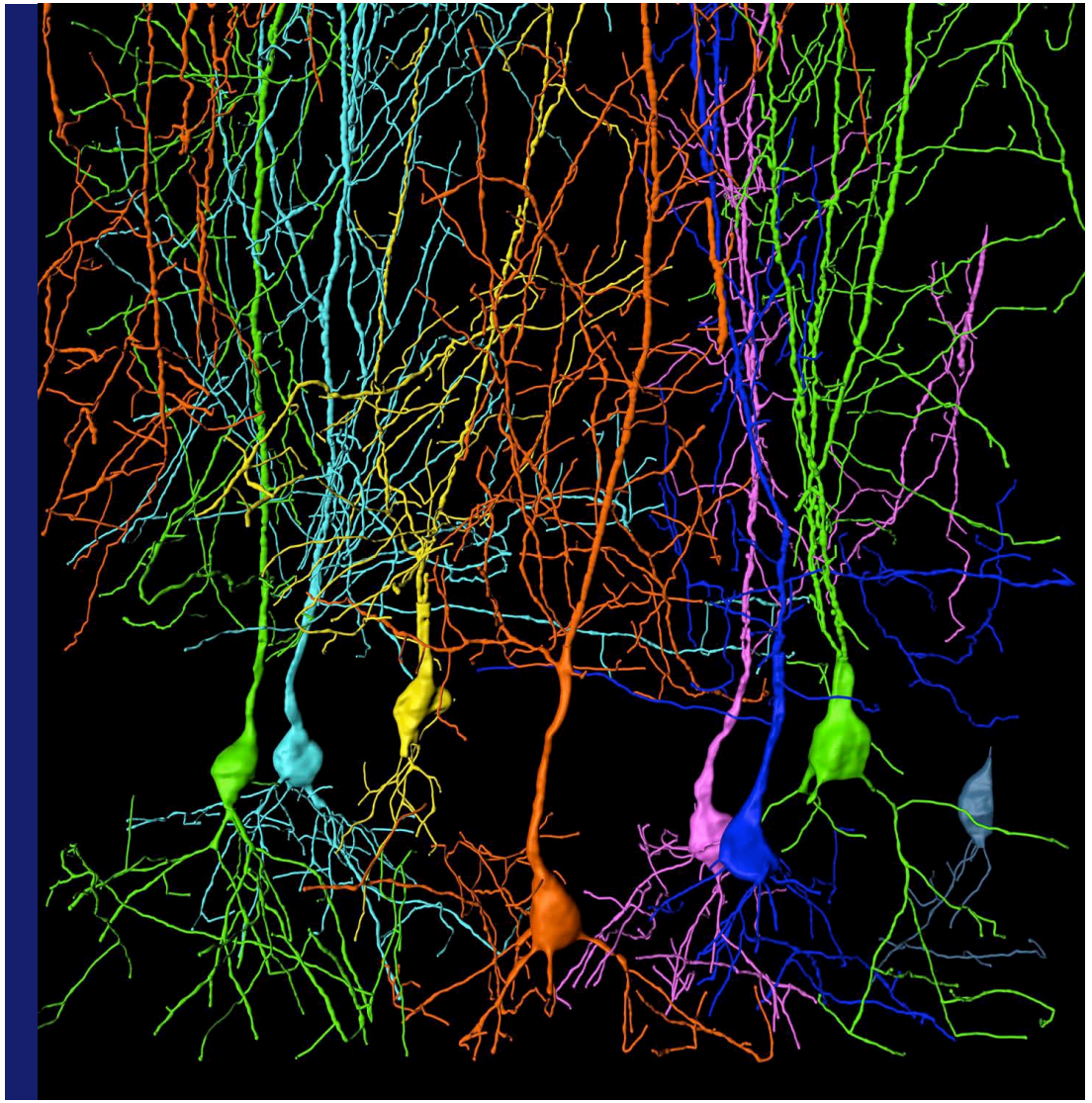


Multi-dimensional Image Analysis

IMARIS

Introduction and Applications

April Hu

Sales Engineer

April.hu@andor.com

Our History

1950s – 1970s | 1980s | 1990s | 2000s | 2020

Foundations

Founded 1959: Oxford Instruments is the first commercial spinout from Oxford University

Oxford Instruments develops the world's first superconducting magnet

World Firsts

1980: Oxford Instruments delivers the world's first MRI system

1983: Floated on the London Stock Exchange

Expansion

The Group expands its global presence opening offices in Japan and China

Broadens portfolio across Semiconductor processing, Analytical Techniques & Medical instrumentation

Acceleration

Nanotechnology Tools strategy & focus drives growth

2016: Horizon Strategy

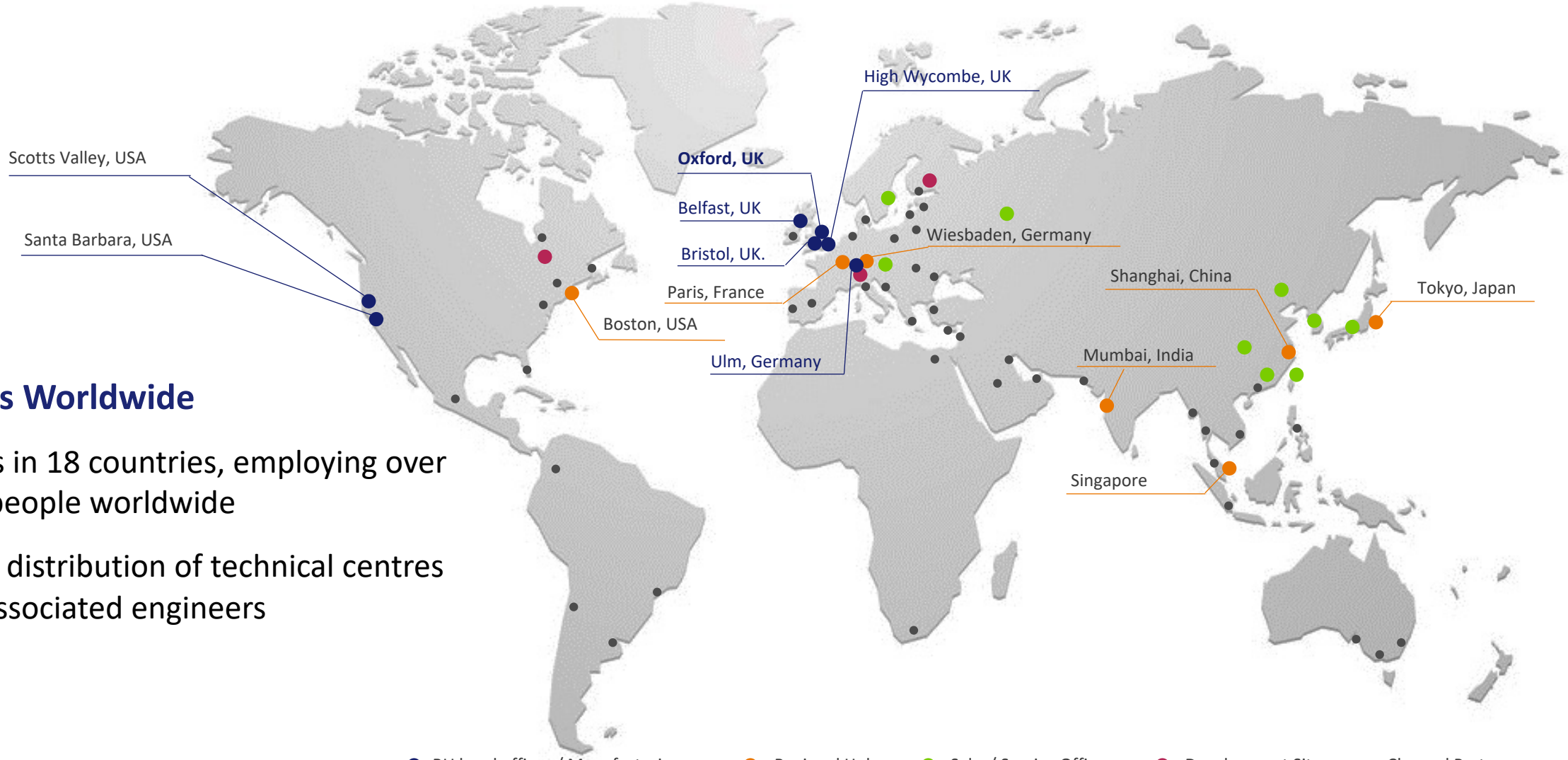
Our core purpose is to support our customers in addressing some of the world's most pressing challenges:

- enabling a greener economy
- increased connectivity
- improved health
- leaps in scientific understanding.

We are a leading provider of high technology products and services to the world's foremost industrial companies and scientific research communities to image, analyse, and manipulate materials down to the atomic and molecular level.

We focus on attractive segments were our key enabling technologies drive long-term growth for customers and where we can maintain leadership positions.

Global Footprint



28 Offices Worldwide

- Offices in 18 countries, employing over 1600 people worldwide
- Global distribution of technical centres with associated engineers

牛津仪器ANDOR发展历程

OXFORD INSTRUMENTS | IMARIS

弱光探测、解析及成像系统

全球制造领跑者

ANDOR

SINCE

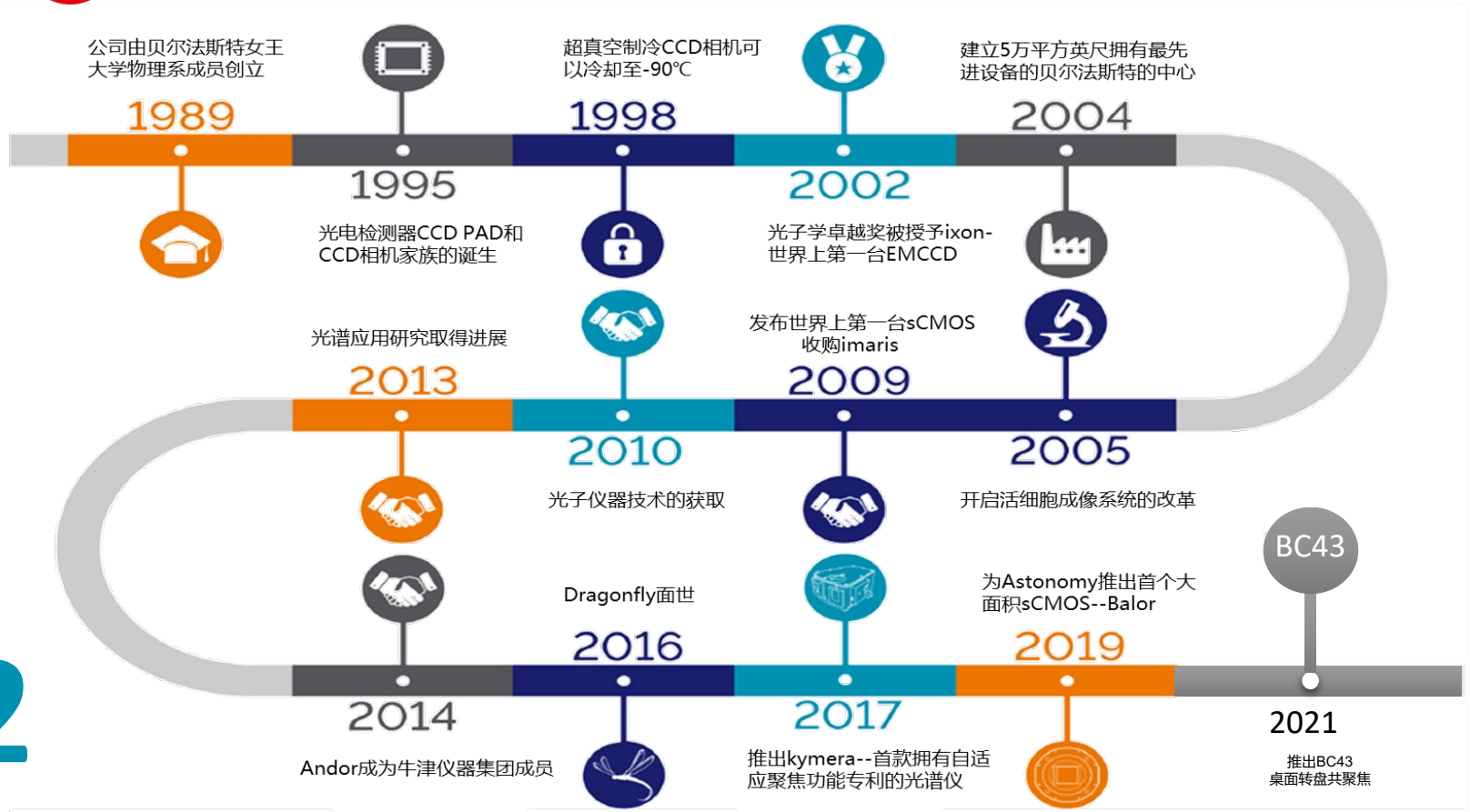
1989

IMARIS

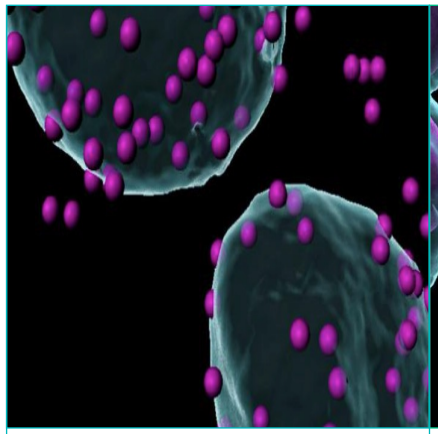
SINCE

1992

QUEEN'S UNIVERSITY BELFAST

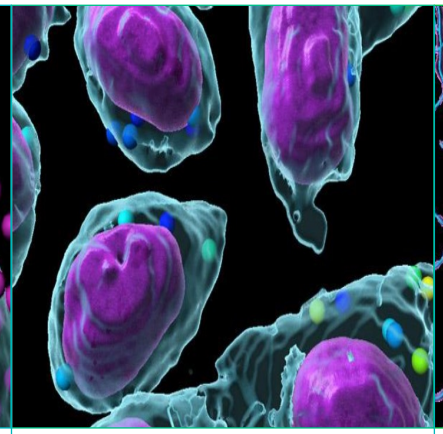


Quantitative Image Analysis for 3D Microscopy



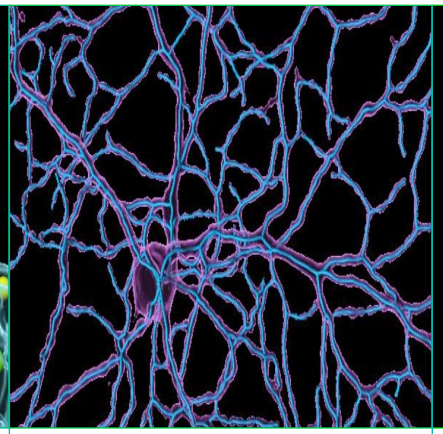
Quantification

- Count of objects
- Area
- Volume
- Intensity
- Position



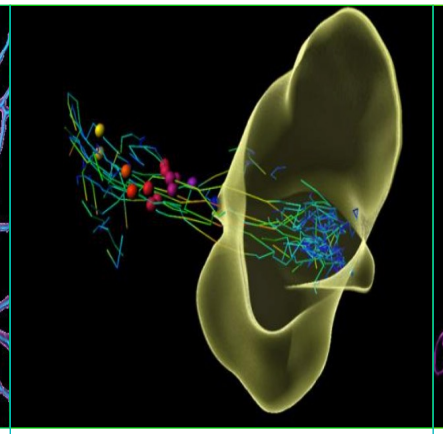
Cell

- Volume
- Vesicles per Cell
- Distance to Membrane
- Vesicles per Nucleus
- Morphology



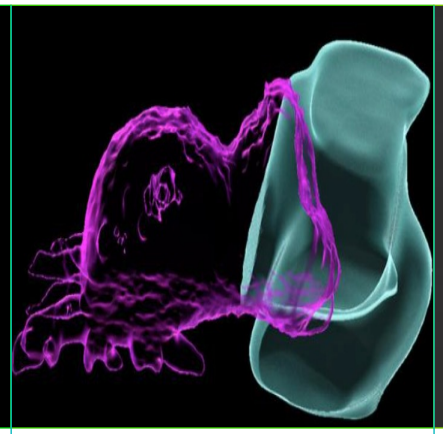
Filaments/Neurons

- Length, Straightness
- Mean Diameter
- Branching Angle
- Spine Density
- Spine Shape



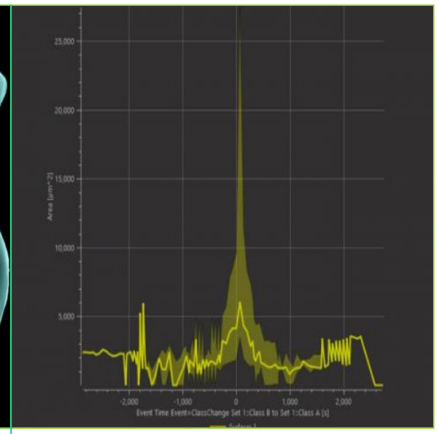
Motion Analysis

- Speed
- Acceleration
- Cell division tracking
- Trajectory
- Event synchronization



Interactions

- Distances between structures
- Volume overlap, contacts
- 3D intensity profiling
- Spatial distribution
- Co-localization

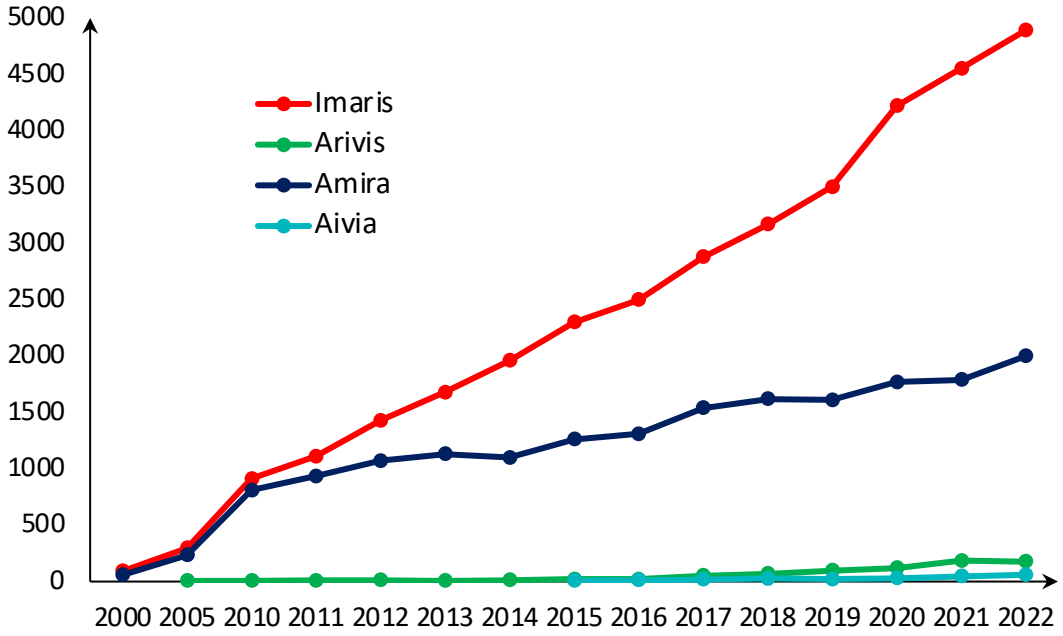


Batch and Plots

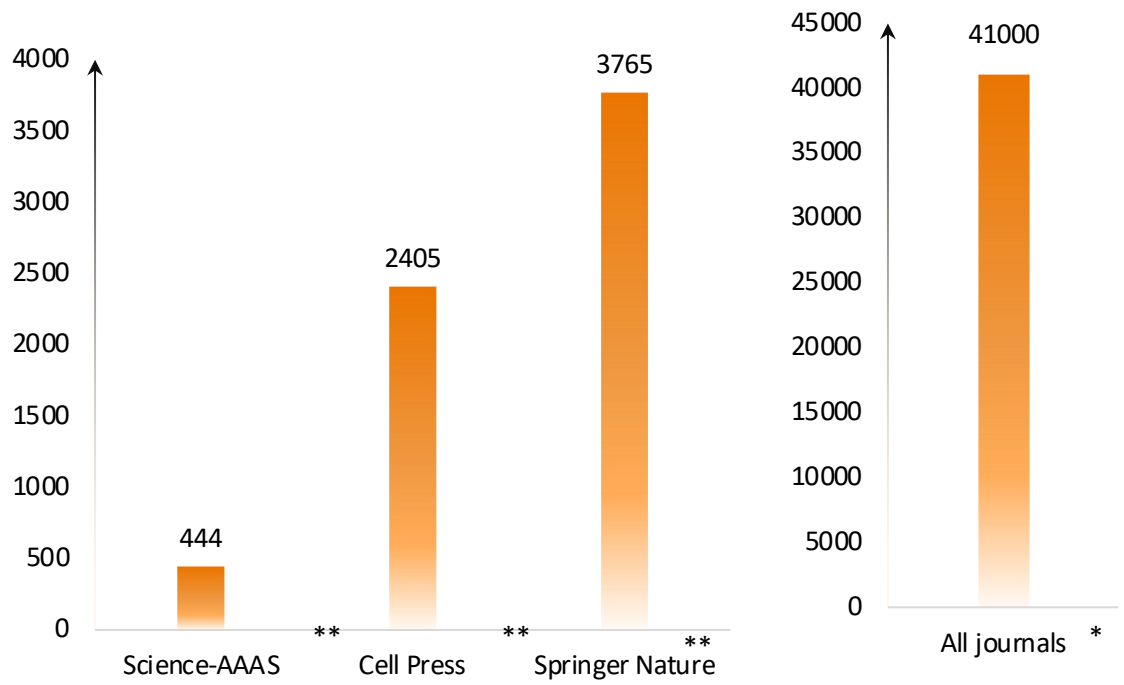
- Image processing
- Measurements
- Interactions
- Group comparisons
- Statistical tests

IMARIS in Publications

IMARIS and competitors' usage in publications overtime* (2000 to 2022)



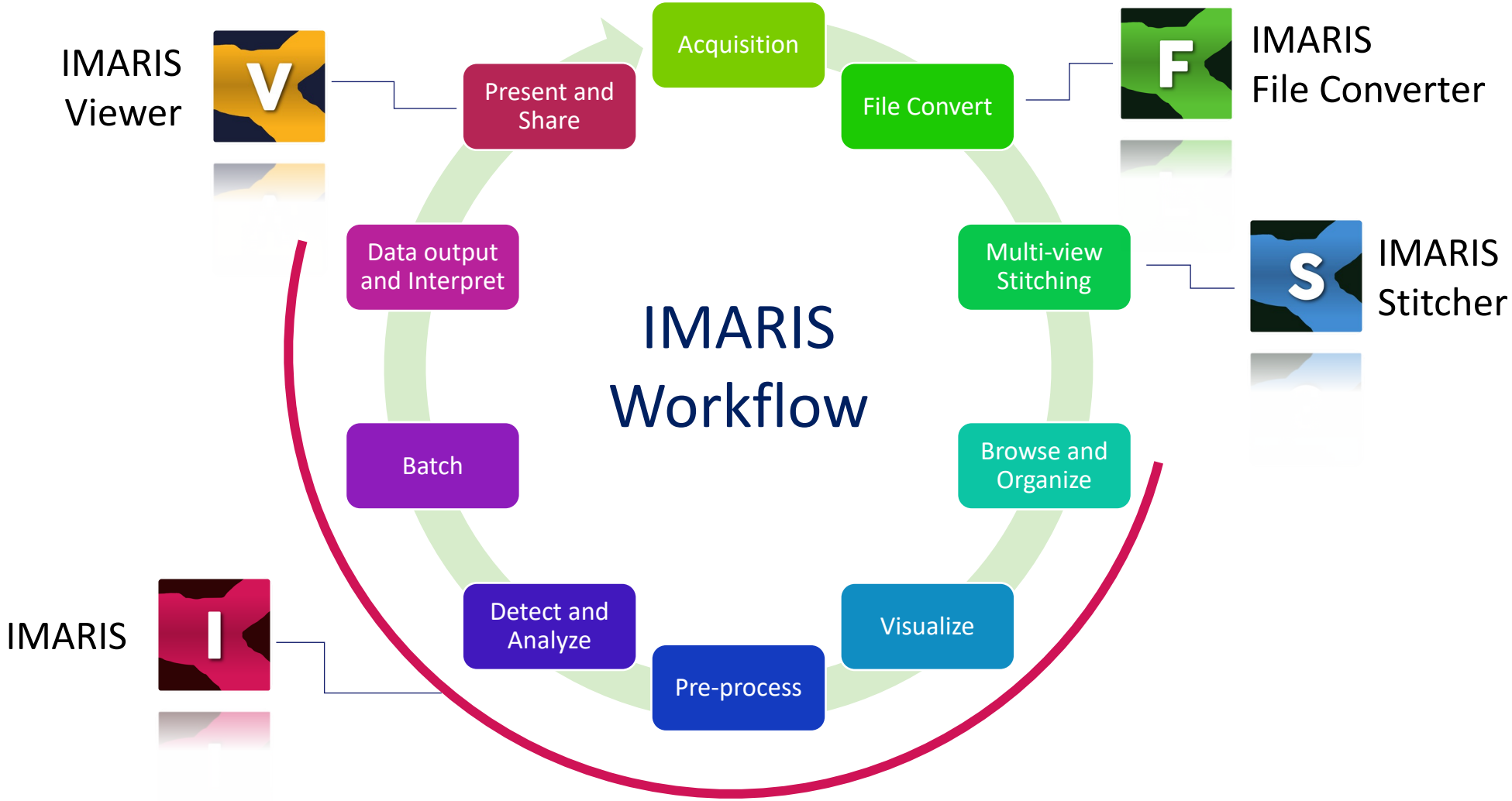
IMARIS usage in publications (2000 to 2023 April)



*Data acquired from Google Scholar

**Data acquired from journal official sites, respectively.

Workflow of image analyzing and processing



IMARIS Microscopy Imaging Software

IMARIS
File Converter

IMARIS
Stitcher

IMARIS

IMARIS
Viewer

IMARIS Microscopy Imaging Software

IMARIS
File Converter

IMARIS File Converter's redesigned GUI and batch conversion efficiently convert multiple large datasets to save you time.

- Conversion is multithreaded (number of cores selected by the user).
- Files dropped to conversion queue and processed with one click.
- Memory allocation increased to handle big data.
- IMARIS Convert Bio-formats.

IMARIS Microscopy Imaging Software

IMARIS
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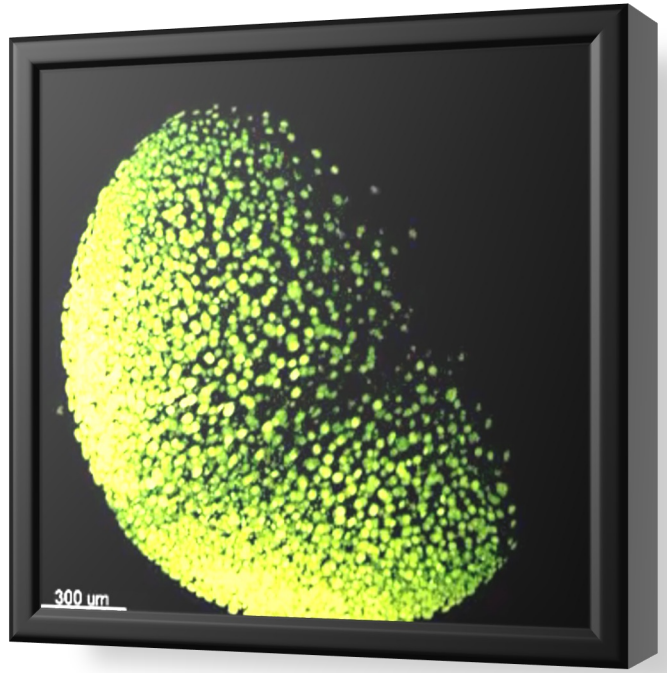
- Memory allocation increased to handle big data.
- IMARIS Convert Bio-formats. New

Data Compatibility Versatile File Formats and Big Data

OXFORD INSTRUMENTS IMARIS

ANDOR
an Oxford Instruments company
OLYMPUS
PerkinElmer
Nikon
ZEISS
Leica MICROSYSTEMS
OME
3i
GATAN
TIFF
DICOM etc...

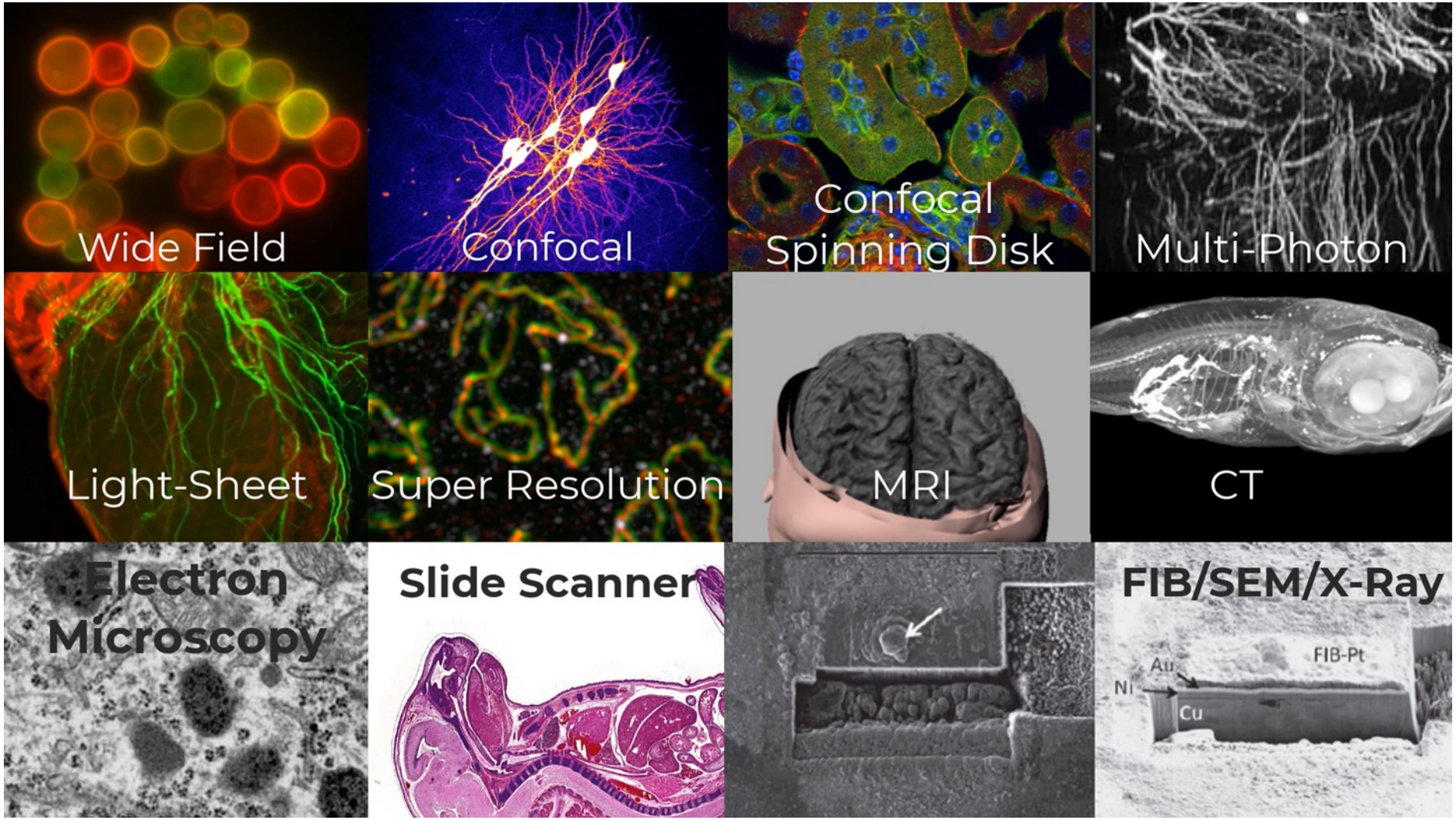
IMARIS
File Converter
+
Bio-Formats
(IMARIS 9.9)
New



Developing Zebrafish Embryo: 1.05TB tiff => 291GB *.ims

Courtesy of K. McDole, HHMI Jamelia Farm research Campus,
Ref: Amat *et al.*, 2014, *Nature Methods*

Hardware Compatibility



IMARIS
File Converter

IMARIS Microscopy Imaging Software

IMARIS
File Converter

IMARIS
Stitcher

IMARIS

IMARIS
Viewer

What is IMARIS – An Overview

IMARIS File Converter

IMARIS Stitcher

IMARIS

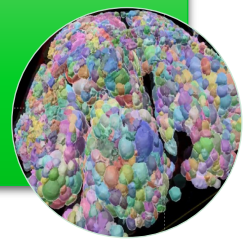
IMARIS Viewer

- Stitcher
- Multi-Modalities & Overlays
- Visualization Tools

Visualization

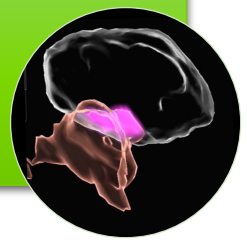
- Spots
- Surfaces
- Cell
- Filament
- Track

