# Connectomics

## Large-scale synaptic-resolution brain mapping in academia-industry collaborations.

Michał Januszewski
Google Research

@michalj

TEAMS ›

# Connectomics

Our goal is to leverage Google expertise and resources to advance understanding of the structure and function of the brain.

## Automated 3d Brain Reconstruction

We develop algorithms and software for automating the process of aligning, segmenting, and annotating petabyte-scale 3d images of brain tissue.

https://research.google/teams/connectomics/

TEAMS ›

# Connectomics

Our goal is to leverage Google expertise and resources to advance understanding of the structure and function of the brain.

## Visualization and Infrastructure

We develop software such as TensorStore and Neuroglancer which helps store, process, and visualize large n-dimensional images and volumes.

https://research.google/teams/connectomics/

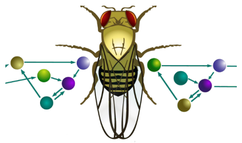
# Connectomics @ **Google**

- Tim Blakely
- Sven Dorkenwald
- Viren Jain
- Michał Januszewski
- Laramie Leavitt
- Peter Li
- Jeremy Maitin-Shepard

# Academic Collaborators

max planck institute of neurobiology

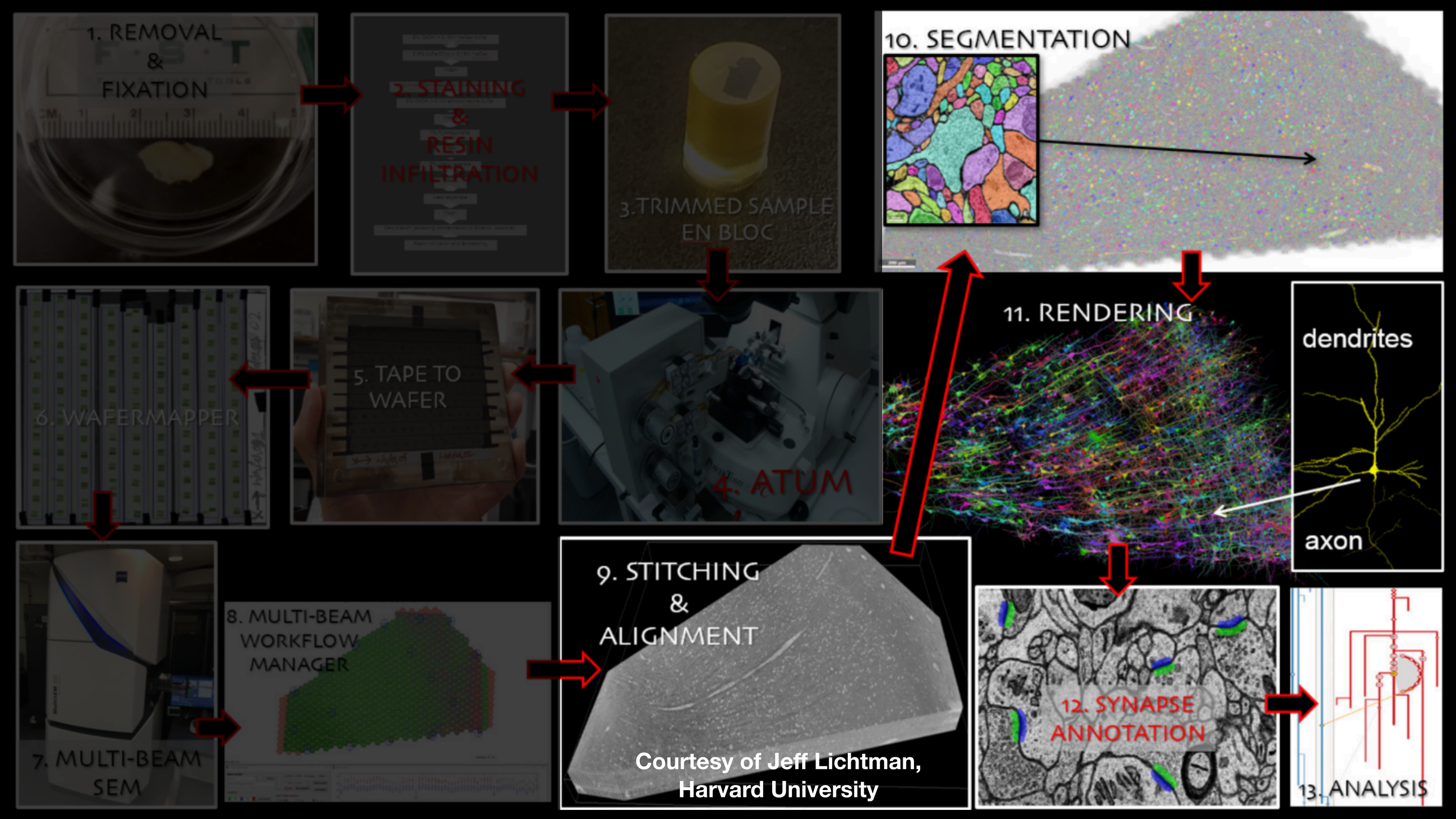
hhmi | janelia Research Campus

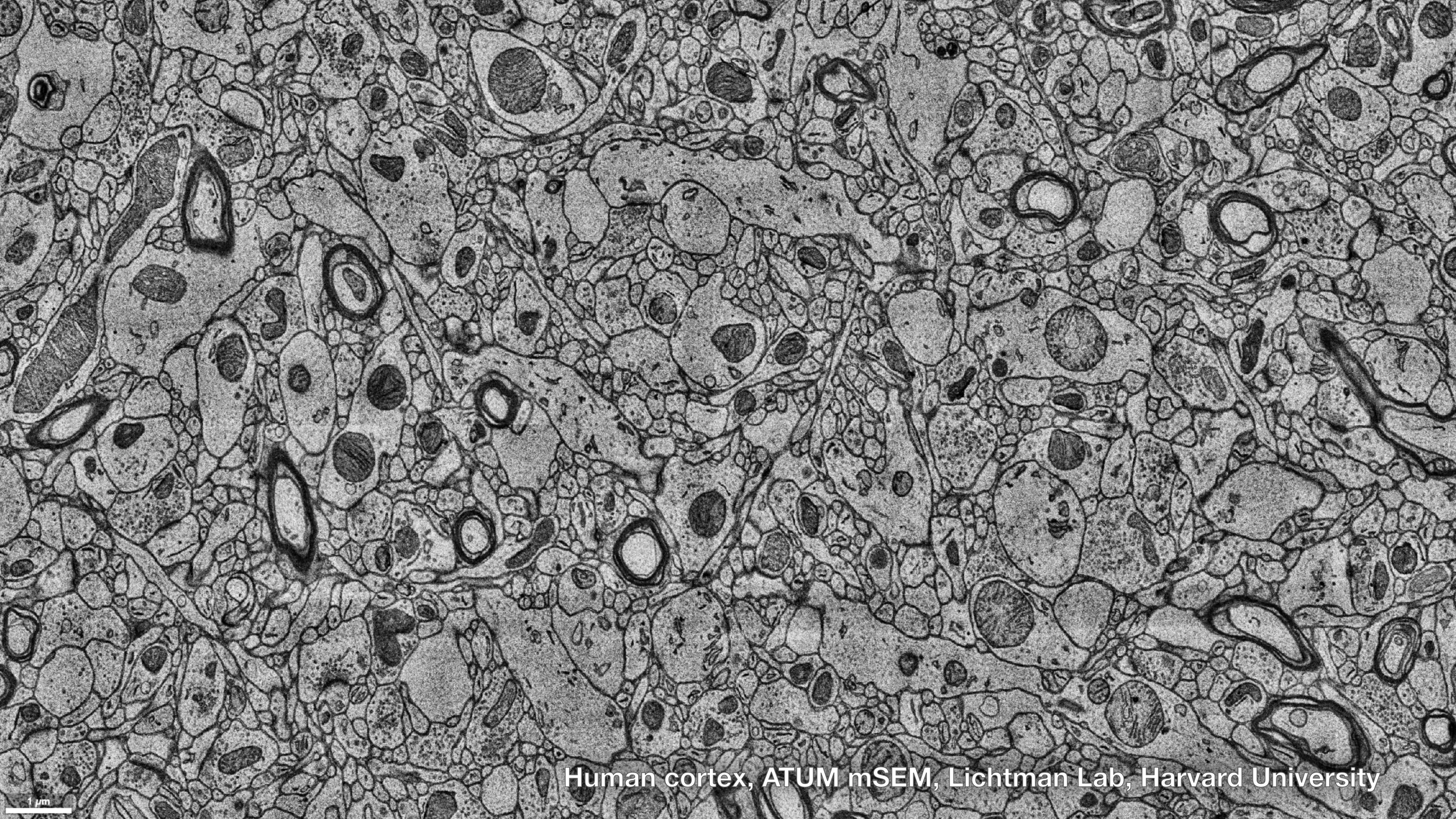


*Fly EM*

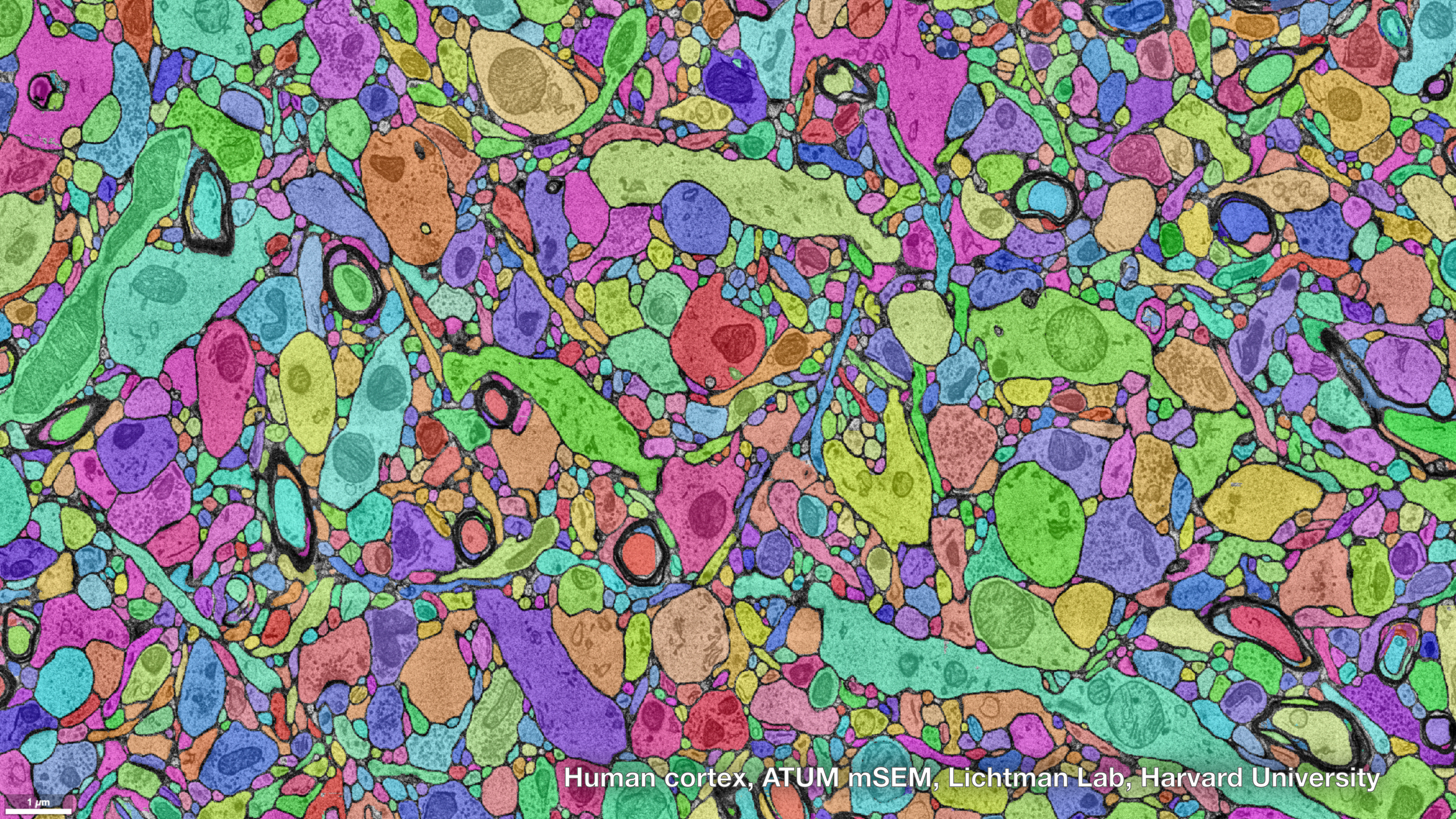
HARVARD UNIVERSITY

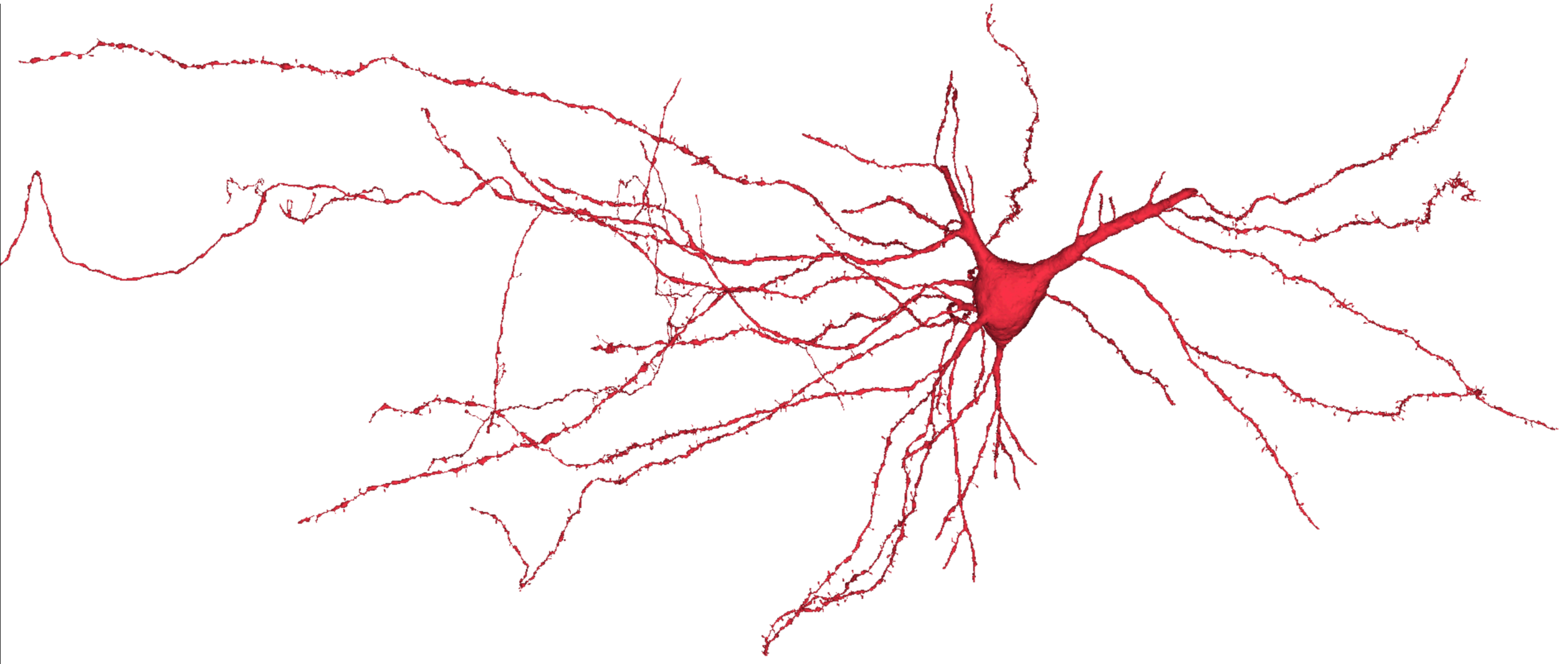
FMI
Friedrich Miescher Institute for Biomedical Research


