Allen Institute Data and Resources: An Interactive Tour

Neurohackademy 2018
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Allen Institute for Brain Science

ALLEN INSTITUTE *for* BRAIN SCIENCE

Overview:

- **Introduction: Allen Institute for Brain Science**
- Allen SDK http://alleninstitute.github.io/AllenSDK/
    - Mouse Connectivity Atlas
    - The Common Coordinate Framework
    - Allen Cell Types Atlas
    - Allen Brain Observatory

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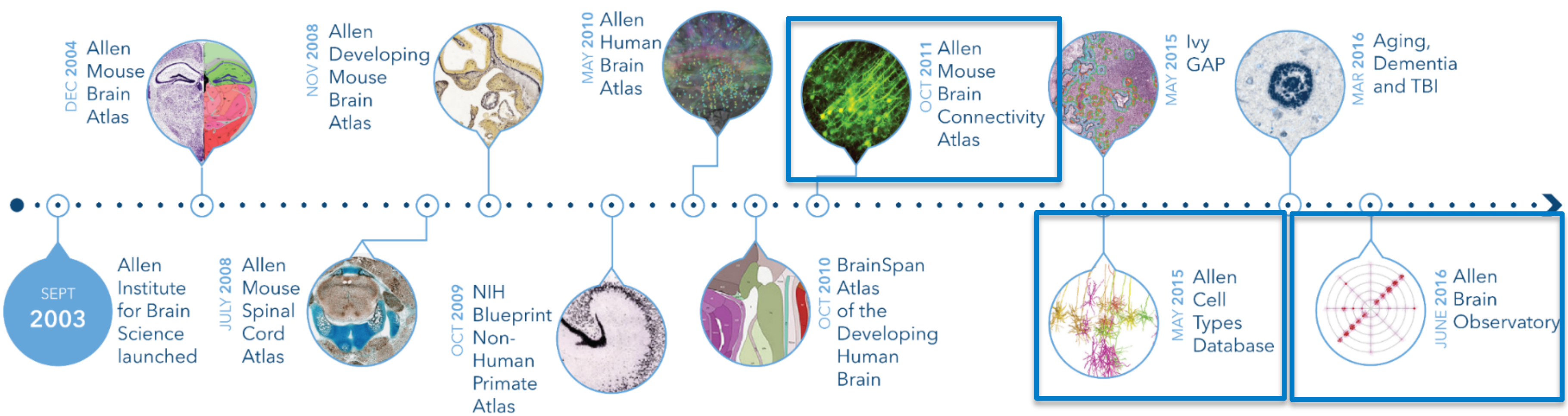
GOAL: What is the data?
- **View it.**
- **Download it.**
- **Access it.**

2003 – Allen Institute for Brain Science
2014 – Allen Institute for Cell Science
2016 – Paul G. Allen Frontiers Group

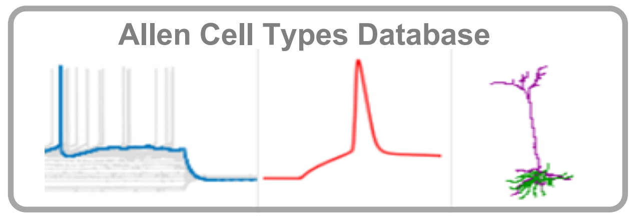
Allen Institute for Brain Science: Online Public Resources

- Data is available for public use
- Data analysis and mining are performed after data release
- Approximately 50,000 visits/month
- More than 5,000,000 cumulative visits
- Global users from academia, biotech/pharma, nonprofit, government

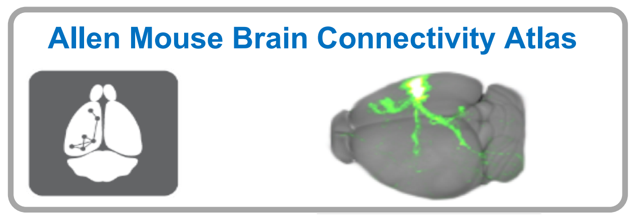


Beyond the Allen Brain Atlases: Recent Projects

What are the components?



What is the wiring logic?



How does the brain compute?

Visual Coding -   What is the functional transform from image to vision?

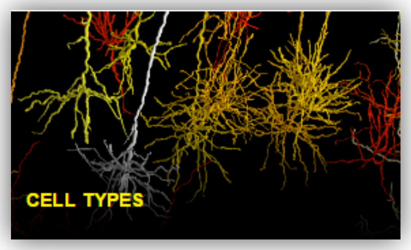
Beyond the Allen Brain Atlases: Recent Projects

Allen Mouse Brain Connectivity Atlas

Brain-wide axonal projection maps

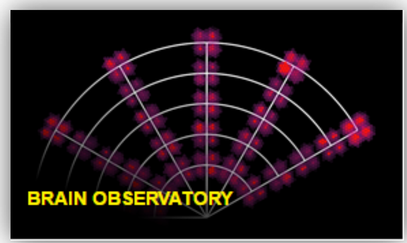
With functional imaging for cortical visual areas

Allen Cell Types Database

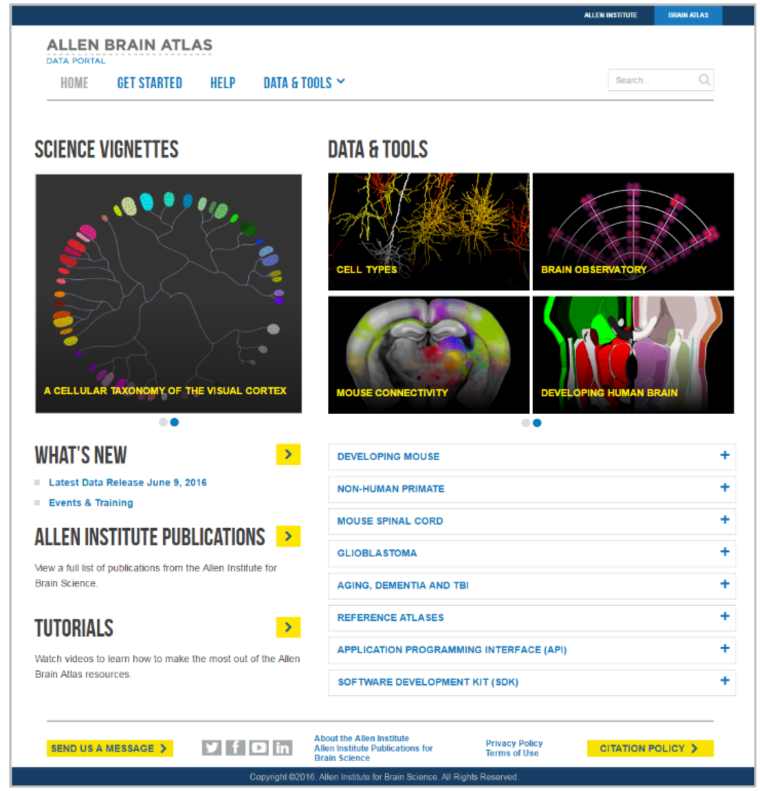


Morpho-electric characterization of neurons in mouse and human

Allen Brain Observatory: Visual Coding



Physiological activity of cells in awake behaving mouse



Web portal: online browse and data search
API: programming interface & data download
SDK: tutorials and use cases

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AllenSDK:

ALLEN INSTITUTE BRAIN ATLAS

ALLEN BRAIN ATLAS
SOFTWARE DEVELOPMENT KIT

CONTENTS

QUESTIONS

Send any questions using the Send Us a Message link below, or submit your question to StackOverflow using with the 'allen-sdk' tag.

