

Brain Connectivity Mapping

IJCNN Tutorial

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Introduction and Overview

Mapping Brain Connectivity



Organism

C57BL/6 mouse

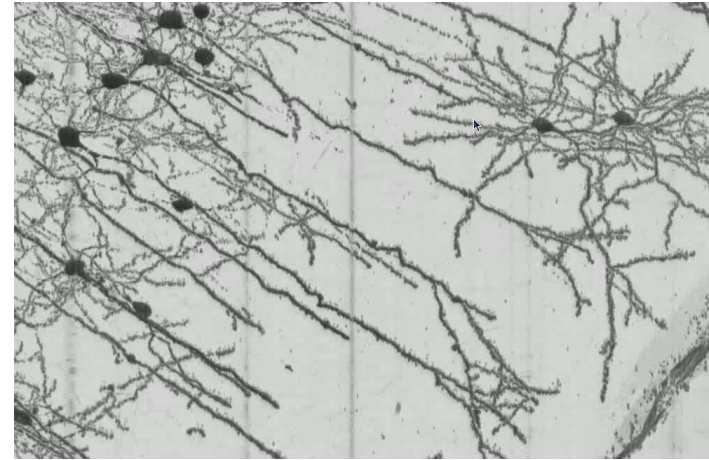
<http://mouseatlas.org>



Brain

Mouse brain

<http://nervenet.org>



Connectivity

Brain circuits (Mouse cortex)

- First step toward Understanding brain function: from structure to function.
- Approach: Omics

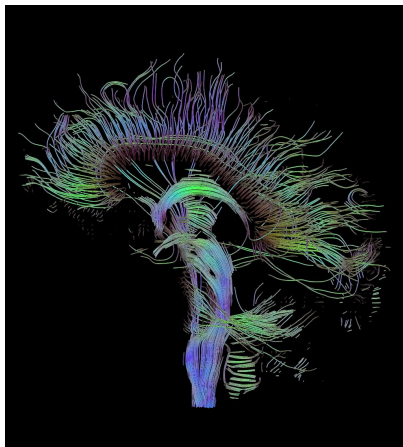
Age of the “Omics”

Biology has entered the age of “Omics”.

- “X-ome” means a complete collection of X
 - Derived from $-\omega\mu\alpha$ (-oma) in Greek.
 - “X-omics” means the study of “X-ome”.
- Examples:
 - genome, proteome, metabolome, physiome, etc.
- Why study “omics”?
 - Can understand how the whole system works.

Connectomics

Connectome: Collection of all connections between all neurons in the brain (Sporns et al. 2005; Sporns 2012; Seung 2012).



Imaging: Diffusion Tensor Imaging (DTI)

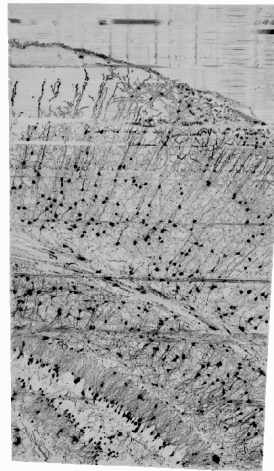
Scale: ~ 10 cm cube

Whole Human brain

Resolution: ~ 1 mm cube

Time: hours

See e.g. Hagmann et al. (2007)



Light Microscopy

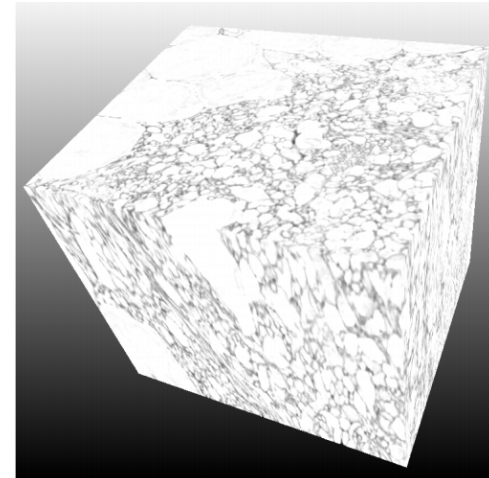
~ 1 cm cube

Whole Mouse brain

~ 1 μ m cube

weeks

Mayerich et al. (2008)



Electron Microscopy

~ 100 μ m cube

Hundreds of neurons

~ 10 nm cube

year

Denk and Horstmann (2004)

Why Connectomics?

- Brain evolution is mostly evolution of the architecture (connectome), not the elements (neurons) (Swanson 2003)
- Current state of neuroscience is too specialized, local, and fragmented.
- Huge accumulation of (local) experimental (anatomical, physiological, genetic, behavioral) data.
- Need a framework to integrate the scattered data for a system-level understanding of the brain.

Current Status of Connectomics

- Nematode *C. elegans*: Only available connectome (White et al. 1986).
- Mostly focused on data acquisition (microscopy and imaging).
- Analysis framework leading behind.

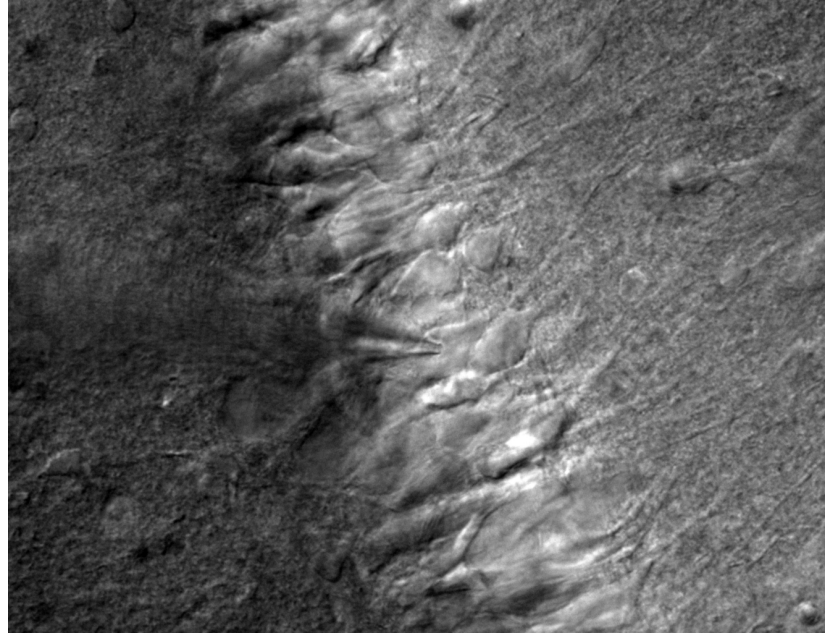
Overview

1. Staining and Labeling
2. Imaging
3. Data and Online Resources
4. Analysis
5. Wrap Up

Part I

Staining and Labeling

Staining and Labeling



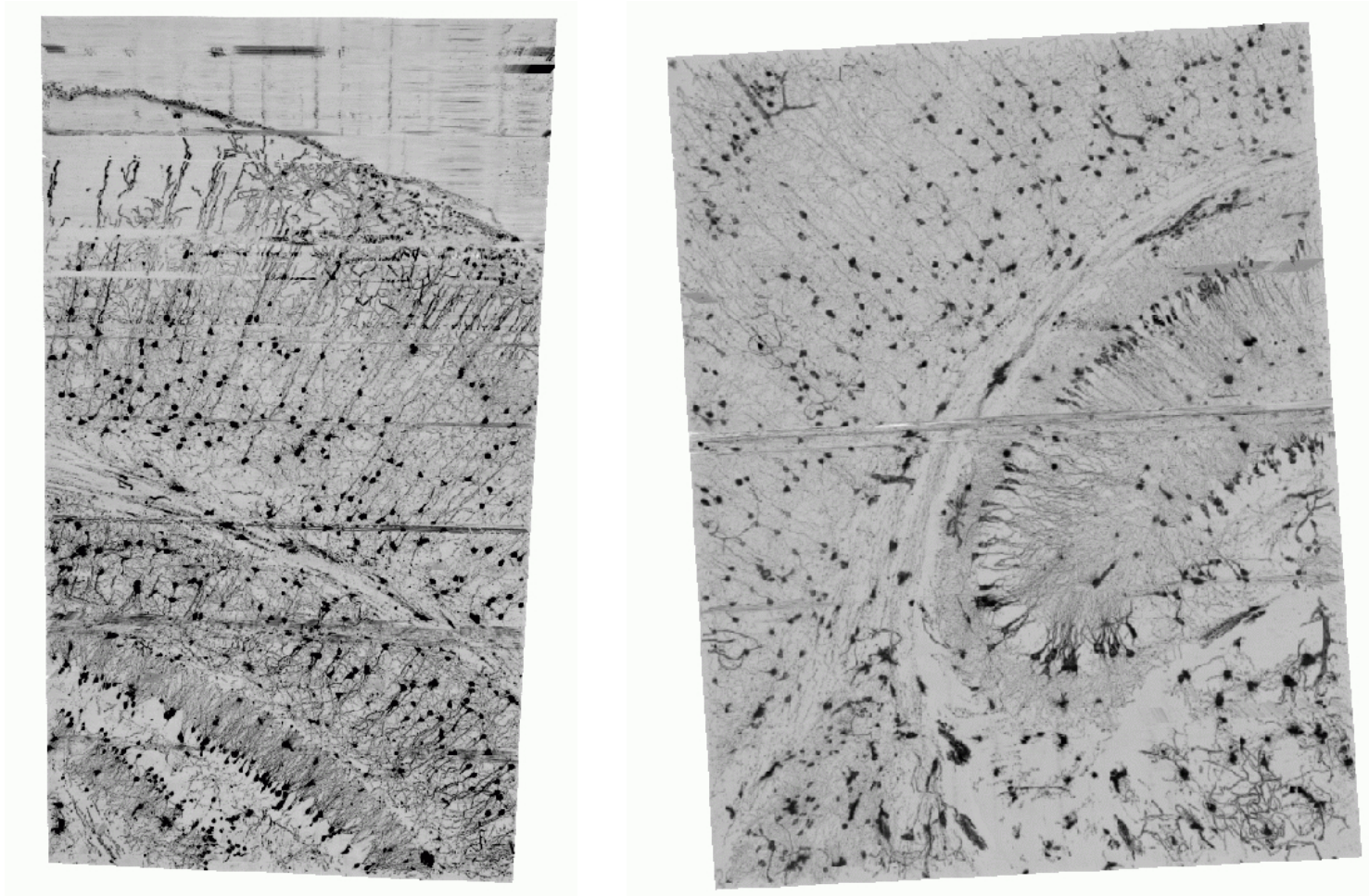
<http://commons.wikimedia.org/wiki/File:WholeCellPatchClamp.jpg>

- Need: Very low contrast between neurons and non-neuronal cells/tissue in the brain (see image above).
- Chemical stains and molecular labels are used to provide contrast.

Types of Stains/Labels

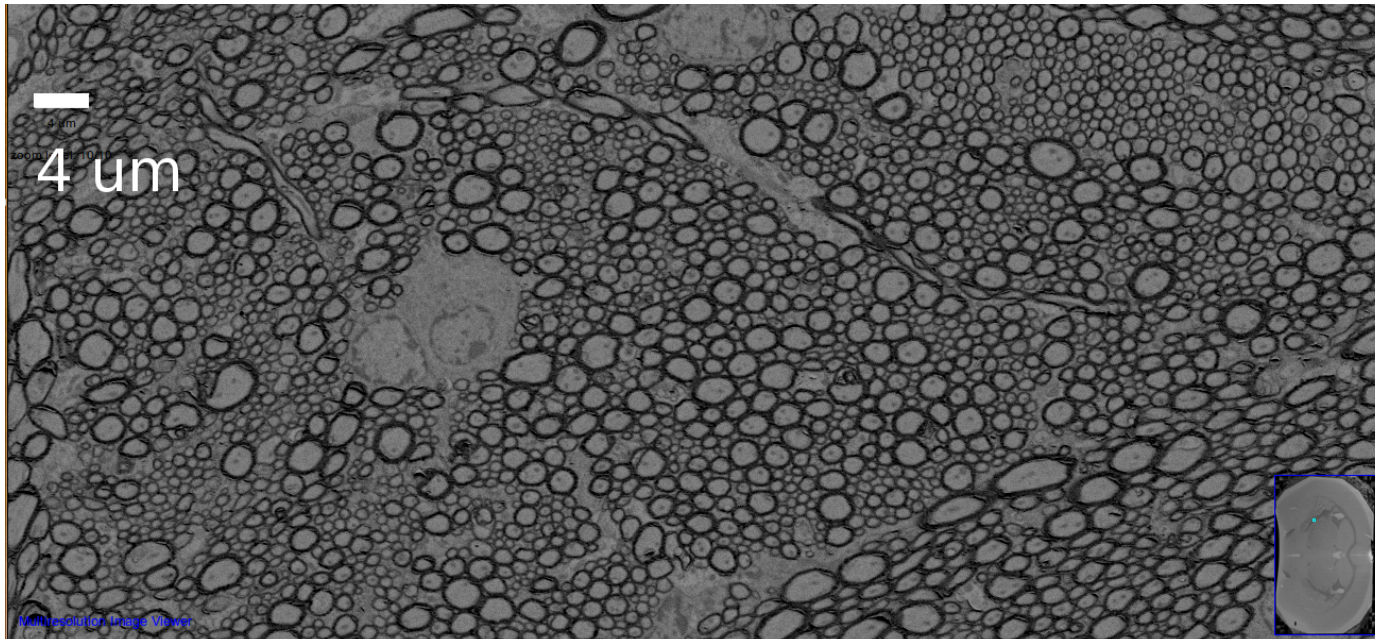
- Sparse (few neurons marked) vs. dense (all neurons marked)
- Random (random population marked) vs. targetted (specific cell types marked).
- For use with different imaging methods: light microscopy, electron microscopy, fluorescence microscopy, etc.

Golgi



- Stains whole neurons (axons unreliably stained): Sparse ($\sim 1\%$ stained), Random, Whole brains can be stained. Ideal for light microscopy.

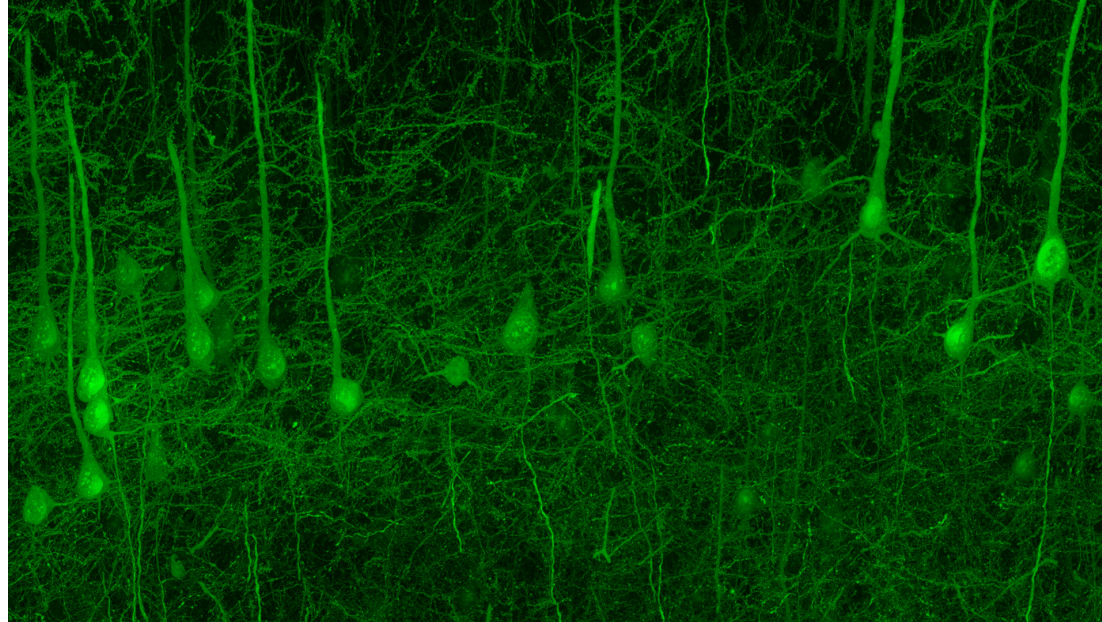
Osmium Tetroxide (OsO_4)



From <http://connectomes.org>. See Mikula et al. (2012). wbPATCO stain (OsO_4 variant)

- Stains lipid (all cell membranes): Dense, Unselective, Whole brains can be stained. Ideal for electron microscopy.

