Brain Mapping @ Argonne

Narayanan ‘Bobby’ Kasthuri
Neuroscience Researcher, Nanosciences Division,
Argonne National Lab
Assistant Professor (*adjunct*), Neurobiology,
University of Chicago

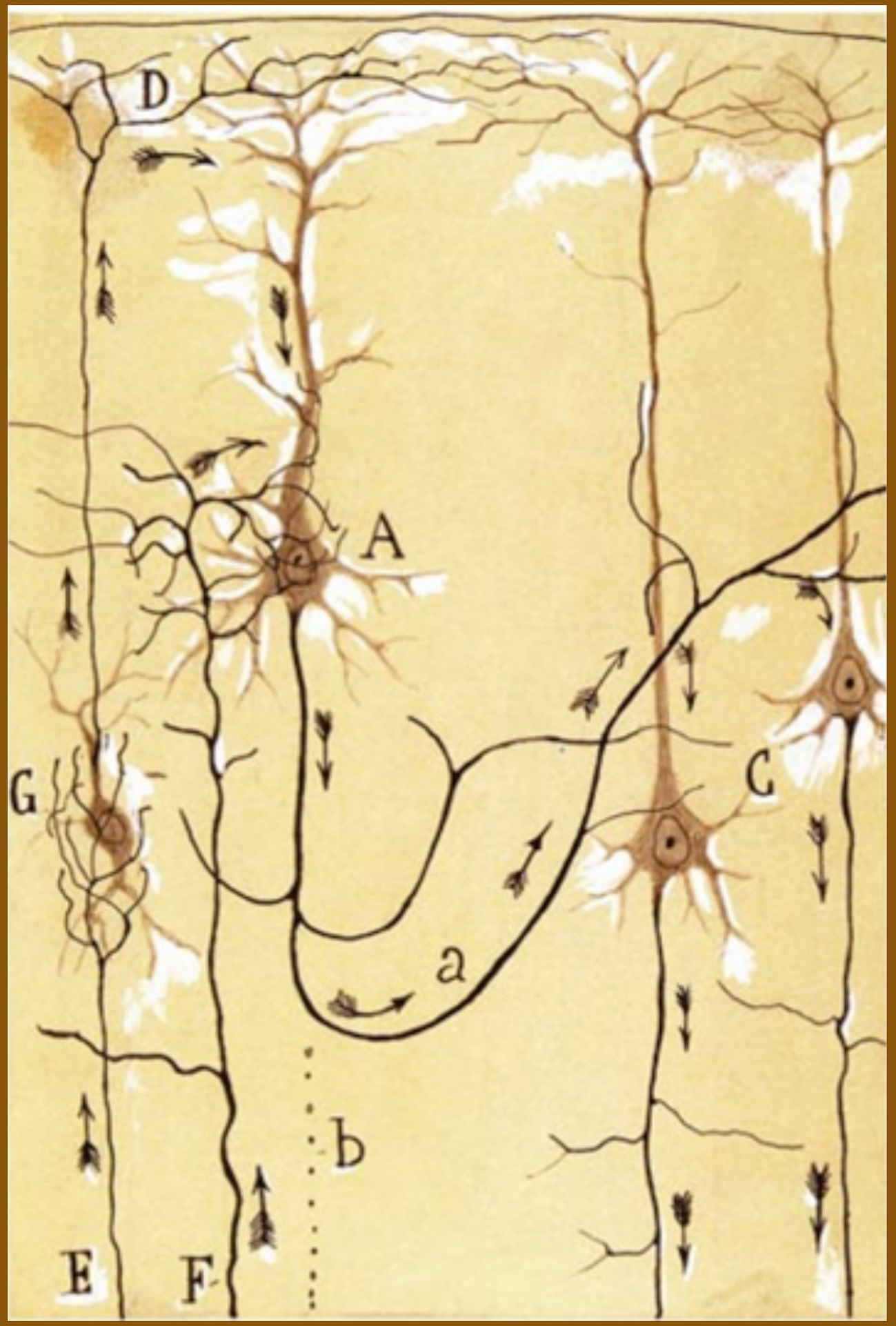
bobbykasthuri@anl.gov

617-335-2518 (c)

1. Technological advance leads to biological insight
2. The ‘control’ is the interesting bit
3. “Anatomy is destiny” - S. Freud (1931)

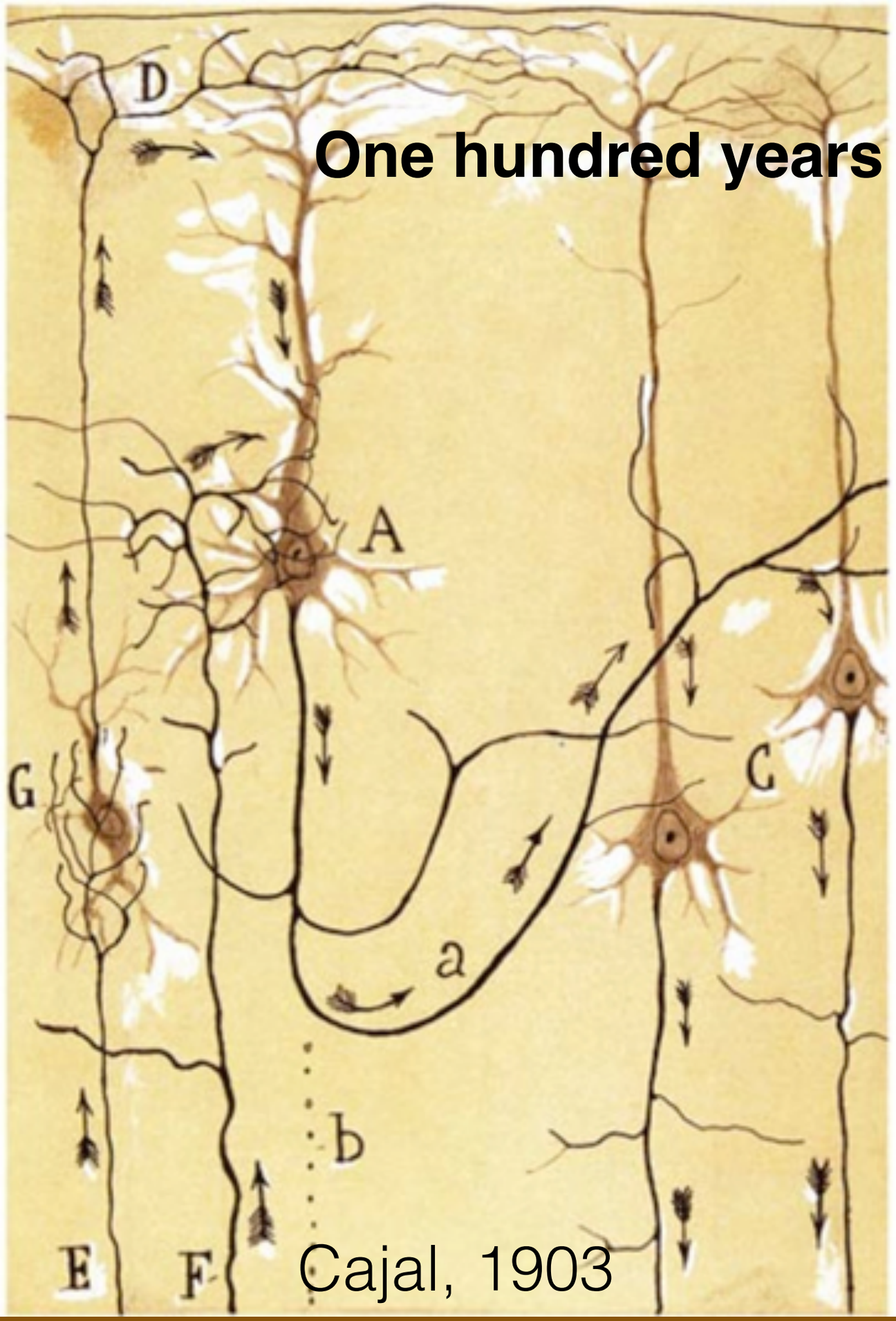
Technology is(can be) the answer:

1. Cajal and Golgi (1906) - Golgi stain and compound microscope
2. Erlanger and Gasser (1944) - Oscilloscope
3. Hodgkin and Huxley (1964) - voltage clamp
4. Katz (1970) - sharp electrodes
5. Hubel and Wiesel (1981) - trans-synaptic tracing, single-unit recording
6. Montalcini and Cohen (1986) - explants and neuronal culture
7. Sakmann and Neher (1991)- patch clamp
8. Lauterbur and Mansfield (2003)- MRI
9. Axel and Buck (2004) - advances in genetic sequencing
10. Betzig, Moerner, and Hell (2014) - super-resolution microscop