If you encounter any problems using the AllenSDK, please create an issue on Github's issue tracker.

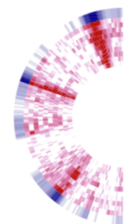
QUICK SEARCH

Go

WELCOME TO THE ALLEN SDK

The Allen Software Development Kit houses source code for reading and processing Allen Brain Atlas data. The Allen SDK focuses on the Allen Brain Observatory, Cell Types Database, and Mouse Brain Connectivity Atlas.

ALLEN BRAIN OBSERVATORY

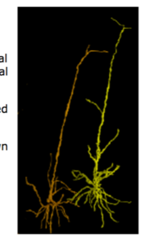


The Allen Brain Observatory is a data resource for understanding sensory processing in the mouse visual cortex. This study systematically measures visual responses in multiple cortical areas and layers using two-photon calcium imaging of GCaMP6-labeled neurons targeted using Cre driver lines. Response characterizations include orientation tuning, spatial and temporal frequency tuning, temporal dynamics, and spatial receptive field structure.

The mean fluorescence traces for all segmented cells are available in the Neurodata Without Borders file format (NWB files). These files contain standardized descriptions of visual stimuli to support stimulus-specific tuning analysis. The Allen SDK provides code to:

- download and organize experiment data according to cortical area, imaging depth, and Cre line
- remove the contribution of neuropil signal from fluorescence traces
- access (or compute) dF/F traces based on the neuropil-corrected traces
- perform stimulus-specific tuning analysis (e.g. drifting grating direction tuning)

ALLEN CELL TYPES DATABASE



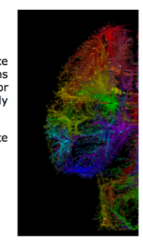
The Allen Cell Types Database contains electrophysiological and morphological characterizations of individual neurons in the mouse primary visual cortex. The Allen SDK provides Python code for accessing electrophysiology measurements (NWB files) for all neurons and morphological reconstructions (SWC files) for a subset of neurons.

The Database also contains two classes of models fit to this data set: biophysical models produced using the NEURON simulator and generalized leaky integrate and fire models (GLIFs) produced using custom Python code provided with this toolkit.

The Allen SDK provides sample code demonstrating how to download neuronal model parameters from the Allen Brain Atlas API and run your own simulations using stimuli from the Allen Cell Types Database or custom current injections:

- Biophysical Models
- Generalized LIF Models

ALLEN MOUSE BRAIN CONNECTIVITY ATLAS



The Allen Mouse Brain Connectivity Atlas is a high-resolution map of neural connections in the mouse brain. Built on an array of transgenic mice genetically engineered to target specific cell types, the Atlas comprises a unique compendium of projections from selected neuronal populations throughout the brain. The primary data of the Atlas consists of high-resolution images of axonal projections targeting different anatomic regions or various cell types using Cre-dependent specimens. Each data set is processed through an informatics data analysis pipeline to obtain spatially mapped quantified projection information.

The Allen SDK provides Python code for accessing experimental metadata along with projection signal volumes registered to a common coordinate framework. This framework has structural annotations, which allows users to compute structure-level signal statistics.

See the mouse connectivity section for more details.

WHAT'S NEW - RELEASE 0.14.2 (AUGUST 17TH, 2017)

The 0.14.2 release is primarily a change in our open source license. We are now using a 2-clause BSD license with an additional clause related to commercial use. If you have any questions, please contact us on our Gitter channel or send us a message.

This release also includes code in the BrainObservatory for mapping stimuli to screens. See this Jupyter example notebook for details.

To find out more, take a look at our CHANGELOG.

SEND US A MESSAGE ❯

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Python API for RMA:

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API ACCESS

The `allensdk.api` package is designed to help retrieve data from the Allen Brain Atlas API. `api` contains methods to help formulate API queries and parse the returned results. There are several pre-made subclasses available that provide pre-made queries specific to certain data sets. Currently there are several subclasses in Allen SDK:

- `CellTypesApi`: data related to the Allen Cell Types Database
- `BiophysicalApi`: data related to biophysical models
- `GlifApi`: data related to GLIF models
- `AnnotatedSectionDataSetsApi`: search for experiments by intensity, density, pattern, and age
- `GridDataApi`: used to download 3-D expression grid data
- `ImageDownloadApi`: download whole or partial two-dimensional images
- `MouseConnectivityApi`: common operations for accessing the Allen Mouse Brain Connectivity Atlas
- `OntologiesApi`: data about neuroanatomical regions of interest
- `ConnectedServices`: schema of Allen Institute Informatics Pipeline services available through the RmaApi
- `RmaApi`: general-purpose HTTP interface to the Allen Institute API data model and services
- `SvgApi`: annotations associated with images as scalable vector graphics (SVG)
- `SynchronizationApi`: data about image alignment
- `TreeSearchApi`: list ancestors or descendents of structure and specimen trees

RMA DATABASE AND SERVICE API

One API subclass is the `RmaApi` class. It is intended to simplify constructing an RMA query.

The RmaApi is a base class for much of the allensdk.api.queries package, but it may be used directly to customize queries or to build queries from scratch.

Often a query will simply request a table of data of one type:

```
from allensdk.api.queries.rma_api import RmaApi

rma = RmaApi()

data = rma.model_query('Atlas',
                        criteria="[name$il'*Mouse*']")
```

This will construct the RMA query url, make the query and parse the resulting JSON into an array of Python dicts with the names, ids and other information about the atlases that can be accessed via the API.

