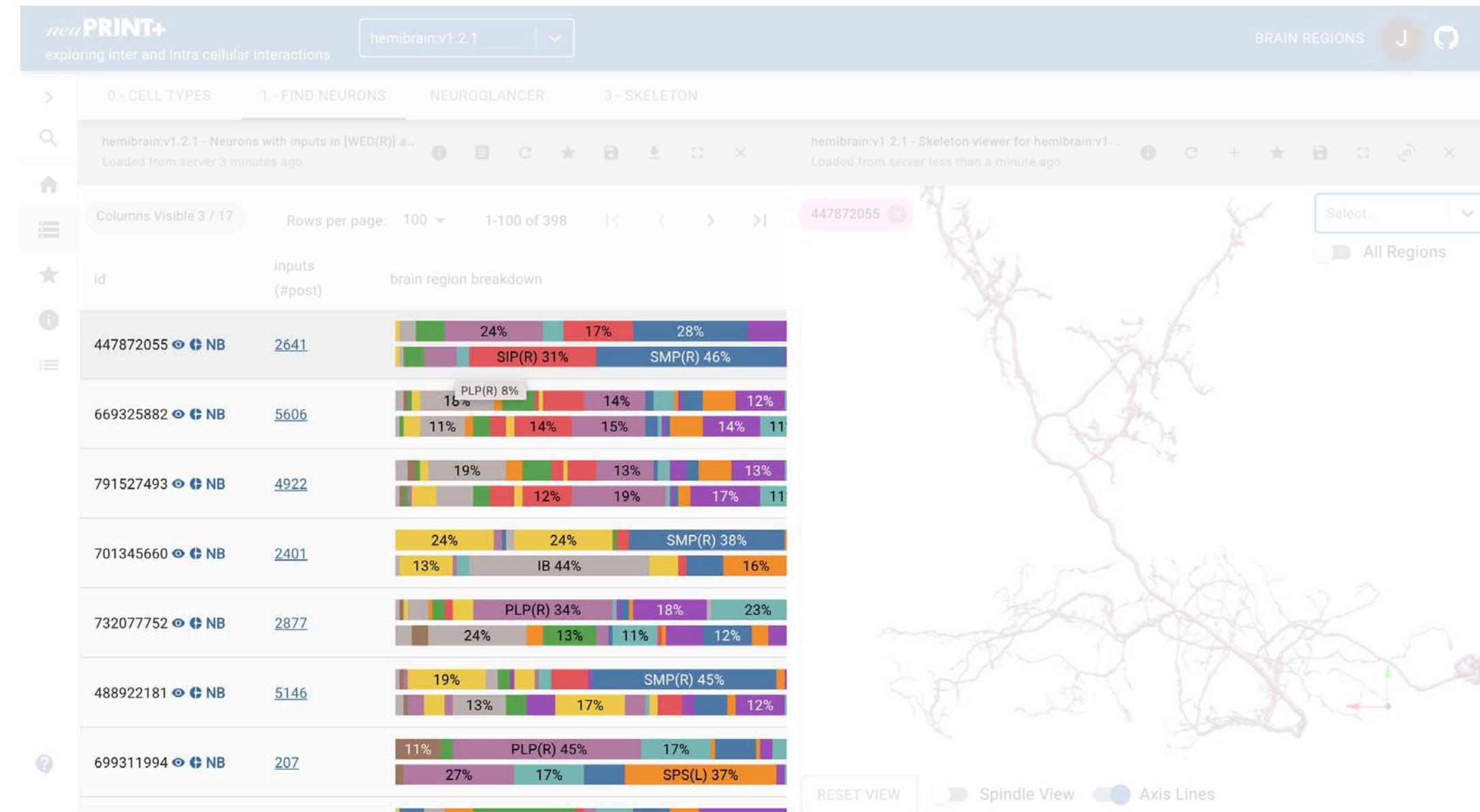


[Clements et al., bioRxiv 2020 - neuPrint]