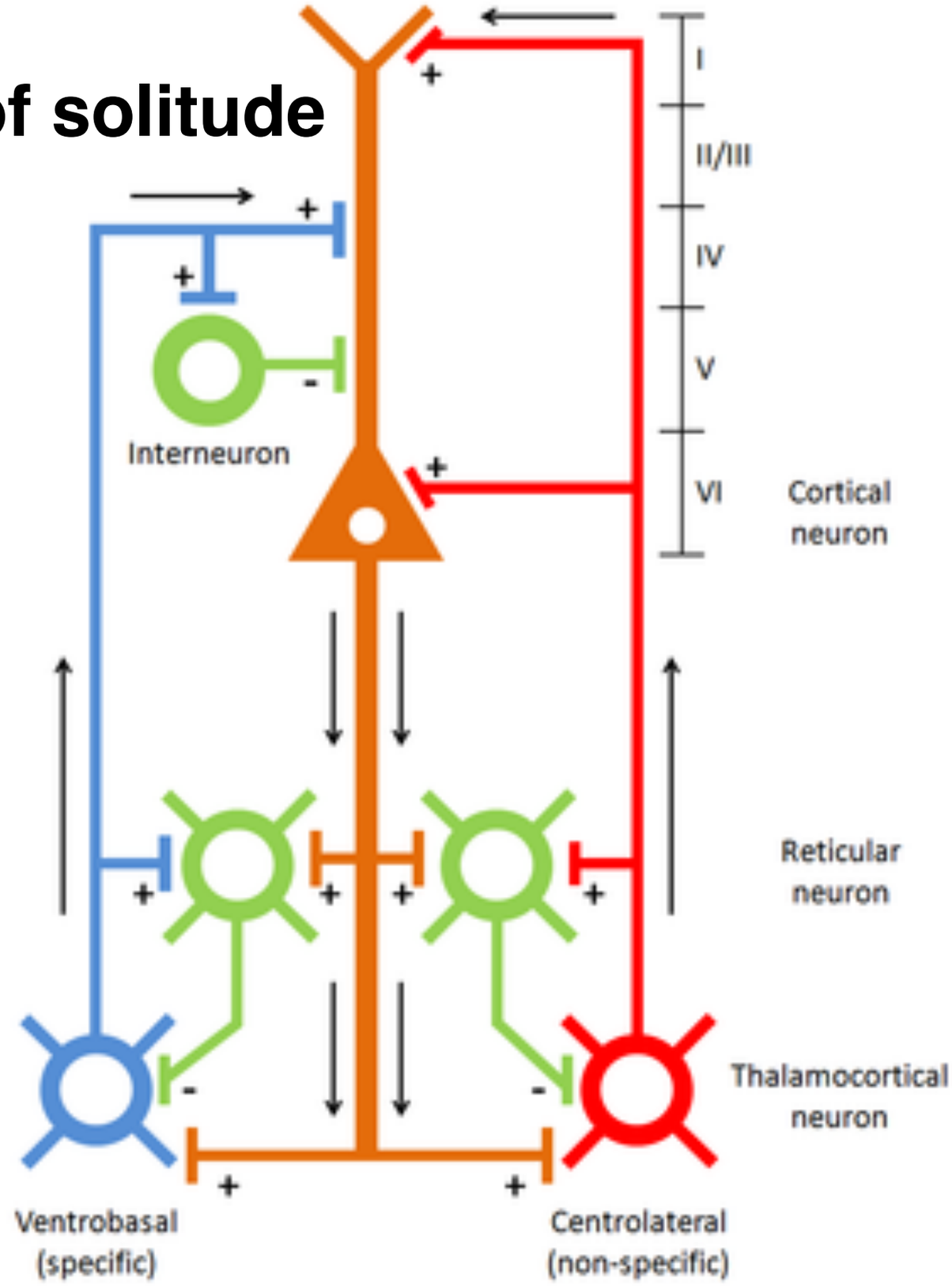


Cajal, 1903

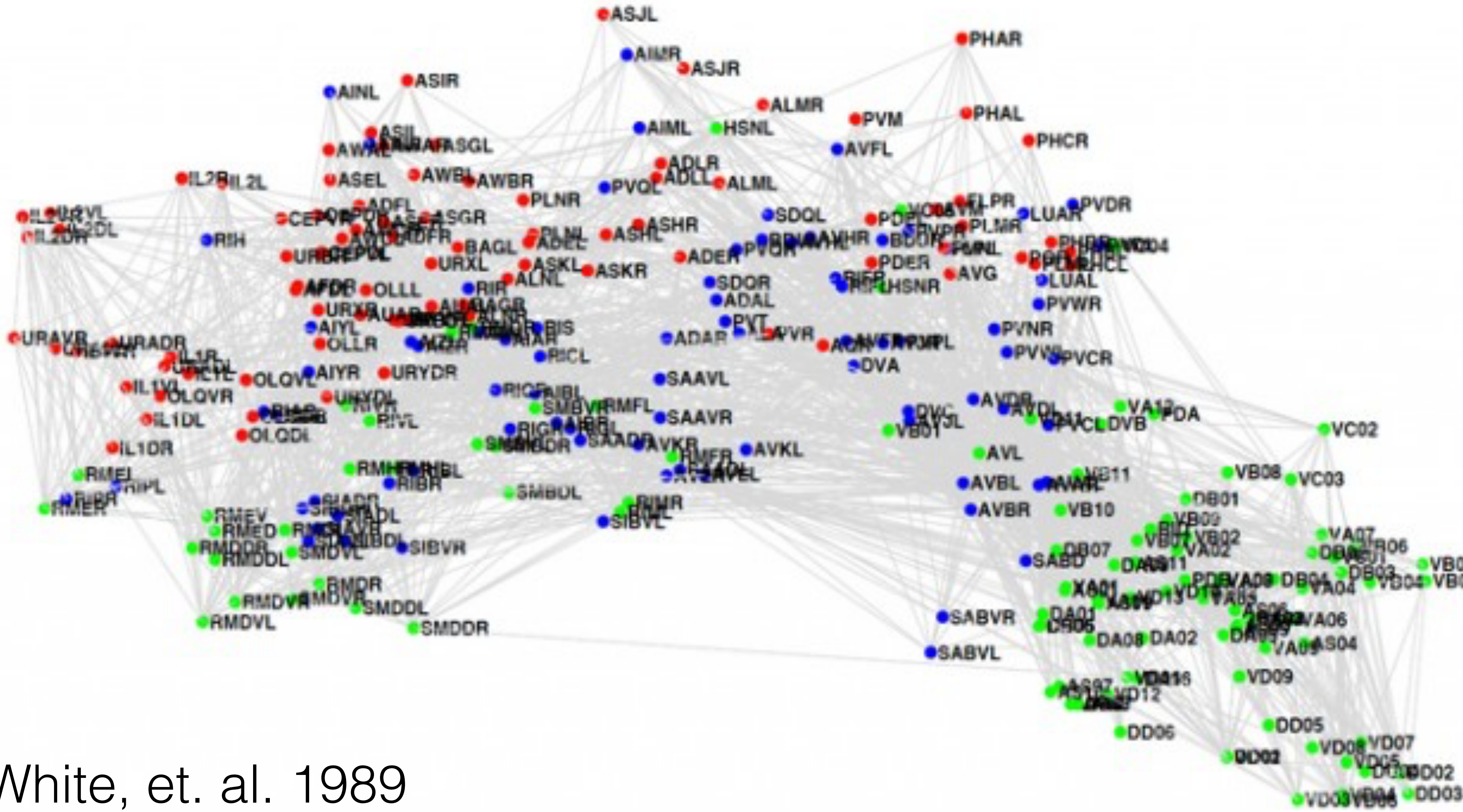
One hundred years of solitude



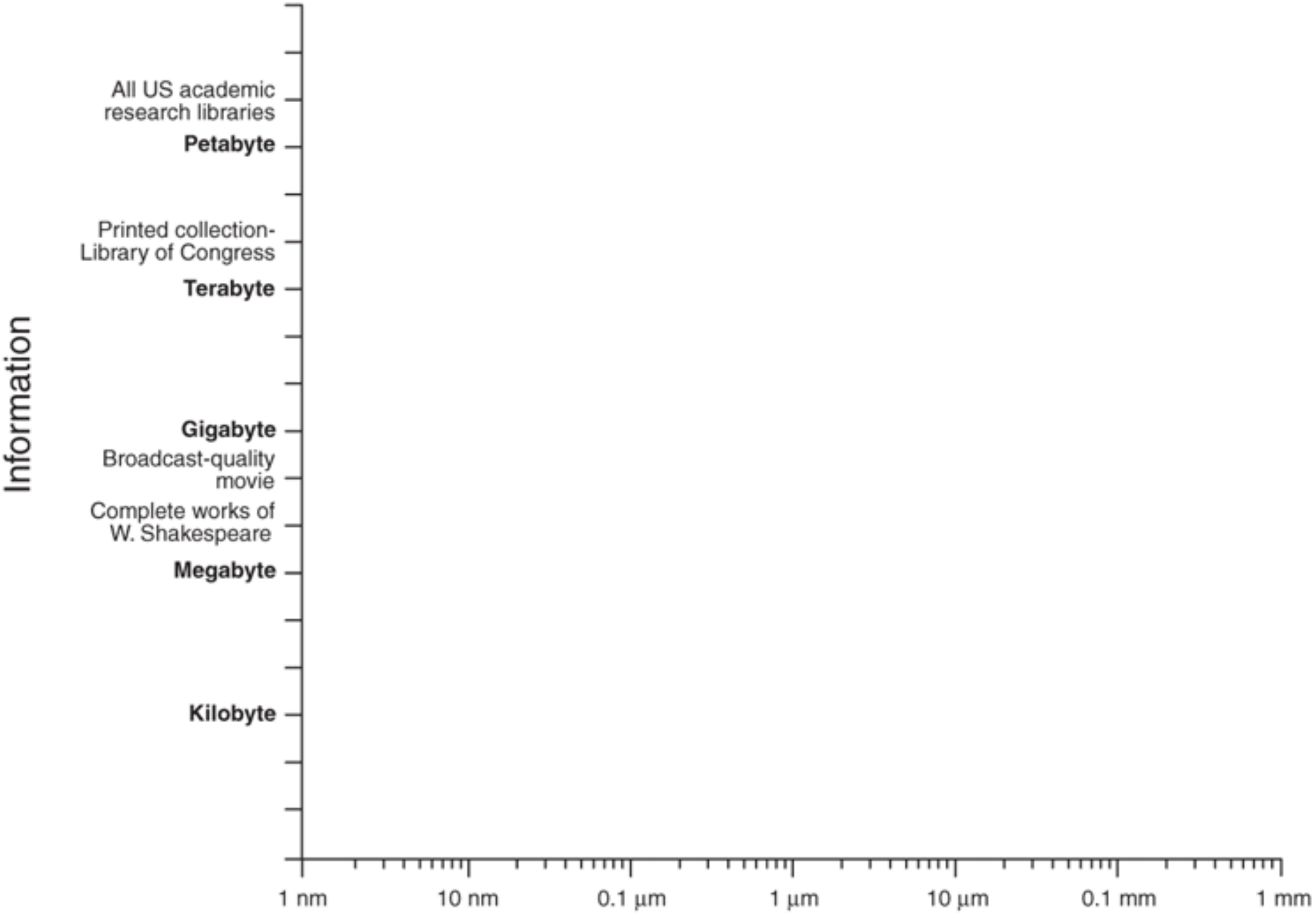
Cajal, 1903



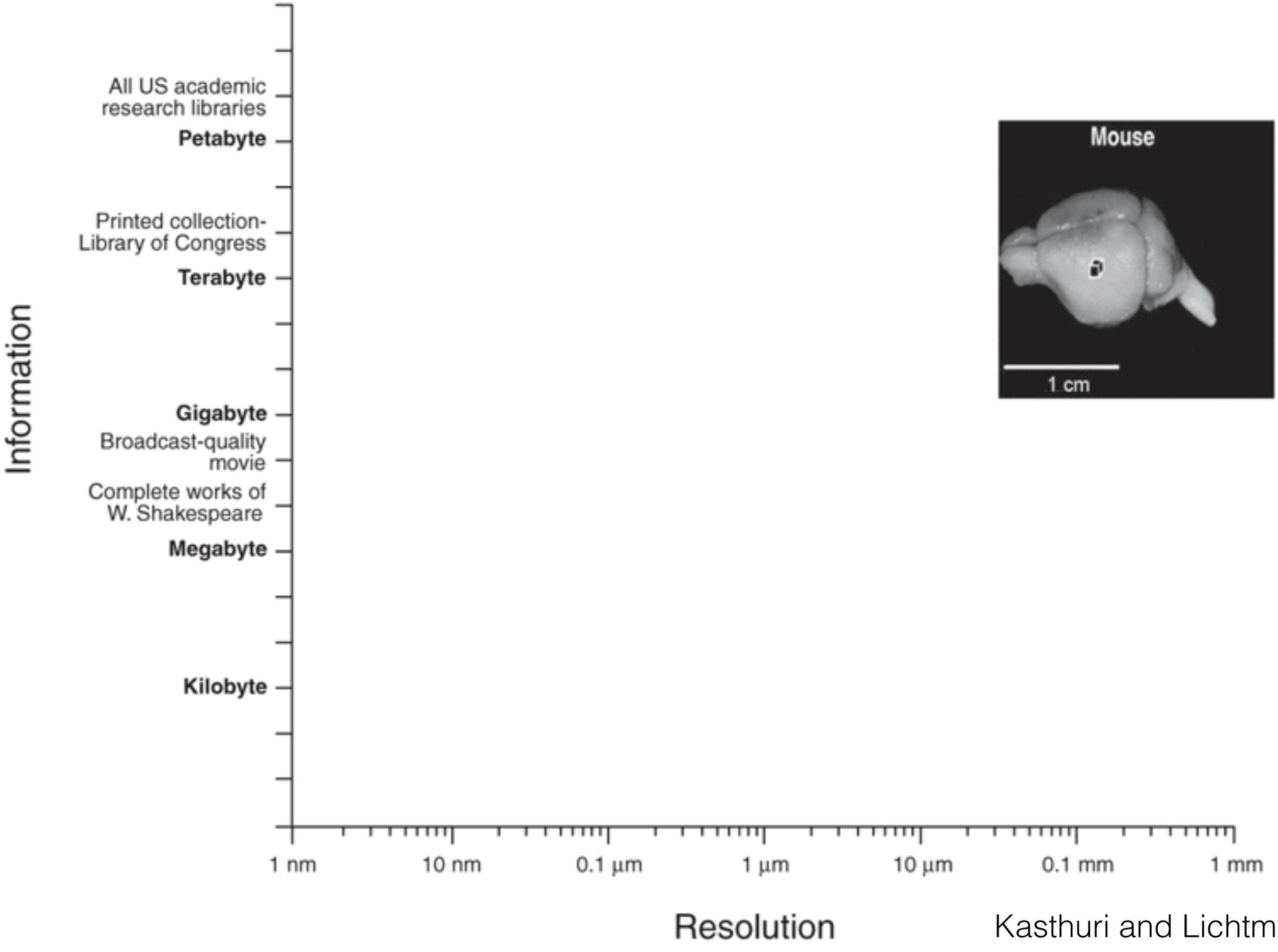
(Llinas, Leznik, Urbano 2002)



White, et. al. 1989



Kasthuri and Lichtman



Kasthuri and Lichtman

Information

All US academic research libraries

Petabyte

Printed collection- Library of Congress

Terabyte

Gigabyte

Broadcast-quality movie

Complete works of W. Shakespeare

Megabyte

Kilobyte

EM

X-ray

Sample Prep

Serial TEM

Serial block-face SEM

PALM/STORM

STED

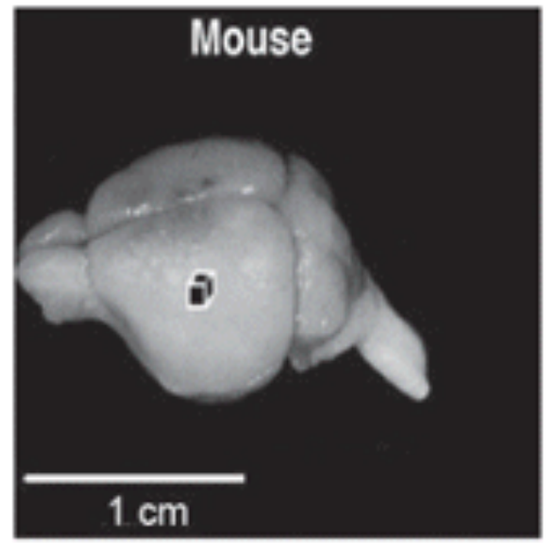
Structured illumination

SPIM*

Confocal

Ultra-microscopy*

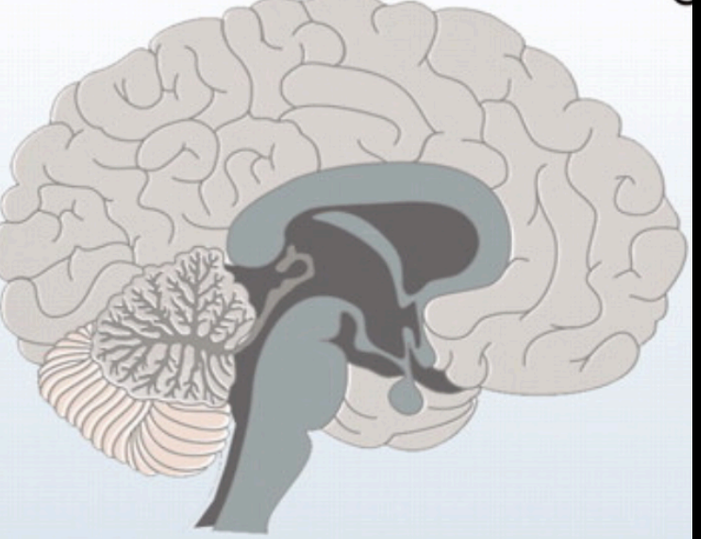
MRI

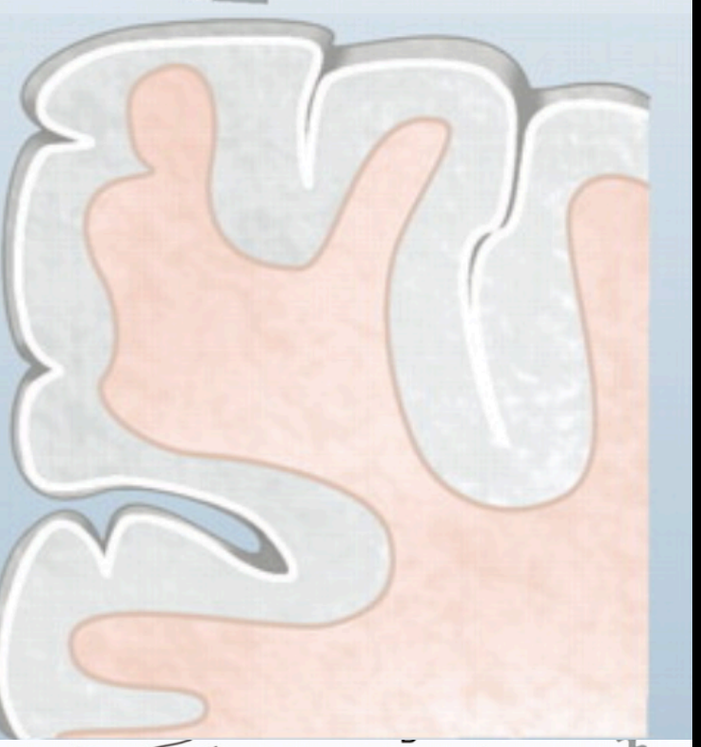


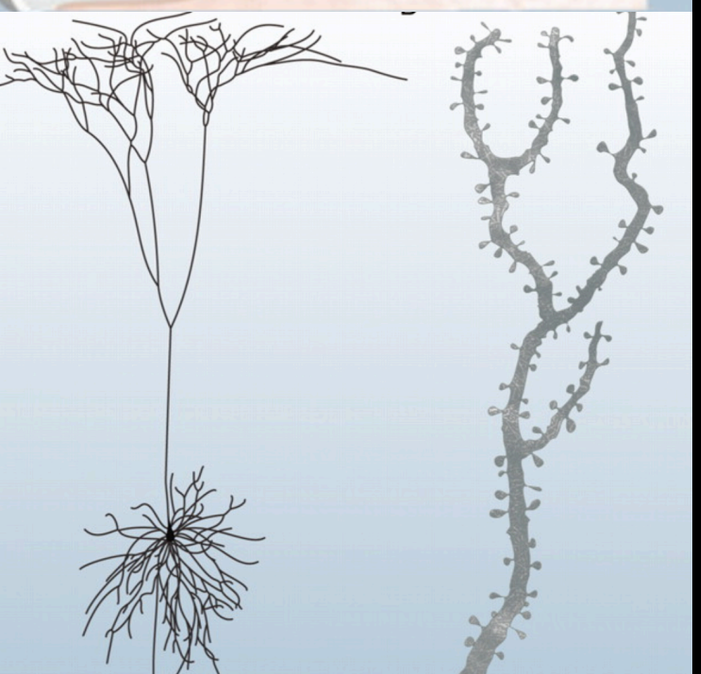
1 nm | 10 nm | 0.1 µm | 1 µm | 10 µm | 0.1 mm | 1 mm

Resolution

Kasthuri and Lichtman







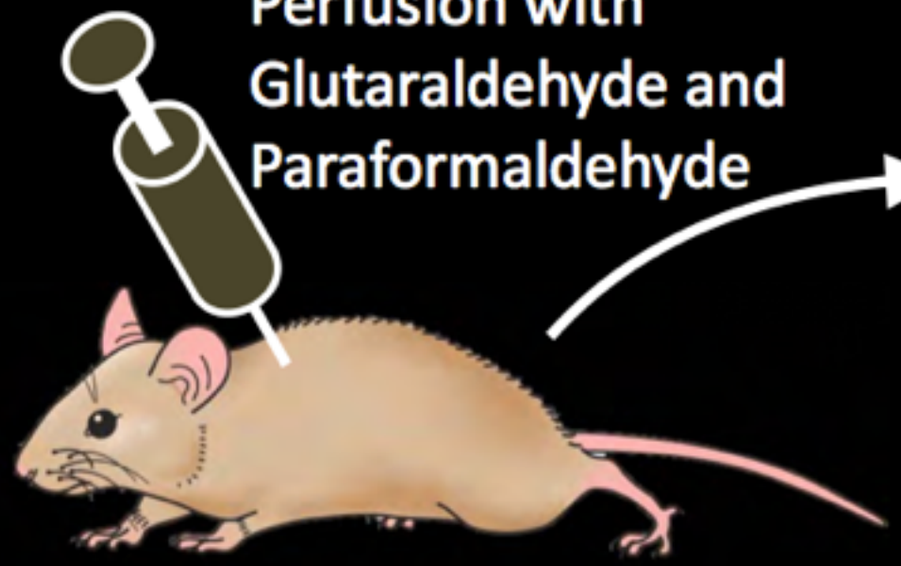
0.1 m

.01 m

.001 m

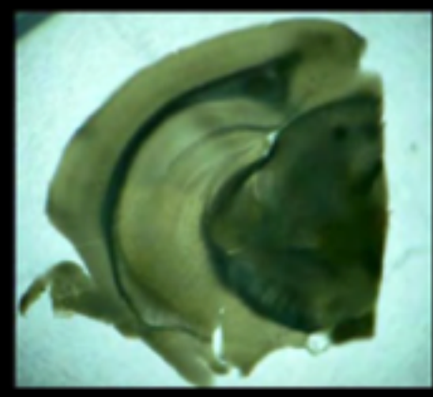
.00001

Sample Preparation



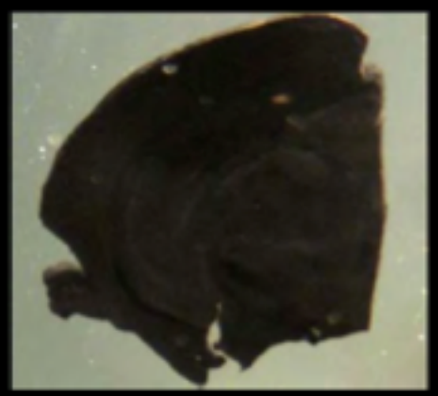
Perfusion with
Glutaraldehyde and
Paraformaldehyde

Vibratome sectioning
(100 or 200 micron slices)



