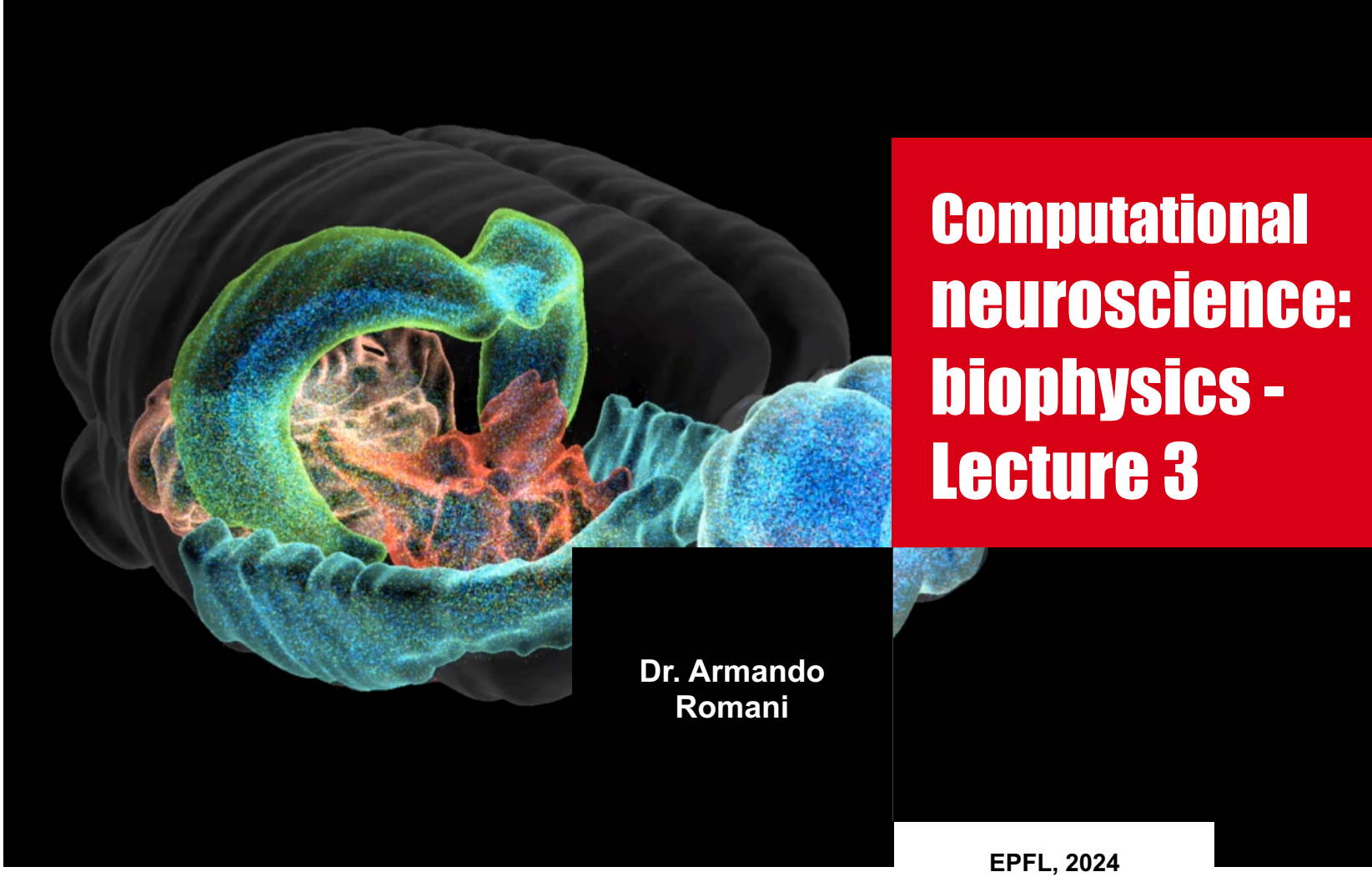


Computational neuroscience: biophysics - Lecture 3

Dr. Armando Romani

- Blue Brain Project

EPFL, 2024

Morphologies

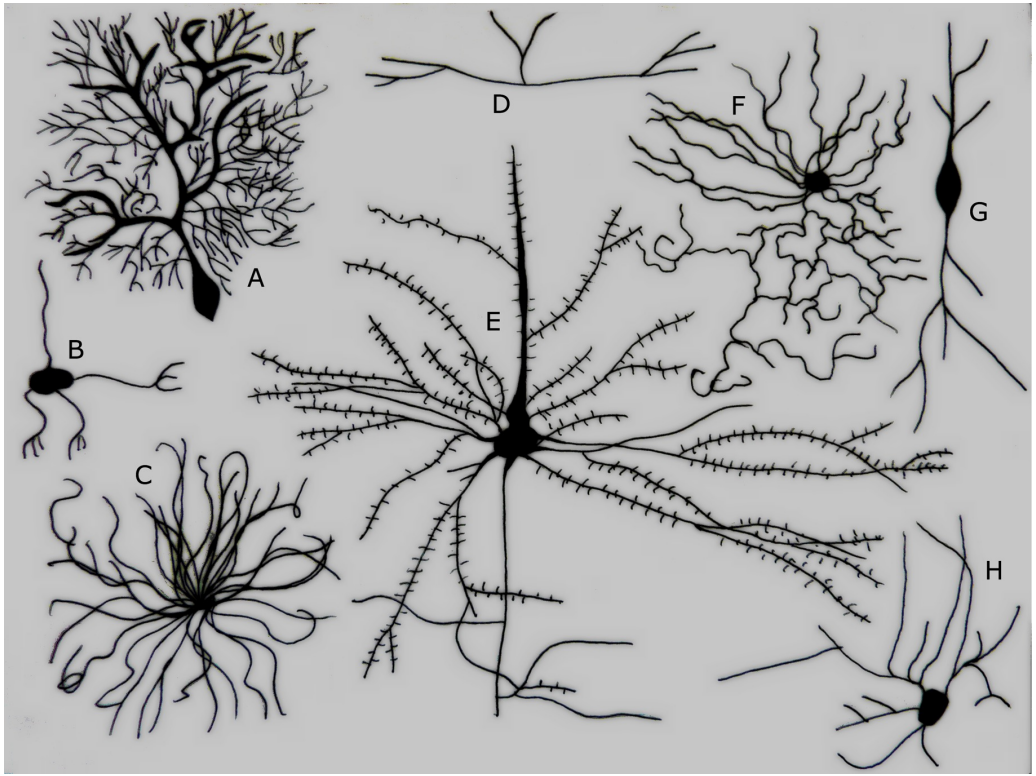
Lecture Overview

- Scope
- Approaches
- Applications

Lecture Overview

- **Scope**
- Approaches
- Applications

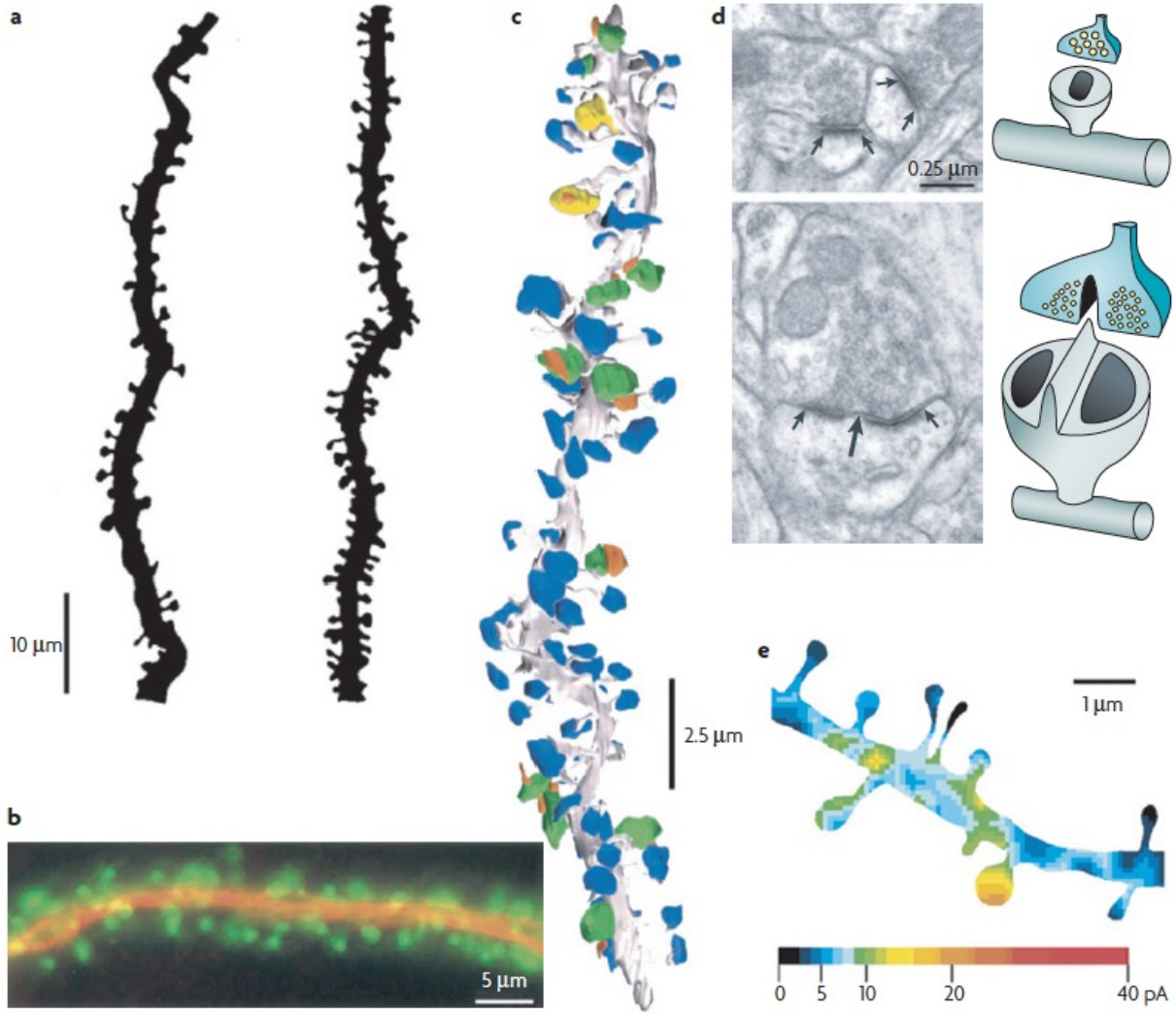
Neuron types
by Santiago Ramón y Cajal (1887)



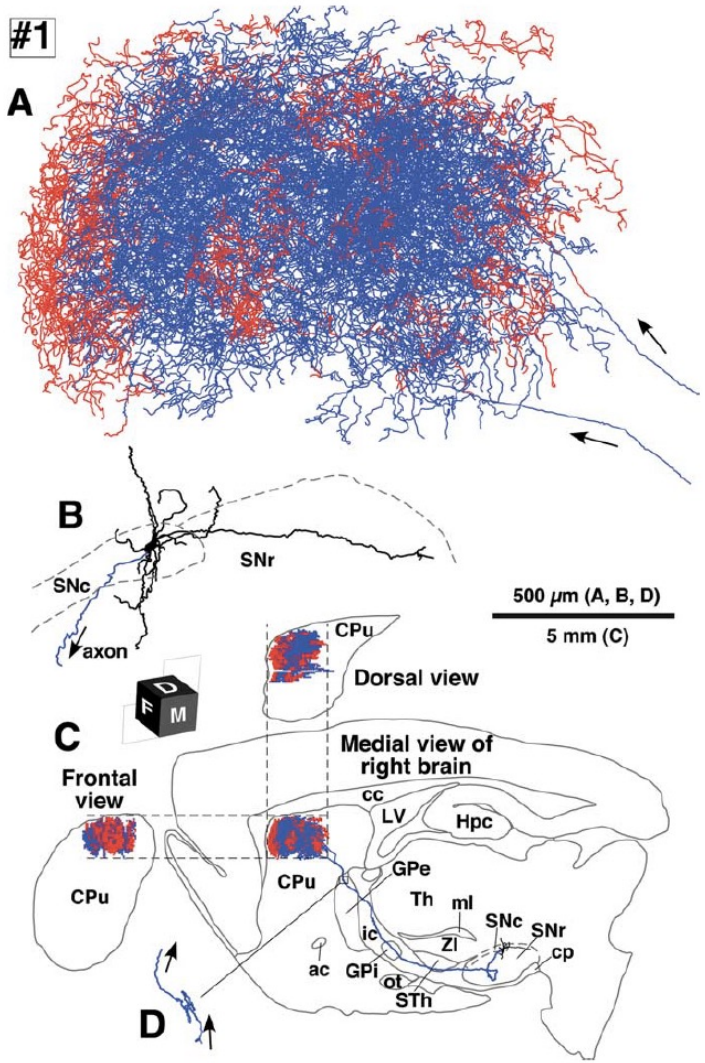
Different Types of Neurons. A. Purkinje cell B. Granule cell C. Motor neuron D. Tripolar neuron E. Pyramidal Cell F. Chandelier cell G. Spindle neuron H. Stellate cell (Credit: Ferris Jabr; based on reconstructions and drawings by Cajal)