Connectivity Analysis

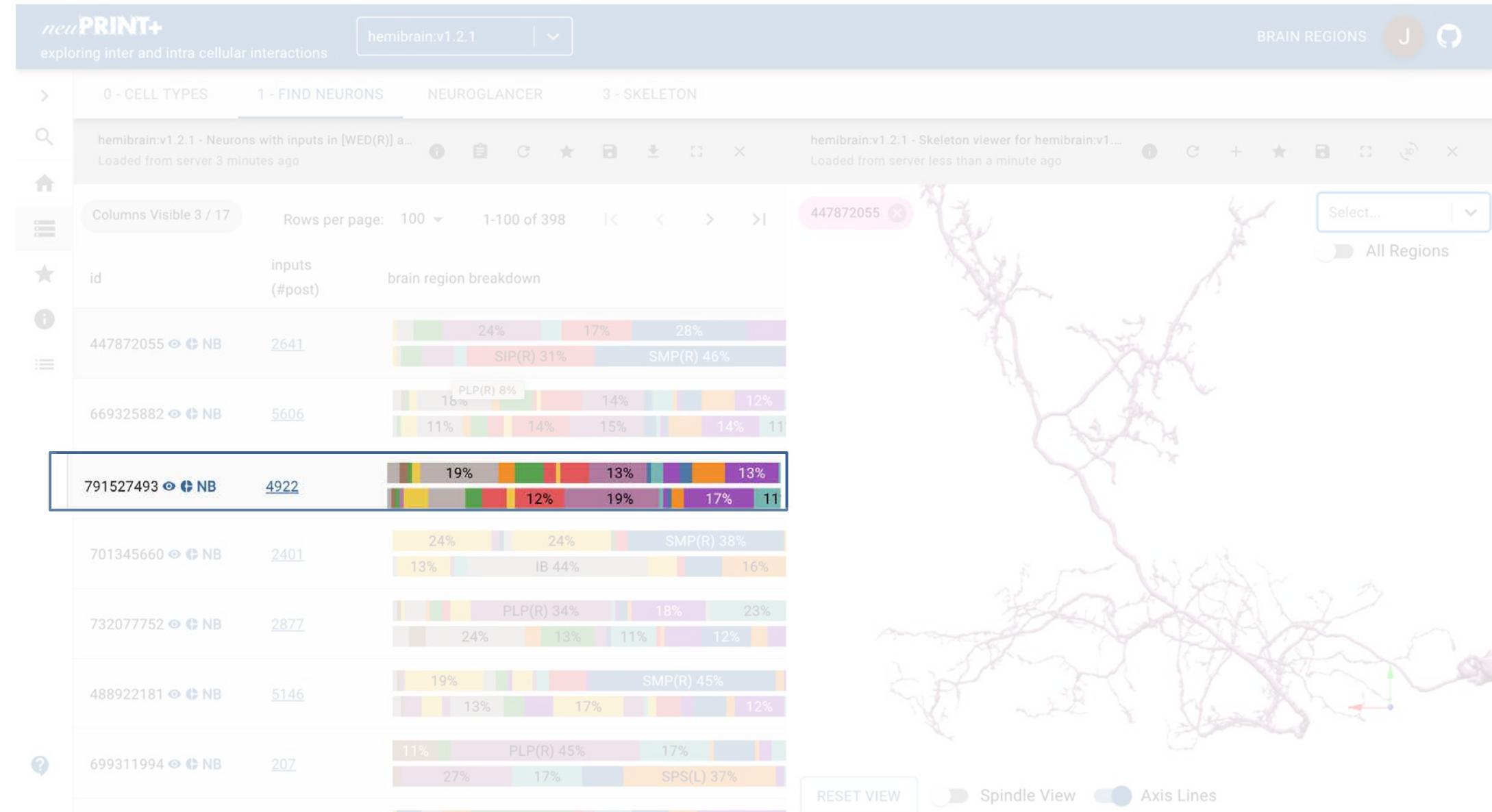


Connectivity Analysis

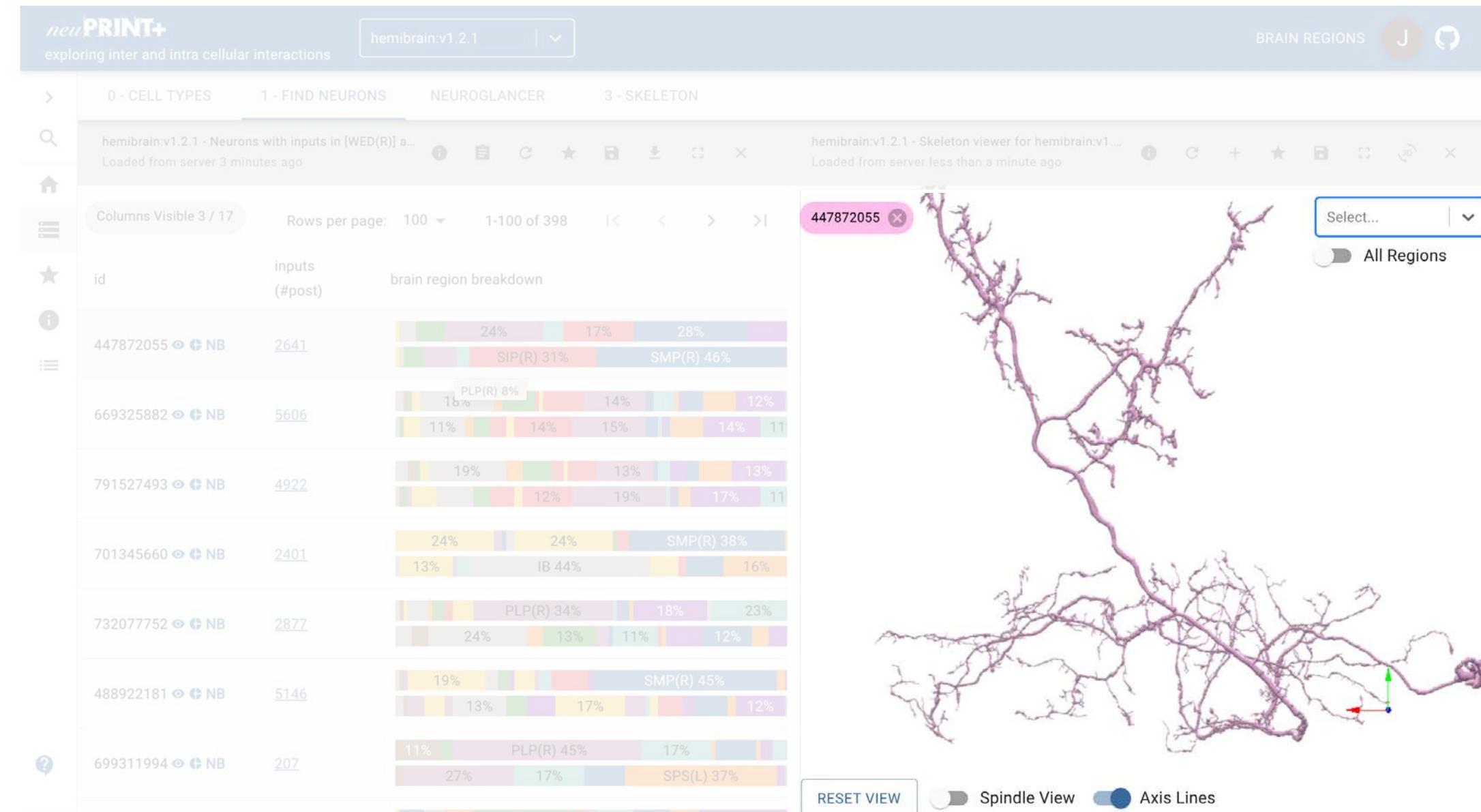


[Clements et al., bioRxiv 2020 - neuPrint]

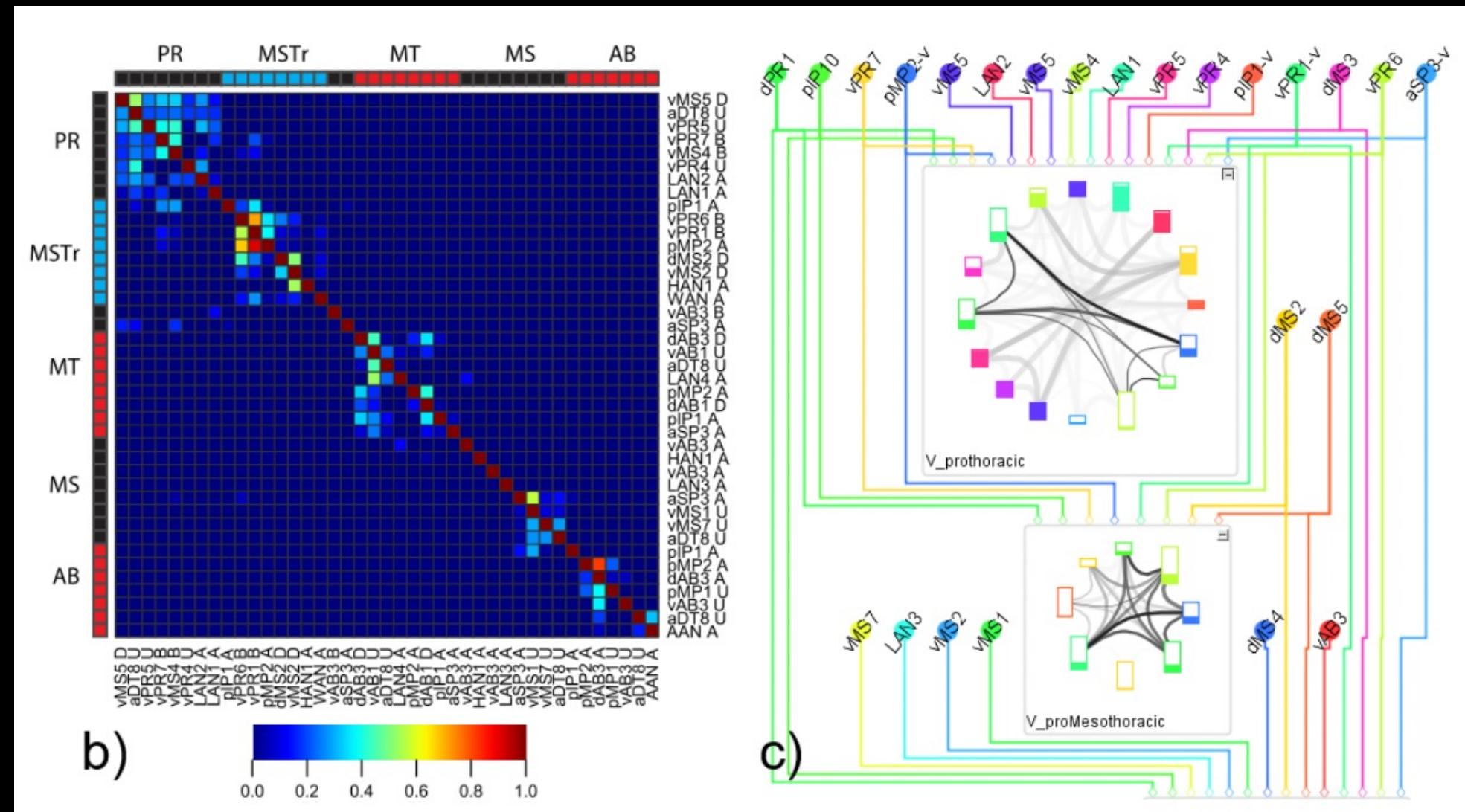
Connectivity Analysis



Connectivity Analysis



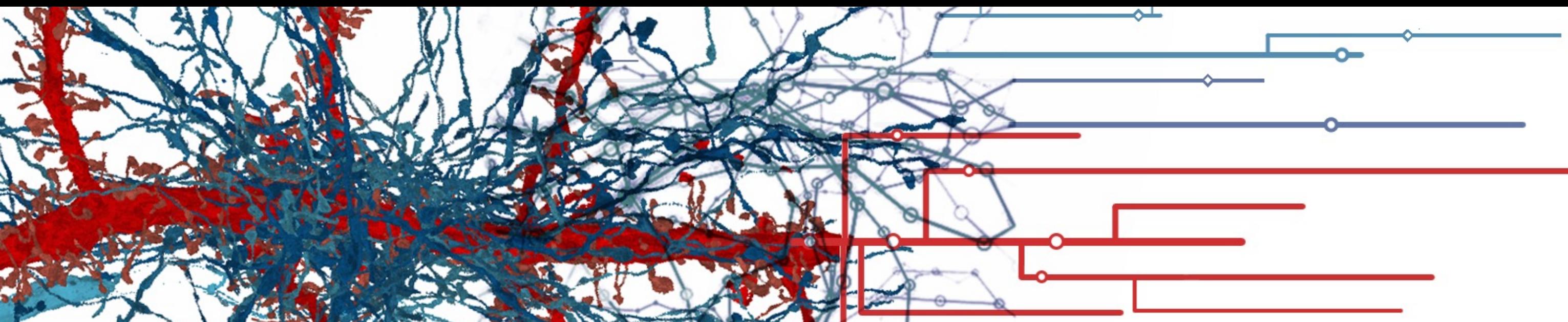
Connectivity Exploration



[Sorger et al., BioVis 2013 - NeuroMAP]