1. REMOVAL & FIXATION
2. STAINING & RESIN INFILTRATION
3. TRIMMED SAMPLE EN BLOC
10. SEGMENTATION
11. RENDERING
dendrites
axon
4. ATUM
5. TAPE TO WAFER
6. WAFERMAPPER
7. MULTI-BEAM SEM
8. MULTI-BEAM WORKFLOW MANAGER
9. STITCHING & ALIGNMENT
12. SYNAPSE ANNOTATION
13. ANALYSIS
Courtesy of Jeff Lichtman, Harvard University

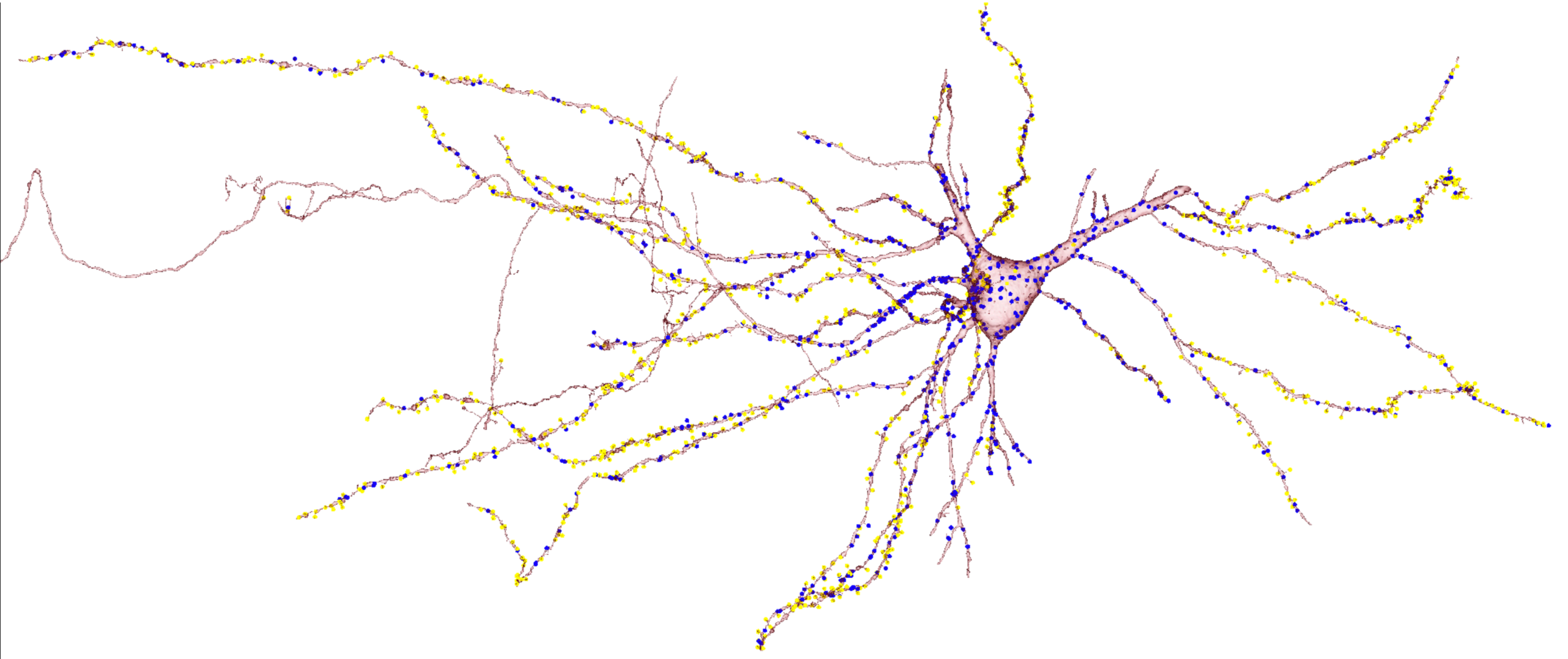



Human cortex, ATUM mSEM, Lichtman Lab, Harvard University

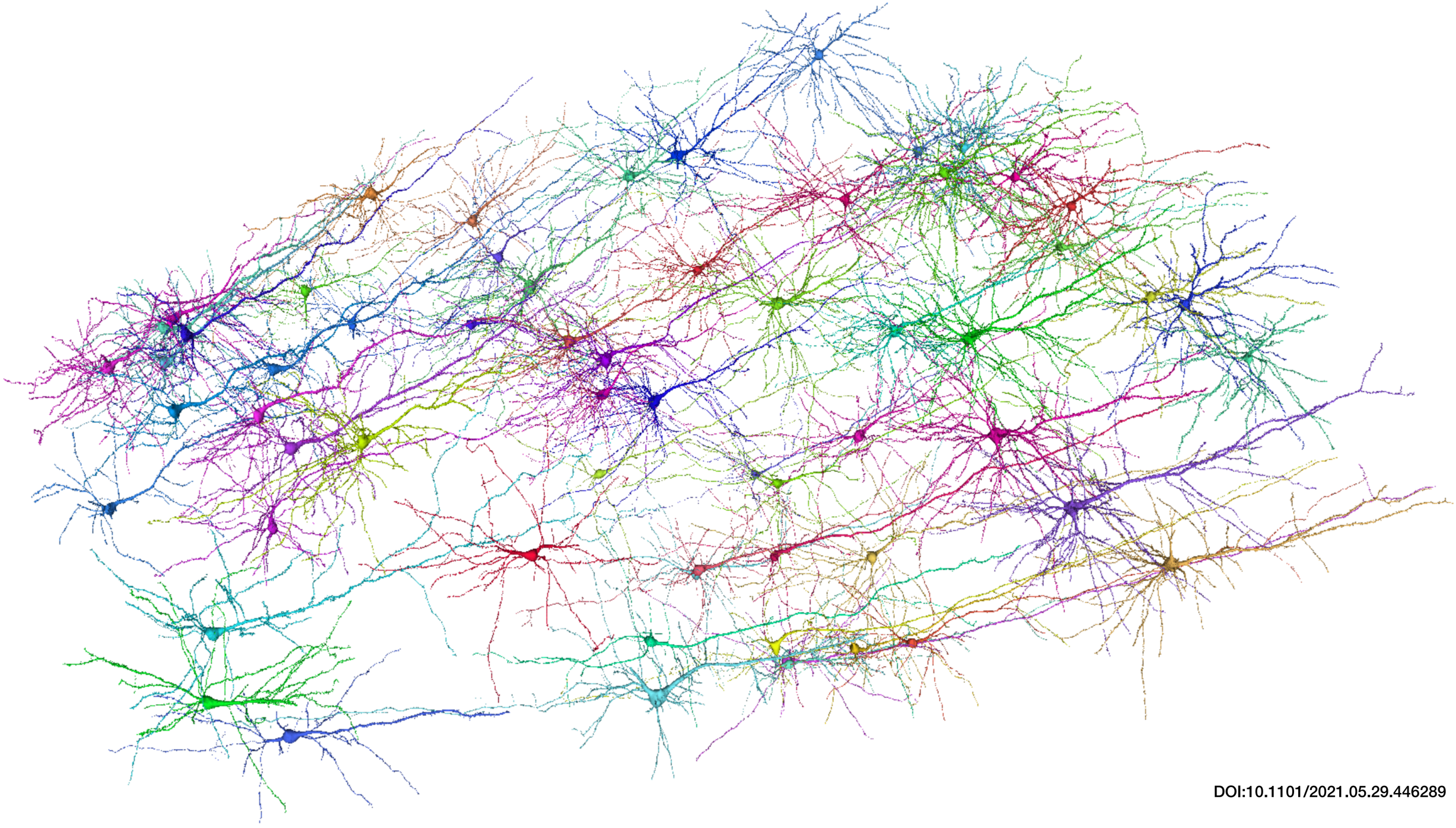

1 µm
Human cortex, ATUM mSEM, Lichtman Lab, Harvard University



DOI:10.1101/2021.05.29.446289



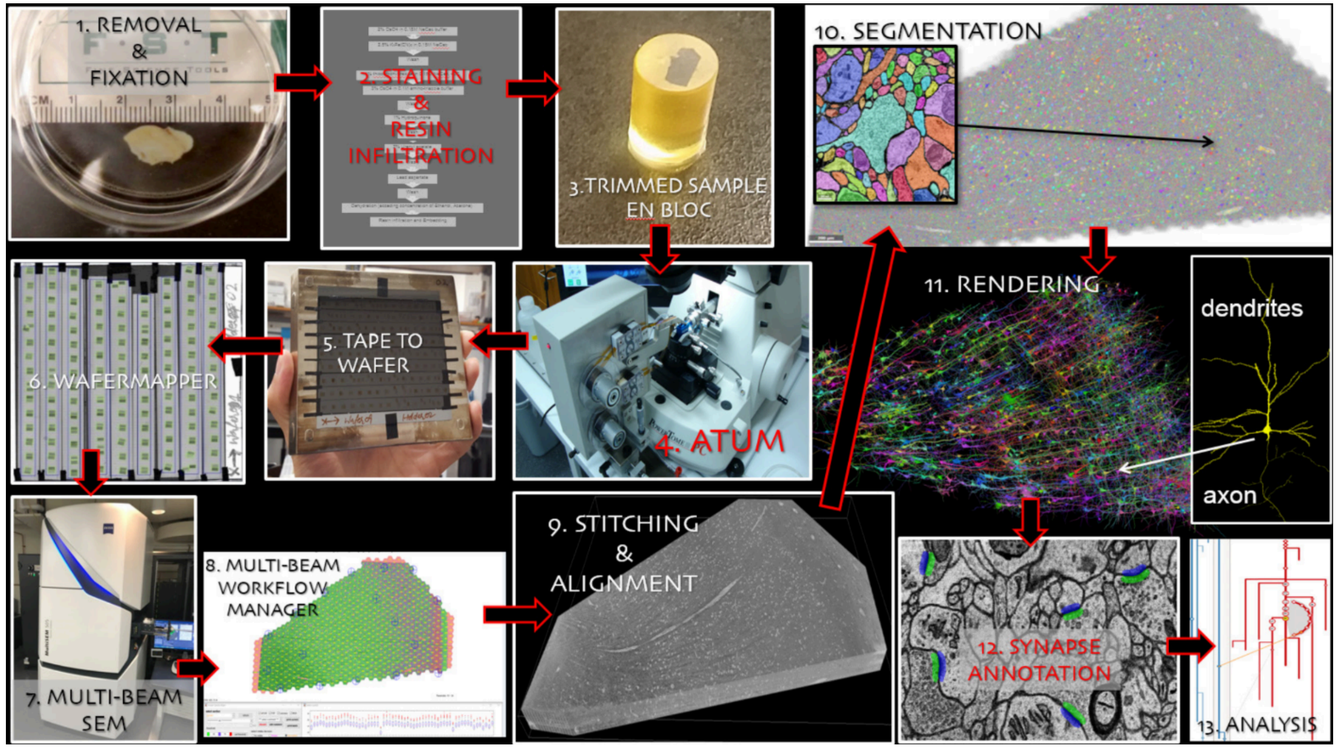
DOI:10.1101/2021.05.29.446289



DOI:10.1101/2021.05.29.446289

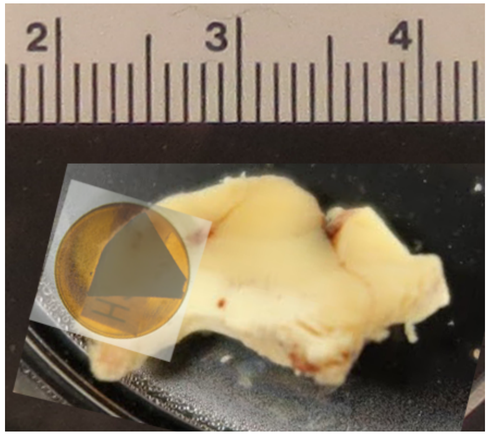
# Why a collaboration?