Immunofluorescence Labeling



http://smithlab.stanford.edu/Smithlab/Array_Tomography.html

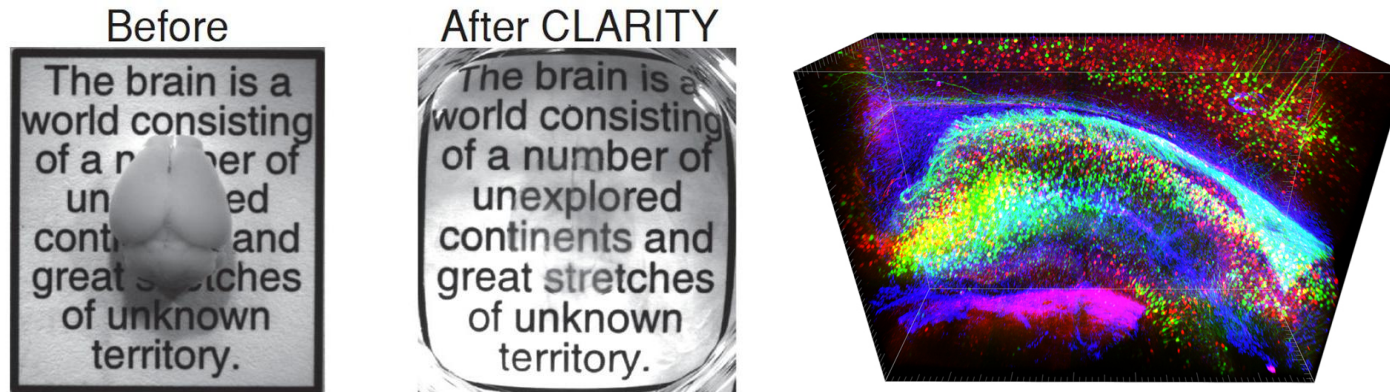
YFP expressed in whole neurons (false color added)

- Targets specific molecules (e.g. proteins): Sparse, Targetted
- Use antibody (to attach to antigen in the target) linked to fluorophore (directly or indirectly).

Tracer Injections

- Fills neurons near injection site (whole neurons):
Sparse (local to injection site), Unselective, Can span long distances.
- Anterograde (soma toward axon terminal),
Retrograde (axon terminal toward soma)
- Viral: anterograde or retrograde. Can cross synapses through infection to highlight higher-order connections (e.g., Pseudorabies virus)

Other Relevant Techniques



<http://directorsblog.nih.gov/the-brain-now-you-see-it-soon-you-wont/>

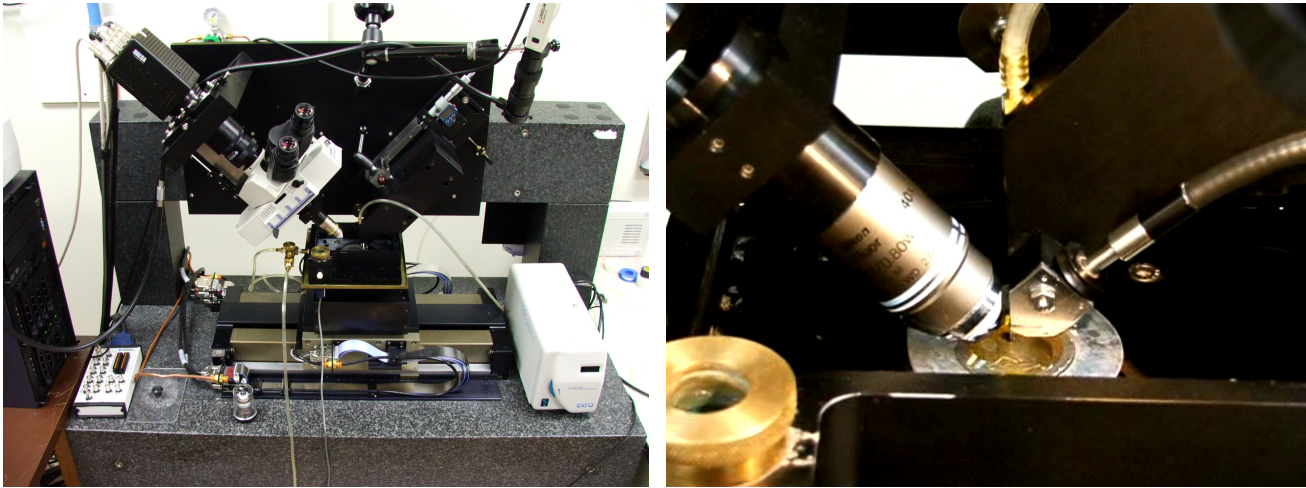
<http://clarityresourcecenter.org/> (Chung and Diesseroth 2013)

- Making brain tissue transparent: remove lipid, replacing with hydrogel for structural support.
- CLARITY: Allows imaging using multiple immunostains over large volumes of brain tissue.

Part II

Imaging

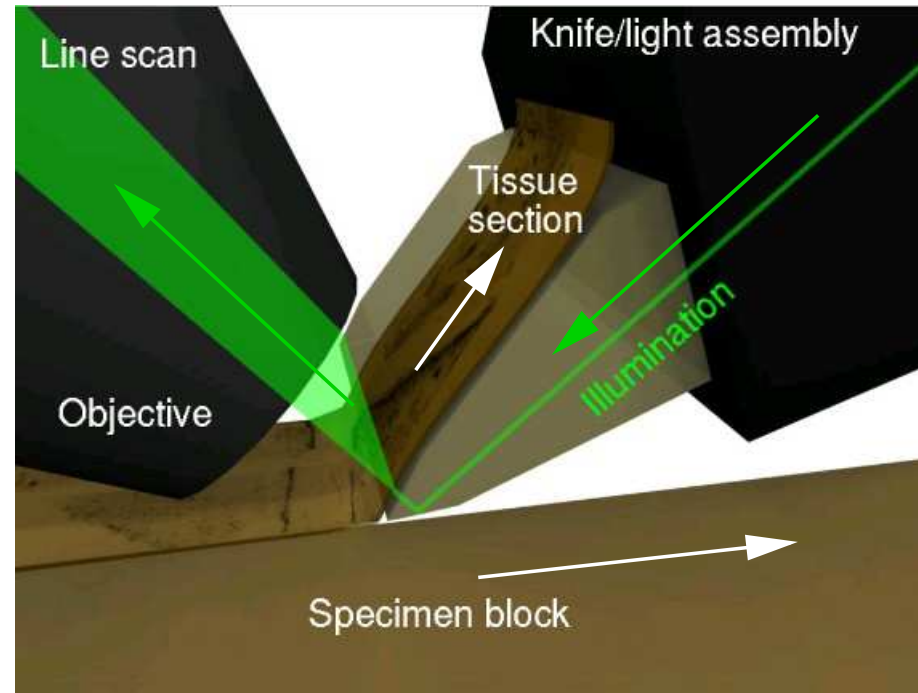
Knife-Edge Scanning Microscope



Mayerich et al. (2008); Chung et al. (2011)

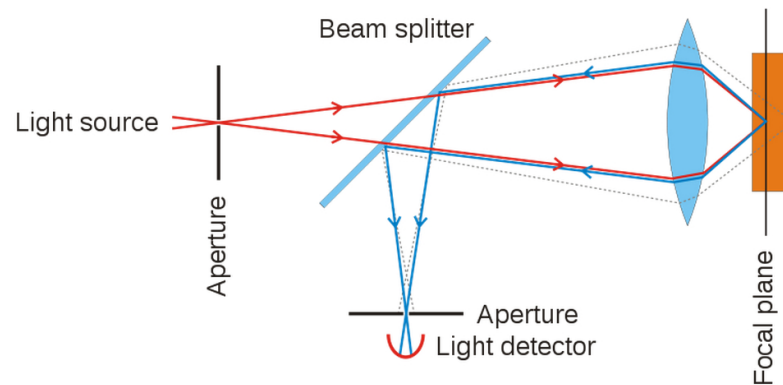
- Physical sectioning, as opposed to optical sectioning (e.g. confocal).
- Light microscopy, bright-field imaging (fluorescence in the works).
- Stains: Golgi (neuron morphology), Nissl (soma), India ink (vasculature). (Fluorescence imaging in the works.)
- $0.6 \mu\text{m} \times 0.7 \mu\text{m} \times 1 \mu\text{m}$ voxel resolution.
- Custom software for control, image capture (Kwon et al. 2008).
- Compare to MOST (based on KESM) (Li et al. 2010).

Imaging Principles of the KESM



- Image while cutting (line-scan at the tip of the knife).
- Transmission illumination through the diamond knife.
- Tissue thickness: 1 μm (or possibly less).

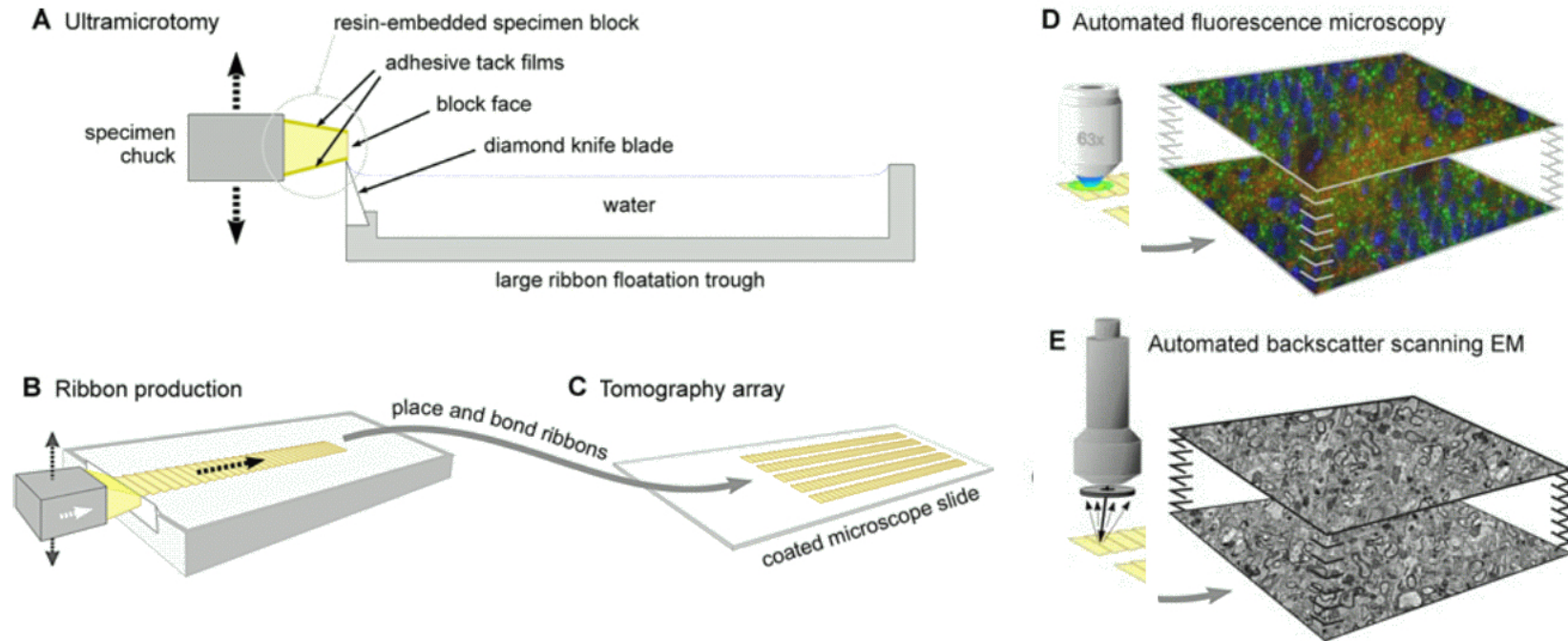
Confocal Microscopy



http://en.wikipedia.org/wiki/File:Confocalprinciple_in_English.svg

- Optical, not physical sectioning: Imaging at a specific focal depth. Scanning. Fluorescence imaging.
- Depth limit (max 1 mm) (Murray 2011).
- Also see two-photon (and multi-photon) imaging.

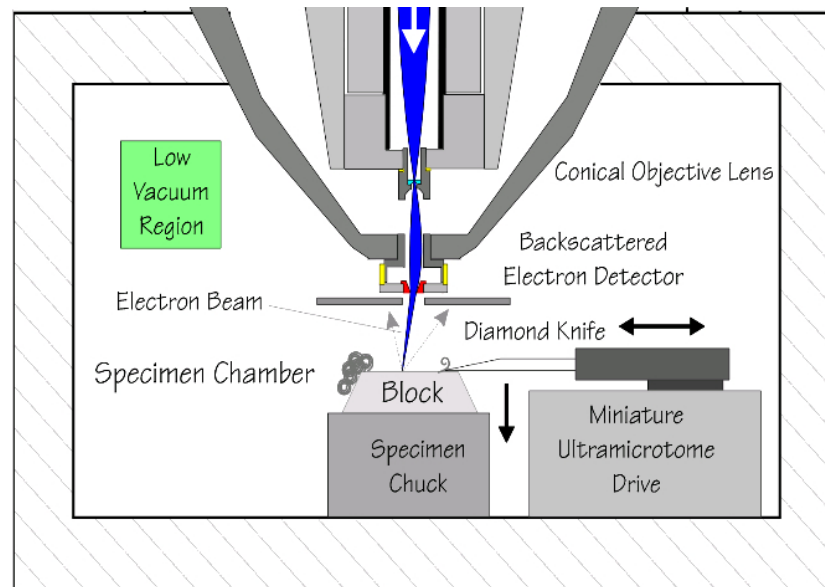
Array Tomography



Micheva and Smith (2007)

- Ultrathin sections transferred on glass slide.
- Repeated washing and staining allows perfectly registered volume data from multiple staining modalities.