Object Detection Modules

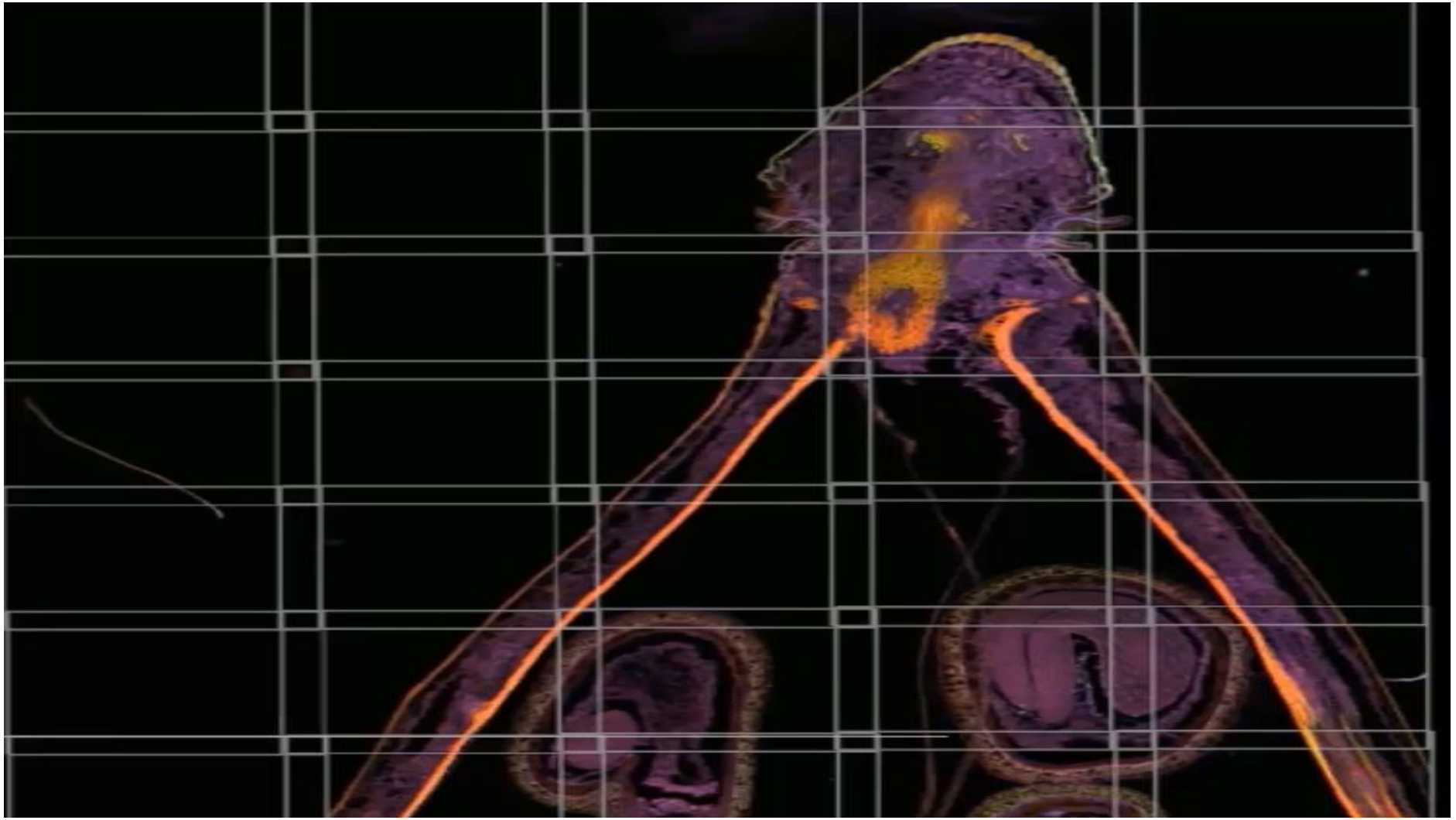


- Colocalization
- Classification
- Affinity
- XTension

Analysis

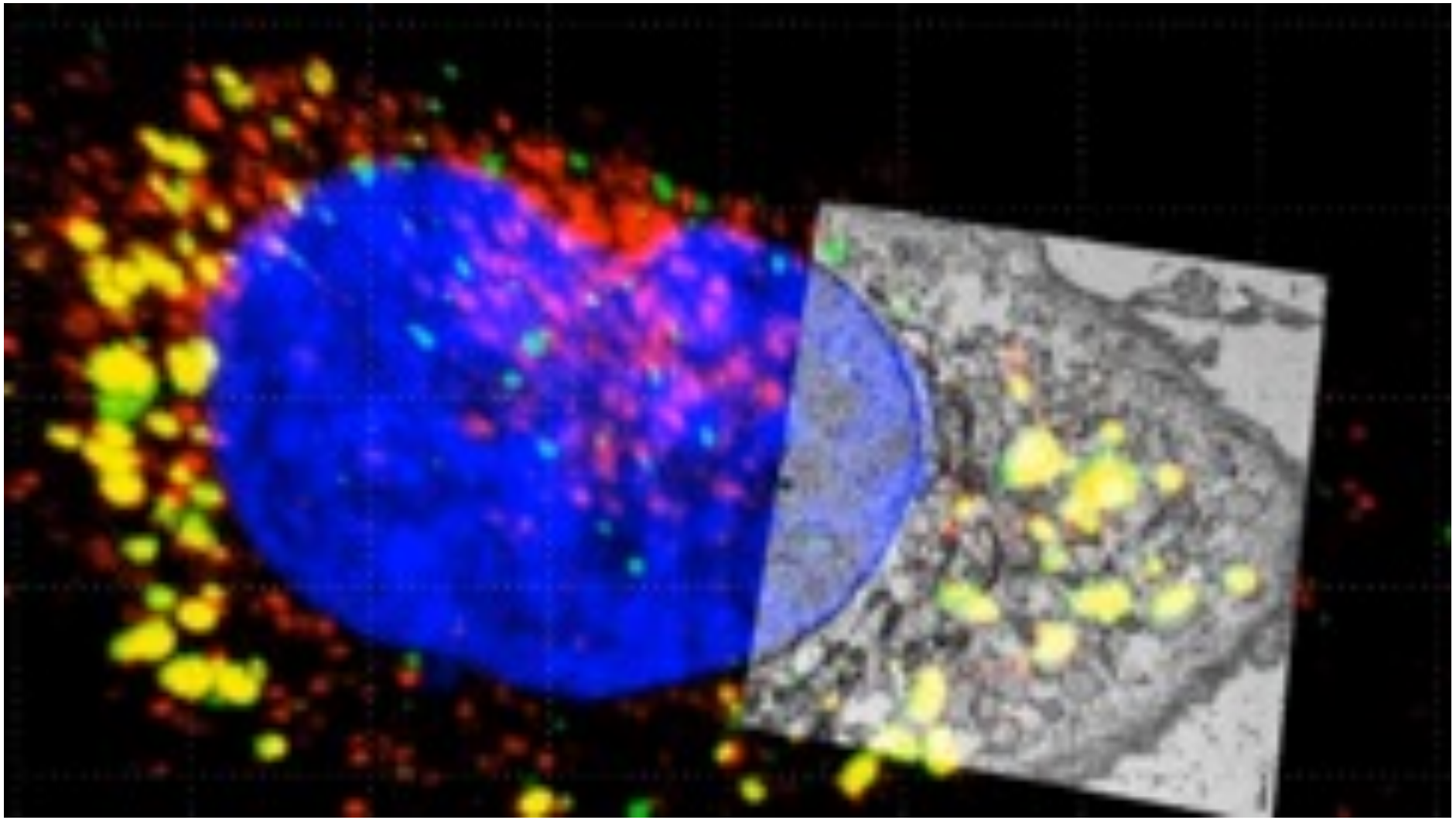


Stitcher Capable of Stitching Large 2D, 3D and 4D tiles



IMARIS
Stitcher

Visualize Multi-Modalities & Overlays

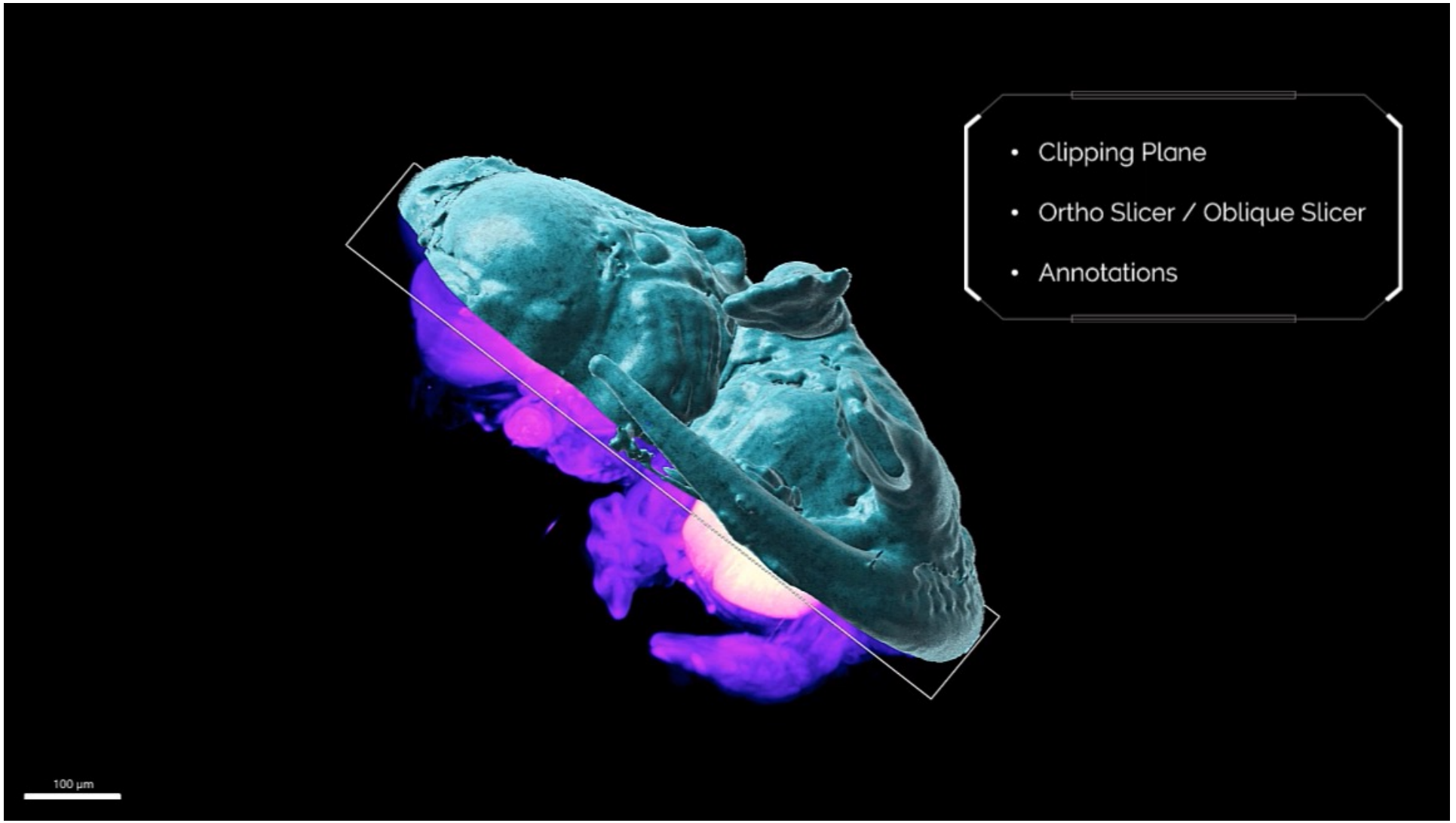


IMARIS

Visualize Visualization Tools

IMARIS

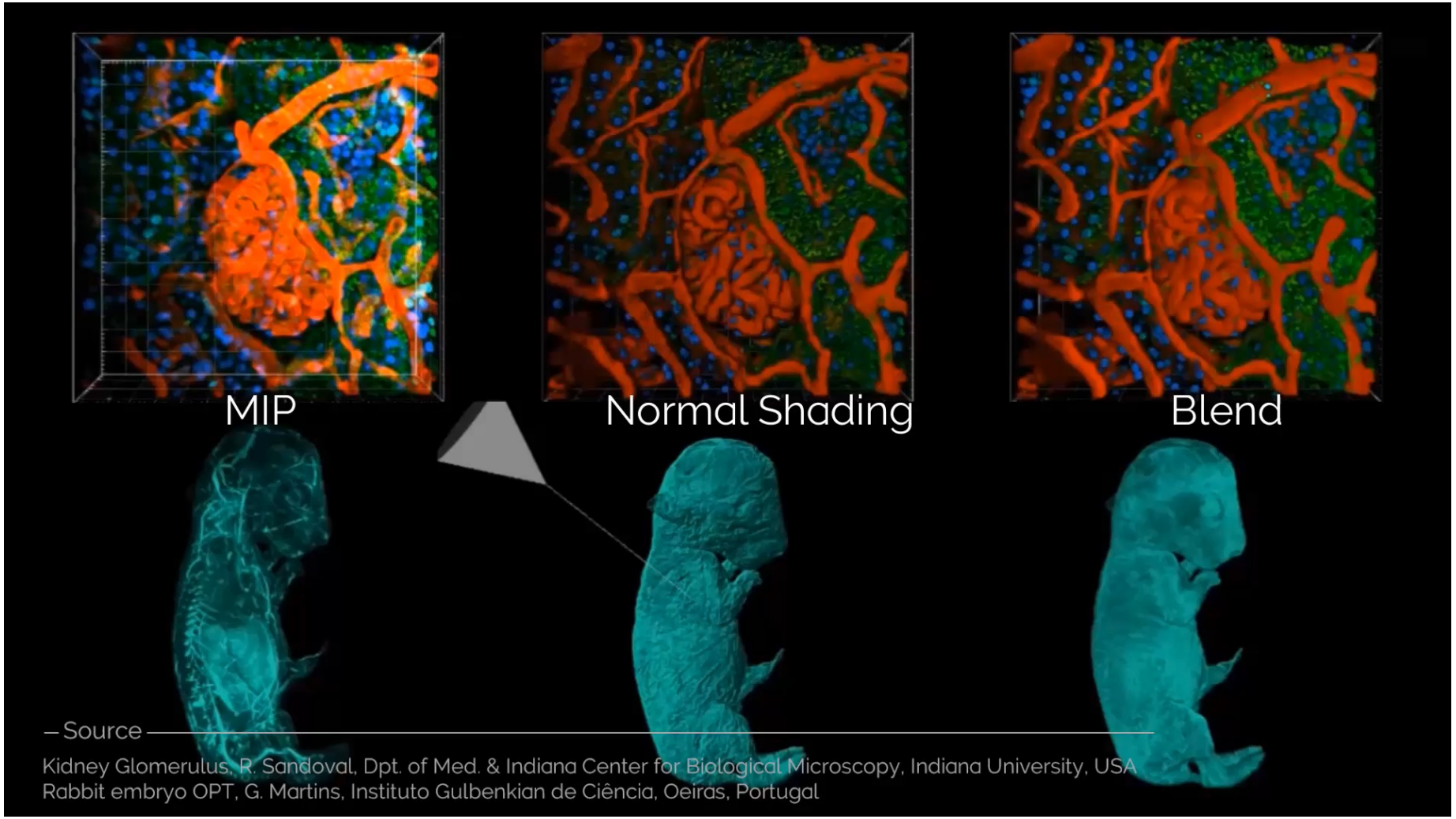
IMARIS Viewer



Visualize Rendering Modes

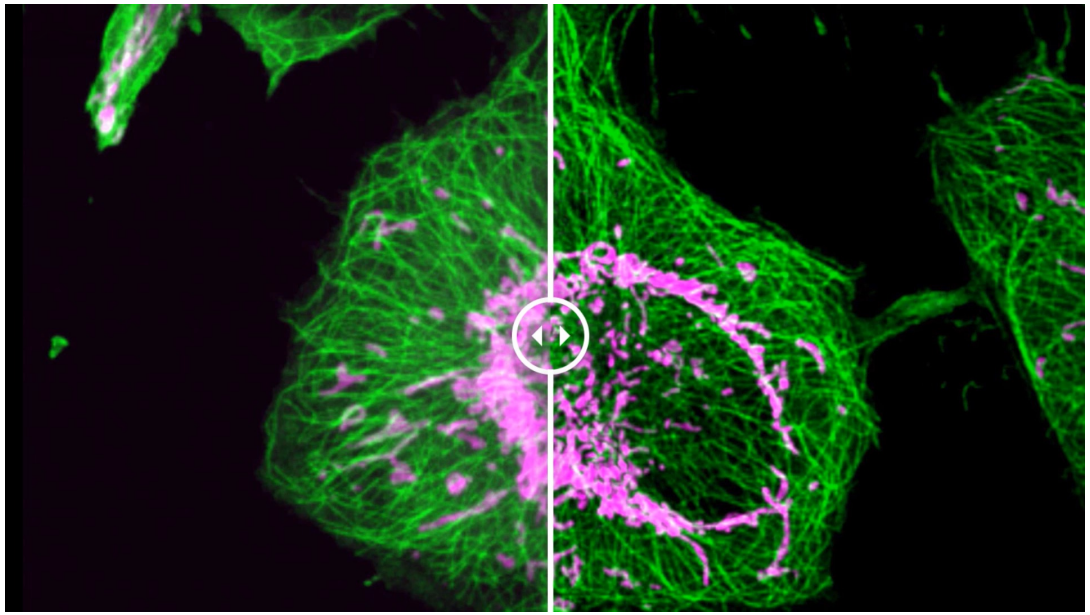
IMARIS

IMARIS Viewer



IMARIS

Deconvolution



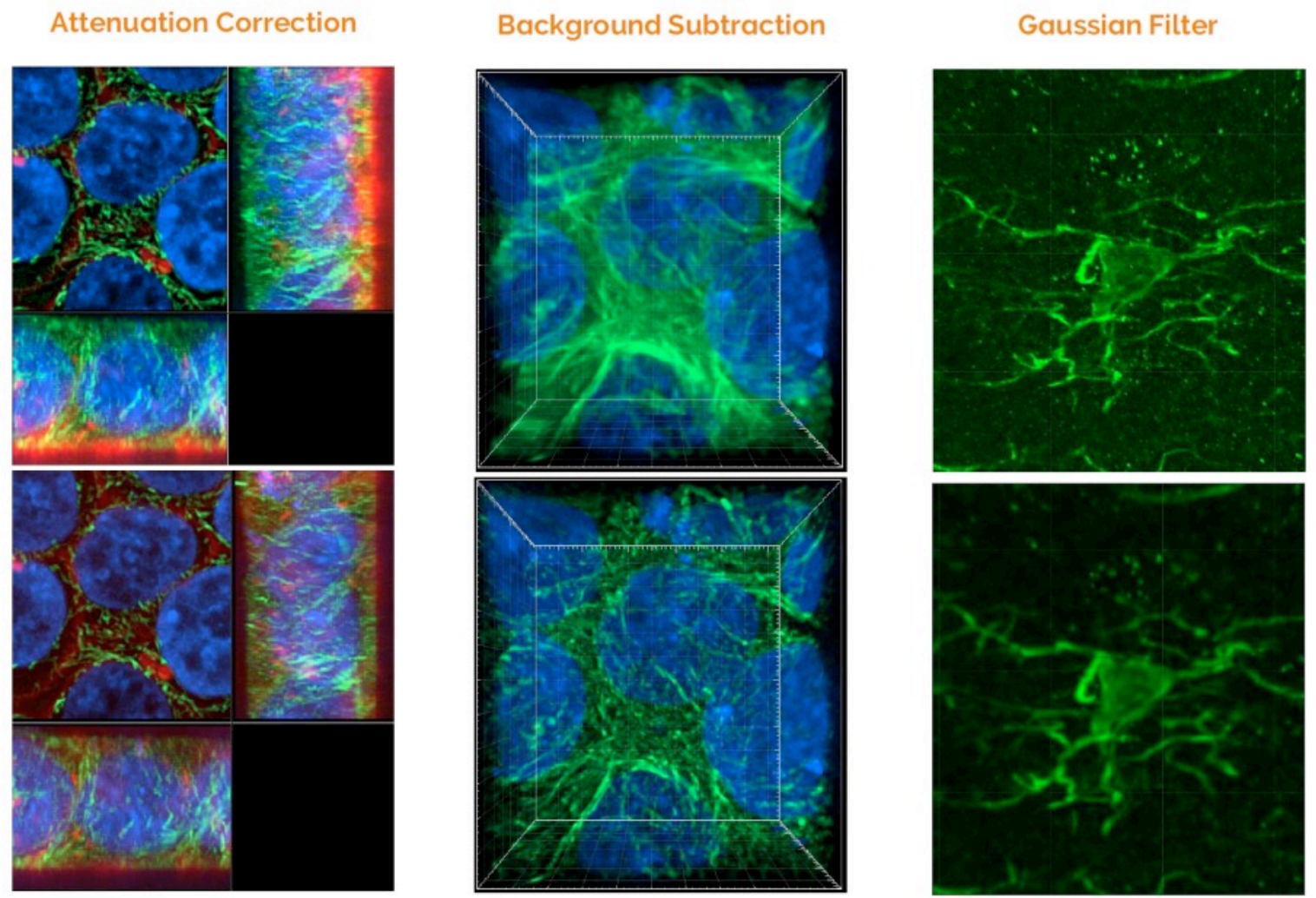
Supported Modalities: WideField, Confocal, Confocal spinning disk, Brightfield, TIRF

Algorithms:

- Qualitative Subtractive : No Neighbour (Fastest)
- Quantitative: Iterative (Robust)

BATCH

Visualize Image Pre-processing

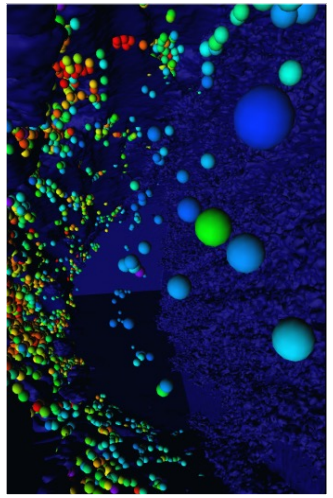


IMARIS

Detect

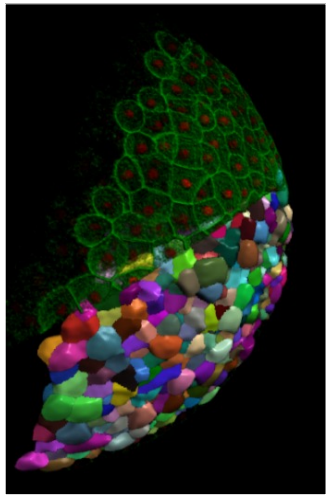
IMARIS

Spot

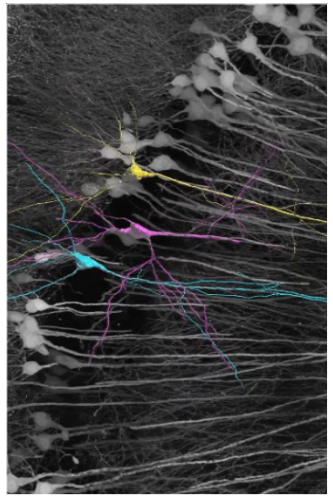


Surface

Cell



Filament



Spot

IMARIS

OXFORD INSTRUMENTS IMARIS

Count

Position

Diameter

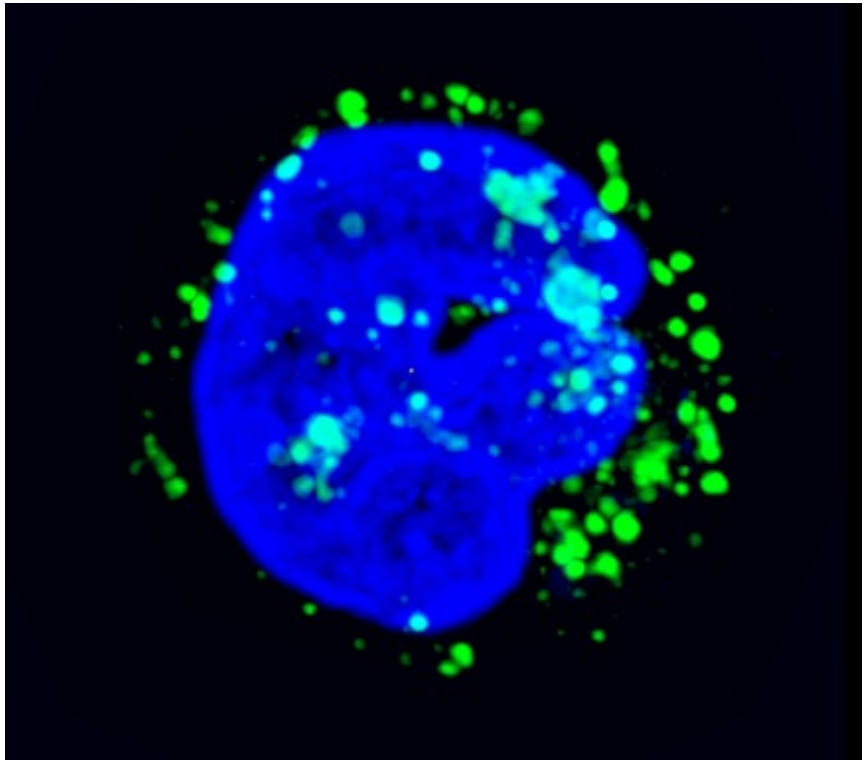
Intensity

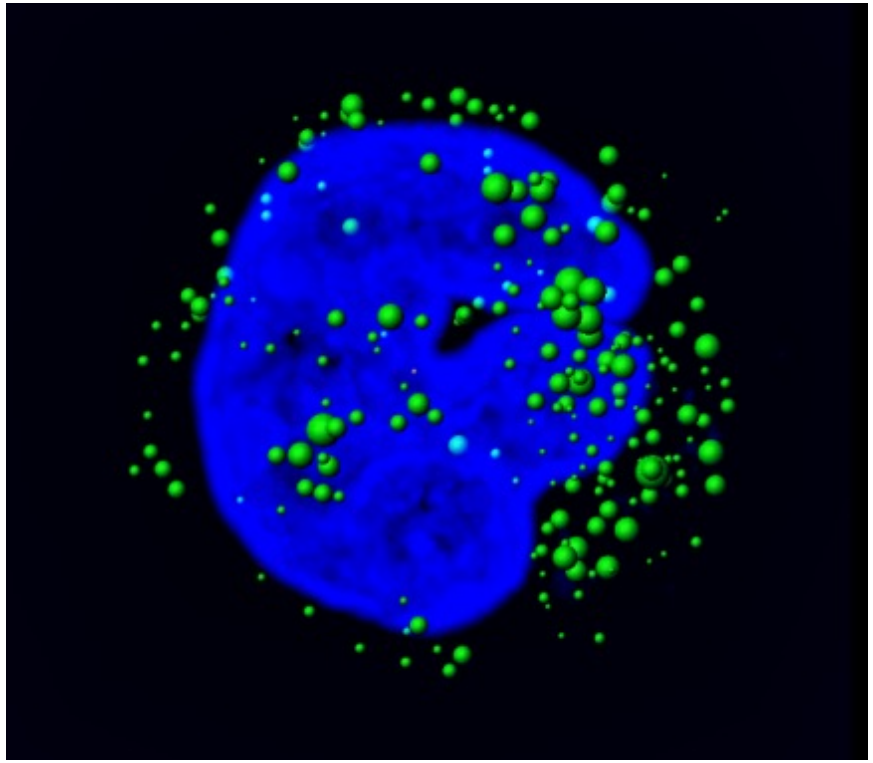
Center

Angle

.....

Spot





Count

Position

Diameter

Intensity

Center

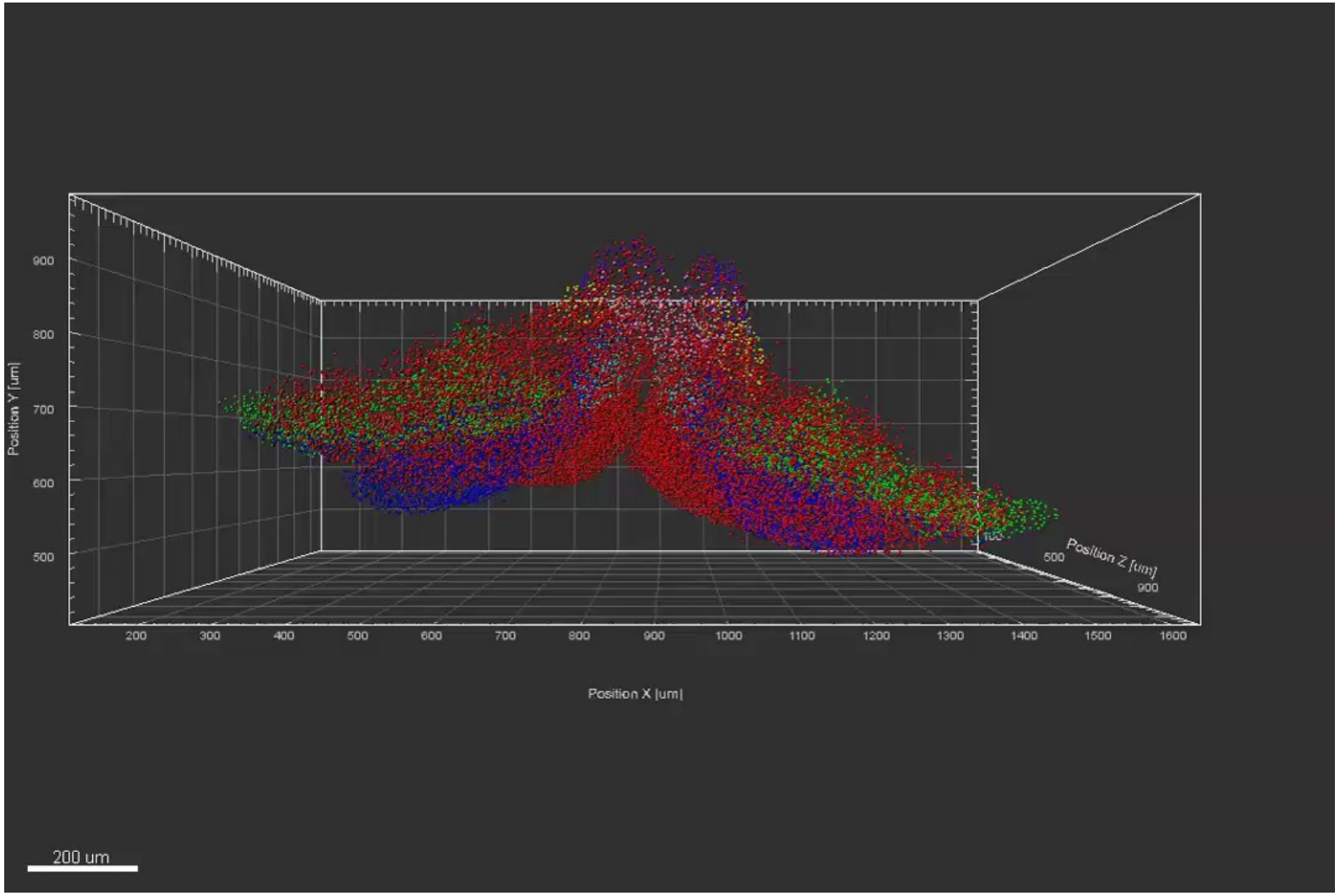
Angle

……

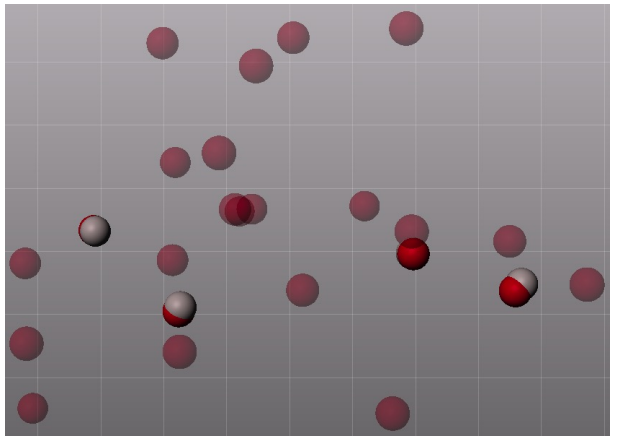
Spot

IMARIS

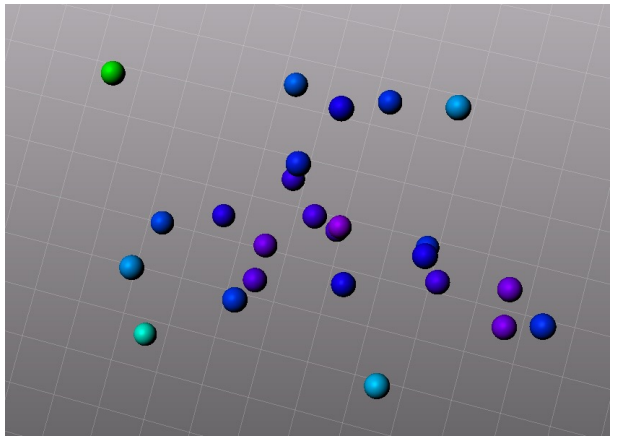
OXFORD INSTRUMENTS IMARIS



Colocolized Spots



Average Distance to Neighbour



Surface

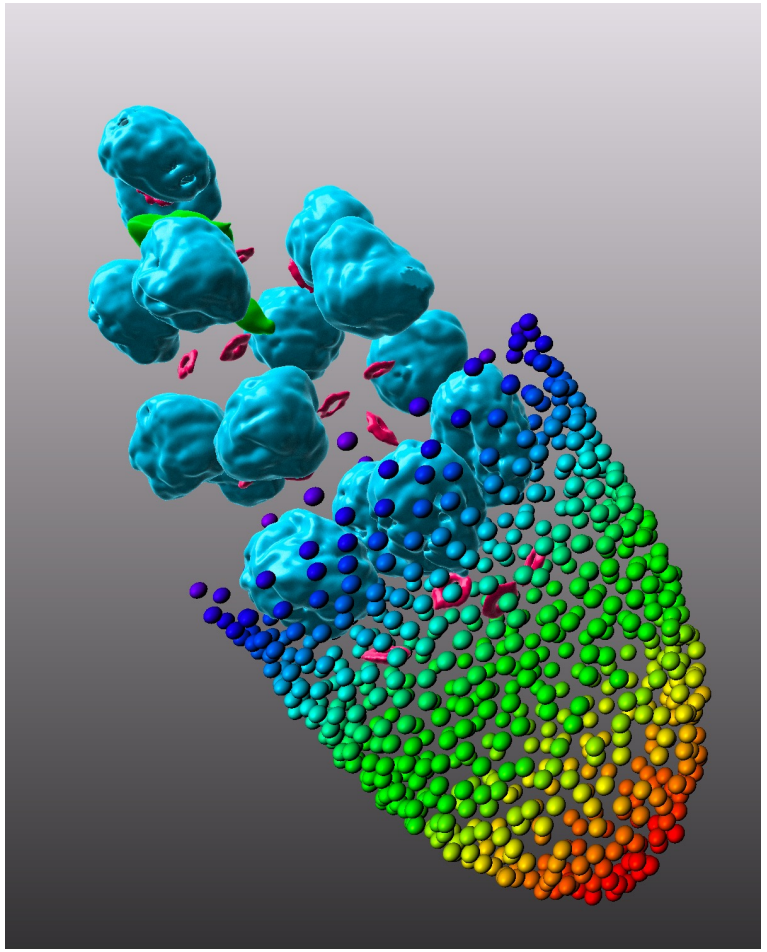
IMARIS

OXFORD INSTRUMENTS IMARIS

Surface

IMARIS

OXFORD INSTRUMENTS IMARIS



Count

Position

Intensity

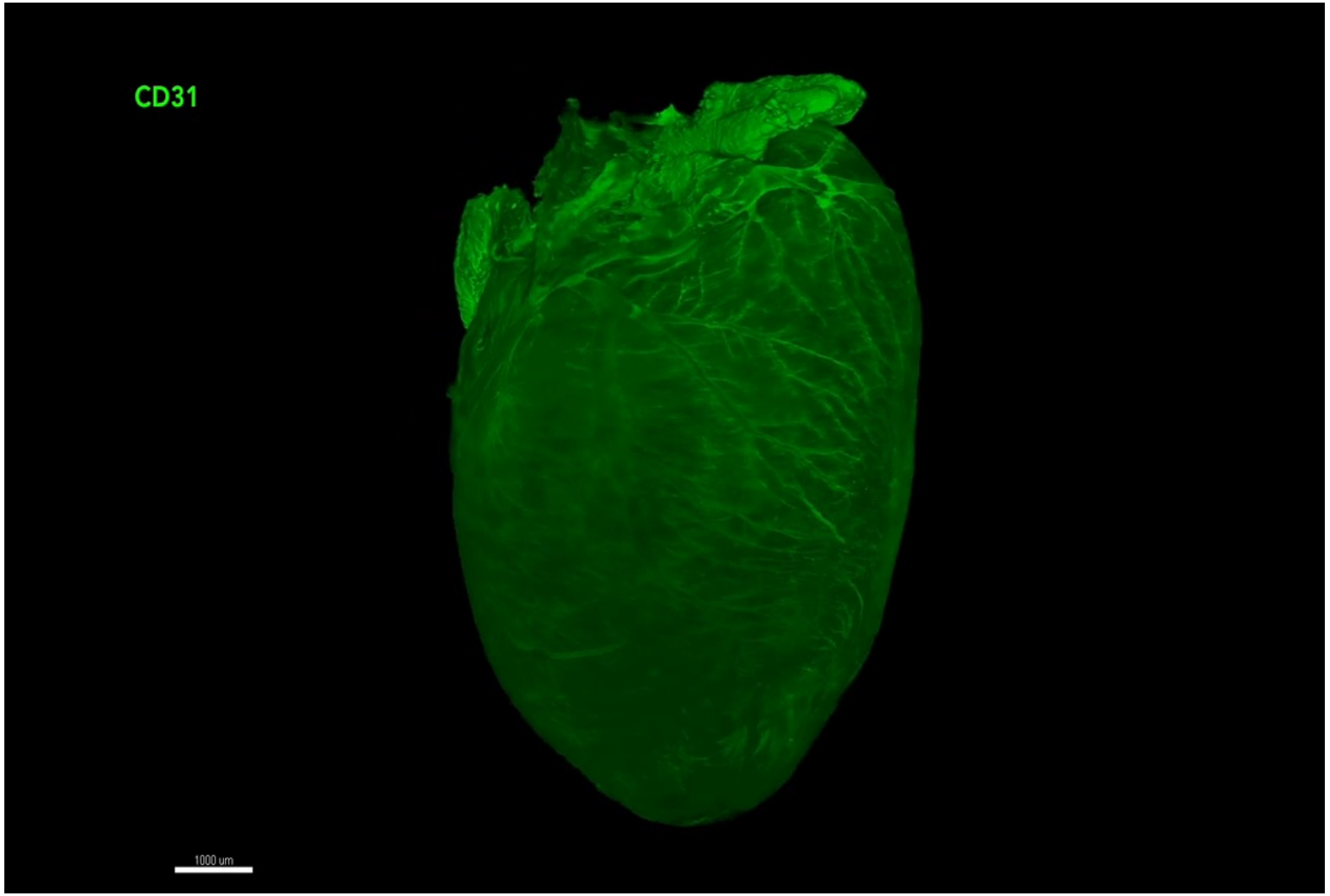
Volume

Area

Morphology

……

Surface



Merz, S.F. et al., Nat Commun. (2019)