EPFL

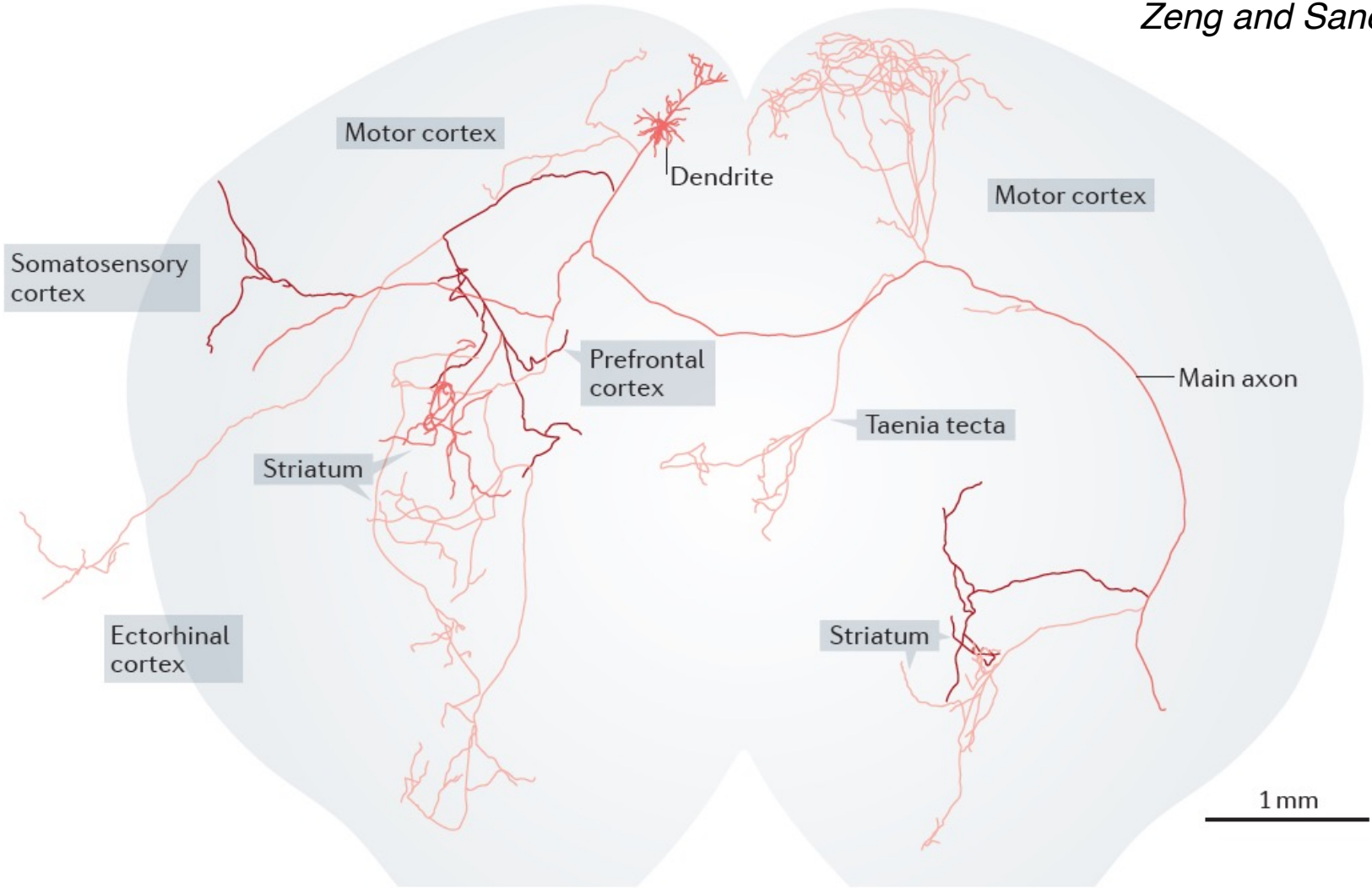
Spruston, 2008



Matsuda et al, 2009



Zeng and Sanes, 2017



Neuron Classification

Why?

- Understand the brain. Dimensionality reduction
- Communication among scientists
- Improve reproducibility
- Study diseases
- Understand evolution. Comparison among species
- Understand development
- Identify new cell types

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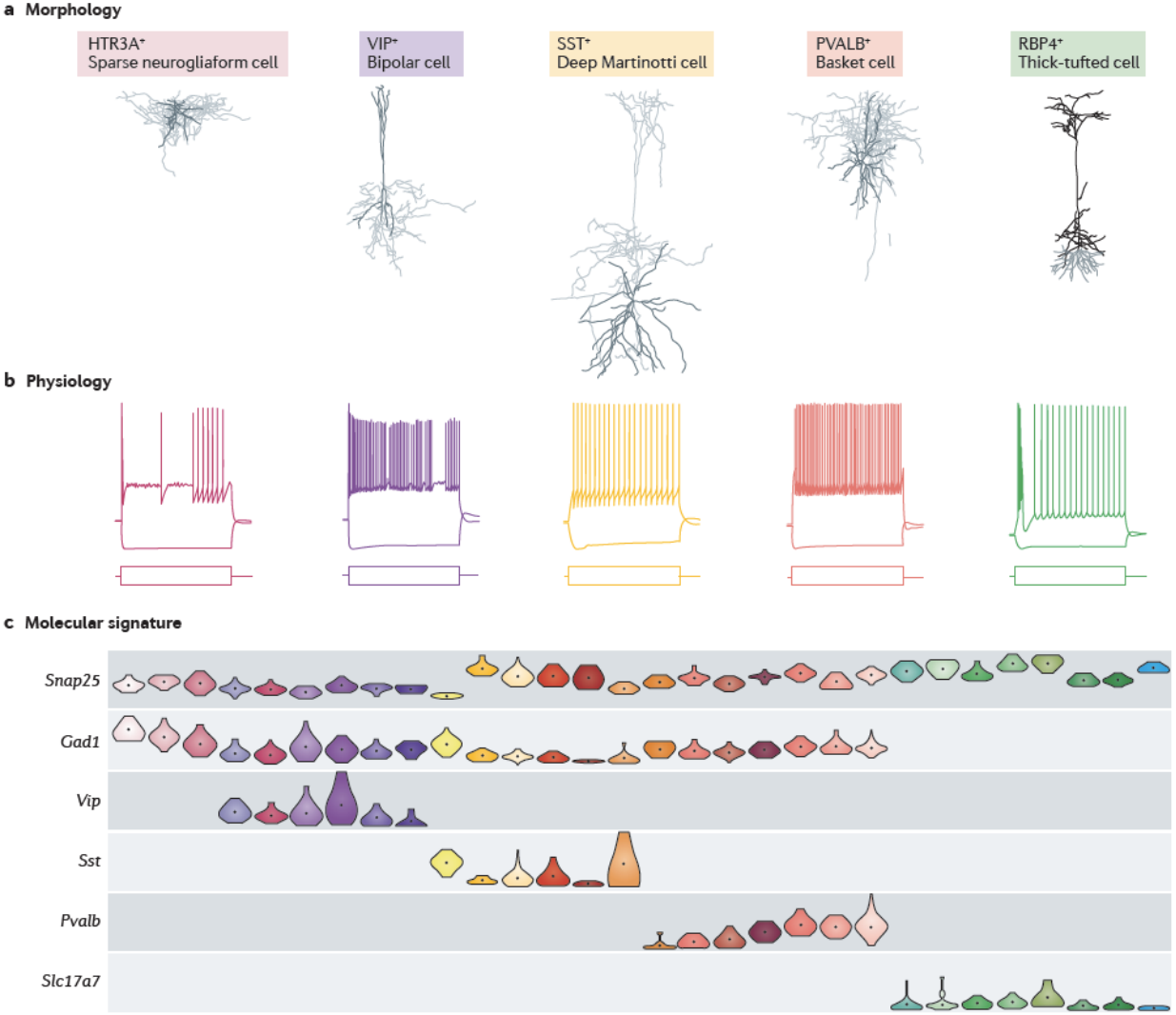
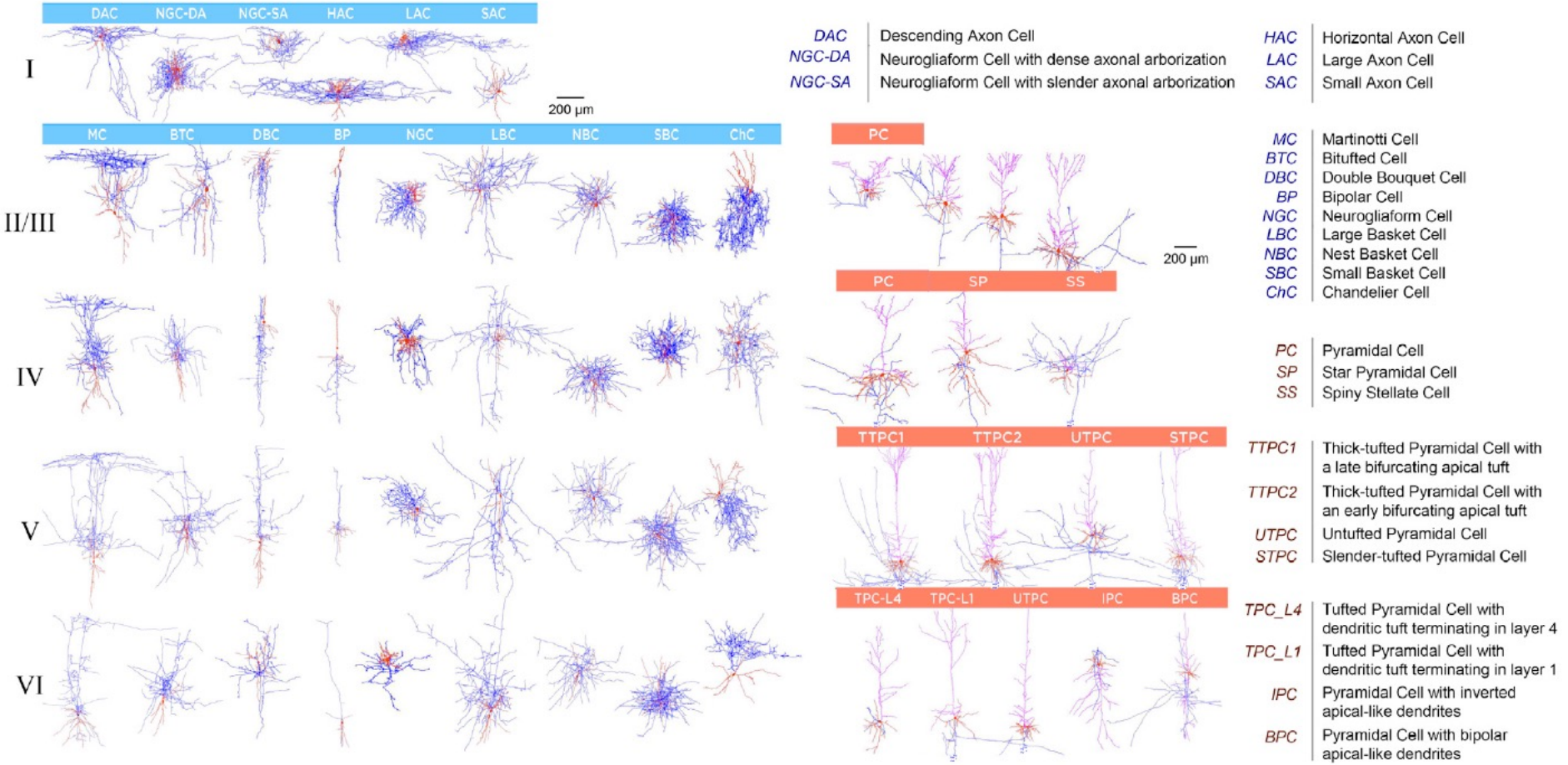
Zeng and Sanes, 2017





Markram et al 2015

Figure 2. Table of Neocortical Neuronal Morphologies

Exemplar 3D reconstructions of 55 m-types. Morphologies in L2 and L3 are not separated. Axon in blue, dendrites in red. Full morphologies are not always shown.

Challenges

- Definition a ‘cell type’ is still elusive
- Find the correct granularity
- Morphologies change during development
- Some features are continuous
- Morphologies change over time due to activity, hormones, …
- The three classification methods not always vary together

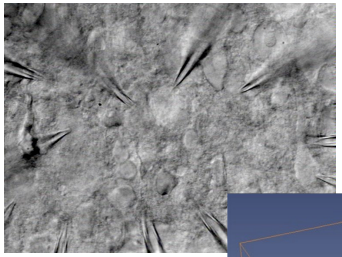
Summary 1

- Research is revealing a wonderful complexity of morphologies
- Morphological diversity correlates with a functional diversity
- We have to bridle this diversity but challenges still exist:
  - Unknown number of morphologies.
  - Define a cell type. Classification.
  - Faithful reconstruction of the morphology.