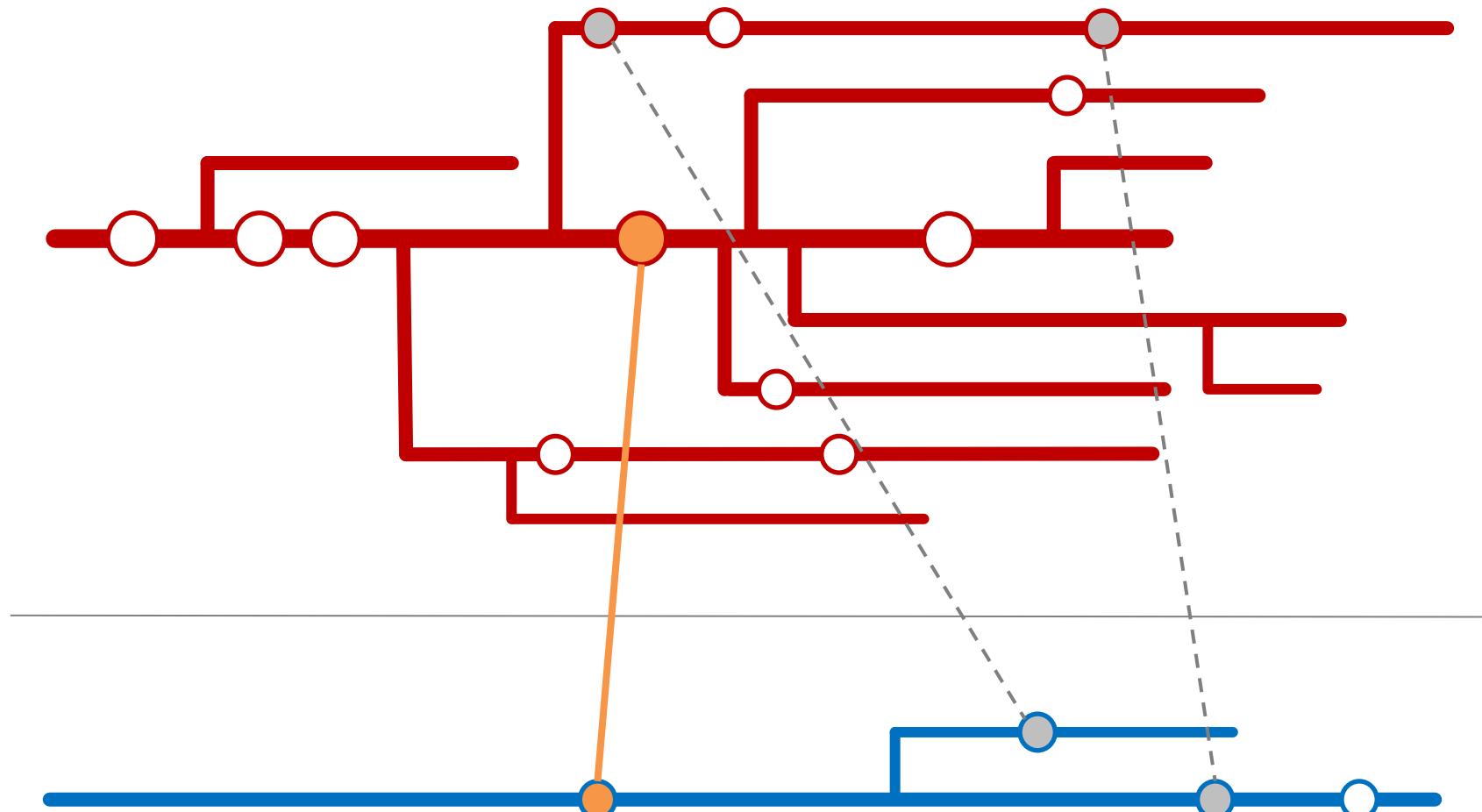
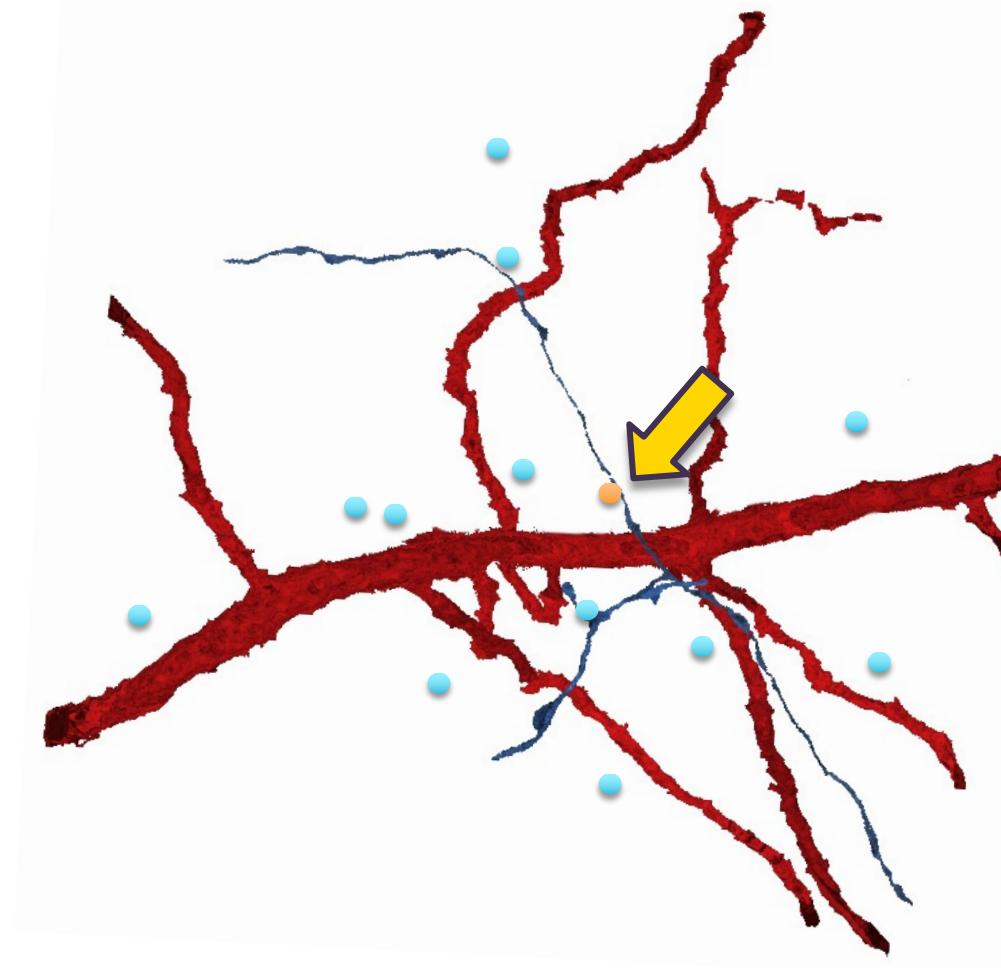
Connectivity Exploration

- Scalable subway map inspired 2D visualization
- Linked with original 3D Data



[Al-Awami et al., IEEE Vis 2014 - Neurolines]

Visual Encoding: Synapse Links

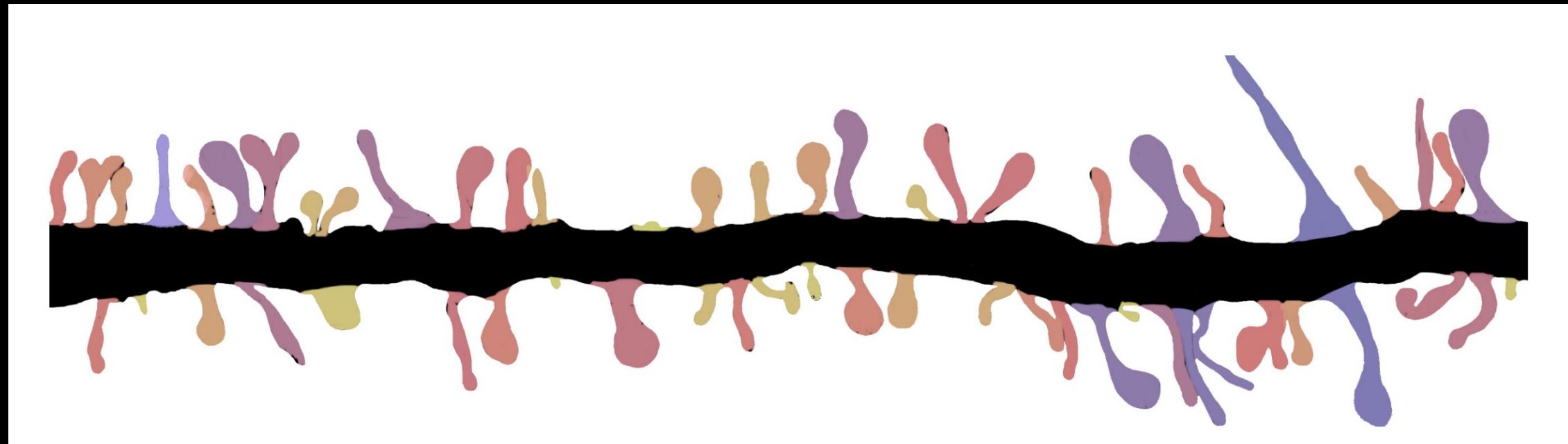


Visualization-Focused Analysis

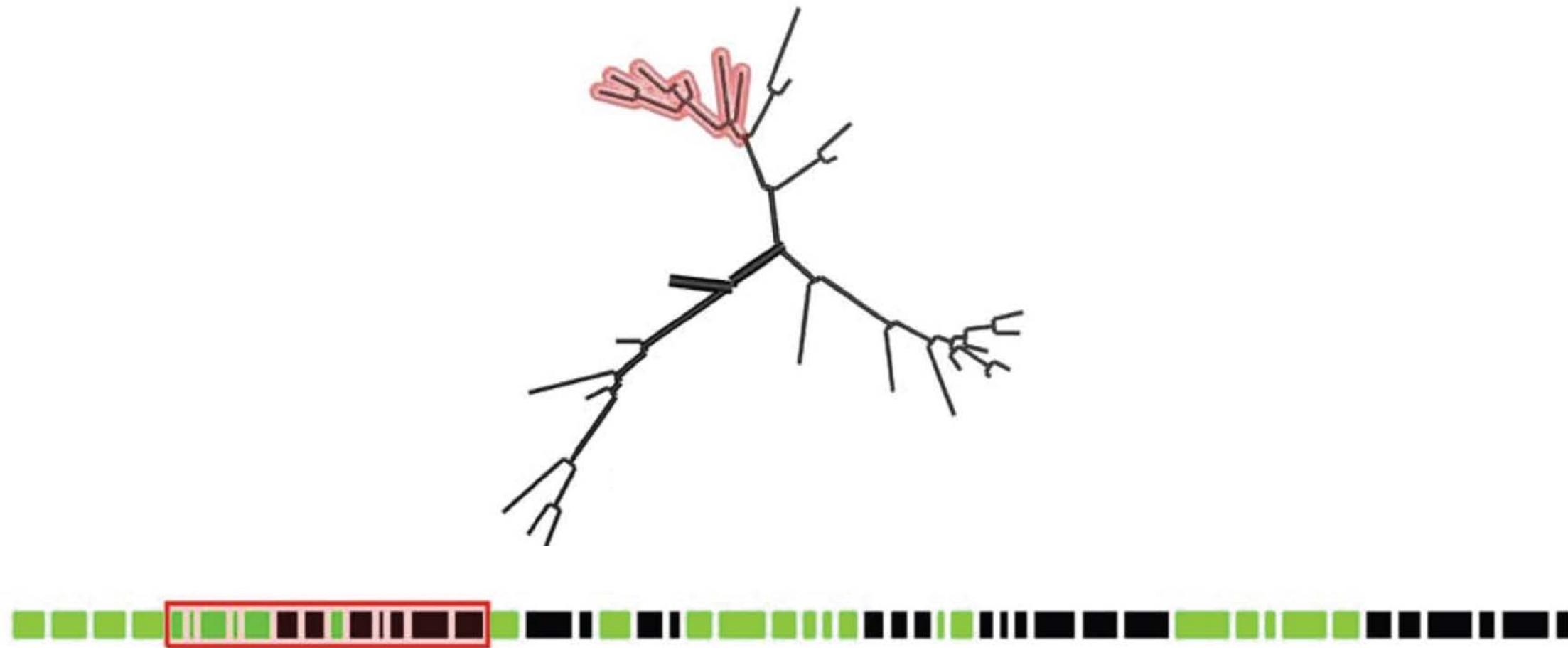
- Approaches:
 - Neuron Analysis
 - Visual Query Systems
 - Neighborhood Analysis