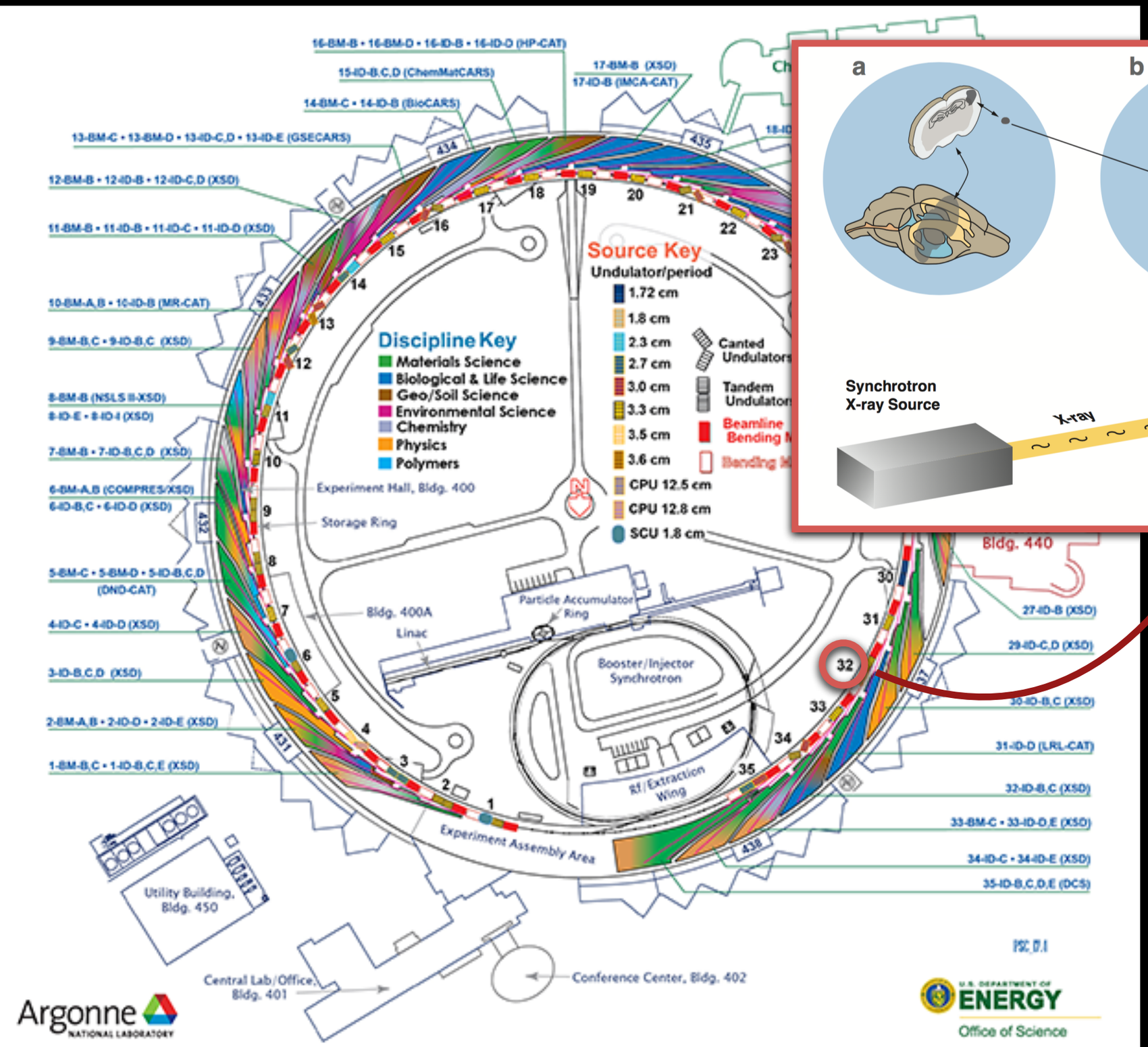
Species Independent

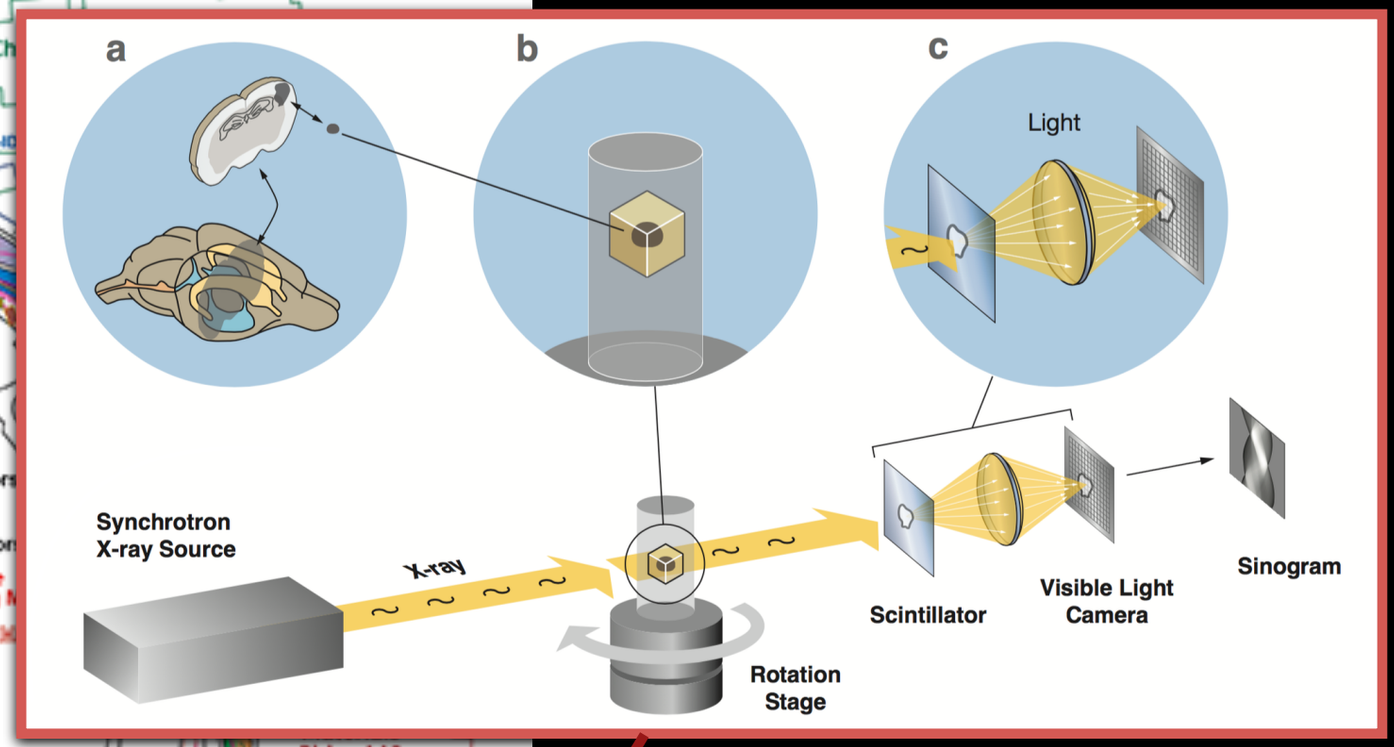
Staining with
heavy metals
(Osmium, Uranium,
Lead)



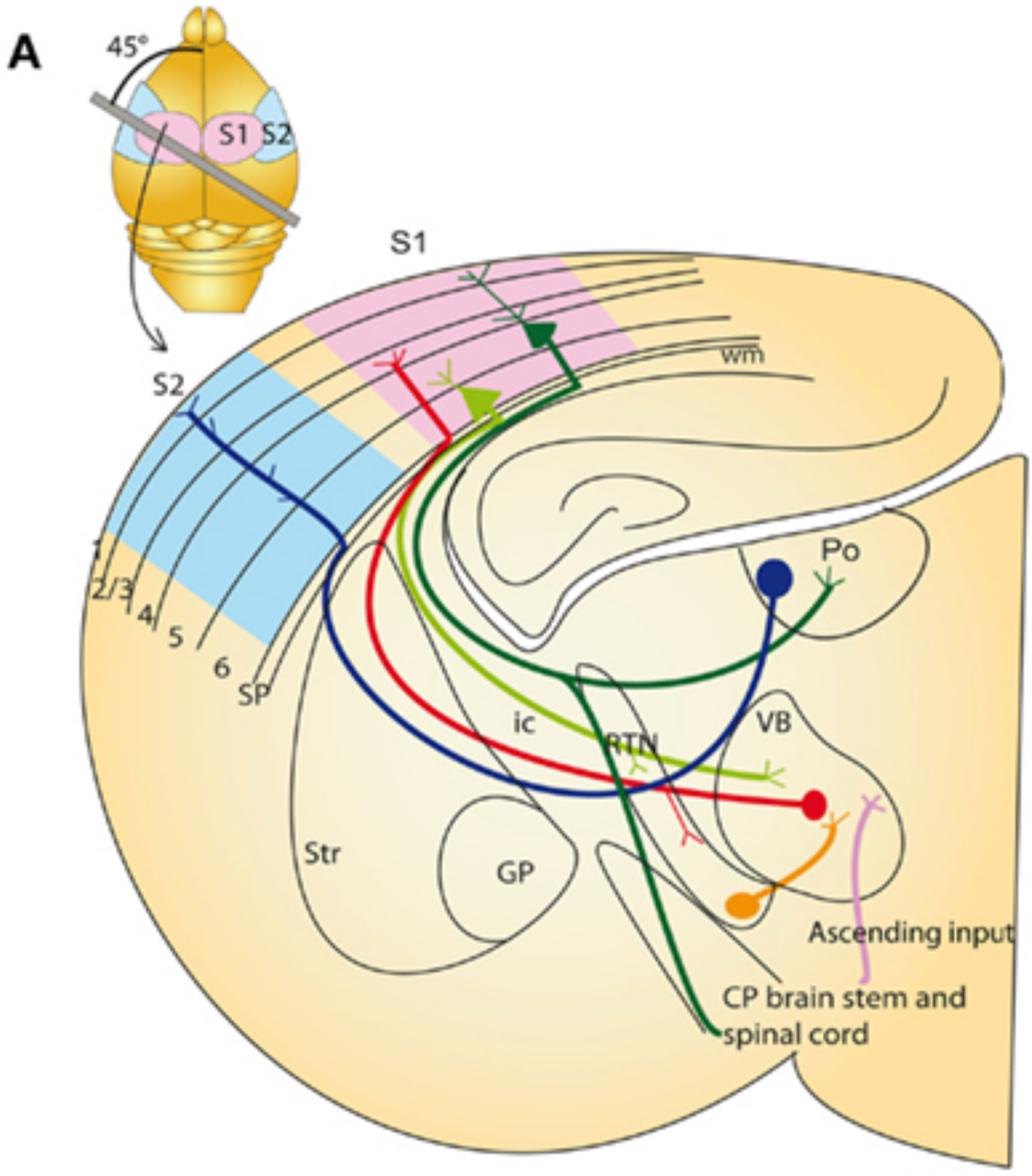
Dehydration and embedding
in epoxy resin (EPON or Durcupan)

~ 450 employees; ~5,000 users per year worldwide.
More protein structures in the Protein Data Bank than any other x-ray light source in the world.

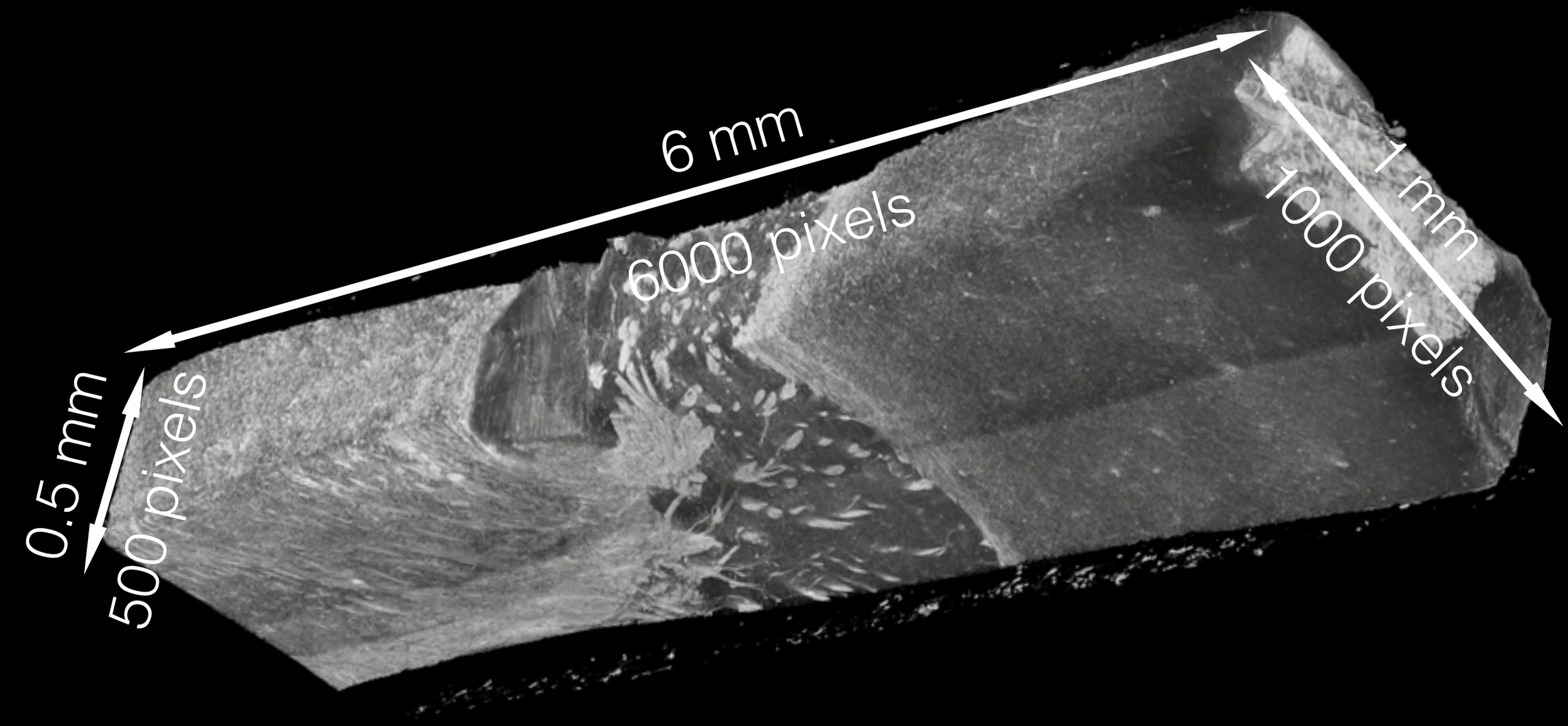




2012 Nobel Prize - Koblika and Lefkowitz - Structure of G-PCR


A
45°
S1
S2
S1
S2
wm
1
2/3
4
5
6
SP
Po
ic
RTN
VB
Str
GP
Ascending input
CP brain stem and
spinal cord

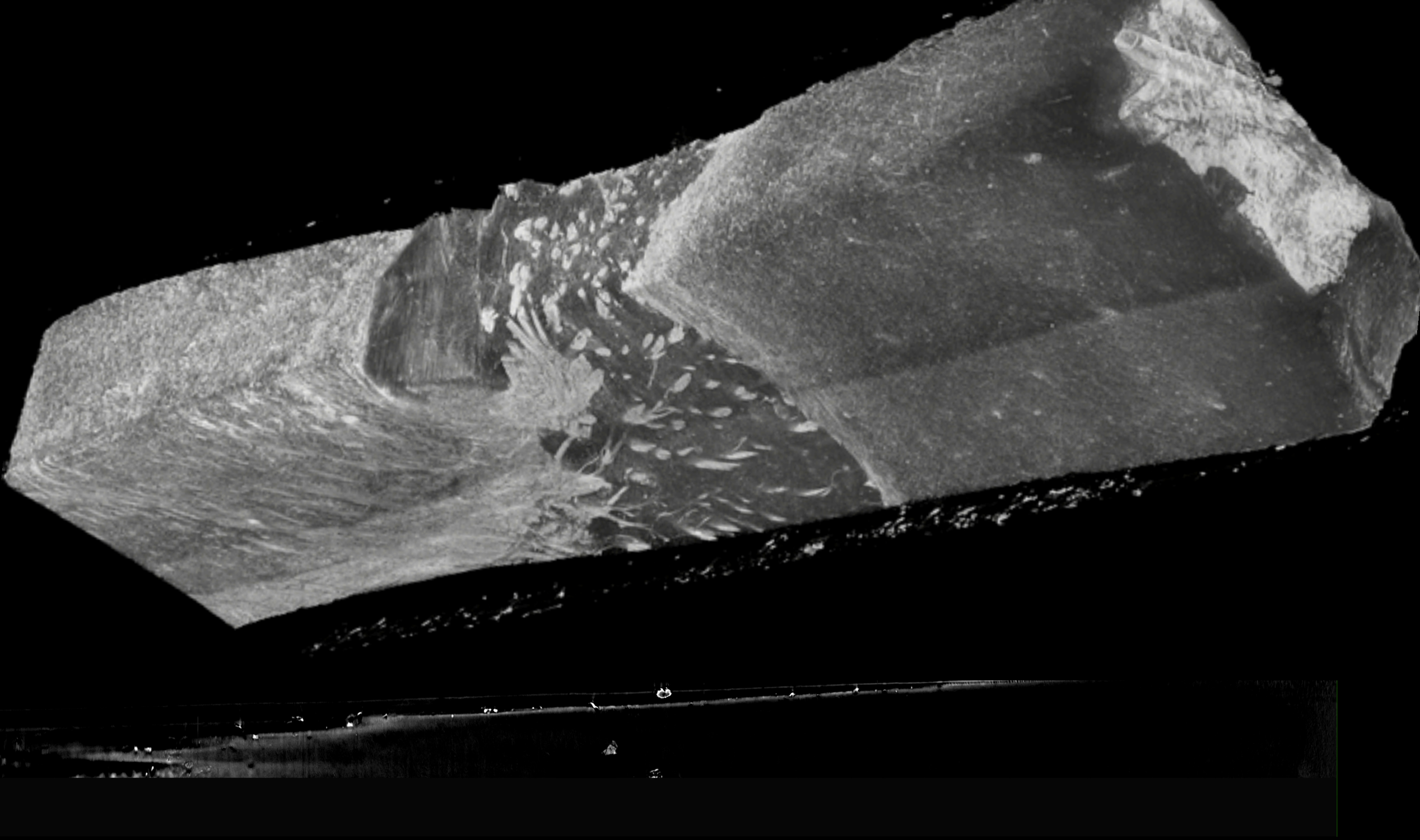
A Thalamocortical Circuit



Judy Prasad, Vandana Sampathkumar, Eva Dyer, Rafael Vescovi, Vincent De Andrade

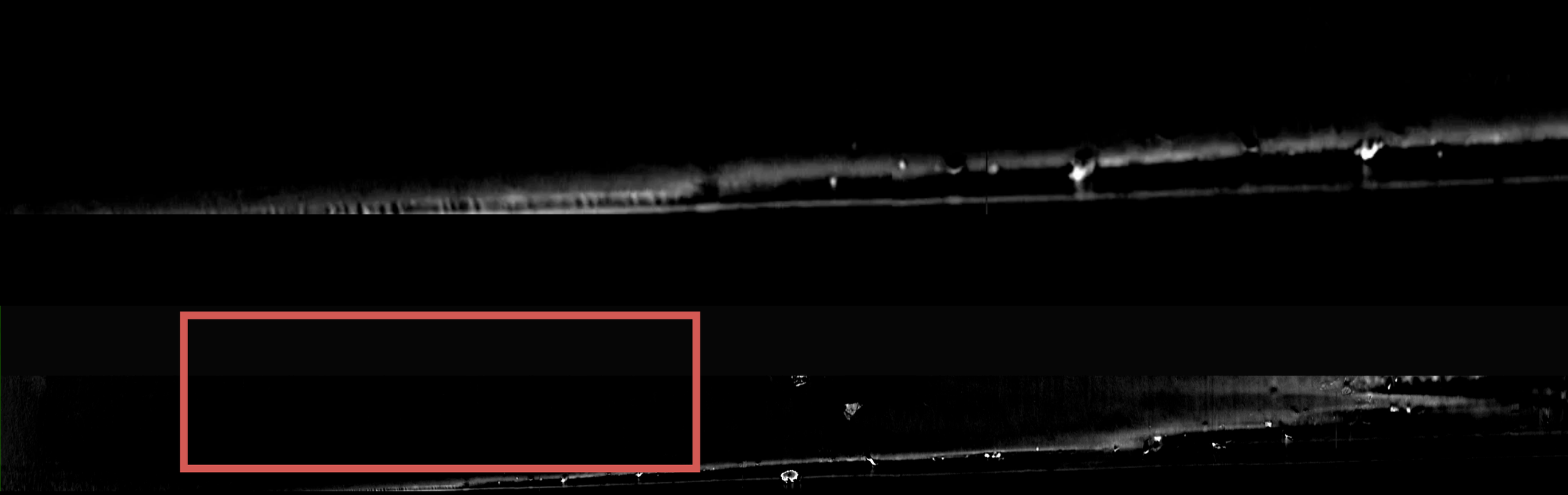
(Agmon and Connors, 1991)