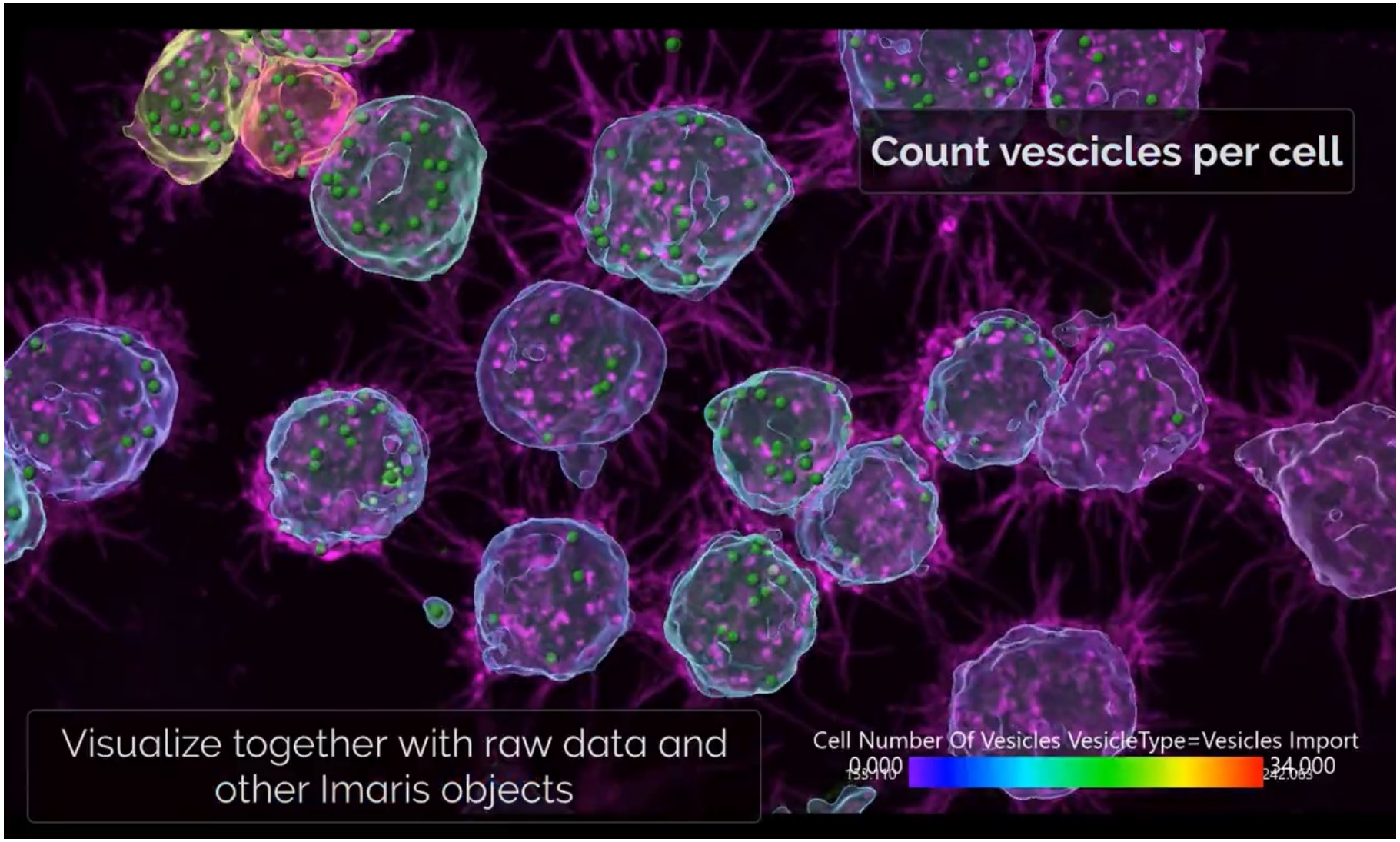
New

Machine Learning Pixel Classification – IMARIS 9.9

IMARIS

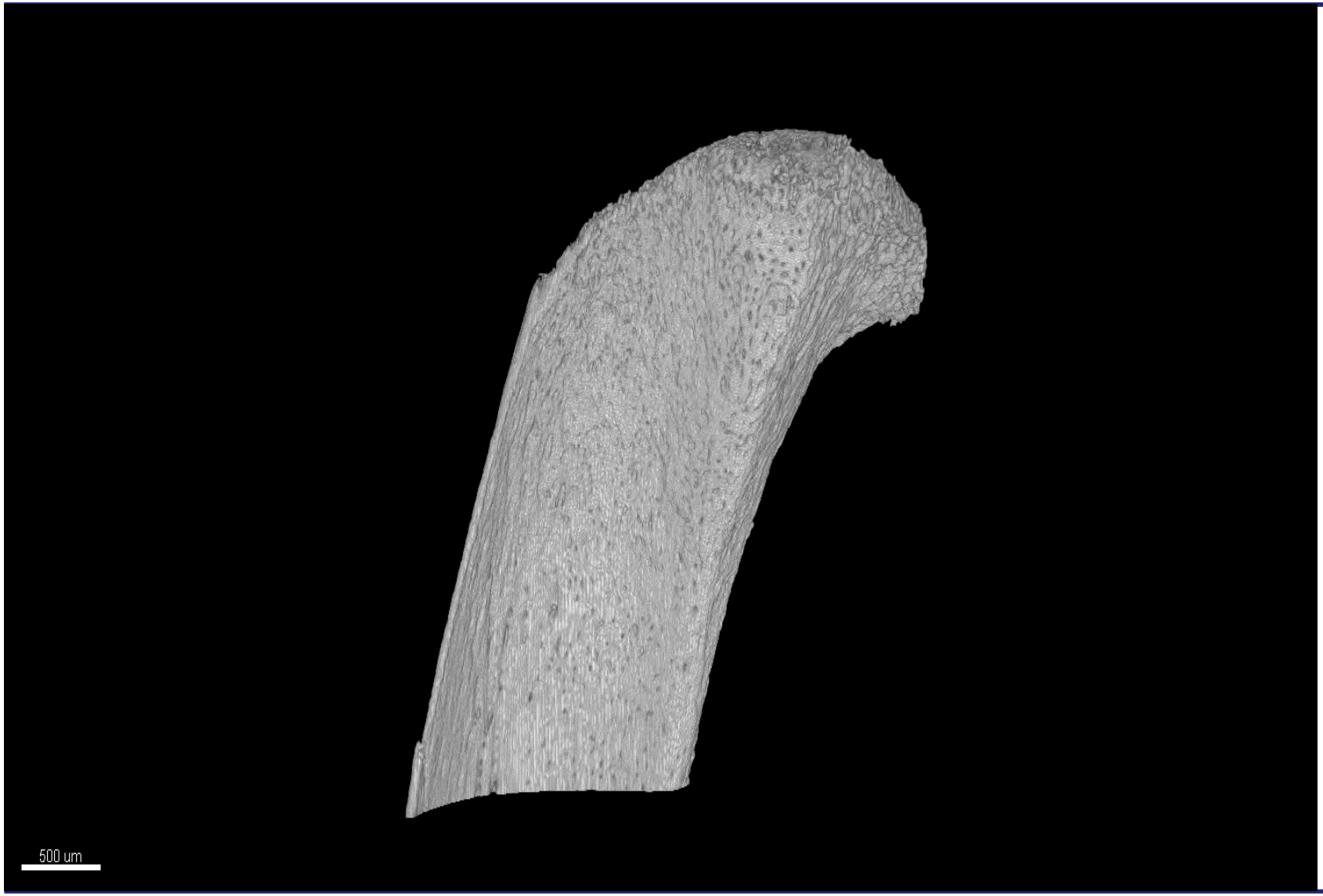
New

Machine Learning Pixel Classification – IMARIS 9.9



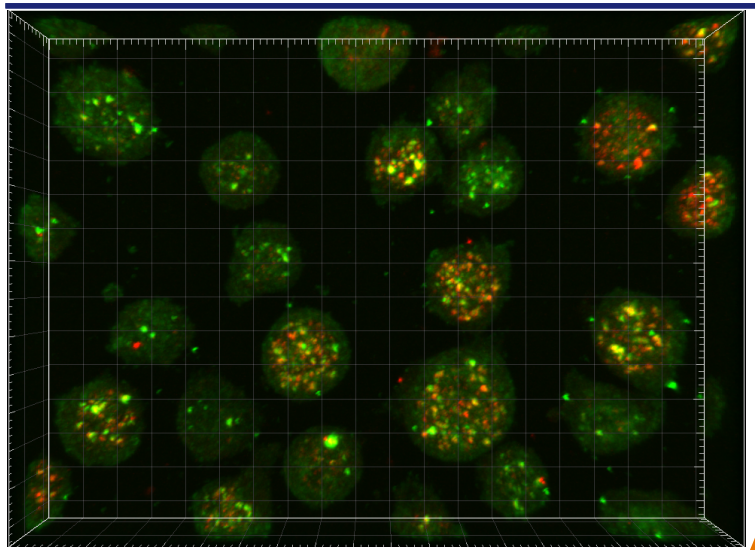
IMARIS

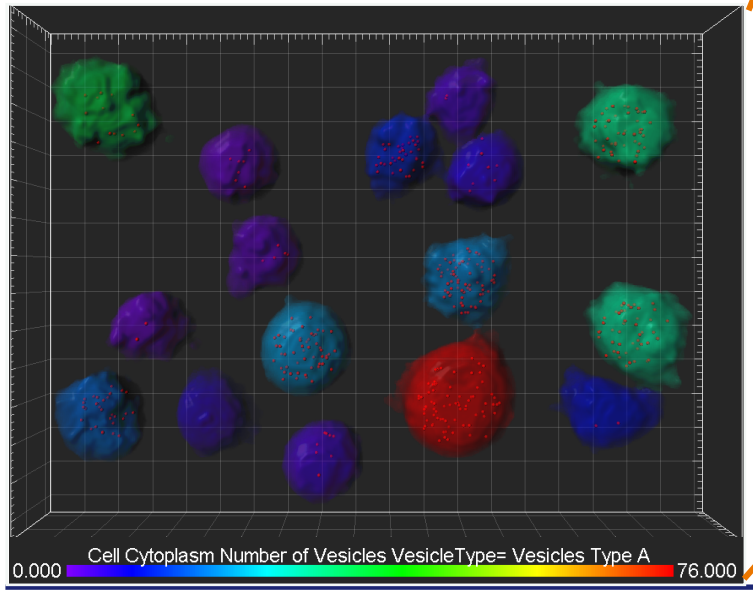
Surface

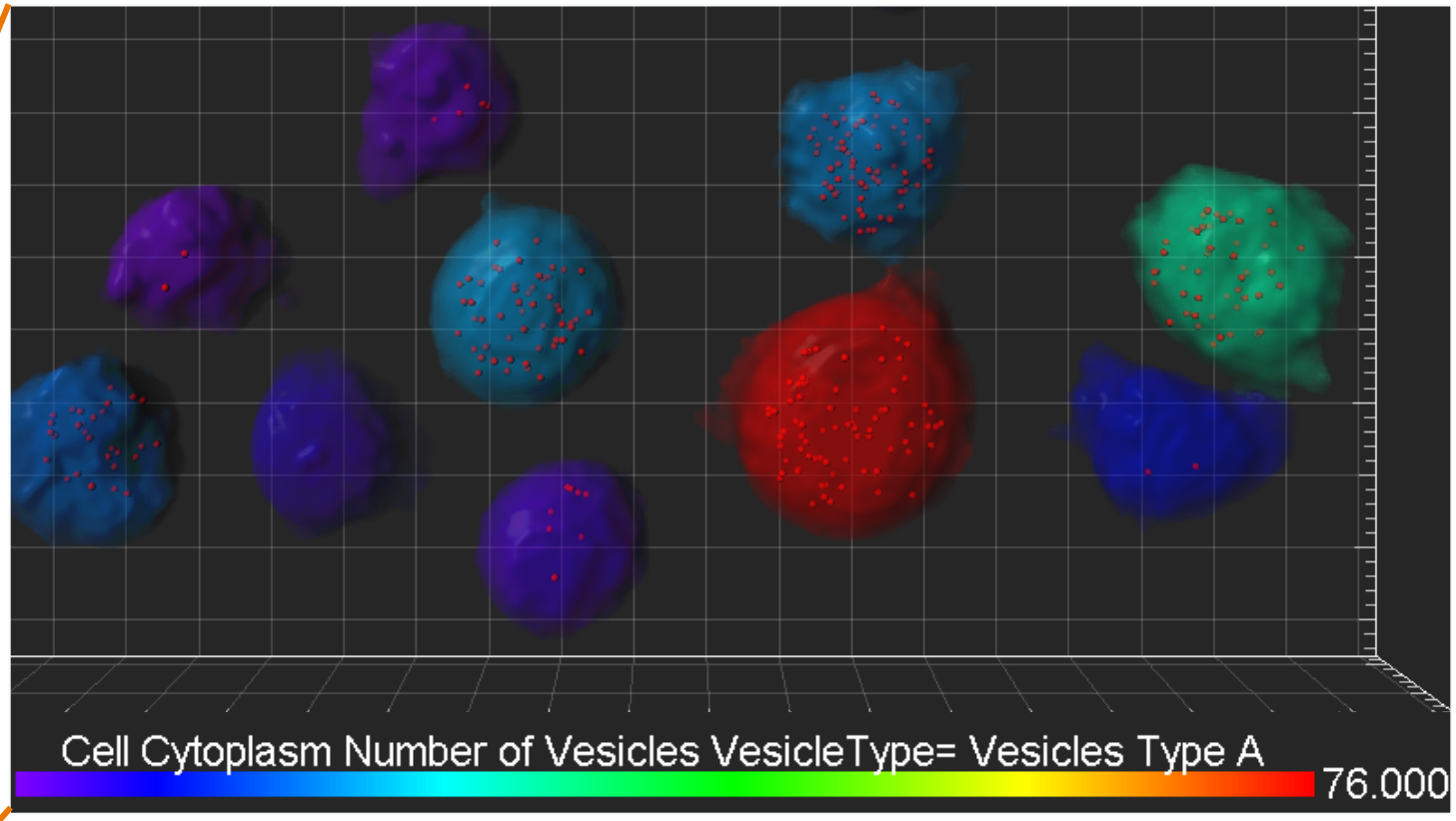


Grüneboom, et al.. Nat Metab (2019)

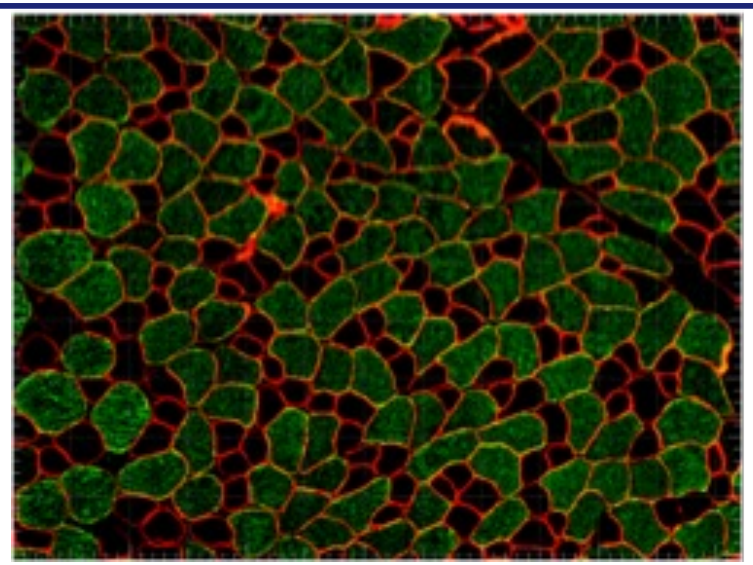
Cell

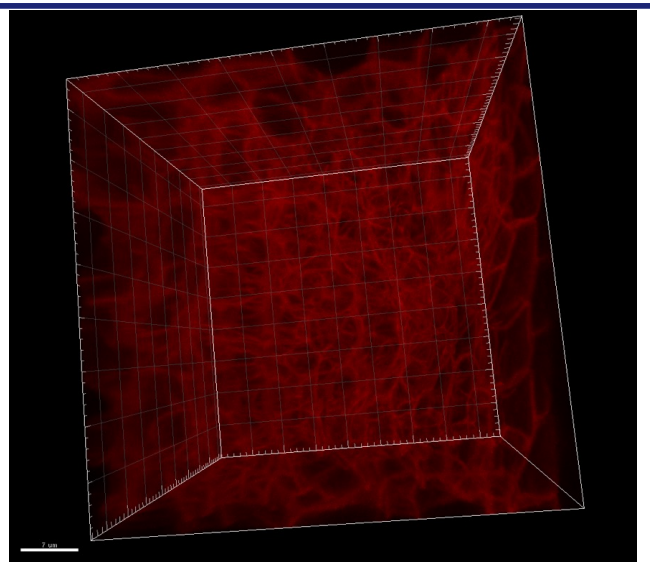


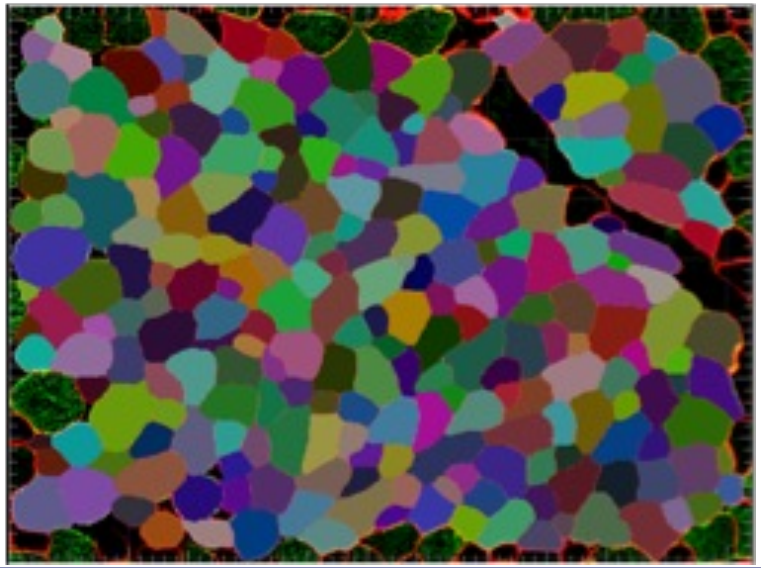


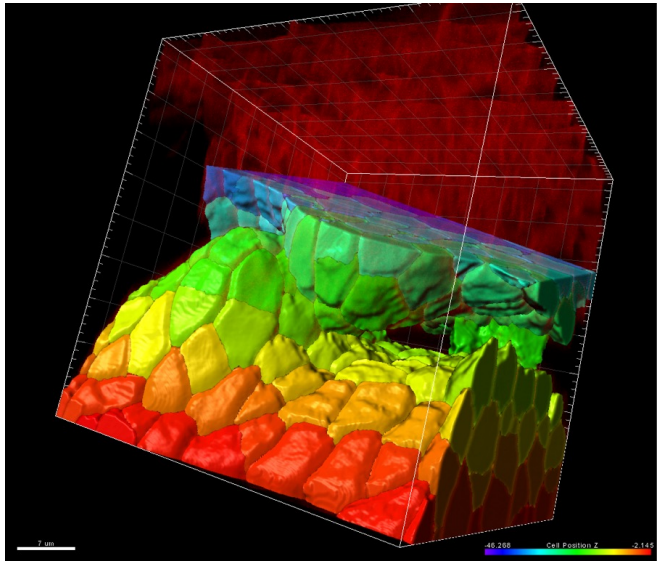


Cell

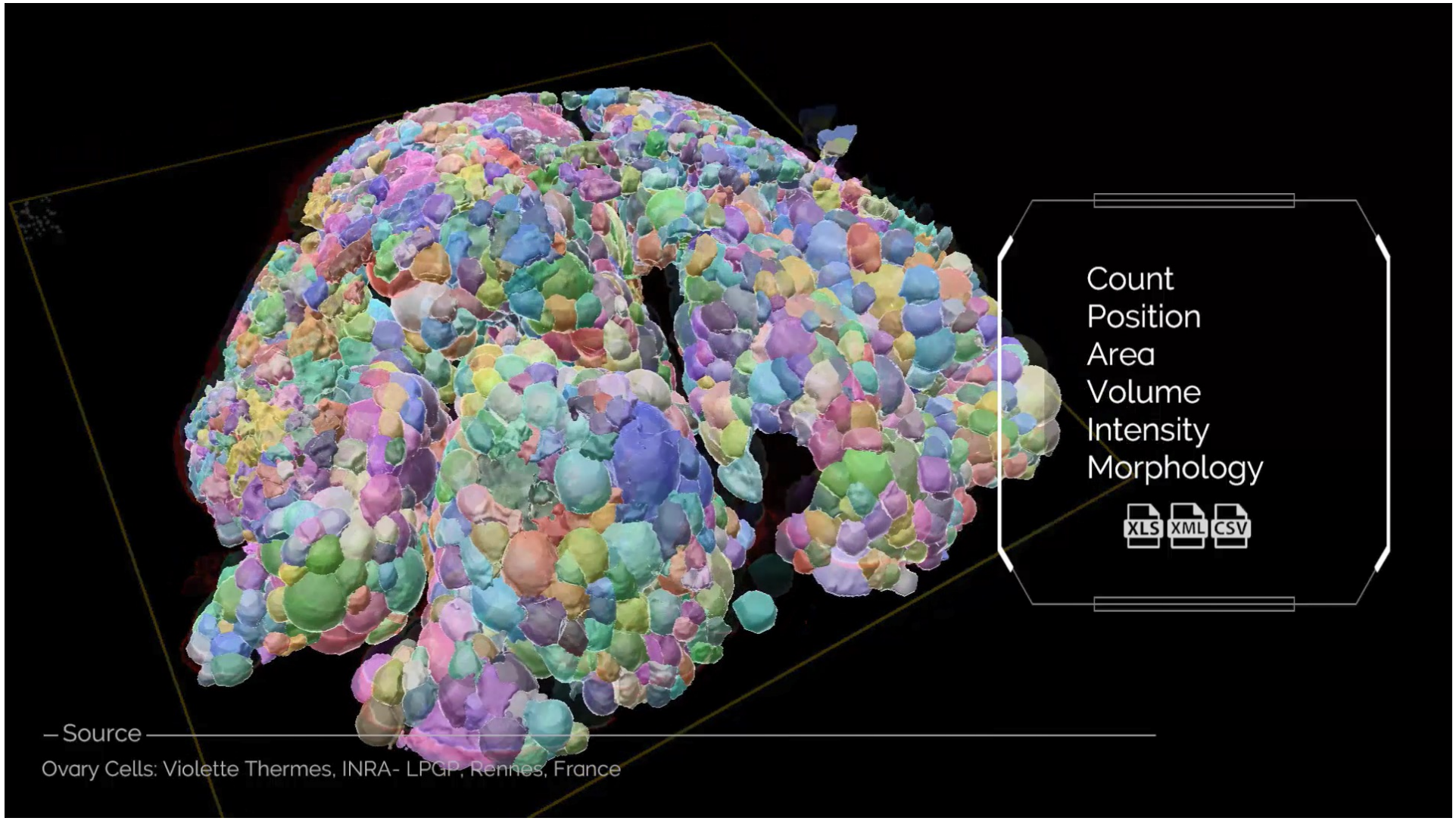






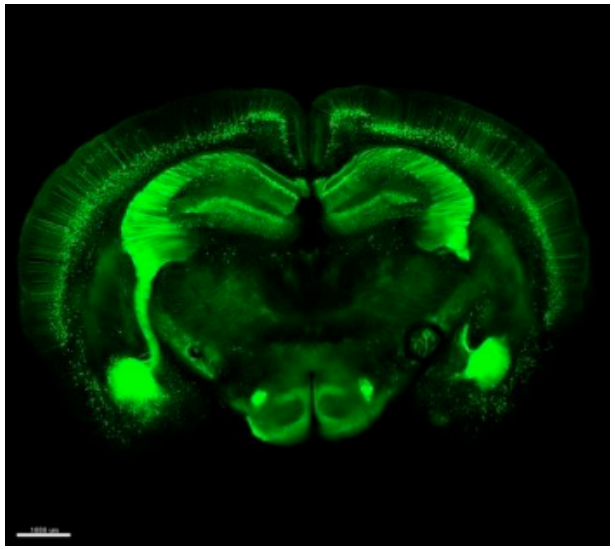


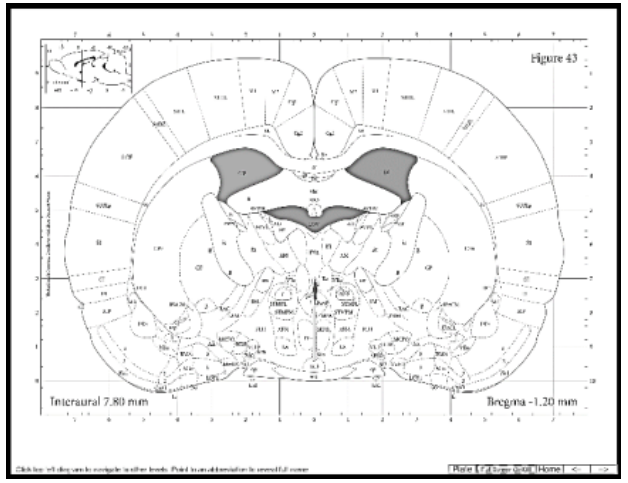
Cell

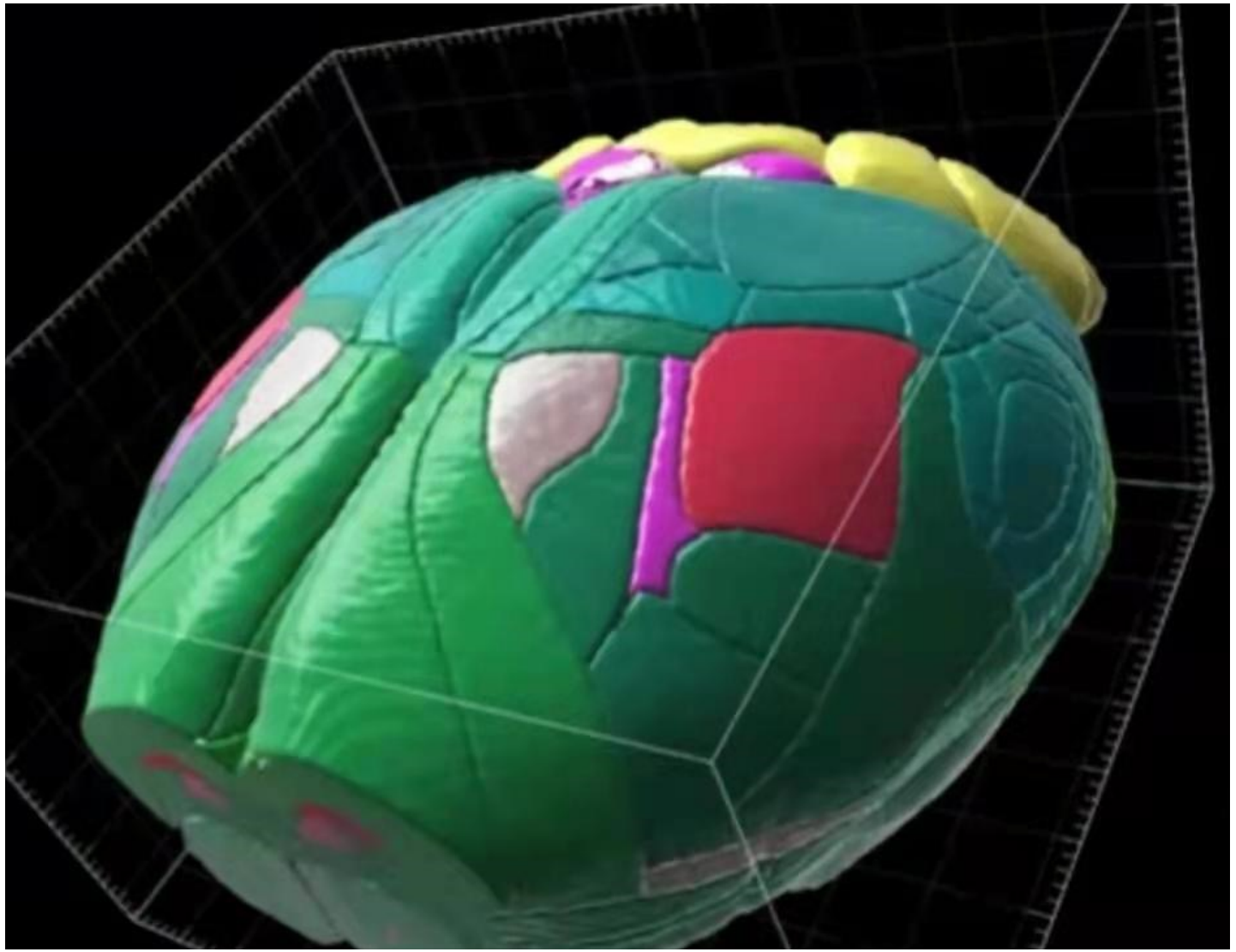


IMARIS

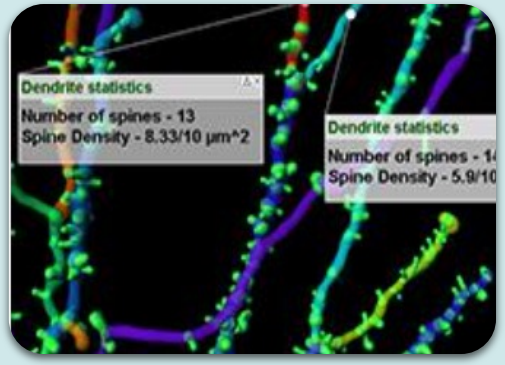
Cell

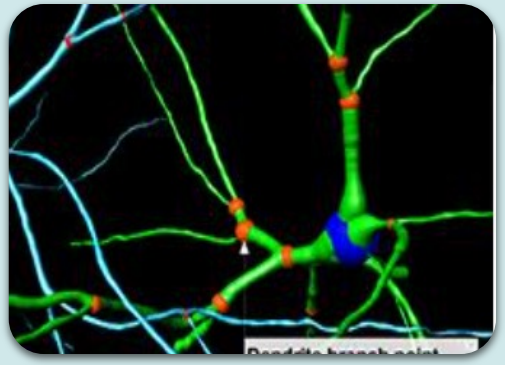


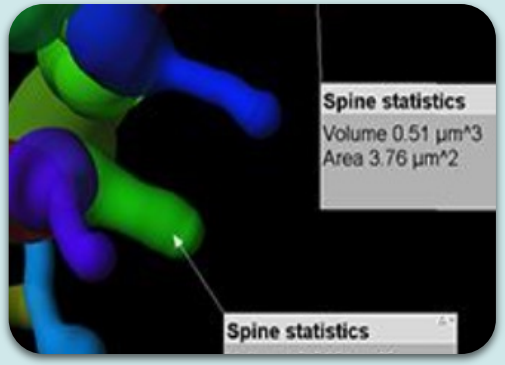


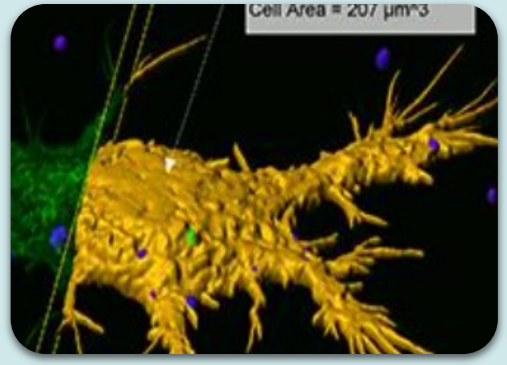


Statistics and measurements for Neuroscience









Dendrites

- Length
- Mean Diameter
- Branching Angle
- Spine Density
- Resistance

Filaments

- Dendrite Branch Points
- Dendrite Terminal Points
- Sholl Intersections
- Spine Terminal Points
- Dendrite Branch Level