Using the criteria, include and other parameter, specific data can be requested.

```
associations = ''.join(['[id$eq1]',
                        'structure_graph(ontology),',
                        'graphic_group_labels'])

atlas_data = rma.model_query('Atlas',
                              include=associations,
                              criteria=associations,
                              only=['atlases.id',
                                    'atlases.name',
                                    'atlases.image_type',
                                    'ontologies.id',
                                    'ontologies.name',
                                    'structure_graphs.id',
                                    'structure_graphs.name',
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```

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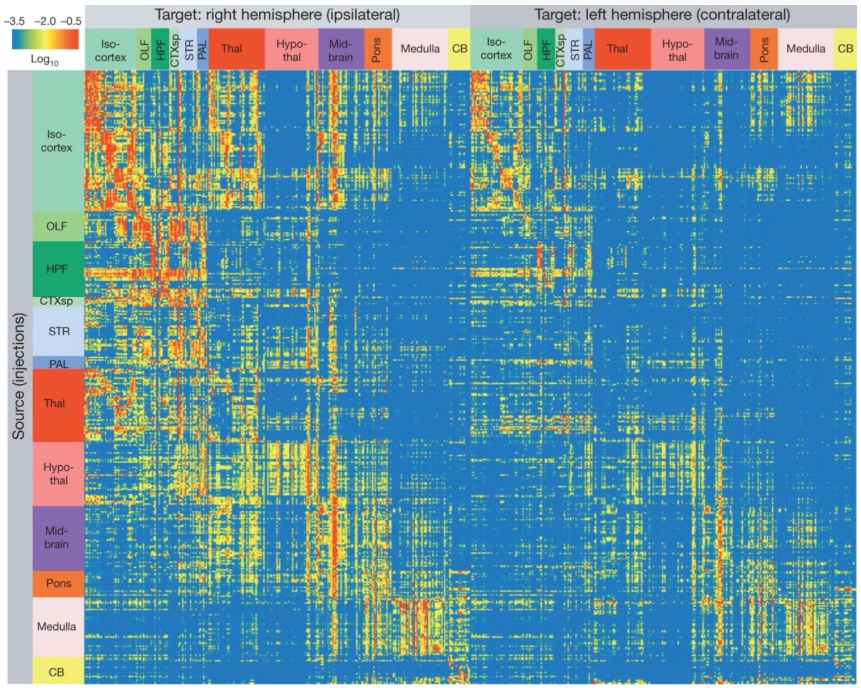
Connectivity Atlas – A Mesoscale Projectome