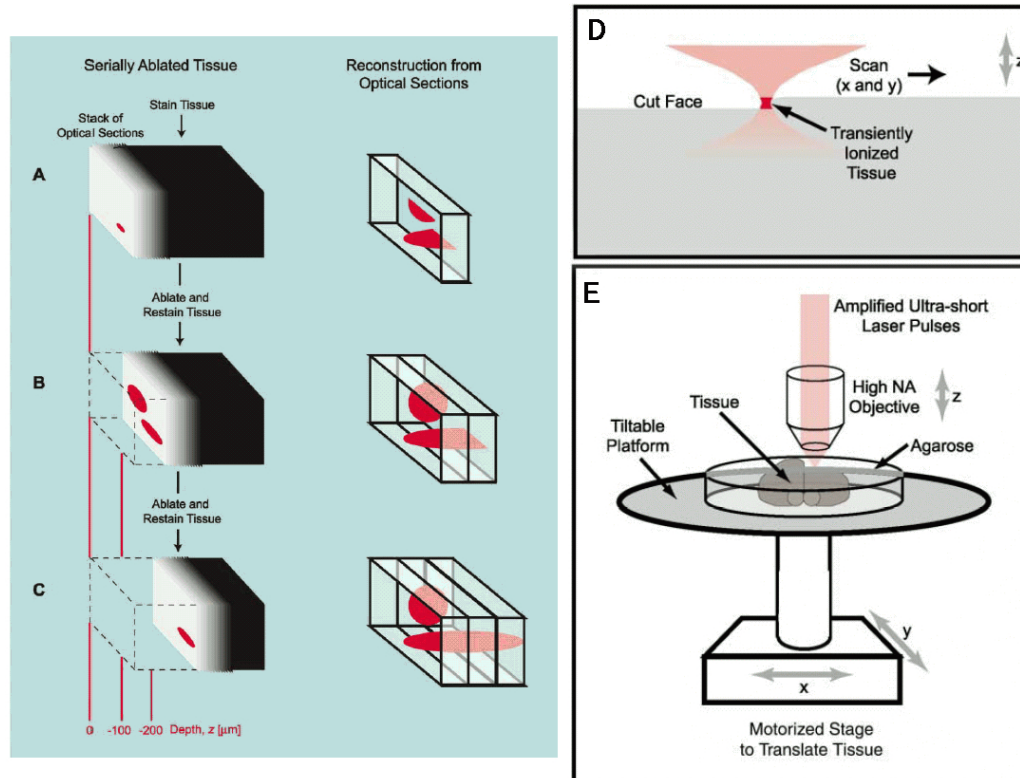
SBF-SEM (or SBEM)



Denk and Horstmann (2004)

- Microtome installed inside the vacuum chamber of an SEM.
- Commercially available from Gatan.

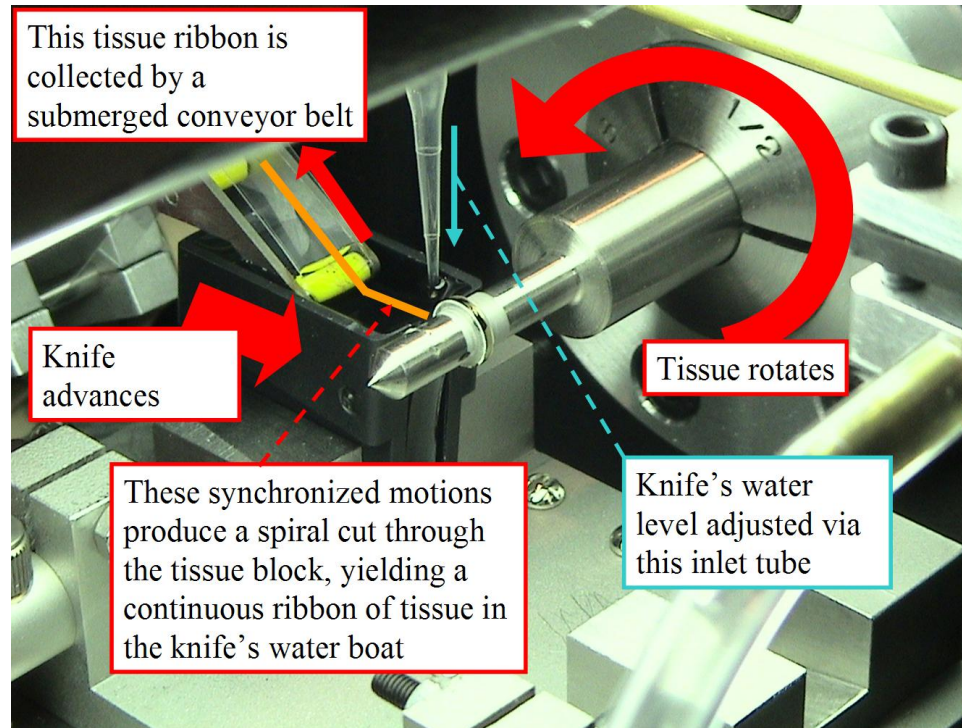
All-Optical Histology



Tsai et al. (2003)

- Hybrid of physical sectioning and optical sectioning (cf. Serial Two-Photon Tomography (Ragan et al. 2012)).
- Femtosecond laser pulses used to ablate $\sim 150 \mu\text{m}$ sections, followed by multiphoton imaging.

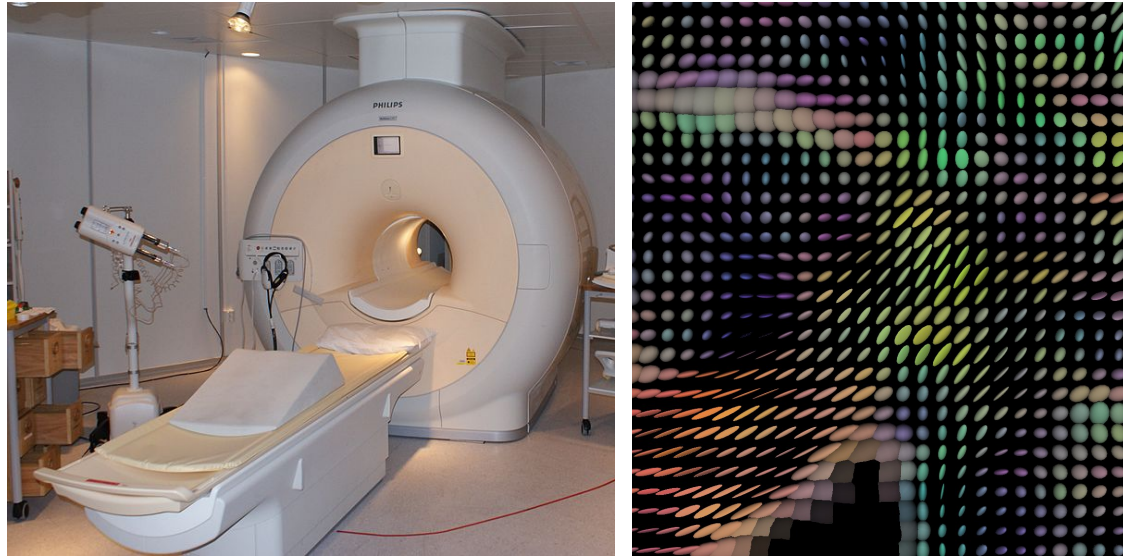
ATLUM



Hayworth et al. (2006)

- Continuous sectioning using a lathe.
- Sectioned tissue collected on adhesive tape.
- Post-staining and imaging of tape library with Transmission EM.

Diffusion Tensor Imaging (DTI)

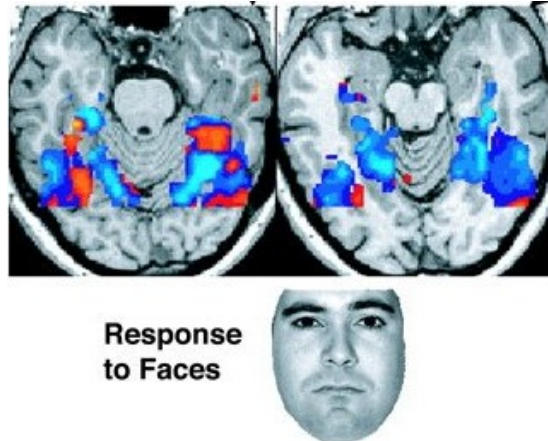


<http://en.wikipedia.org/wiki/File:MRI-Philips.JPG>

<http://en.wikipedia.org/wiki/File:DTI-axial-ellipsoids.jpg>

- Based on Magnetic Resonance Imaging (MRI). Low resolution ($\sim 100 \mu\text{m}$).
- Detect anisotropic diffusion patterns of water molecules along fiber tracts.

functional MRI (fMRI)



Haxby et al. (2001) (image cropped)

- Brain activity measured through BOLD (blood oxygen level dependent signal).
- Region-to-region connectivity can be inferred based on activity correlation or causality (dynamic causal model, Granger causal model): (Friston 2009).

Comparison

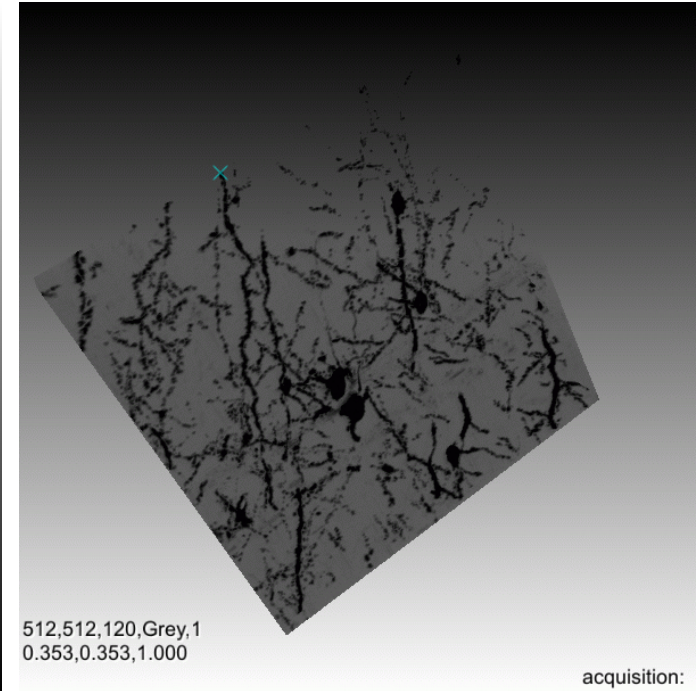
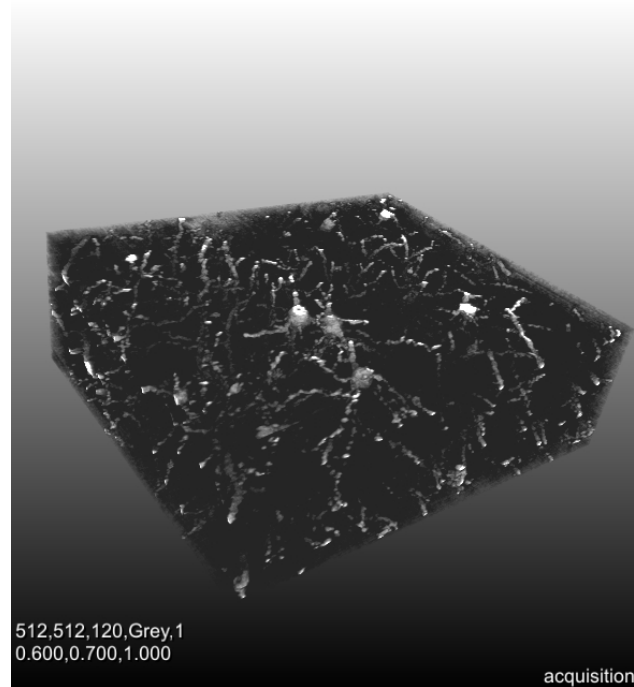
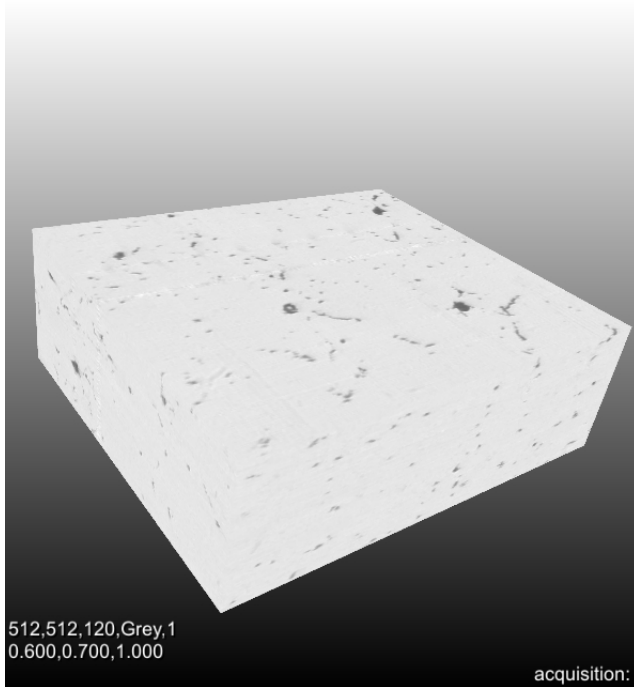
Table 1: Summary Comparison.

Method	nm-scale	μm -scale	High-Volume	High-Throughput
KESM (Mayerich et al. 2008) (cf. Li et al. 2010)	–	○	○	○
Confocal	–	○	–	–
All-Optical Hist. (Tsai et al. 2003)	–	○	○	–
Serial Two-Photon Tomography (Ragan et al. 2012)	–	○	○	–
Array Tomography (Micheva and Smith 2007)	○	○	–	–
SBF-SEM (Denk and Horstmann 2004)	○	–	–	–
ATLUM (Hayworth et al. 2006)	○	–	○	–
MRI/diffusion MRI (Jacobs et al. 1999; Haggmann et al. 2007)	–	–	○	○
nm-scale: ~ 10 nm (thickness of cell membrane) μm -scale: ~ 1 μm (diameter of dendrites, axons, capillaries, etc.) High-Volume: > 1 cm^3 (approximate volume of mouse brain and other organs) High-Throughput: < 100 hours (for ~ 50 scanned organs per year)				

Part III

Data and Online Resources (with Demo)

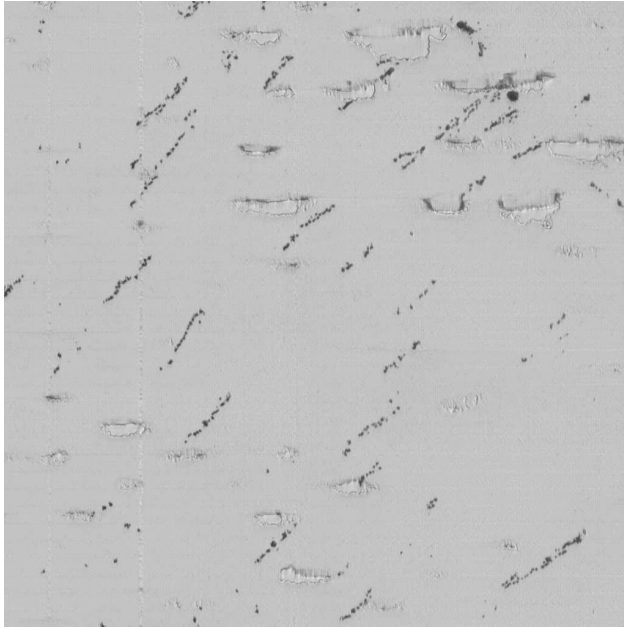
KESM Data



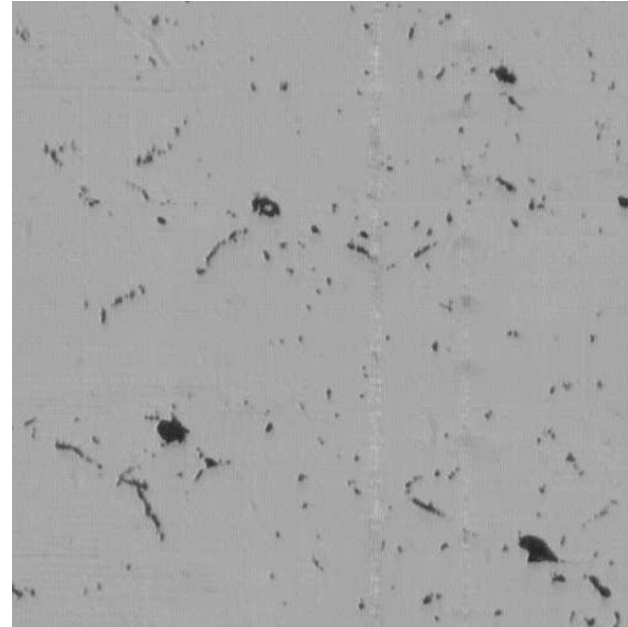
300 μm \times 350 μm \times 120 μm block

- Basically a huge 3D stack made up of 2D images.
- Details such as dendritic spines can be observed.