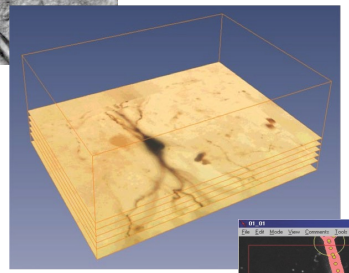
Lecture Overview

- Scope
- **Approaches**
- Applications

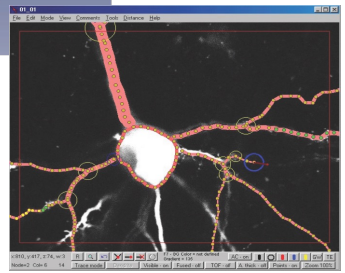
How to reconstruct a morphology



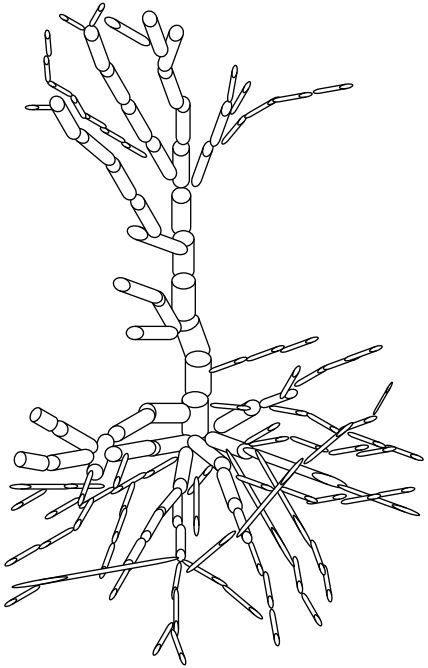
Labeling of cells



Histology



3D reconstruction



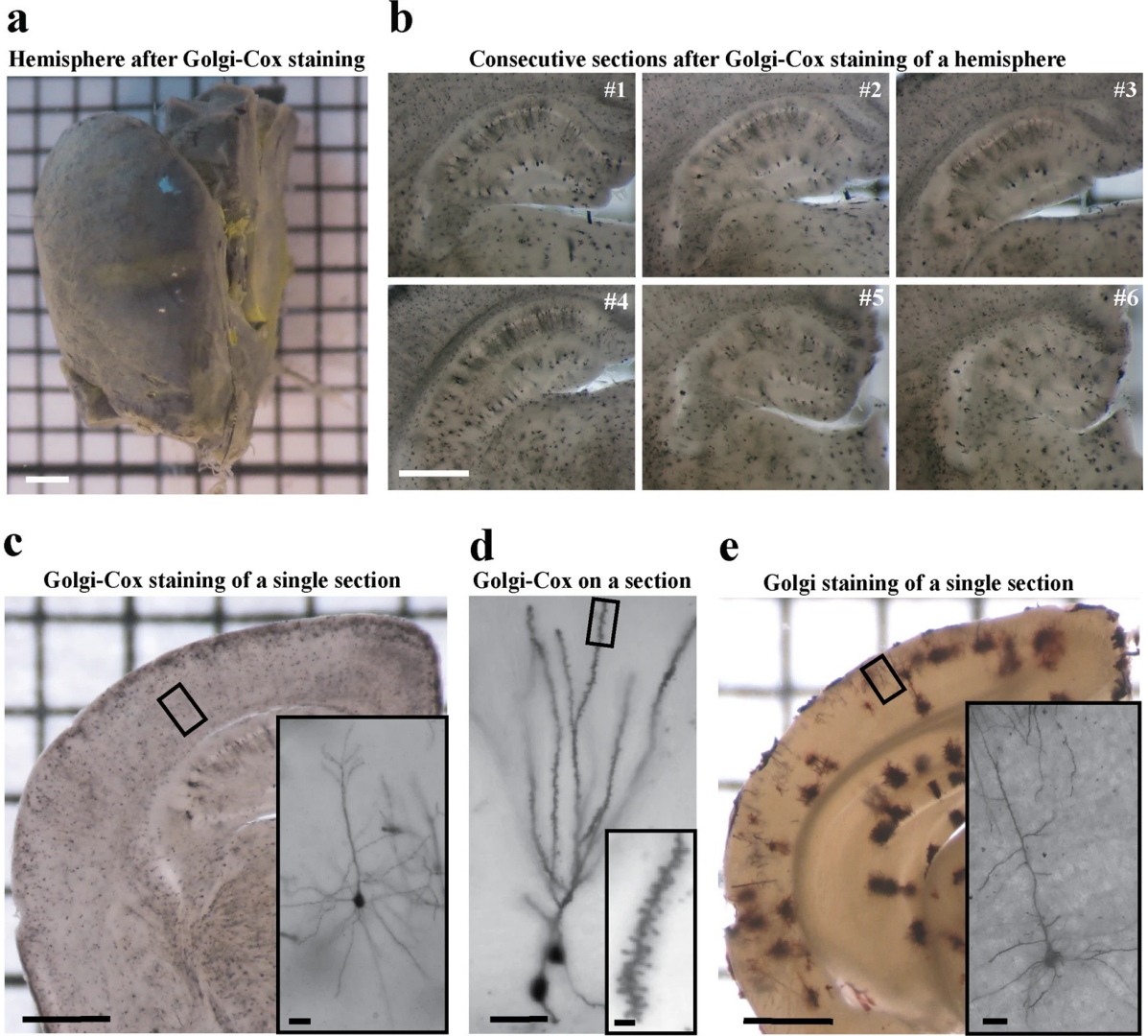
Staining techniques

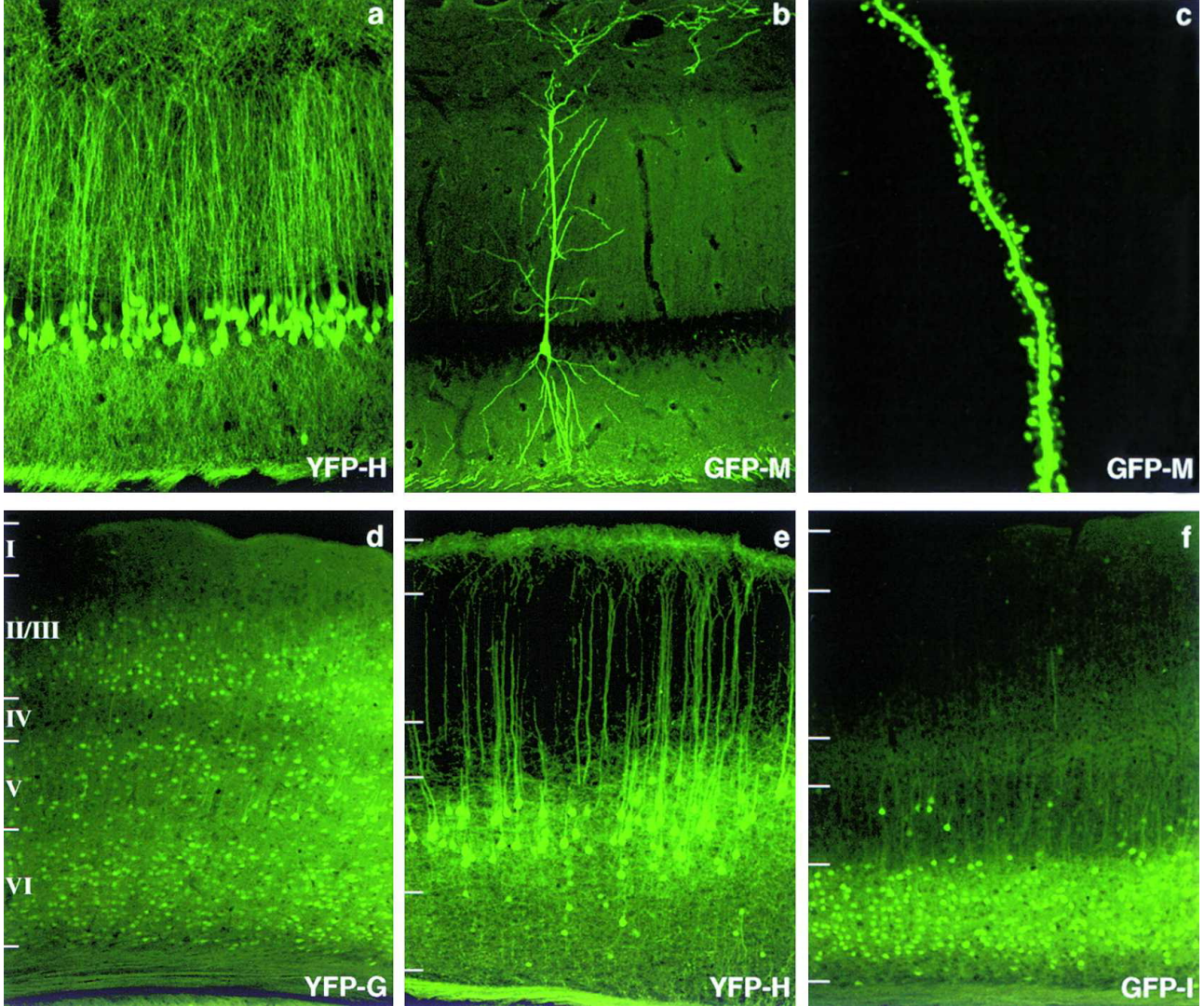
- In-vitro staining
- In-vivo staining

Staining techniques

- Staining with heavy metals (Golgi). Light microscopy (LM)
- Fluorescence proteins (GFP, RFP, YFP) introduced transgenically in selected cells. Fluorescence microscopy
- Immunostaining. Antibody labelled with fluorescent or chromogenic tags. Light, fluorescent, or electron microscopy (EM) depending on the label.
- Direct injection of fluorescent dyes or biotin variants (biocytin or neurobiotin) *in-vivo* or *in-vitro* (during electrophysiology experiments).

Vints et al., 2019





Feng et al., 2000

Immuno-staining

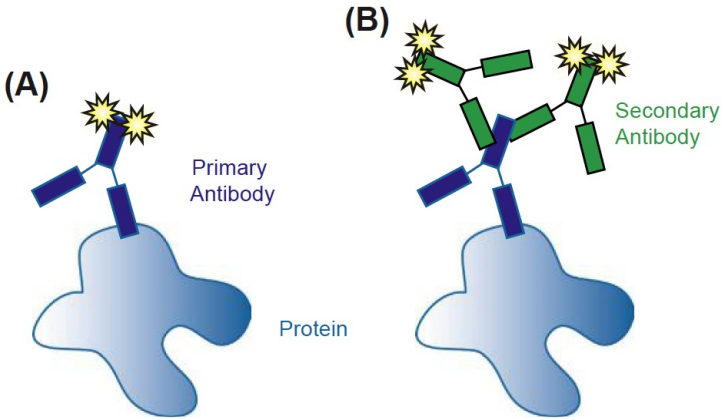


FIGURE 6.6 Immunohistochemistry (IHC). (A) In direct IHC, primary antibodies are conjugated directly to a label that can be visualized. (B) In indirect IHC, primary antibodies attract labeled secondary antibodies, further amplifying the signal.

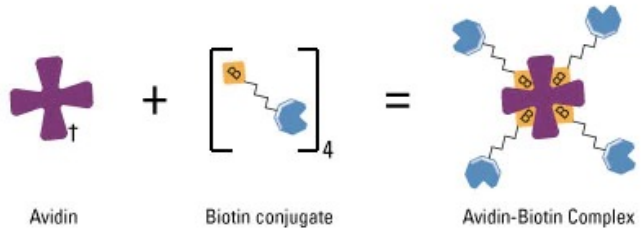
TABLE 6.3 Commonly Used Antibodies that Label Specific Neural Cell Types

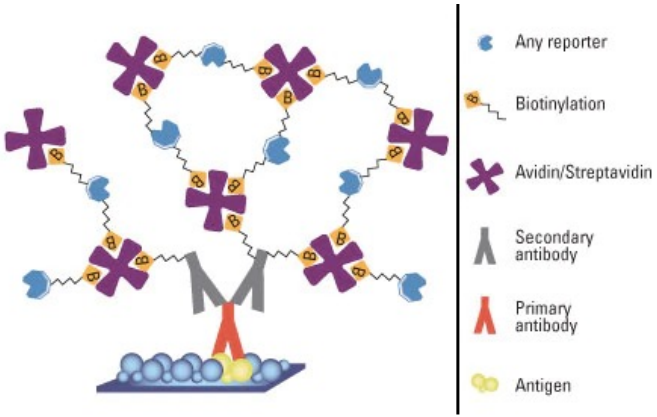
Cell Type	Antibodies
Progenitors/radial glia	Nestin; Pax6; RC2; vimentin; NF (neurofilament)
Young neurons	Doublecortin (DCX); NeuroD
Neurons	Tuj1 (neuron-specific β-tubulin); NeuN
Dendrites	MAP2
Axons	Tau-1, L1, Tag-1
Synapses	PSD95, synapsin
Neuronal subtypes	GAD (GABAergic neurons); vGLUT (glutamatergic); TH (dopaminergic); 5-HT (serotonergic); AChE (cholinergic)
Glia	GFAP (astrocytes); MBP (oligodendrocytes, myelin); PLP
Oligodendrocyte progenitor cells (OPC)	NG2, A2B5, O4 (late progenitor)

Carter and Shieh, 2015

Avidin-Biotin Complex (ABC)

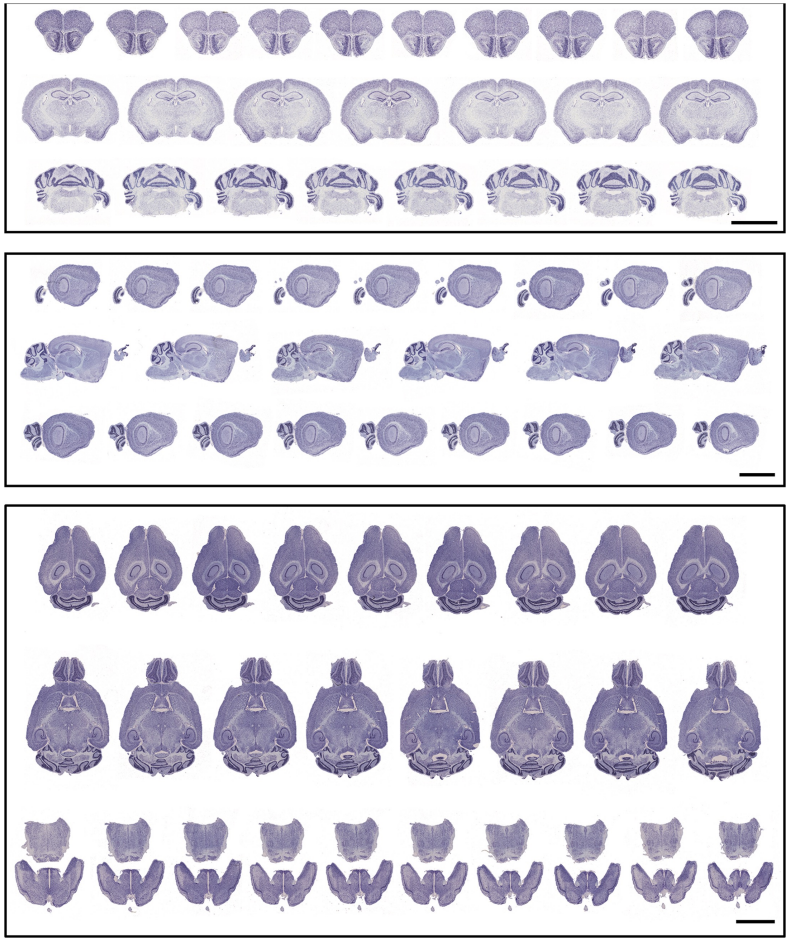
- Fluorophore conjugated to biotin
- The complex can amplify the signal