Neuron Analysis

- Visualize & quantify neuron shapes
- Compare neurons

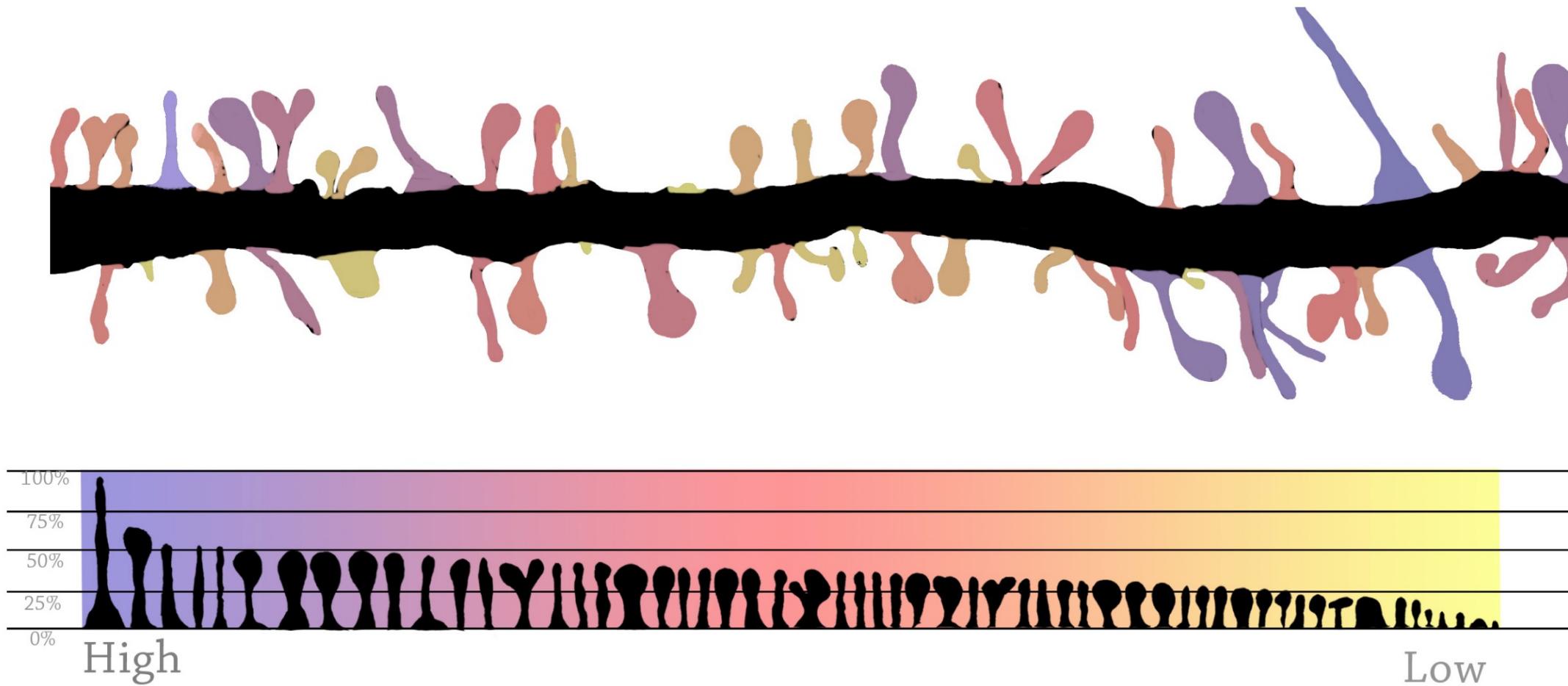


Neuron Analysis



[Cuntz et al., PLOS Computational Biology 2010]

Neuron Analysis



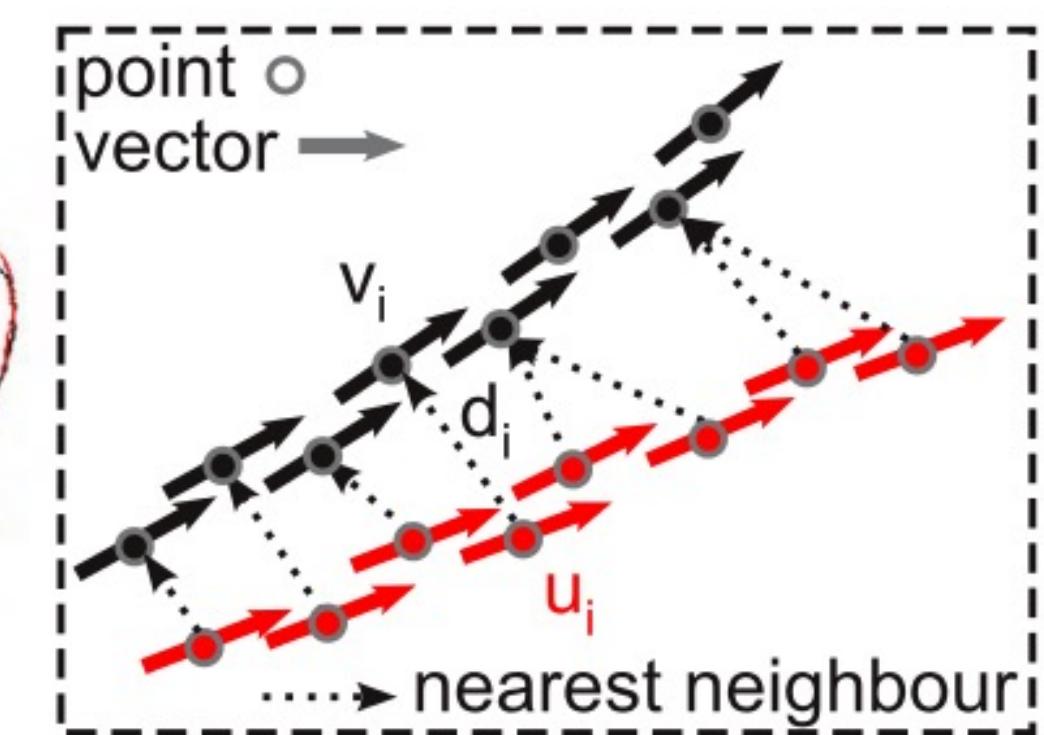
[Pastor et al., Applied Sciences 2021]

Neuron Analysis

NBLAST: pairwise similarity computation for (fly) neurons. Organizing & searching large datasets

Identifying the same neuron imaged with different modalities and across hemispheres

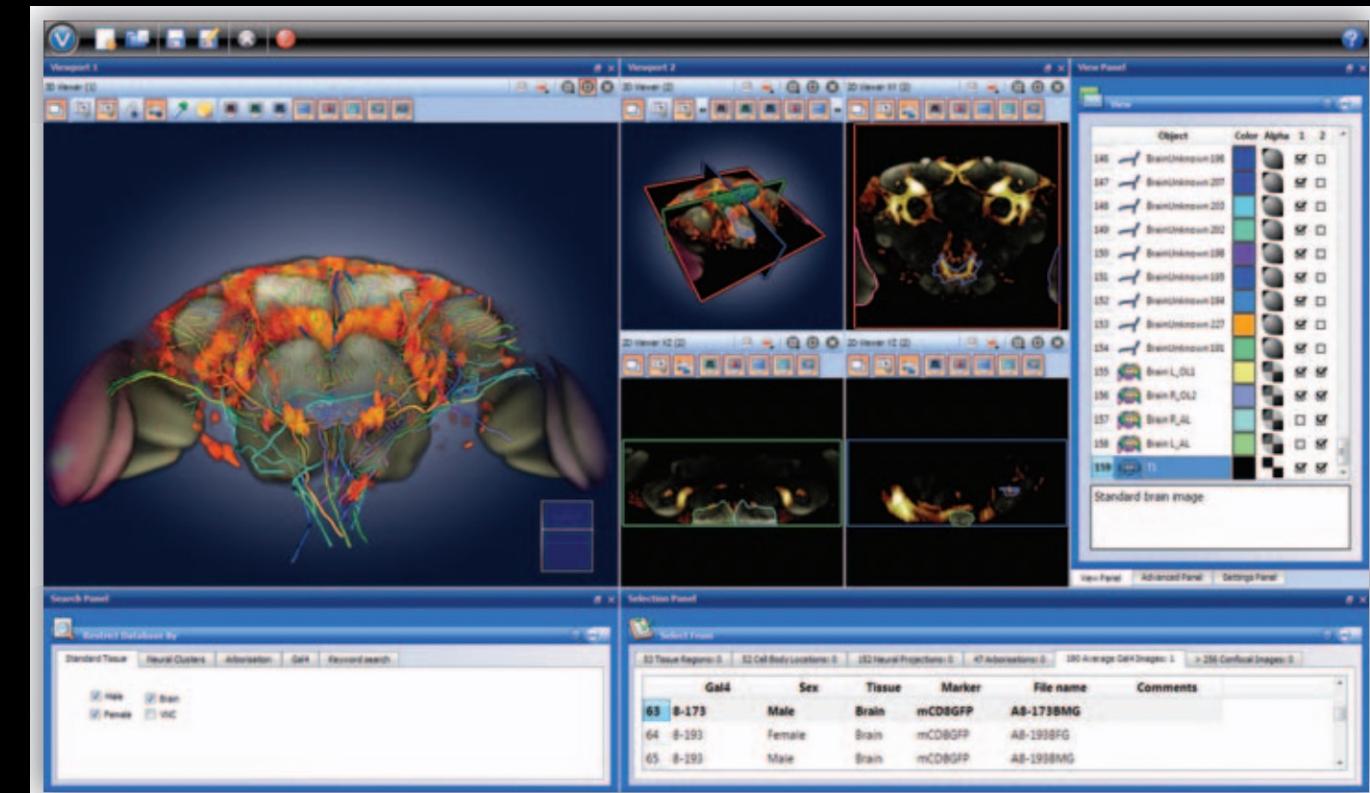
Depends on position and local geometry



[Image by P. Schlegel, NAVis documentation]