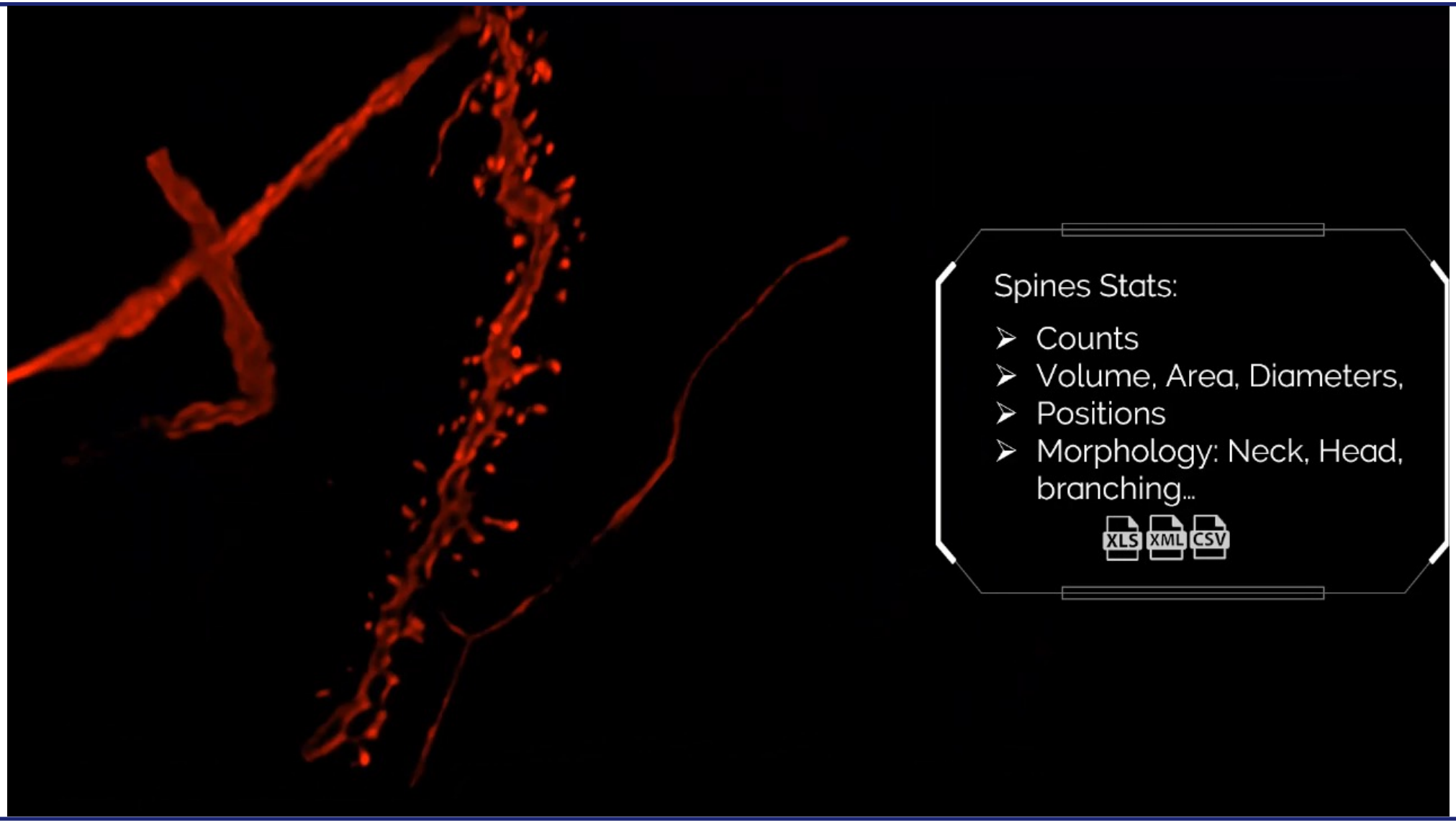
Spines

- Length
- Volume
- Mean Diameter
- Area
- Terminal Point Diameter

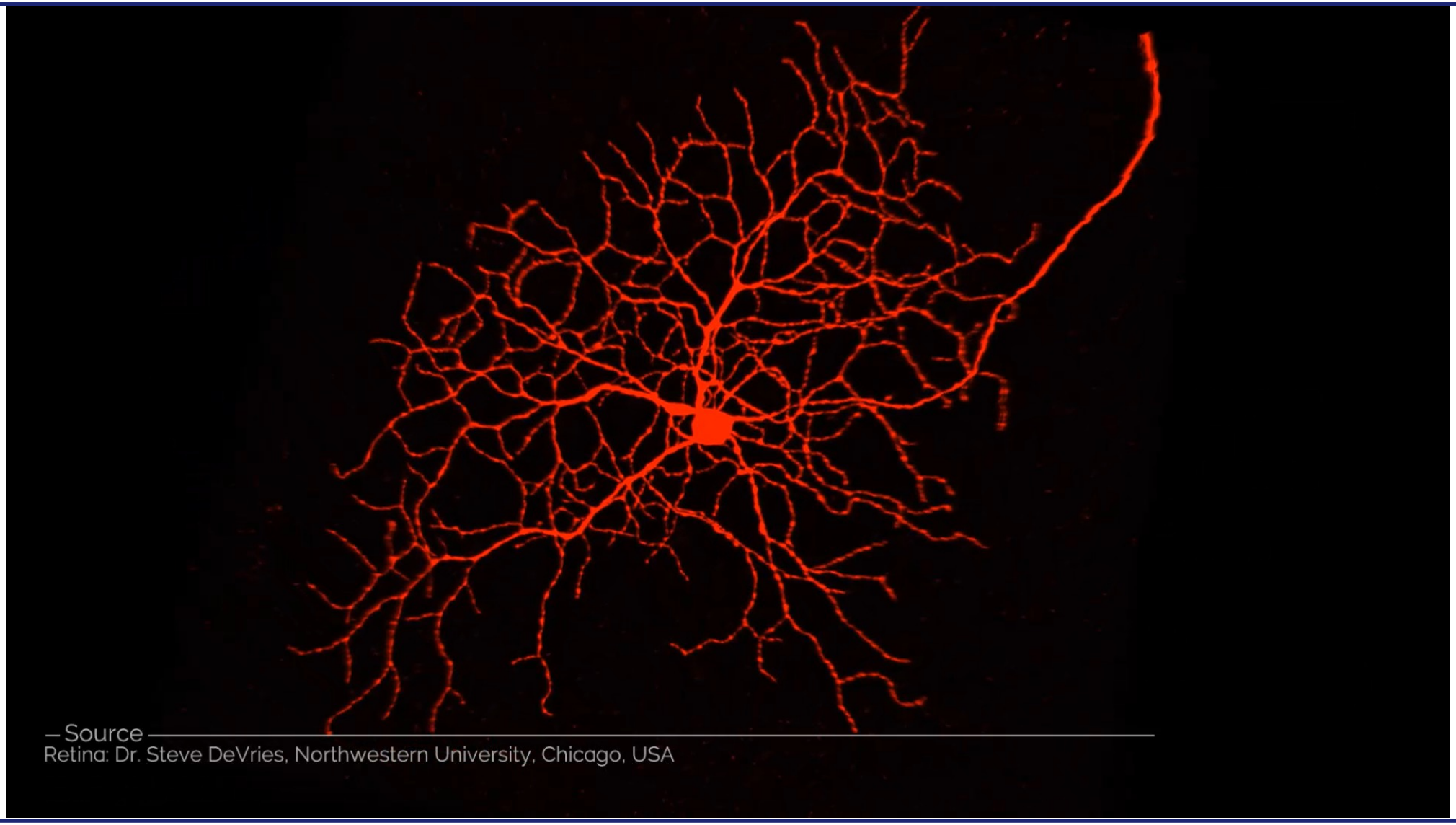
Surfaces

- Area
- Volume
- Intensity
- Position (x, y, z)
- Number (counting objects)

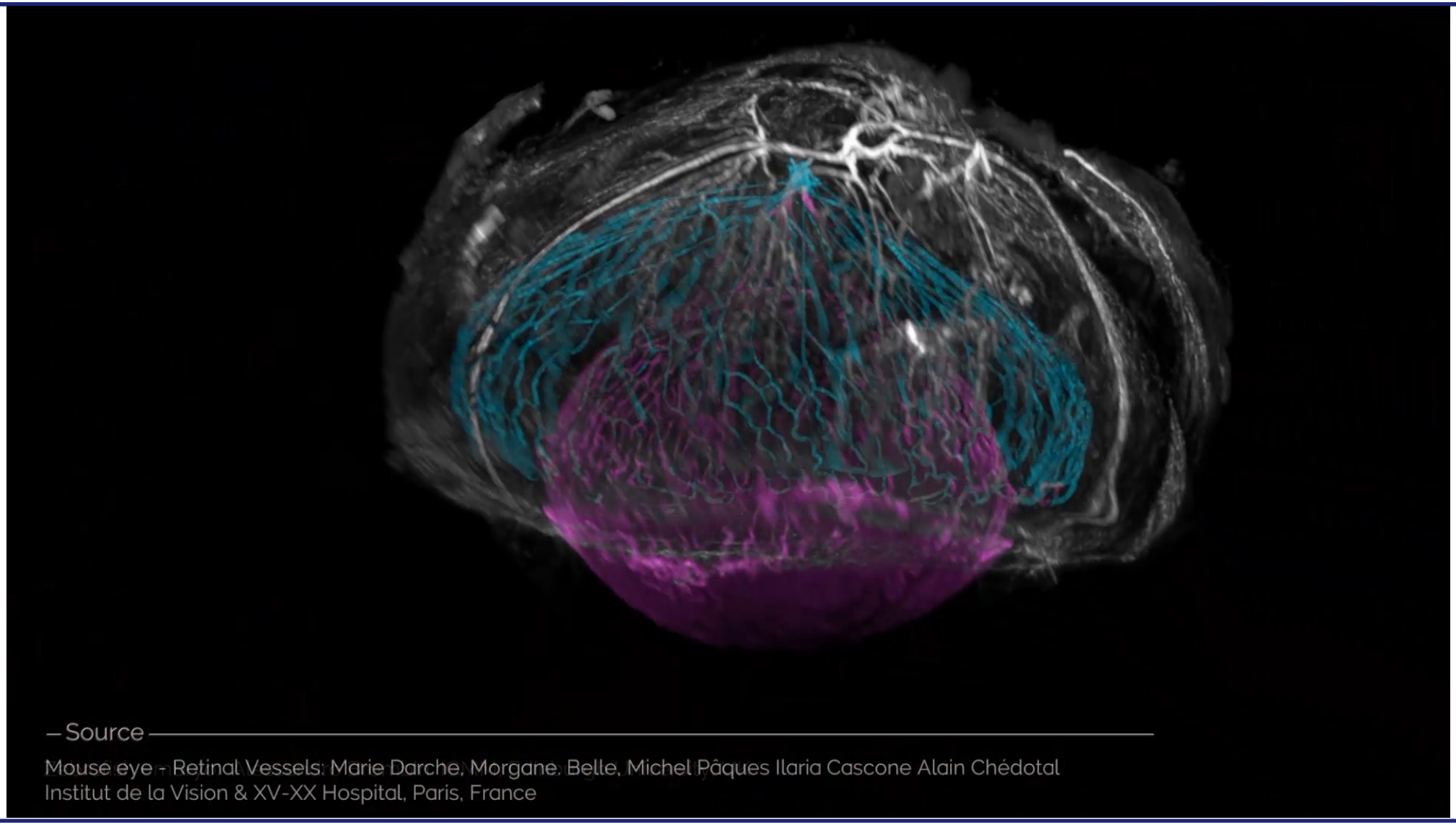
Filament



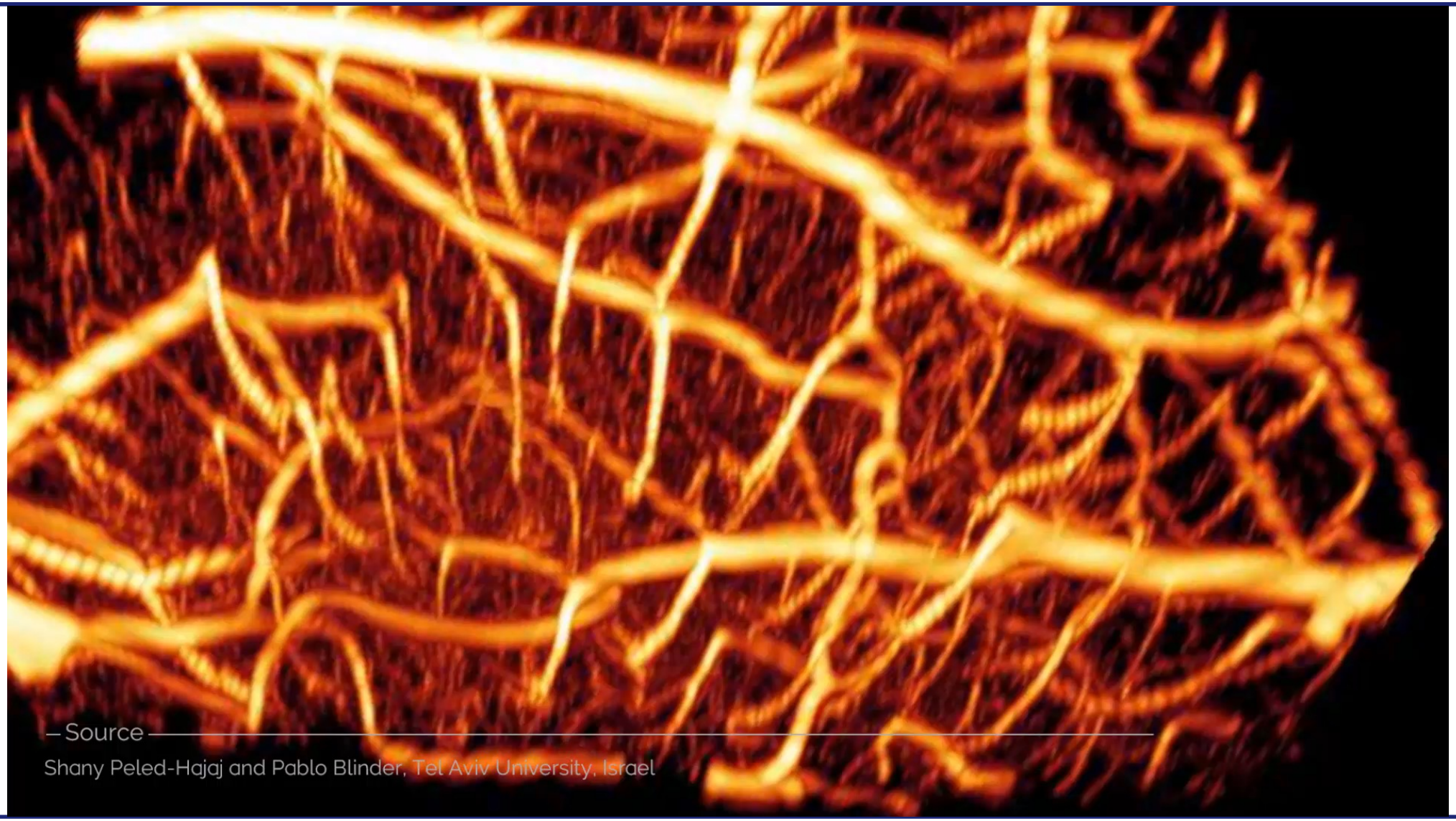
Filament



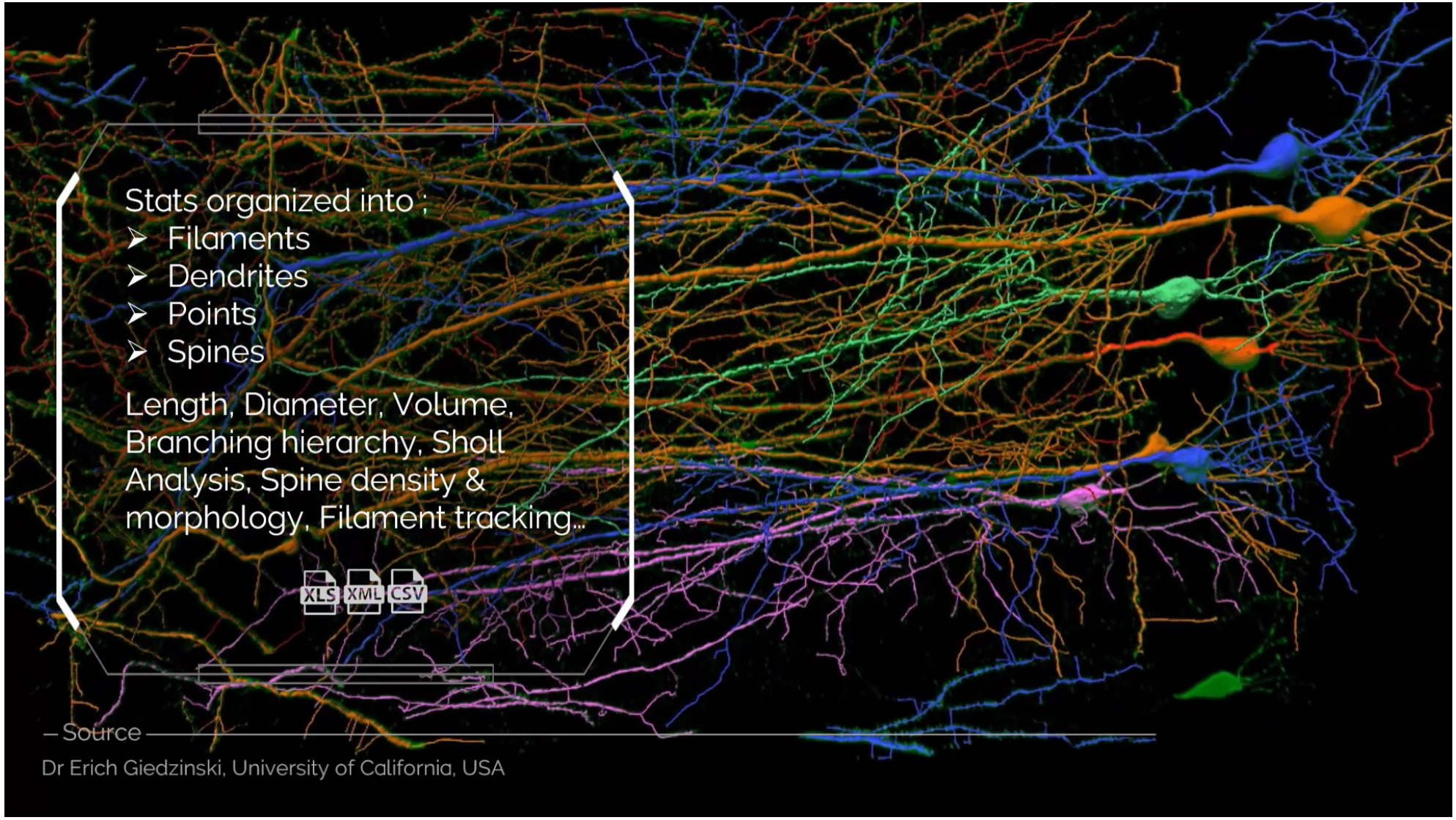
Filament



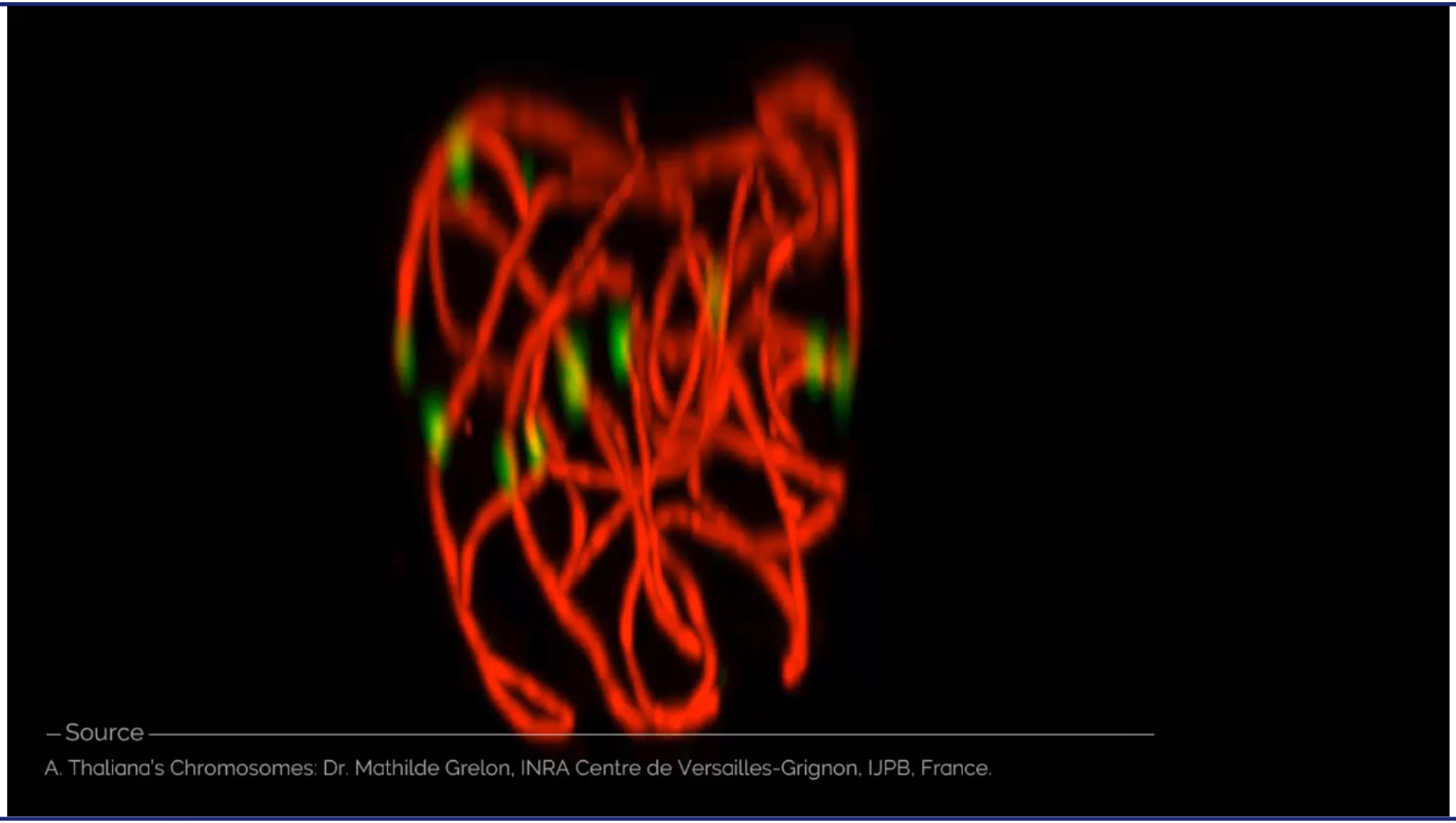
Filament



Filament



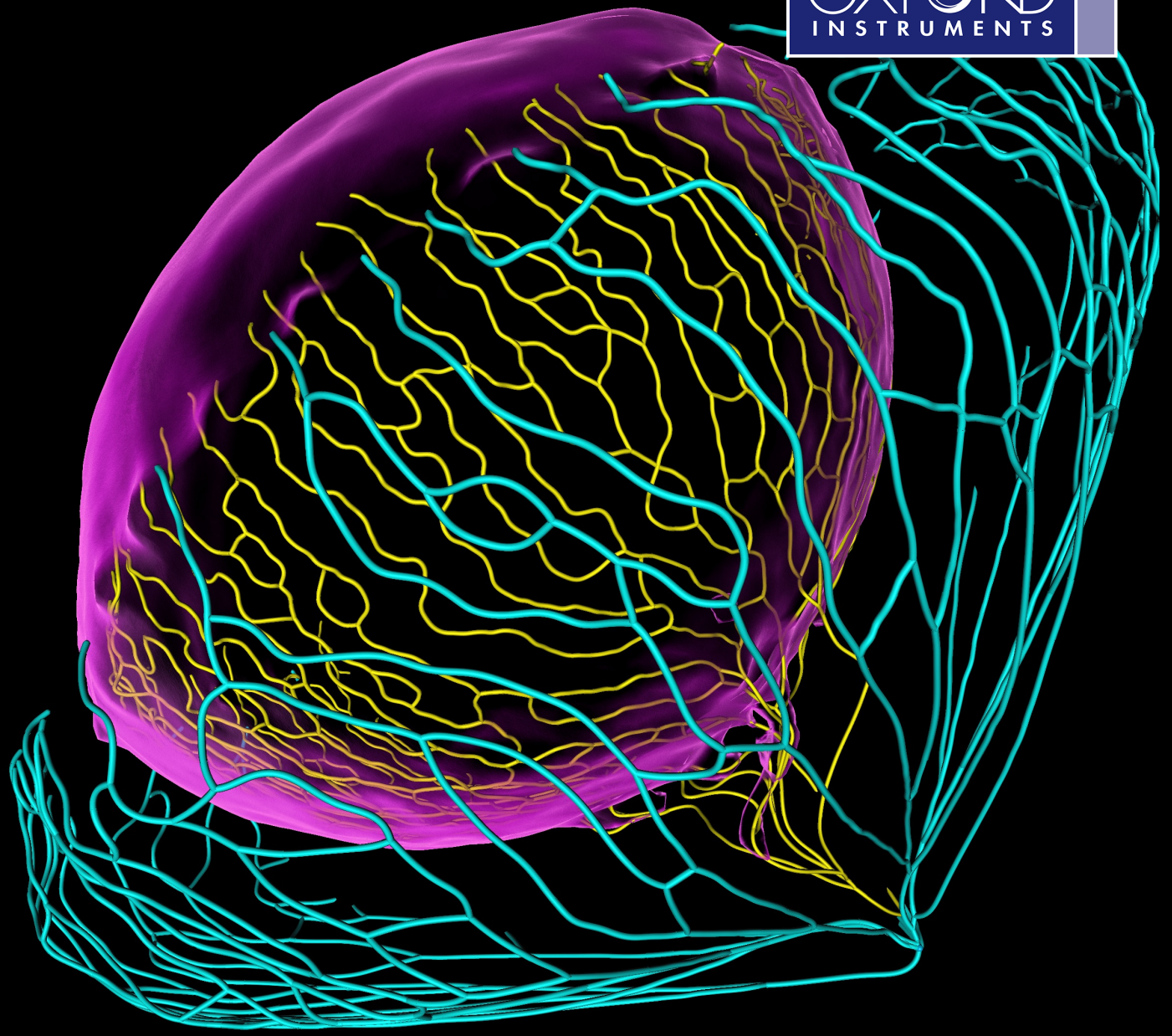
Filament



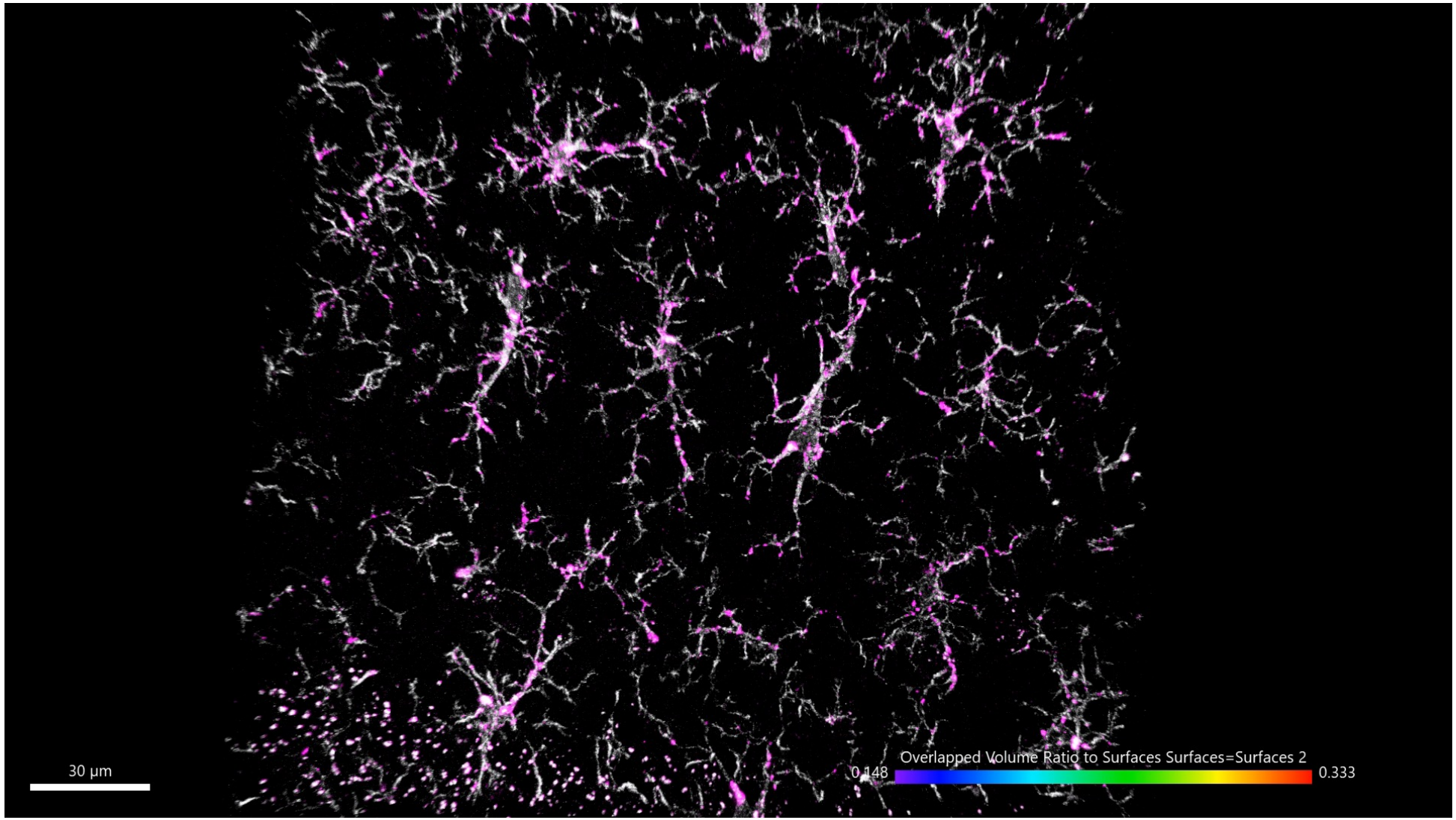
Imaris 10

AI Powered

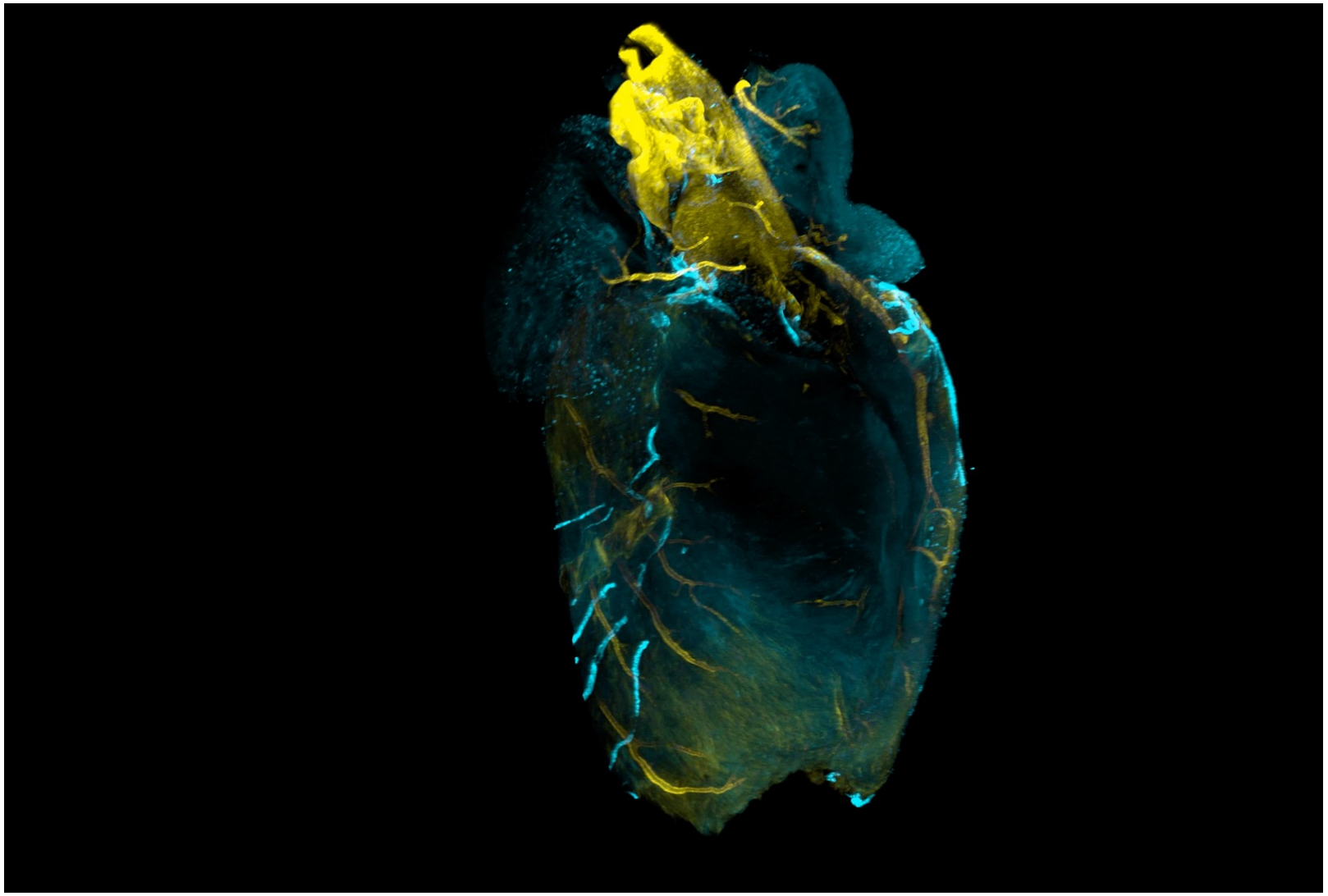
Filament Tracing



Imaris 10.0 – AI Powered Filament Tracer



Imaris 10.0 – AI Powered Filament Tracer



- Higher Throughput
  - Blockwise Calculation
  - Improved Rendering
  - AI Powered Creation
  - Usability tools
- Flexibility in sample
  - Multi-scale spots
  - New network model
- Easier to Learn
  - Less training
  - Less Support