Prepare the tissue for microscope

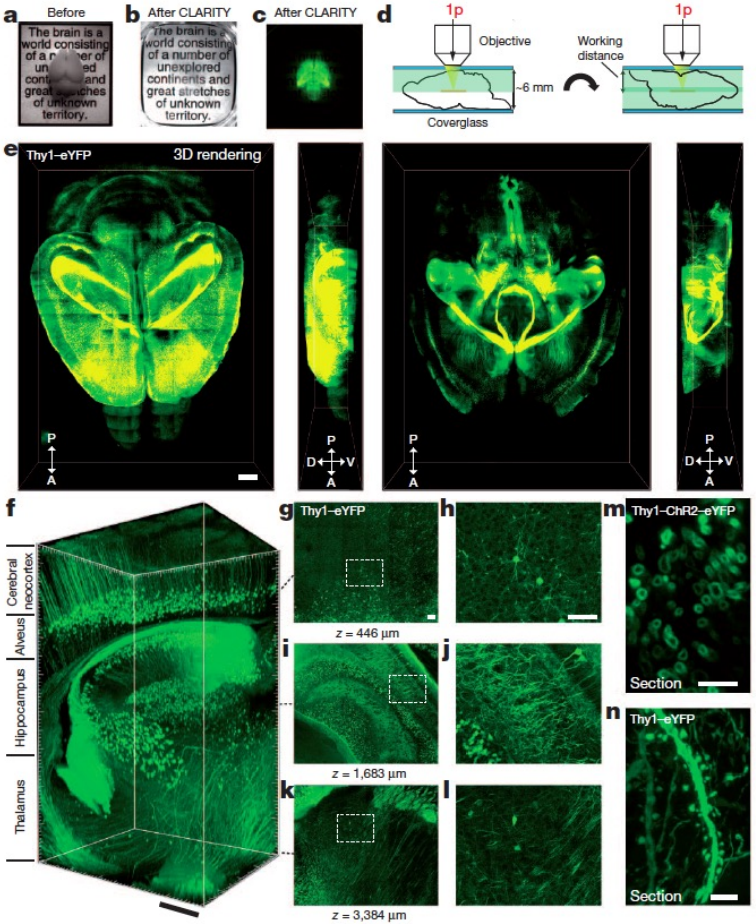
- Sectioning



Pinskiy et al., 2015

Prepare the tissue for microscope

- Sectioning
- CLARITY

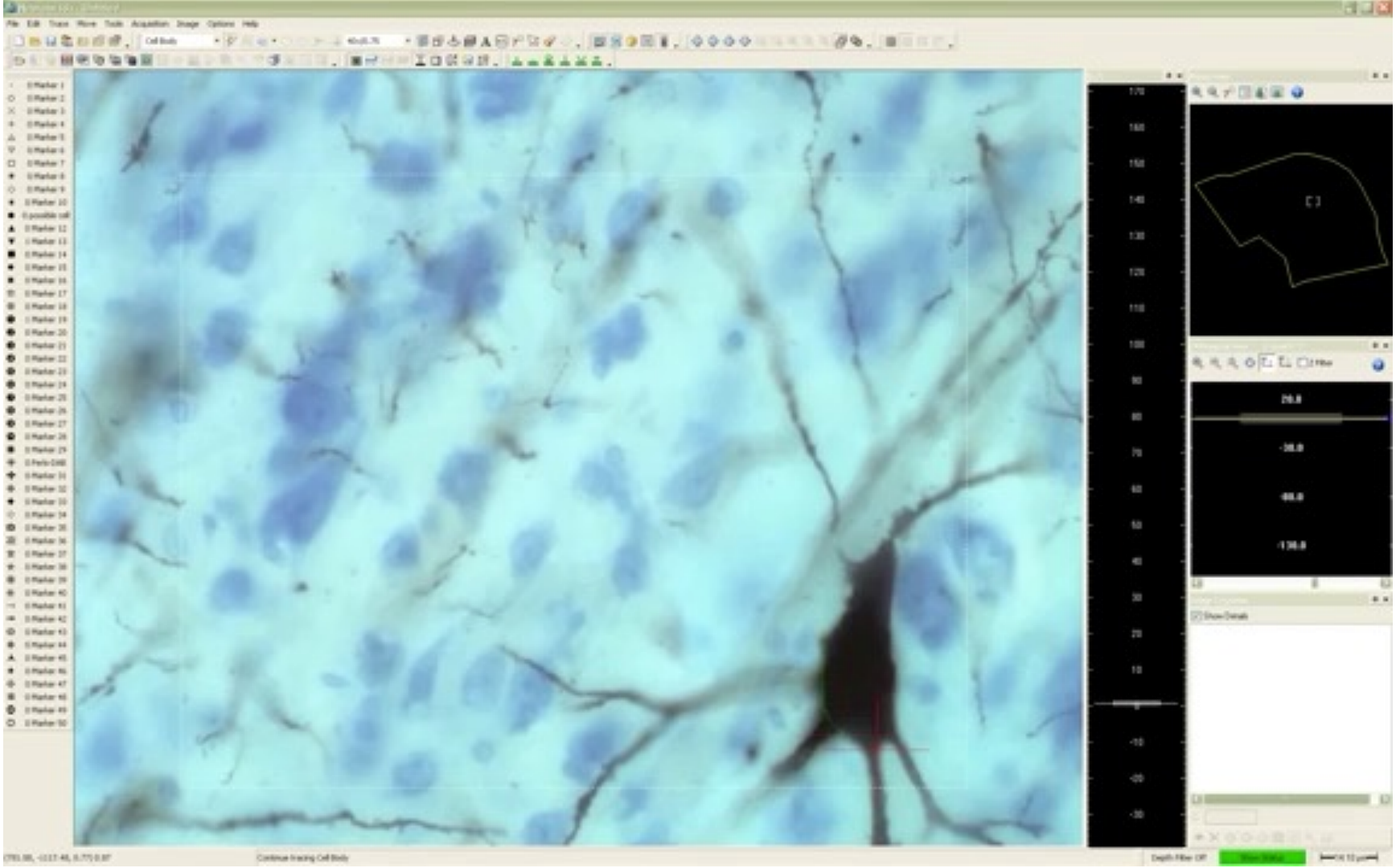


Chung et al., 2013

Microscopy

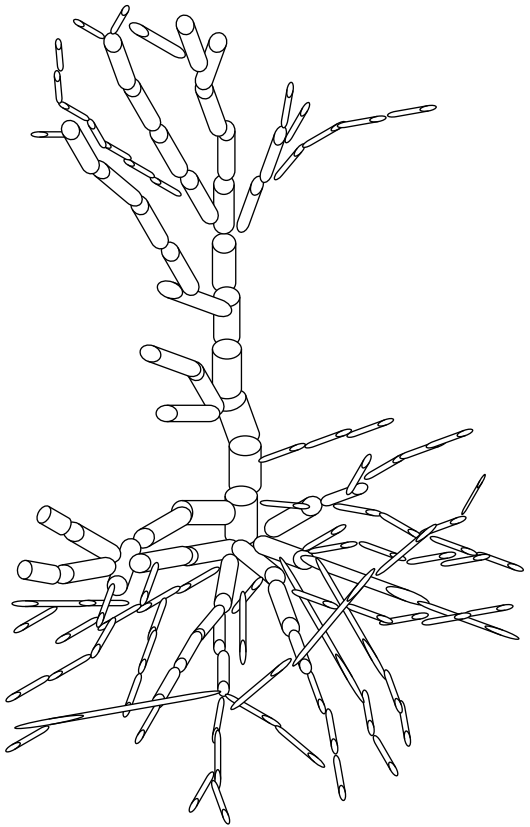
- Light microscopy
- Fluorescence microscopy
- Electron microscopy (EM)

Neurolucida tracing

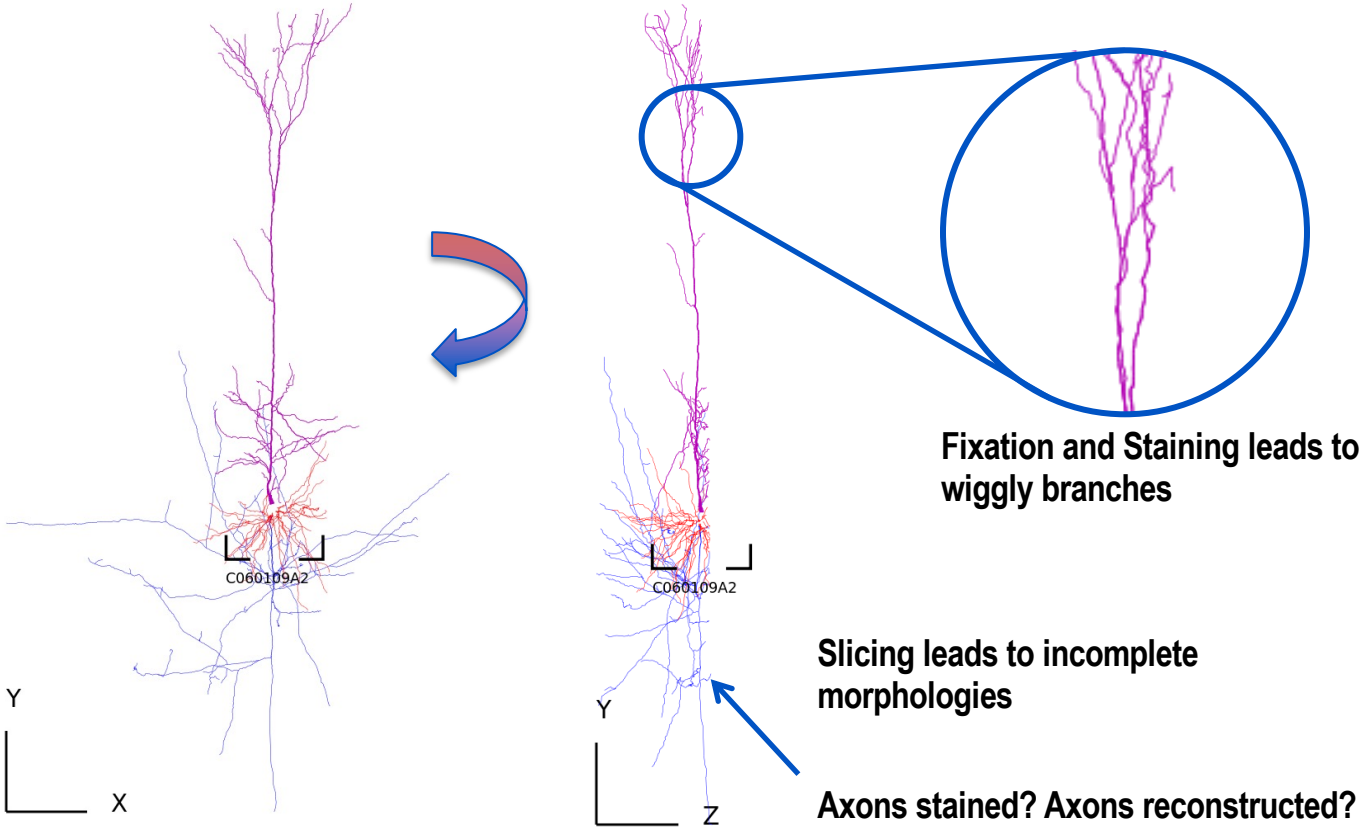


Reconstruction result

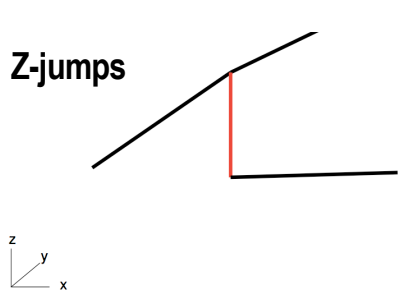
- We assume that the morphology can be faithfully described as a series of truncated cones or frusta
- To increase the precision of our approximation, we can increase the number of segments

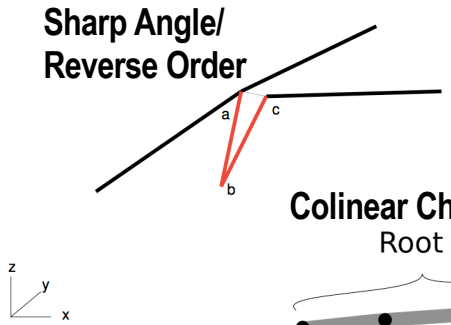


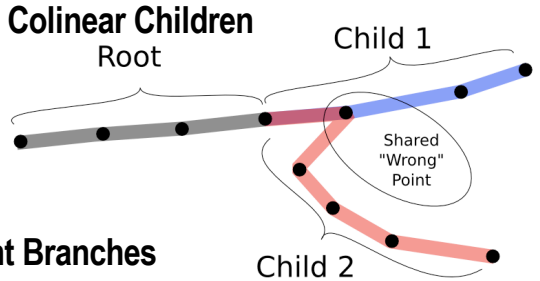
Beware of Systematic Artifacts!

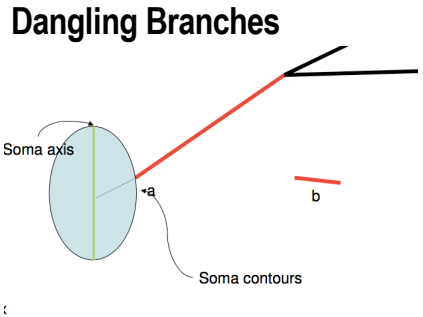


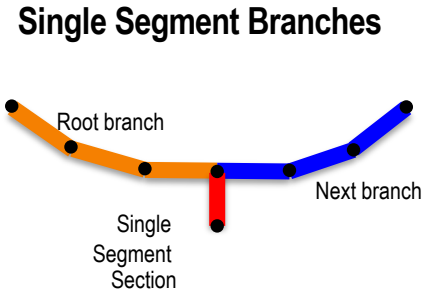
Reconstruction Artifacts











These artifacts may not matter when publishing a morphology in a paper...
For electrical modeling they matter a lot!