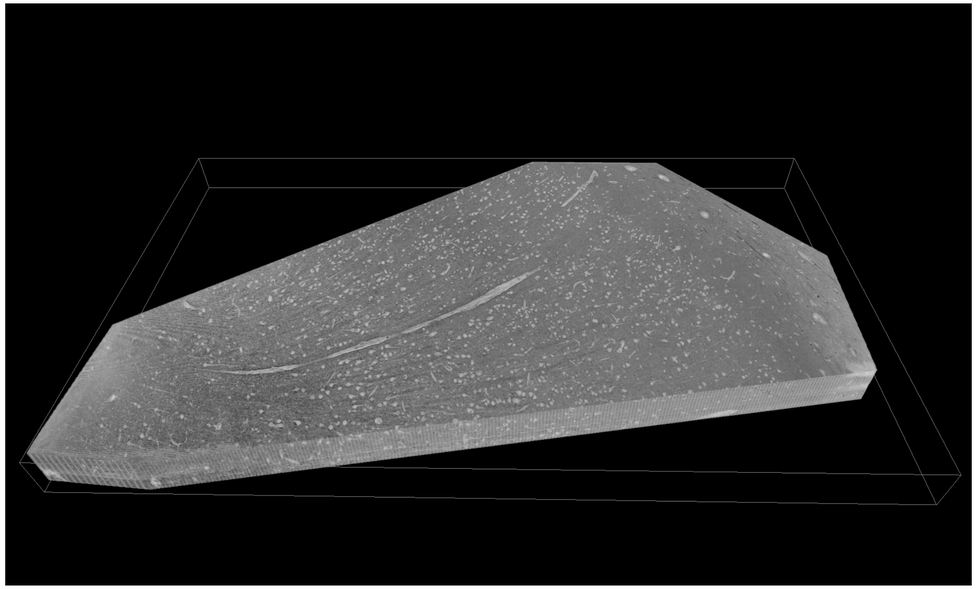
- Common goal.
- Large-scale, complex project.
- **Complementary expertise.**
- Sufficient shared understanding of the involved domains.



# h01: 1 $mm^3$ of human cortex

- Collaboration with Lichtman lab, Harvard University
- 5,000 sections
- 326 days of imaging time
- 1.4 PB of imagery
- 57,216 cells
- 133.7M synapses
- Available online: https://h01-release.storage.googleapis.com/landing.html

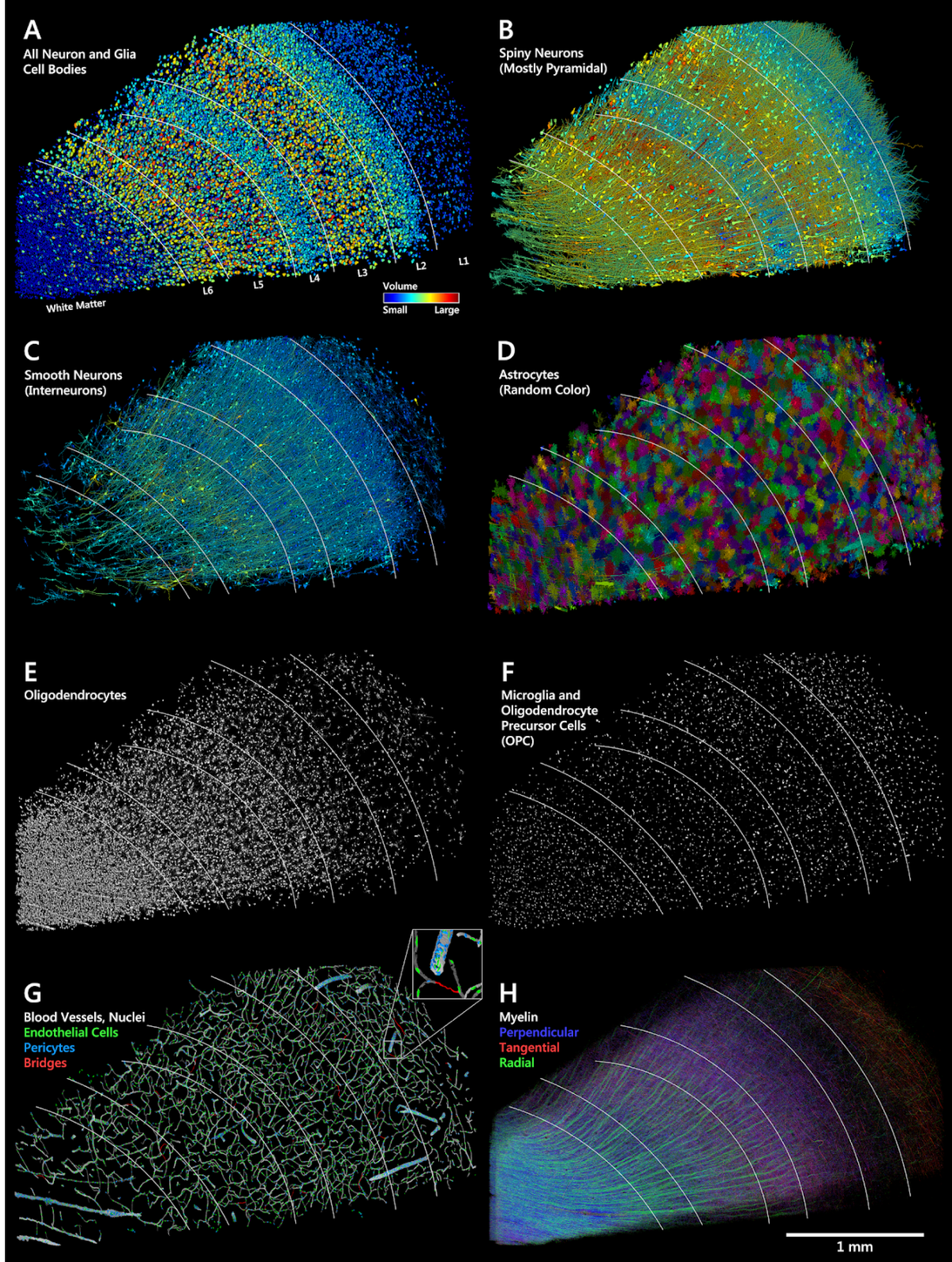


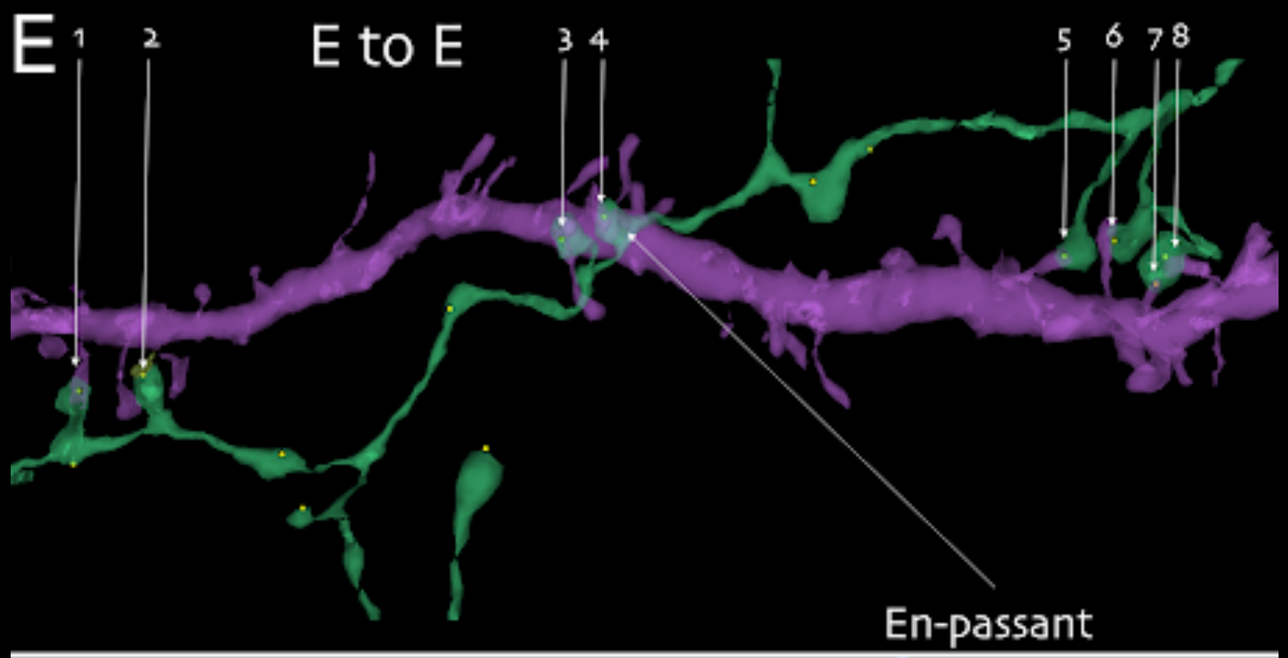



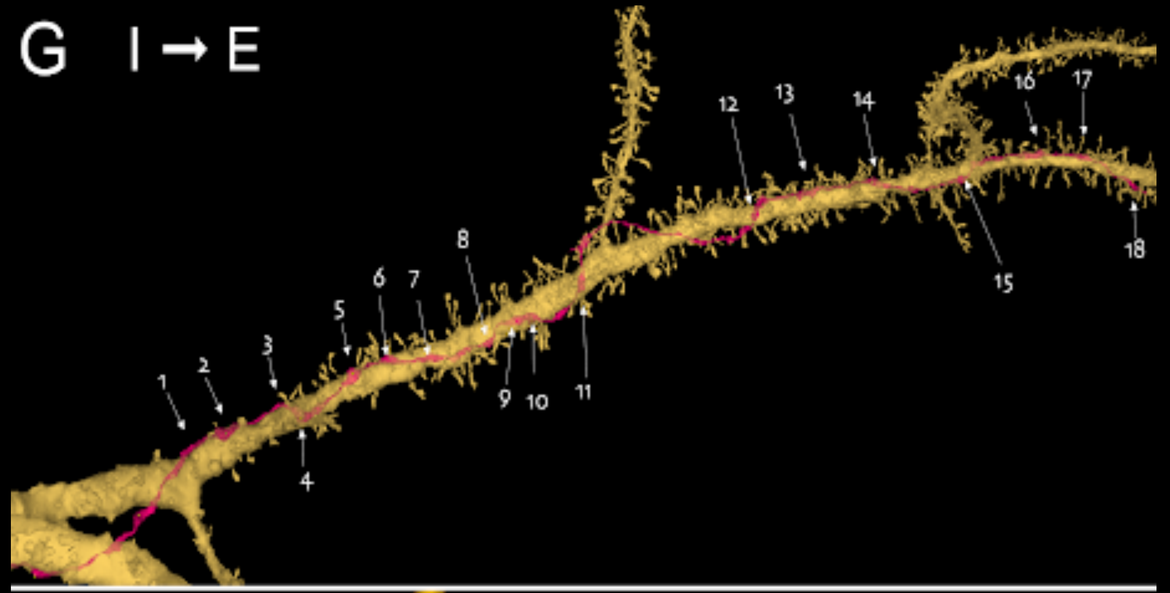
Shapson-Coe, Alexander, et al. "A connectomic study of a petascale fragment of human cerebral cortex." *bioRxiv* (2021) DOI: 10.1101/2021.05.29.446289

# Initial findings

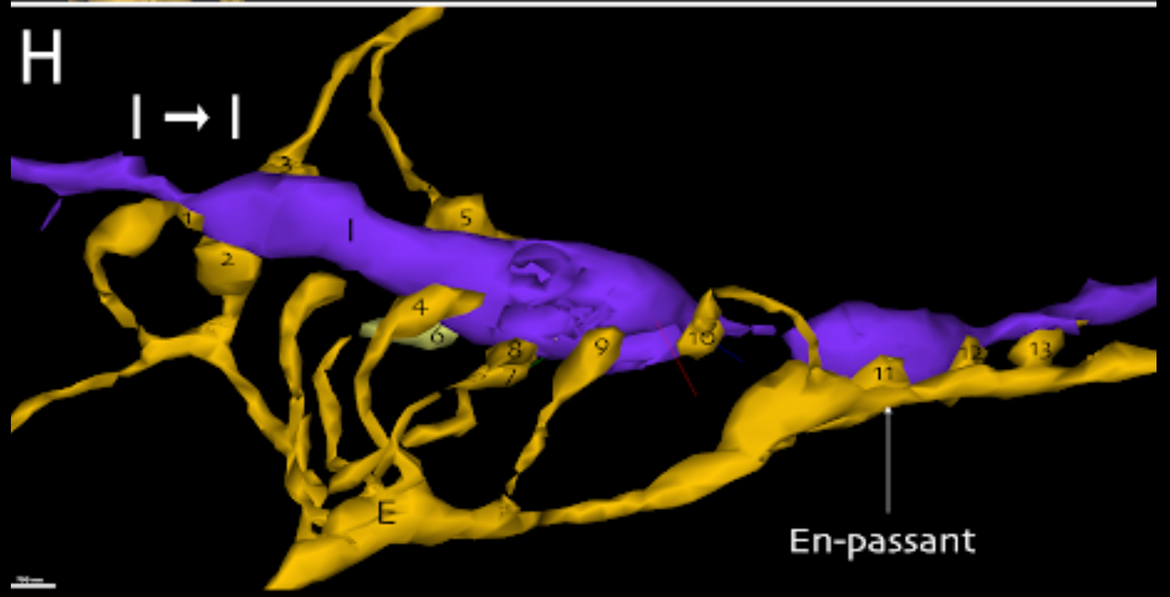
- Complete cell census;
  ~2:1 glia:neuron ratio.
- Presence of axons with unusual morphology ("whorls").
- Chandelier interneurons innervating each other's axon initial segments.
- Presence of rare multi-synaptic contacts.