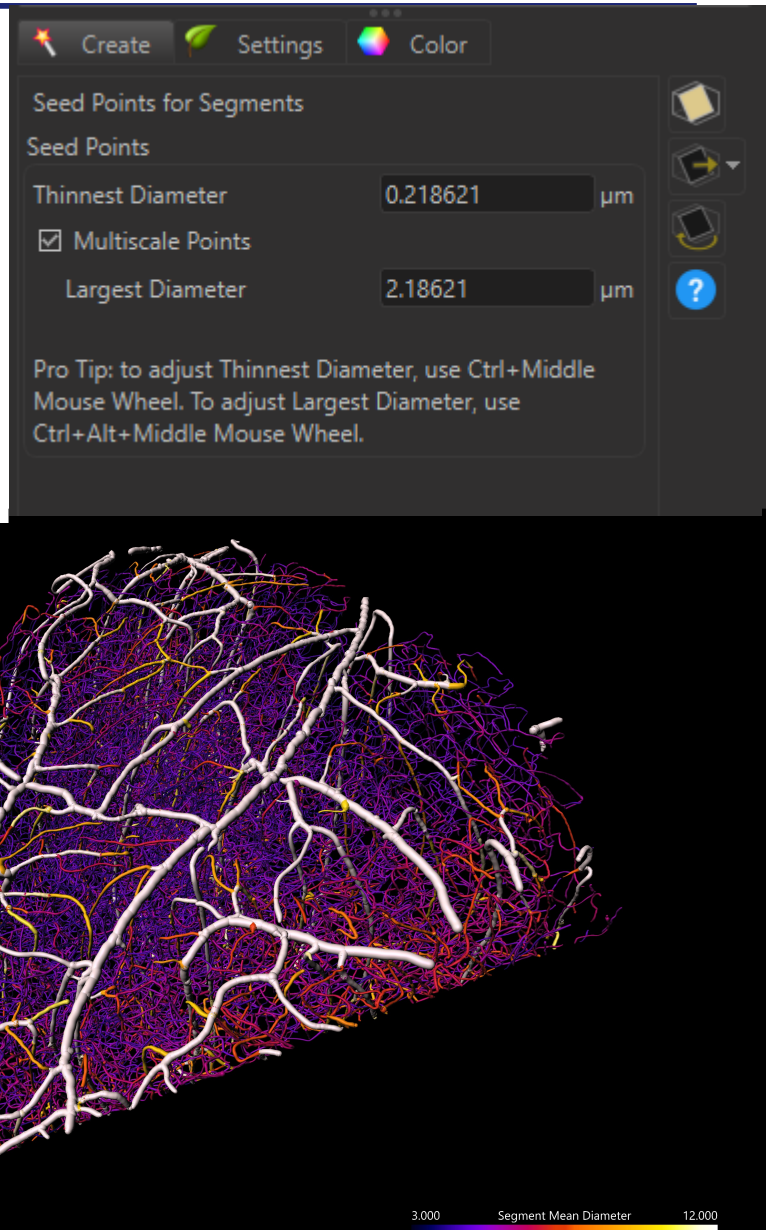
New Features of Imaris 10.0

Filament Feature

1. Blockwise calculation of images
2. Faster Filament object rendering
3. Machine Learning point classification
4. Multiscale Seedpoints

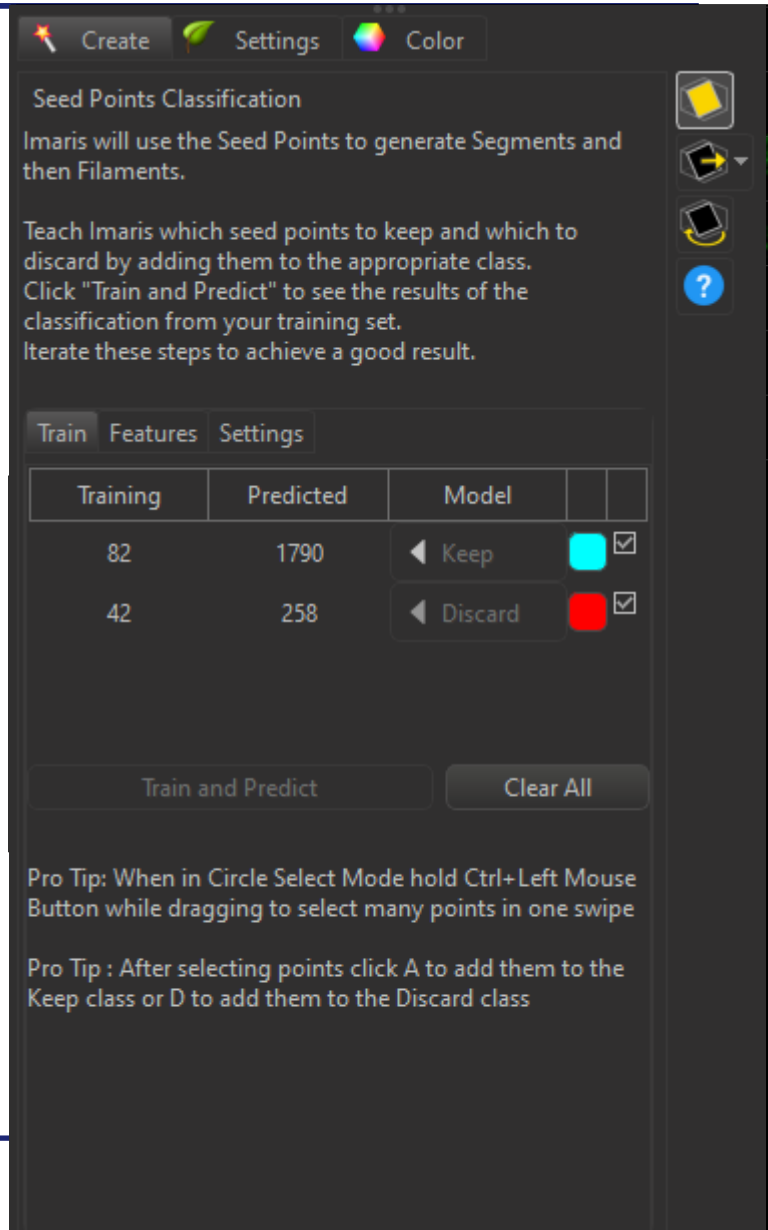
Benefit

1. Trace images greater than 2GB and faster
2. Smooth interaction (rotation, selection, etc.)
3. Improves quality of results for poor quality images
4. Improves quality of results and throughput



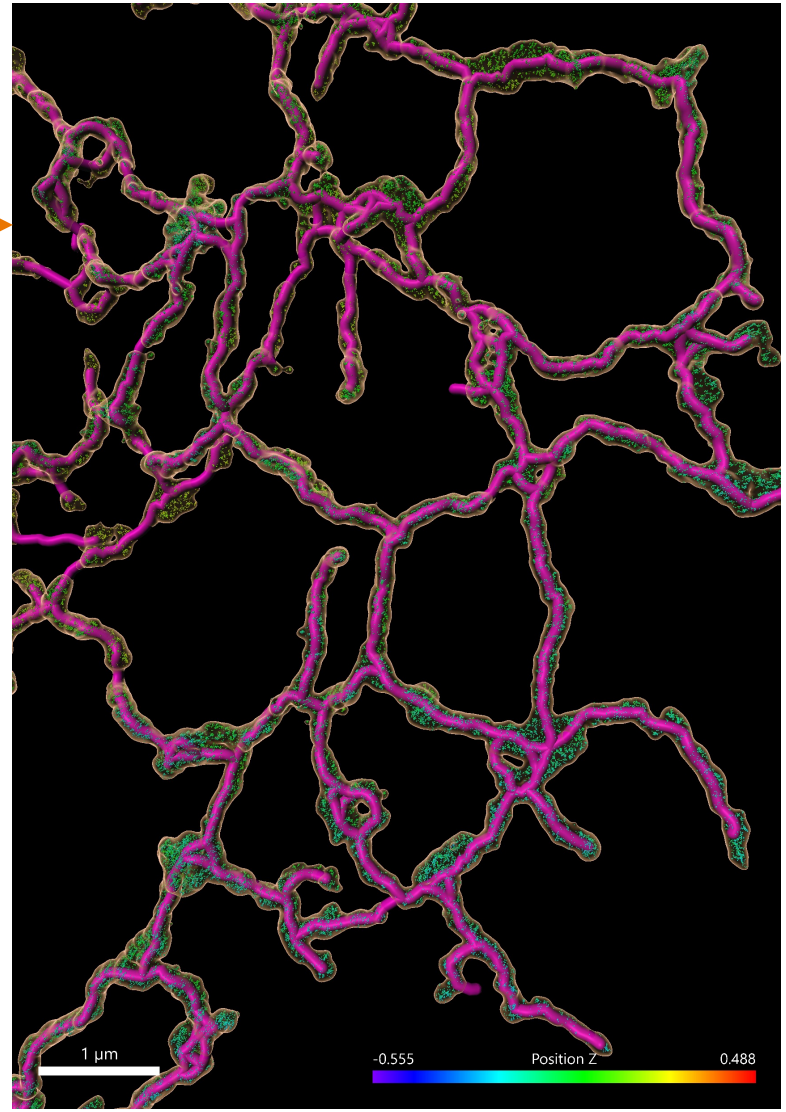
New Features of Imaris 10.0

Filament Feature	Benefit
1. Blockwise calculation of images	1. Trace images greater than 2GB and faster
2. Faster Filament object rendering	2. Smooth interaction (rotation, selection, etc.)
3. Machine Learning point classification	3. Improves quality of results for poor quality images
4. Multiscale Seedpoints	4. Improves quality of results and throughput
5. Visual Aides for detection type	5. Users pick the correct path every time
6. Dynamic 3D measurement of somas and seed points linked to wizard input boxes	6. Stay in wizard for all steps
7. Pro Tips for keyboard shortcuts	7. Potentially overlooked EoU features are prominent
8. ? Button for Reference Manual	8. Easy Reference Manual Link
9. Machine Learning point classification	9. Training data can be reused
10. Swiping selection tool	10. Faster and easier editing
11. **HDF5 “position” reader	11. Load Picasso localizations as Spots

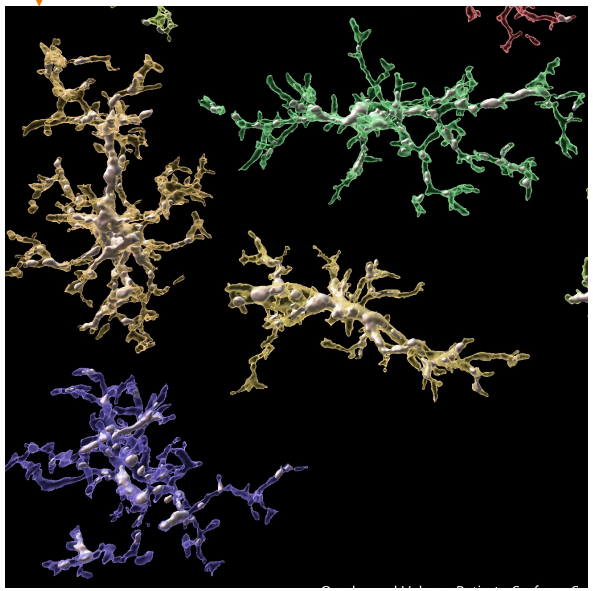


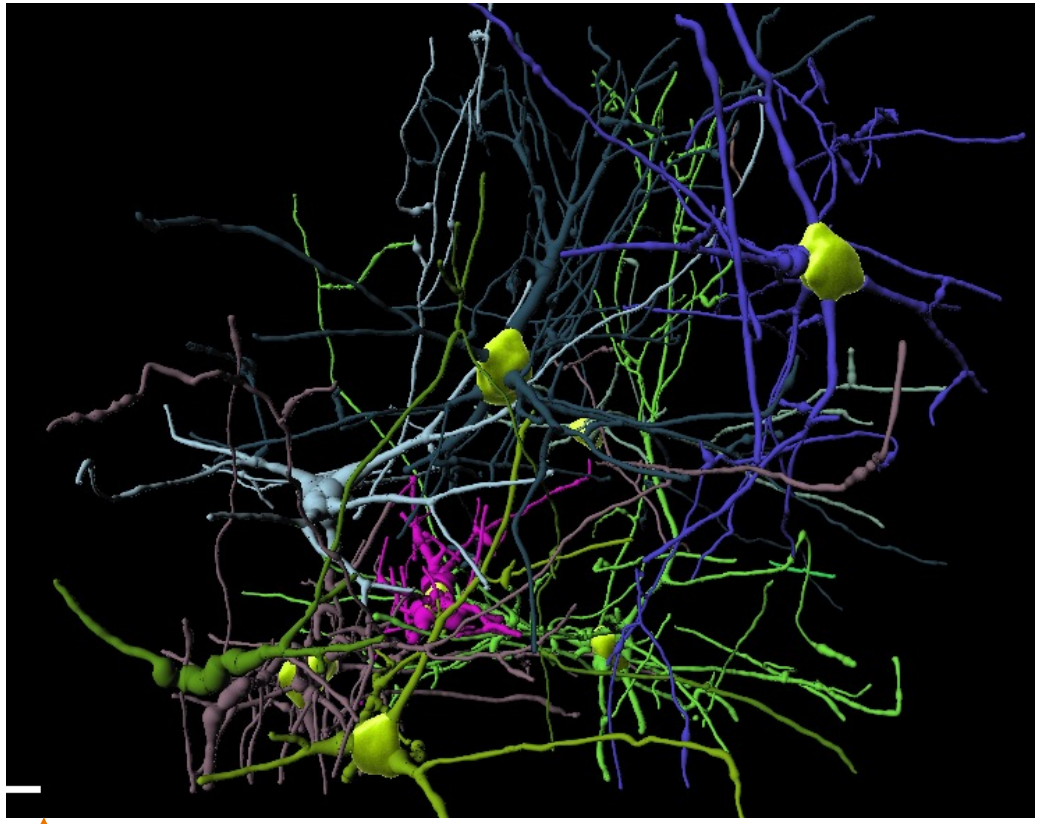
Imaris 10.0 – Applications

Sub-cellular endoplasmic reticulum network imaged with DF600 super-resolution microscopy and traced with Imaris 10.0



Microglia traced in Imaris 10.0 with additional analysis via Surfaces to determine activation state



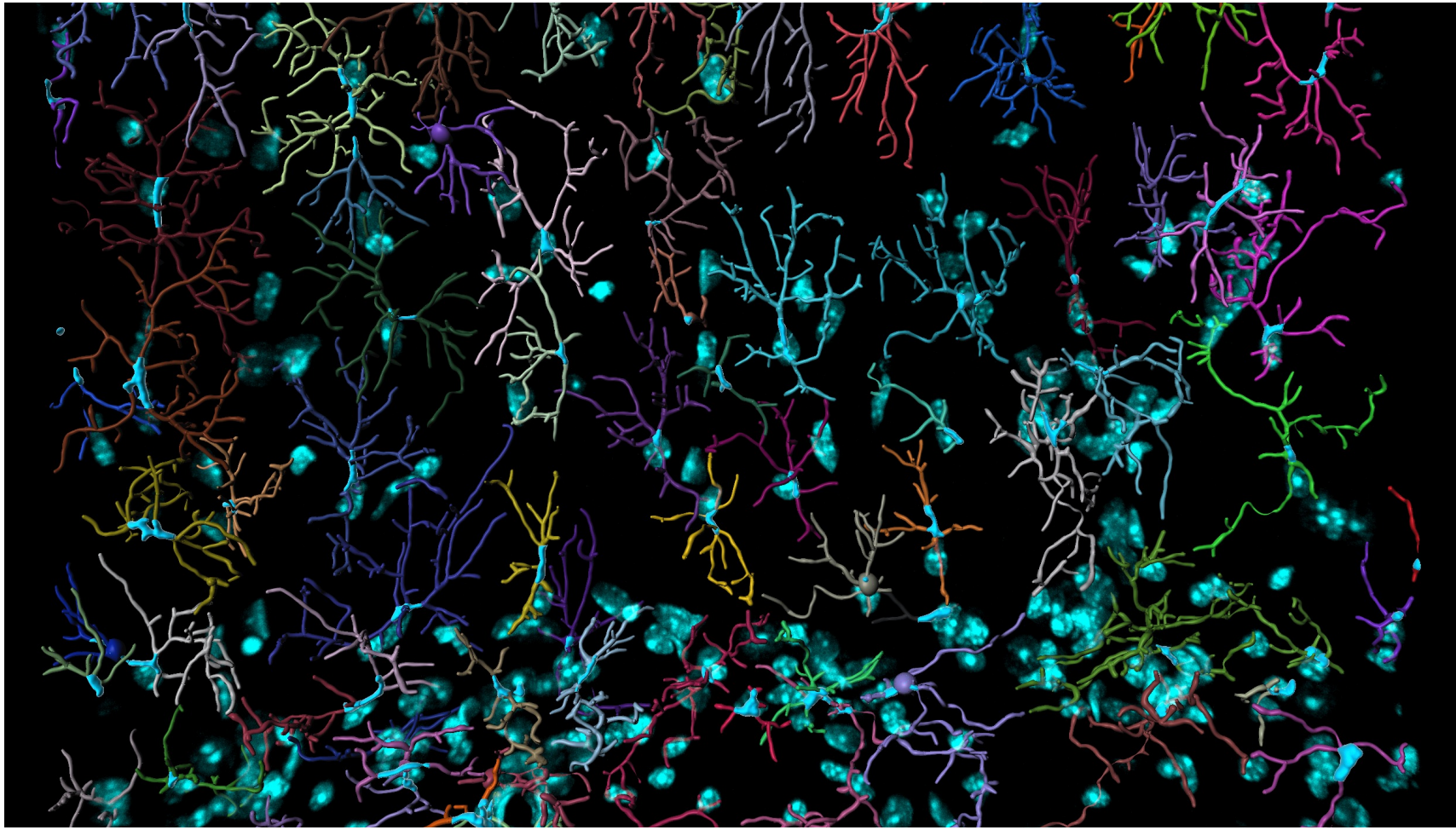


Neurons in a cleared mouse brain. Pre-10.0 analysis required ½ day of work by an experienced Imaris user. The above result was completed in 13 minutes.

Imaris 10.0 – Neuroscience

Neuroscience

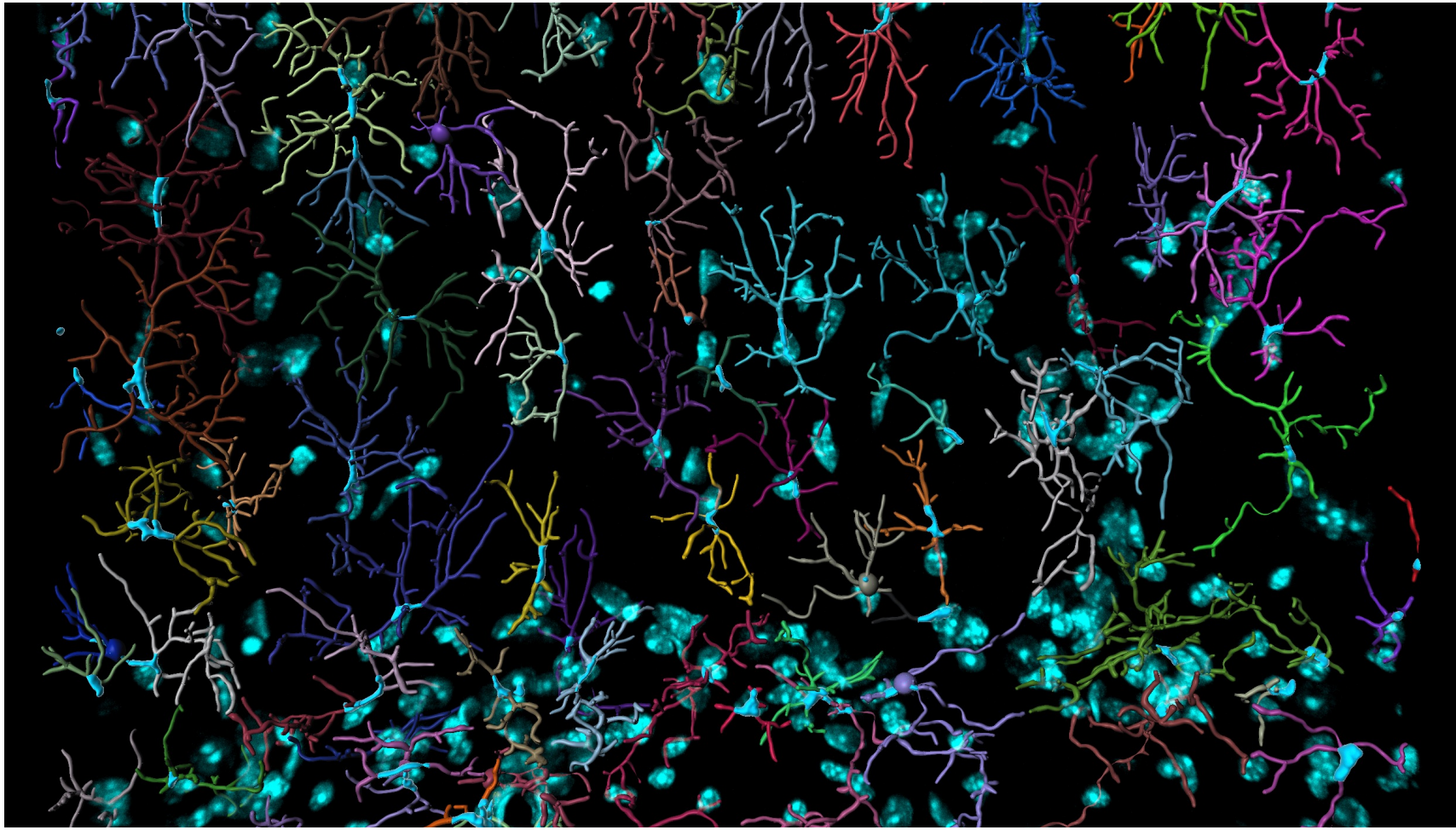
- **Intensity**
- **Distance to Spots**
  - Colocalization
- **ML-based creation**
  - Batchability
- **EoU Improvements**



Imaris 10.0 – Neuroscience

Neuroscience

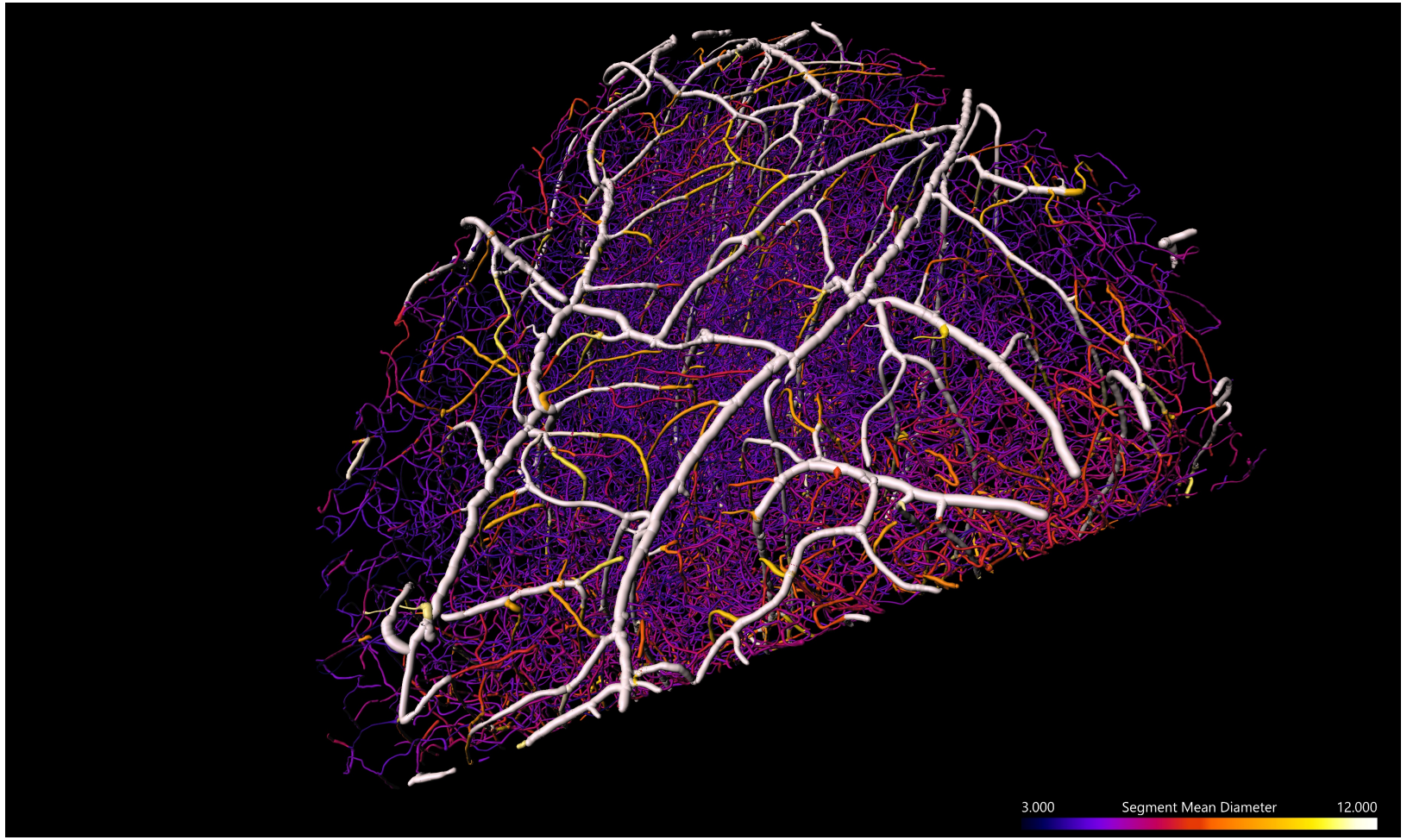
- **Tree Structure for Neurons**
  - Branching
  - Diameter
- **Spine characterization**
- **Microglia**
  - Alzheimer’s Disease
- **Astrocytes**
- **Axons**



Imaris 10.0 – AI Powered Filament Tracer

Vasculature

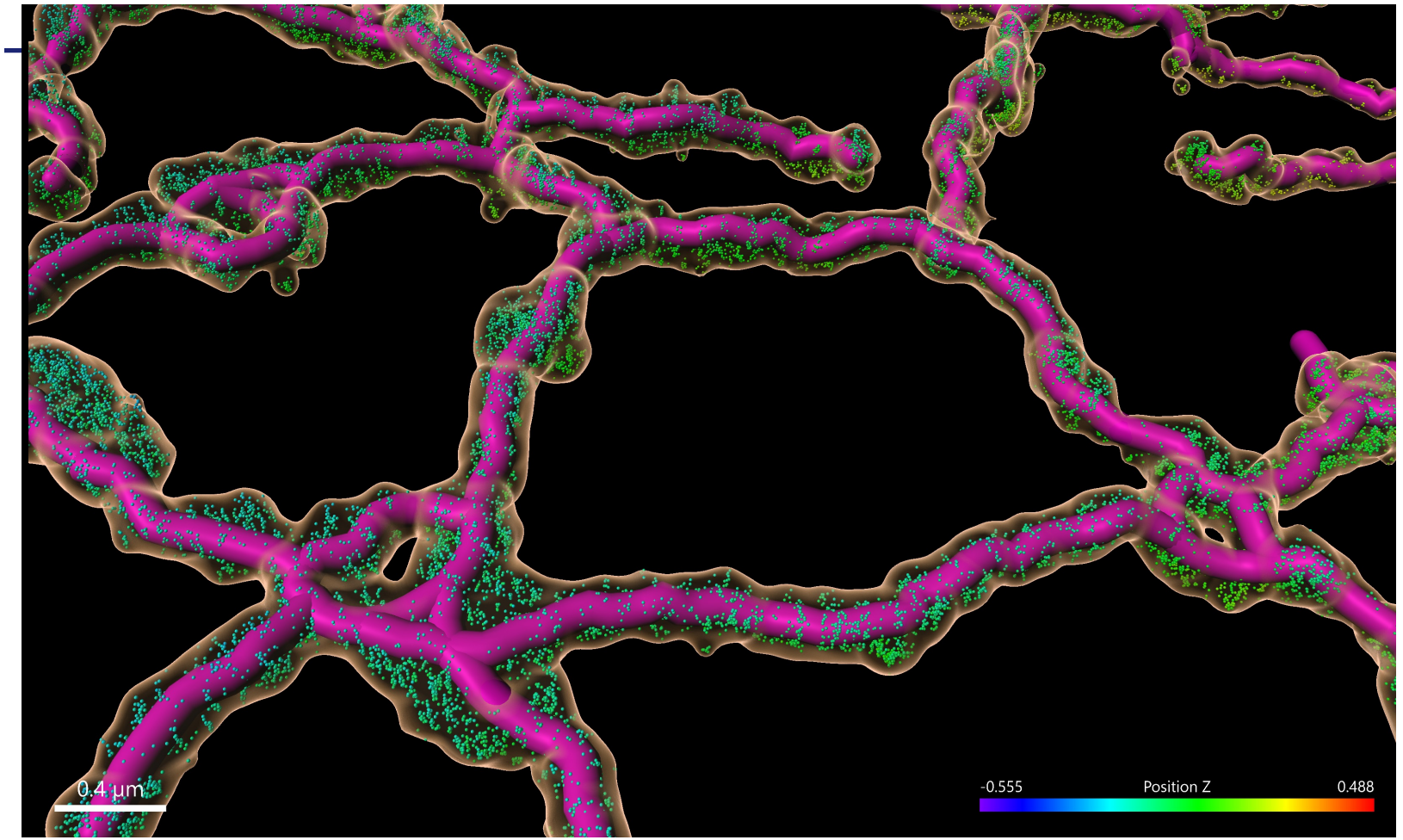
- **Network**
  - Multi-scale diameter
- **Vast speed increase**
- **Distance to Spots**
  - Colocalization
- **ML-based creation**
  - Batchable
- **EoU Improvements**



Imaris 10.0 – AI Powered Filament Tracer

Sub-cellular Organelles

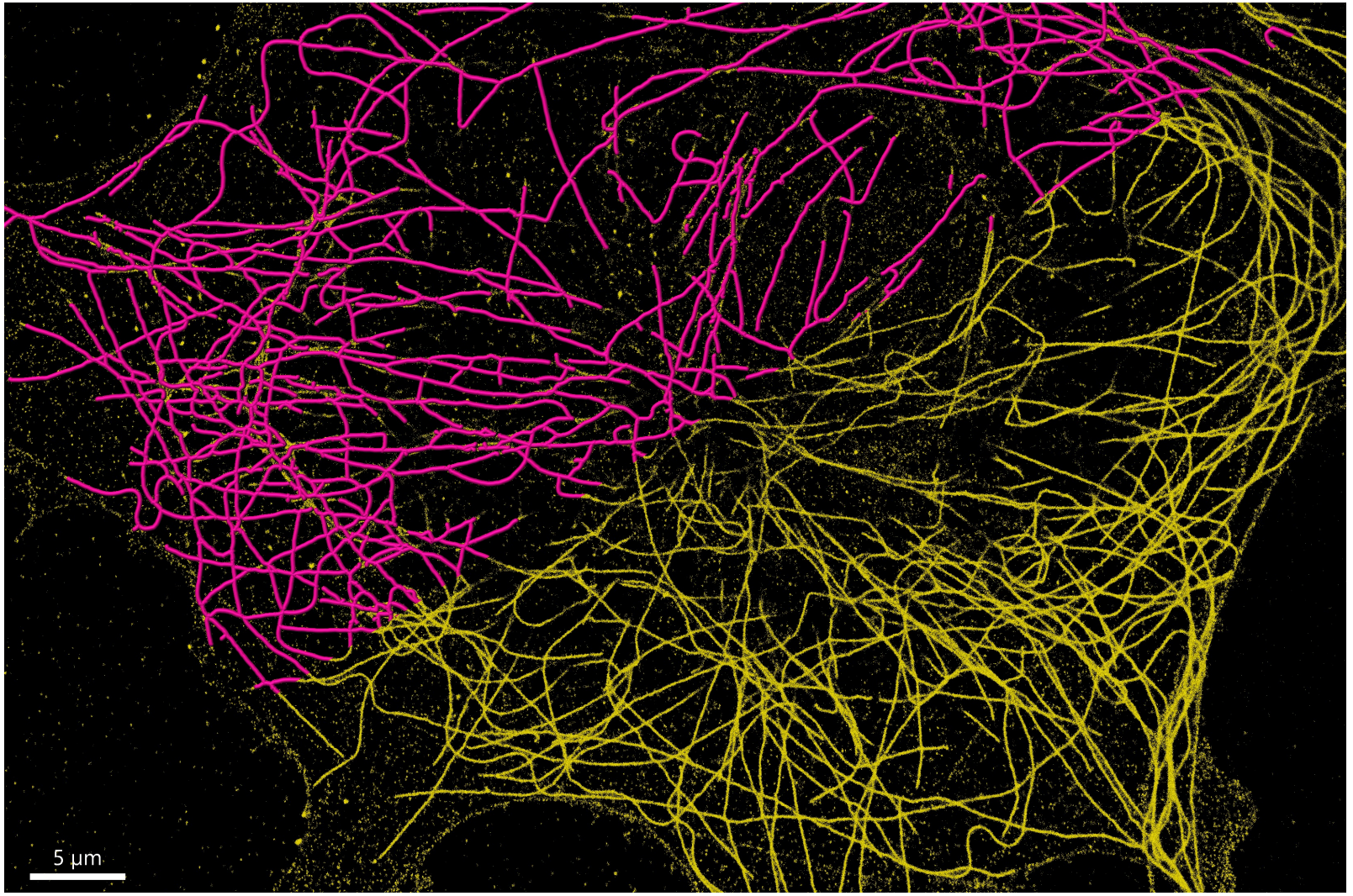
- **In harmony with DF600**
- **Vast speed increase**
- **Distance to Spots**
  - Colocalization
- **ML-based creation**
  - Batchable
- **EoU Improvements**



Imaris 10.0 – Sub-cellular Organelles, etc.