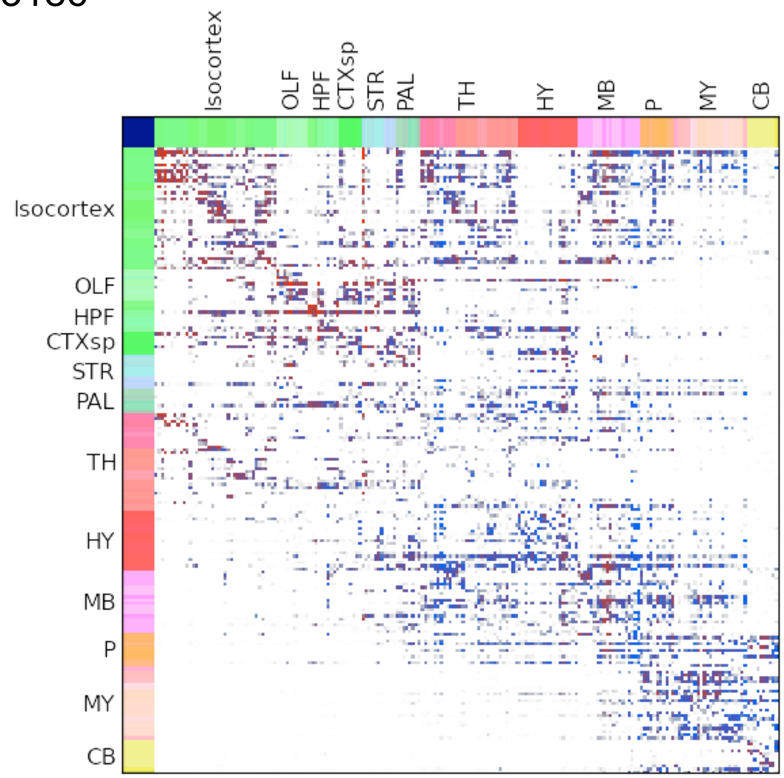
Summary:
- Whole brain mesoscale projectome
  - standardized
  - quantified
- High-precision co-registration of datasets into common reference space
- Retaining realistic 3D spatial location and topography of projection targets as well as fiber tracts

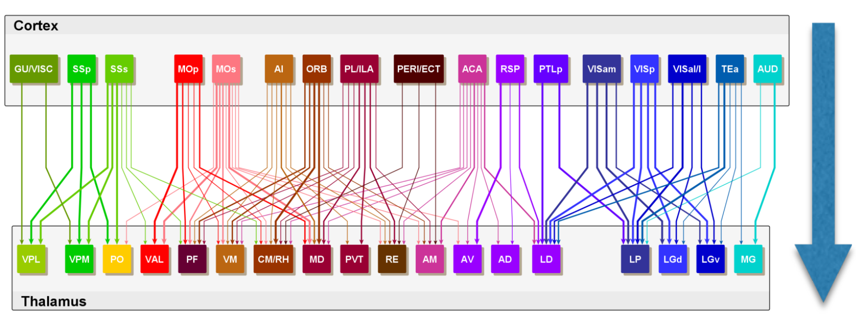
Facilitates:
- Computational network analysis: sub-networks, motifs, hubs, etc.
- More refined delineation of anatomical boundaries in 3D: improving traditional chemo- and cytoarchitecture based brain atlases
- Anterograde (from sources) and virtual retrograde (from targets) searches and comparisons
- Global connectivity based physiological and functional studies

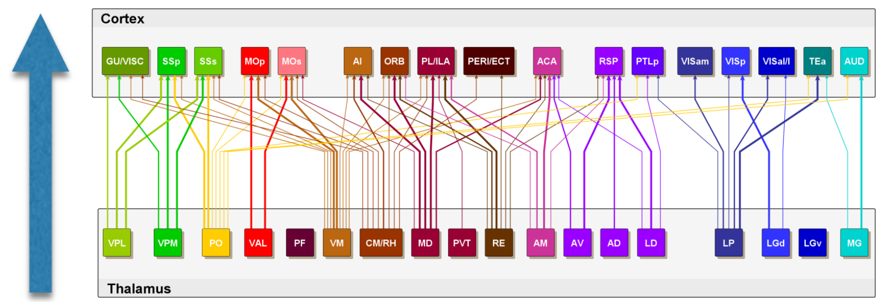
Whole Brain Connectivity Matrix

- SW Oh *et al. Nature*, 1-8 (2014) doi:10.1038/nature13186



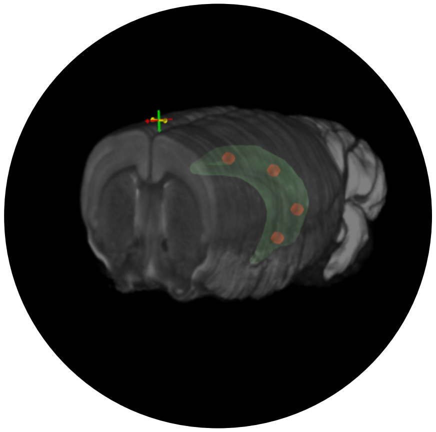






Allen Mouse Brain Connectivity Atlas