How to deal with artifacts?

- Manual curation
- Automatic correction

Most Common Morphology Formats

Neurolucida ASCII

```
;       V3 text file written for MicroBrightField products.
(Sections)

("CellBody"
  (Color Red)
  (CellBody)
  (    43.94     27.22     -8.51      0.28)  ;  1, 1
  (    46.63     24.62     -8.51      0.28)  ;  1, 2
  (    47.56     19.11     -8.51      0.28)  ;  1, 3
  (    47.23     16.02     -8.90      0.28)  ;  1, 4
  (    46.54     13.75     -8.90      0.28)  ;  1, 5
  (    42.23     11.77     -7.41      0.28)  ;  1, 6
  (    38.09     11.20     -7.46      0.28)  ;  1, 7
  (    36.08     12.18     -7.46      0.28)  ;  1, 8
  (    34.00     13.99     -7.46      0.28)  ;  1, 9
  (    33.43     18.13     -9.39      0.28)  ;  1, 10
  (    34.60     21.28     -9.39      0.28)  ;  1, 11
  (    34.63     24.91     -9.39      0.28)  ;  1, 12
  (    36.10     27.80    -12.04      0.28)  ;  1, 13
  (    39.36     28.86    -12.02      0.28)  ;  1, 14
)  ;  End of contour

( (Color Blue)  ; [10,21]
  (Axon)
  (    37.98     12.22     -6.49      1.39)  ; Root
  (    38.15      9.73     -6.49      1.39)  ; R, 14
  (    37.82      6.63     -6.49      1.11)  ; R, 2
  (    36.33      4.02     -8.67      1.11)  ; R, 3
  (    35.65     -2.16    -10.20      0.83)  ; R, 4
  (    36.65     -4.59    -11.55      0.83)  ; R, 5
  (    39.33    -10.10     -5.05      0.83)  ; R, 6
  (    41.24    -17.49     -5.05      0.83)  ; R, 7
  (    42.86    -20.72     -5.05      0.83)  ; R, 8

  (
    (    49.78    -66.77     -9.80      0.56)  ; R-1, 1
    (
      (    50.16    -66.18     -6.76      0.28)  ; R-1-1, 1
      (    52.61    -65.45     -6.52      0.28)  ; R-1-1, 2
      (    53.00    -62.92     -6.76      0.28)  ; R-1-1, 3
```

SWC (e.g. NeuroMorpho)

Sample StructureType X Y Z radius parent

---

1 1 40.03 19.34 -8.95 8.592 -1
2 1 40.03 27.93 -8.95 8.592 1
3 1 40.03 10.75 -8.95 8.592 1
4 2 99.36 -13.16 -63.91 0.14 1
5 2 104.33 -12.54 -64 0.14 4
6 2 111.2 -15.13 -59.85 0.14 5
7 2 114.84 -15.43 -62.52 0.14 6
8 2 115.89 -14.52 -62.52 0.14 7
9 2 118.18 -15.47 -62.52 0.14 8
10 2 123.96 -18.42 -62.95 0.14 9
11 2 134.11 -20.21 -62.28 0.14 10
12 2 138.22 -23.27 -62.28 0.14 11
13 2 142.22 -24.66 -62.28 0.14 12
14 2 154.66 -27.42 -62.28 0.14 13
15 2 160.08 -31.22 -58.66 0.14 14
16 2 168.86 -33.39 -58.66 0.14 15
17 4 33.54 16.22 -7.52 1.665 1
18 4 32.45 15.86 -7.52 1.665 17