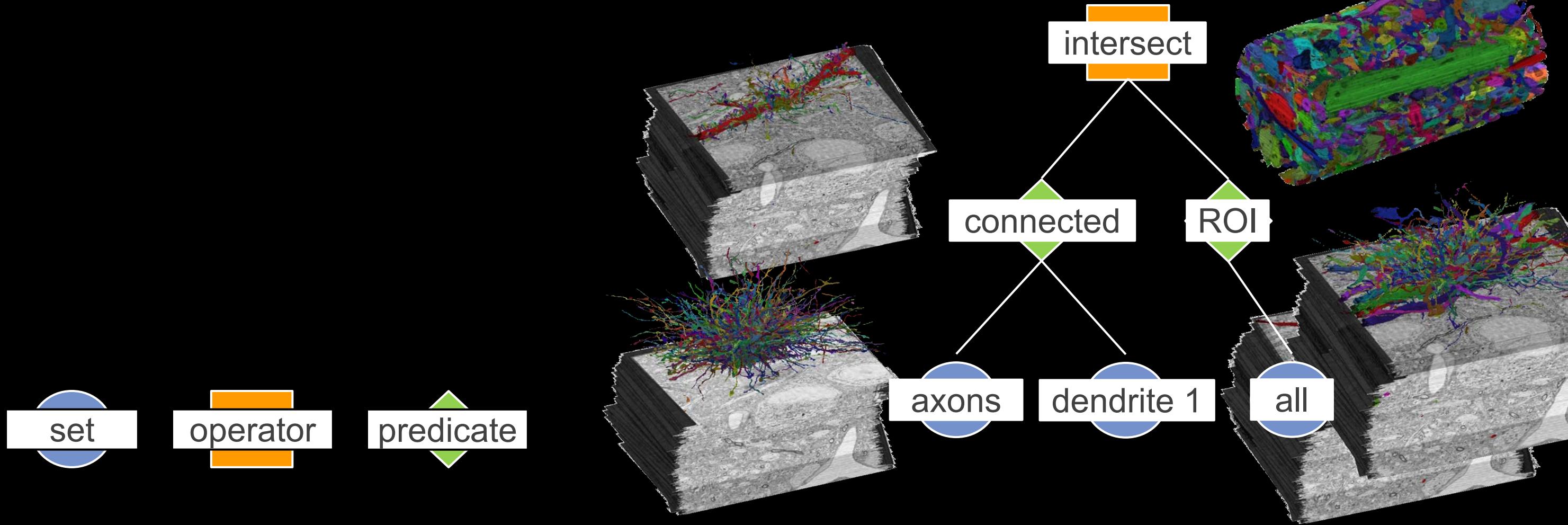
Visual Query Systems

- Interactive analysis of connectomics data
- Easy-to-use for domain scientist
- Scalable & flexible



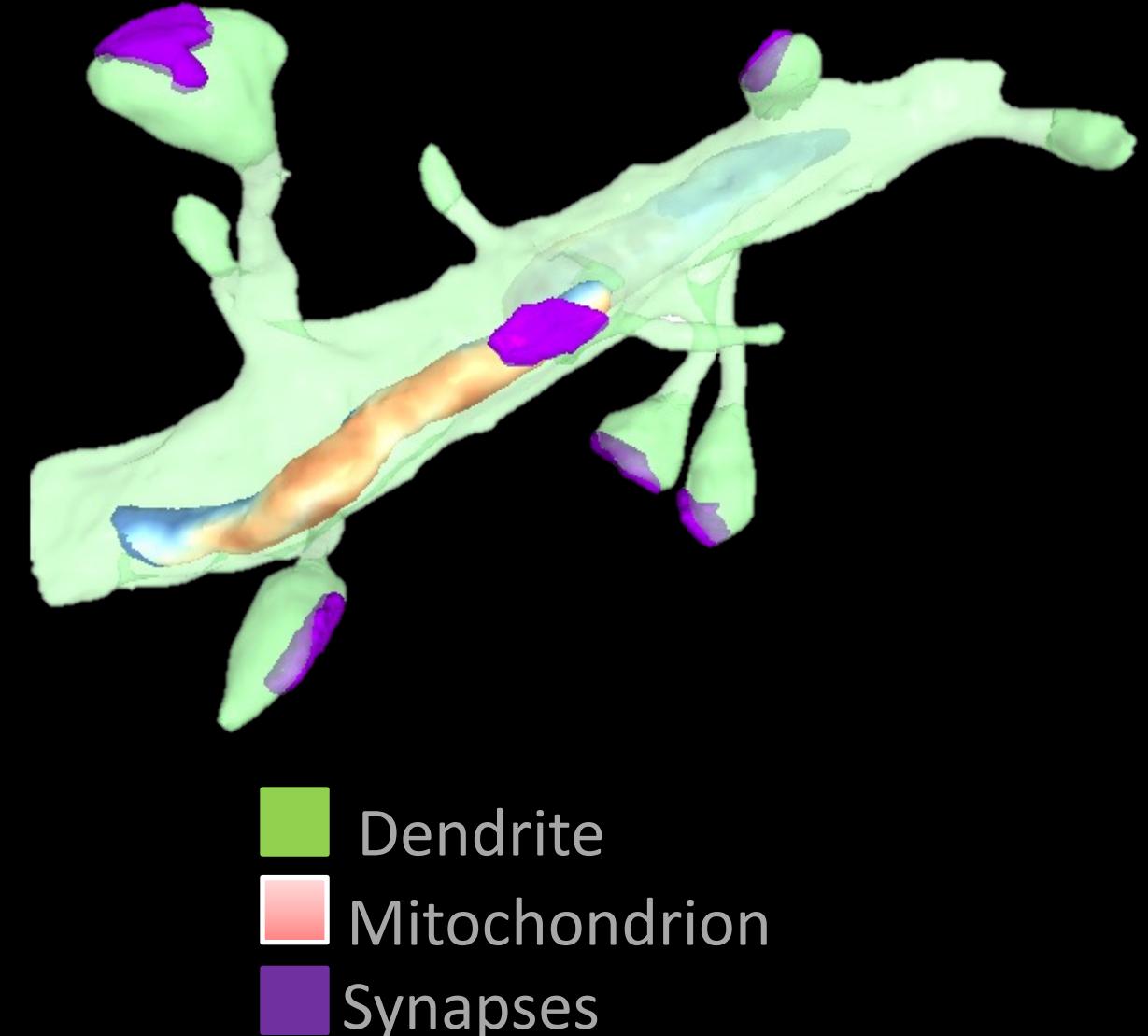
[Bruckner et al., IEEE Vis 2009]

Visual Query Systems

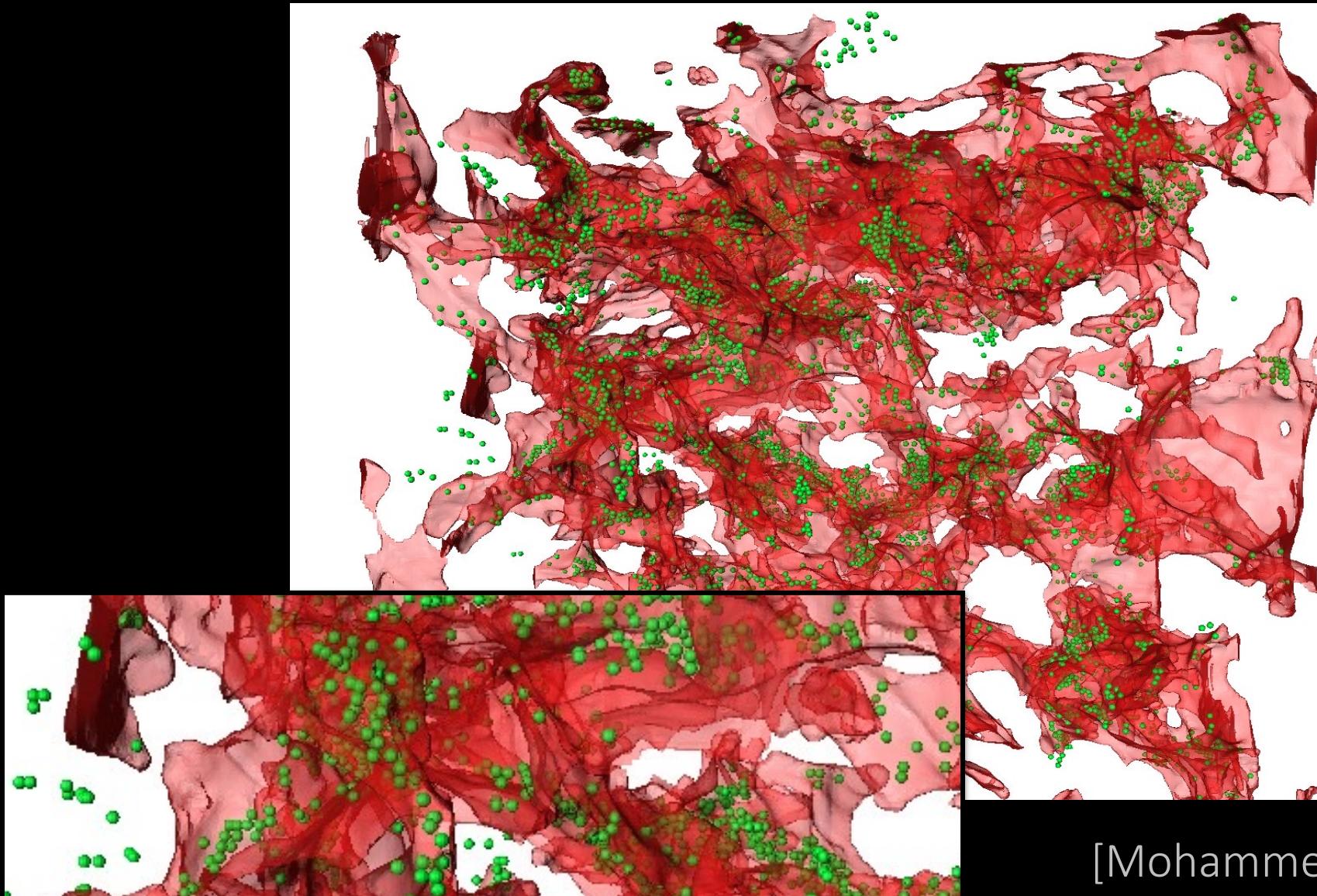


Neighborhood Analysis

- Beyond pure connectivity
- Analyze cell organelles and local spatial neighborhoods
- Examples:
 - Astrocytes
 - Glycogen
 - Mitochondria