Stereotaxic or Functionally targeted Injections
(300-500 brain regions, >100 cell-type specific Cre mice)



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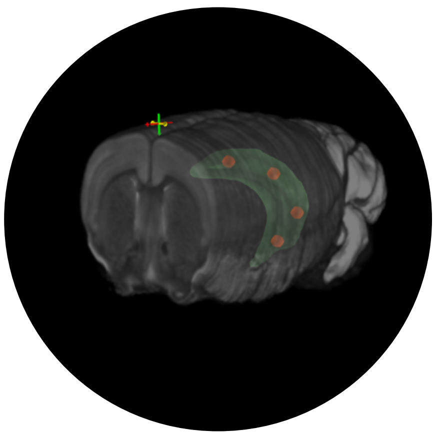
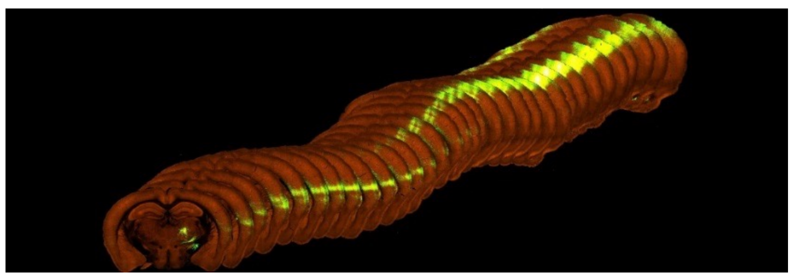
→

High-throughput Fluorescence Imaging

→





Allen Mouse Brain Connectivity Atlas

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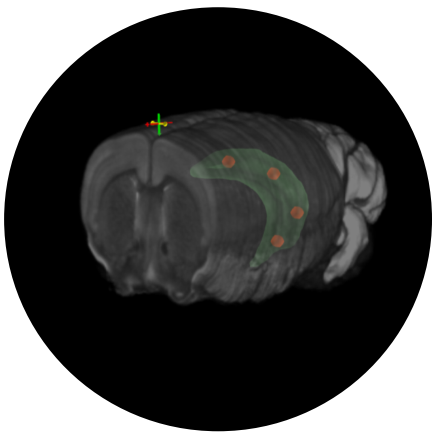
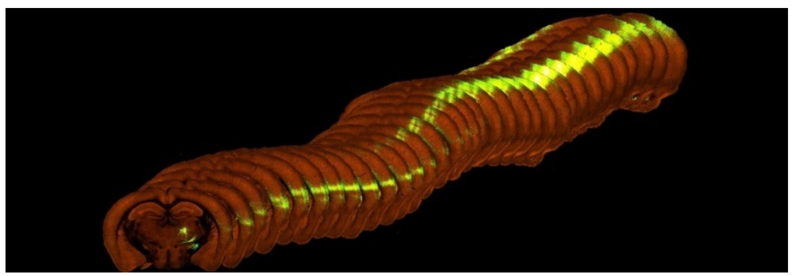
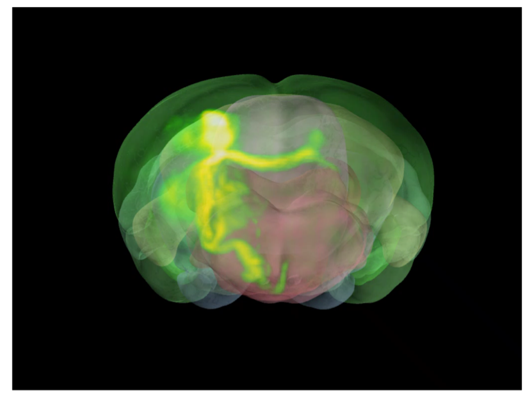
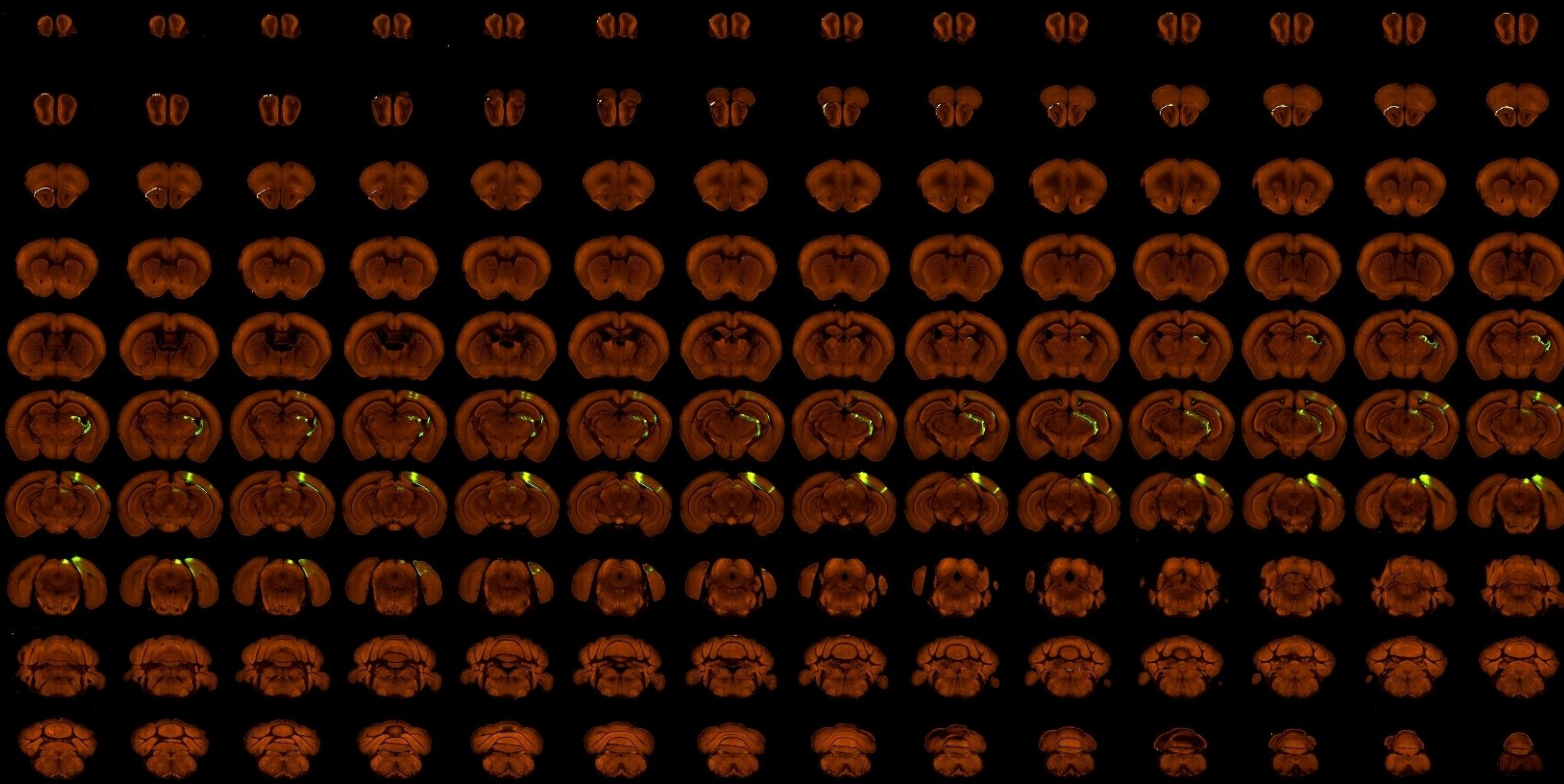
→ **High-throughput Fluorescence Imaging**
→ **3D Connectivity Map & Model**





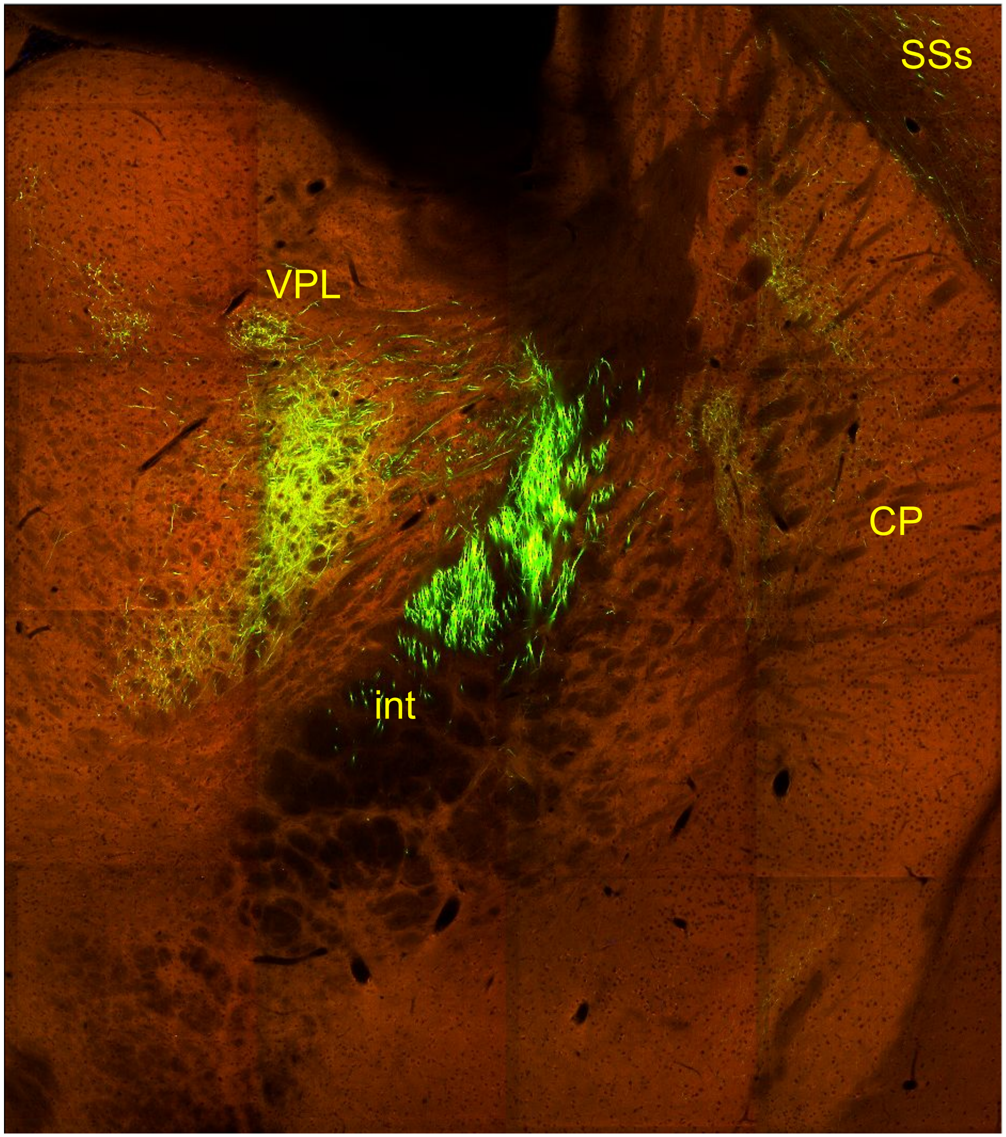


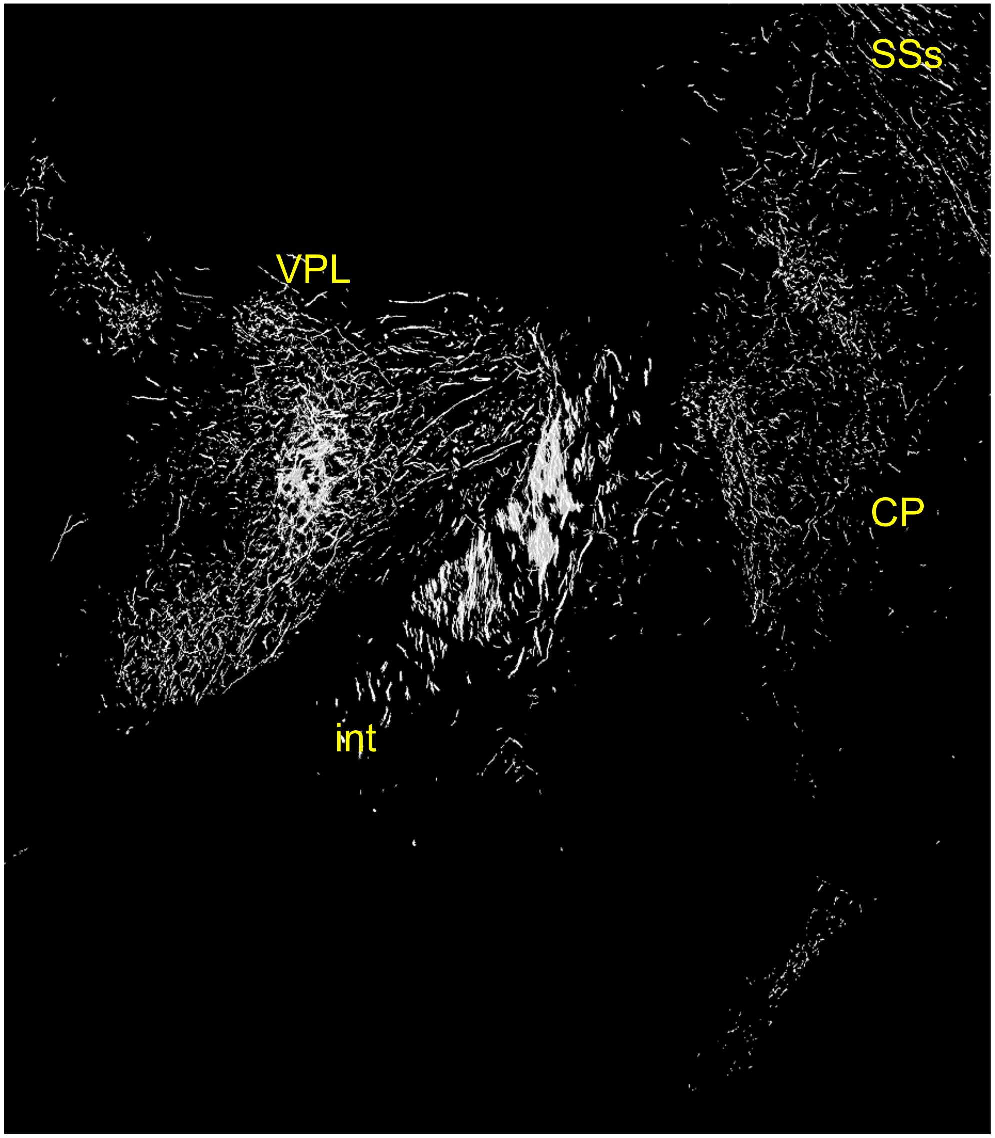
A Single Experiment



hSyn-EGFP-WPRE injection VISp, 21 day survival.
140 serial 100 μm vibratome sections, imaged with 2P at 20X, one optical section (z) per slice.
TissueCyte1000, TissueVision (Ragan et al., 2012, Nature Methods)

Signal detection