KESM Data (Image Stack)



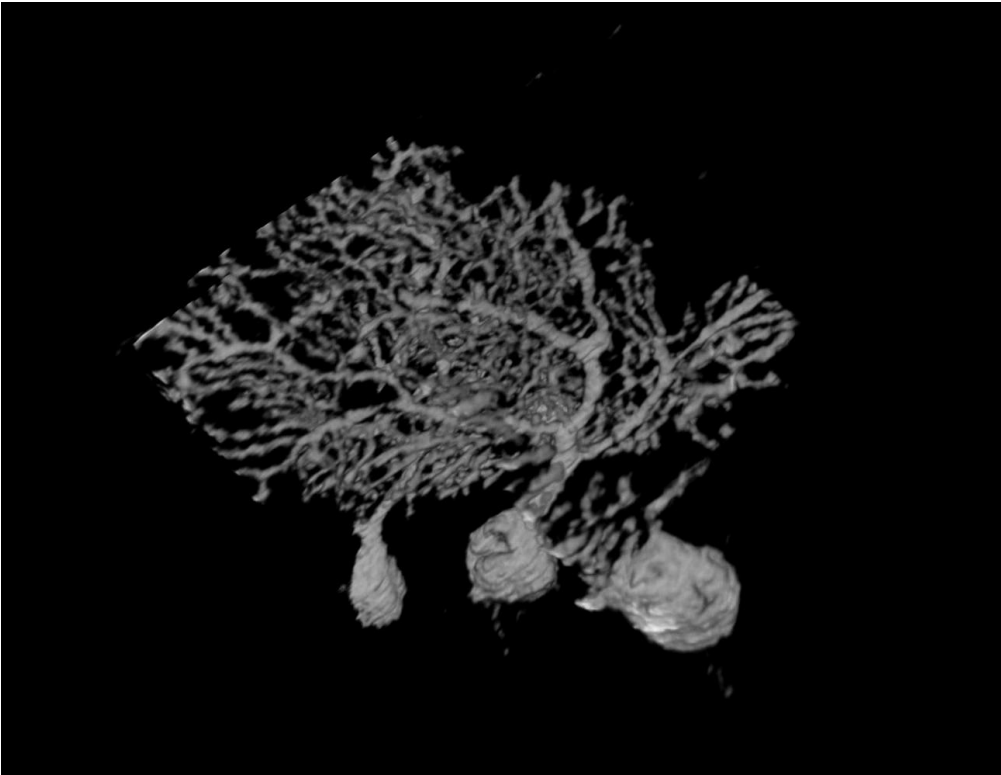
Cerebellum (Golgi)



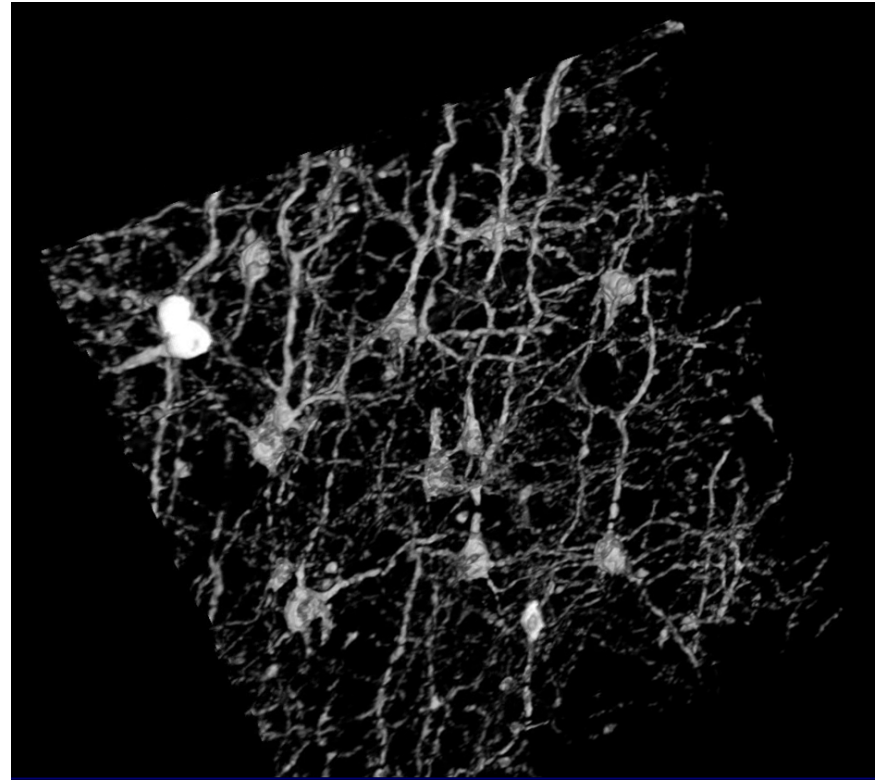
Cortex (Golgi)

- Flythrough of 3D stack: Looks like a movie in 2D.
- Each frame = 1 μm -thin section.

KESM: Volume Visualization



Golgi (Cerebellum)

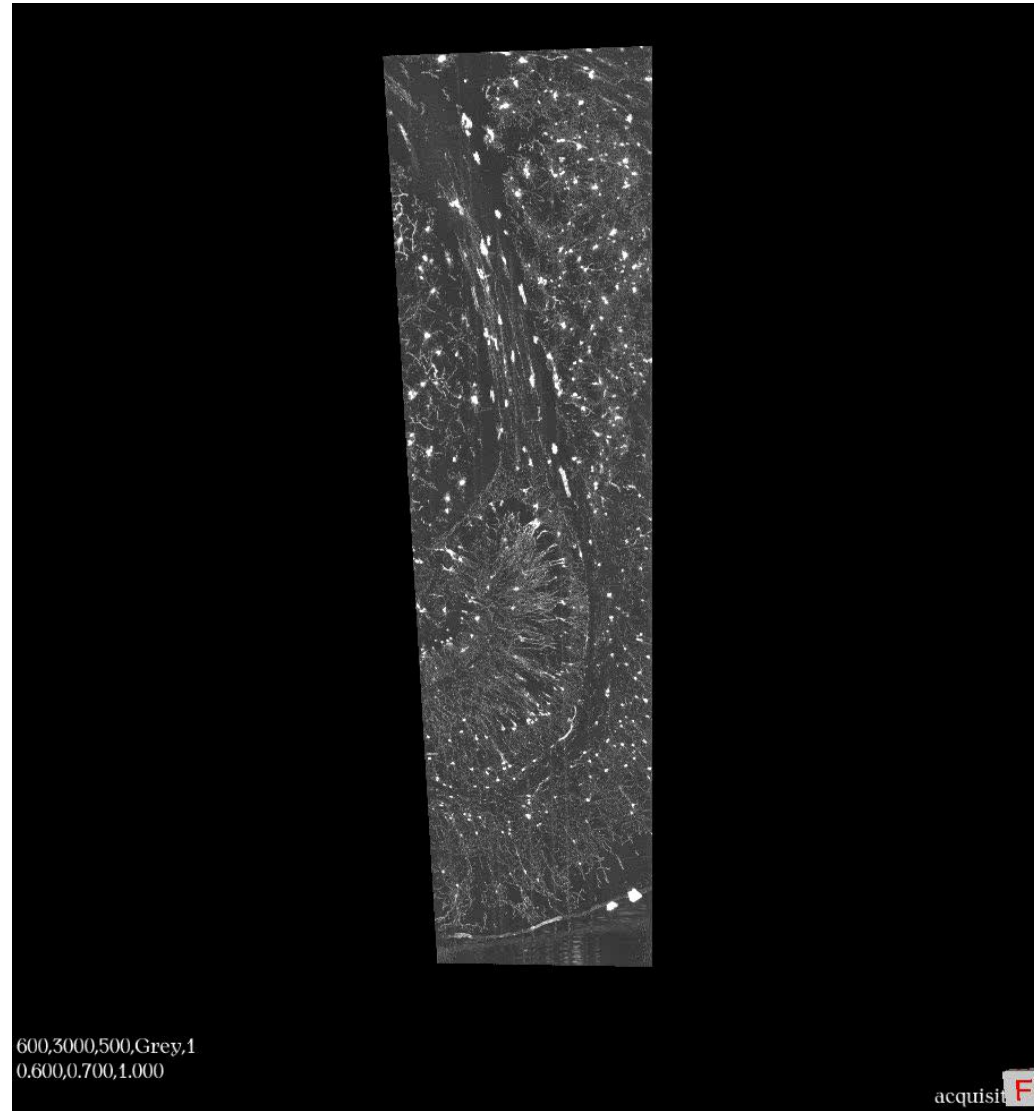


Golgi (Cortex)

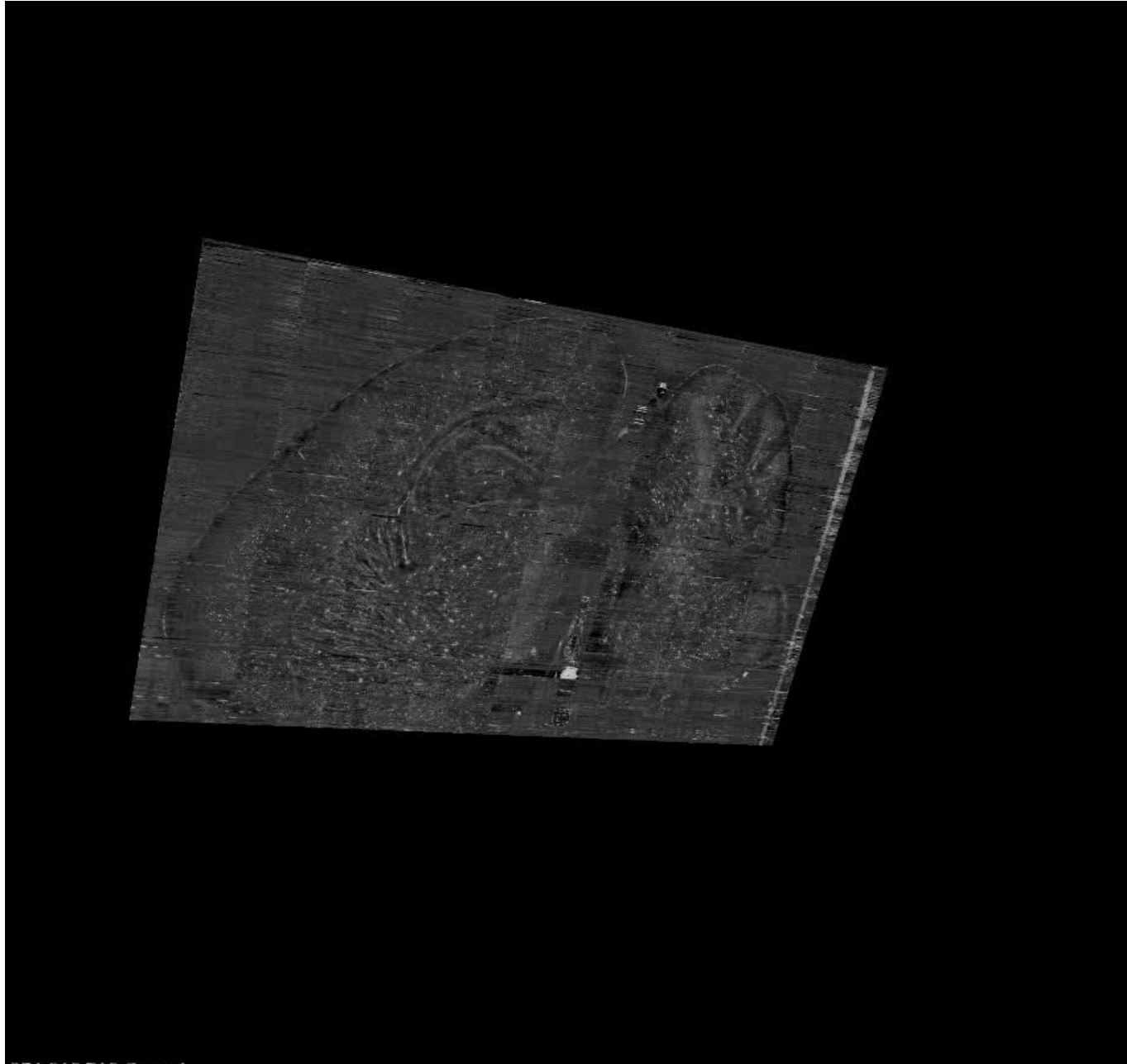
3D visualization of

- Purkinje cells and pyramidal cells.