32-ID, APS

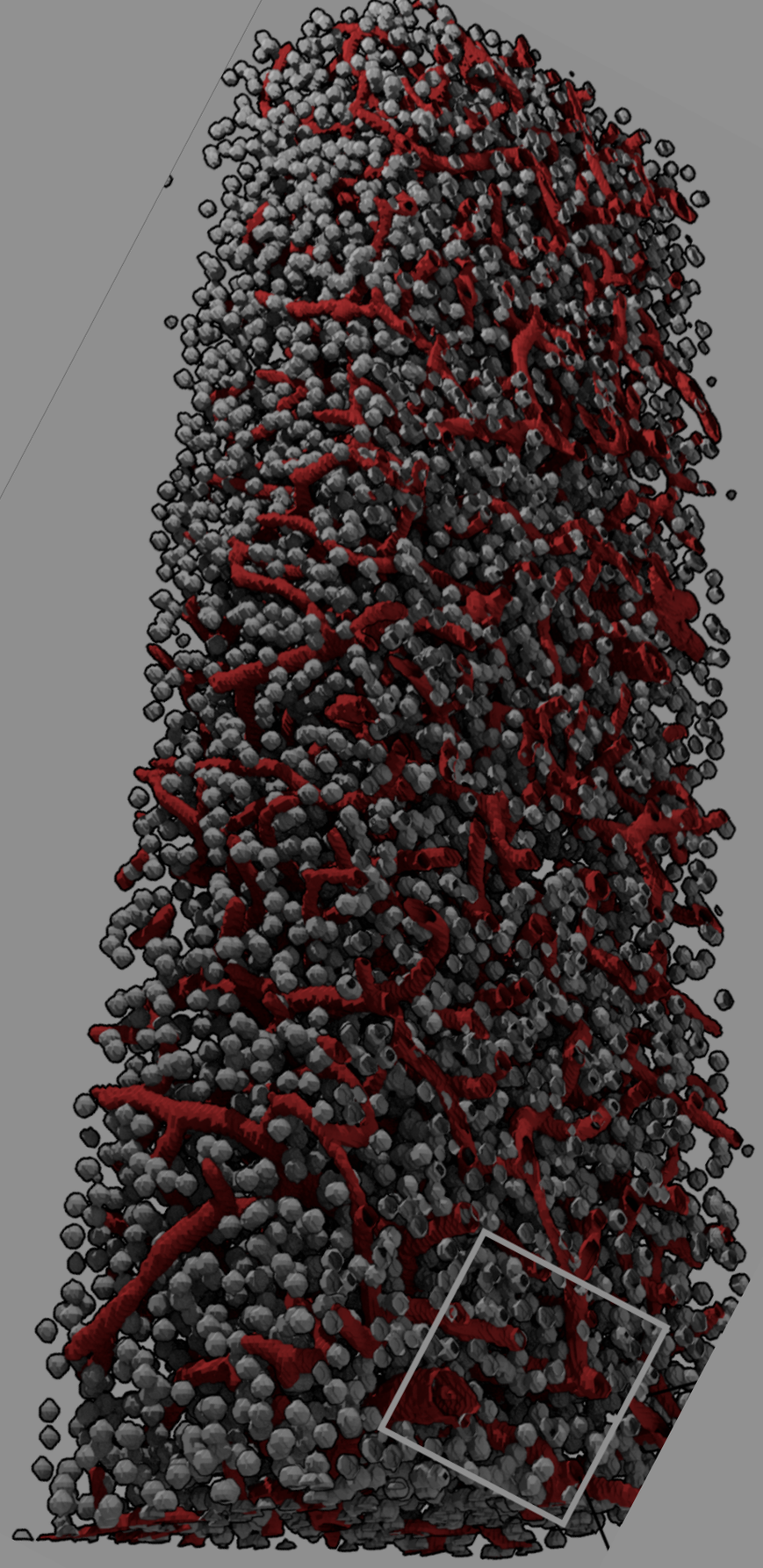


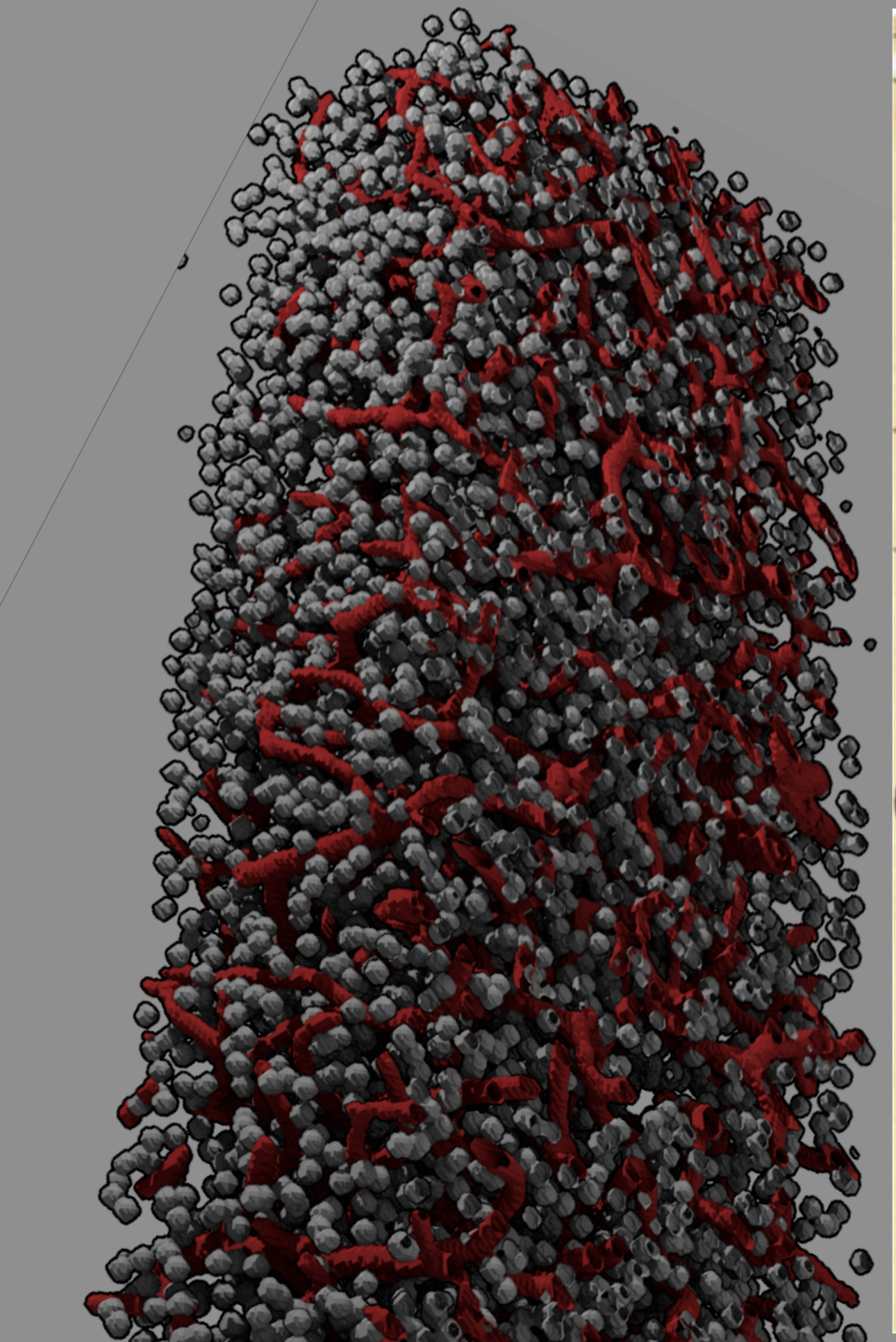
Thalamus

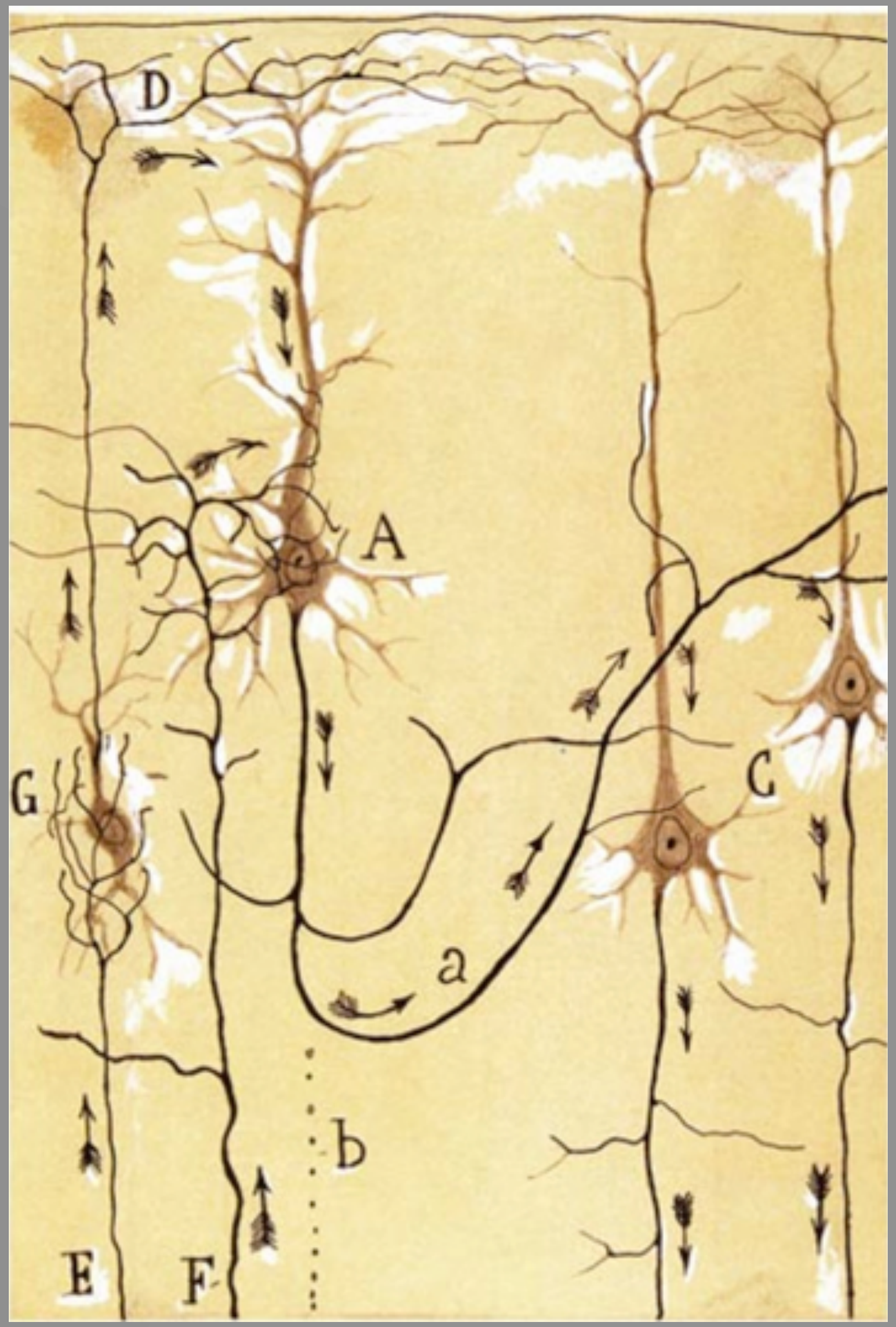
Cortex

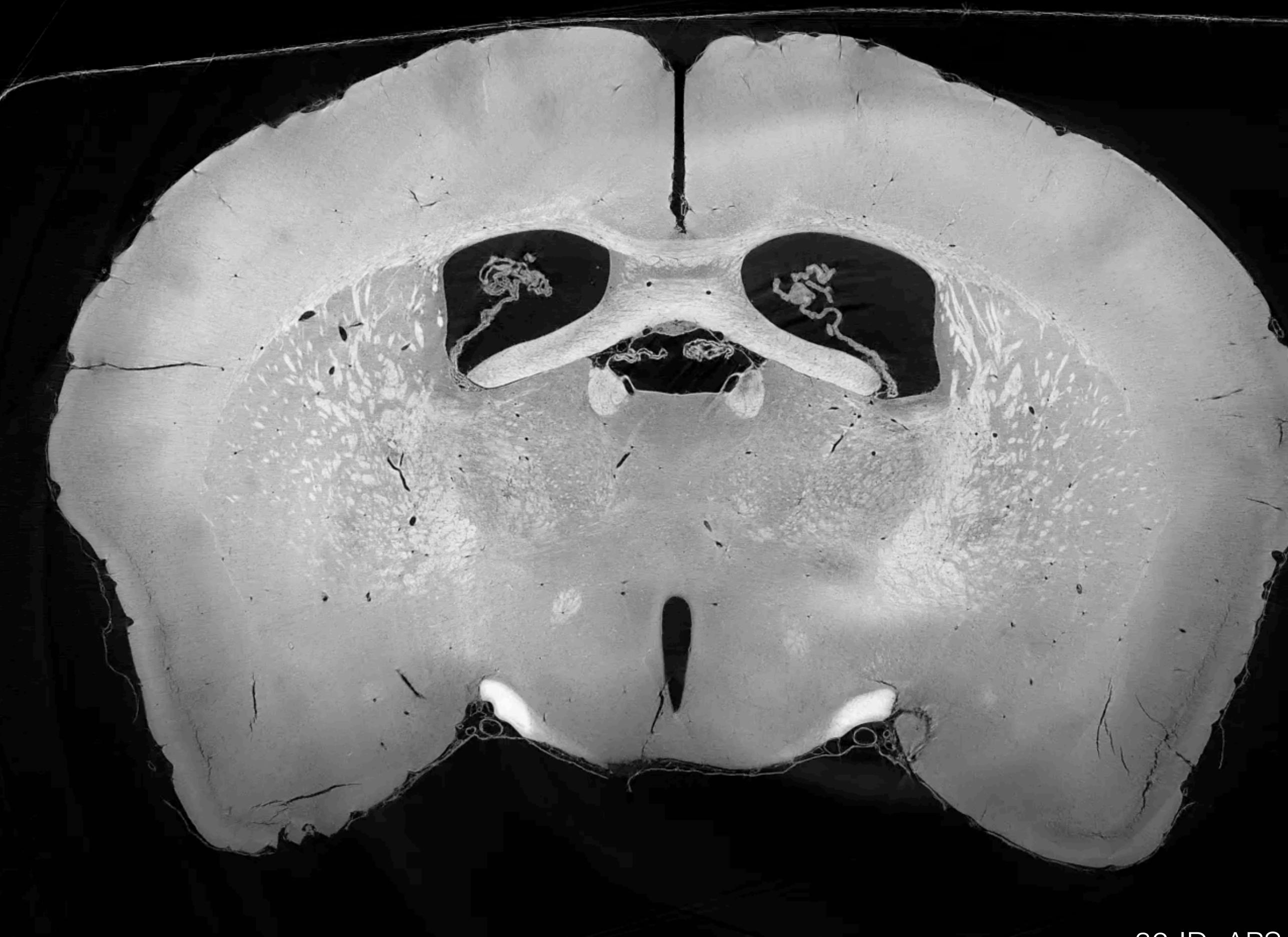



Eva Dyer

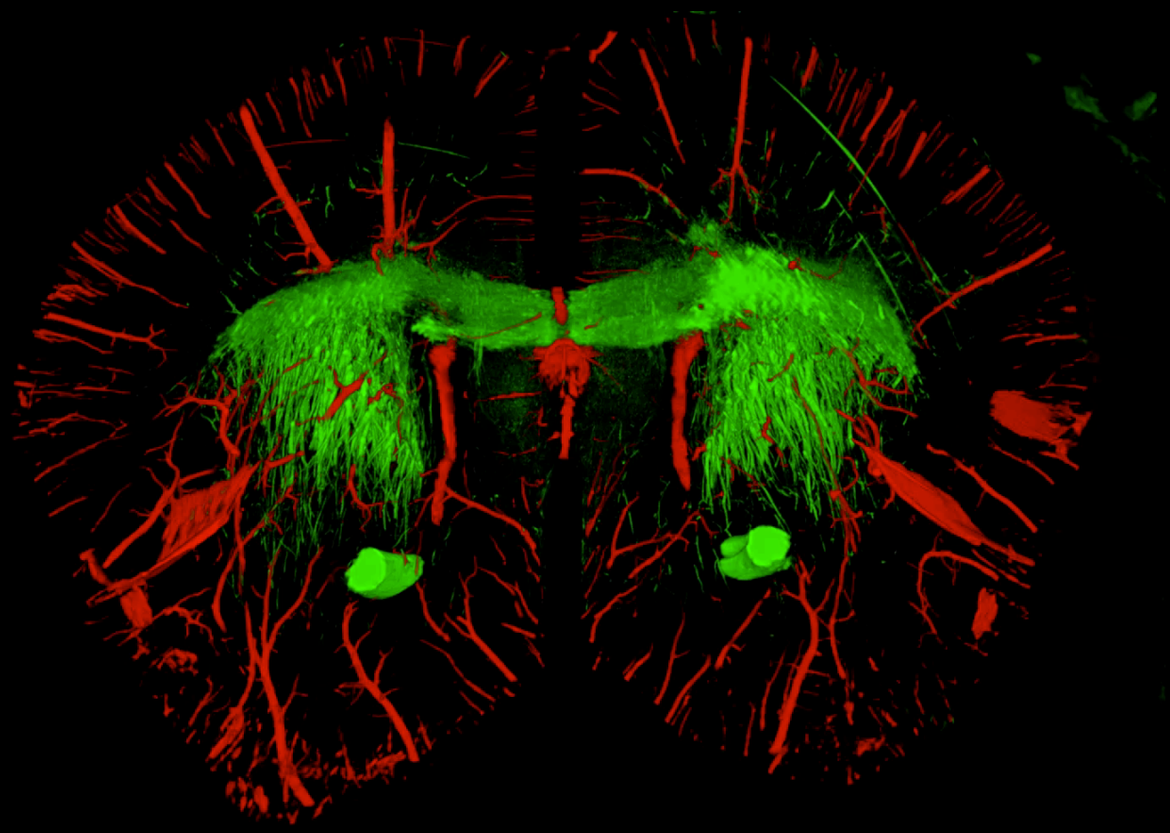


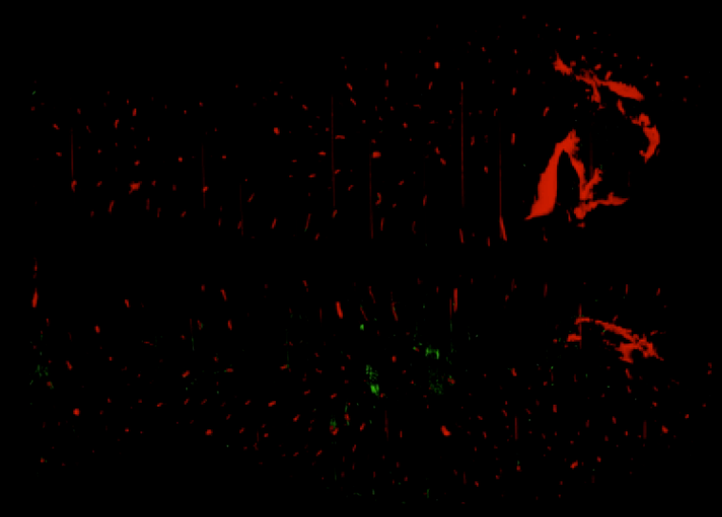


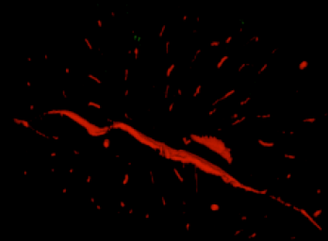

D
A
G
C
a
b
E
F

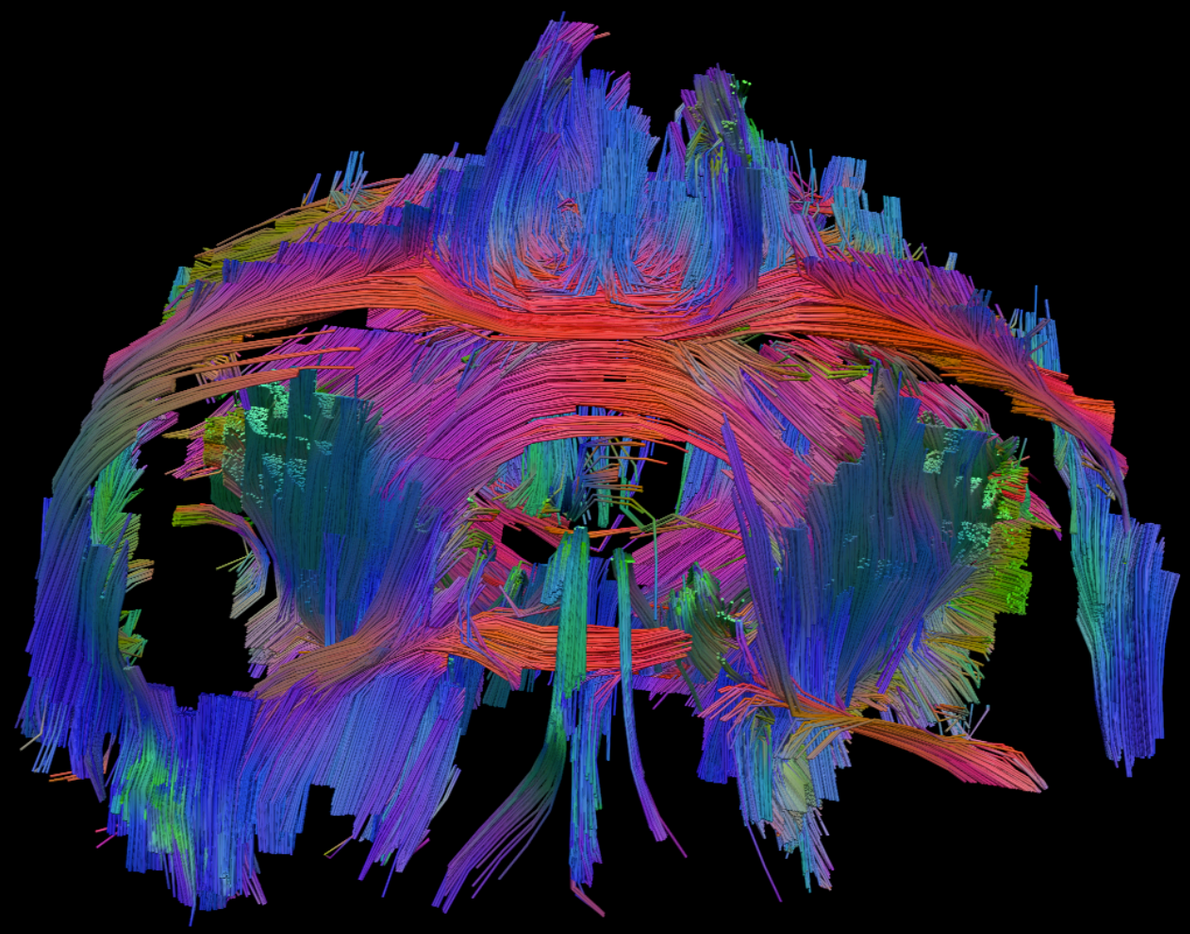


Shawn Mikula, Rafael Vescovi, Vincent De Andrade, Ming Du, Doga Gursoy, Chris Jacobsen 32-ID, APS