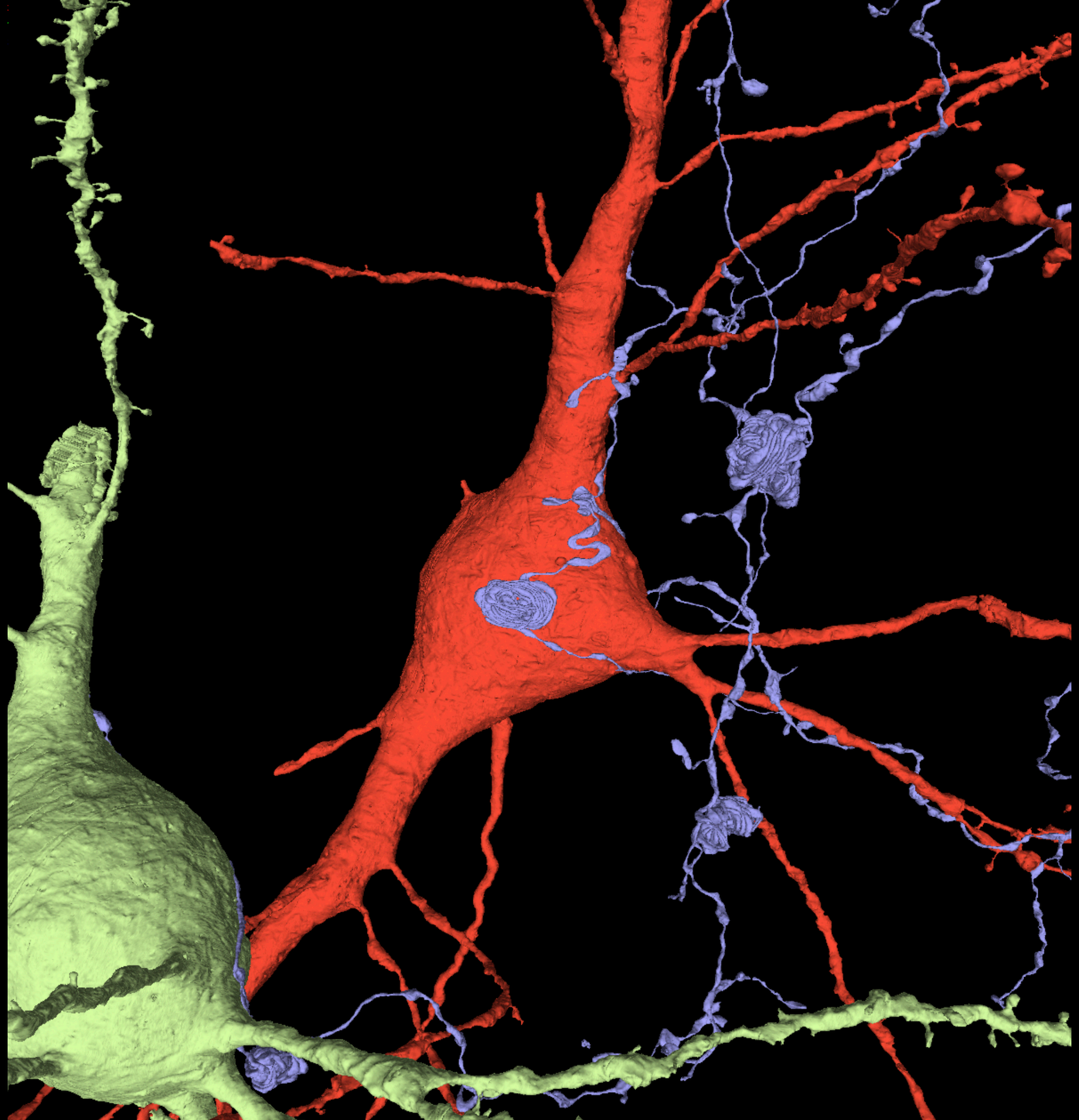


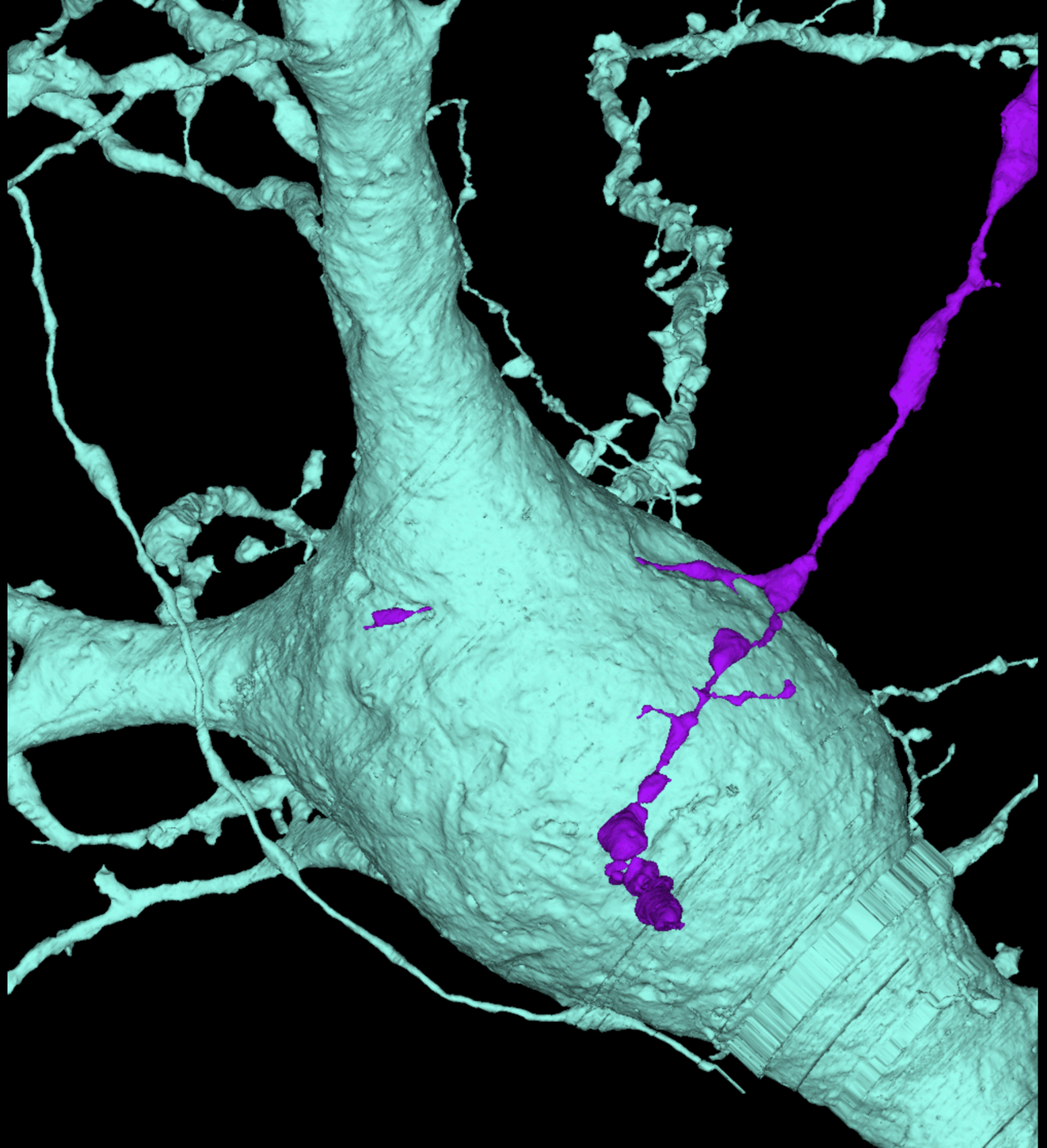

E
E to E
1
2
3
4
5
6
7
8
En-passant


G
I → E
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18

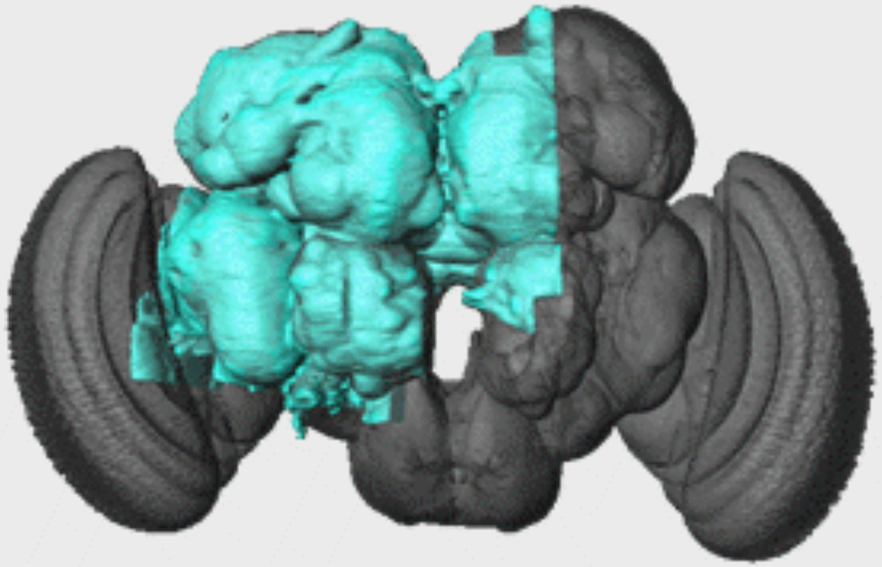
F
E → I
En-passant


H
I → I
I
E
En-passant





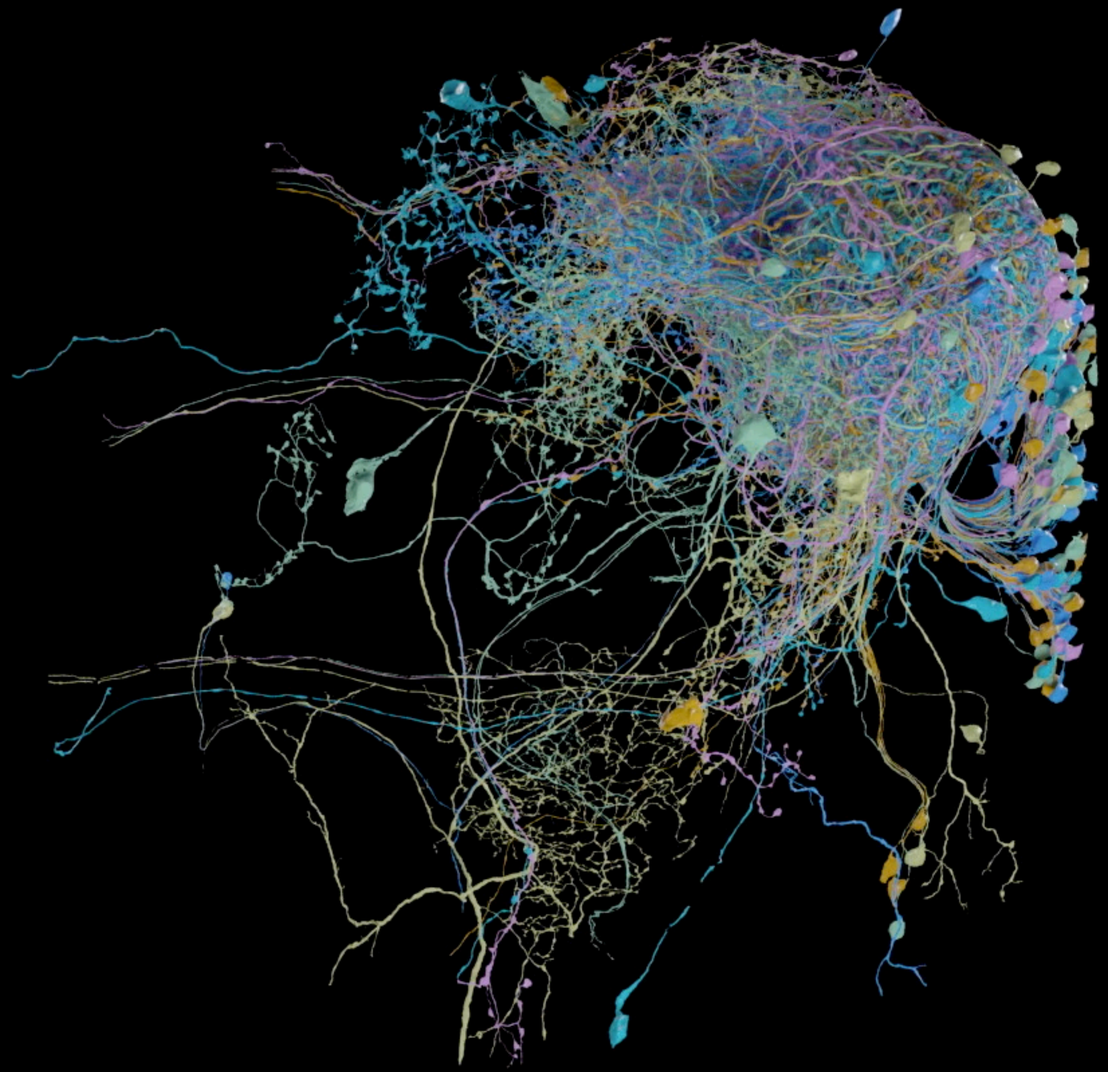
# Hemibrain



The hemibrain dataset encompasses the part of the fly brain highlighted here in blue. This region includes neurons involved in learning, navigation, smell, vision, and many other functions.

- Central part of the Drosophila brain
- 25,000 neurons
- 50 person-years of proofreading
- Public resource: https://www.janelia.org/project-team/flyem/hemibrain

Details in:
Scheffer, Louis K., et al. "A connectome and analysis of the adult Drosophila central brain." *Elife* 9 (2020): e57443.