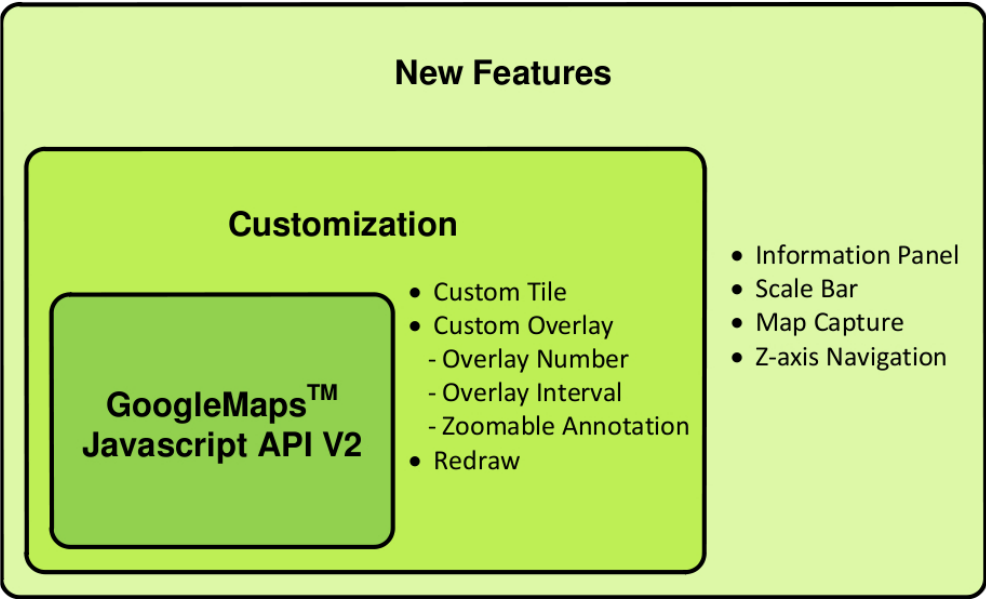
KESM: Local Circuits (Hippocampus)



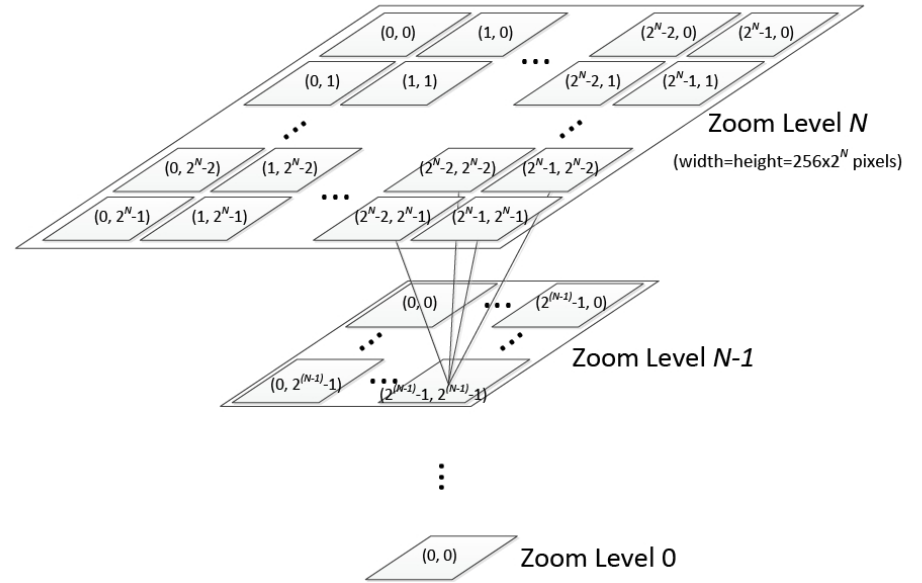
KESM Whole Brain: Neurons (Golgi)



KESM Brain Atlas



API layers

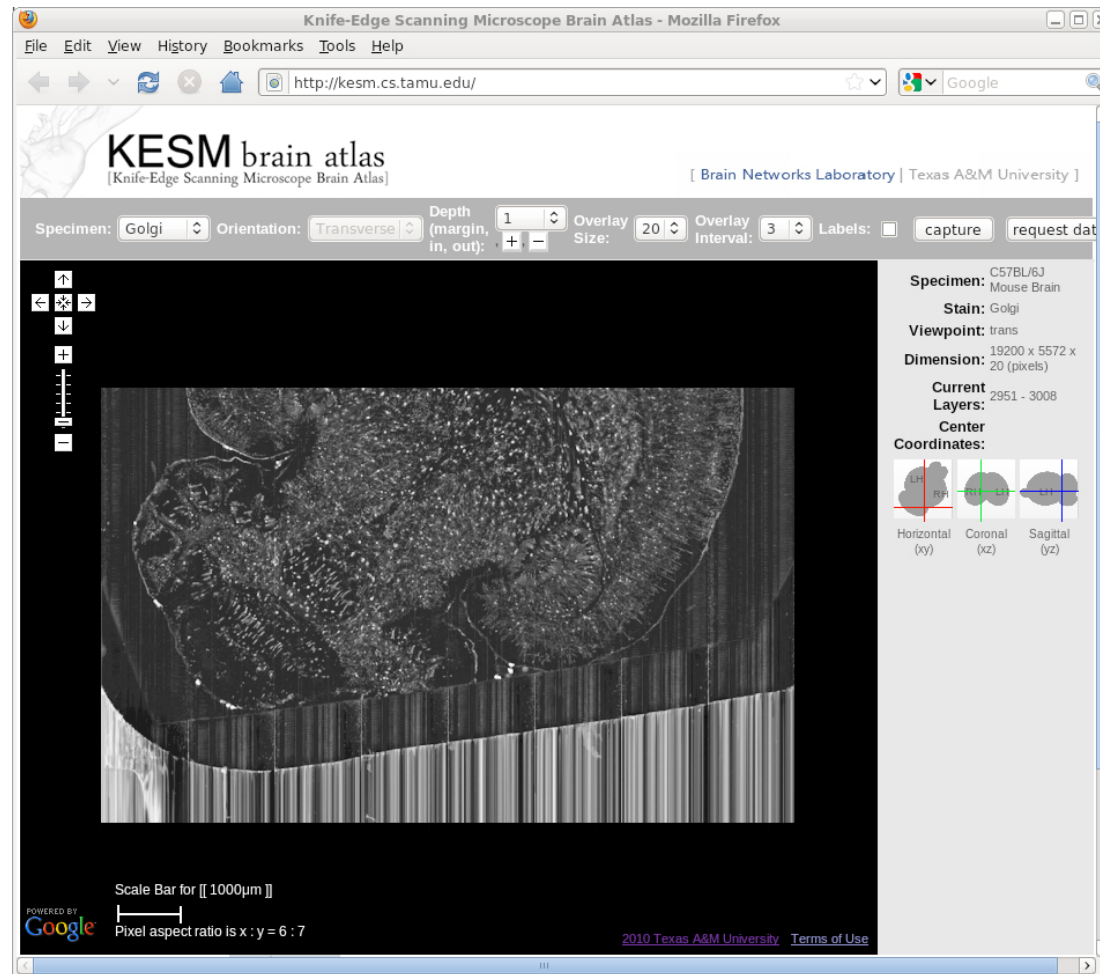


Tiling Scheme

- Multi-scale tiles.
- Semi-transparent images.
- Google Maps API (v2).

→ KESM Brain Atlas

KESM Brain Atlas (KESMBA)



- <http://kesm.org> (Chung et al. 2011).
- Open to all! Even runs on smartphone browsers (can be slow).

KESMBA: Single Overlay

The screenshot displays the KESM brain atlas web application in a Mozilla Firefox browser window. The browser's address bar shows the URL <http://kesm.cs.tamu.edu/>. The page header includes the KESM brain atlas logo and the text "[Knife-Edge Scanning Microscope Brain Atlas]" and "[Brain Networks Laboratory | Texas A&M University]".

The main interface features a control bar with the following settings:

- Specimen: Golgi
- Orientation: Transverse
- Depth (margin, in, out): 1
- Overlay Size: 1
- Overlay Interval: 1
- Labels:
- Buttons: capture, request data

The central area shows a large, dark image of Golgi-stained mouse brain tissue with white, filamentous structures. On the left side of the image, there is a vertical toolbar with navigation and zoom controls. At the bottom left of the image, there is a scale bar labeled "Scale Bar for [100µm]" and a note "Pixel aspect ratio is x : y = 6 : 7".

On the right side, a metadata panel provides the following information:

- Specimen: C57BL/6J Mouse Brain
- Stain: Golgi
- Viewpoint: trans
- Dimension: 19200 x 5572 x 1 (pixels)
- Current Layers: 2951 - 2951
- Center Coordinates: Three small diagrams showing the brain in Horizontal (xy), Coronal (xz), and Sagittal (yz) views.

At the bottom of the page, there is a "POWERED BY Google" logo and a footer with the text "2010 Texas A&M University Terms of Use".

KESMBA: 20 Overlays

The screenshot shows the KESM brain atlas web application in a Mozilla Firefox browser window. The browser's address bar displays the URL <http://kesm.cs.tamu.edu/>. The page header includes the KESM logo and the text "KESM brain atlas [Knife-Edge Scanning Microscope Brain Atlas]" and "[Brain Networks Laboratory | Texas A&M University]".

The main interface features a control panel with the following settings:

- Specimen: Golgi
- Orientation: Transverse
- Depth (margin, in, out): 1
- Overlay Size: 20
- Overlay Interval: 1
- Labels:
- Buttons: capture, request data

The central area displays a grayscale micrograph of Golgi-stained mouse brain tissue. On the left side of the image, there is a vertical toolbar with navigation and zoom controls. At the bottom left of the image, a scale bar is labeled "Scale Bar for [100µm]" and a note states "Pixel aspect ratio is x : y = 6 : 7".

On the right side, a metadata panel provides the following information:

- Specimen: C57BL/6J Mouse Brain
- Stain: Golgi
- Viewpoint: trans
- Dimension: 19200 x 5572 x 20 (pixels)
- Current Layers: 2951 - 2970
- Center Coordinates: Three small brain diagrams showing the current slice location in Horizontal (xy), Coronal (xz), and Sagittal (yz) planes.

At the bottom of the page, there is a "POWERED BY Google" logo and a footer that reads "KESM 2010 Texas A&M University · Terms of Use".

KESMBA: Zoomed Out

Knife-Edge Scanning Microscope Brain Atlas - Mozilla Firefox

File Edit View History Bookmarks Tools Help

http://kesm.cs.tamu.edu/

KESM brain atlas
[Knife-Edge Scanning Microscope Brain Atlas]

[Brain Networks Laboratory | Texas A&M University]

Specimen: Golgi Orientation: Transverse Depth (margin, in, out): 1 Overlay Size: 20 Overlay Interval: 3 Labels: capture request data

Specimen: C57BL/6J Mouse Brain
Stain: Golgi
Viewpoint: trans
Dimension: 19200 x 5572 x 20 (pixels)
Current Layers: 2951 - 3008
Center Coordinates:

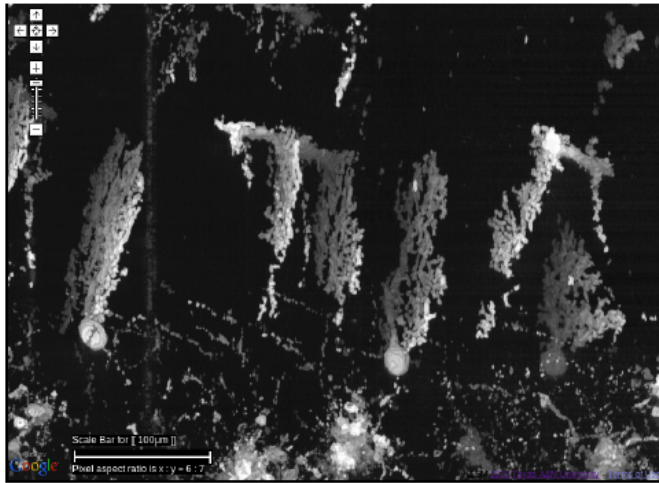
Horizontal (xy) Coronal (xz) Sagittal (yz)

Scale Bar for [100µm]
Pixel aspect ratio is x : y = 6 : 7

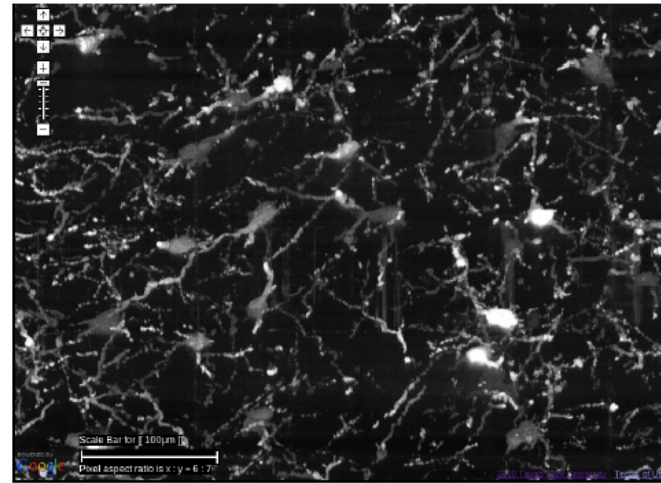
POWERED BY Google

KESM 2010 Texas A&M University Terms of Use

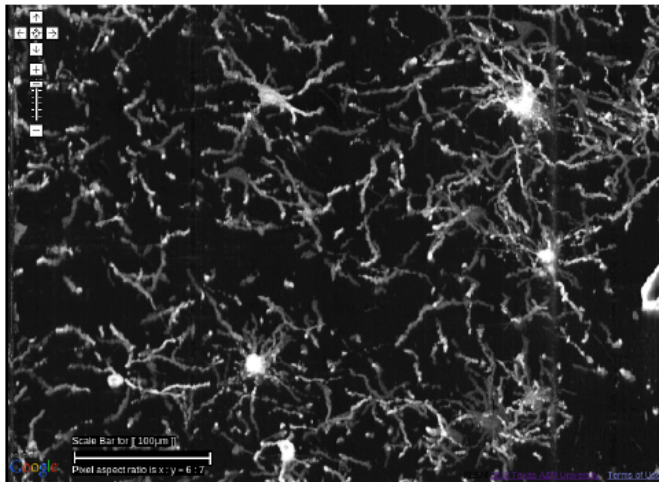
KESMBA: Some Samples



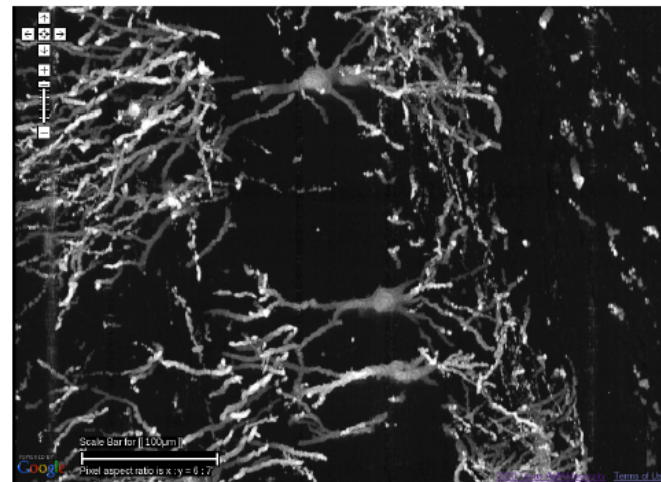
A



B



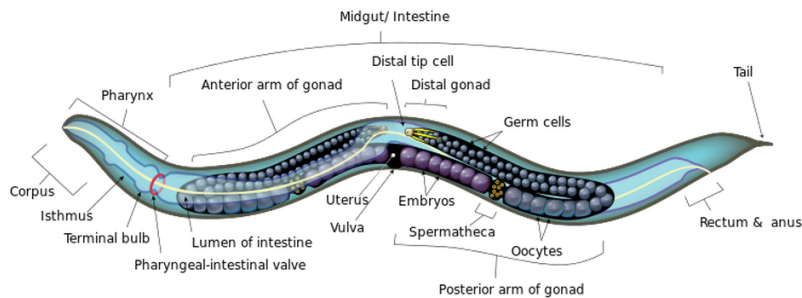
C



D

A: Cerebellum, B: Inferior colliculus, C: Thalamus, D: Hippocampus

OpenWorm Project



http://en.wikipedia.org/wiki/File:Caenorhabditis_elegans_hermaphrodite_adult-en.svg

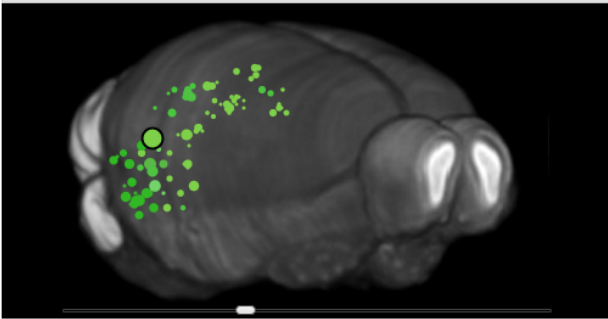
<http://www.openworm.org/>

- C. elegans connectome, downloadable in XML (NeuroML), for multicompartment models.
- Ultimate goal of constructing a detailed simulation of the whole worm.