Neighborhood Analysis - Astrocytes



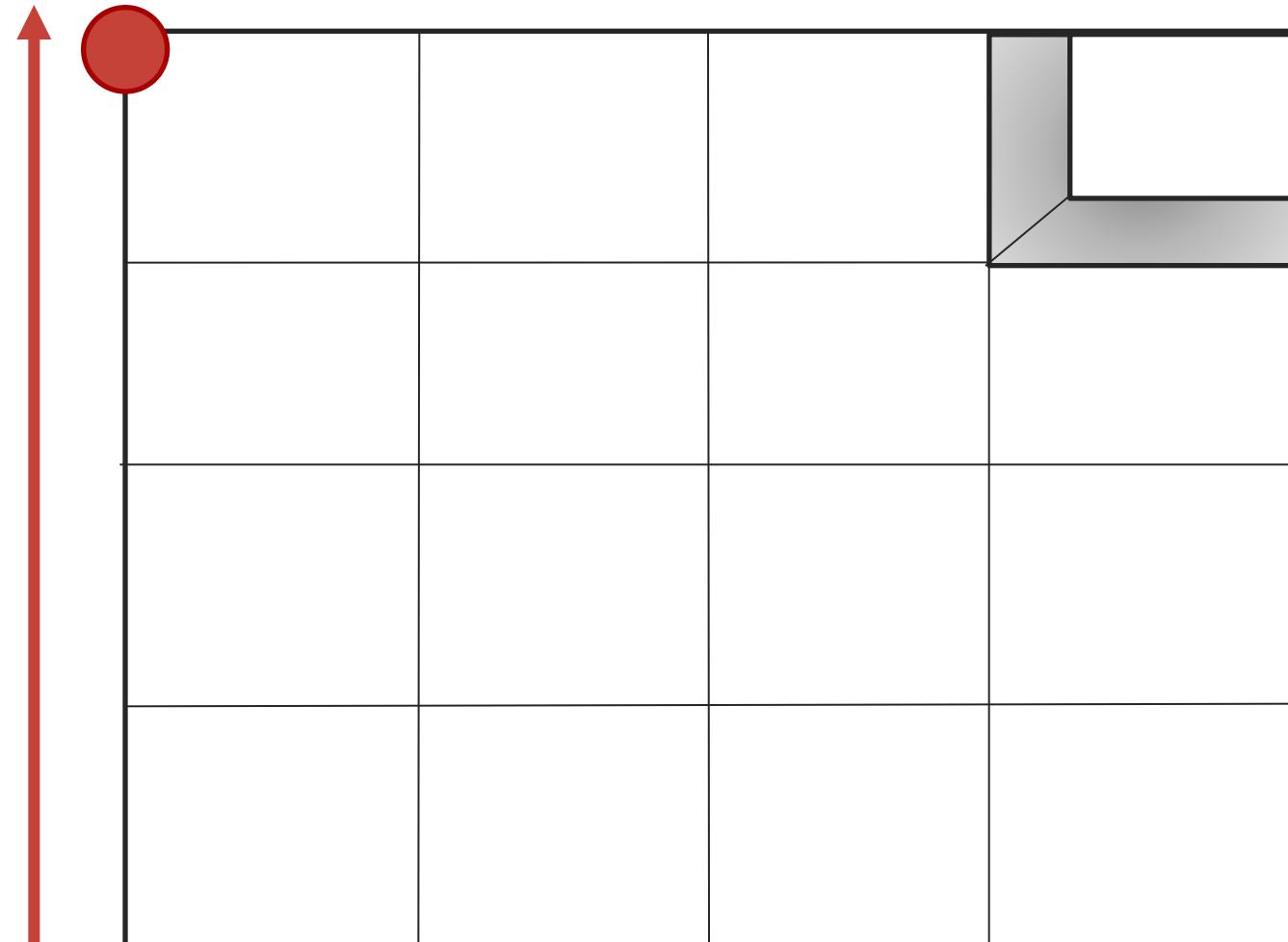
[Mohammed et al., IEEE Vis 2017]

3D Abstraction of Neurites

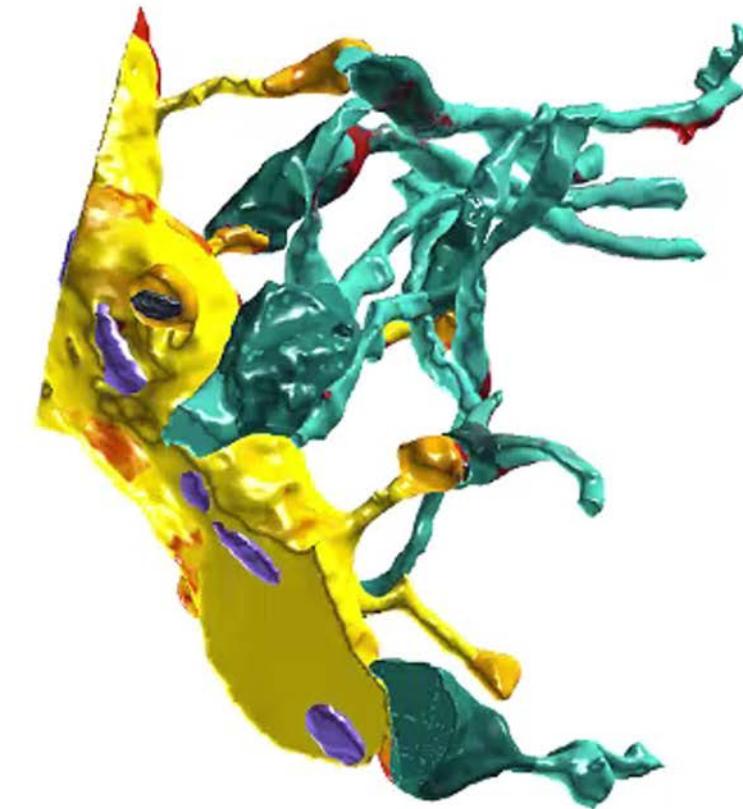


abstract

ASTROCYTES

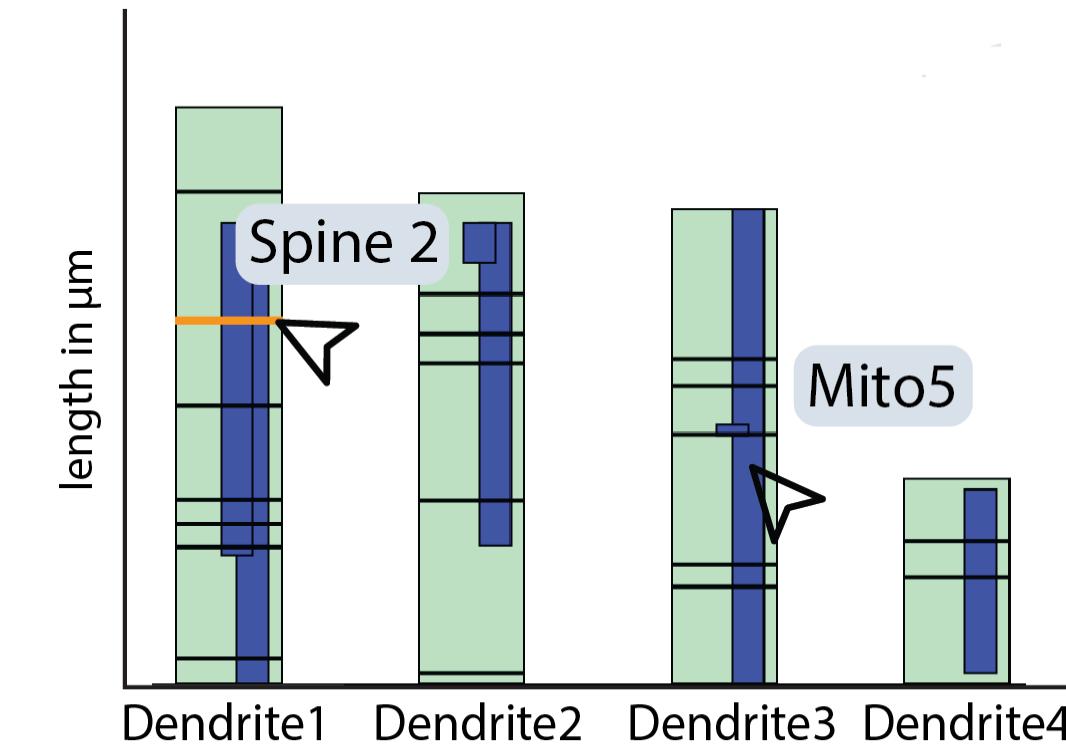
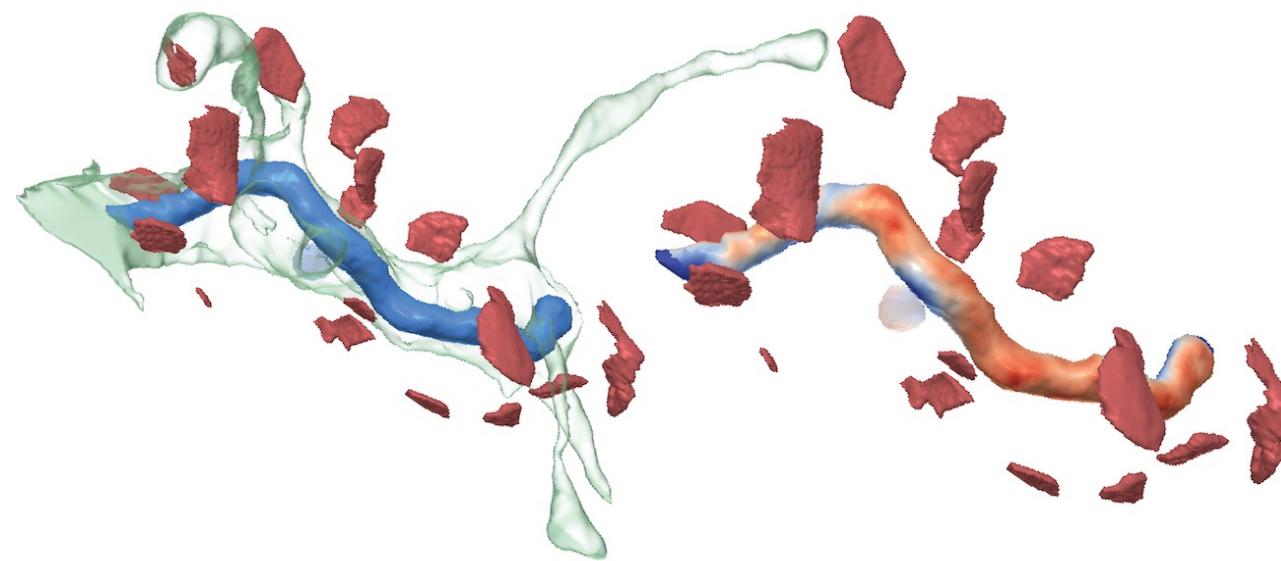