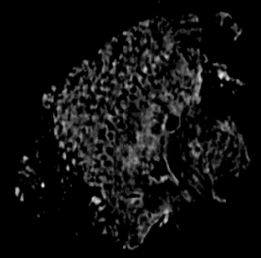


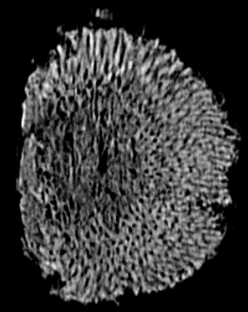




Hanyu Li

Rafael Vescovi, Sean Foxley, Patrick LaRiviere, Doga Gursoy





Gregg Wildenberg, Markus Kornfrost, Rafael Vescovi, Vincent DeAndrade

32-ID, APS

Serial ultra-thin slicing

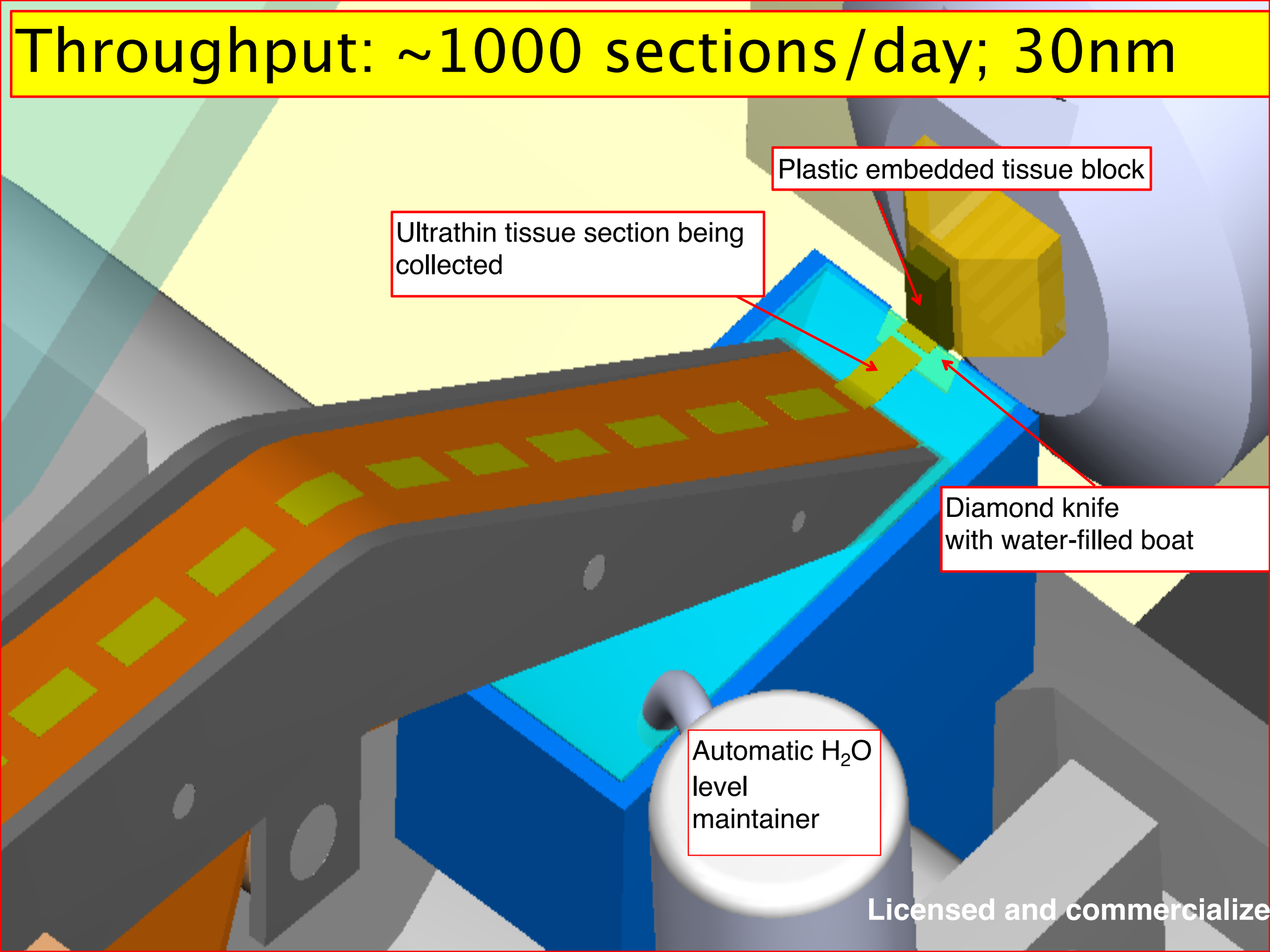
EM imaging

Image alignment

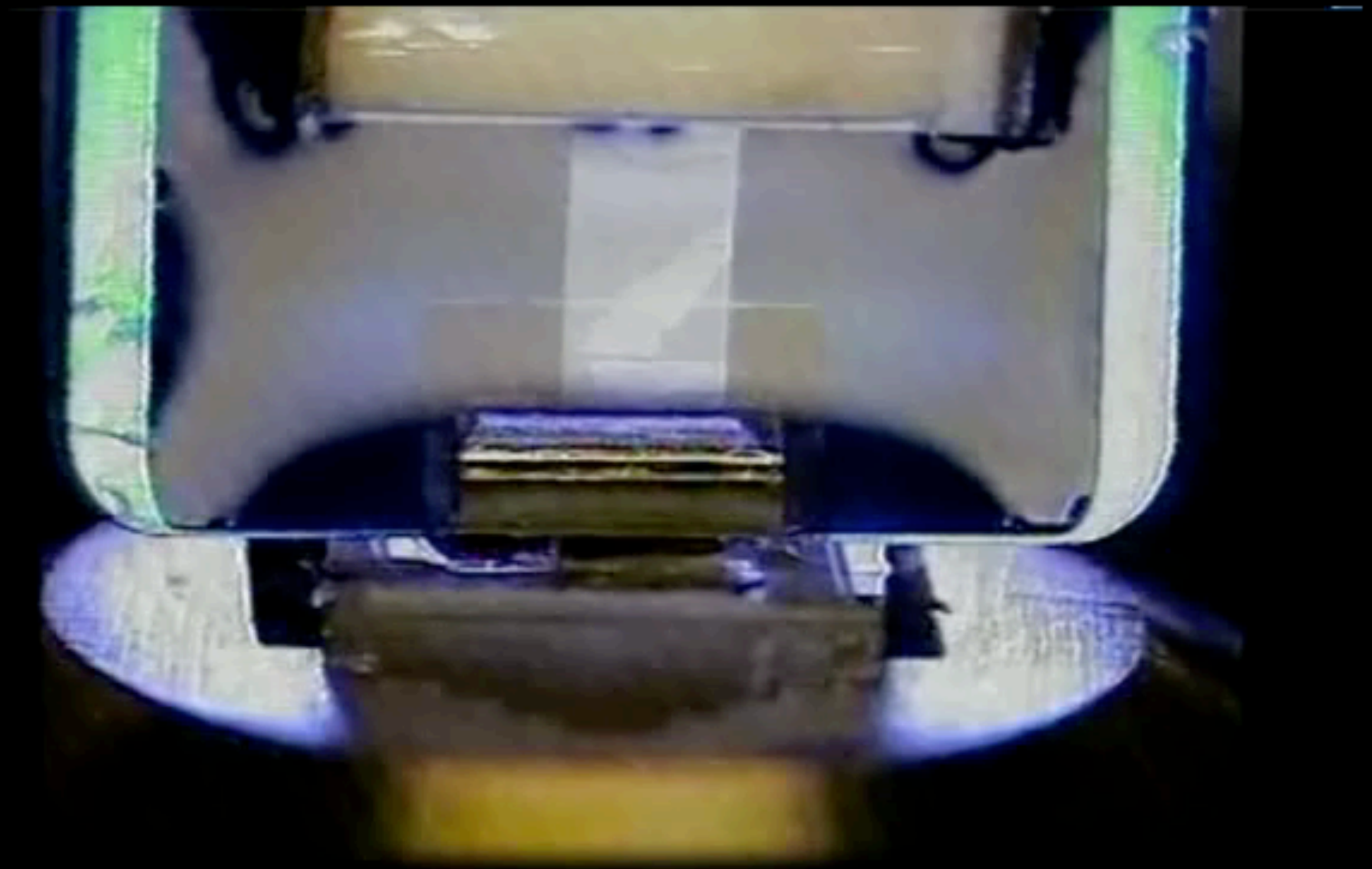
2D Object Segmentation