Allen Brain Atlas: Mouse Connectivity

Search Results Permalink

Injection Sites - Showing 86 Experiments

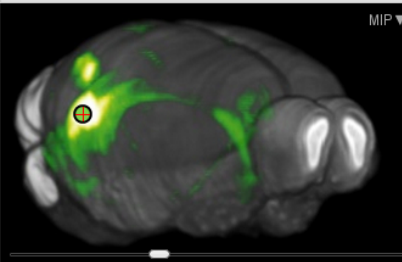


Injection Structure(s)	Mouse Line	Inj Vol
<input checked="" type="checkbox"/> CA1 - VISal, CA2, CA3, DG, SUB	Etv1-CreERT2	0.456
<input checked="" type="checkbox"/> CA1 - SSp-tr6a, SSp-tr6b, CA2	C57BL/6J	0.145
<input type="checkbox"/> CA1 - MOp, PTLp	C57BL/6J	0.204
<input type="checkbox"/> CA1	C57BL/6J	0.037
<input type="checkbox"/> CA1 - SSp-tr, PTLp	Vipr2-Cre_K...	0.186
<input type="checkbox"/> CA1 - DG	Kcnc2-Cre	0.362
<input type="checkbox"/> CA1	C57BL/6J	0.014
<input type="checkbox"/> CA1	Vipr2-Cre_K...	0.146
<input type="checkbox"/> CA1 - SUBv	Vipr2-Cre_K...	0.203
<input type="checkbox"/> CA1	Sim1-Cre	0.033
<input type="checkbox"/> CA1 - CA3, SUBv	Etv1-CreERT2	0.222
<input type="checkbox"/> CA3	C57BL/6J	0.040
<input type="checkbox"/> CA3 - CA1, DG	C57BL/6J	0.489
<input type="checkbox"/> CA3 - DG	C57BL/6J	0.294
<input type="checkbox"/> CA3 - CA2	C57BL/6J	0.018
<input type="checkbox"/> CA3 - DG	Grik4-Cre	0.451
<input type="checkbox"/> CA3 - DG	Prkcd-GluCla...	0.011
<input type="checkbox"/> CA3	C57BL/6J	0.081

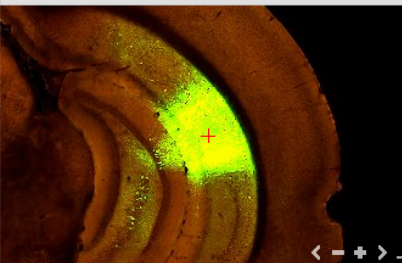
View Selections (0) Clear Selections

Experiment 181093729 - CA1 3D MIP

Projection Density



Section Images



Transgenic Line Etv1-CreERT2

Enriched in neocortical layer 5, and restricted populations within the cerebellum, thalamus, hippocampus, piriform cortex, and cortical subplate (amygdala)

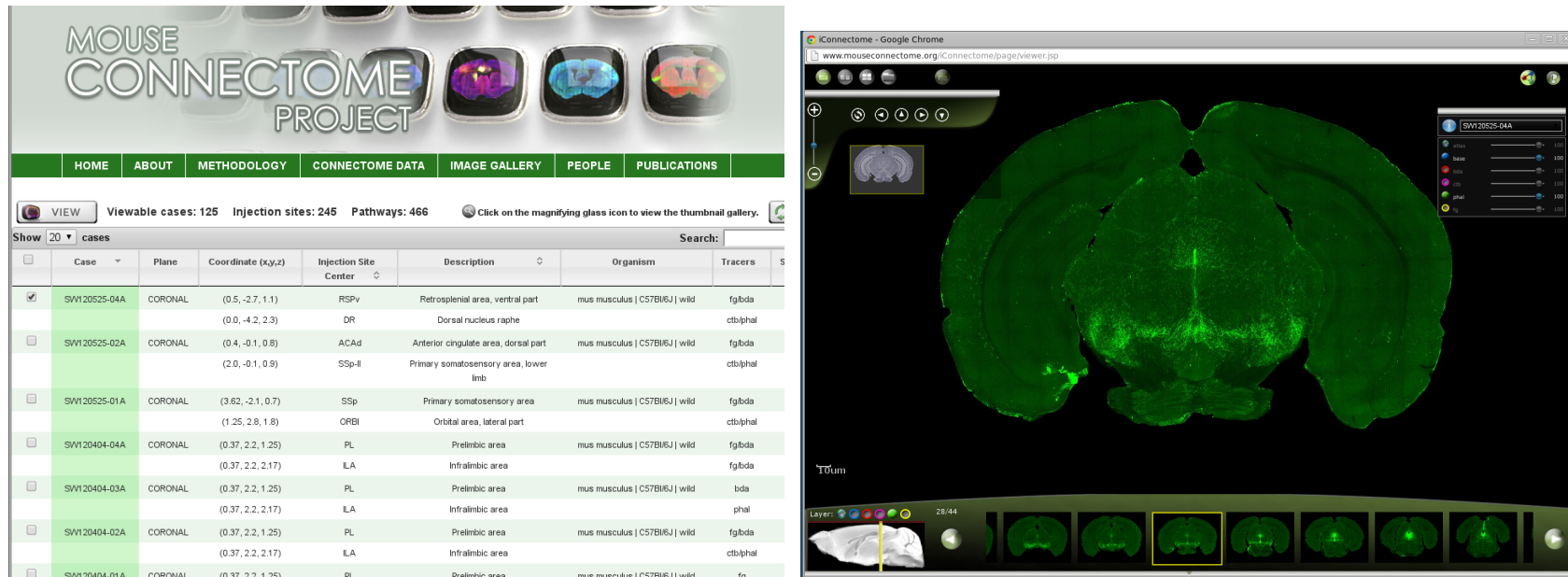
Correlative Search ?

Basic cell groups and regions (grey) Search

<http://connectivity.brain-map.org>

- Tracer injection-based (1010 injection sites).
- Fluorescence microscopy.

Mouse Connectome Project (UCLA)



The image shows two parts of the Mouse Connectome Project interface. On the left is a screenshot of the website's data table, and on the right is a screenshot of the 3D brain viewer.

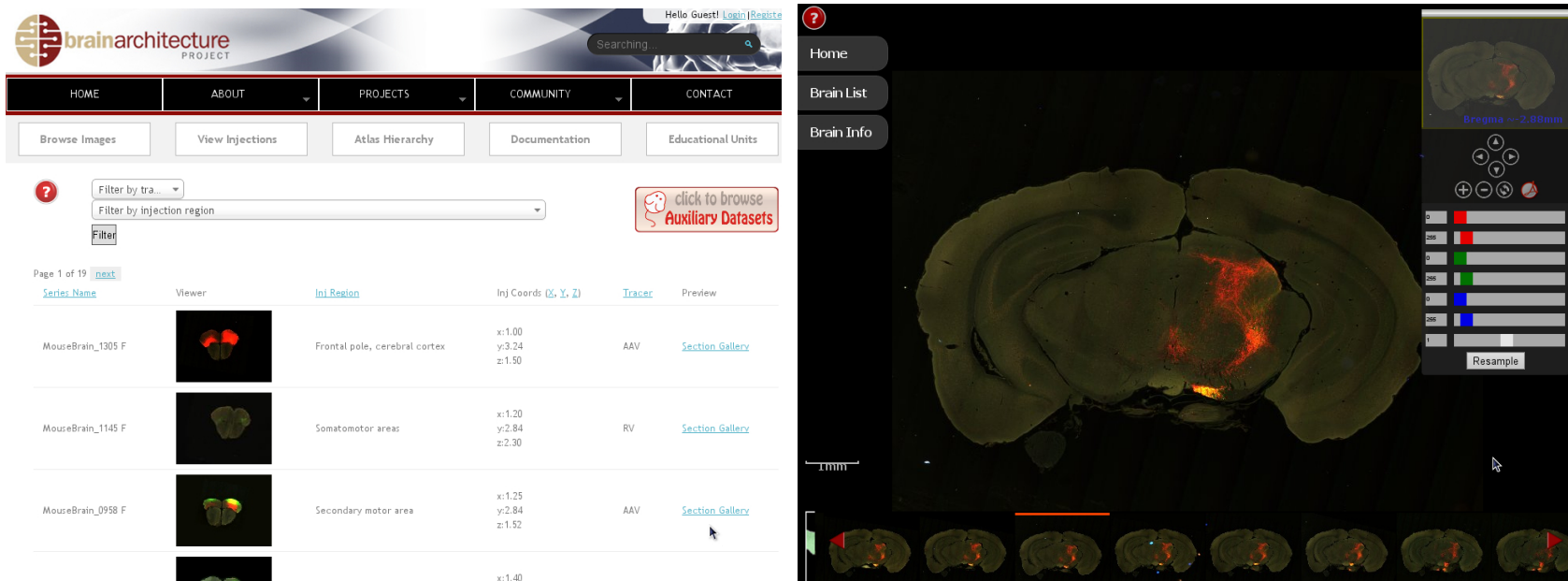
Case	Plane	Coordinate (x,y,z)	Injection Site Center	Description	Organism	Tracers
SW120525-04A	CORONAL	(0.5, -2.7, 1.1)	RSPV	Retrosplenial area, ventral part	mus musculus C57Bl/6J wild	fgbda
		(0.0, -4.2, 2.3)	DR	Dorsal nucleus raphe		ctb phal
SW120525-02A	CORONAL	(0.4, -0.1, 0.8)	ACAd	Anterior cingulate area, dorsal part	mus musculus C57Bl/6J wild	fgbda
		(2.0, -0.1, 0.9)	SSp-II	Primary somatosensory area, lower limb		ctb phal
SW120525-01A	CORONAL	(3.62, -2.1, 0.7)	SSp	Primary somatosensory area	mus musculus C57Bl/6J wild	fgbda
		(1.25, 2.8, 1.8)	ORB1	Orbital area, lateral part		ctb phal
SW120404-04A	CORONAL	(0.37, 2.2, 1.25)	PL	Prelimbic area	mus musculus C57Bl/6J wild	fgbda
		(0.37, 2.2, 2.17)	ILA	Infralimbic area		fgbda
SW120404-03A	CORONAL	(0.37, 2.2, 1.25)	PL	Prelimbic area	mus musculus C57Bl/6J wild	bda
		(0.37, 2.2, 2.17)	ILA	Infralimbic area		phal
SW120404-02A	CORONAL	(0.37, 2.2, 1.25)	PL	Prelimbic area	mus musculus C57Bl/6J wild	fgbda
		(0.37, 2.2, 2.17)	ILA	Infralimbic area		ctb phal
SW120404-01A	CORONAL	(0.37, 2.2, 1.25)	PL	Prelimbic area	mus musculus C57Bl/6J wild	fg

The 3D viewer on the right shows a coronal section of a mouse brain with green fluorescent tracers. A control panel on the right side of the viewer allows for adjusting the opacity of different tracers. A thumbnail gallery at the bottom shows a series of brain slices with the current slice highlighted.

<http://www.mouseconnectome.org/> (Hintiryan et al. 2012)

- Tracer injection-based (245 injection sites).
- Fluorescence microscopy.

Brain Architecture Project (CSHL)



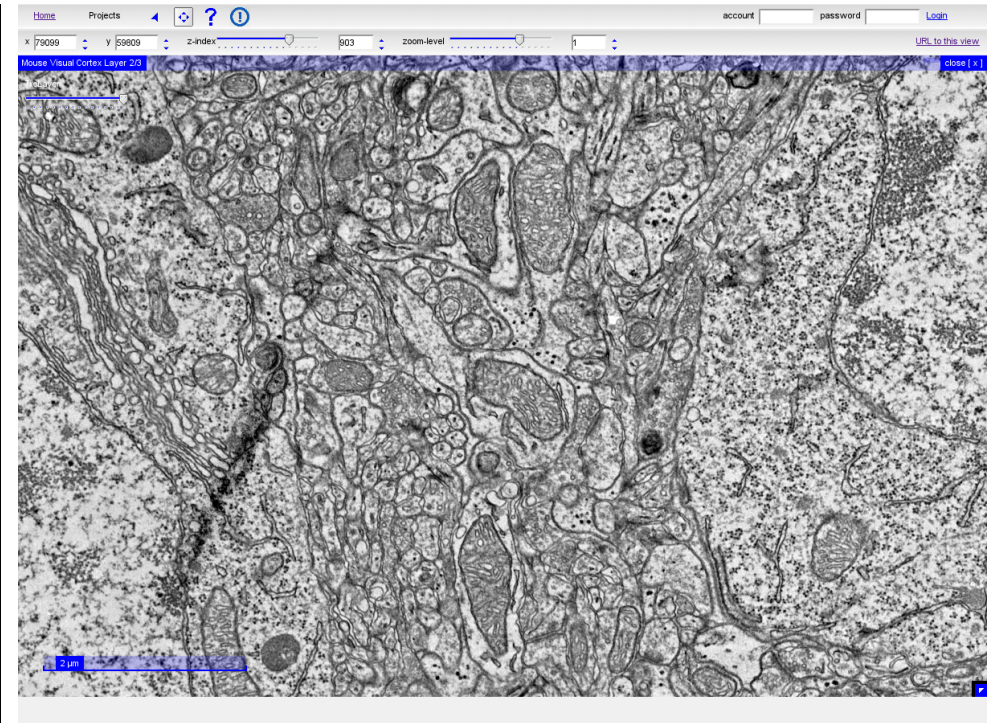
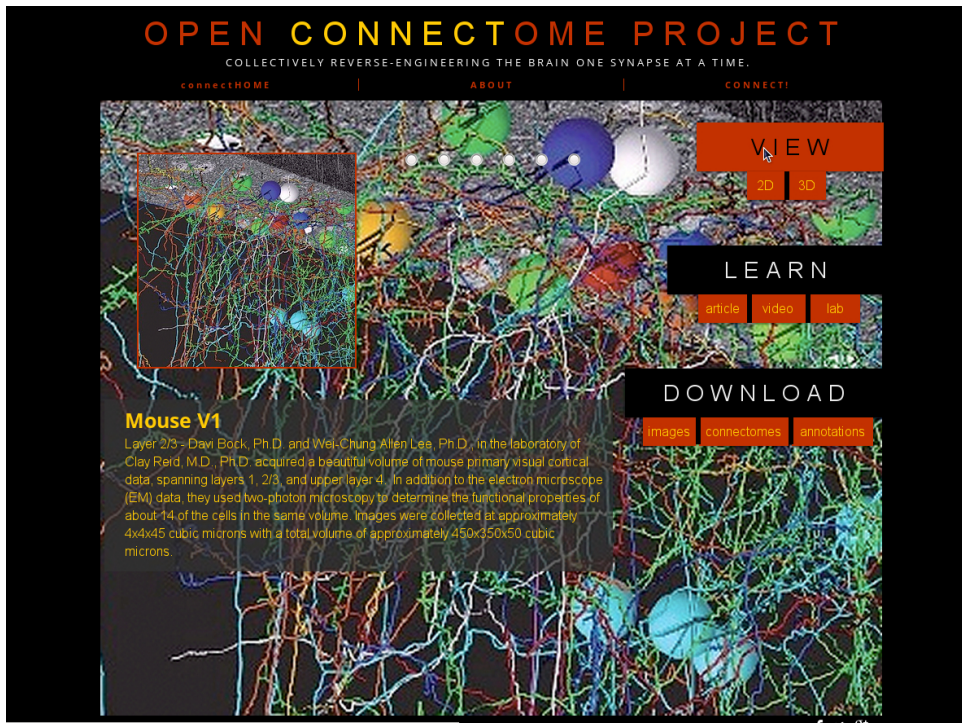
The screenshot displays the Brain Architecture Project website interface. On the left, a navigation menu includes 'HOME', 'ABOUT', 'PROJECTS', 'COMMUNITY', and 'CONTACT'. Below the menu are buttons for 'Browse Images', 'View Injections', 'Atlas Hierarchy', 'Documentation', and 'Educational Units'. A search bar and a 'Filter by injection region' dropdown are visible. A table lists injection sites with columns for 'Series Name', 'Viewer', 'Inj Region', 'Inj Coords (X, Y, Z)', 'Tracer', and 'Preview'. The table contains three rows of data for mouse brains. On the right, a large brain image shows a fluorescence tracer injection site in red. A control panel on the right side of the image includes a 'Brain List' and 'Brain Info' menu, a 'Resample' button, and a 'click to browse Auxiliary Datasets' button.