abstract



Neighborhood Analysis

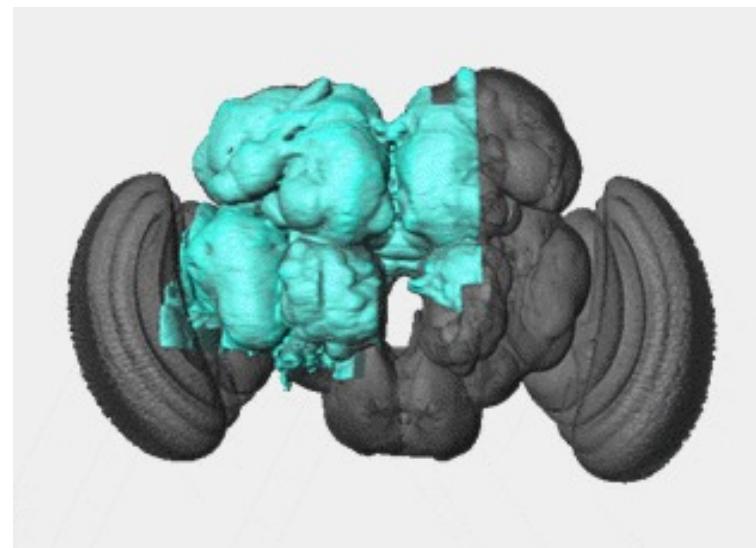
Our current EuroVis paper “Barrio: Customizable Spatial Neighborhood Analysis and Comparison for Nanoscale Brain Structures”



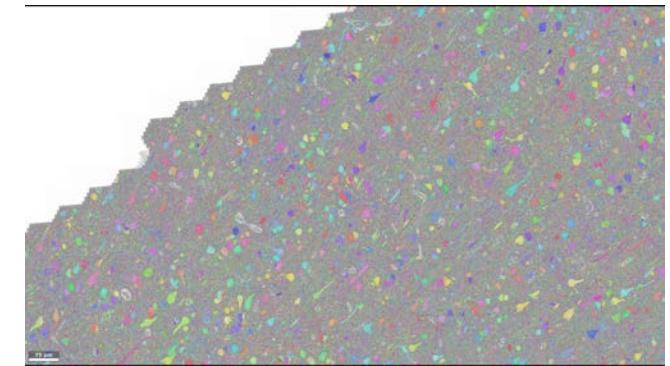
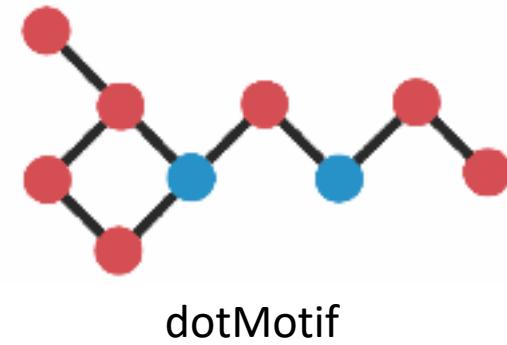
Datasets & Open-Source Tools

Commonly used datasets are listed in paper

Links and resources of ready to use open-source tools



FlyEM Hemibrain dataset

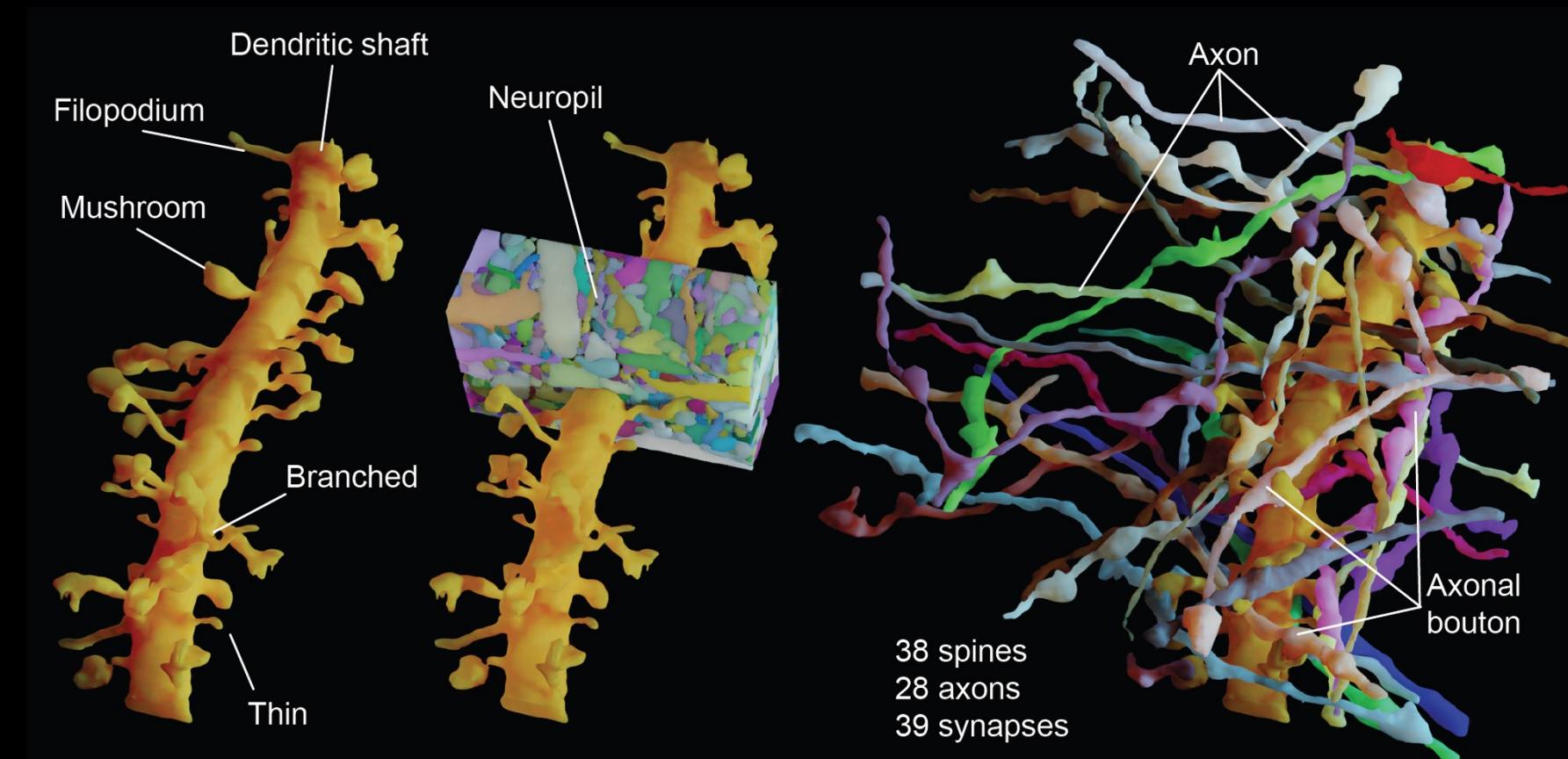


H01 dataset

... and many many more!!!

Future Research: Multimodal Data

- Optical imaging is limited in resolution
- EM can only image dead tissue
- How to **visualize living tissue?**
- How can we combine modalities to get the best of both worlds?