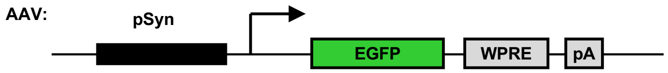


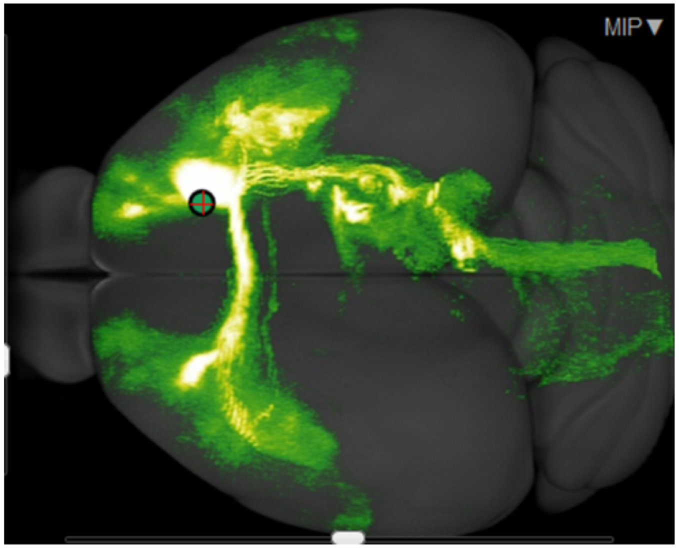
Intensity scaling, noise reduction, edge and dense cloud signal detection

Components of the Connectivity Atlas

Regular rAAV as tract tracer (non-Cre-dependent)

- Mapping all axonal projections from injection sites (300-500 sites covering the entire brain)
- Comparison with conventional tracer BDA





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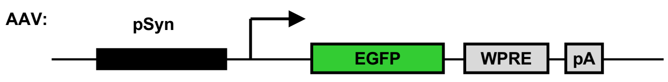
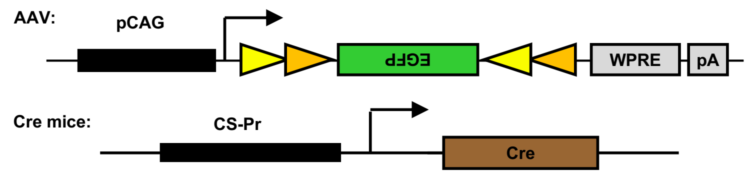
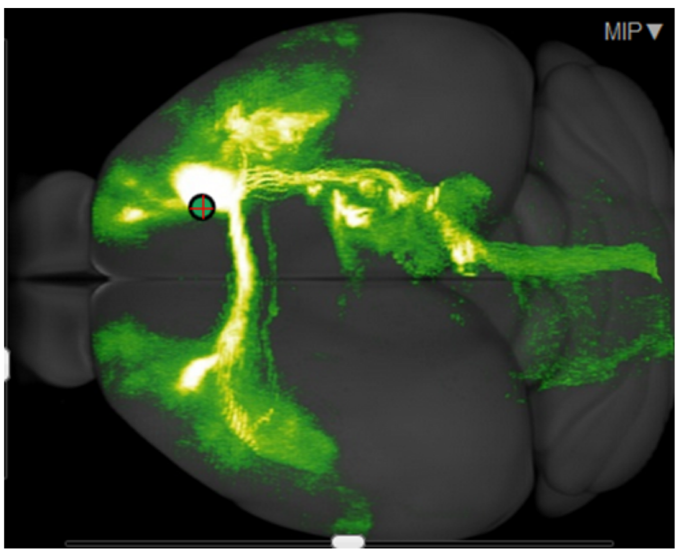
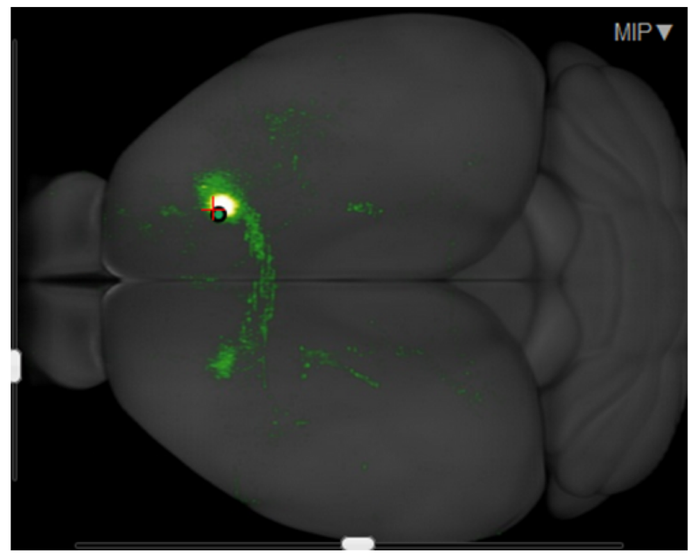


Cre lines + Cre-dependent rAAV

- Cell-type-specific mapping of projections from injection sites
- Use >100 Cre lines







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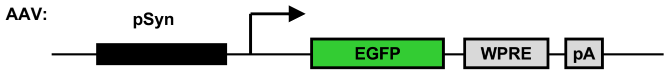

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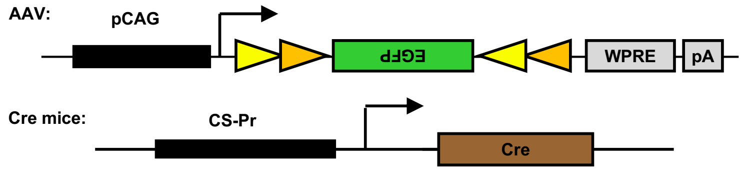