Resolution, resolution, resolution!

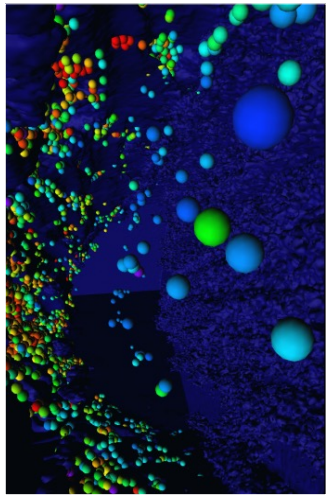
- **Requires acquisition with a super-res technique**
  - DF600 with SMLM
  - SIM



Detect

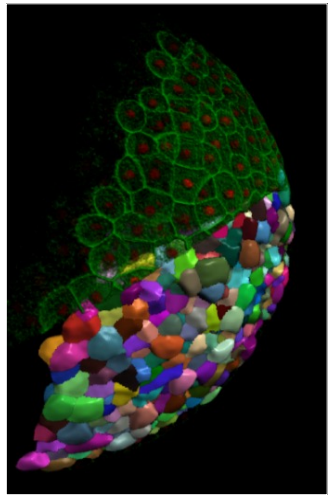
Track

Spot

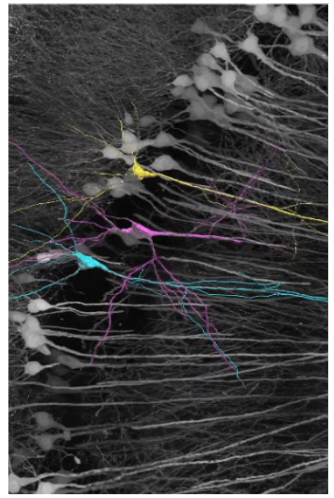


Surface

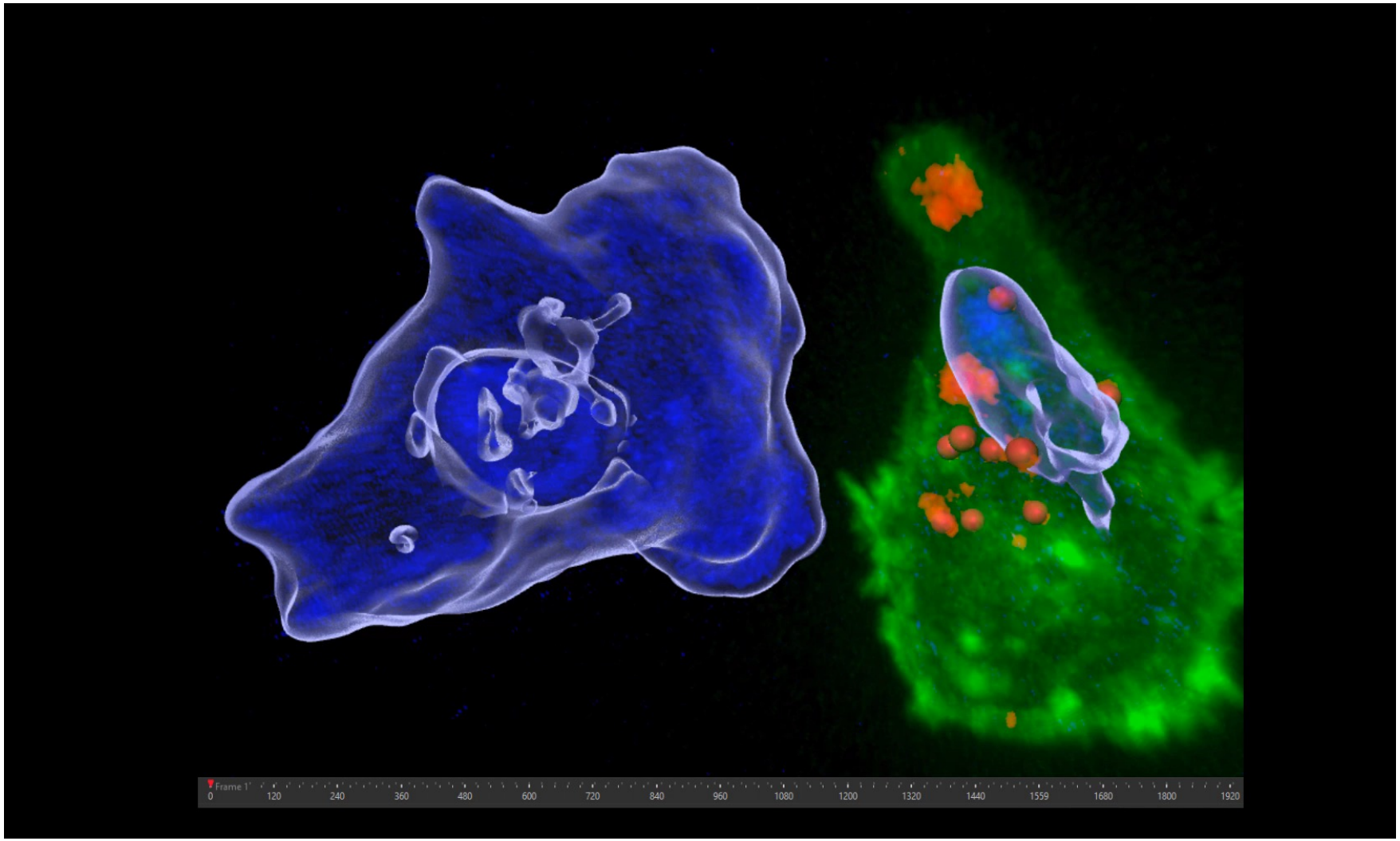
Cell



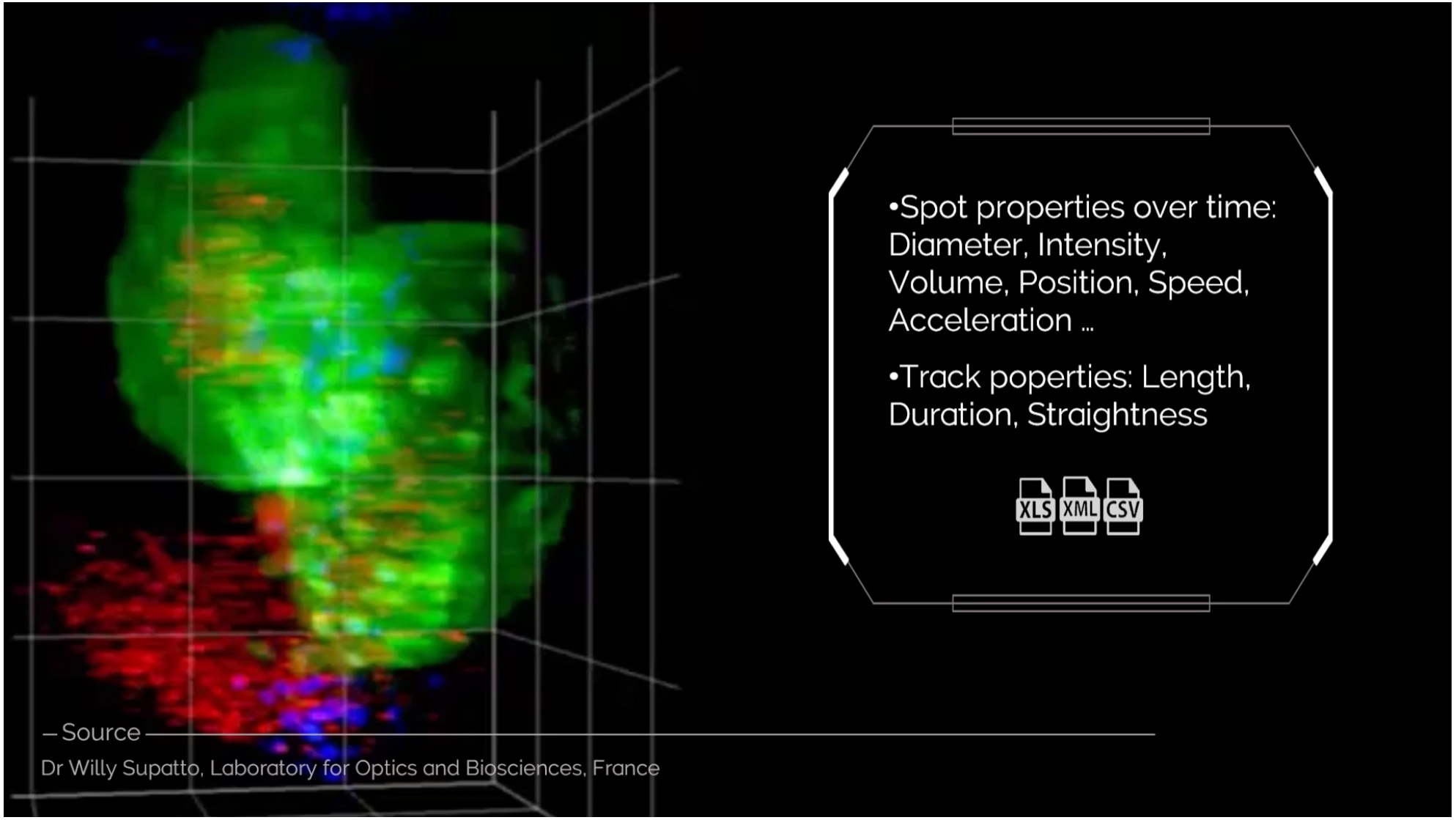
Filament



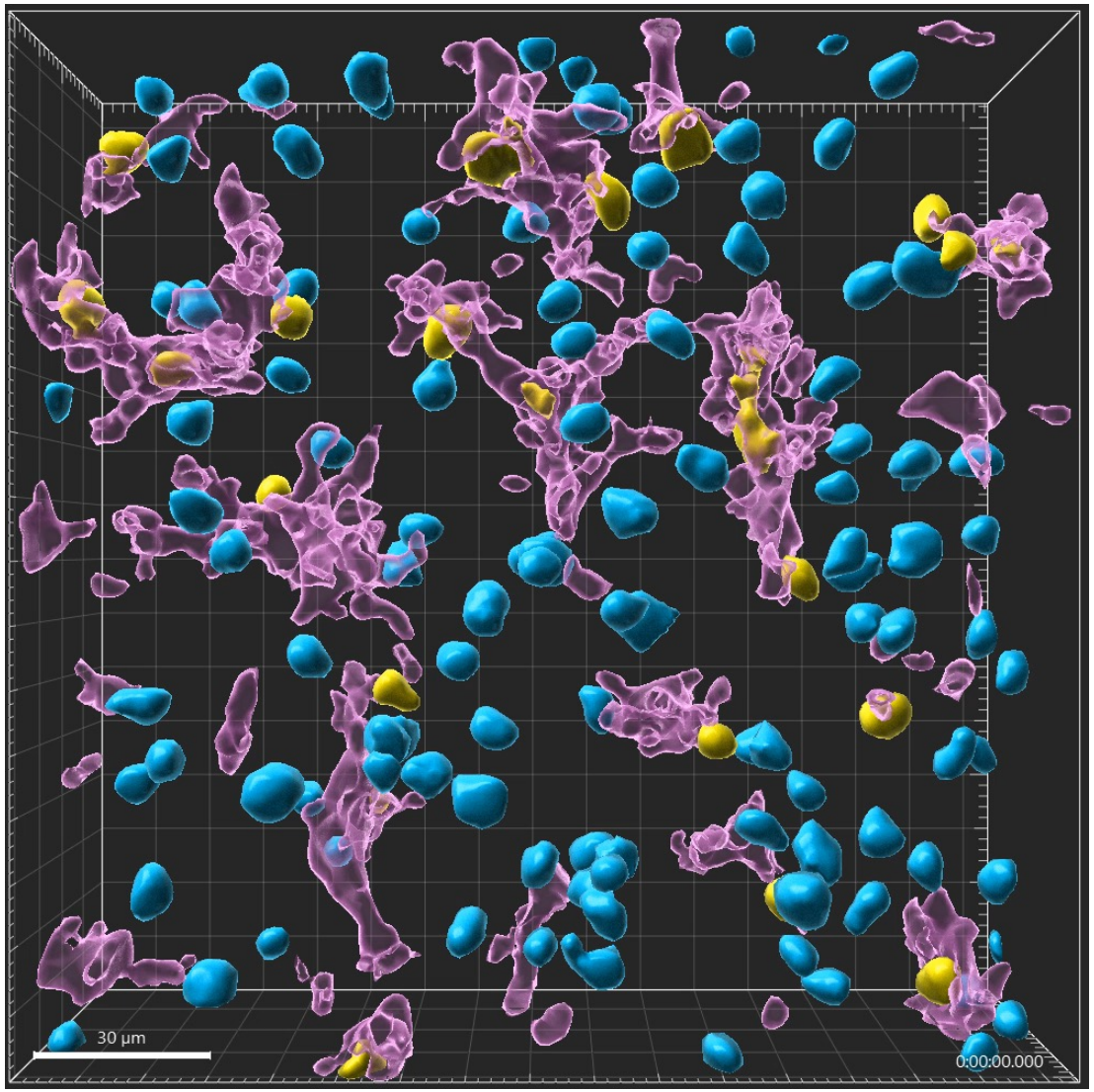
Track



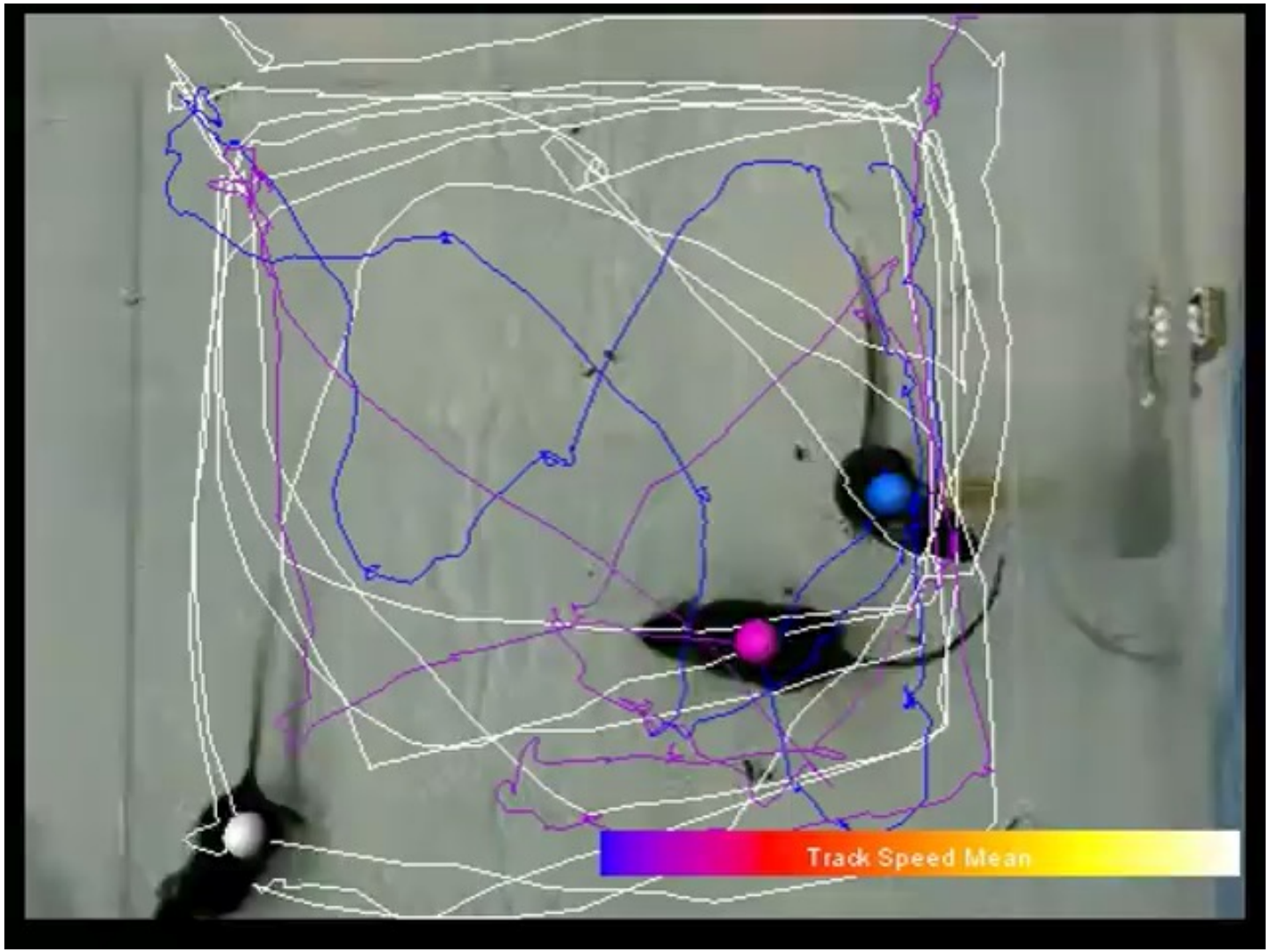
Track



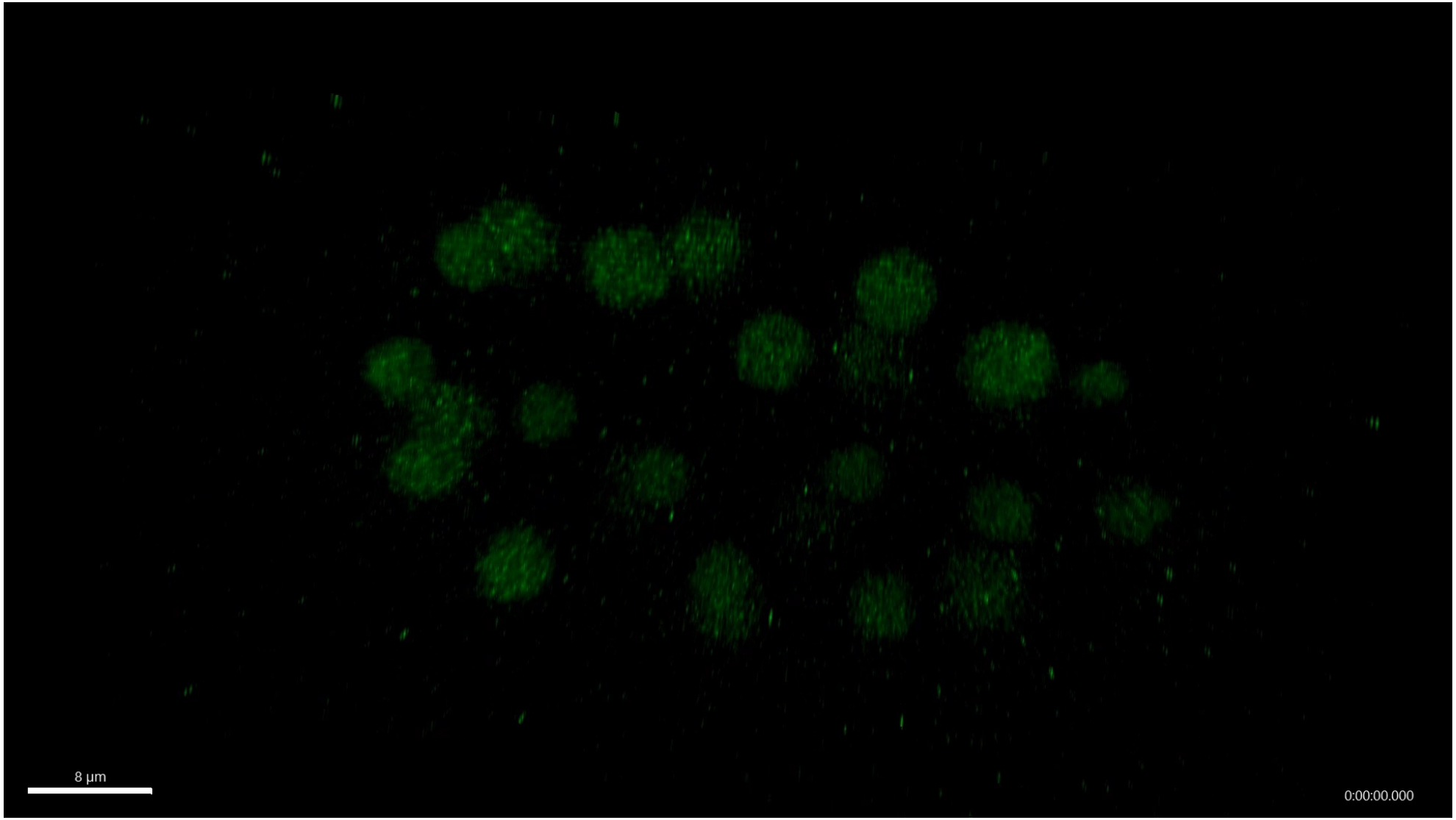
Track



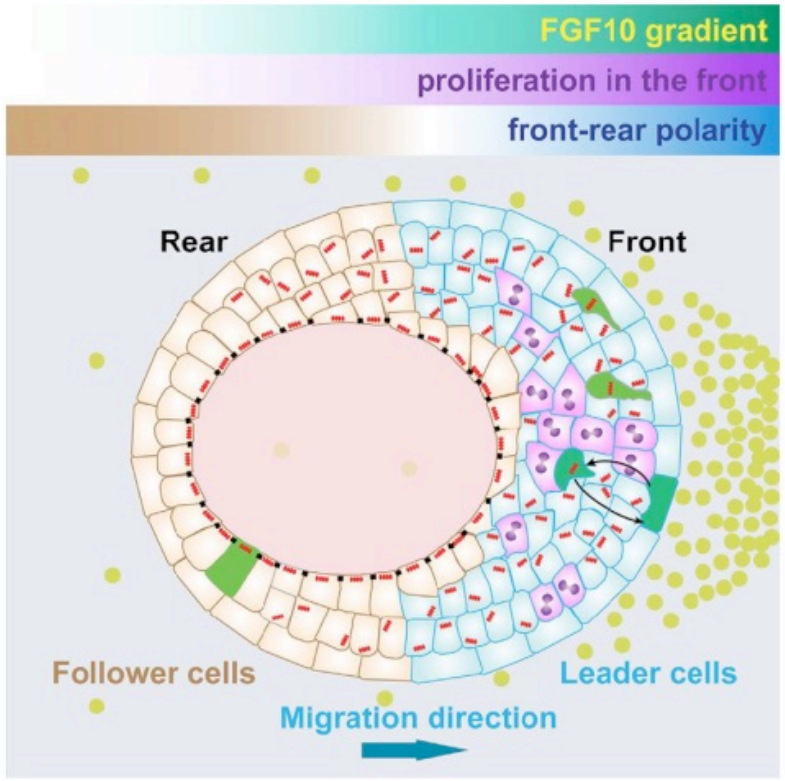
Track



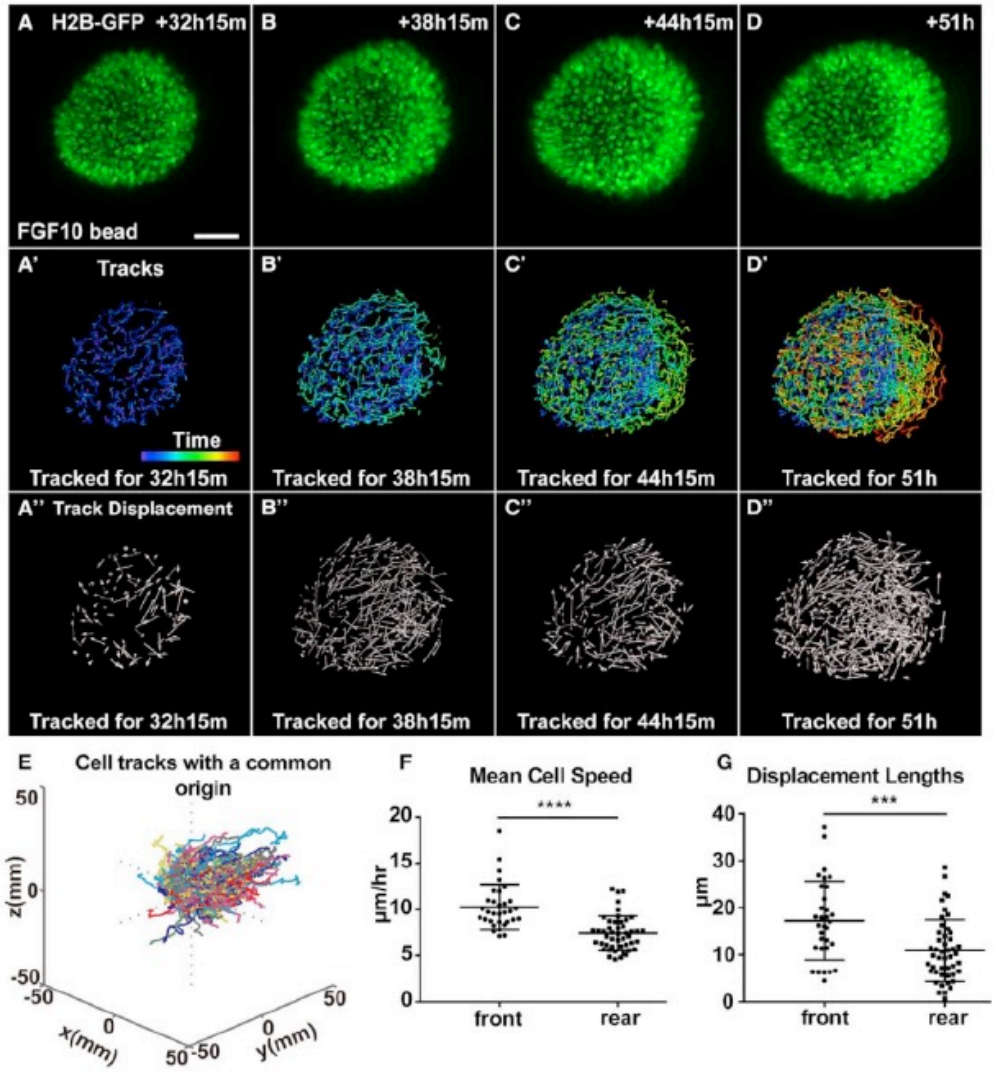
Track



Application



Lu et al. Cell Reports. 2020

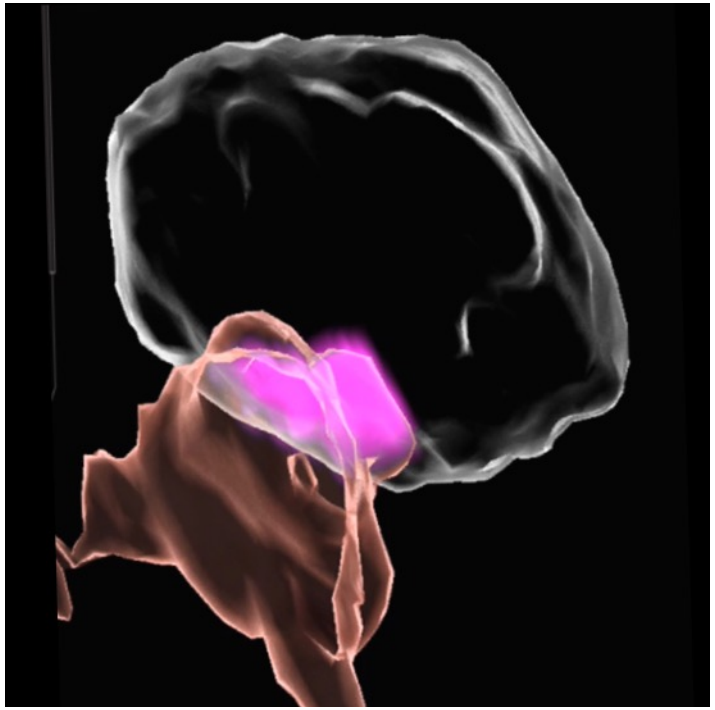


Detect Summary

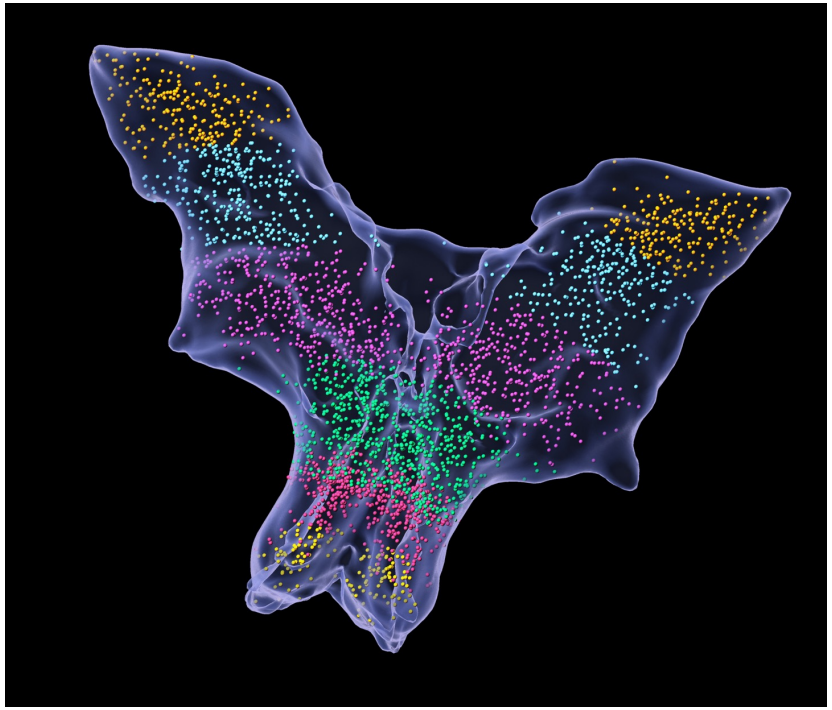
	Spot	Surface	Cell	Filament
Intensity	√	√	√	X
Counts. Positions	√	√	√	√
Diameters	√	X	√	√
Volume, Area & Morphology	X Est. Volume	√	√	X Est. Volume
Intercellular Component Analysis: Num. Vesicles/Cell&Nucleus Num. Nuclei/Cell	X	X	√	X
Membrane Staining	X	X	√	X
Network Complexity: Lengths, Branches, Scholl, Straightness, Orientation, Spines…	X	X	X	√
Track	√	√	√	√