MorphML

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"http://morphml.org/metadata/schema" xmlns: xsi =
"http://www.w3.org/2001/XMLSchema-instance" xsi: Schema Location =
"http://morphml.org/morphml/schema
http://morphml.org:8080/NeuroMLValidator/NeuroMLFiles/
Schemata/v1.5/Level1/MorphML_v1.5.xsd" lengthUnits = "micron">
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<meta:notes>A Simple cell</meta:notes> <segments>
<segment id = "0" name = "SomaSegment" cable = "0">
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<distal x = "0.0" y = "0.0" z = "0.0" diameter = "16.0"/>
</segment>
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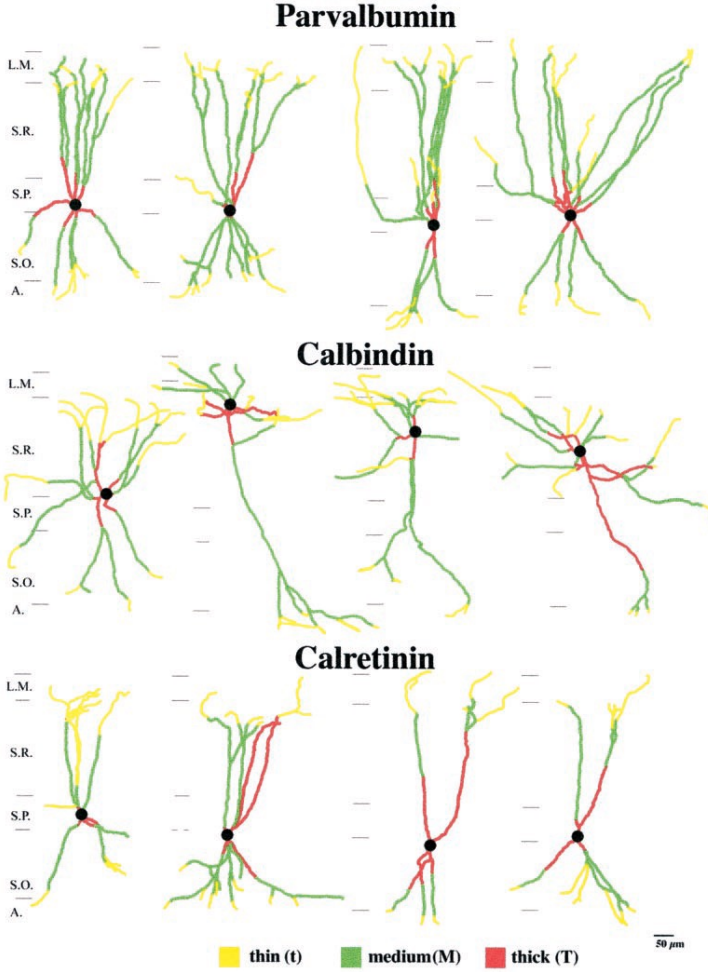
</segment>
```

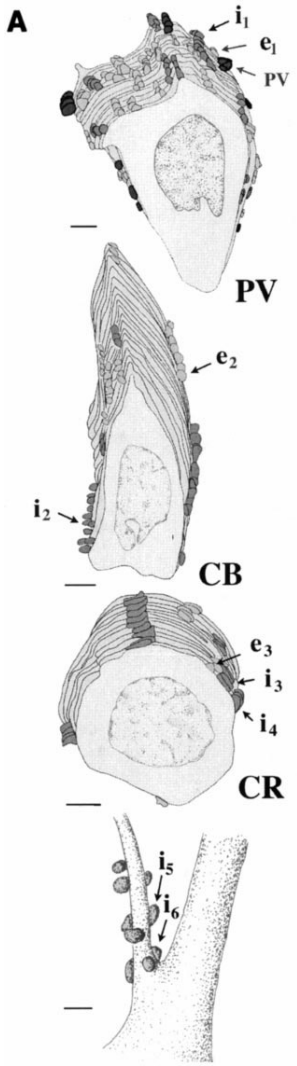
For a good description: http://www.neuroconstruct.org/docs/import.html

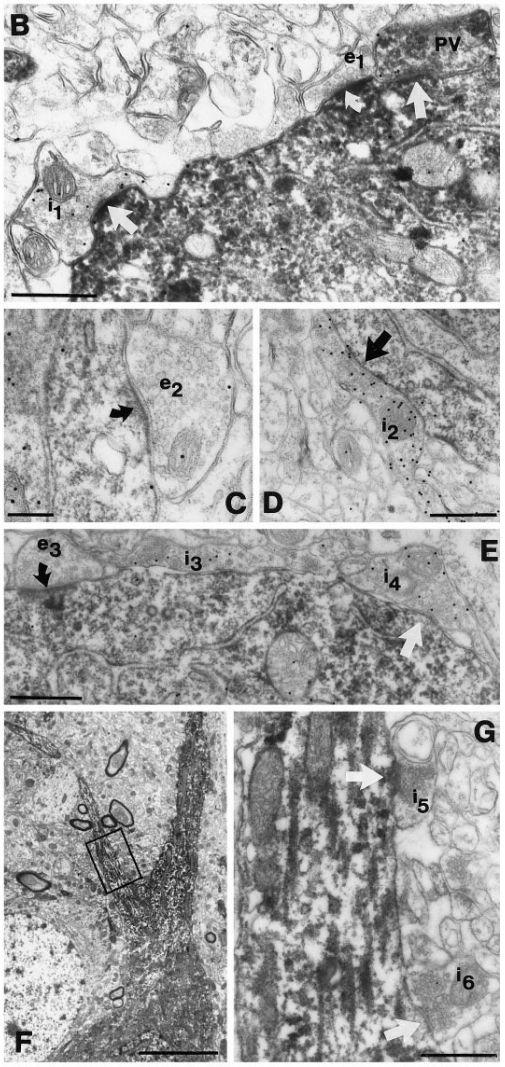
EPFL

Challenge: find the correct granularity

- Incorporate the salient features given our scope
- Do no incorporate noise (staining artefacts)







EPFL

Gulyas et al 1999

Summary 2

- Reconstruction is still a quite manual process.
- There is no perfect method. Each method has pros and cons.
- Data format is still an open problem.

Lecture Overview

- Scope
- Approaches
- **Applications**

Table 1.1 List of frequently used morphometric measures to quantify neuronal morphologies

Property	Brief description
Number of stems[a]	Total number of segments leaving from the dendritic root
Number of branch points[a]	Total number of branch points in the tree
Branch order	Topological distance from the dendritic root. The root has order 0, and the order of a segment in the tree equals the number of branch points along the path to the root + 1
Maximum branch order[a]	Maximum branch order in a neuron
Degree	Number of termination points downstream of the node under investigation
Maximum degree[a]	Maximum degree in a tree. By definition the degree at the dendritic root
Total length[a]	Summed segment lengths of all segments in a tree (see next)
Segment length	Path length of the incoming segment toward a node
Stem length	Path length between a branch point with order = 1 and the dendritic root
Interbranch length	Path length between branch points
Terminal segment length	Path length between the termination point and the last branch point
Euclidean distance	Can be applied in a similar fashion as the path length. Often used to measure the distance between the soma and the termination points
Dimension[a]	Width, height, and depth of the bounding box
Taper rate[a]	The uniform decrease in diameter across a dendritic branch
Somatofugal tropism[a]	Quantification of the preference of a neurite to grow away from the soma. Defined as the ratio of a segment's path length and the Euclidean distance between its starting and end point
Fractal dimension[a]	Fractal dimension used as a measure of space-filling
Contraction	Quick proxy of the fractal dimension: the Euclidean length of a branch divided by the path length
Partition asymmetry[a]	Topological complexity of a tree. A completely asymmetric tree has PA = 1, symmetric has PA = 0
Lacunarity[a]	A measure of "holes" in a volume spanned by a tree. See Sect. 1.4.2
Horton–Strahler index	Measure of topological complexity of a tree relating the order and asymmetry in that tree. Computed for each branch point. See Sect. 1.4.1
Strahler number[a]	The Horton–Strahler index associated with the root of the tree

Light shading—topological measures
Medium shading—geometrical measures
Dark shading—compound measures
[a]Global measure as opposed to distribution of local measures. However, often derived features are used as global feature. For instance, to describe the branch order in a tree, a distribution of all orders can be given, or the distribution can be characterized by considering the maximum branch order, the average branch order, etc. This holds for all local measures

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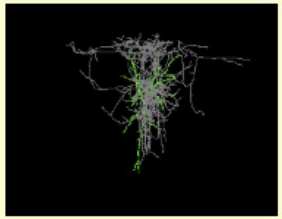
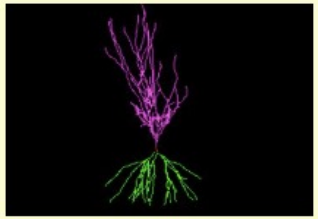
NeuroMorpho.Org

Version 7.9 - Released: 12/13/2019 - Content: 121544 neurons

Total number of downloads: 13894177 Total site hits since August 1, 2006: 4911911

itors from 194 countries 121544 digital reconstructions Contribu





NeuroMorpho.Org is a centrally curated inventory of **digitally reconstructed neurons** associated with peer-reviewed publications. It contains contributions from over 500 laboratories worldwide and is continuously updated as new morphological reconstructions are collected, published, and shared. To date, NeuroMorpho.Org is the largest collection of publicly accessible 3D neuronal reconstructions and associated metadata.

The goal of NeuroMorpho.Org is to provide dense coverage of available reconstruction data for the neuroscience community. Data sharing through NeuroMorpho.Org enables the full and continuing research potential of existing digital reconstruction data.

NeuroMorpho.Org

Version 7.9 - Released: 12/13/2019 - Content: 121544 neurons

Animal
Species
Gender
Minimum Weight
Maximum Weight
Development
Minimum Age
Maximum Age

Experiment
Protocol
Experimental Condition
Stain
Slicing Thickness
Slicing Direction
Tissue Shrinkage
Reconstruction Method
Objective Type
Objective Magnification

Anatomy
Brain Region
Cell Type

Source
Archive
PMID
Original Format
Date of Deposition
Date of Upload

Completeness
Structural Domain
Physical Integrity
Morphological Attributes

Hits from current criteria

Your search results can be arranged:

By animal species | By brain region | By cell type | By archive

NeuroMorpho.Org

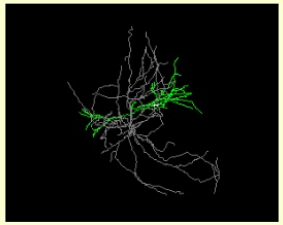
Version 7.9 - Released: 12/13/2019 - Content: 121544 neurons

73 Neurons found

- Esclapez
  - rat
    - hippocampus
      - Trilaminar
        - DEV104T1
        - DEV119T4
        - DEV166T1
      - Perforant pathway-associated
        - DEV119T3
        - DEV122T3
        - DEV131T3
        - DEV133T2
        - DEV157T2
      - perisomatic targeting
        - DEV125T1
        - DEV128T2
        - DEV133T3
        - DEV174T1
        - R155T1
        - R61
        - R75C1
      - oriens-lacunosum moleculare
        - DEV127T1
        - DEV159T2
        - DEV169T1
        - DEV95T7
        - DEV82T1m