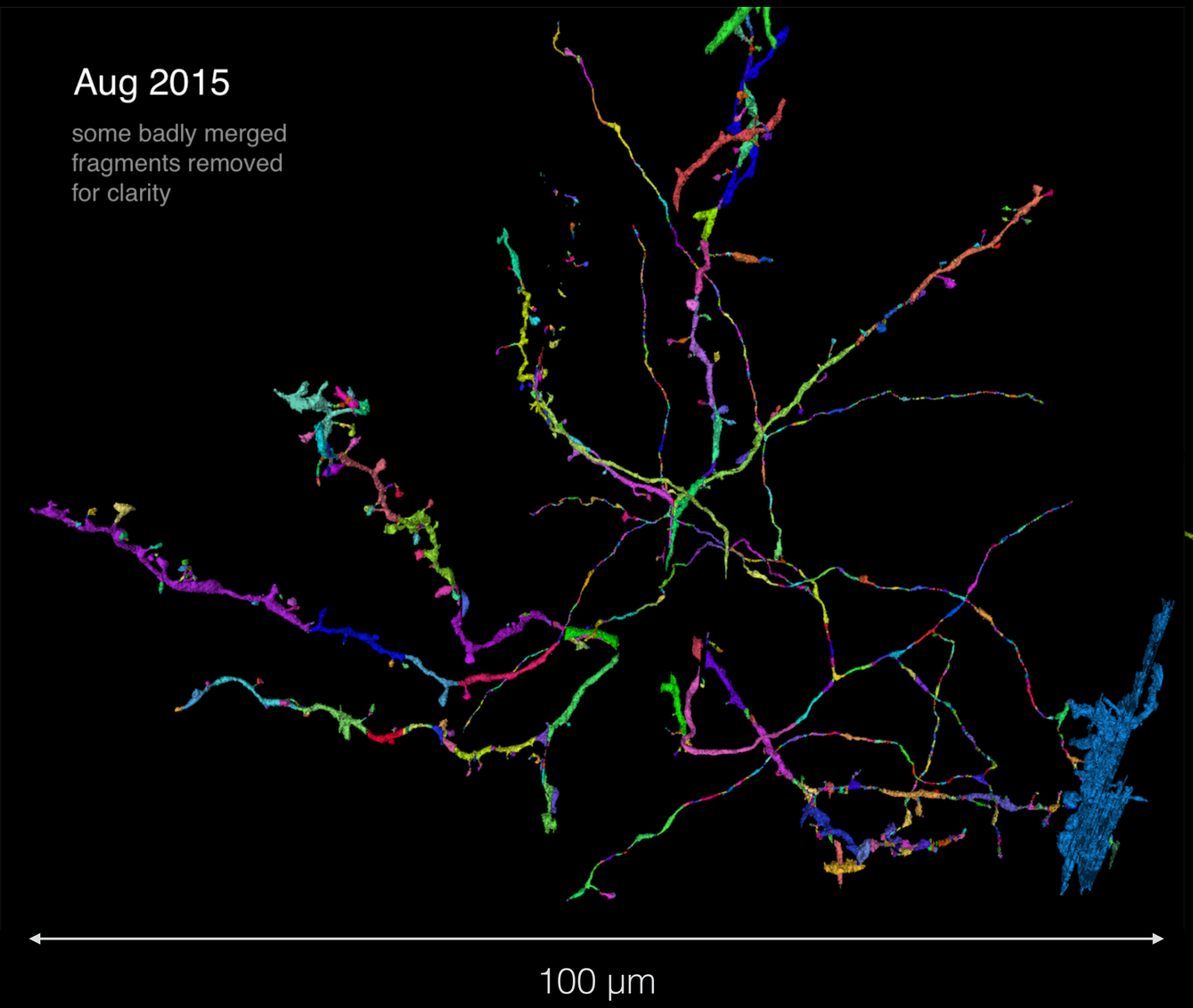


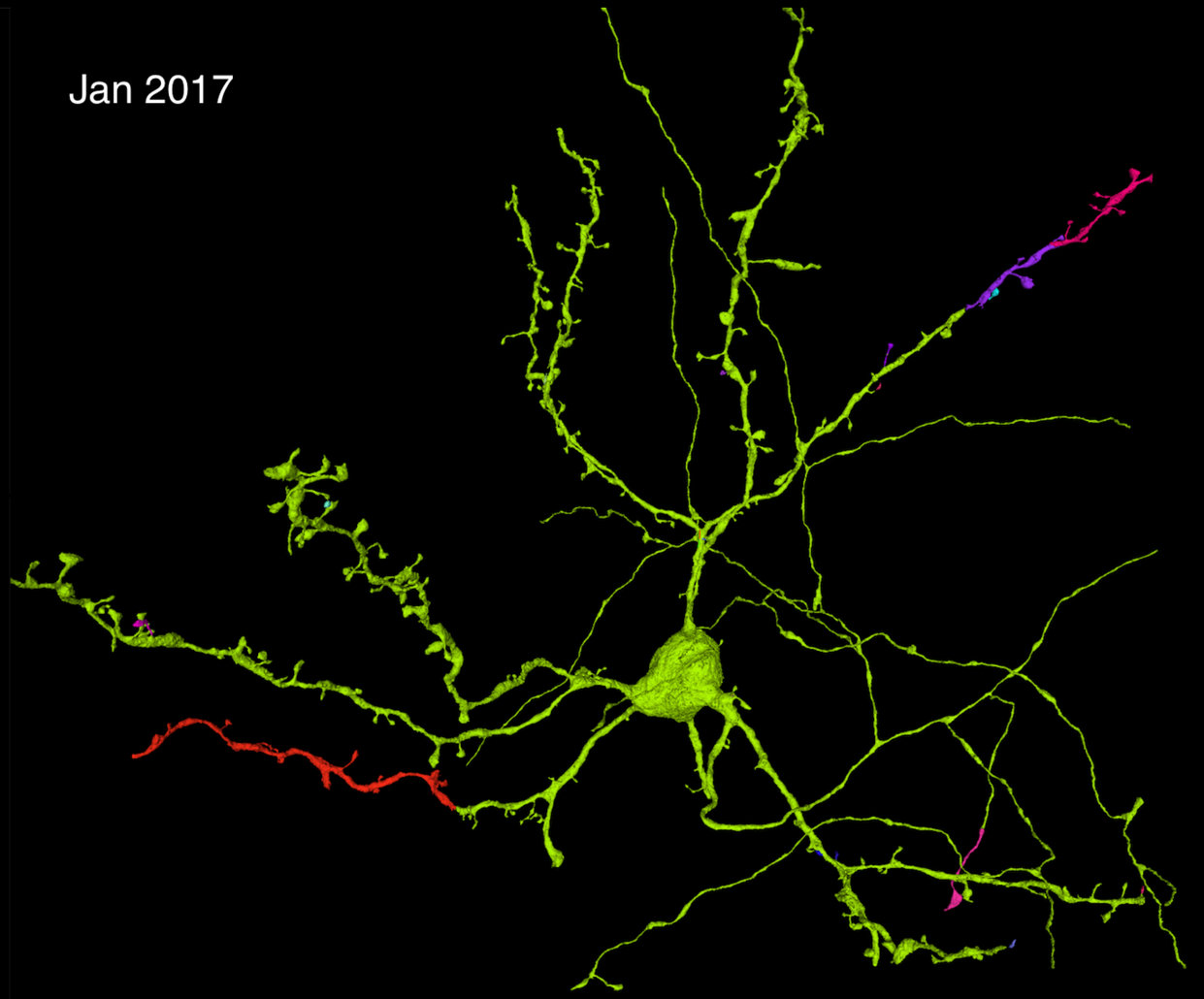
Olfactory

Drosophila hemibrain
Google Connectomics & FlyEM, HHMI Janelia

*It should be kept in mind that although most of the currently operating systems make extensive use of the computer for bookkeeping, 3-D display, and data analysis, they still require the slow manual input of graphical information. However, it seems quite clear that the rapid advances in electronics will make* ***more and more automation possible*** *at a reasonable cost.* ***Within a few years we can expect that systems will be available that can easily recognize and digitize some features automatically, leaving for the investigator only those cases that are difficult or ambiguous.*** *The greater speed with which the analysis can then be done should make possible a great increase in the use of such systems for both basic research and practical problems, such as those of the clinical pathologist. Thus two quite separate issues will be involved in future developments of this technique: (a) the technical problems associated with increasing automation and reducing equipment cost; and (b) the expanded exploration of ways in which these techniques can be applied to new and different scientific as well as clinical problems*

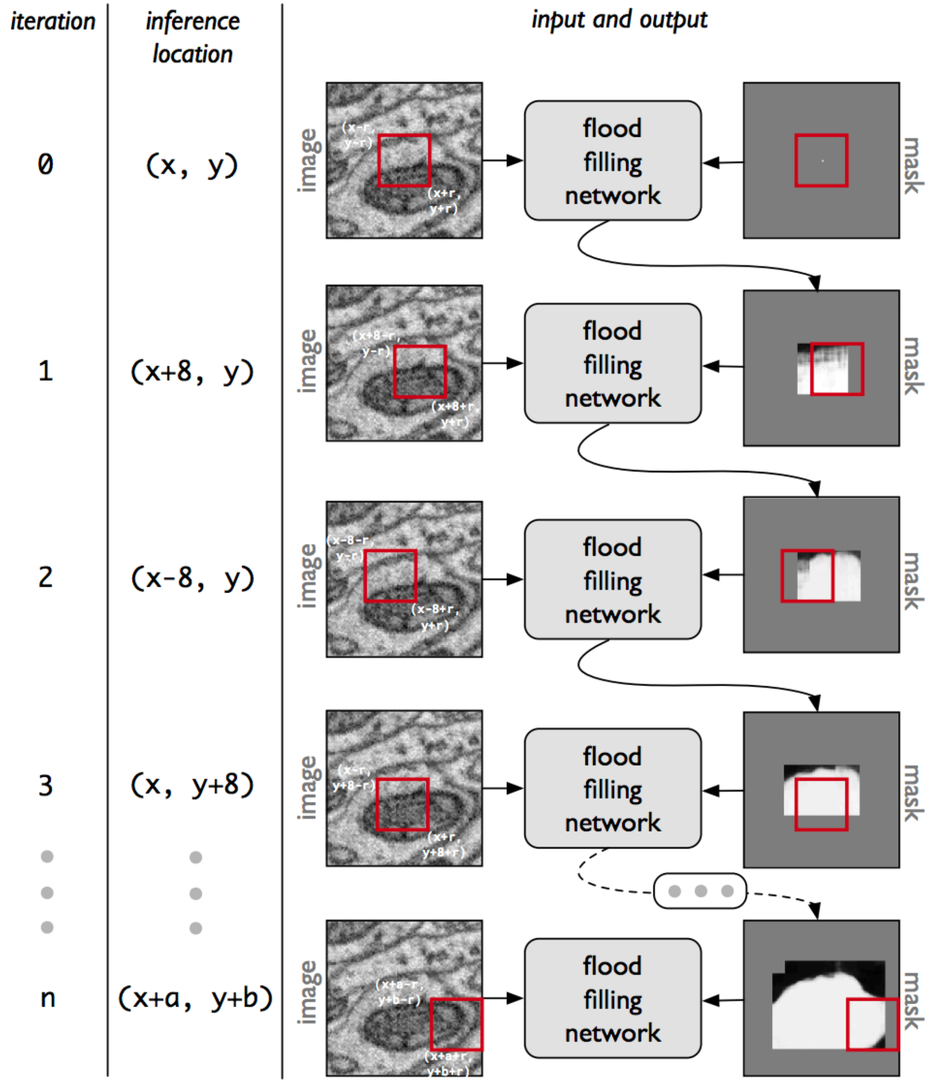
Macagno, Levinthal, Sobel (**1979**)