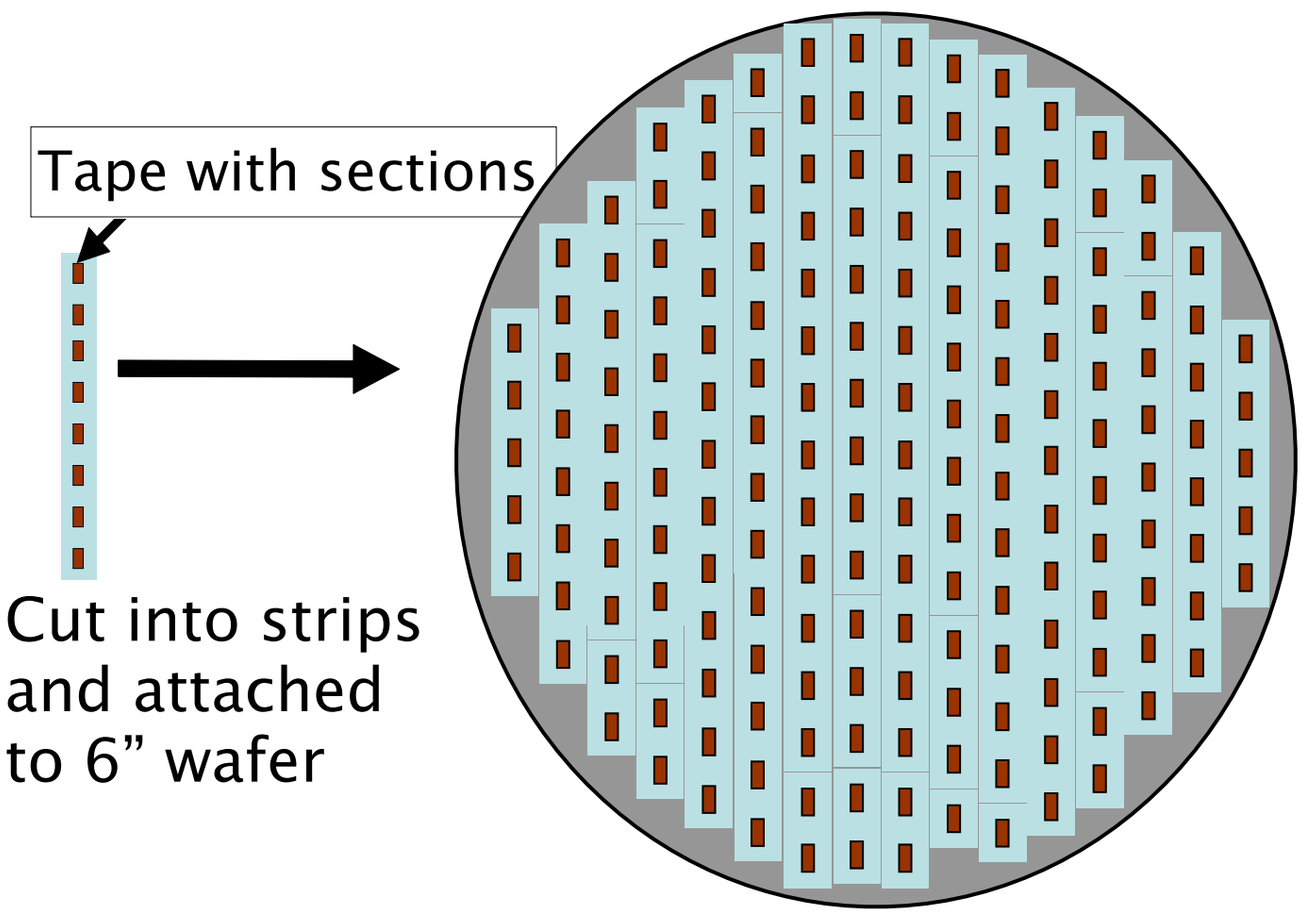
3D Object Segmentation

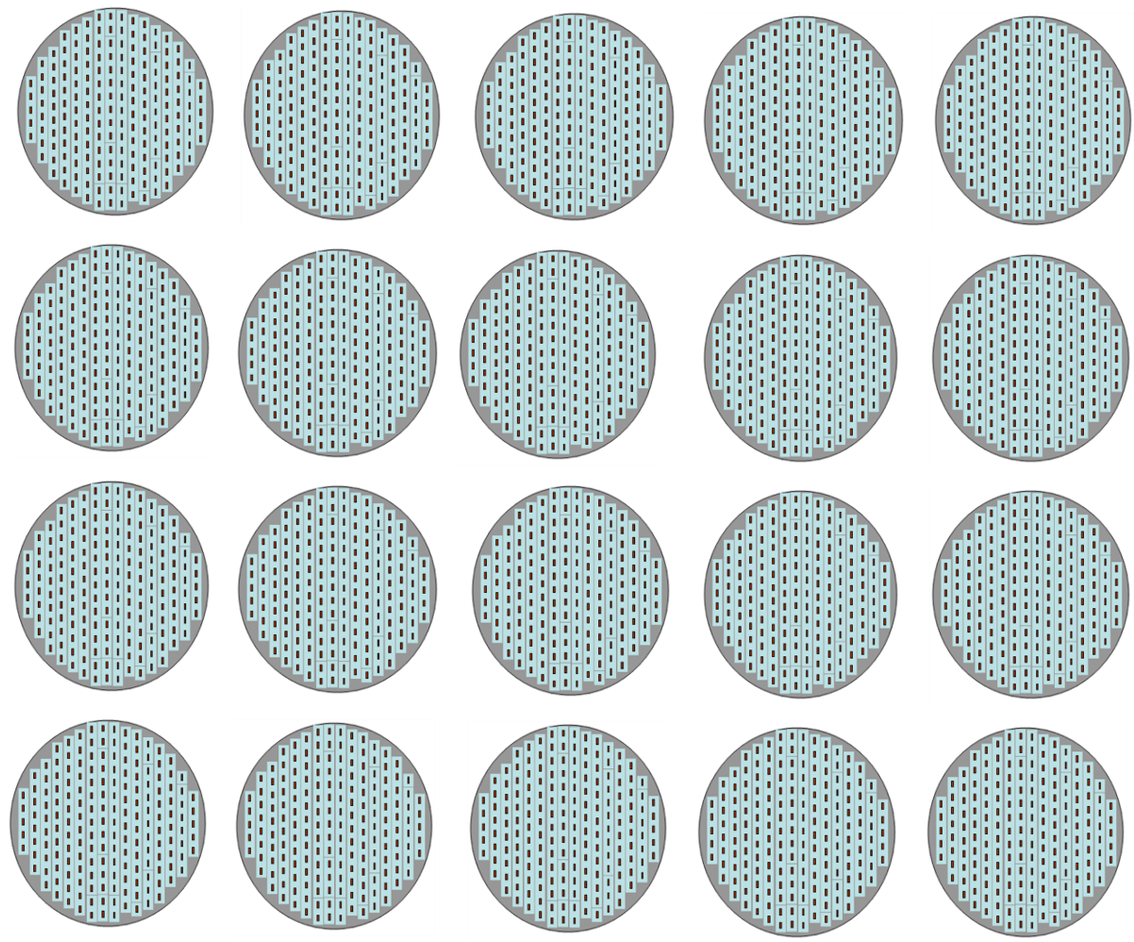
Throughput: ~1000 sections/day; 30nm



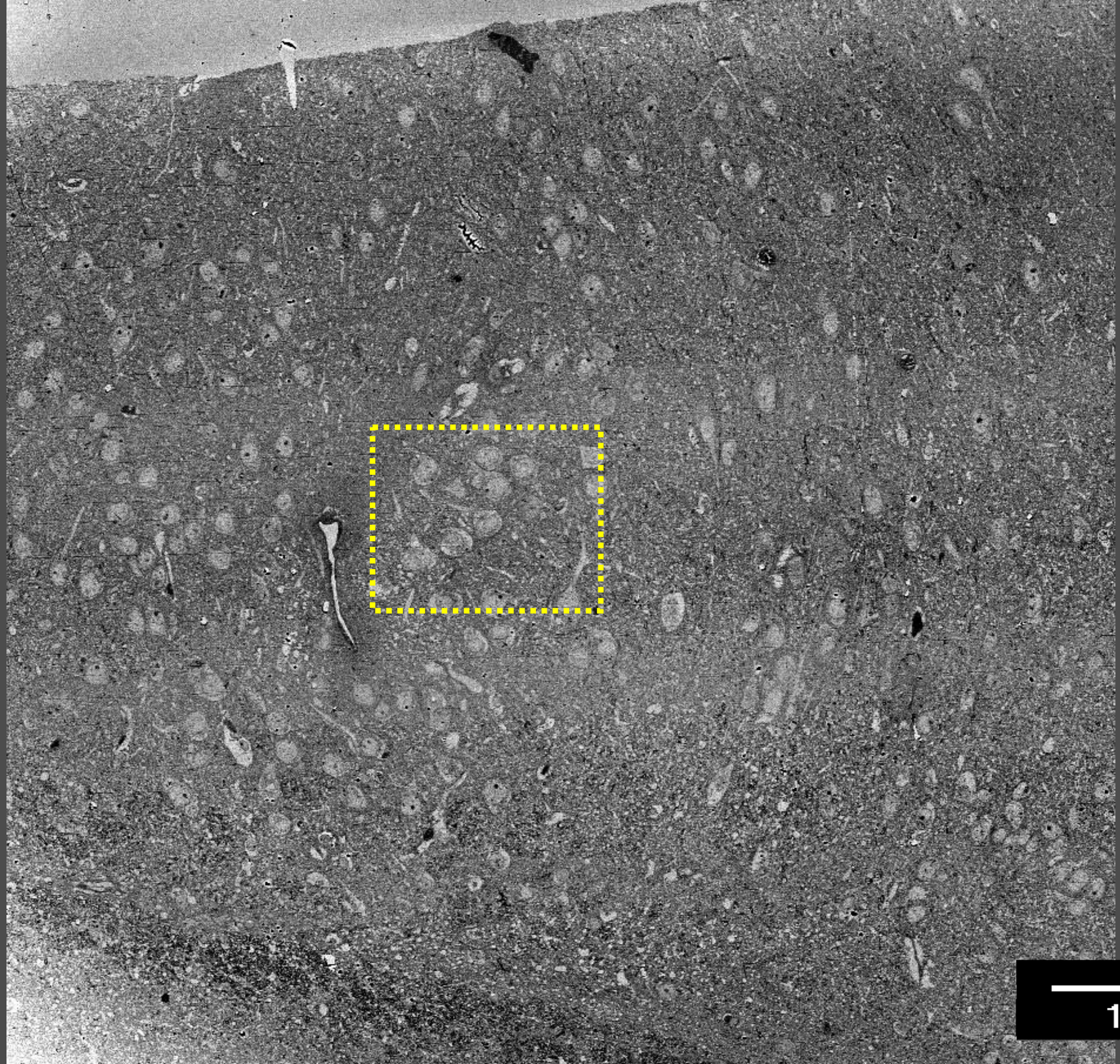
Licensed and commercialize

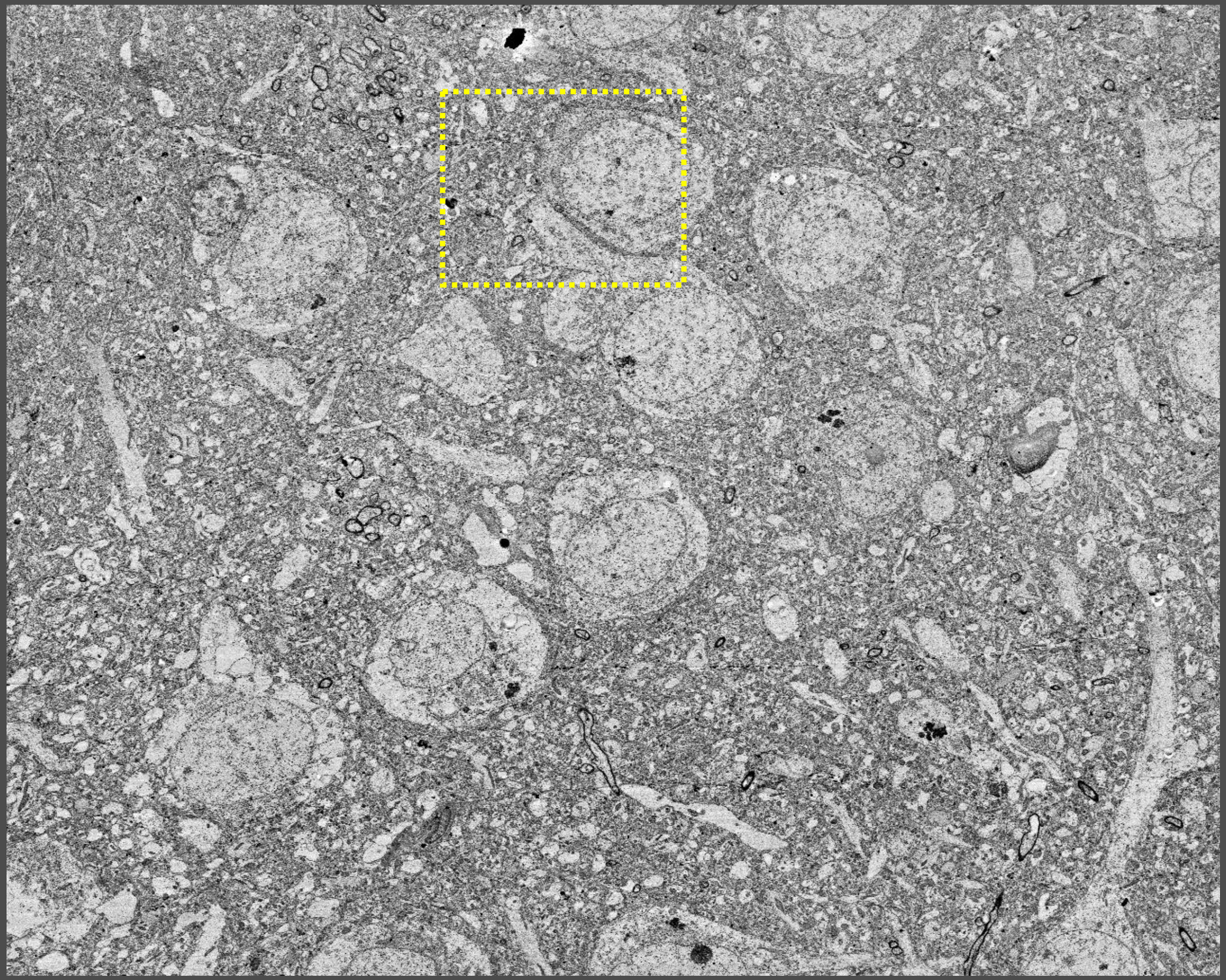


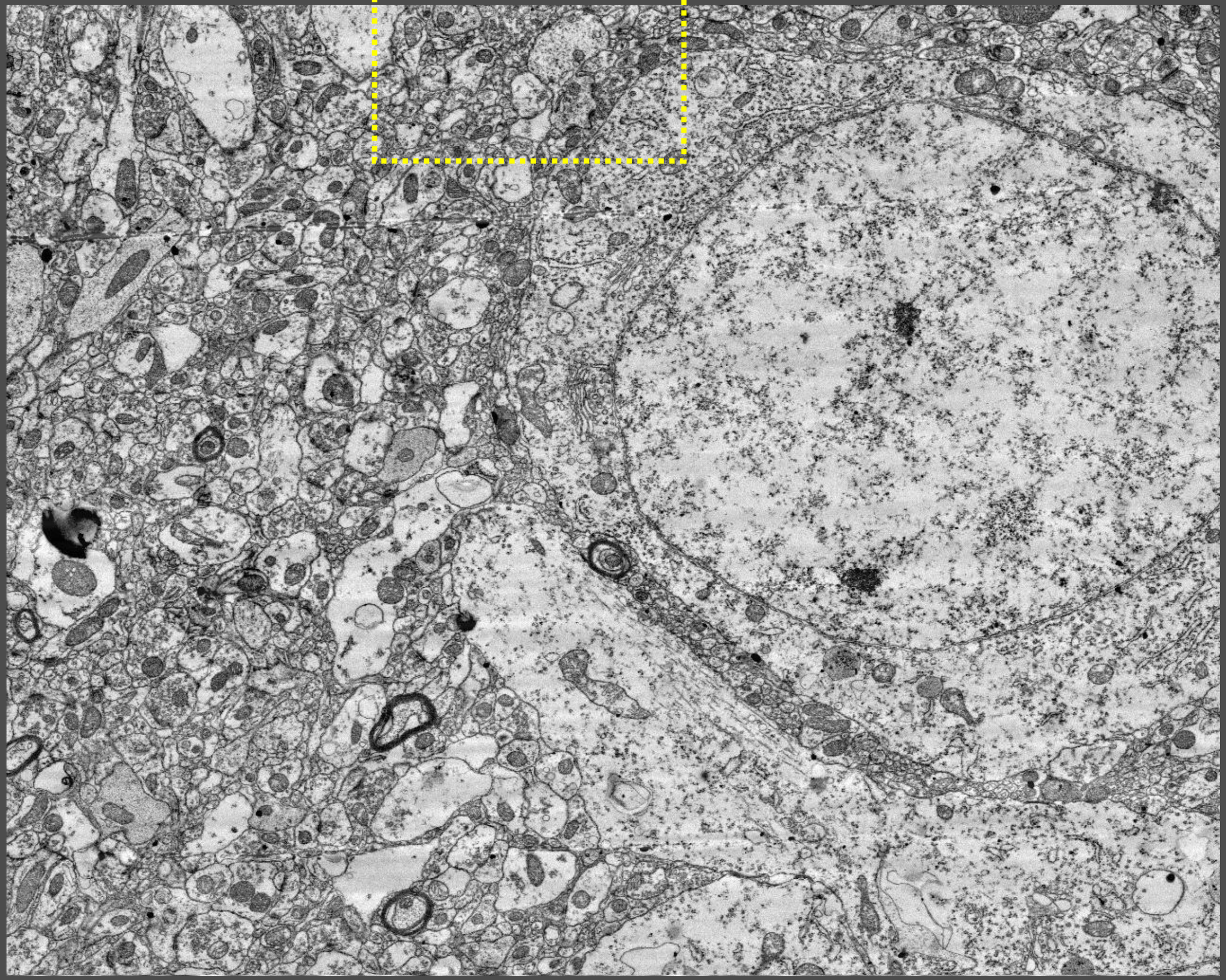

Tape with sections
Cut into strips
and attached
to 6” wafer

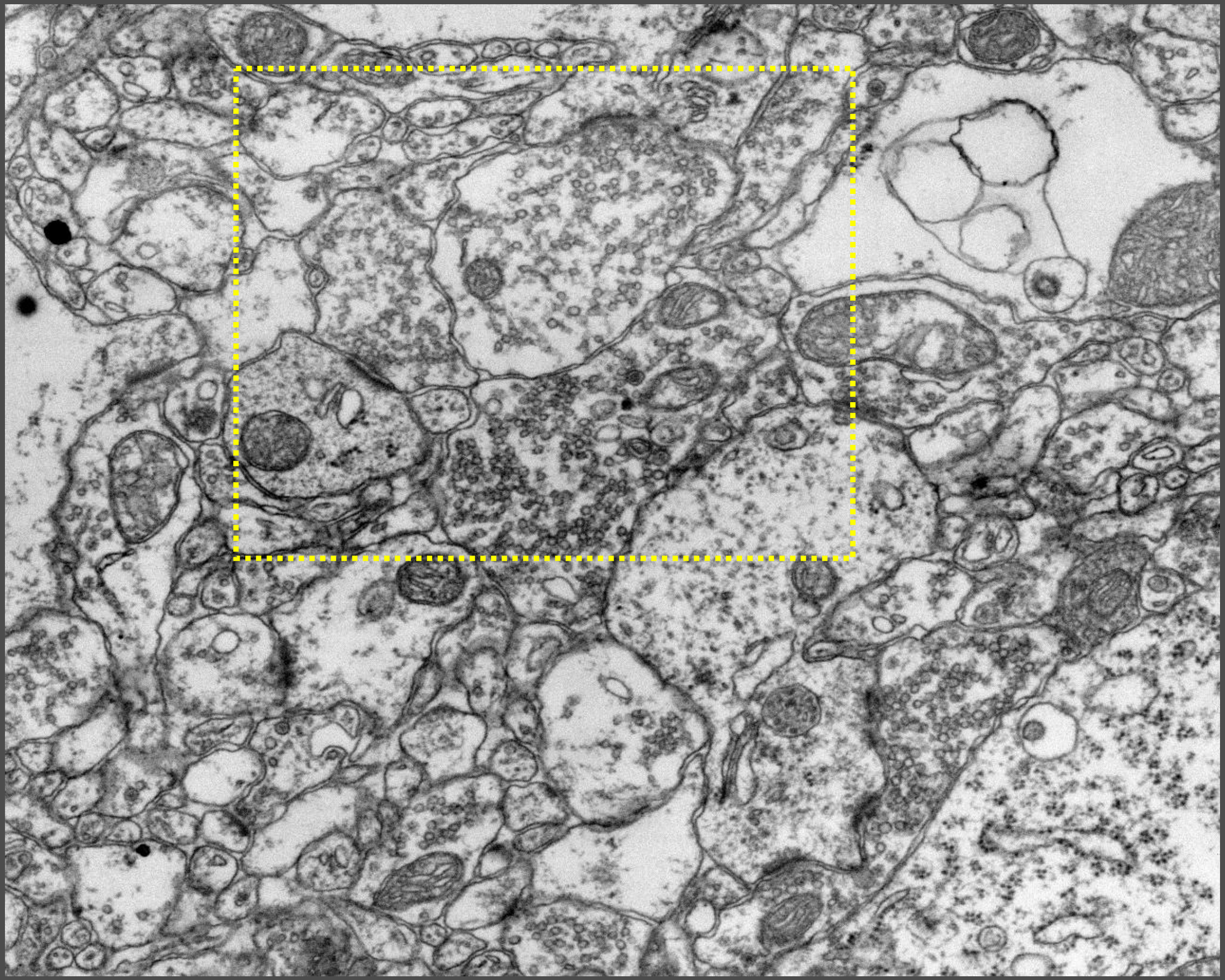


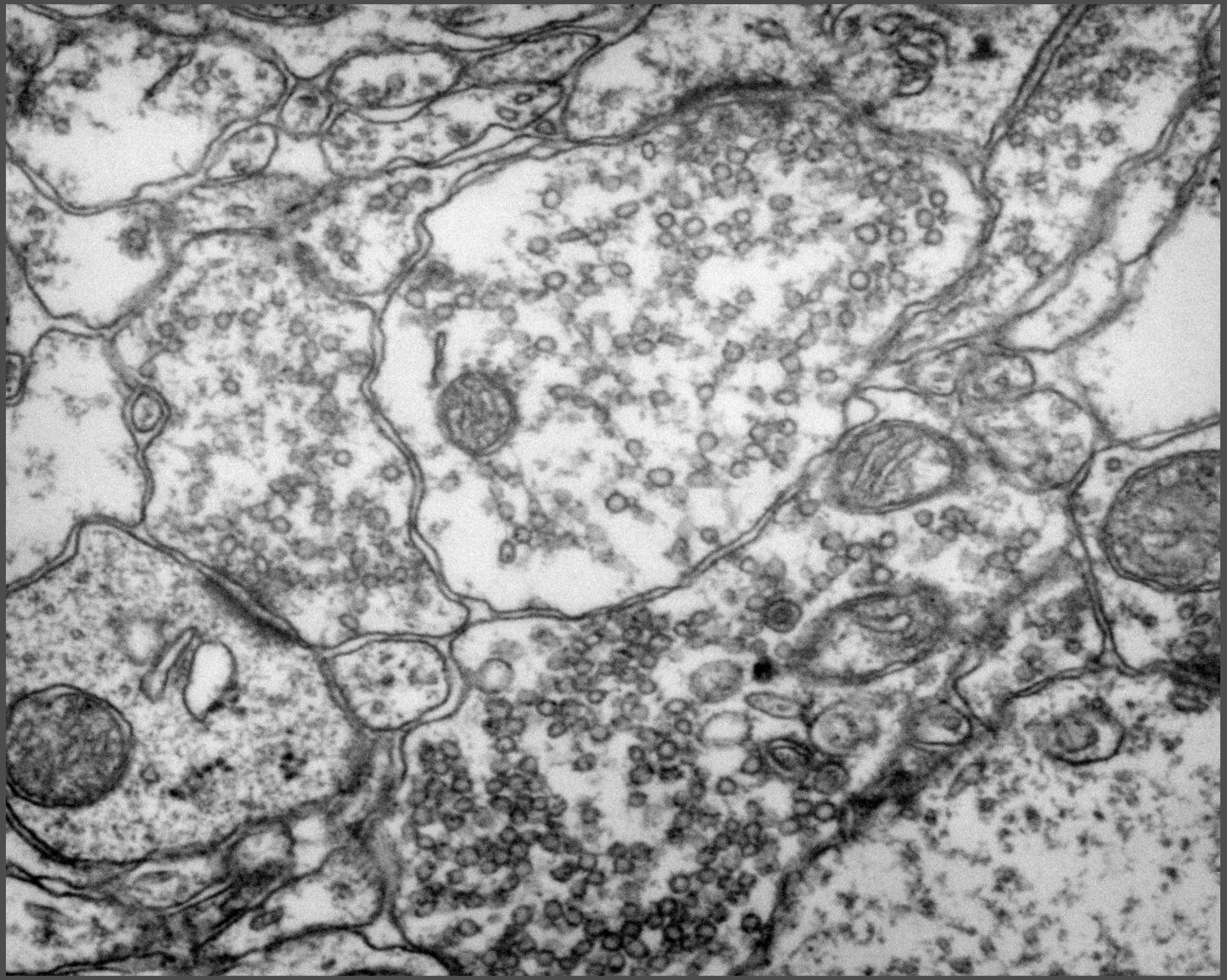