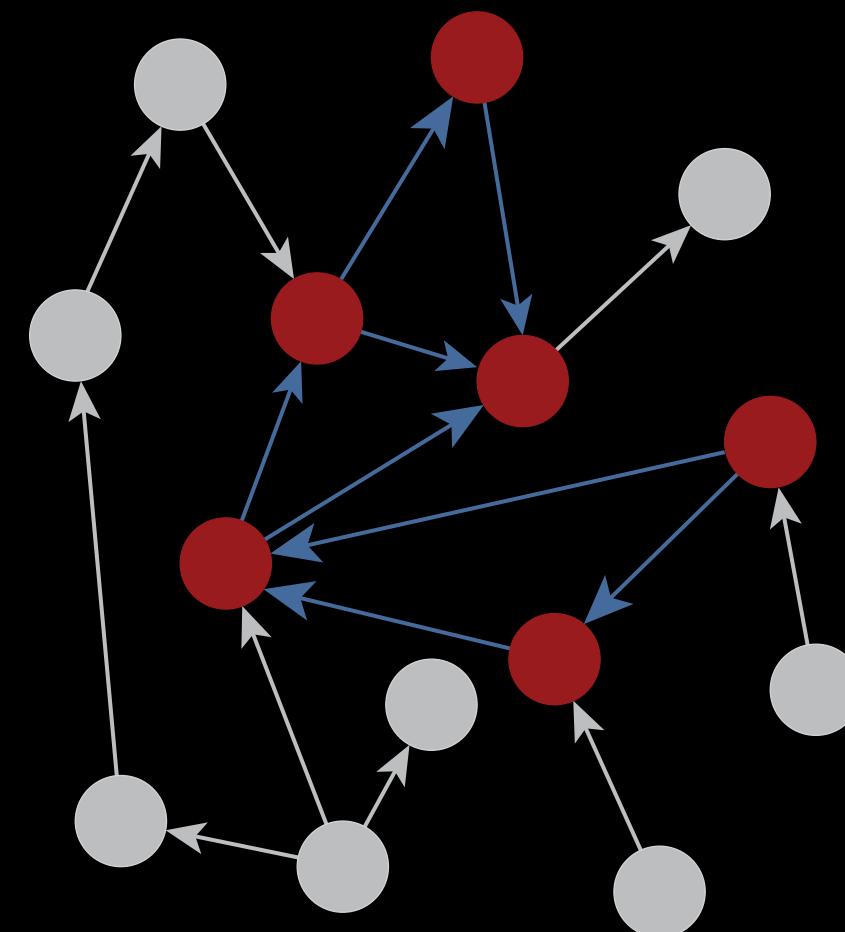


[Velicky et al., bioRxiv 2022]

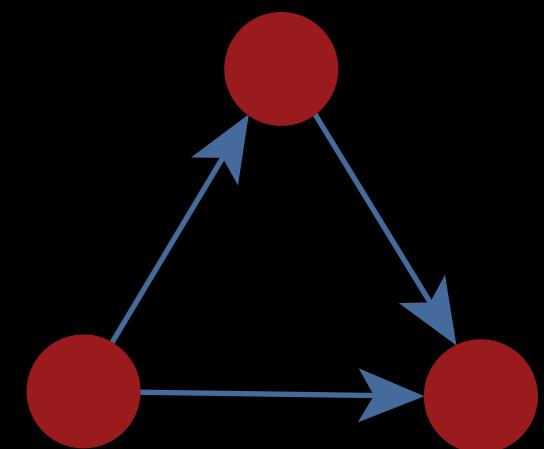
Future Research: Large Connectivity Graph Exploration

Large and dense brain networks are available now How to **query and (visually) analyze** such networks

Network



Motif



Future Research: Scalability

Future (whole brain) connectomics datasets will be an **order of magnitude larger** than current data sets

How can we **process & visually analyze** such datasets efficiently?

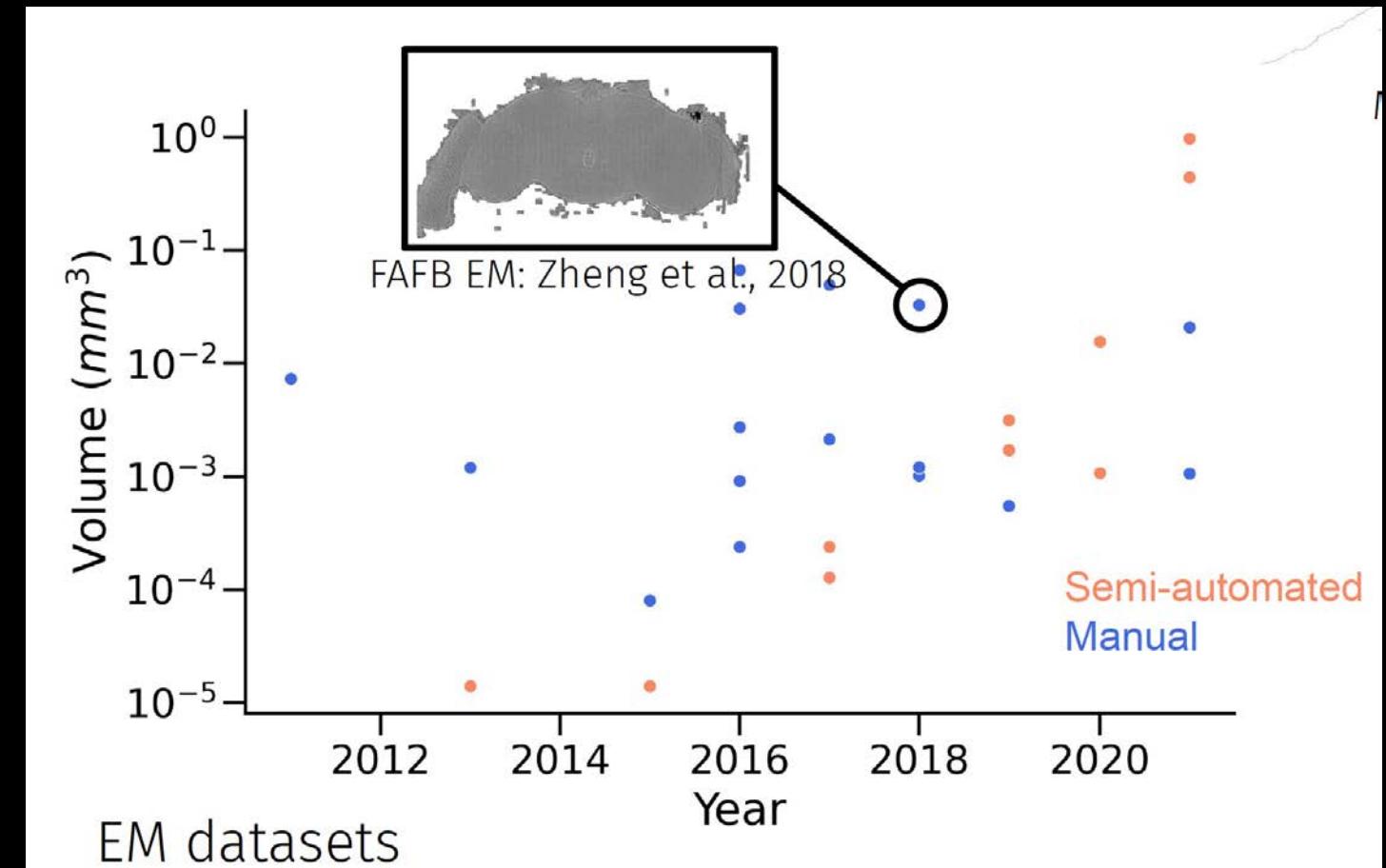


Image by Sven Dorkenwald

Take This With You

- Visual Computing needed in all steps of connectomics pipeline
- Challenges:
 - Scalability
 - Computational
 - Visual Complexity
 - Accessibility

Thank You!

CONNECTOMICS VIS SURVEY

A survey visualization research in high-resolution connectomics.

Paper
Please contribute if you think a relevant paper is missing.
View on GitHub

Select filters:
210 / 210 items (show all)

Acquisition	Microscale	Nanoscale	Vis-for-Acquisition
Alignment	2D-Alignment	3D-Registration	
Segmentation	Automatic	Interactive	
	Connectivity-Extraction	Provenance-Tracking	
Proofreading	Manual	Semi-Automatic	
	Guided-Automatic	Crowdsourced	
Analysis	Data-Structures	Spatial-Exploration	Connectivity-Exploration
	Vis-focused-Analysis	Communication	

Filter by tag

- GitHub
- Executable
- LM
- EM
- Dataset

Website template by Sarah Schöttler.

The collage consists of a grid of 210 small images, each representing a research paper. Each image includes a thumbnail of the paper's content, the title, and a brief abstract. The titles and abstracts are as follows:

- D** Proofread PyC
- d** Chandelier cell anatomy and function reveal a variability distributed but common signal.
- d** Binary and analog variation of synapses between cortical pyramidal neurons.
- d** Structured dendritic inhibition supports branch-selective integration in CA1 pyramidal cells.
- d** Synaptic molecular imaging in spared and deprived columns of mouse barrel cortex array tomography.
- d** Interactive Visualization of Terascale Data in the Browser: Fact or Fiction?
- d** SparseLeap: Efficient Empty Space Skipping for Large-Scale Volume Rendering
- d** NeuroBlocks - Visual Tracking of Segmentation and Proofreading for Large Connectomics Projects
- FluoRender: An Application of 2D Image Space Methods for 3D and 4D Confocal Microscopy Data Visualization in Neurobiology Research**
- EyeWire**
- A Virtual Reality Visualization Tool for Neuron Tracing**
- BrainGazer - Visual queries for neurobiology research**
- FluoRender: joint freehand segmentation and visualization for many-channel fluorescence data**
- VICE: Visual Identification and Correction of Neural Circuit Errors**
- Improving the Usability of Virtual Reality Neuron Tracing with Topological Elements**
- Semi-automatic stitching of filamentous structures in image stacks from serial-section electron tomography**
- VAST (Volume Annotation and Segmentation Tool): Efficient Manual and Semi-Automatic Labeling of Large 3D Image Stacks**
- TrakEM2 Software for Neural Circuit Reconstruction**
- Absorption map**
- Interactive Volumetric Visual Analysis of Glycogen-derived Energy Absorption in Nanometric Brain Structures**
- neuroMAP — Interactive graph-based visualization of the fruit fly's neural circuit**
- ilastik: Interactive learning and segmentation toolkit**
- Seerett and NeuroTrace: Interactive Visualization and Analysis Tools for Large-Scale Neuroscience Data Sets**
- Scalable Interactive Visualization for Connectomics**
- GPU-Accelerated Brain Connectivity Reconstruction and Visualization in Large-Scale Electron Micrographs**
- Demand-driven volume rendering of terascale EM data**
- NeuroLines: A Subway Map Metaphor for Visualizing Nanoscale Neuronal Connectivity**
- Scalable and Interactive Segmentation and Visualization of Neural Processes in EM**

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