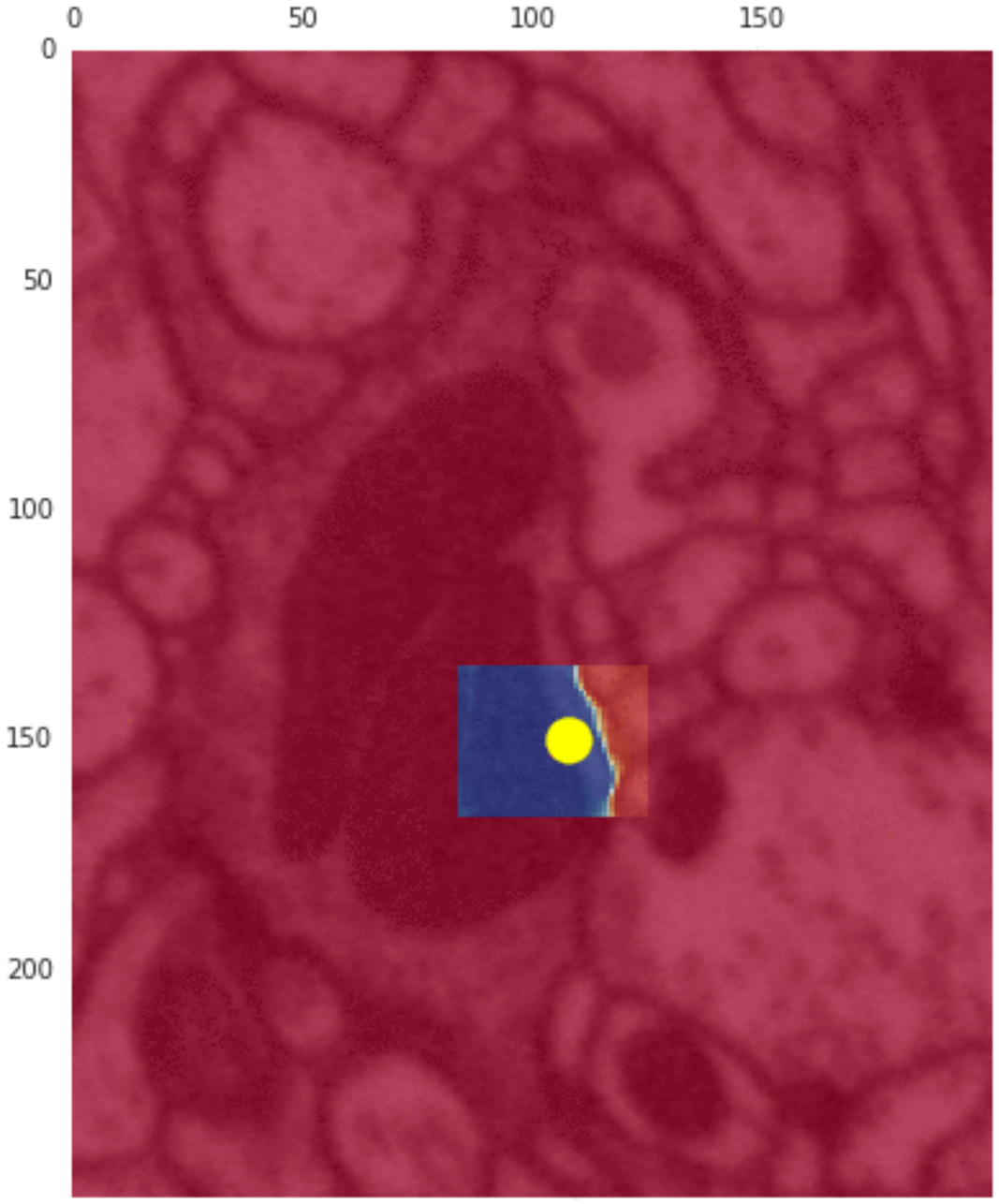


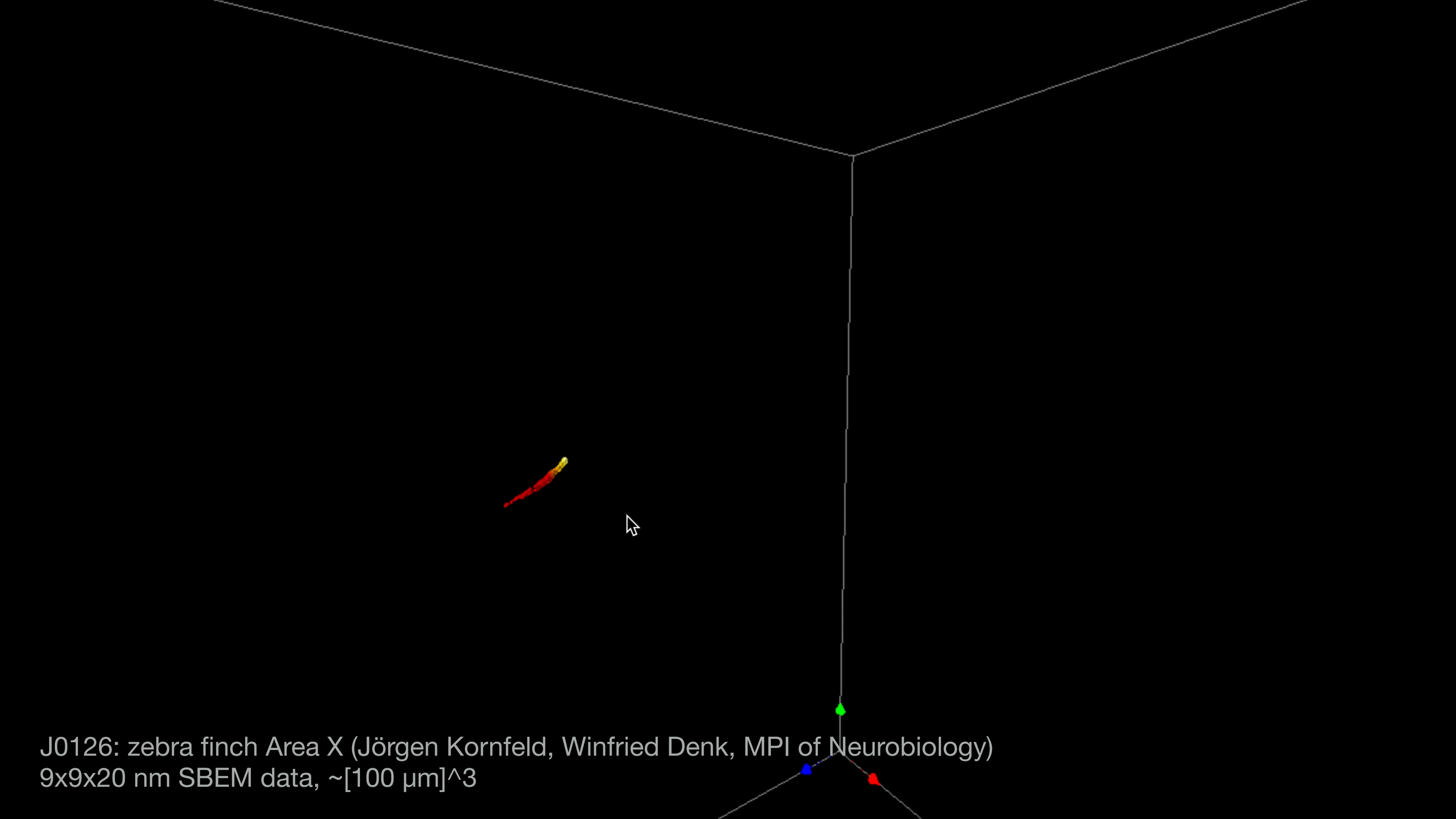




J0126: Zebra Finch Area X
Jörgen Kornfeld, Winfried Denk, MPI of Neurobiology
9x9x20 nm SBEM data

# Flood-Filling Networks

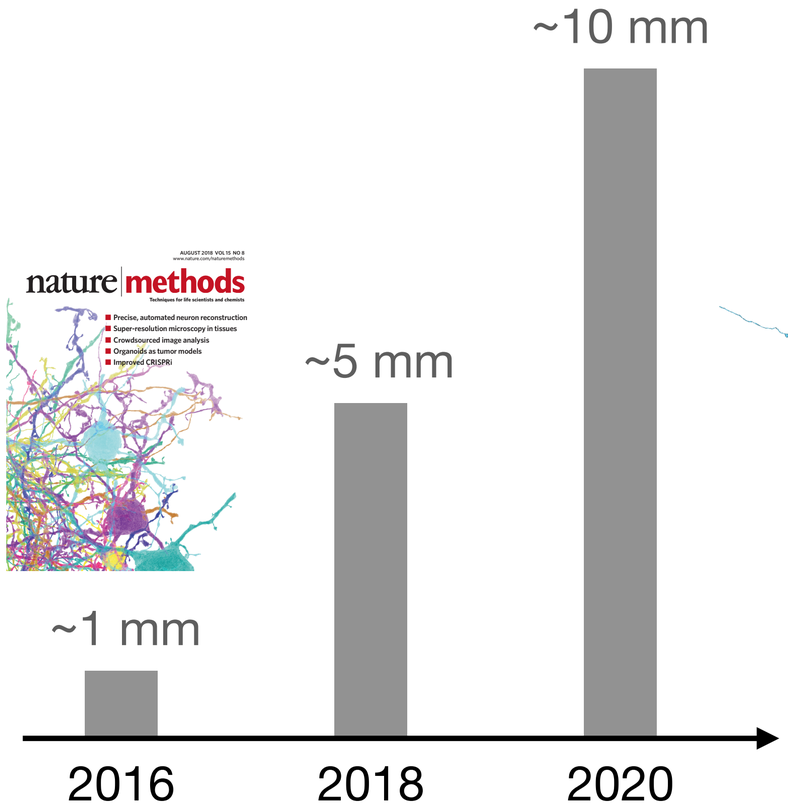


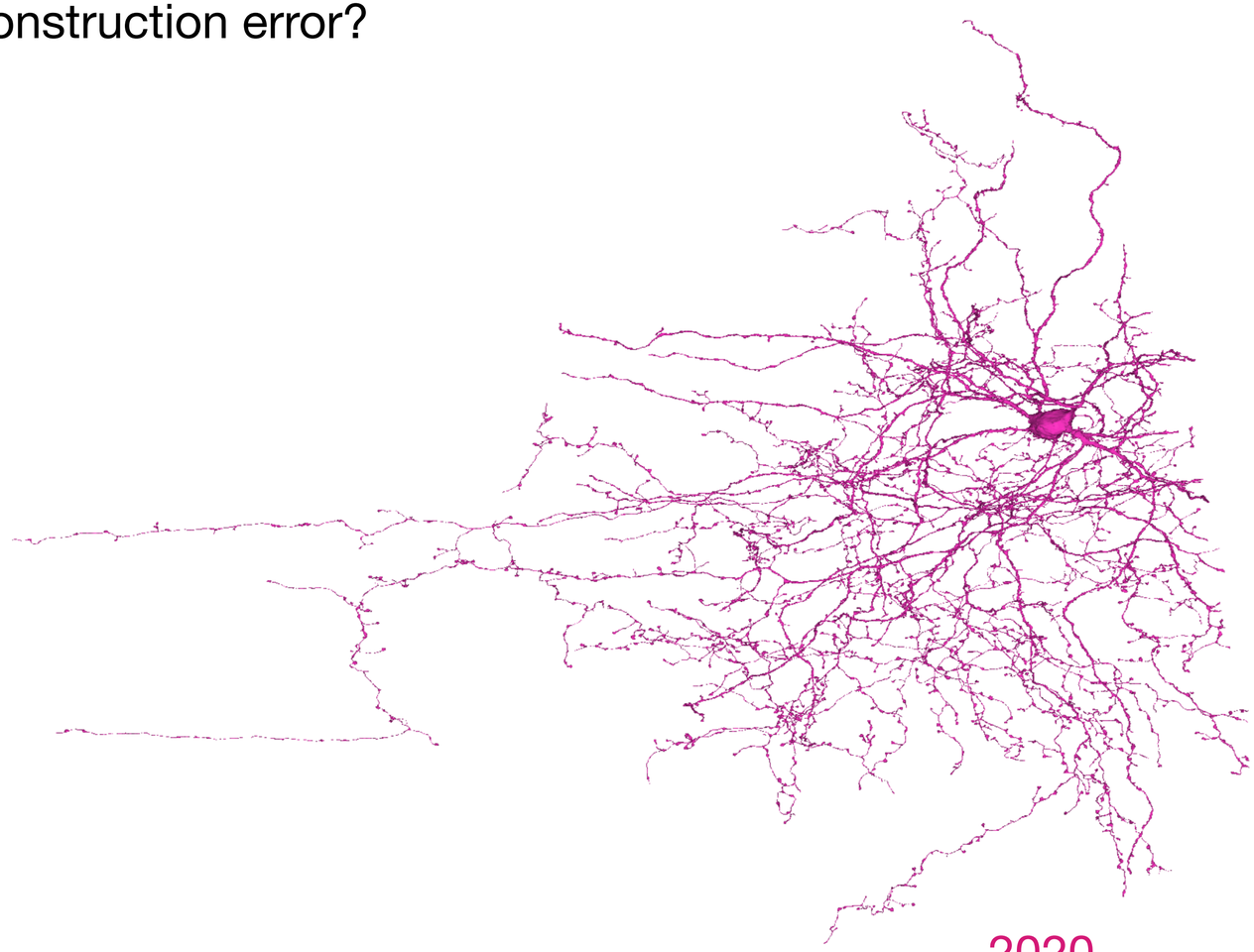

J0126: zebra finch Area X (Jörgen Kornfeld, Winfried Denk, MPI of Neurobiology)
9x9x20 nm SBEM data, ~[100 µm]^3

# Reconstruction quality

**Expected Run Length (ERL):** how far can a system automatically trace from a randomly selected point before encountering a reconstruction error?