ZEISS
ΣIGMA | HD
ZEISS

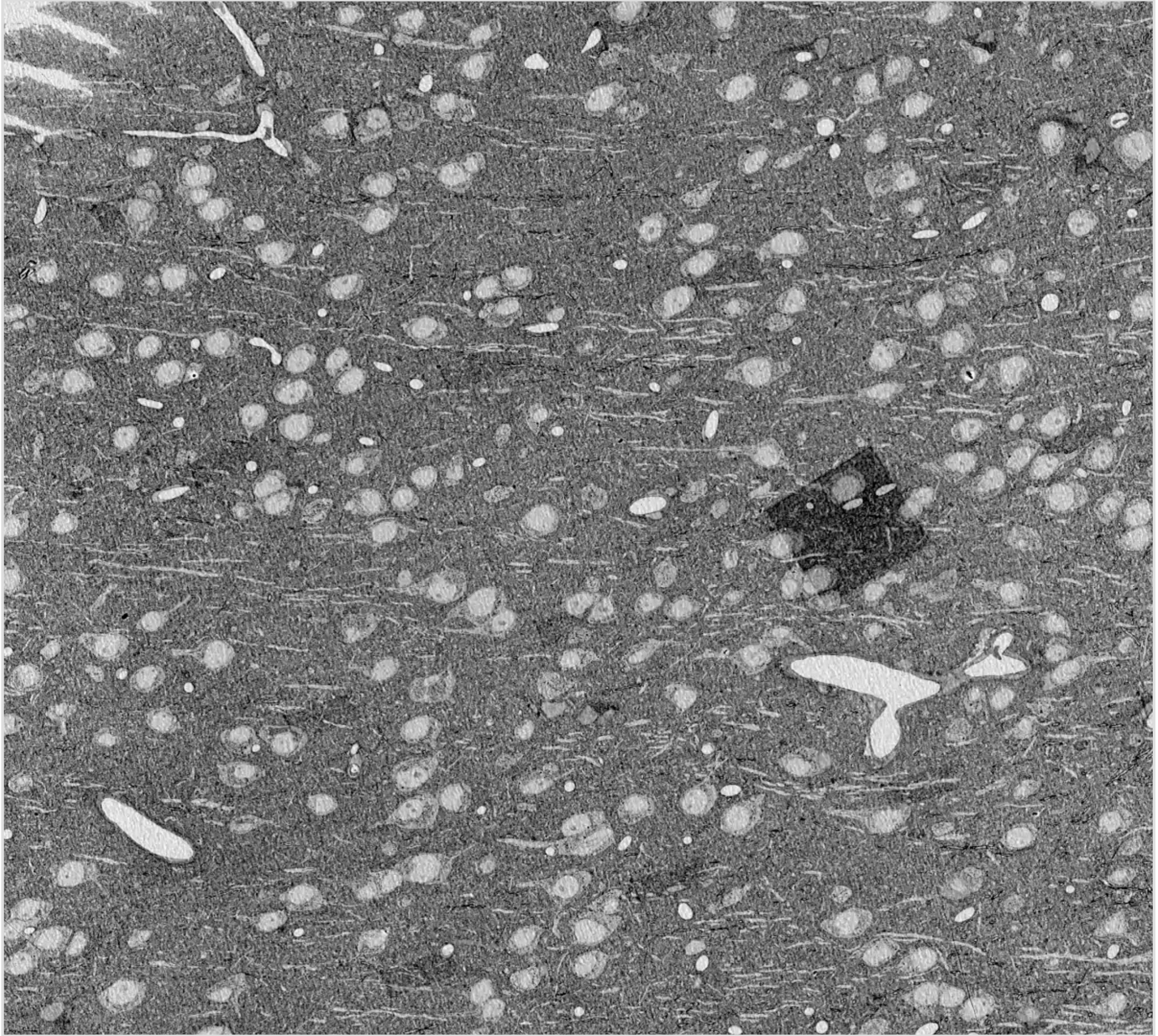

100μm

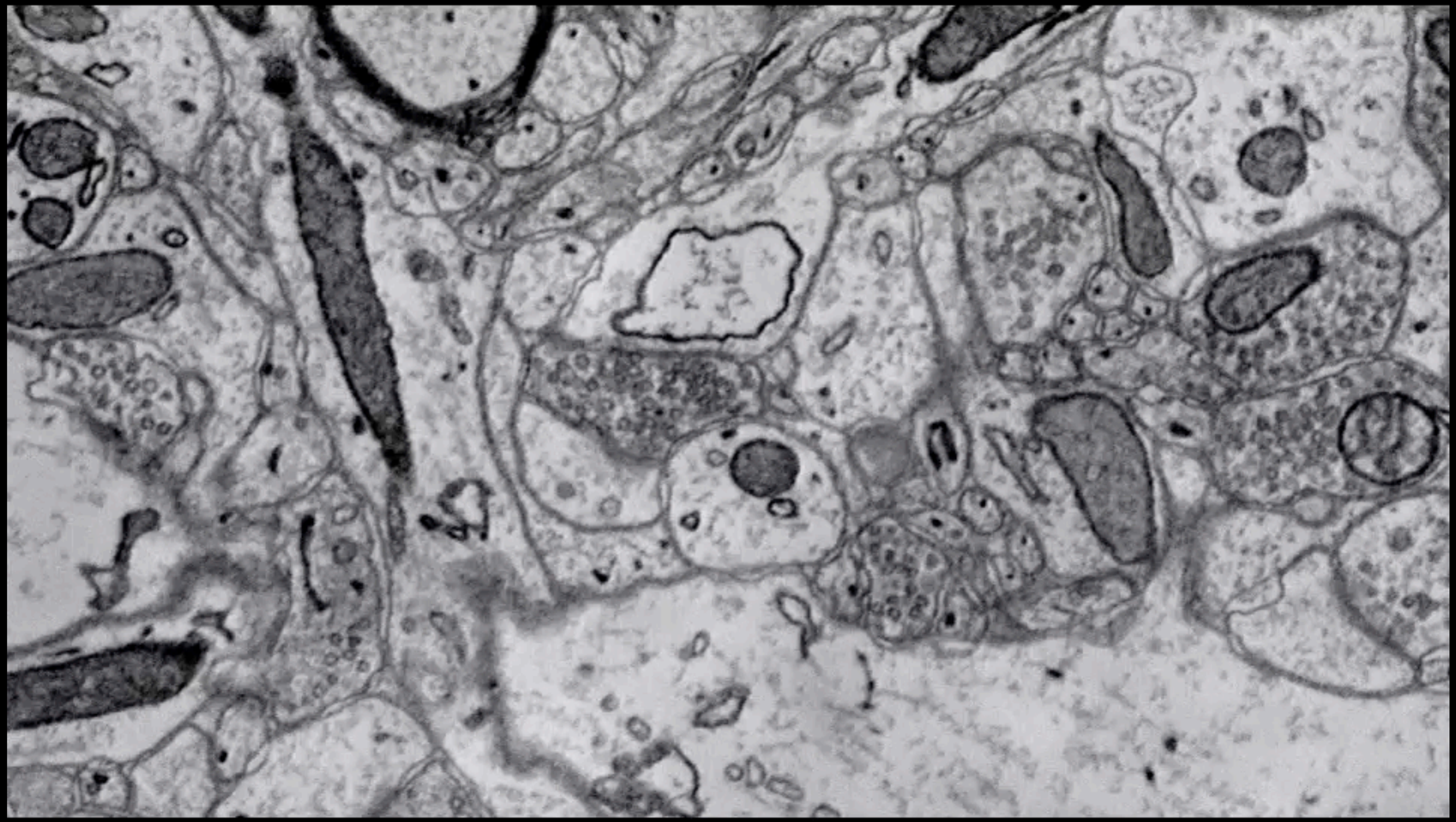


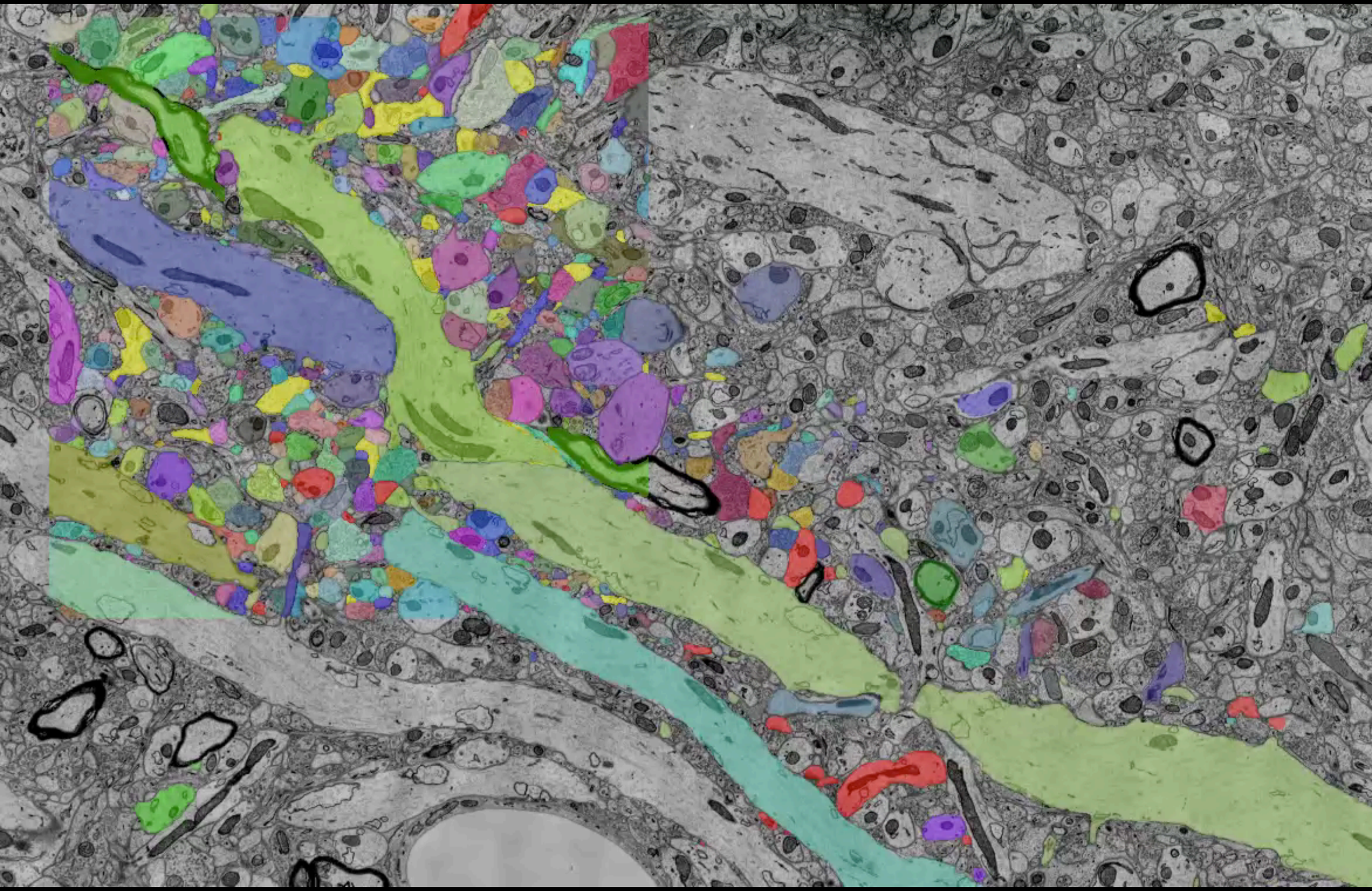


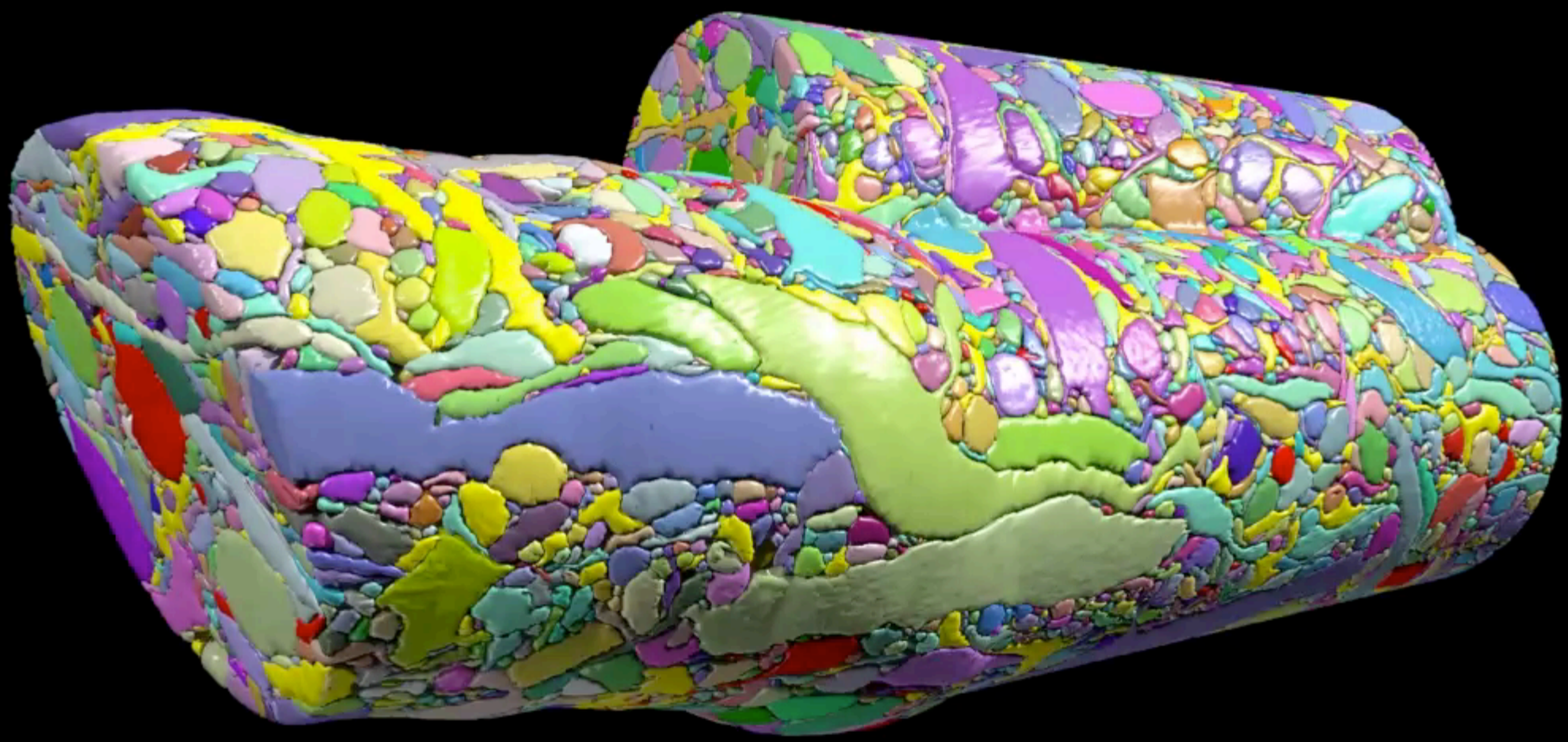












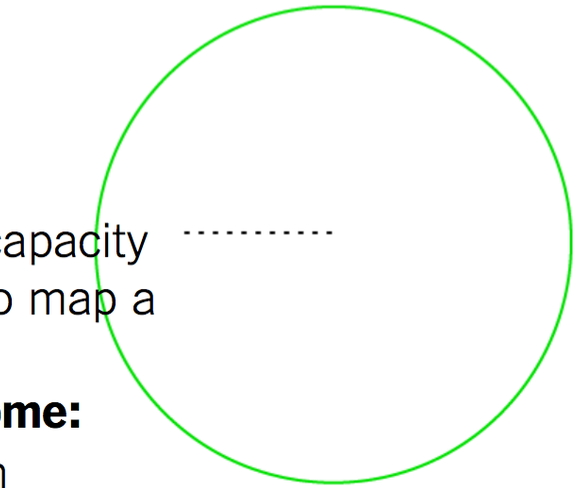
Kasthuri, et. al. 2015

Visualizing the brain at the level of the connectome would consume nearly half the world's current digital storage capacity.