      - Schaffer-collateral associated
        - DEV127T3
        - DEV160T3
        - DEV172T1
        - DEV52T1
        - Dev97T1
        - R161T1m
      - bistratified
        - DEV174T4
        - DEV50T2

NeuroMorpho.Org

Version 7.9 - Released: 12/13/2019 - Content: 121544 neurons



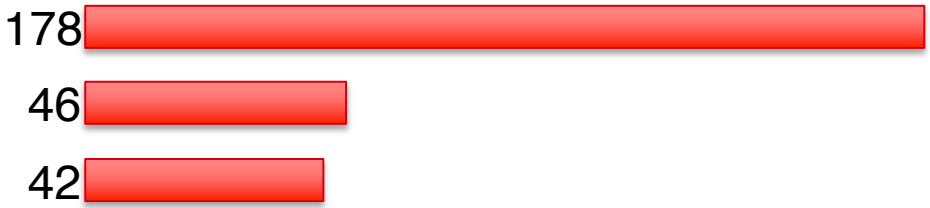
Morphology File (Standardized)
Morphology File (Original)
Log File (Standardized)
Log File (Original)

Get above files zipped

3D Neuron Viewer - Java, legacy
3D Neuron Viewer - WebGL, novel
Animation

Details about selected neuron	
NeuroMorpho.Org ID :	NMO_02325
Neuron Name :	DEV104T1
Archive Name :	Esclapez,Cossart_Bernard
Species Name :	rat
Strain :	Wistar
Structural Domains :	Dendrites, Soma, Axon
Physical Integrity :	Dendrites Complete, Axon Moderate
Morphological Attributes :	Diameter, 3D, Angles
Min Age :	14.0 days
Max Age :	21.0 days
Gender :	Not reported
Min Weight :	Not reported
Max Weight :	Not reported
Development :	young
Primary Brain Region :	hippocampus
Secondary Brain Region :	CA1
Tertiary Brain Region :	stratum radiatum
Primary Cell Class :	interneuron
Secondary Cell Class :	Trilaminar
Tertiary Cell Class :	Not reported
Original Format :	Neurolucida.dat
Experiment Protocol :	in vitro
Experimental Condition :	Control
Staining Method :	biocytin
Slicing Direction :	horizontal
Slice Thickness :	400 µm
Tissue Shrinkage :	Not reported
Objective Type :	Not reported
Magnification :	Not reported

Neuromorpho.org



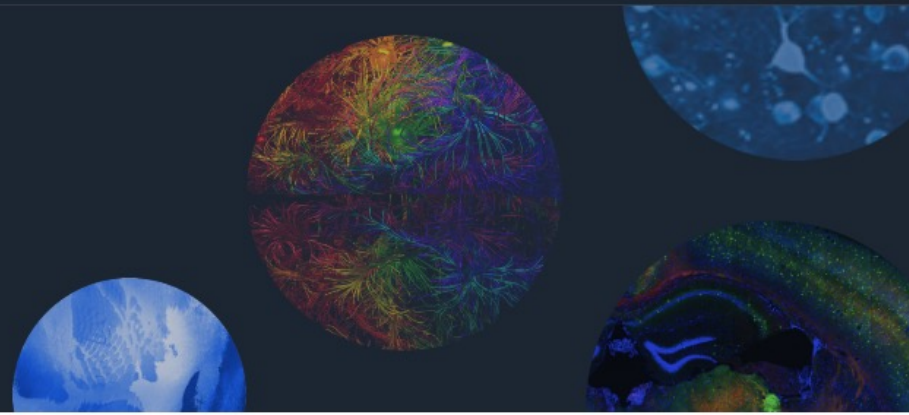
CA1 interneurons

classified

with an axon

	With axon	Layer info	Orientation hints	Soma	Complete axon
BC	33	8	8	2d	33
OLM	2	2	2	3d , 2d	0
SCA	6	6	6	3d (1), 2d (5)	6
IS3	1	1	1	2d	1

Accelerating progress toward understanding the brain.



New Data and Tools

MOUSE TRANSCRIPTOMIC CELL TYPES

Explore the latest dataset and

HUMAN TRANSCRIPTOMIC CELL TYPES

Explore the latest dataset and

VISUAL CODING WITH NEUROPIXELS

The latest from Allen Brain

SYNAPTIC PHYSIOLOGY

Dive into the first Synaptic Physiology dataset, which brings together

Cell Types: Overview of the Data

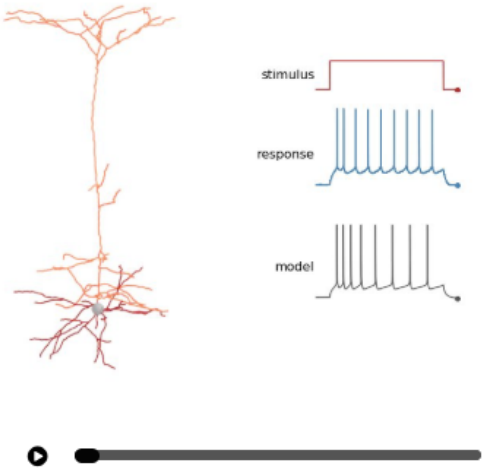
This brain cell database contains a survey of biological features derived from single cell data, from both human and mouse. It is part of a multi-year project to create a census of cells in the mammalian brain.

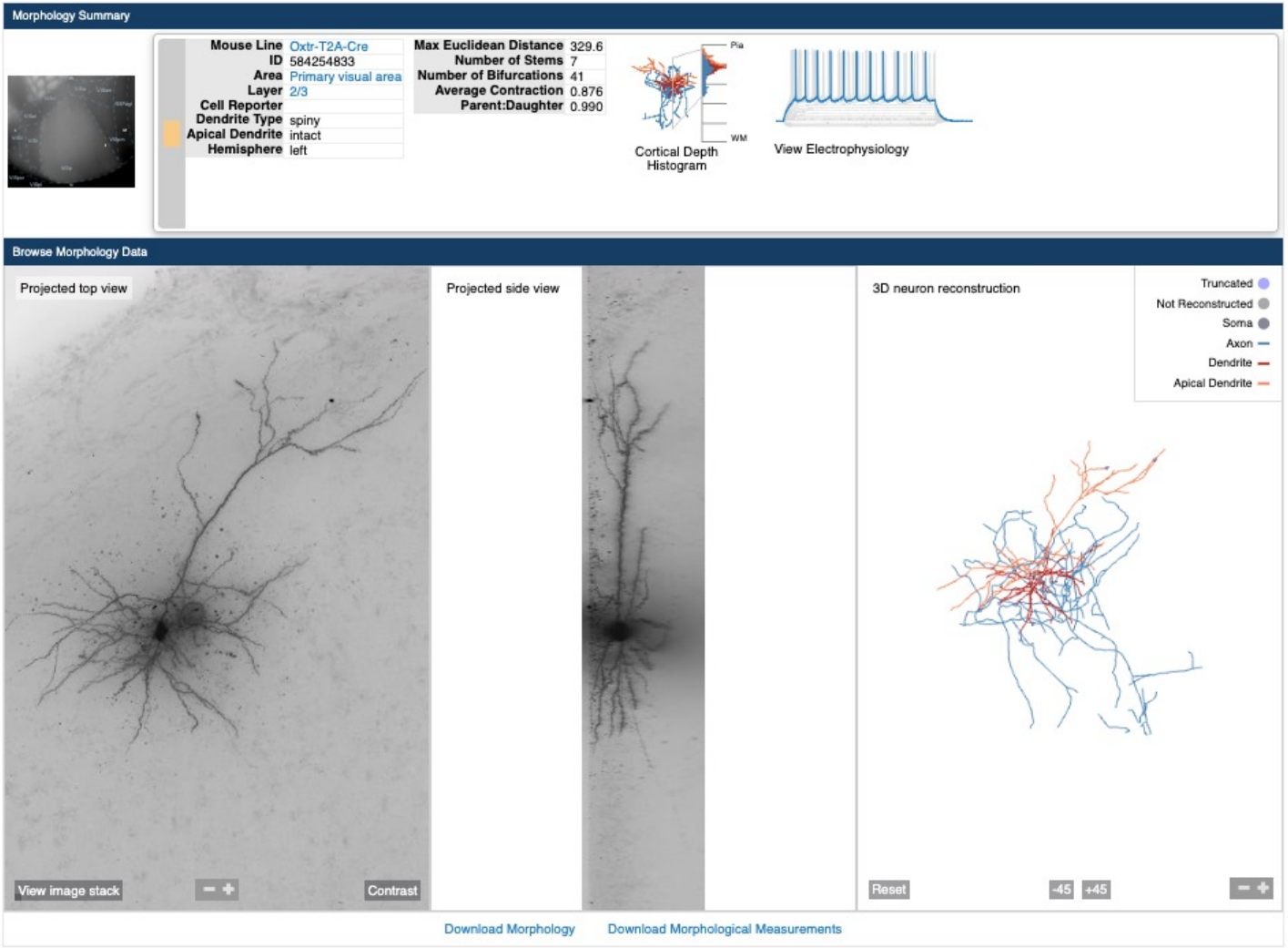
The database contains electrophysiological, morphological, and transcriptomic data measured from individual cells, as well as models simulating cell activity. Thus far, data generation has focused on select areas of cerebral cortex, and thalamic neurons.

Browse electrophysiological response data and reconstructed neuronal morphologies using the Cell Feature Search tool. Single cell gene expression data is described on the RNA-Seq Data page.

Use the Allen Software Development Kit (SDK) to programmatically access and analyze raw data, and to run models.

Data can be downloaded by selecting individual experiments in the Cell Feature Search tool, by accessing transcriptomic RNA-Seq files, or through the Allen SDK or API.




Morphology Summary
Mouse Line Oxtr-T2A-Cre
ID 584254833
Area Primary visual area
Layer 2/3
Cell Reporter
Dendrite Type spiny
Apical Dendrite intact
Hemisphere left
Max Euclidean Distance 329.6
Number of Stems 7
Number of Bifurcations 41
Average Contraction 0.876
Parent:Daughter 0.990
Pia
WM
Cortical Depth Histogram
View Electrophysiology
Browse Morphology Data
Projected top view
Projected side view
3D neuron reconstruction
Truncated
Not Reconstructed
Soma
Axon
Dendrite
Apical Dendrite
View image stack
Contrast
Reset
-45
+45
Download Morphology
Download Morphological Measurements

MouseLight / NeuronBrowser

This is an interactive web platform to explore, search, filter and visualize single neuron reconstructions generated by the Janelia MouseLight project.

Reconstructions are presented registered to the Allen Reference Atlas. Queries for neuronal morphology can be made based on soma position or location of projection targets within the brain. Filtered results can be visualized in 3-D along with the Allen brain compartments. We will periodically add to this collection of reconstructed neurons in future releases. Query results can also be downloaded for offline analysis (see Terms of Use).

A quick overview of currently available features and how to use the NeuronBrowser can be found in a Tutorial Video here.

For additional information on how the data was generated please refer to the documentation in the Resources section. A description of the core MouseLight technology can also be found here.

Connect With Us

For data feedback, questions, and comments please contact us.

Email Us Today

Join in on the conversation and follow us on Twitter.

Follow Us

MouseLight Neuron Browser

hhmi janelia Research Campus

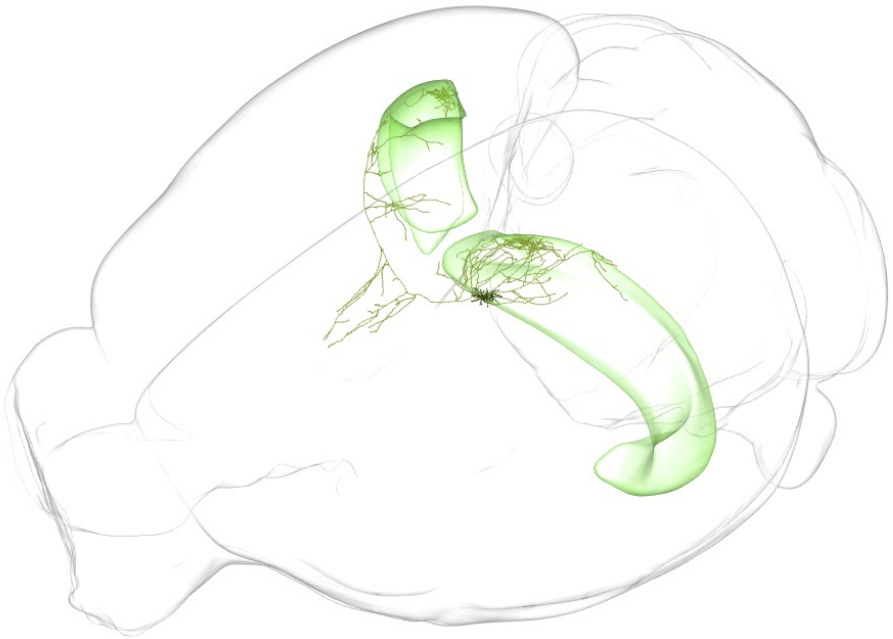
Tutorial Video | Examples - Try It Now! | MouseLight Home | Help

Reset | Matched 155 of 1094 neurons in 6.007 seconds | Add Filter | Search

Neurons

☐	All	☐	AA0960	CA2	
☑	All	☐	AA0959	CA1	
☐	All	☐	AA0910	CA1	
☐	All	☐	AA0909	CA1	
☐	All	☐	AA0894	SUB	
☐	All	☐	AA0891	SUB	
☐	All	☐	AA0890	SUB	
☐	All	☐	AA0881	PRE	
☐	All	☐	AA0879	POST	
☐	All	☐	AA0878	PRE	
☐	All	☐	AA0877	PRE	
☐	All	☐	AA0875	PRE	
☐	All	☐	AA0871	SUB	
☐	All	☐	AA0869	DG-mo	
☐	All	☐	AA0864	SUB	
☐	All	☐	AA0855	SUB	
☐	All	☐	AA0851	CA1	
☐	All	☐	AA0850	SUB	
☐	All	☐	AA0849	SUB	
☐	All	☐	AA0848	SUB	

Show Search



Compartments

History

- ☑ Whole Brain
- ☑ Field CA1

All Compartments

Filter compartments...

- ☑ Whole Brain
  - ☐ Basic cell groups and regions
    - ☐ Brain stem
    - ☐ Cerebellum
    - ☐ Cerebrum
      - ☐ Cerebral cortex
        - ☐ Cortical plate
          - ☐ Hippocampal formation
            - ☐ Hippocampal region
              - ☐ Ammon's horn
                - ☑ Field CA1
                - ☐ Field CA2
                - ☐ Field CA3
              - ☐ Dentate gyrus
              - ☐ Fasciola cinerea
              - ☐ Induseum griseum
            - ☐ Retrohippocampal region
          - ☐ Isocortex
          - ☐ Olfactory areas
        - ☐ Cortical subplate
          - ☐ Basolateral amygdalar nucleus
          - ☐ Basomedial amygdalar nucleus
          - ☐ Claustrum