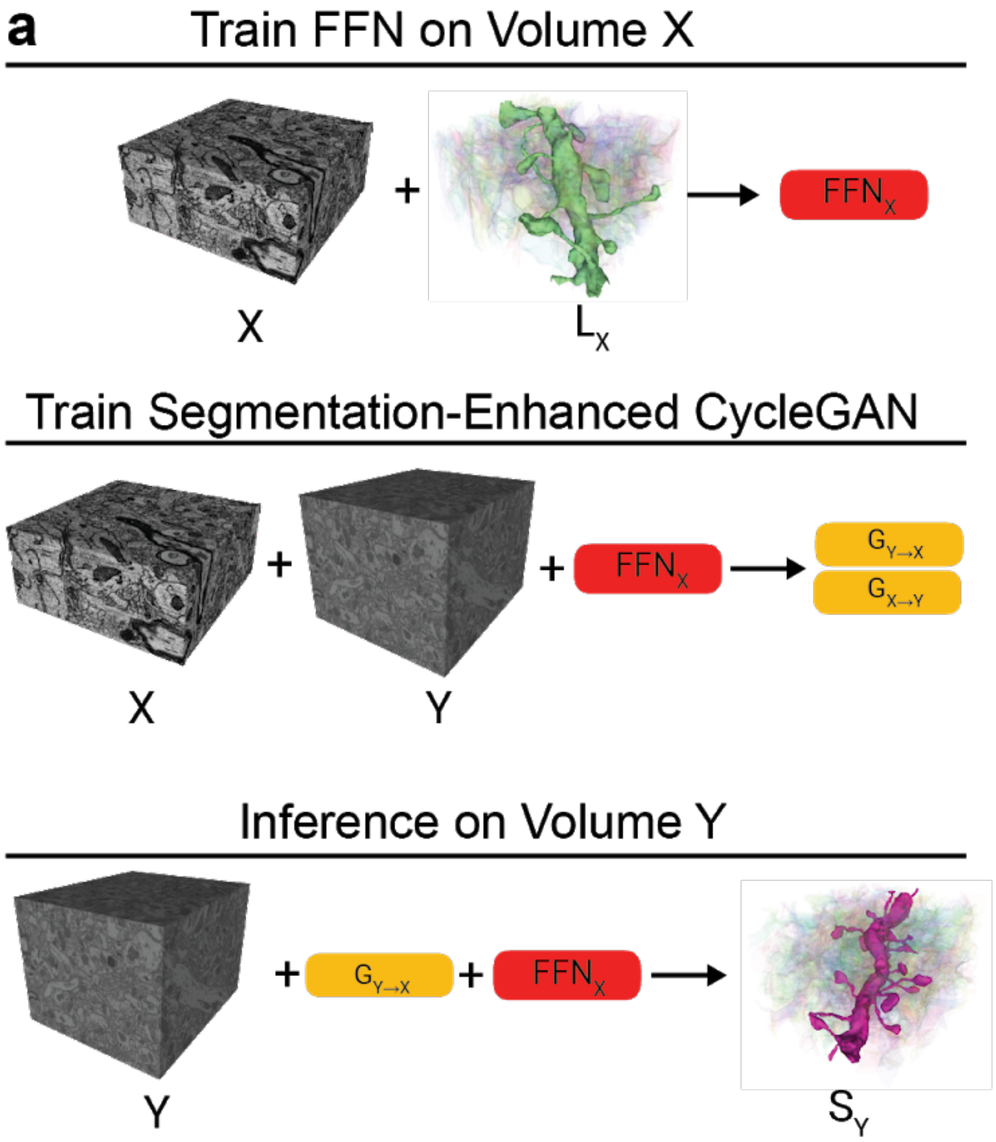
2016

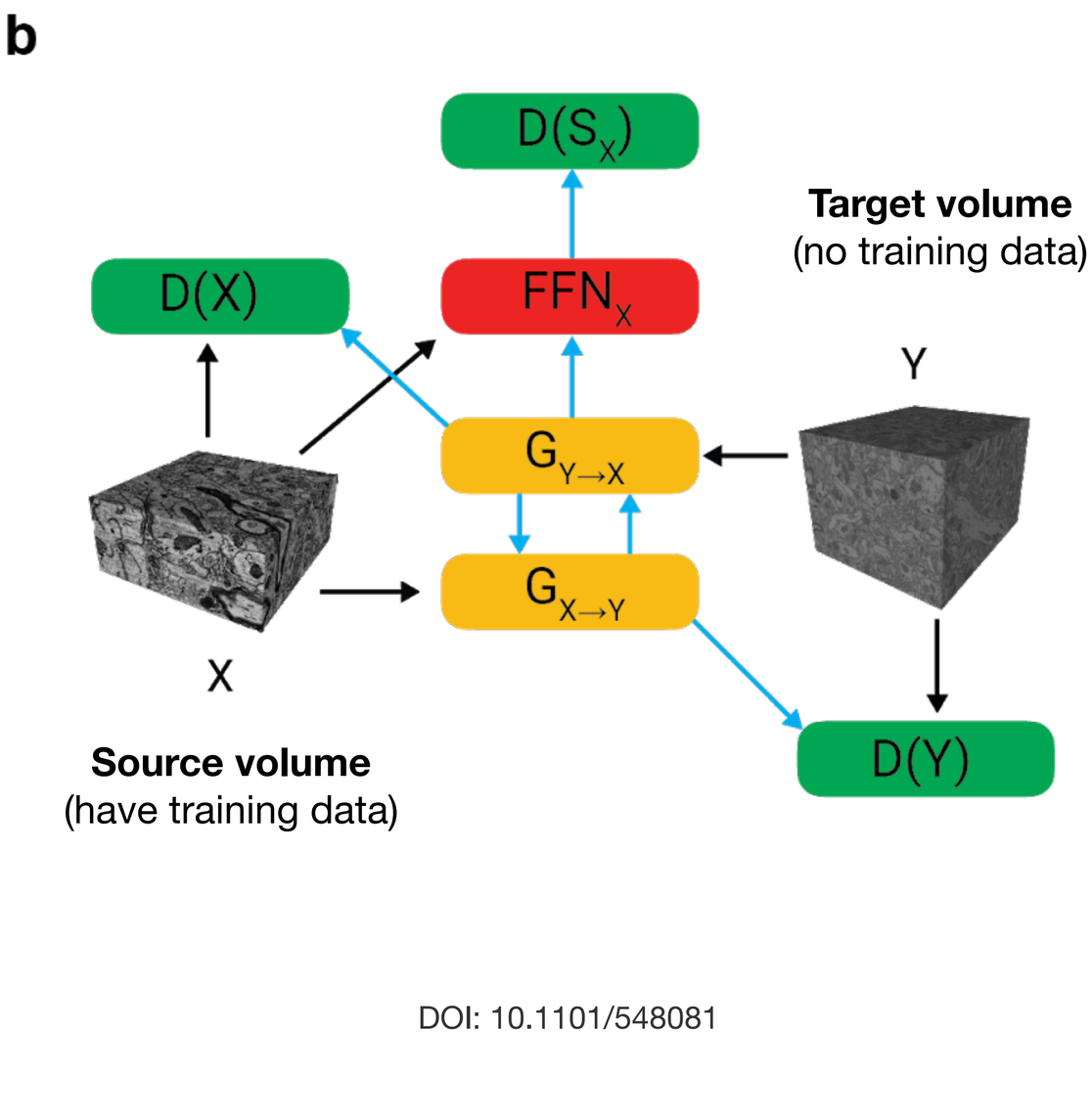


2020

Nat Methods 15, 605–610 (2018)
DOI: 10.1038/s41592-018-0049-4

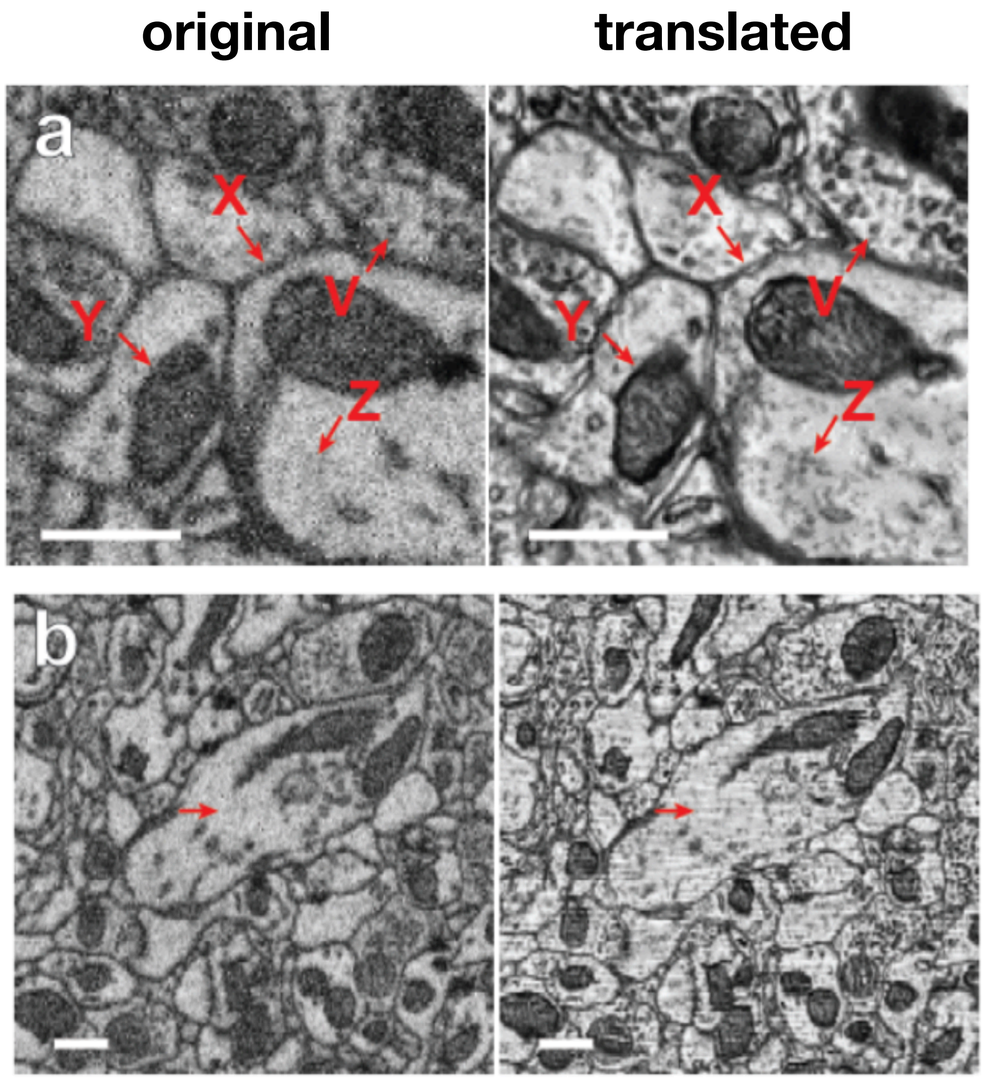
# SECGAN: Segmentation-Enhanced CycleGAN