Storage capacity **needed to map a mouse connectome:** 450,000 terabytes

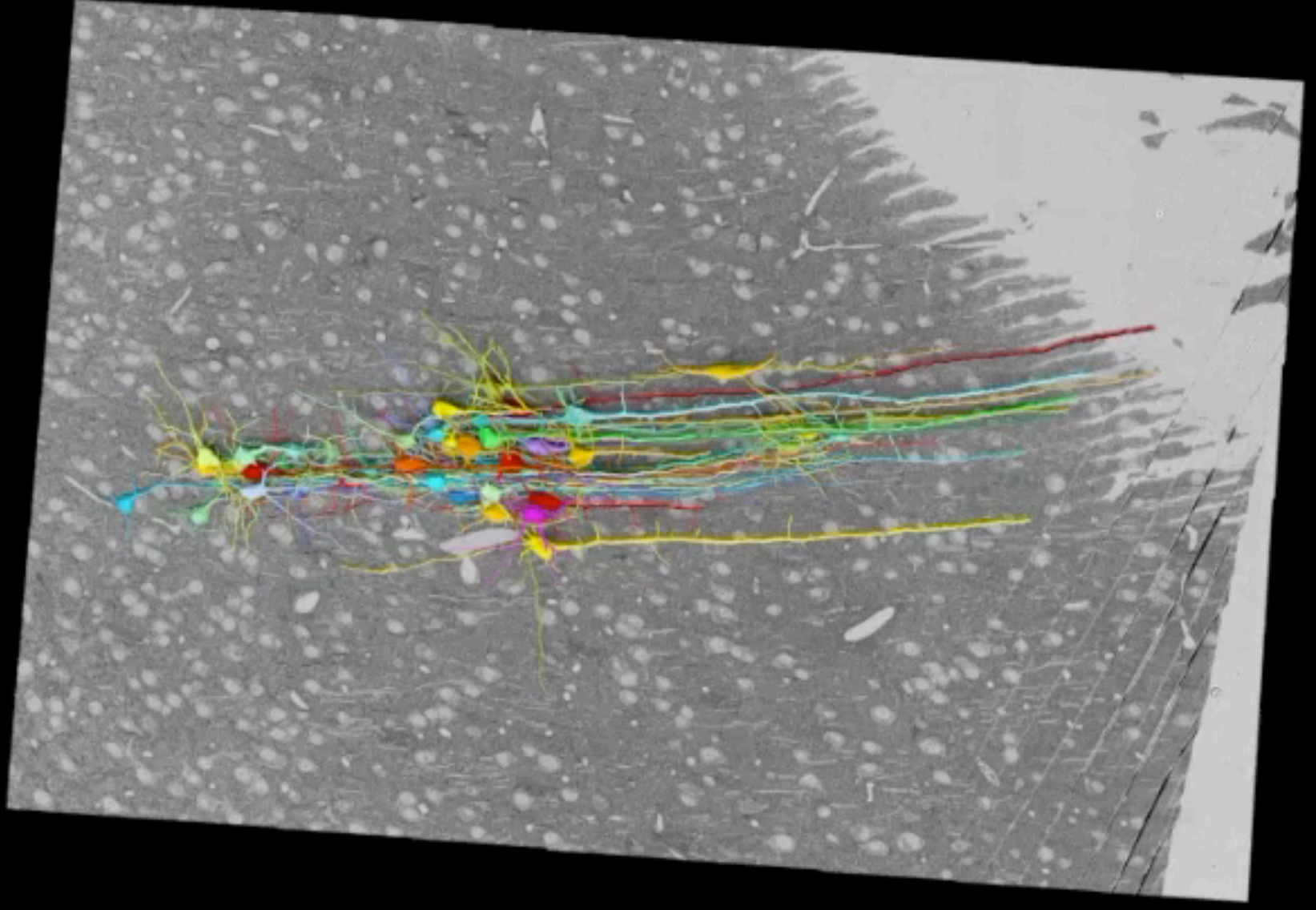
Storage capacity needed to map a **human connectome:** 1.3 billion terabytes

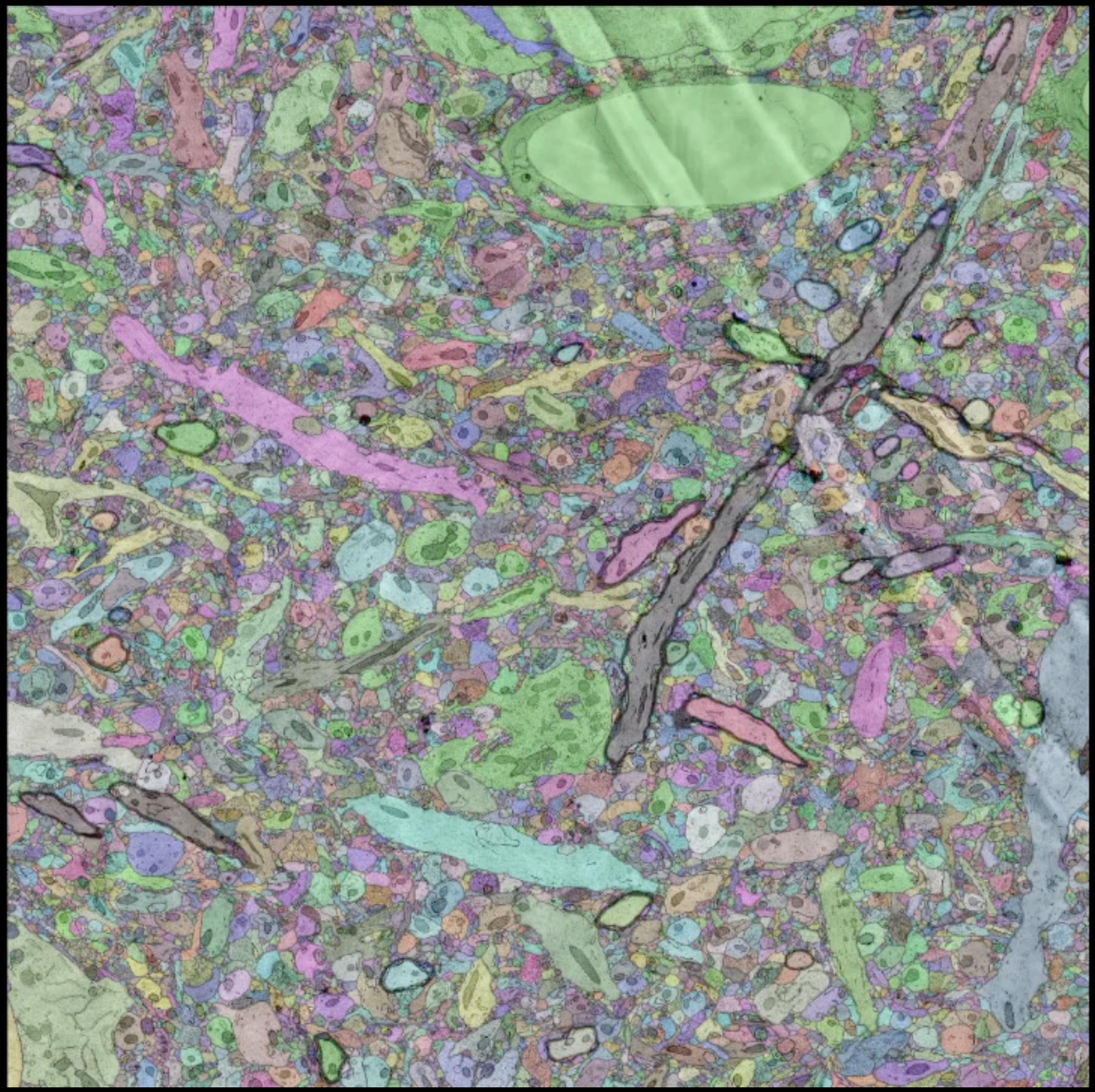
Global hard drive storage, 2014: 2.6 billion terabytes



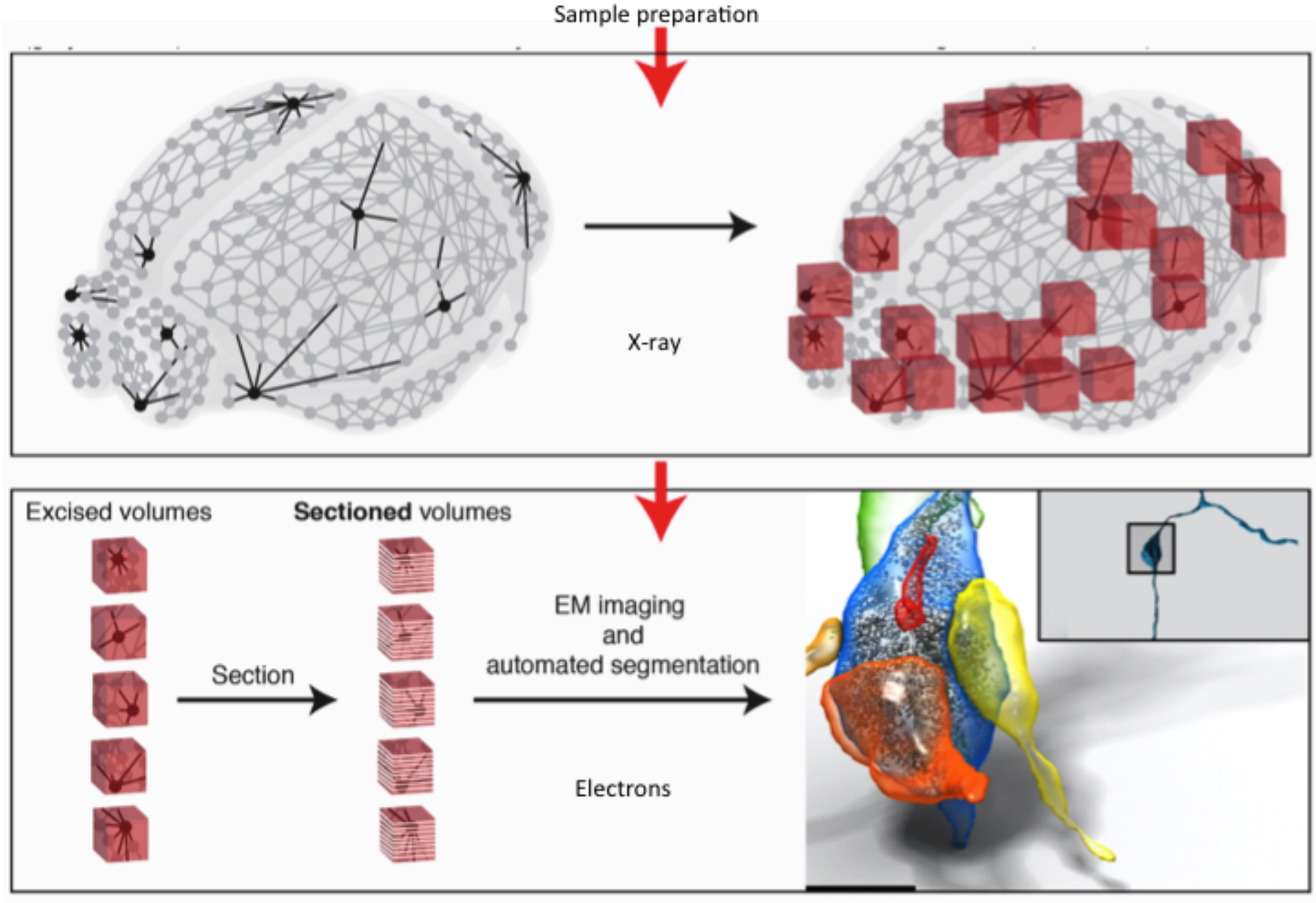
Source: Bobby Kasthuri, International Data Corporation (global hard drives)

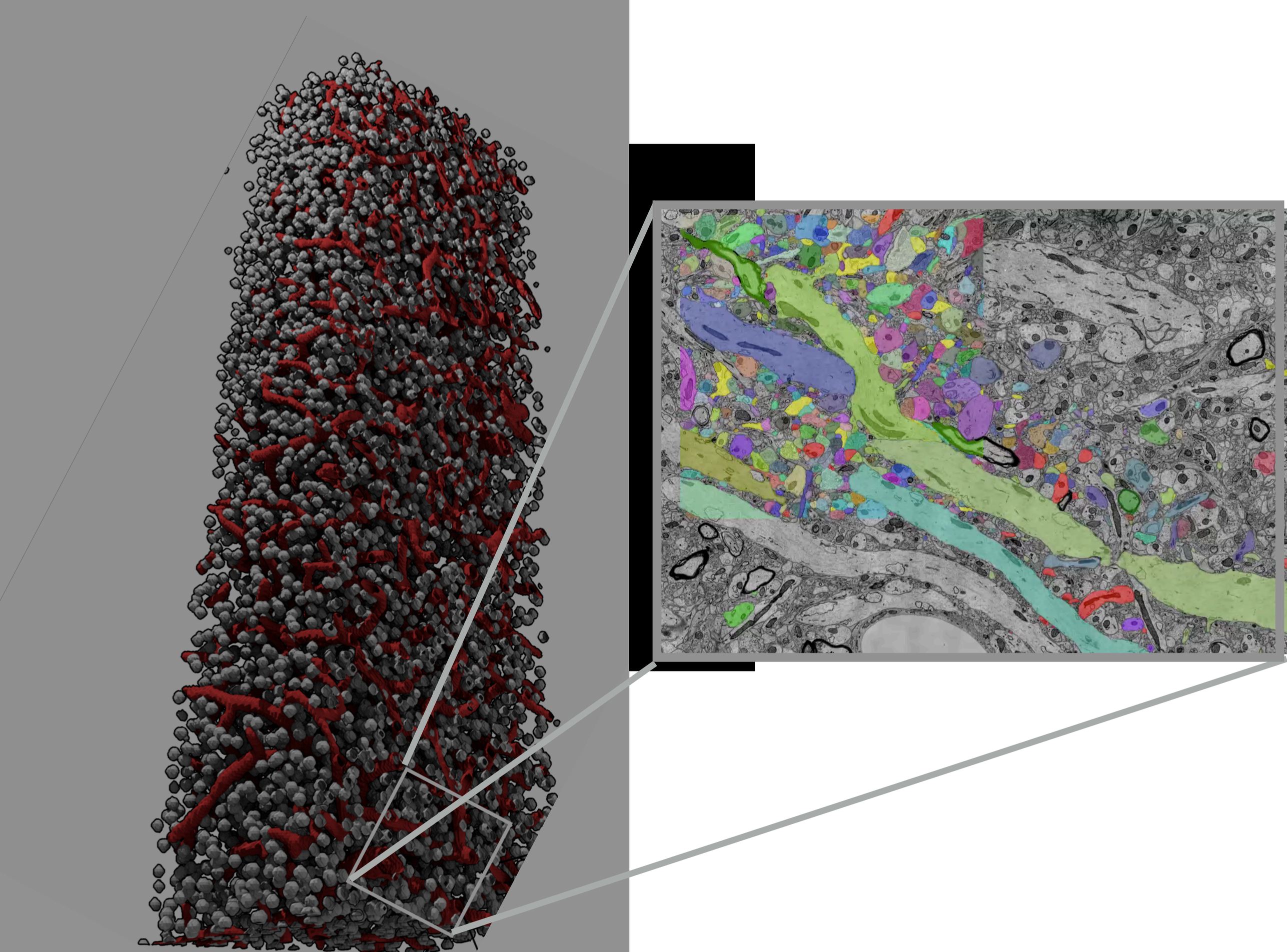
By The New York Times





XEM


Sample preparation
X-ray
Excised volumes
Sectioned volumes
Section
EM imaging
and
automated segmentation
Electrons



We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win.

But why, some say, the Moon? Why choose this as our goal? And they may well ask, why climb the highest mountain? Why, 35 years ago, fly the Atlantic? Why does Rice play Texas?

JFK, Rice University, ~1962

IARPA, NIH, NSF, McKnight Foundation, Argonne LDRD