Analyse

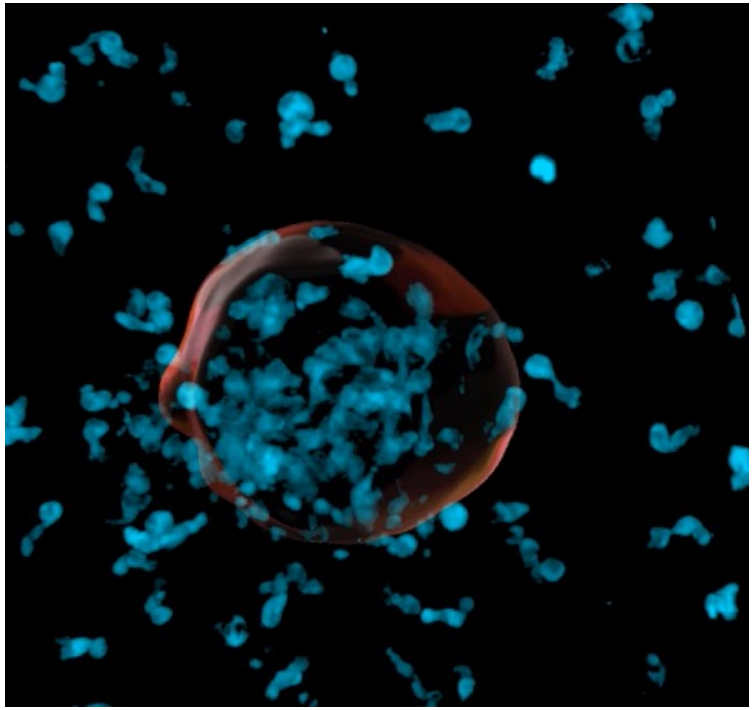
Colocalization



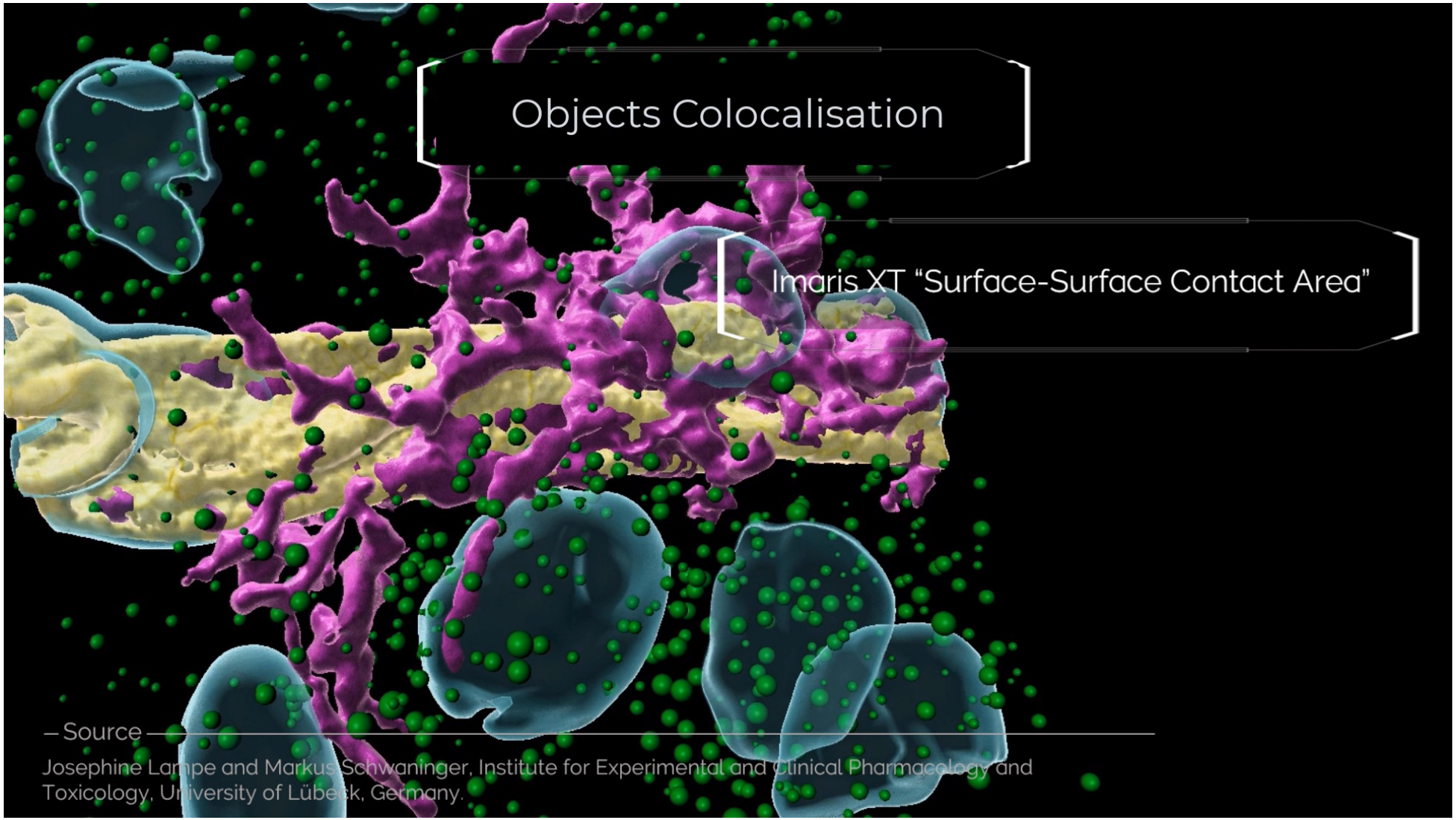
Object Classification



Affinities

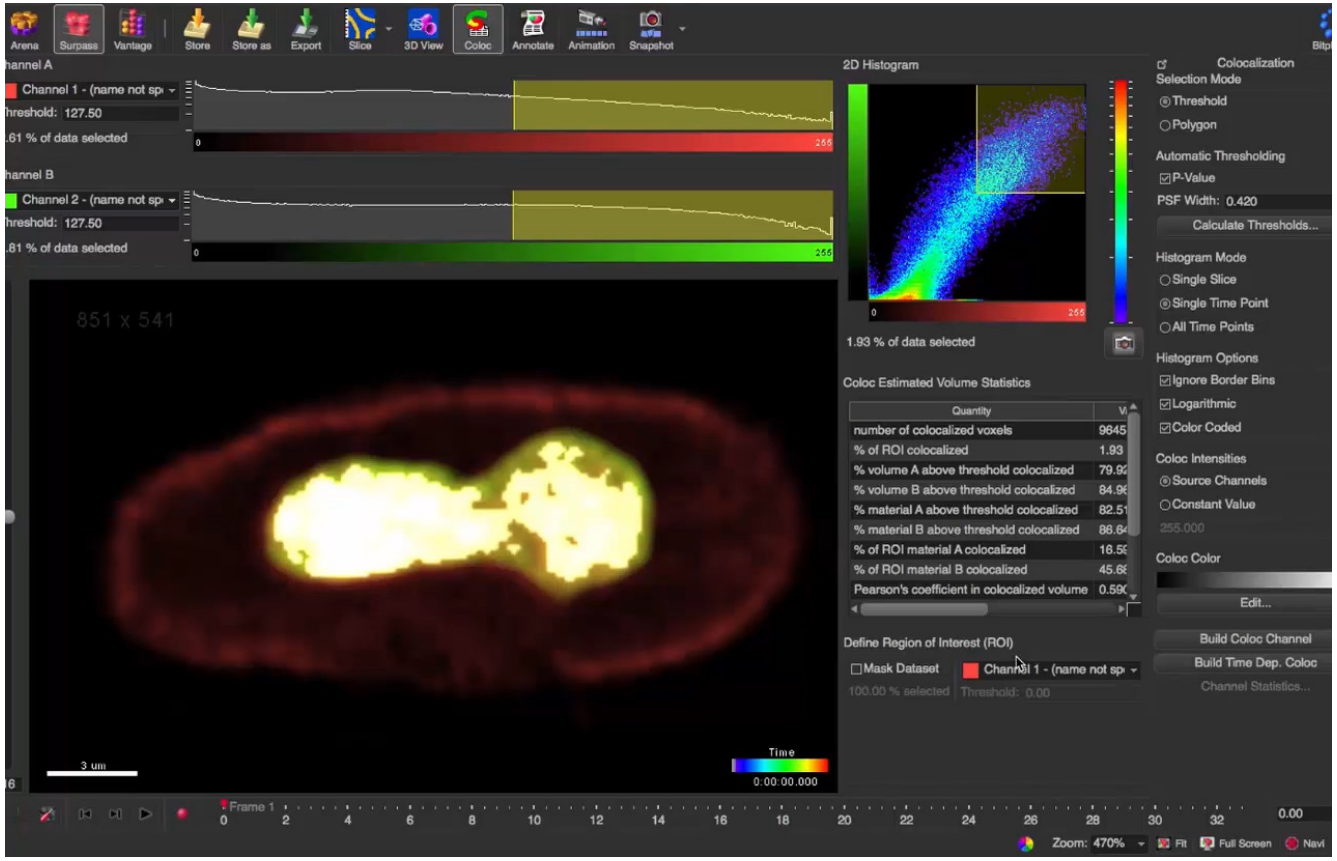


Colocalization



Colocalization – ImarisColoc

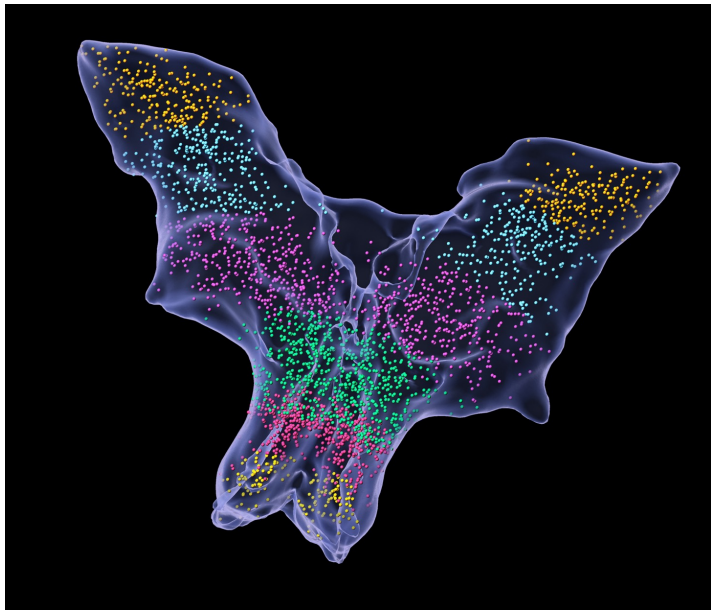
- ImarisColoc is the most powerful colocalization analysis tool to quantify and document codistribu-tion of multiple stained biological components.
  - Co-localization available for 2D, 3D data and time series
  - Co-localized regions can be presented as new 3D or 4D color channel
  - Users can expand or narrow the region from which histograms for colocalize-tion are computed
  - Automatic calculations: **Pearson's coefficient**, **Mander's coefficient**, co-localized voxels, co-localized percentages



Object Classification

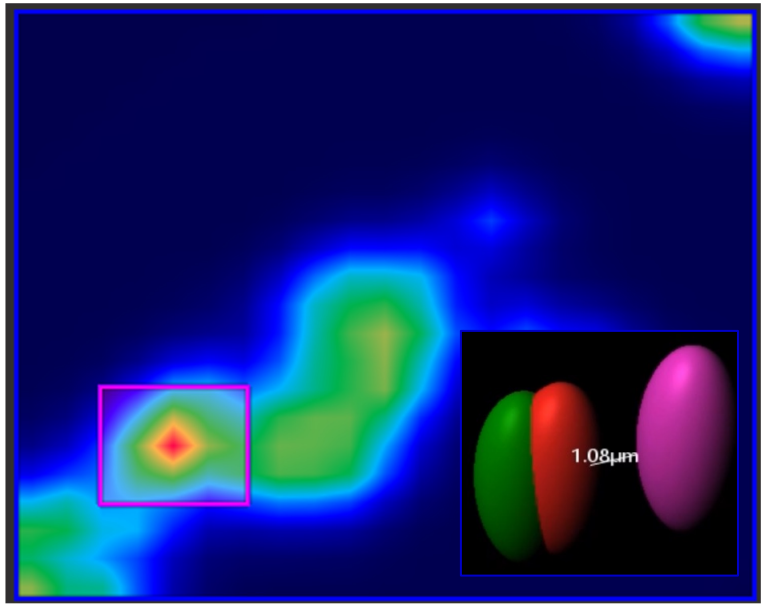
1 Parameter

Ex: Cell migration



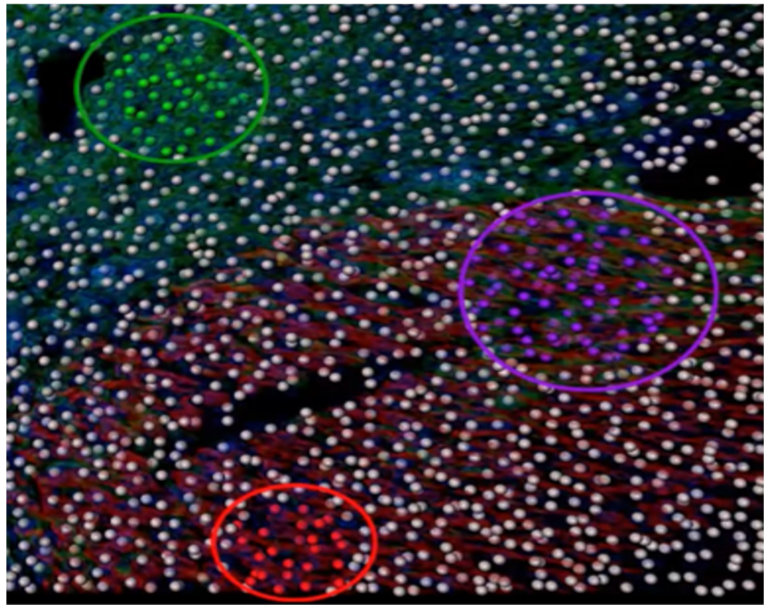
2 Parameters

Ex: Triplets colocalization

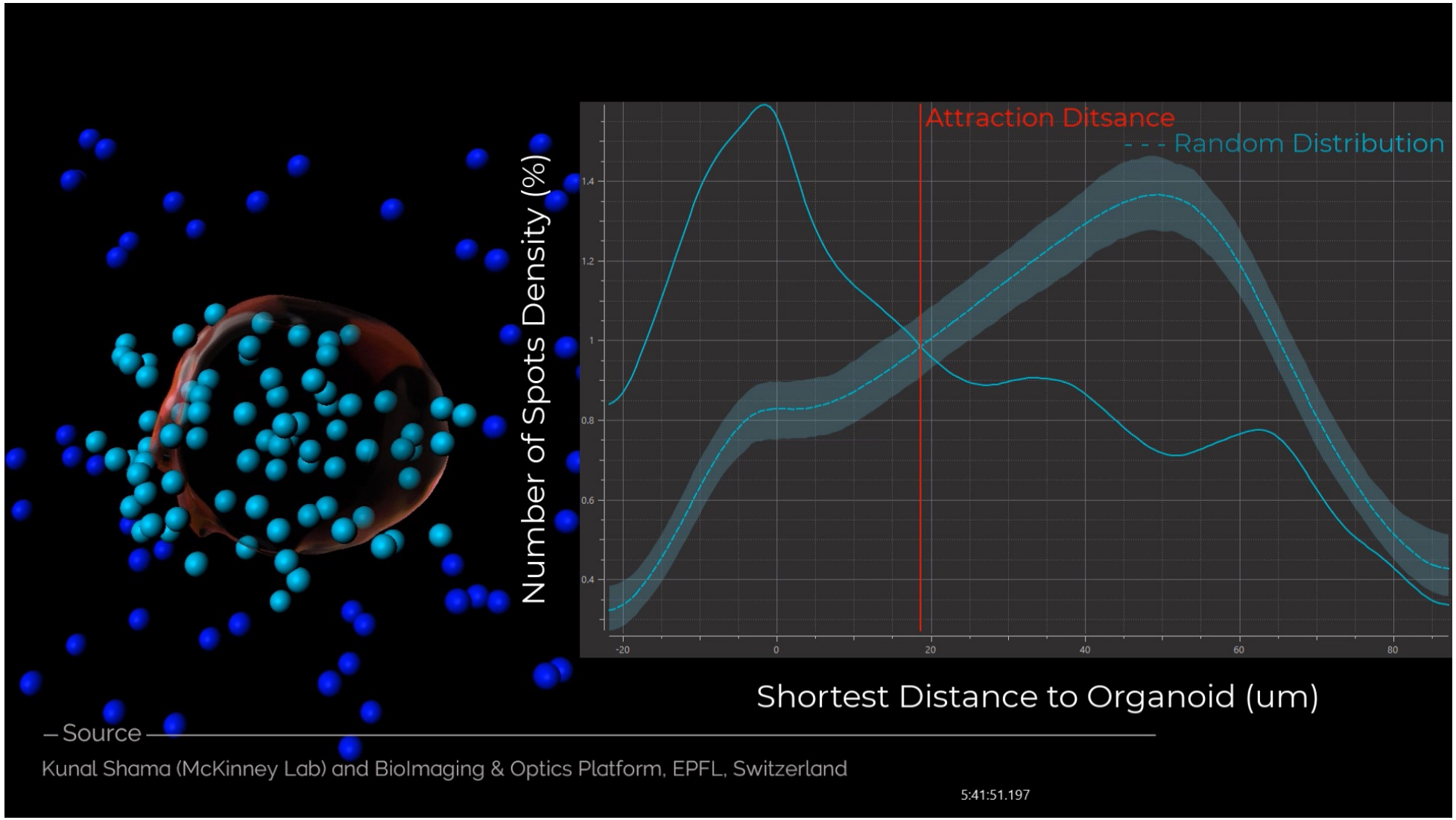


Machine Learning

Ex: Identification of regions



Affinities



Customization

Expand IMARIS power with Imaris XTension (plugins)

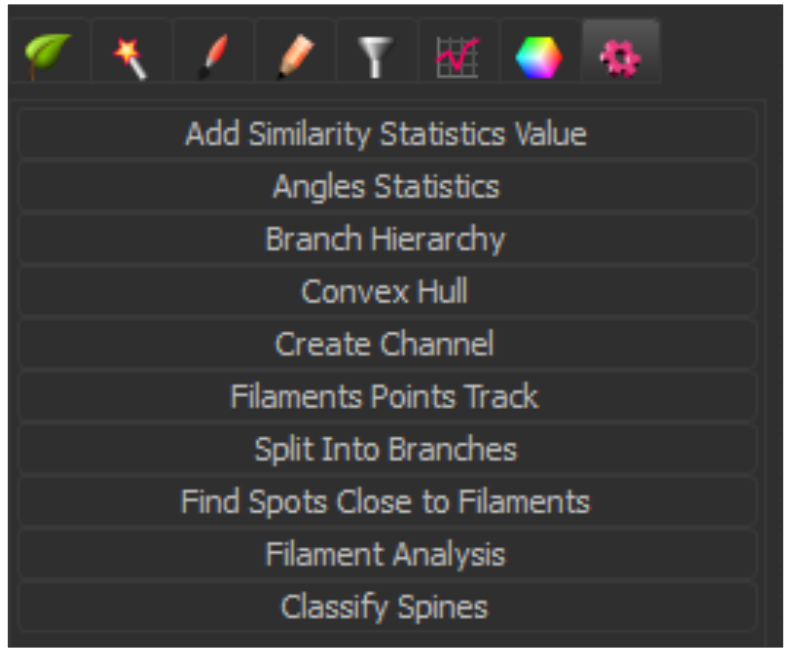
Write Your Own XTensions

Java

Python

Matlab

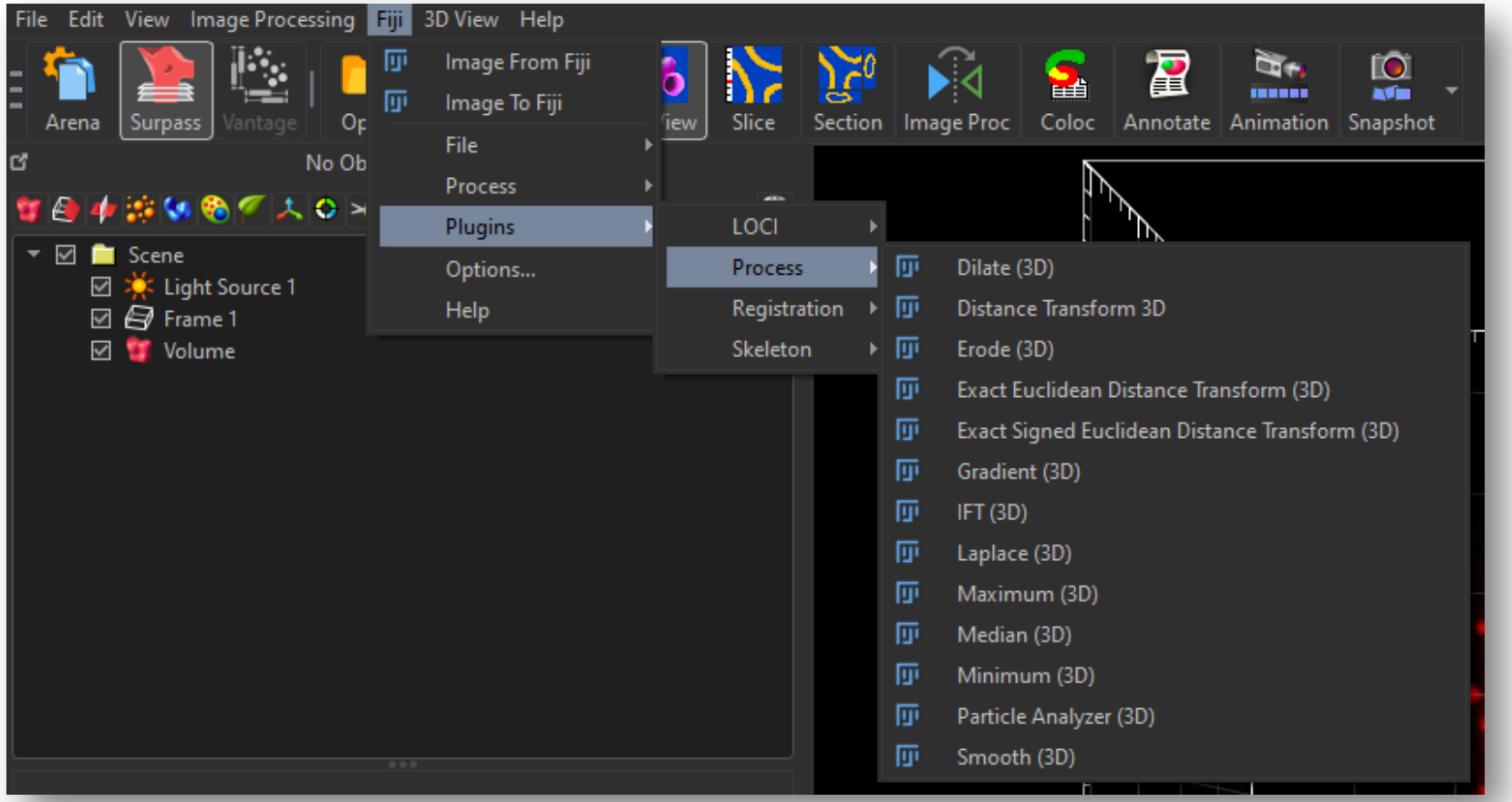
Integrate Xtensions



Customization

Connect to Fiji & ImageJ

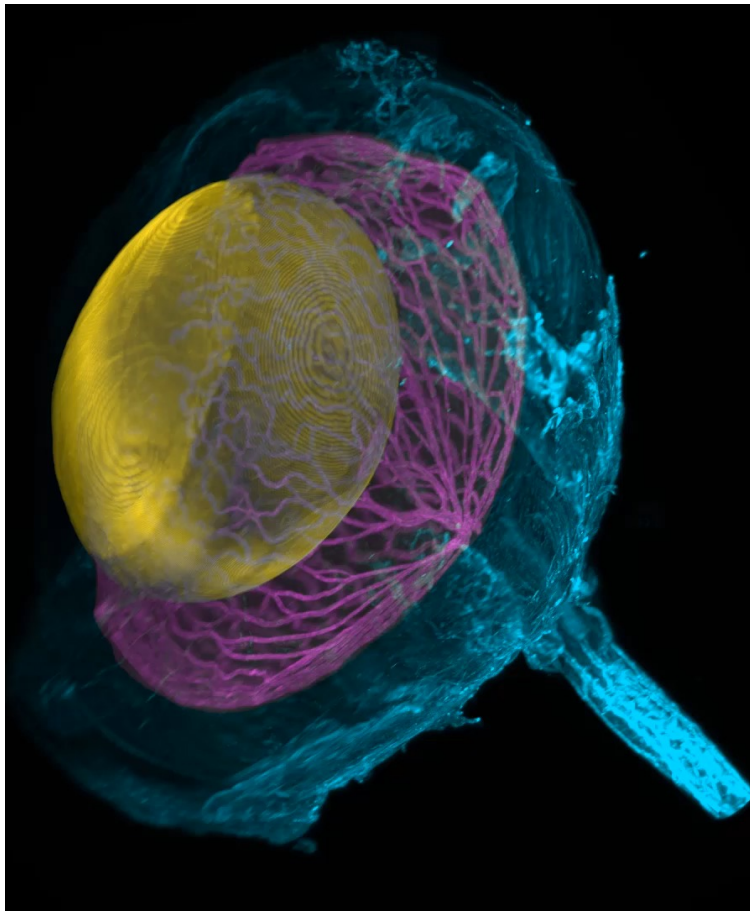
ImageJ



- Multiple plugins already incorporated
- Direct Bridging

Share

Animation

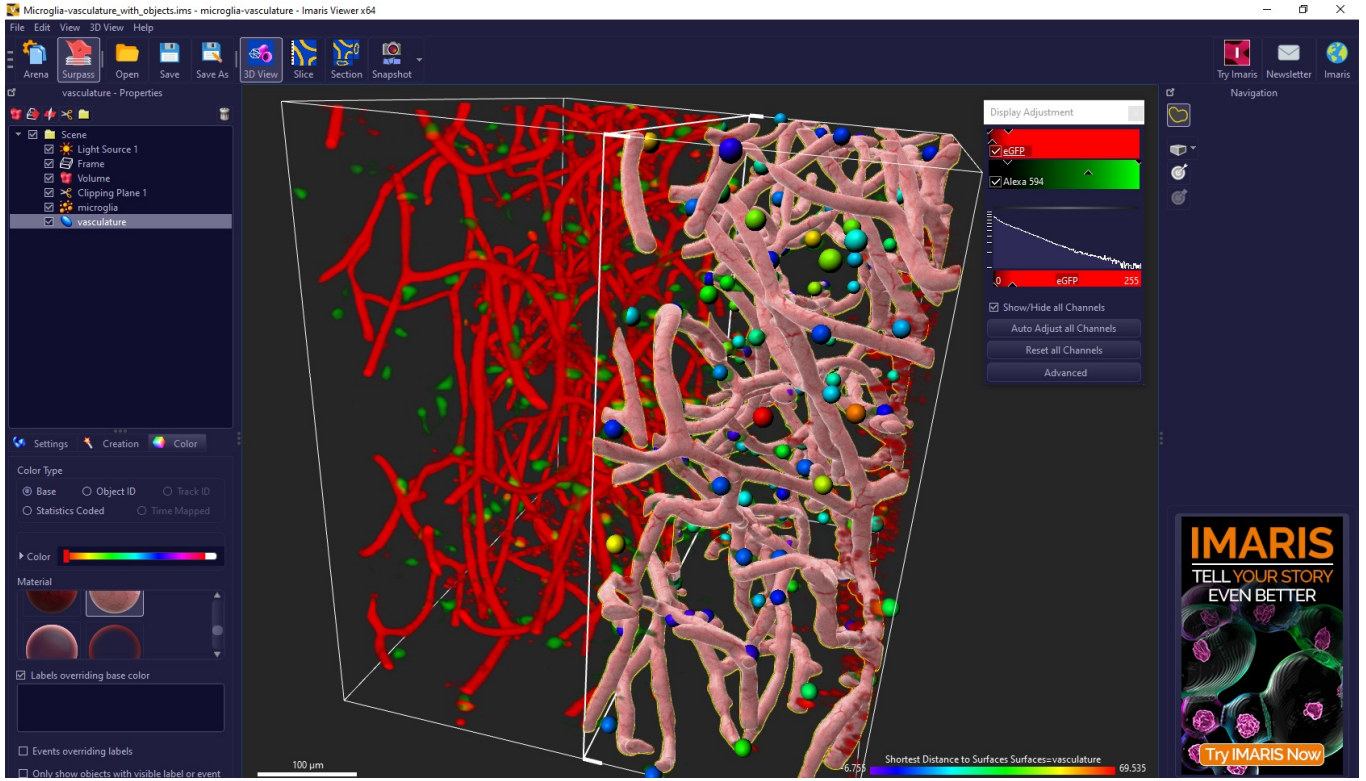


Snapshot

Share Result

Share Support OXFORD INSTRUMENTS IMARIS

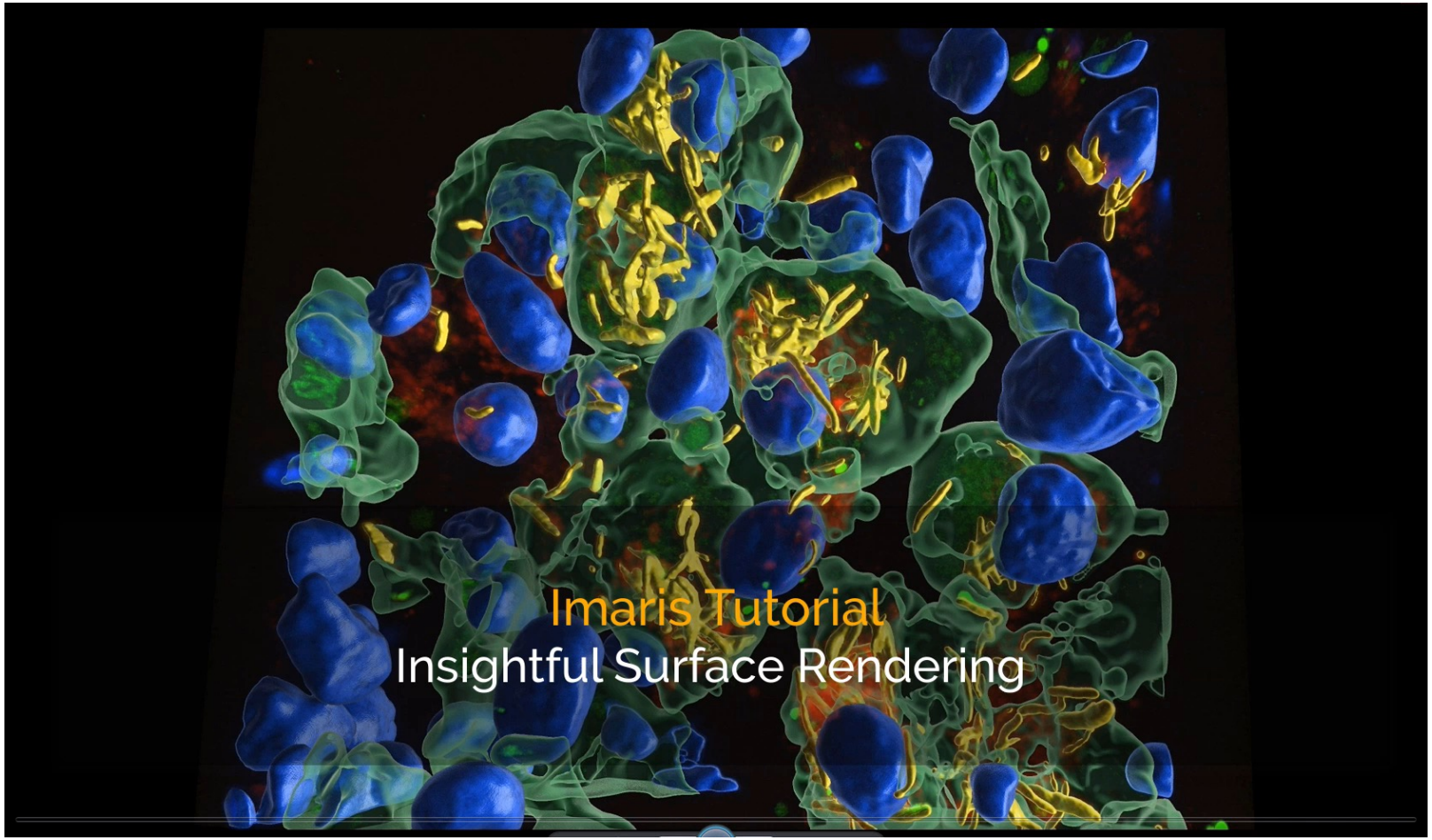
Imaris viewer



Learning center

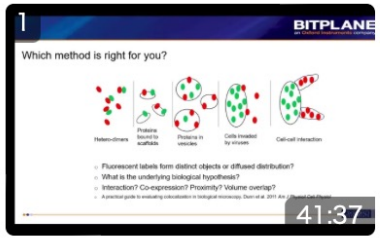
imaris.oxinst.com/learning/

- Webinar recordings
- Customer case Study
- Tutorial videos
- IMARIS Homeschools



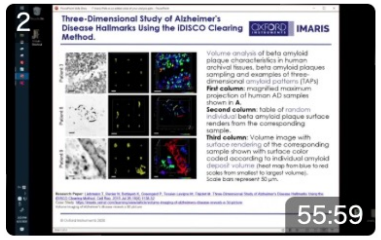
Support Bilibili: 牛津仪器 - Imaris

操作教程



Various ways of solving the colocalization problem

1521 2020-5-28

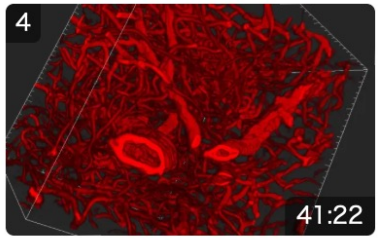


Imaris Plots as an added value of your analysis

685 2020-6-2

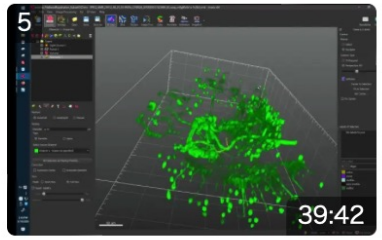
Batch-make your workflows more efficient

666 2020-5-27



Analysis of Vasculature-Combining multiple Imaris

1834 2020-5-21



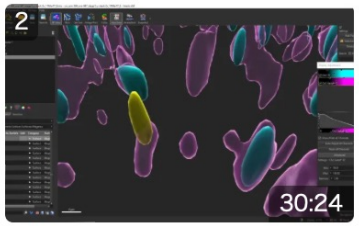
Filament Tracer manual

1651 2020-5-19

新版本发布

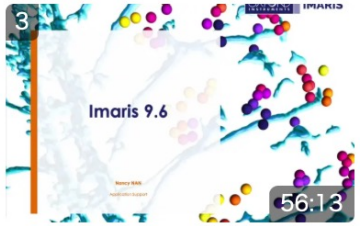
Imaris 9.8 | I can see clearly now!