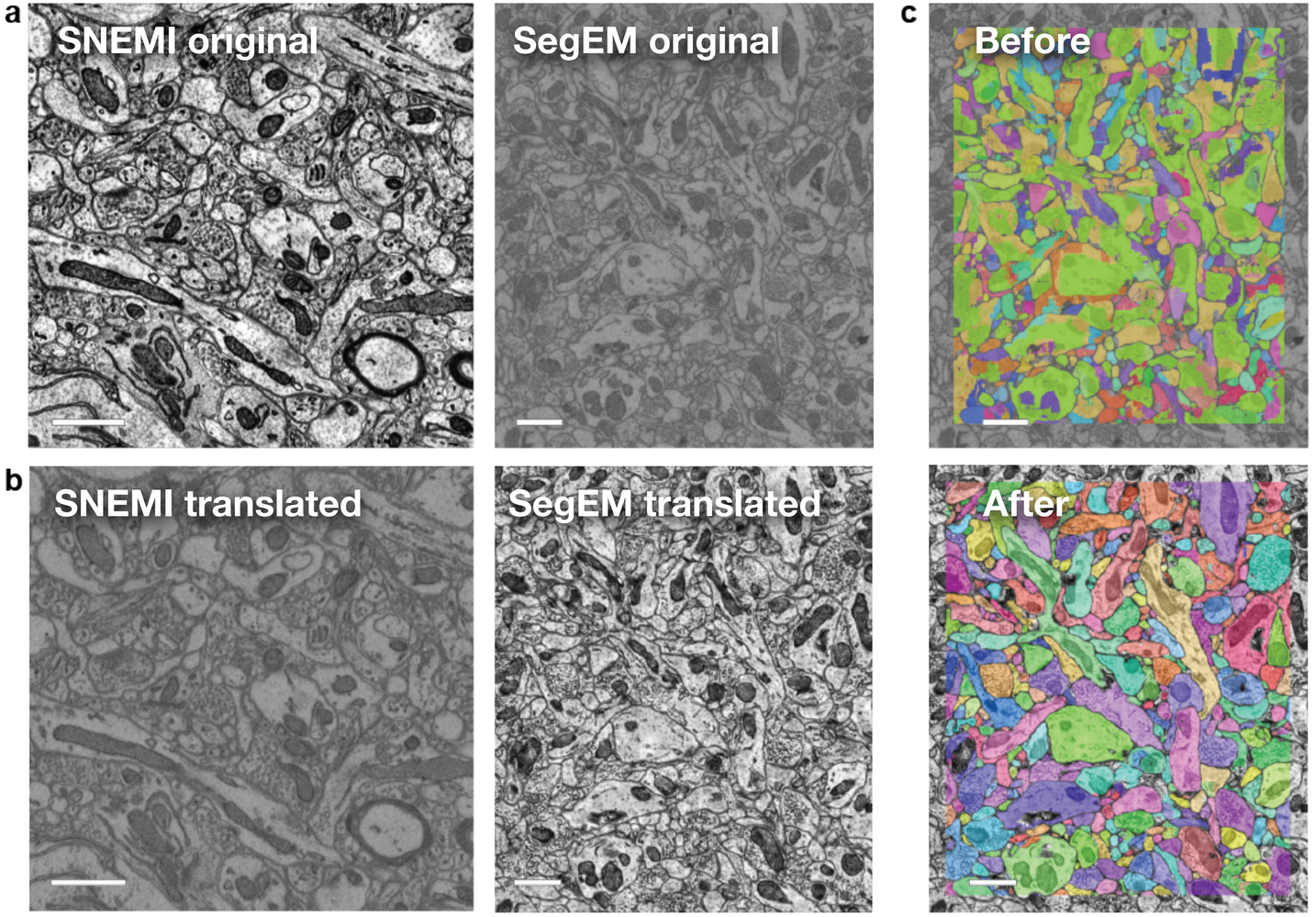


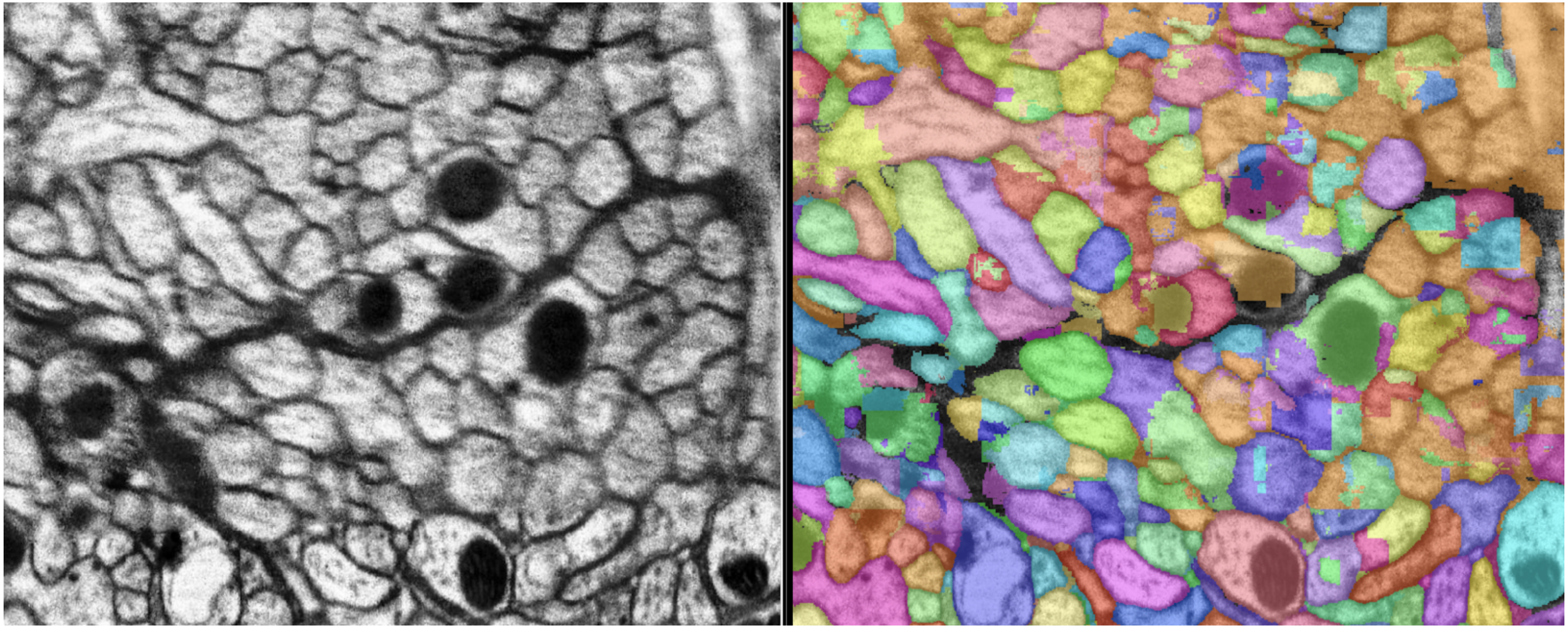

DOI: 10.1101/548081

# Sample results

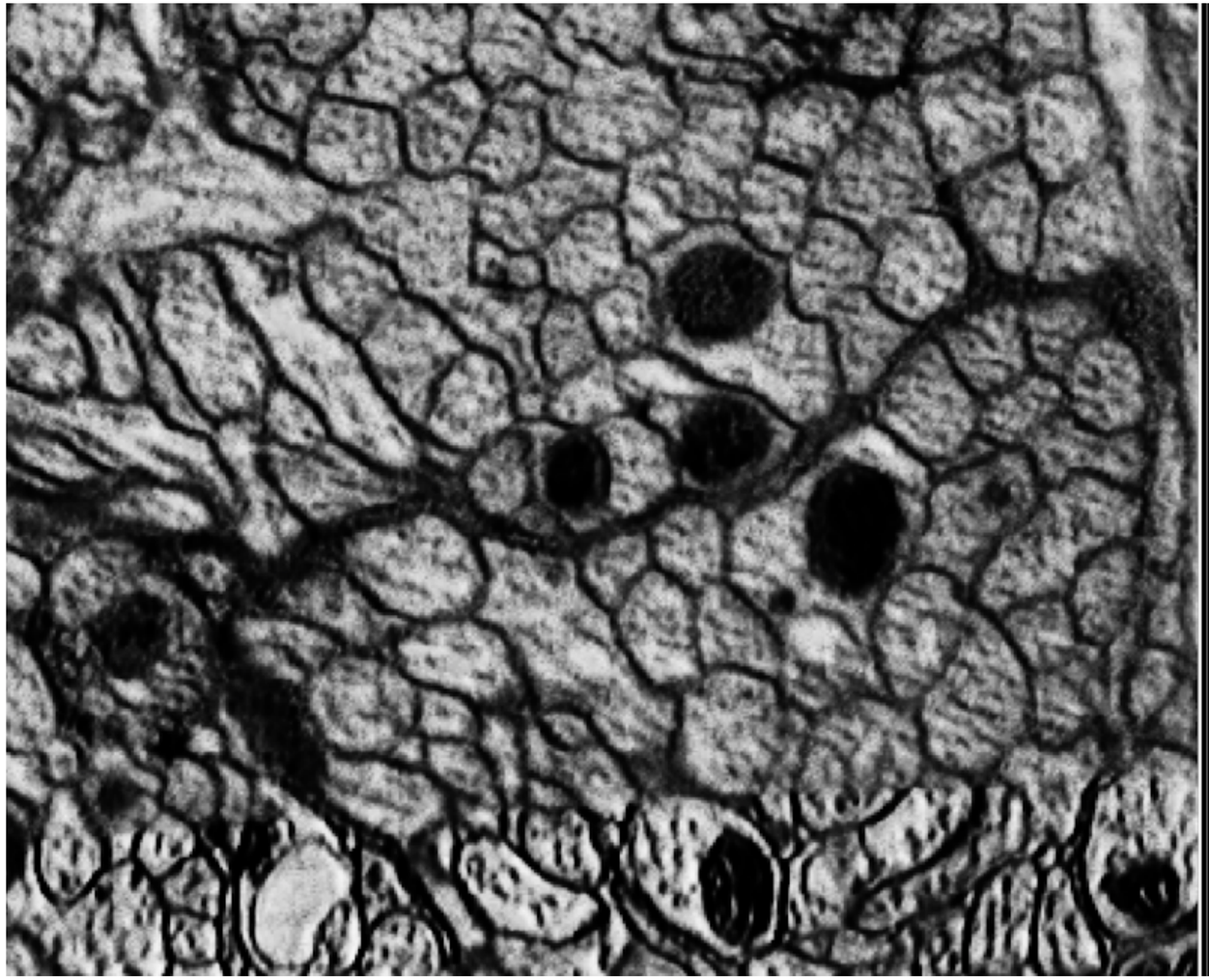


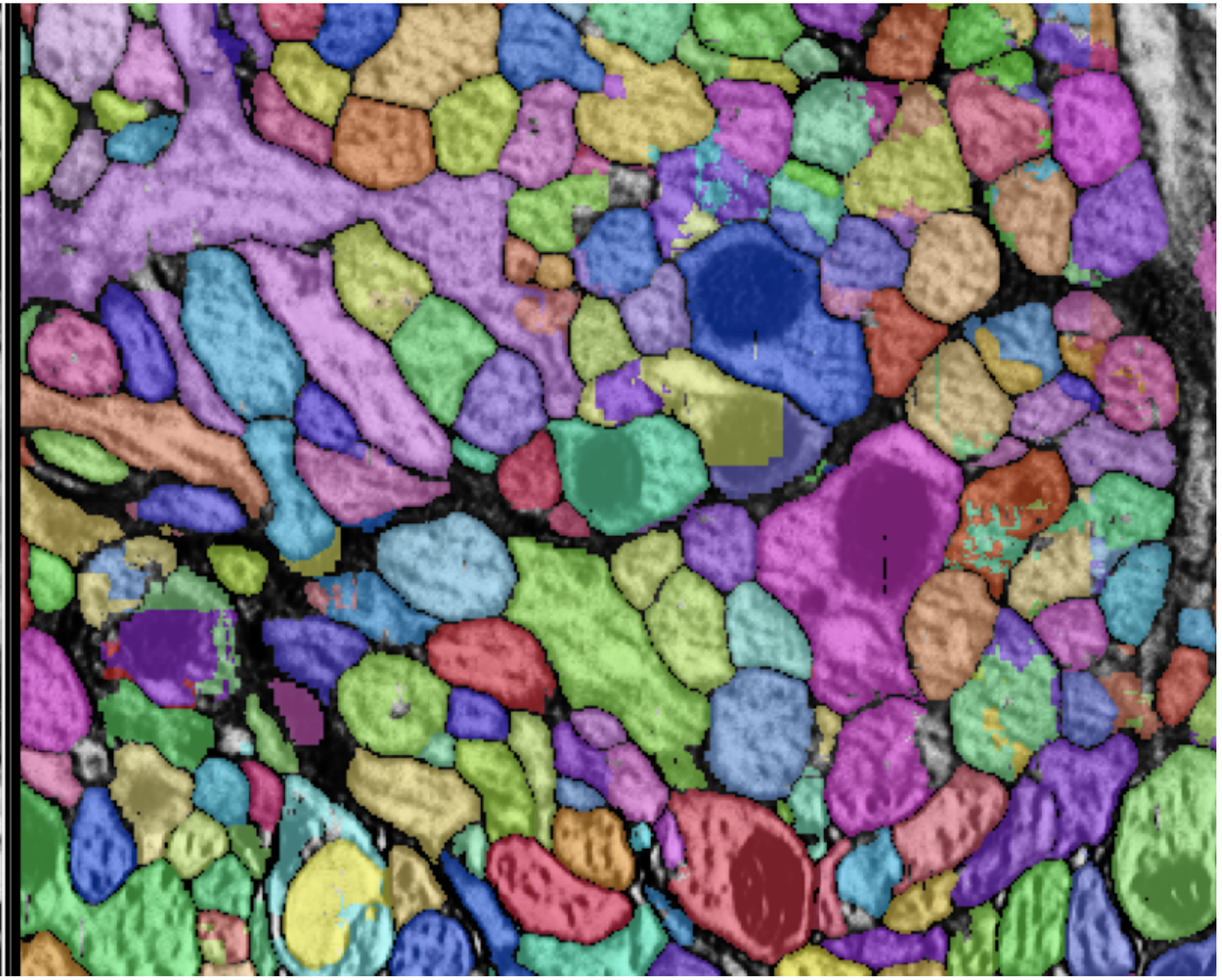



# Applications: image correction

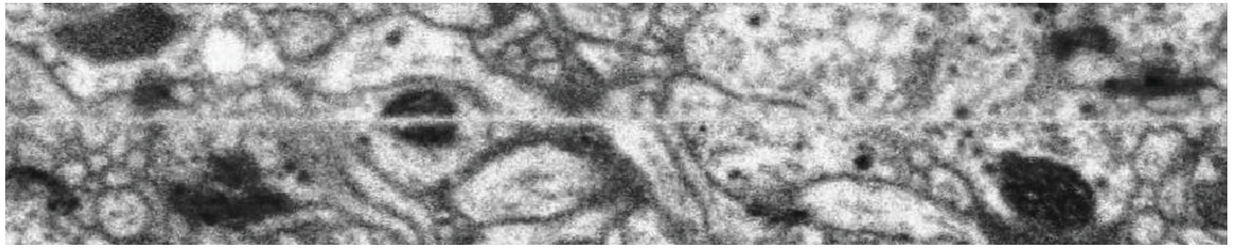


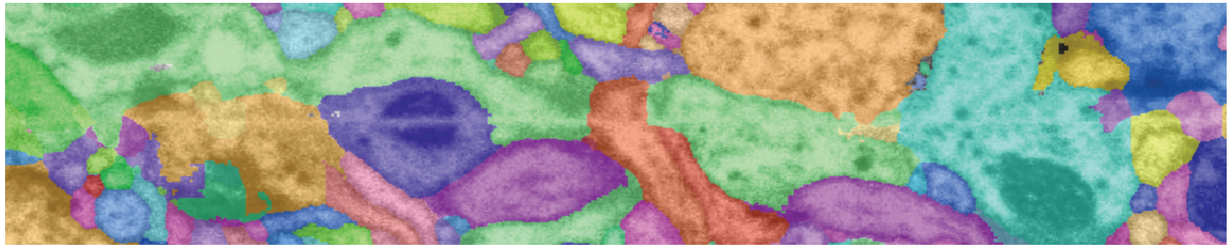
# Applications: image correction

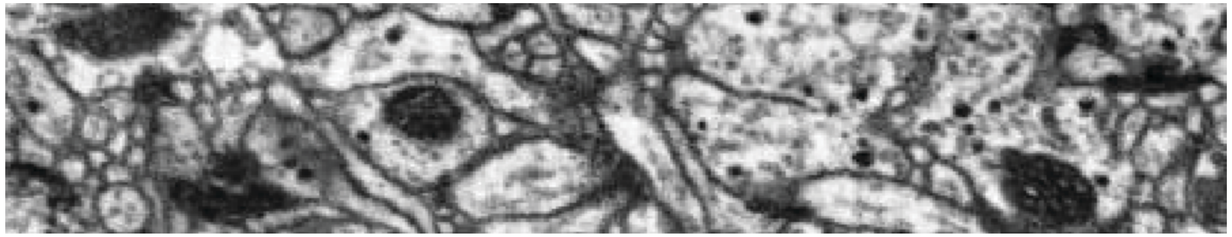


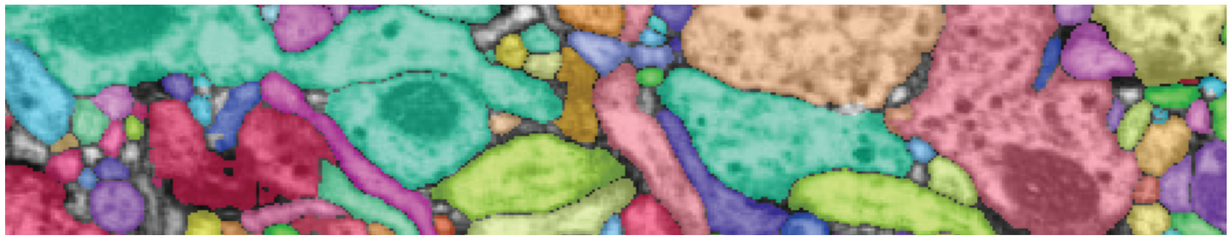


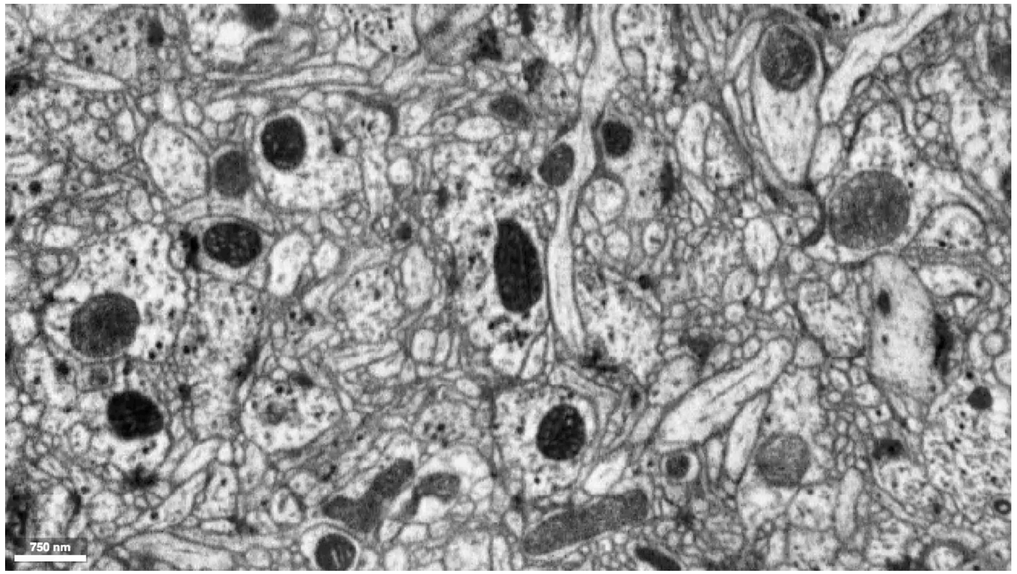
# Applications: image restoration

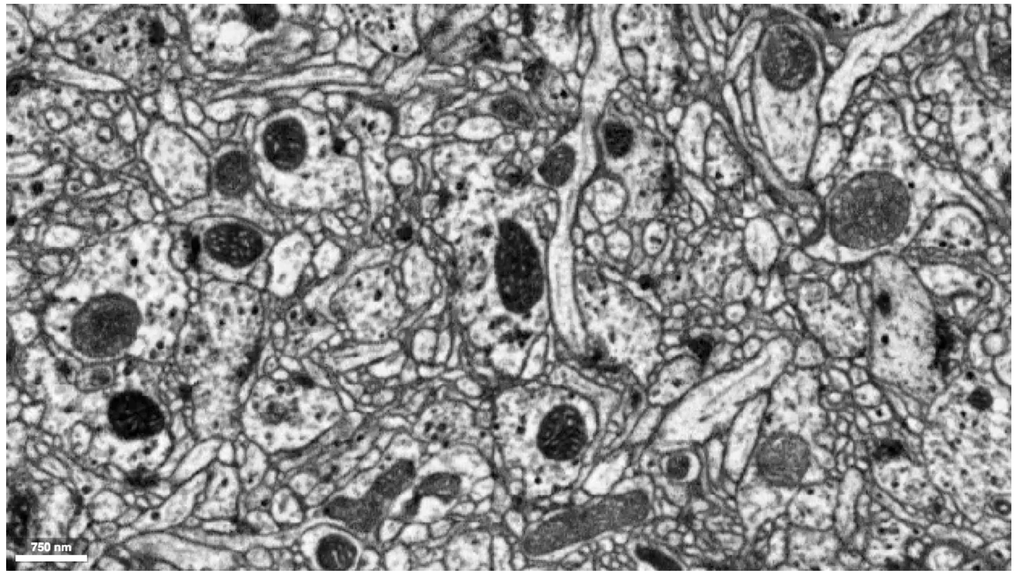










# Summary

- Connectomics demands **extreme accuracy and scale.** Customized ML approaches make this possible.
- Successful projects bring together lots of complementary expertise to a single collaboration.
- More about our work:

https://research.google/teams/connectomics

- Open source code:

https://github.com/google/neuroglancer (WebGL-based N-d data browser)

https://github.com/google-research/sofima (alignment & stitching of large volumes)

https://github.com/google/tensorstore (N-d data storage library)

@michalj mjanusz@google.com