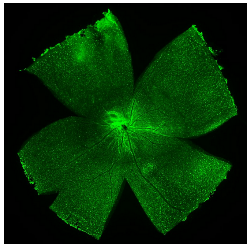
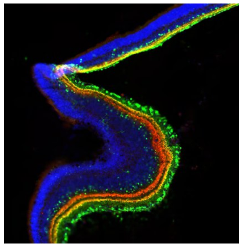


Retinal Projectome

- Axonal projections from retinal ganglion cells (RGC) to the brain
- 26 Cre lines
- Whole retinal mount





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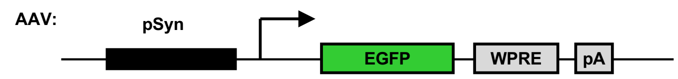

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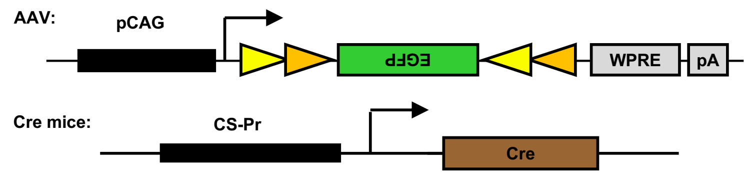

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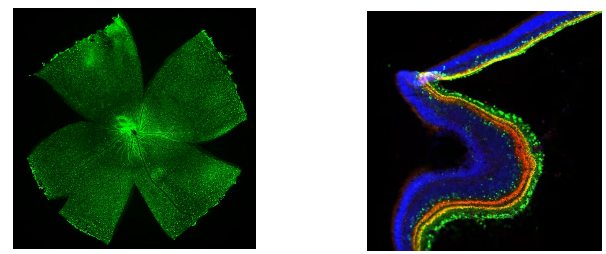
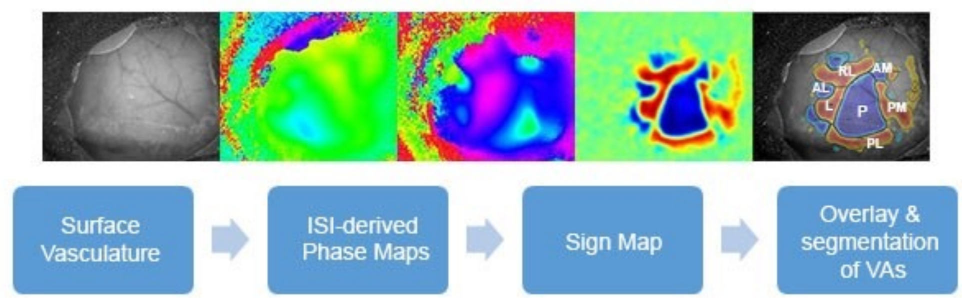


Targeting of Functional Areas

- Retinotopic mapping and Intrinsic Signal Imaging to target visual-associated areas



https://goo.gl/D41Myu

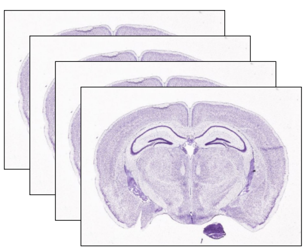
Annotated 3D Reference Space

Registration to a canonical space enables comparison of information within and across datasets

Common Coordinate Framework: 3D Reference Space

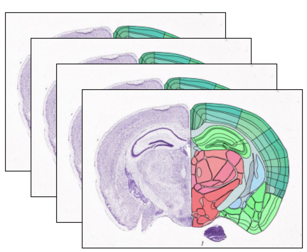
Allen Reference Atlas