          - ☐ Endopiriform nucleus
          - ☐ Lateral amygdalar nucleus
          - ☐ Posterior amygdalar nucleus
      - ☐ Cerebral nuclei
    - ☐ fiber tracts
    - ☐ ventricular systems

1094 neurons available

OXFORD

Cerebral Cortex, 2019;00: 1–23

doi: 10.1093/cercor/bhz122
Advance Access Publication Date: 02 July 2019
Feature Article

FEATURE ARTICLE

Differential Structure of Hippocampal CA1 Pyramidal Neurons in the Human and Mouse

Ruth Benavides-Piccione[1,2,*], Mamen Regalado-Reyes[2], Isabel Fernaud-Espinosa[2], Asta Kastanauskaite[2], Silvia Tapia-González[2], Gonzalo León-Espinosa[2,3], Concepcion Rojo[4], Ricardo Insausti[5], Idan Segev[6,7] and Javier DeFelipe[1,2]

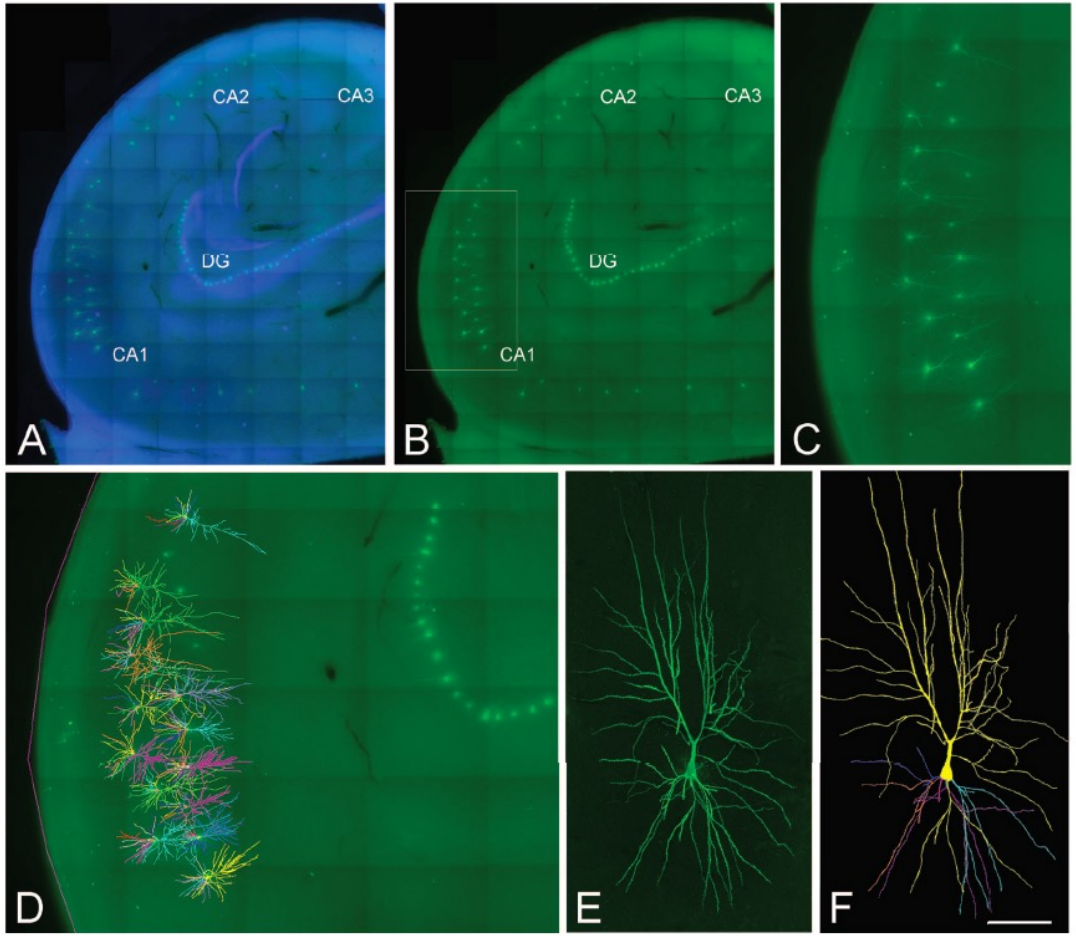
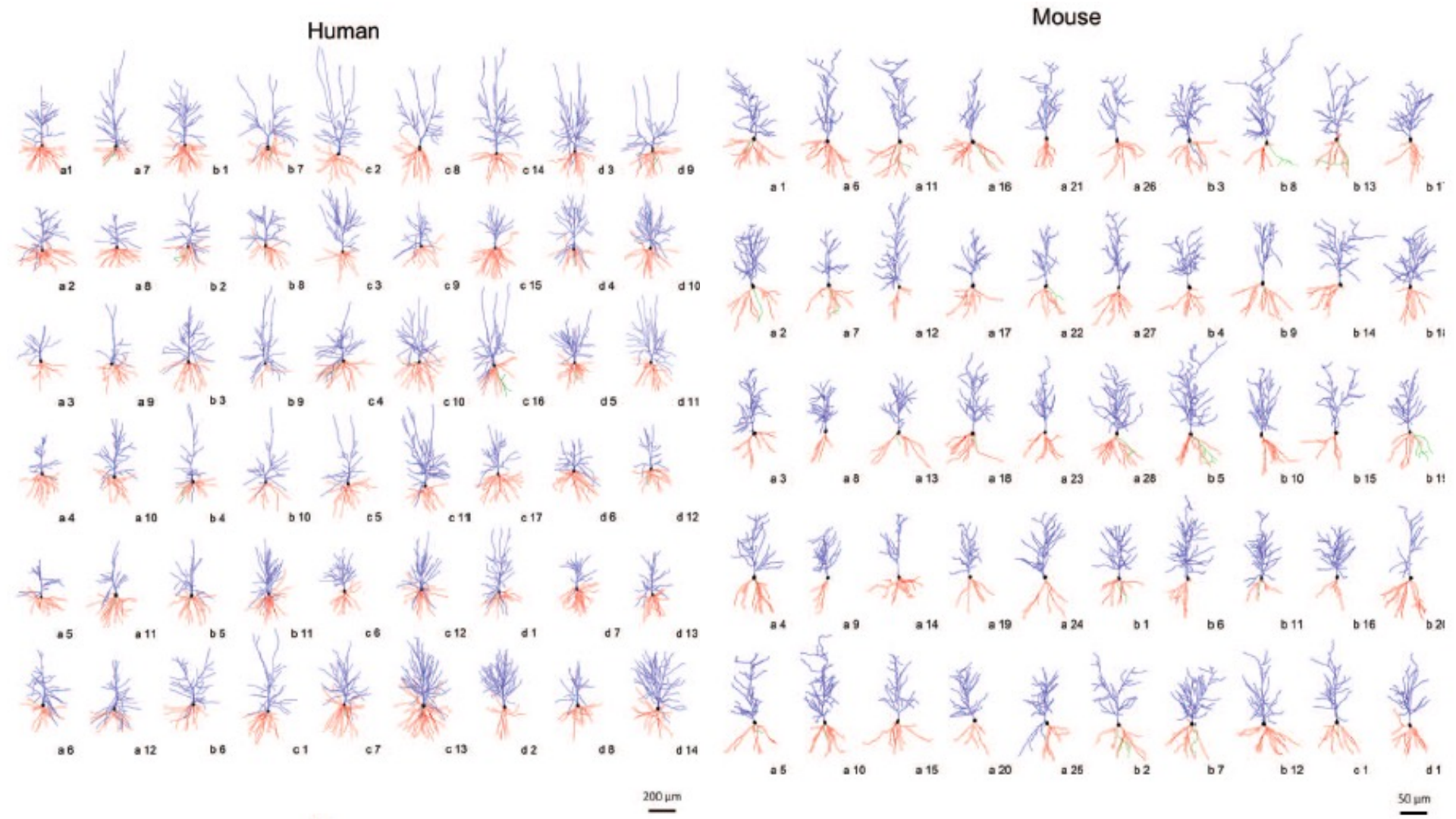
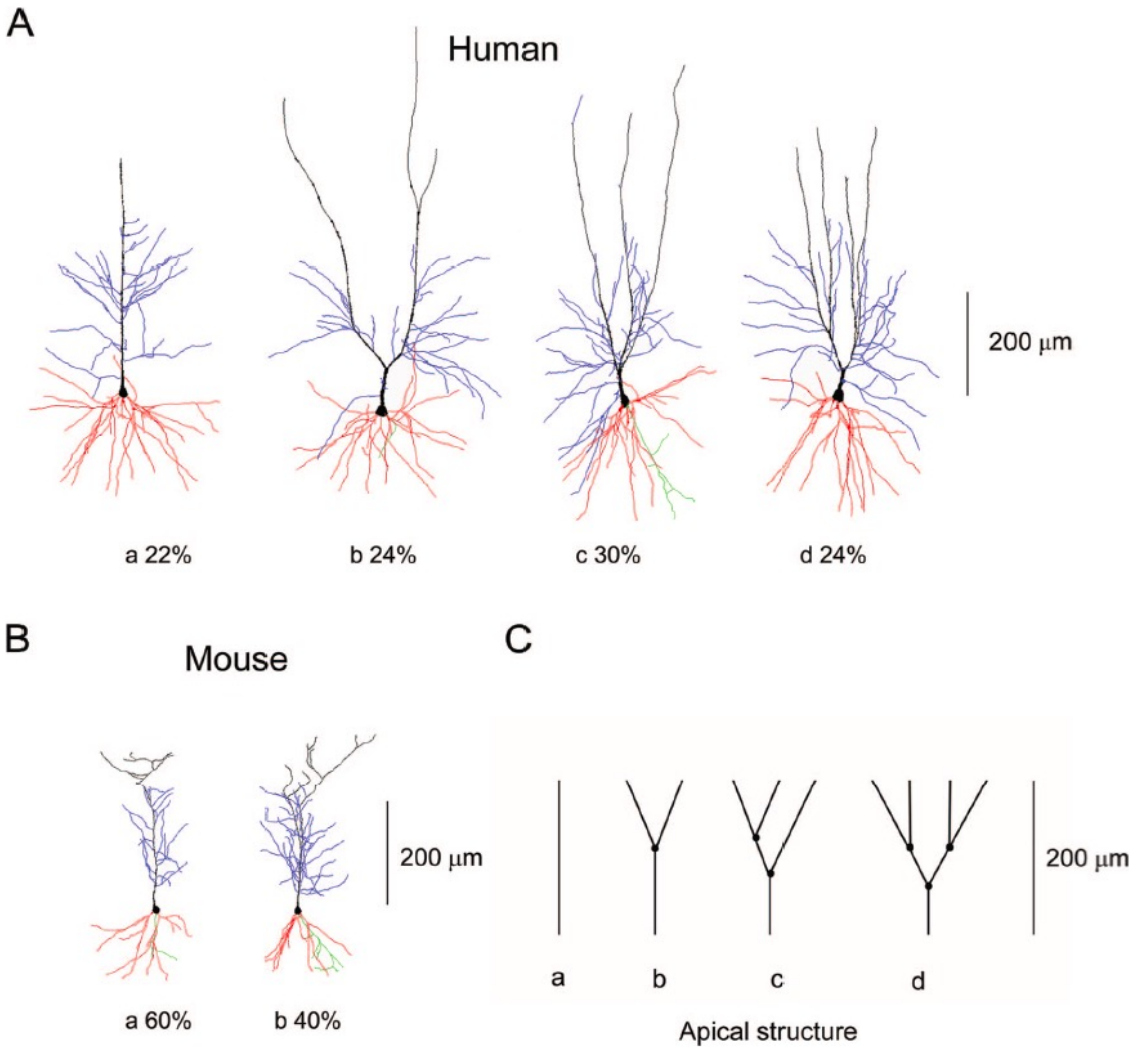


Figure 2. Confocal microscopy images of human neurons injected with LY in the hippocampus. (A and B) Labeled pyramidal cells (green) and DAPI staining (blue) in different regions of the human hippocampus, including CA1, CA2, CA3, and the dentate gyrus (DG) region. (C) Higher magnification image of the boxed region shown in (B). (D) 3D-reconstructed cells superimposed on the confocal image shown in (C). (E and F) High-magnification image z projection showing an injected CA1 pyramidal cell (E) and the 3D reconstruction of the same cell (F). Scale bar (in panel F) is equal to 1100 µm in (A) and (B); 460 µm in (C) and (D); 100 µm in (E) and (F).


Human
Mouse
200 µm
50 µm

	Human	Mouse	% Difference
Area of the maximum perimeter of the soma (μm^2)	350 ± 9.7	137 ± 3.0	255
Number of primary basal dendrites	6.37 ± 0.25	3.04 ± 0.15	209
Basal extent (μm)	300	190	158
Distance peak basal nodes (μm)	40	30	133
Segment diameter first-order main apical (μm)	5.74 ± 0.18	1.82 ± 0.05	302
Segment diameter second-order main apical (μm)	3.31 ± 0.15	1.19 ± 0.04	278
Segment diameter first-order apical collateral (μm)	1.33 ± 0.02	0.71 ± 0.01	187
Segment diameter second-order apical collateral (μm)	1.07 ± 0.01	0.65 ± 0.005	165
Segment diameter first-order basal (μm)	1.98 ± 0.04	1.19 ± 0.04	166
Segment diameter second-order basal (μm)	1.50 ± 0.02	0.88 ± 0.02	170
Segment length first-order main apical (μm)	84.77 ± 10.75	157.6 ± 13.54	54
Segment length second-order main apical (μm)	130.9 ± 21.08	124 ± 14.60	105
Segment length first-order apical collateral (μm)	60.99 ± 2.36	60.48 ± 1.33	101
Segment length second-order apical collateral (μm)	99.4 ± 2.94	64.54 ± 1.45	154
Segment length first-order basal (μm)	16.63 ± 0.80	11.48 ± 0.98	145
Segment length second-order basal (μm)	48.32 ± 3.28	33.64 ± 3.30	144
Segment branching diameter apical collateral (μm)	1.41 ± 0.02	0.81 ± 0.01	175
Segment terminal diameter apical collateral (μm)	0.96 ± 0.004	0.65 ± 0.002	148
Segment branching diameter basal (μm)	1.63 ± 0.01	0.90 ± 0.01	181
Segment terminal diameter basal (μm)	1.01 ± 0.005	0.64 ± 0.005	159
Segment branching length apical collateral (μm)	25.32 ± 0.80	14.57 ± 0.64	174
Segment terminal length apical collateral (μm)	147.1 ± 1.64	77.9 ± 0.78	188
Segment branching length basal (μm)	20.55 ± 0.66	16.43 ± 0.73	125
Segment terminal length basal (μm)	169.2 ± 1.78	93.51 ± 1.76	180
Average diameter at 10 μm Sholl main apical distance (μm)	7.19 ± 0.21	3.12 ± 0.15	230
Average diameter at 10 μm Sholl collateral distance (μm)	1.87 ± 0.33	0.80 ± 0.07	234
Average diameter at 10 μm Sholl basal distance (μm)	2.36 ± 0.20	1.36 ± 0.07	173
Average diameter at 10 μm Sholl axon distance emerging from soma (μm)	3.92 ± 0.42	1.18 ± 0.05	332
Average diameter at 10 μm Sholl axon distance emerging from dendrite (μm)	1.88 ± 0.25	0.85 ± 0.23	221
Average diameter of basal dendrites containing an emerging axon (μm)	4.97 ± 0.27	2.4 ± 0.18	207


A
Human
200 µm
a 22%
b 24%
c 30%
d 24%
B
Mouse
200 µm
a 60%
b 40%
C
200 µm
a
b
c
d
Apical structure

Key points

- On average human cells are 2 times bigger than mouse cells
- Human brain is 2800 times bigger. There is a biophysical limit for the size of a neuron.
- Human cells are not just a larger version of the mouse cells
- There is no linear scaling for all the characteristics
- The morphologies appear larger and more complex
- This may correspond to more complex information processing. Multiple semi-independent dendritic subunits

EPFL

Cell

Resource

Reconstruction of 1,000 Projection Neurons Reveals New Cell Types and Organization of Long-Range Connectivity in the Mouse Brain

Johan Winnubst,[1] Erhan Bas,[1,5] Tiago A. Ferreira,[1] Zhuhao Wu,[2] Michael N. Economo,[1] Patrick Edson,[3] Ben J. Arthur,[1] Christopher Bruns,[1,6] Konrad Rokicki,[1] David Schauder,[1] Donald J. Olbris,[1] Sean D. Murphy,[1] David G. Ackerman,[1] Cameron Arshadi,[1] Perry Baldwin,[1] Regina Blake,[1] Ahmad Elsayed,[1] Mashtura Hasan,[1] Daniel Ramirez,[1] Bruno Dos Santos,[1] Monet Weldon,[1] Amina Zafar,[1] Joshua T. Dudman,[1] Charles R. Gerfen,[4] Adam W. Hantman,[1] Wyatt Korff,[1] Scott M. Sternson,[1] Nelson Spruston,[1] Karel Svoboda,[1] and Jayaram Chandrashekar[1,7,*]

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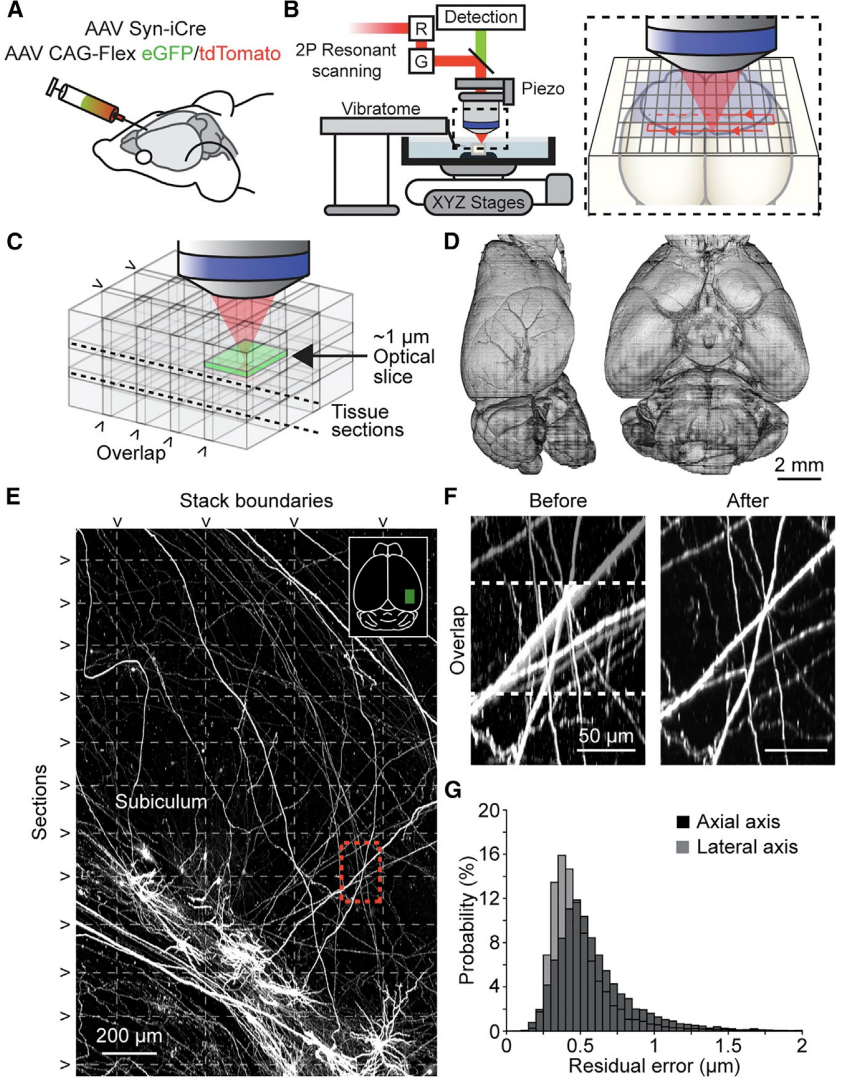
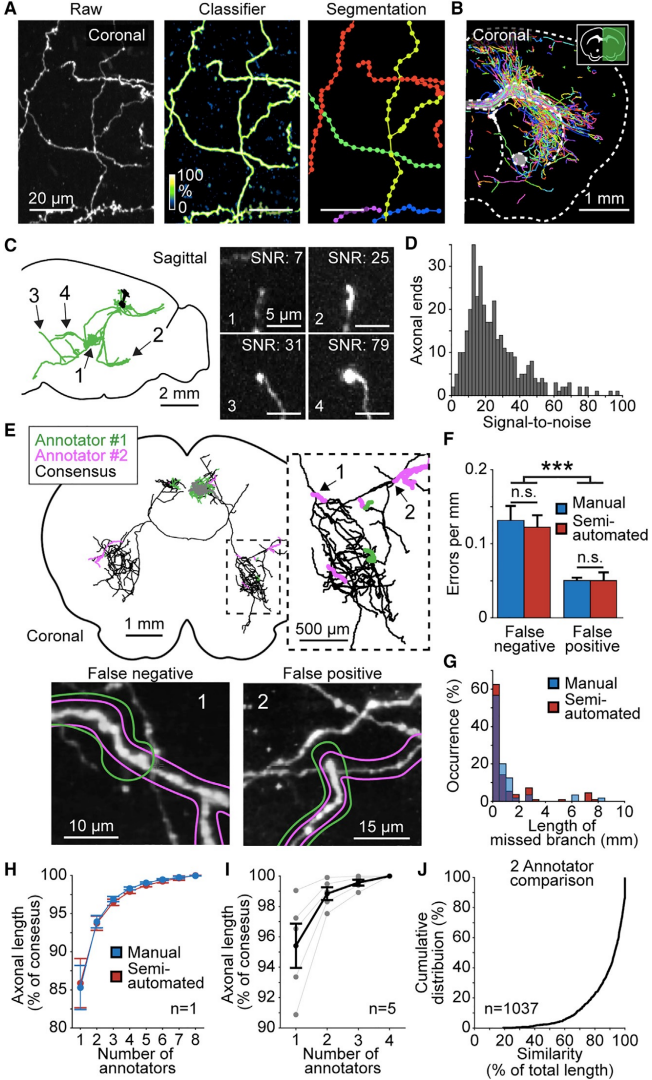
https://doi.org/10.1016/j.cell.2019.07.042

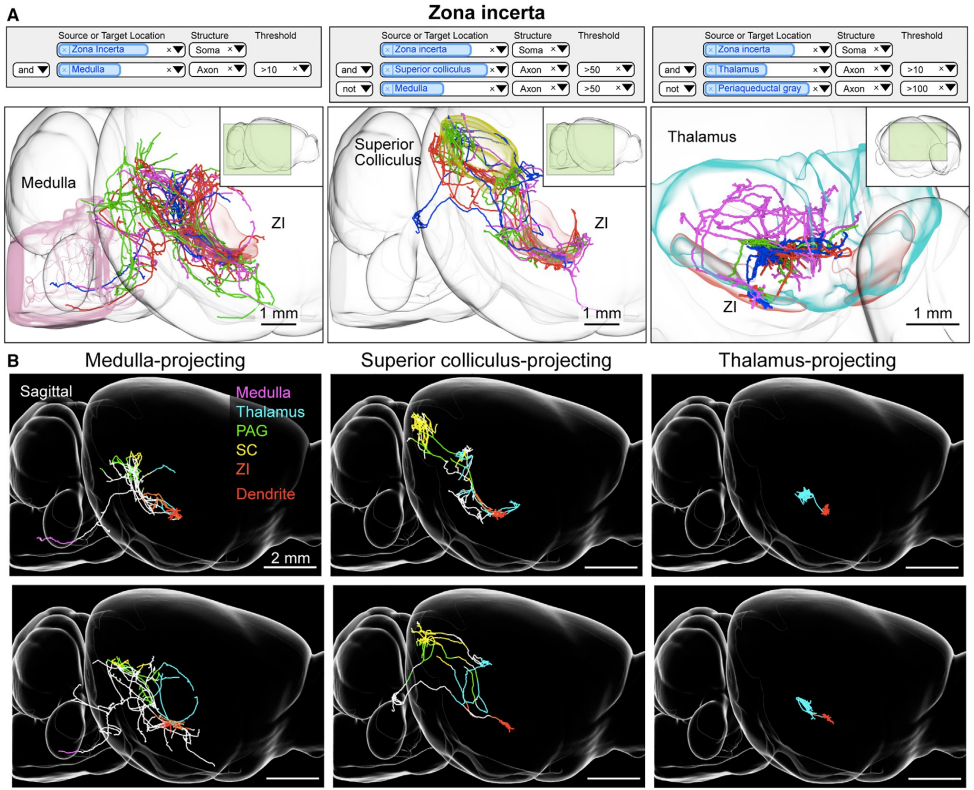
- Fluorescence labelling
- > 100 labelled neurons / brain
- Brain optically cleared
- Re-assemble of 40,000 stack images



- Semi-automatic reconstruction
- Automatic segmentation
- Segments were broken at each branchpoints and close cross points
- Manual linking and proofreading
- Multiple annotators
- +5-fold increase in speed compare to pure manual reconstruction without loose in precision



- Register the morphologies in Allen Mouse Common Coordinate Framework
- Collect and organize data highlights patters
- New projecting classes



Summary 3

- More systematic analysis of the morphologies
- High throughput technologies are emerging
- Databases allow users to access better data and
- organized in a better way
  - Metadata
  - Quality, completeness
  - Registered in atlas

What you have learnt

- Cell type.
- Cell classification.
- Reconstruction process.
- Reconstruction artefacts.
- File formats.
- Morphometrics.
- Familiarize with database of morphological reconstructions (e.g., neuromorpho.org)