1006 2021-11-9



Imaris 9.7 Diving into Structure and Dynamics

922 2021-3-3



【合集】Imaris9.6 新功能介绍

2809 2020-8-21

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前沿应用分享

Imaris for Immunology Research

734 2021-10-19

Imaris for Cancer Research

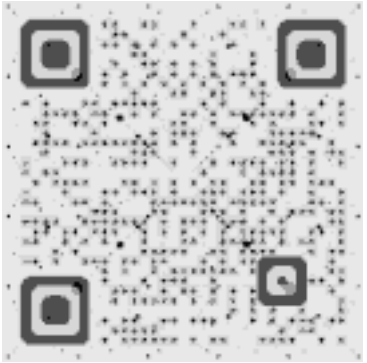
242 2021-10-19

Bone Analysis with Surface Tool~~

734 2020-11-20

IMARIS Resources

- Free Imaris File Converter:
  https://imaris.oxinst.com/microscopy-imaging-software-free-trial
- Free Imaris Viewer:
  https://imaris.oxinst.com/imaris-viewer
- Free 10 Days Trail:
  https://imaris.oxinst.com/microscopy-imaging-software-free-trial
- System Requirement for Windows and Mac:
  https://imaris.oxinst.com/support/system-requirements
- Imaris Home School
  https://imaris.oxinst.com/homeschool
- Bilibili, Account：牛津仪器-Imaris
  https://space.bilibili.com/512602011/video



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IMARIS in Publications

SCIENCE ADVANCES | RESEARCH ARTICLE

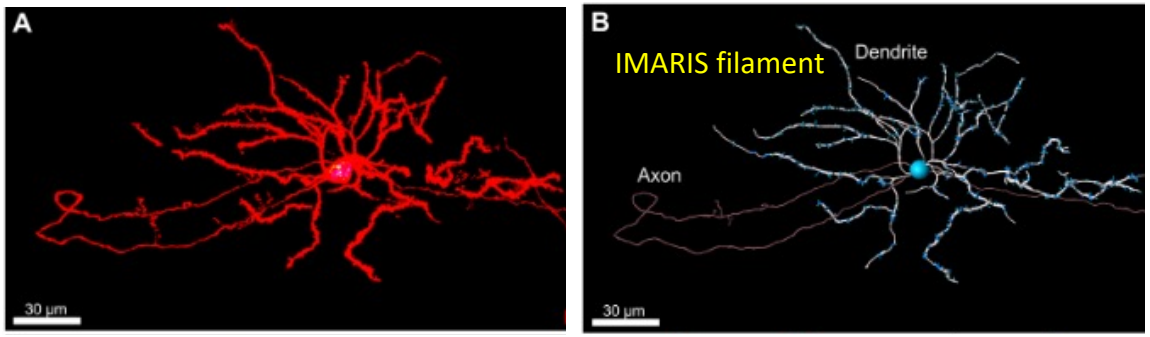
NEUROSCIENCE

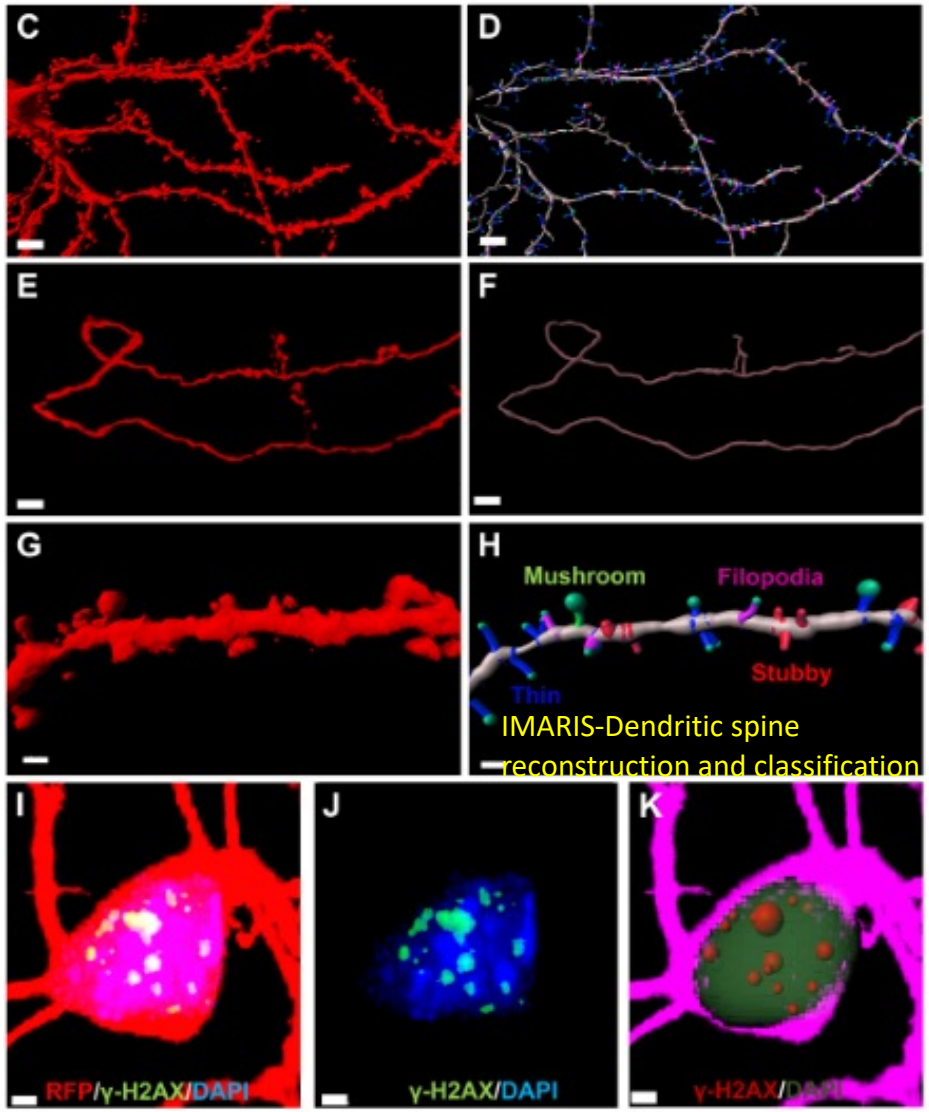
Tracing brain genotoxic stress in Parkinson's disease with a novel single-cell genetic sensor

Madison Wynne El-Saadi[1], Xinli Tian[1], Mychal Grames[1], Michael Ren[1], Kelsea Keys[1], Hanna Li[1], Erika Knott[1], Hong Yin[2], Shile Huang[3], Xiao-Hong Lu[1]*

To develop an in vivo tool to probe brain genotoxic stress, we designed a viral proxy as a single-cell genetic sensor termed PRISM that harnesses the instability of recombinant adeno-associated virus genome processing and a hypermutable repeat sequence–dependent reporter. PRISM exploits the virus-host interaction to probe persistent neuronal DNA damage and overactive DNA damage response. A Parkinson's disease (PD)–associated environmental toxicant, paraquat (PQ), inflicted neuronal genotoxic stress sensitively detected by PRISM. The most affected cell type in PD, dopaminergic (DA) neurons in substantia nigra, was distinguished by a high level of genotoxic stress following PQ exposure. Human alpha-synuclein proteotoxicity and propagation also triggered genotoxic stress in nigral DA neurons in a transgenic mouse model. Genotoxic stress is a prominent feature in PD patient brains. Our results reveal that PD-associated etiological factors precipitated brain genotoxic stress and detail a useful tool for probing the pathogenic significance in aging and neurodegenerative disorders.

El-Saadi, M. W. *et al.* Tracing brain genotoxic stress in Parkinson's disease with a novel single-cell genetic sensor. *Sci. Adv.* **8**, eabd1700 (2022).





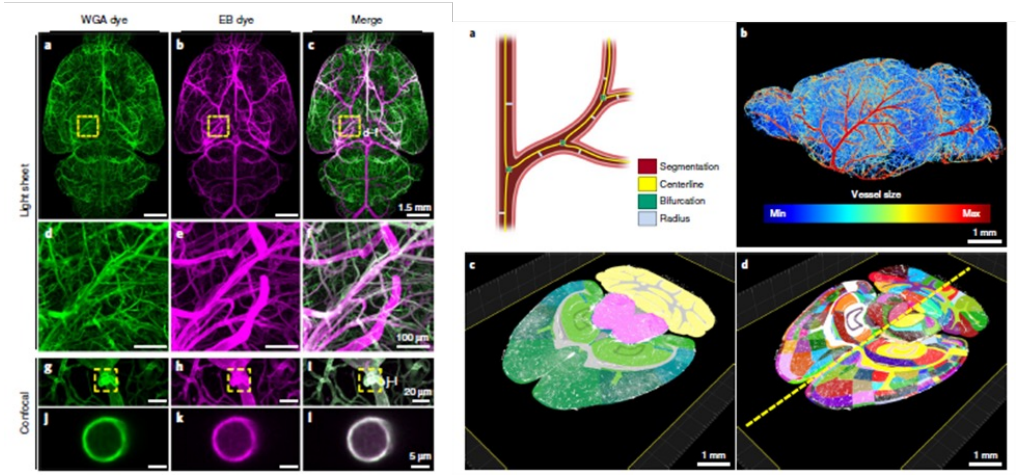
IMARIS in Publications

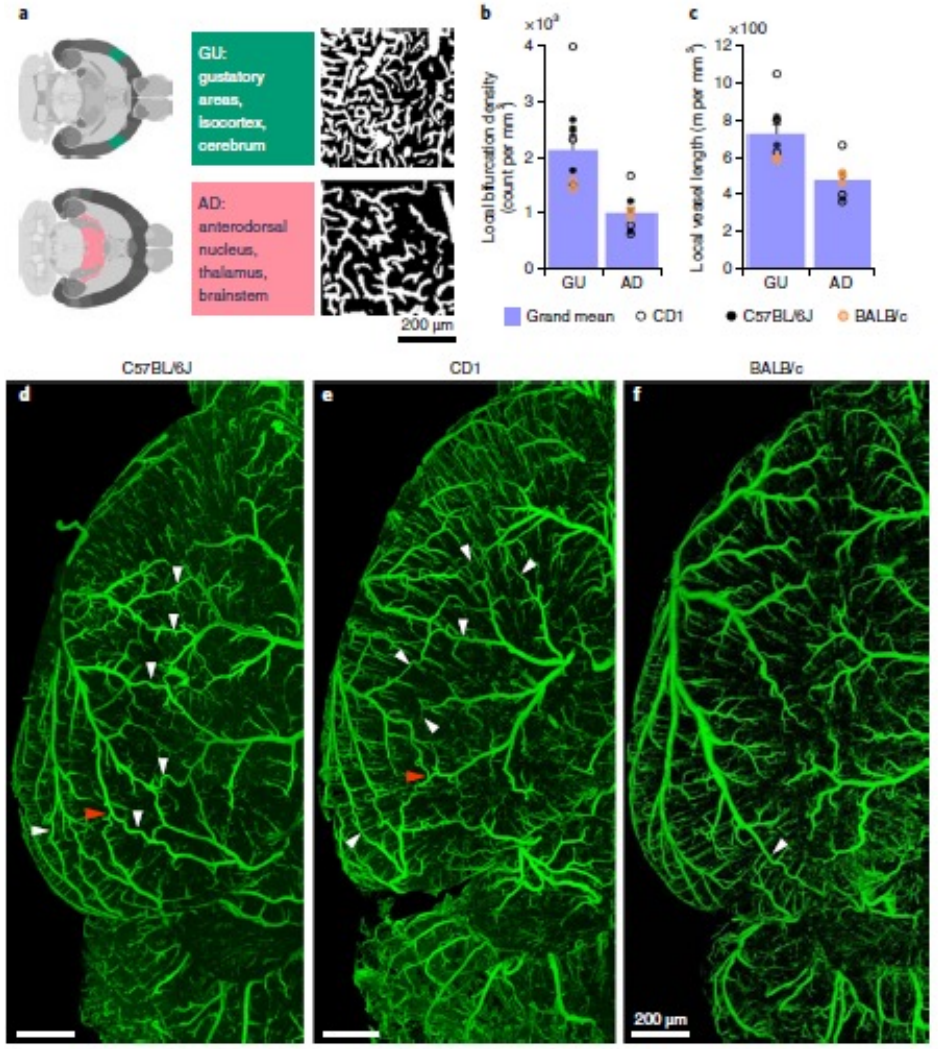
ARTICLES
https://doi.org/10.1038/s41592-020-0792-1
nature methods

Machine learning analysis of whole mouse brain vasculature

Mihail Ivilinov Todorov[1,2,3,10], Johannes Christian Paetzold[4,5,6,10], Oliver Schoppe[4,5], Giles Tetteh[4], Suprosanna Shit[4,5,6], Velizar Efremov[4,7], Katalin Todorov-Völgyi[2], Marco Düring[2,8], Martin Dichgans[2,8,9], Marie Piraud[4], Bjoern Menze[4,5,6,11] and Ali Ertürk[1,2,8,11]

Tissue clearing methods enable the imaging of biological specimens without sectioning. However, reliable and scalable analysis of large imaging datasets in three dimensions remains a challenge. Here we developed a deep learning-based framework to quantify and analyze brain vasculature, named Vessel Segmentation & Analysis Pipeline (VesSAP). Our pipeline uses a convolutional neural network (CNN) with a transfer learning approach for segmentation and achieves human-level accuracy. By using VesSAP, we analyzed the vascular features of whole C57BL/6J, CD1 and BALB/c mouse brains at the micrometer scale after registering them to the Allen mouse brain atlas. We report evidence of secondary intracranial collateral vascularization in CD1 mice and find reduced vascularization of the brainstem in comparison to the cerebrum. Thus, VesSAP enables unbiased and scalable quantifications of the angioarchitecture of cleared mouse brains and yields biological insights into the vascular function of the brain.





Todorov, M. I. *et al.* Machine learning analysis of whole mouse brain vasculature. *Nat Methods* **17**, 442–449 (2020).

IMARIS in Publications

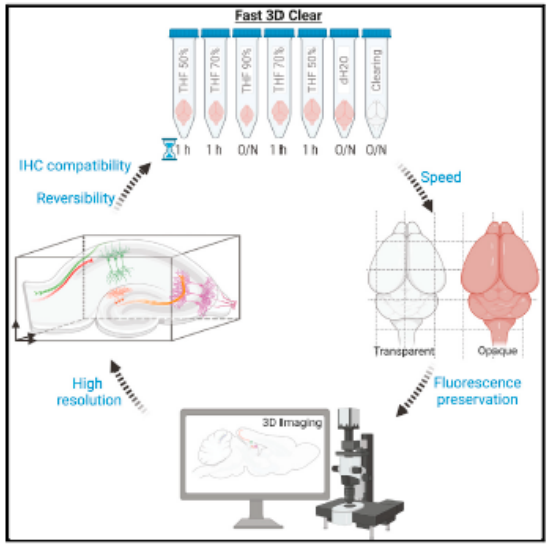
OXFORD INSTRUMENTS | IMARIS

Cell Reports
Methods

Report

A fast, aqueous, reversible three-day tissue clearing method for adult and embryonic mouse brain and whole body

Graphical abstract



Authors

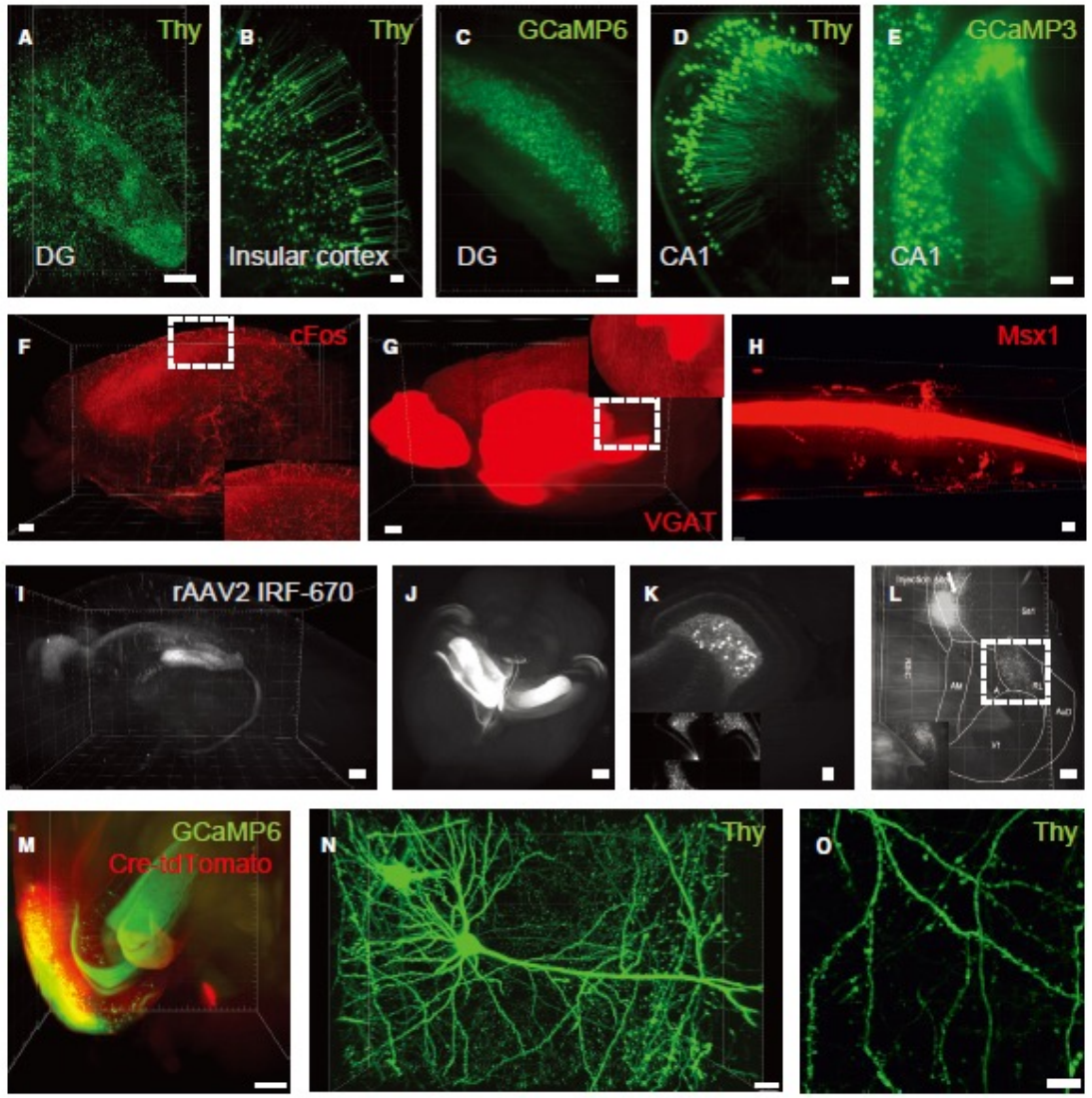
Stylianos Kosmidis, Adrian Negrean, Alex Dranovsky, Attila Losonczy, Eric R. Kandel

Correspondence

erk5@columbia.edu (E.R.K.), sk3440@columbia.edu (S.K.)

In brief

Tissue clearing enables the study of cells as units and as components of a network within intact organs. Kosmidis et al. develop an easy and speedy method for clearing large tissues and visualizing individual cells and their connections within the brain in 3D.



Kosmidis, S., Negrean, A., Dranovsky, A., Losonczy, A. & Kandel, E. R. A fast, aqueous, reversible three-day tissue clearing method for adult and embryonic mouse brain and whole body. *Cell Reports Methods* **1**, 100090 (2021).

IMARIS in Publications

nature medicine

ARTICLES

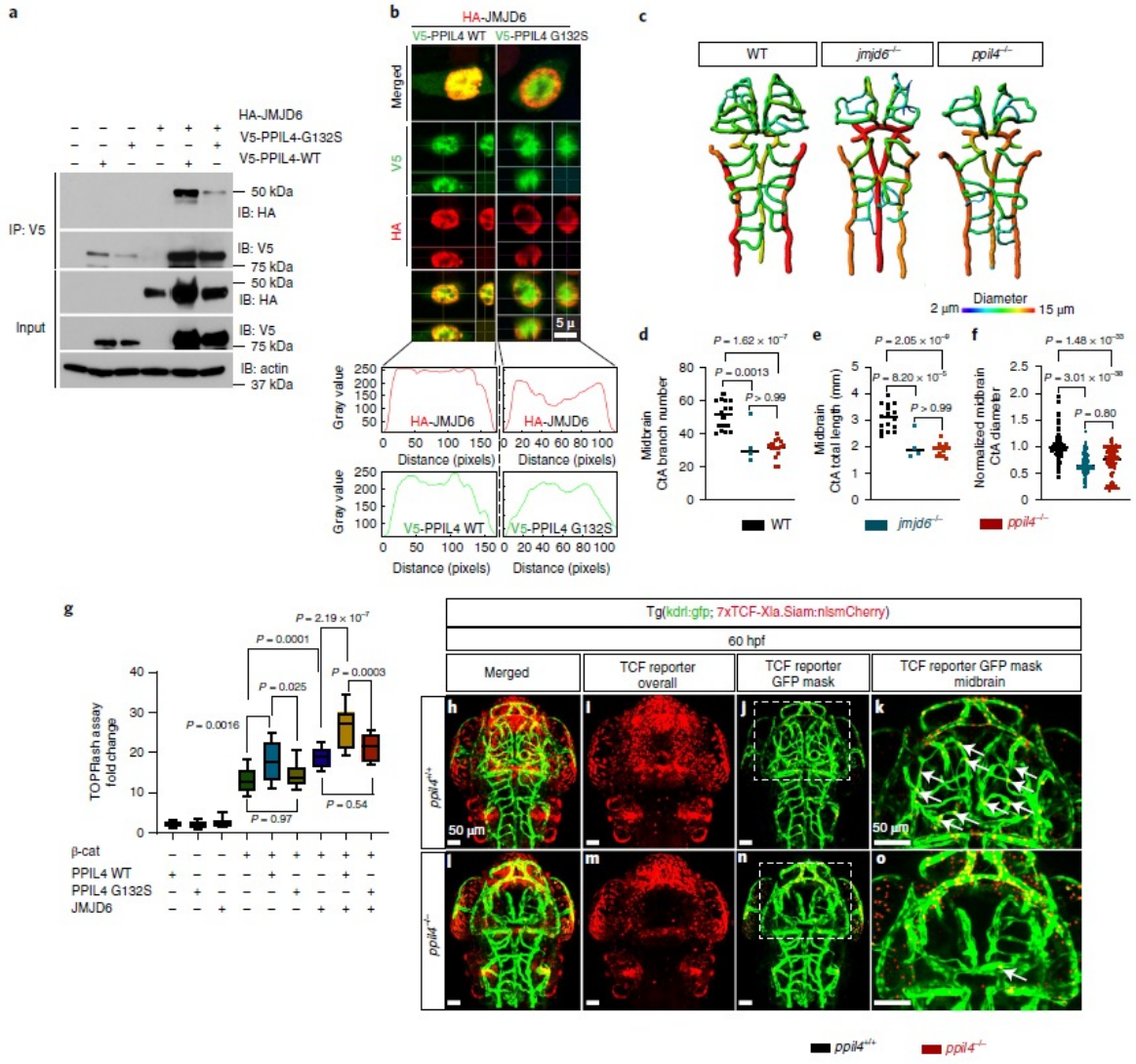
https://doi.org/10.1038/s41591-021-01572-7

Check for updates

PPIL4 is essential for brain angiogenesis and implicated in intracranial aneurysms in humans

Tanyeri Barak[1,2,3,4,18], Emma Ristori[2,5,18], A. Gulhan Ercan-Sencicek[1,2,3,4], Danielle F. Miyagishima[1,2,3,4], Carol Nelson-Williams[2], Weilai Dong[2,6], Sheng Chih Jin[2,6,7], Andrew Prendergast[5], William Armero[2,5], Octavian Henegariu[1,2,3,4], E. Zeynep Erson-Omay[1,2,3,4], Akdes Serin Harmancı[1,2,3,4], Mikhael Guy[8], Batur Gültekin[1], Deniz Kilic[1], Devendra K. Rai[1,2,3,4], Nükte Goc[1], Stephanie Marie Aguilera[1], Burcu Gülez[1], Selin Altinok[1], Kent Ozcan[1], Yanki Yarman[1], Süleyman Coskun[1,2,3,4], Emily Sempou[9], Engin Deniz[9], Jared Hintzen[5], Andrew Cox[2], Elena Fomchenko[1], Su Woong Jung[10], Ali Kemal Ozturk[11], Angeliki Louvi[1,4], Kaya Bilgüvar[2,4,12], E. Sander Connolly Jr.[13], Mustafa K. Khokha[2,9], Kristopher T. Kahle[1,14,15,16], Katsuhito Yasuno[1,2,3,4], Richard P. Lifton[2,6], Ketu Mishra-Gorur[1,2,3,4] ✉, Stefania Nicoli[2,5,17] ✉ and Murat Günel[1,2,3,4] ✉

Intracranial aneurysm (IA) rupture leads to subarachnoid hemorrhage, a sudden-onset disease that often causes death or severe disability. Although genome-wide association studies have identified common genetic variants that increase IA risk moderately, the contribution of variants with large effect remains poorly defined. Using whole-exome sequencing, we identified significant enrichment of rare, deleterious mutations in *PPIL4*, encoding peptidyl-prolyl *cis-trans* isomerase-like 4, in both familial and index IA cases. *Ppil4* depletion in vertebrate models causes intracerebral hemorrhage, defects in cerebrovascular morphology and impaired Wnt signaling. Wild-type, but not IA-mutant, PPIL4 potentiates Wnt signaling by binding JMJD6, a known angiogenesis regulator and Wnt activator. These findings identify a novel PPIL4-dependent Wnt signaling mechanism involved in brain-specific angiogenesis and maintenance of cerebrovascular integrity and implicate *PPIL4* gene mutations in the pathogenesis of IA.



Barak, T. *et al.* PPIL4 is essential for brain angiogenesis and implicated in intracranial aneurysms in humans. *Nat Med* **27**, 2165–2175 (2021).

IMARIS in Publications

nature neuroscience

ARTICLES

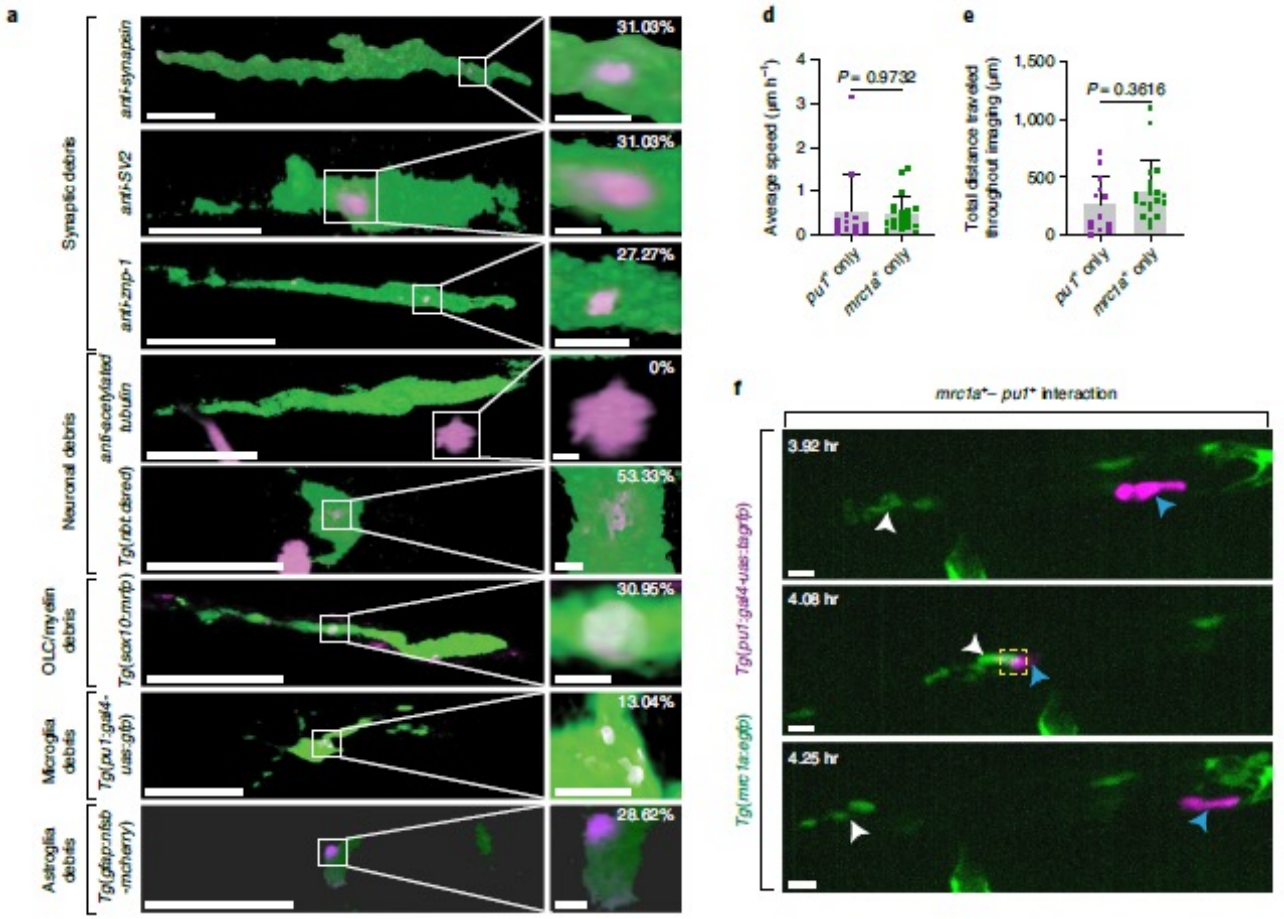
https://doi.org/10.1038/s41593-022-01091-9

Check for updates

The embryonic zebrafish brain is seeded by a lymphatic-dependent population of *mrc1*+ microglia precursors

Lauren A. Green[1,2,3], Michael R. O'Dea[1,3], Camden A. Hoover[1,2], Dana F. DeSantis[1,2] and Cody J. Smith[1,2]

Microglia are the resident macrophages of the CNS that serve critical roles in brain construction. Although human brains contain microglia by 4 weeks gestation, an understanding of the earliest microglia that seed the brain during its development remains unresolved. Using time-lapse imaging in zebrafish, we discovered a *mrc1a*+ microglia precursor population that seeds the brain before traditionally described microglia. These early microglia precursors are dependent on lymphatic vasculature that surrounds the brain and are independent of *pu1*+ yolk sac-derived microglia. Single-cell RNA-sequencing datasets reveal *Mrc1*+ microglia in the embryonic brains of mice and humans. We then show in zebrafish that these early *mrc1a*+ microglia precursors preferentially expand during pathophysiological states in development. Taken together, our results identify a critical role of lymphatics in the microglia precursors that seed the early embryonic brain.



Green, L. A., O'Dea, M. R., Hoover, C. A., DeSantis, D. F. & Smith, C. J. The embryonic zebrafish brain is seeded by a lymphatic-dependent population of mrc1+ microglia precursors. *Nat Neurosci* (2022) doi:10.1038/s41593-022-01091-9.

IMARIS in Publications

nature metabolism

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Article | Published: 28 November 2022

Maternal diet disrupts the placenta–brain axis in a sex-specific manner

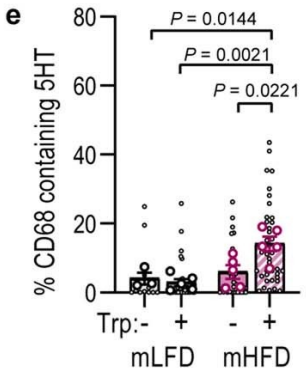
Alexis M. Ceasrine, Benjamin A. Devlin, Jessica L. Bolton, Lauren A. Green, Young Chan Jo, Carolyn Huynh, Bailey Patrick, Kamryn Washington, Cristina L. Sanchez, Faith Joo, A. Brayan Campos-Salazar, Elana R. Lockshin, Cynthia Kuhn, Susan K. Murphy, Leigh Ann Simmons & Staci D. Bilbo

Nature Metabolism **4**, 1732–1745 (2022) | Cite this article

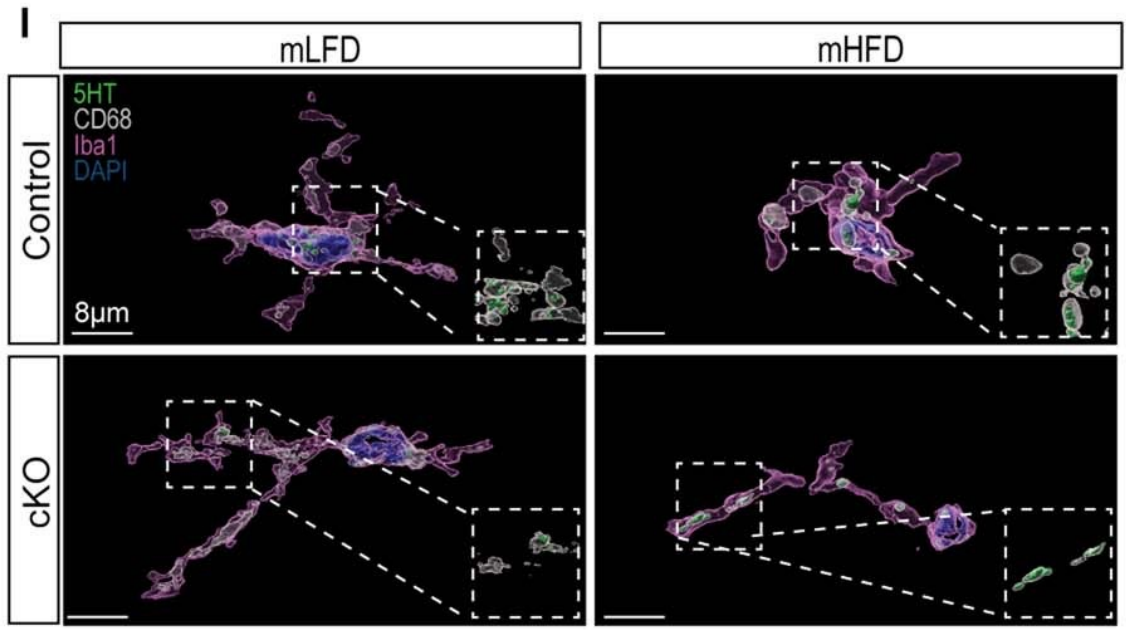
3865 Accesses | **1** Citations | **220** Altmetric | Metrics

Abstract

High maternal weight is associated with detrimental outcomes in offspring, including increased susceptibility to neurological disorders such as anxiety, depression and communicative disorders. Despite widespread acknowledgement of sex biases in the development of these disorders, few studies have investigated potential sex-biased mechanisms underlying disorder susceptibility. Here, we show that a maternal high-fat diet causes endotoxin accumulation in fetal tissue, and subsequent perinatal inflammation contributes to sex-specific behavioural outcomes in offspring. In male offspring exposed to a maternal high-fat diet, increased macrophage Toll-like receptor 4 signalling results in excess microglial phagocytosis of serotonin (5-HT) neurons in the developing dorsal raphe nucleus, decreasing 5-HT bioavailability in the fetal and adult brains. Bulk sequencing from a large cohort of matched first-trimester human samples reveals sex-specific transcriptome-wide changes in placental and brain tissue in response to maternal triglyceride accumulation (a proxy for dietary fat content). Further, fetal brain 5-HT levels decrease as placental triglycerides increase in male mice and male human samples. These findings uncover a microglia-dependent mechanism through which maternal diet can impact offspring susceptibility for neuropsychiatric disorder development in a sex-specific manner.



Extended Fig 7e, IMARIS reconstruction quantification from female e14.5 dorsal raphe nucleus microglia. Statistics shown for animal averages (large circles), small circles are individual microglia. (n = 3 mLFD, 5, mLFD+Trp, 6 mHFD, 5 mHFD+Trp from 3 litters/diet).



Extended Fig 7l, IMARIS reconstructions from female mLFD and mHFD control and cKO e14.5 DRN. Statistics ran for animal averages (large circles), small circles are individual microglia. (n = 7 mLFD control, 5 mLFD cKO, 5 mHFD control, and 4 mHFD cKO from 7 mLFD and 5 mHFD litters)