Series Name	Viewer	Inj Region	Inj Coords (X, Y, Z)	Tracer	Preview
MouseBrain_1305 F		Frontal pole, cerebral cortex	x:1.00 y:3.24 z:1.50	AAV	Section Gallery
MouseBrain_1145 F		Somatomotor areas	x:1.20 y:2.84 z:2.30	RV	Section Gallery
MouseBrain_0958 F		Secondary motor area	x:1.25 y:2.84 z:1.52	AAV	Section Gallery

<http://brainarchitecture.org> (Mitra 2012)

- Tracer injection-based (235 injection sites, mouse).
- Fluorescence microscopy. Other species also available.

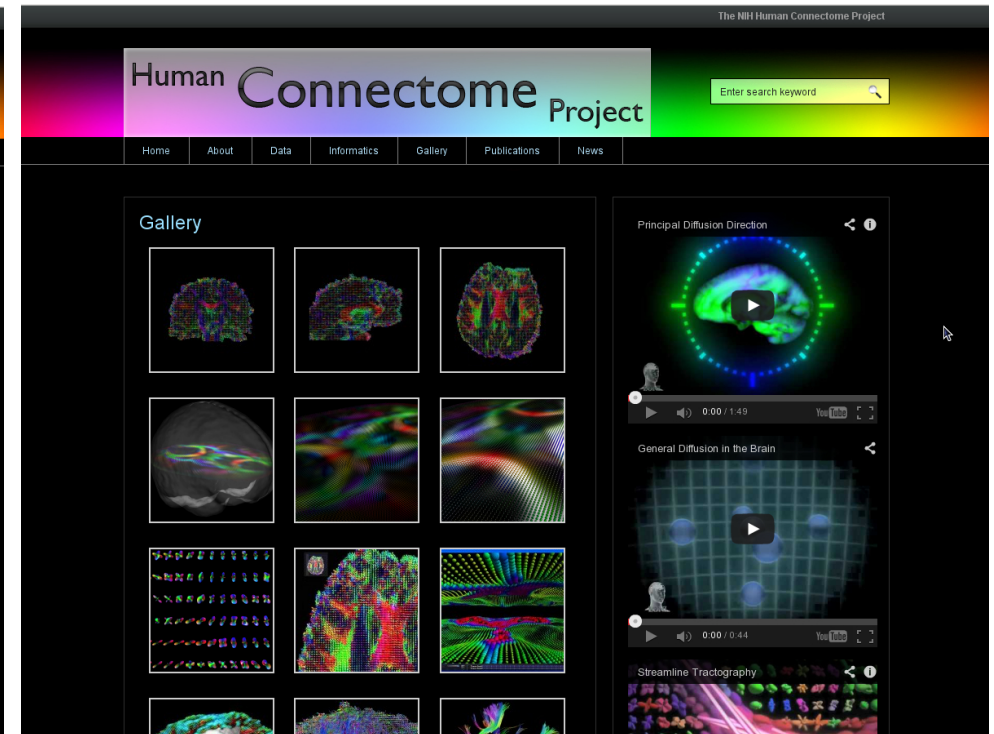
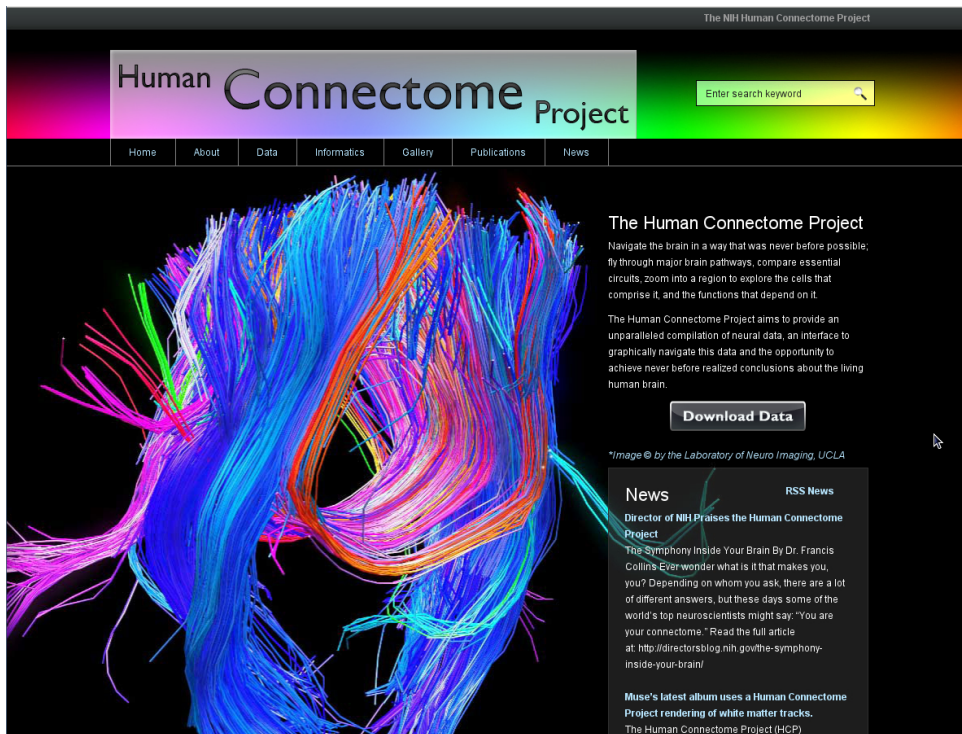
Open Connectome Project



<http://www.openconnectomeproject.org>

- EM data from mouse visual cortex (Bock et al. 2011).

Human Connectome Project



<http://www.humanconnectomeproject.org>

- DTI data from human (Van Essen et al. 2012).
- Also see (Hagmann et al. 2007).

CoCoMac

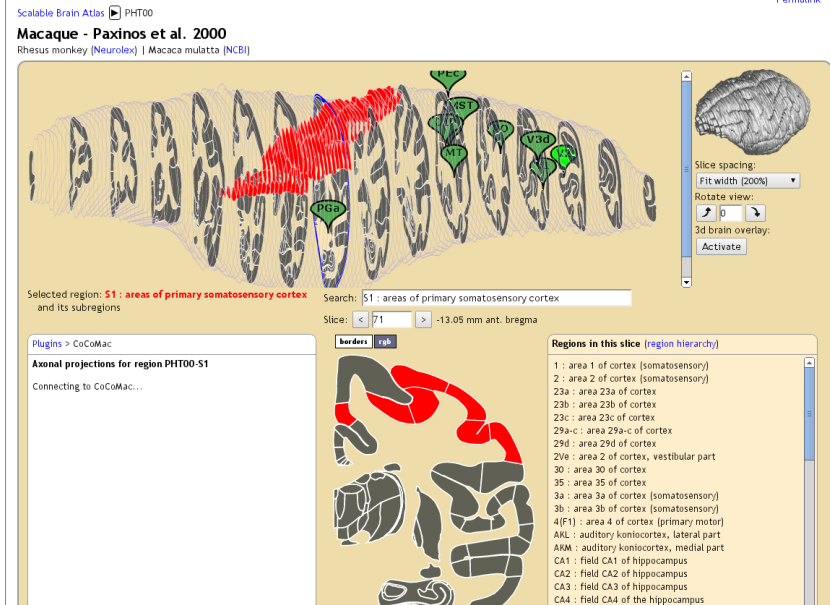
Connectivity of somatomotor and visual areas

anatomical projections

	target areas															
source areas	FA	FB	FBA	FCBm	46	PC	PEp	PF	PG	TA	TE	TEO	IF	OA	OB	OC
FA	1	1	1	1	0	0	1	0	0	1	0	0	0	0	0	0
FB	1	1	1	1	1	1	0	0	0	1	0	0	0	0	0	0
FBA	1	1	1	1	1	1	0	0	0	1	0	0	0	0	0	0
FCBm	1	1	1	1	1	1	0	0	0	1	0	0	0	0	0	0
46	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0
PB	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0
PC	1	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0
PEp	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
PF	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
PG	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
TA	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
TE	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
TEO	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
IF	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
OA	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
OB	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1
OC	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1

functional projections

	target areas															
stimulated areas	FA	FB	FBA	FCBm	46	PC	PEp	PF	PG	TA	TE	TEO	IF	OA	OB	OC
FA	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FB	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FBA	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FCBm	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
46	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
PB	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
PC	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
PEp	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
PF	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PG	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
TA	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
TE	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
TEO	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
IF	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0
OA	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
OB	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
OC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1



<http://cocomac.org> <http://scalablebrainatlas.incf.org>

- Macaque brain connectivity (based on 2508 tracer injections, 39,748 connection details, collected from the literature).
- Second version under preparation:
<http://cocomac.g-node.org/>

UCLA Multimodal Connectivity DB

[login | register | lost password?]

UCLA Multimodal Connectivity Database

Home About Analyze Network Compare Networks Browse All Data Upload New Data

The UCLA Multimodal Connectivity Database (UMCD) is a web-based repository and analysis site for connectivity matrices that have been derived from de-identified neuroimaging data. Users can analyze connectivity matrices that have been shared publicly and upload their own matrices to share or analyze privately.

Analyze a Brain Network

To analyze any shared brain network, choose a study name, a network name from that study, a weighting scheme, and the percentage of edges to include, then click Analyze. Momentarily, you'll get a full breakdown of the chosen network, including study info and network analysis.

Study Name: Choose from the list of available studies

Network Name: Choose from the list of shared networks for the chosen study

Weighting scheme: Choose a weighting scheme for the network, either weighted or binarized edges

Percentage of connections: Choose the percent of connections

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Browse All Data

All datasets that are viewable here have been publicly shared. Click on the links to view, download or analyze a specific dataset. If you're logged in, you can also see

Display 25 entries Search:

Details Page	Analyze	Study Name	Network Name	Atlas	Imaging Modality
View/Download	Analyze	ICBM	UCLA_ICBM_1004_DTI	Freesurfer_85	DTI
View/Download	Analyze	ICBM	ICBM_thickness_cormat	Freesurfer_88	Structural MRI
View/Download	Analyze	ICBM	ICBM_DTI_tractography	Freesurfer_88	DTI
View/Download	Analyze	ADHD200_CC200	KKI_2371032	Craddock 200	fMRI
View/Download	Analyze	ADHD200_CC200	KKI_2026113	Craddock 200	fMRI
View/Download	Analyze	ADHD200_CC200	KKI_3434578	Craddock 200	fMRI
View/Download	Analyze	ADHD200_CC200	KKI_8629223	Craddock 200	fMRI
View/Download	Analyze	ADHD200_CC200	KKI_1623716	Craddock 200	fMRI
View/Download	Analyze	ADHD200_CC200	KKI_1594156	Craddock 200	fMRI

<http://umcd.humanconnectomeproject.org>

- MRI-based connectivity database.

Part IV

Analysis

Geometric Reconstruction

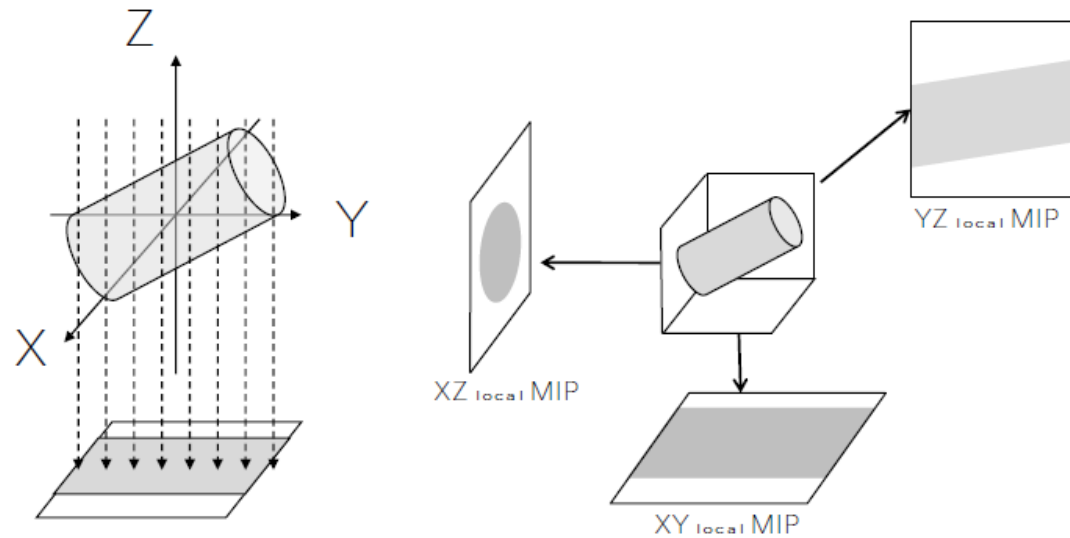
Raw data or volume visualization is not enough:

- We need to reconstruct the geometric structure of the objects in the data.
- Data can be huge (several TB): manual tracing is not an option.
- We need automated algorithms.

Reconstruction Approaches

- Segment-then-connect: the most common approach
- 3D convolutional network: Jain et al. (2010)
- Template-matching-based vector tracing: Al-Kofahi et al. (2002); Han et al. (2009b,a); Han (2009); Luisi et al. (2011)
- Semi-automated reconstruction: Yang and Choe (2011b)
- Topology-constrained reconstruction: Yang and Choe (2011a); Jain et al. (2007)
- Crowd sourcing: Eyewire.org (Seung and Burnes 2012).

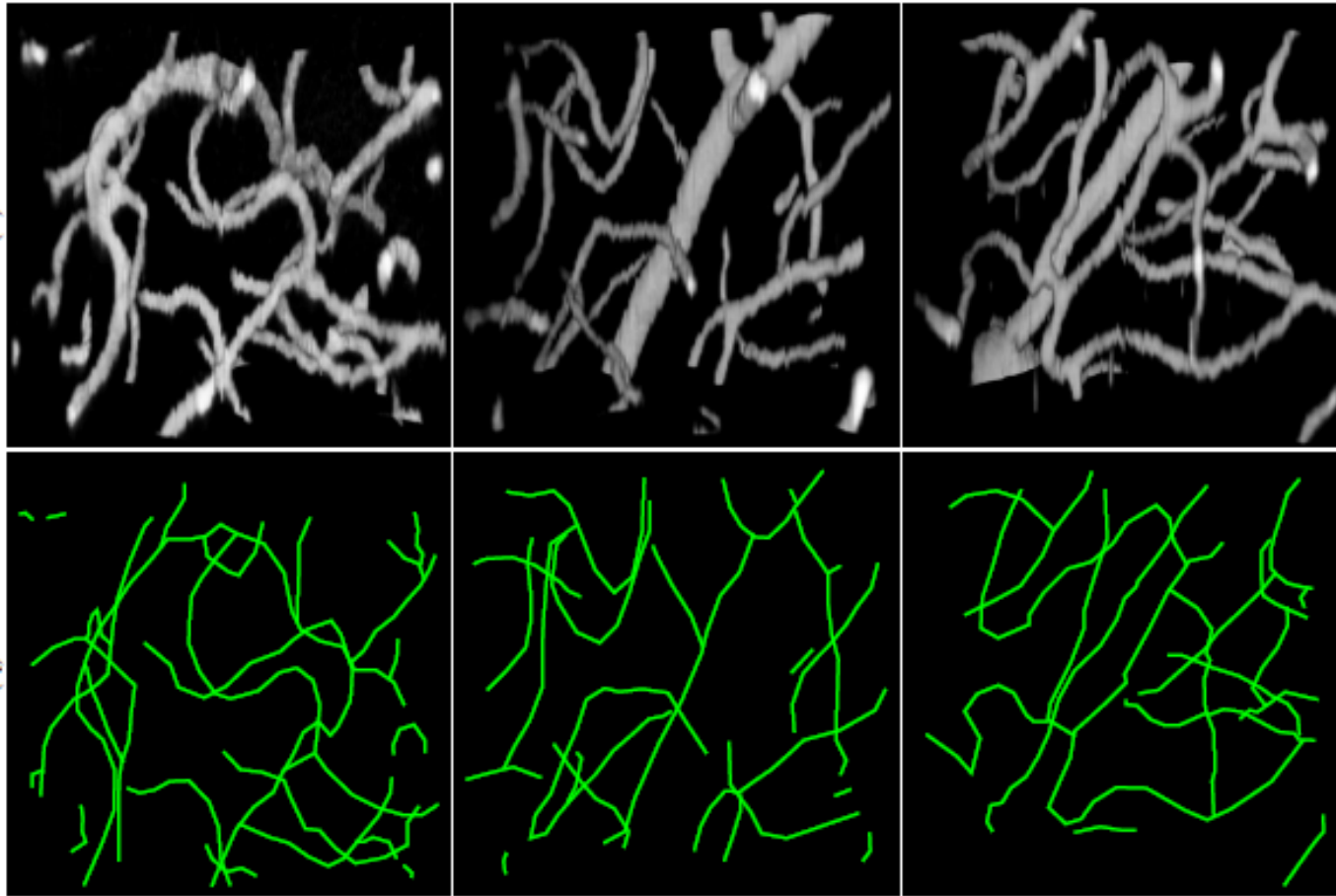
Tracing Example: MIP-Based Tracing



Han (2009)

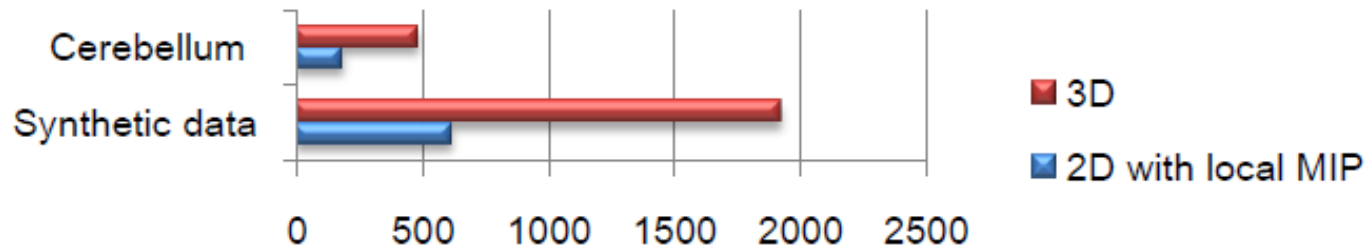
- Maximum-Intensity Projection (MIP).
- MIP-based tracing: Trace on projected 2D images.

MIP-Based Tracing Results



- KESM mouse vasculature data.

MIP-Based Tracing Performance



- MIP-based approach about $3\times$ faster than 3D version.

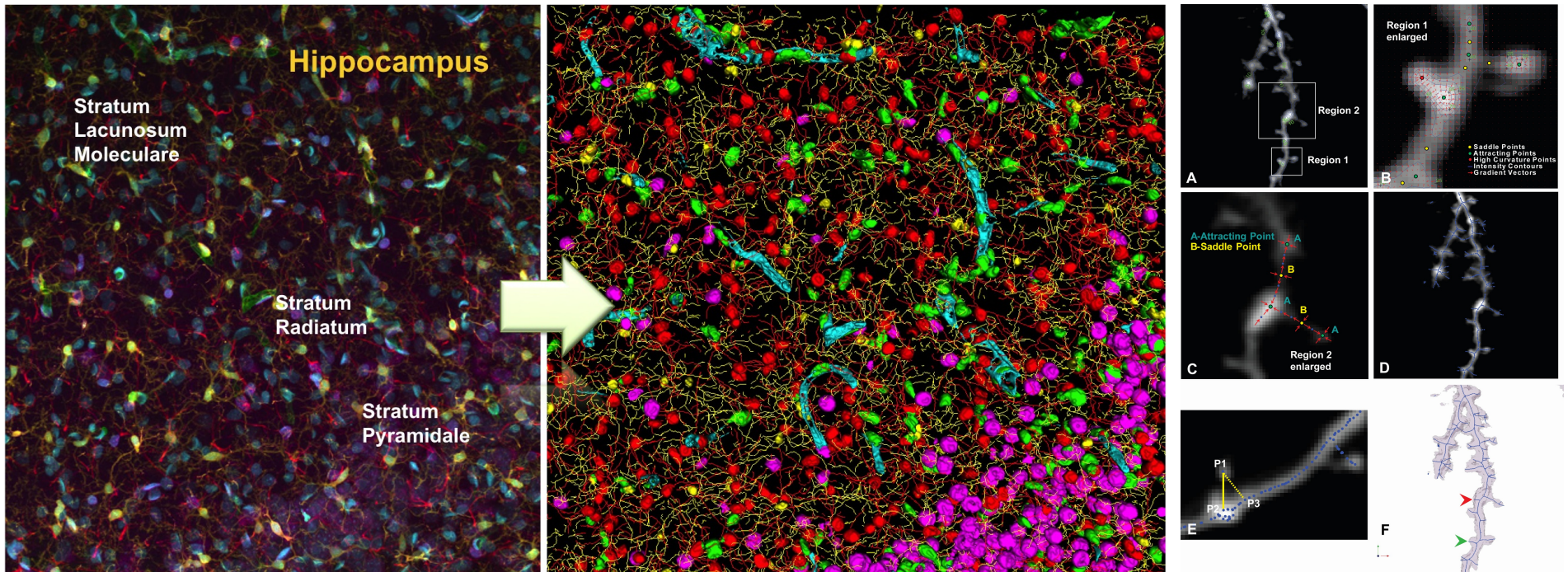
MIP-Based Tracing: Validation

	ϕ			φ		
	μ	σ	p -value	μ	σ	p -value
R1	0.1518	0.1762	0.4188	1.2131	0.3529	0.6853
R2	0.1325	0.1804		1.1294	0.3016	

Error

- Validation against small manual ground-truth (R1 and R2).
- ϕ = centerline deviation, φ = length difference.

FARSight Toolkit (U Houston)



<http://www.farsight-toolkit.org> (Luisi et al. 2011)

- 2D and 3D image analysis toolkit.

Other Reconstruction Tools

- KNOSSOS: 3D image data (mostly for EM) analysis tool (mostly manual). <http://www.knossostool.org/>
- EyeWire: crowd-sourcing EM reconstruction portal.
<http://eyewire.org/>
- Reconstruct: EM reconstruction tool (manual).
<http://synapses.clm.utexas.edu/tools/reconstruct/reconstruct.stm>
- Generic (yet powerful) tools:
 - ImageJ: <http://rsbweb.nih.gov/ij/>
 - ITK: <http://www.itk.org/>

Connectivity Analysis

- Graph-theory based analysis (Sporns 2002, 2011)
 - In-degree, out-degree, cluster index, power law
- Motif analysis (Milo et al. 2002).
 - Statistics of small sub-graph patterns.
- Dynamics (Thiel et al. 2003; Sporns and Tononi 2002)
- Large-scale simulation based on DTI (Izhikevich and Edelman 2008)
- Time is a crucial factor in connectivity analysis (Choe 2004).

Part V

Theoretical Insights

Wrap Up

Thinking Beyond Connectomics

Connections alone not enough:

- Sign: excitatory/inhibitory
- Weight: synaptic strength
- Delay: both conduction delay and integration time
- Molecular dynamics and gene expression
- Plasticity

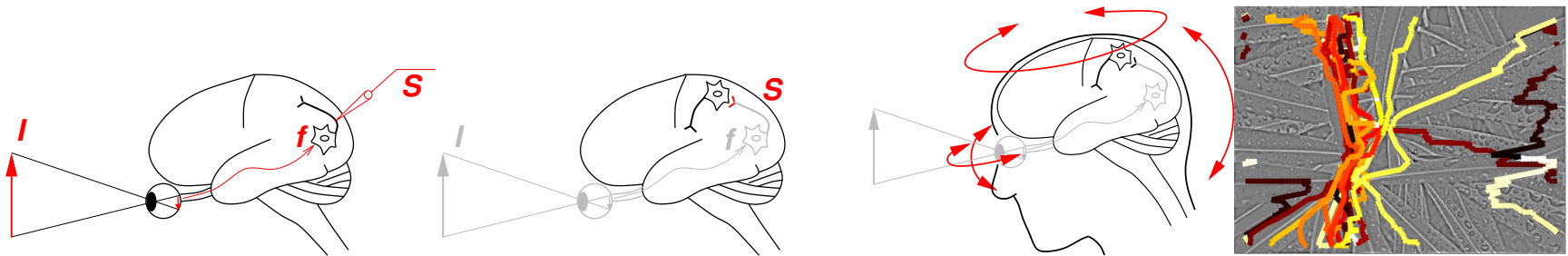
Is the Brain Enough? – Will Need the Body

- Brain is part of the body and a lot of function is performed by the spinal cord and the peripheral nervous system.
- To fully understand brain function, it must be understood in the context of the entire body.
- Imaging whole organisms may be necessary for a true understanding of brain function.

Risk of Doubling our Task?

- Without a proper theoretical framework for analysis, the resulting simulation can be as complex and hard to understand as the real brain.
- Such blind simulation could double our task.
- However, it has distinct merits:
 - Full read/write access and localized lesions.
 - Can investigate subjective phenomena such as consciousness (have the brain simulation study itself!).
 - Systematic, programmatic investigation becomes possible (automated science).

Conceptual Breakthroughs Needed

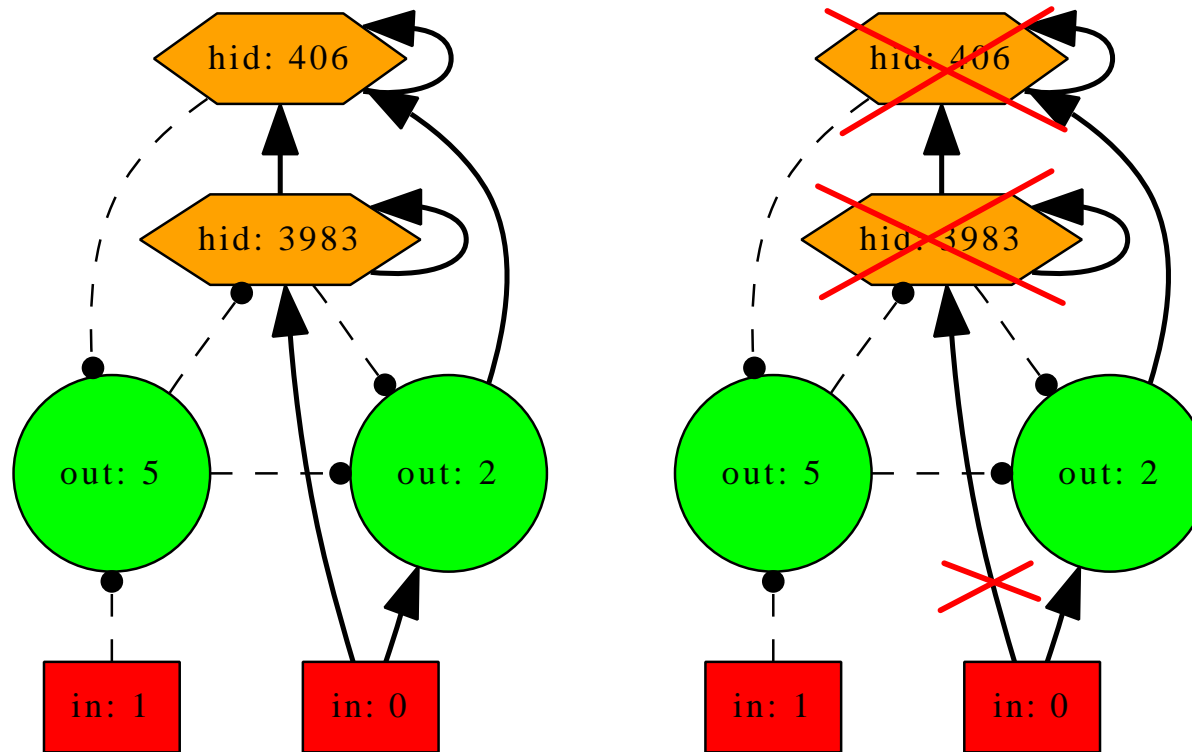


Choe and Smith (2006); Choe et al. (2007)

- Posing the right questions (Choe and Mann 2012): Internal perspective, problems faced by the brain itself.
- Sensorimotor perspective (Choe and Smith 2006; Choe et al. 2007).
- Developmental perspective.
- Evolutionary perspective (Chung and Choe 2011; Kwon and Choe 2008; Choe et al. 2012).
- Temporal perspective (Choe 2004; Lim and Choe 2008).

Inferring Function from a Brain

Network: A Cautionary Tale



Analyze this!

- hid = hidden neuron, out = output neuron, in = input unit, arrow = excitatory connection, disc = inhibitory connection

Conclusion

- Understanding brain function requires a system-level investigation at a microscopic resolution.
- Innovative microscopy technologies are enabling a data-driven investigation linking the microstructure to the system level.
- A robust, accessible informatics platform is needed for knowledge discovery.
- Deep theoretical insights are needed to guide our investigation.

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