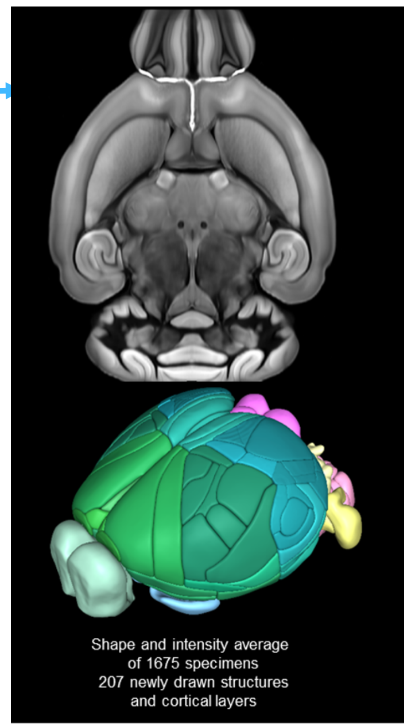
~500 Nissl sections



132 annotated sections

~800 structures





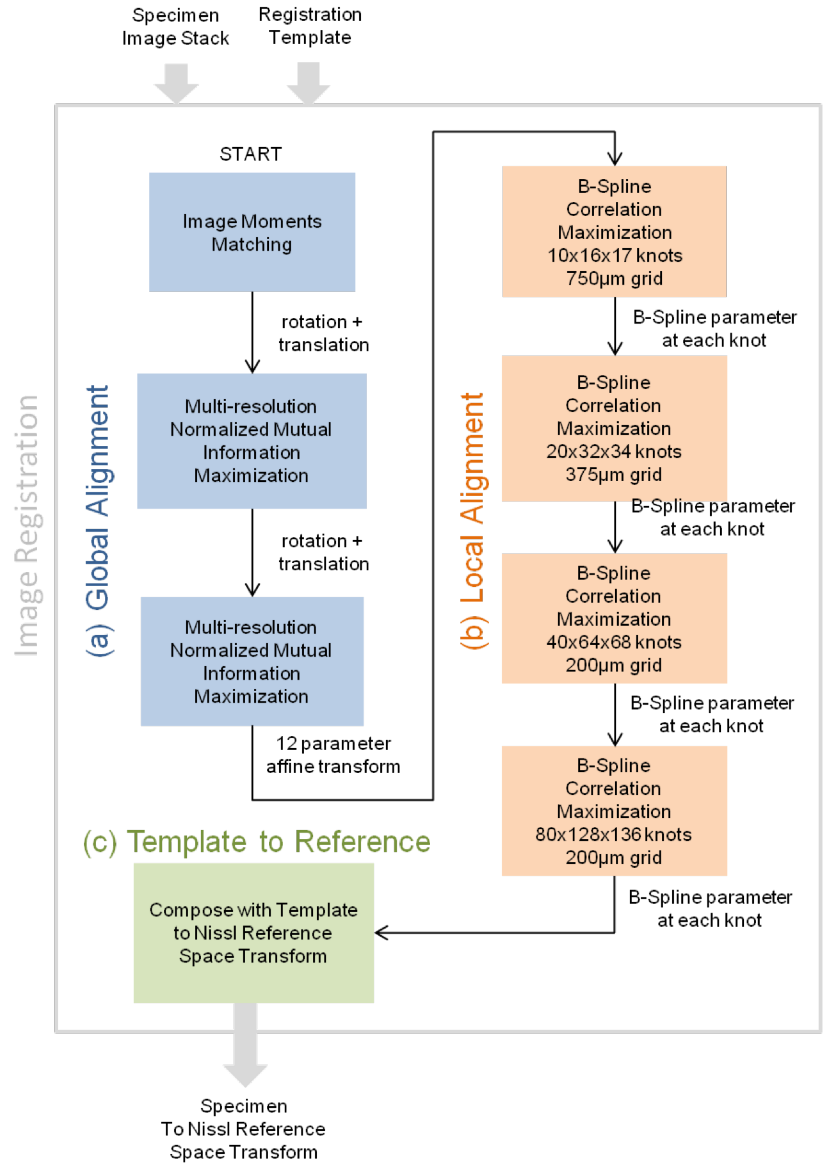


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Image Registration

Chicken or the egg?

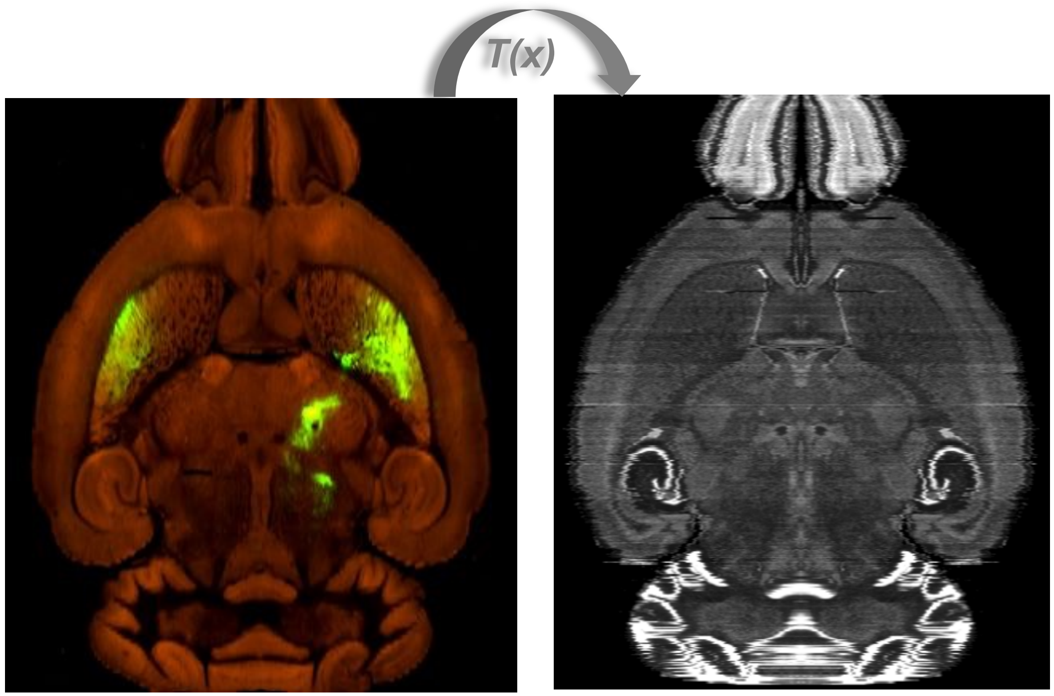
- You need a good registration to get a good averaged brain
- You need a good averaged brain to get good registration
- Start with a rough template and iteratively improve both

Perfused brain

2P Tomography Imaging

Background autofluorescne

Sections 100µm apart



Fresh frozen brain

Reconstructed from Nissl sections

25µm thick sections

Averaged brain as registration template

Chicken or the egg?

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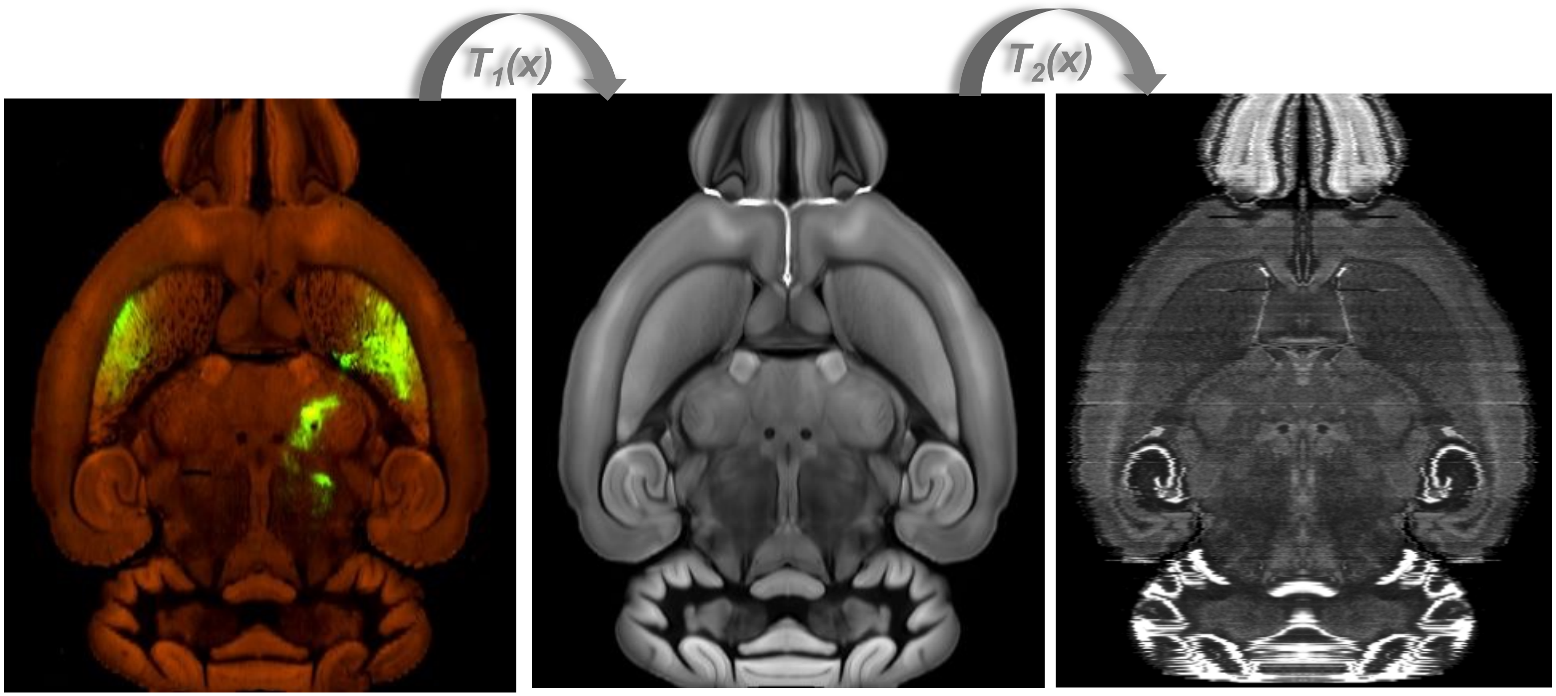
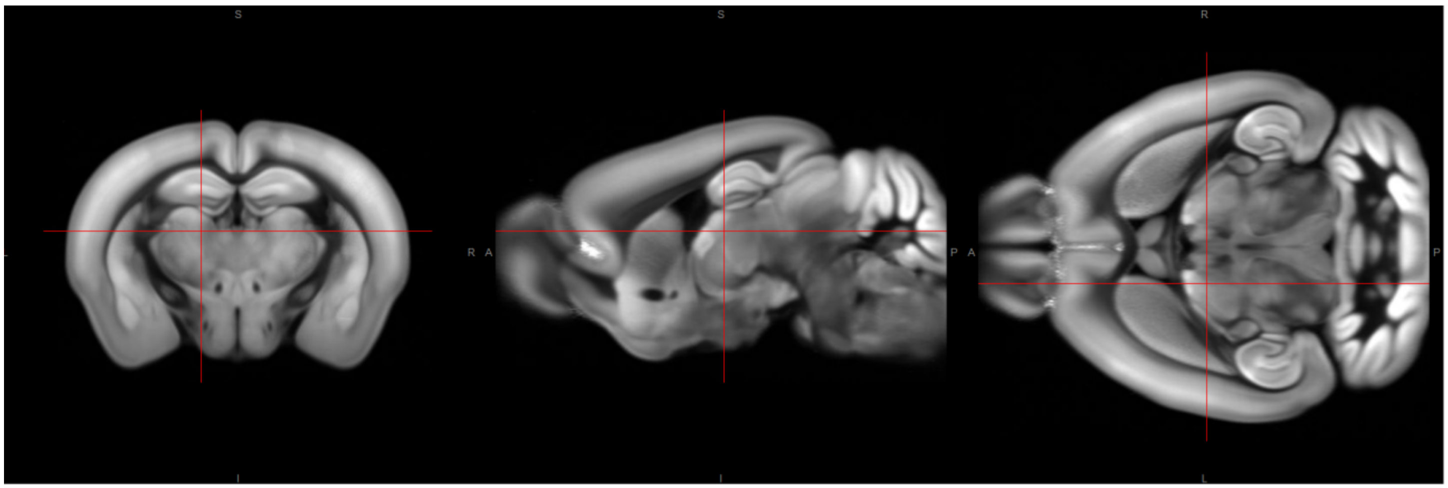
- You need a good averaged brain to get good registration
- Start with a rough template and iteratively improve both

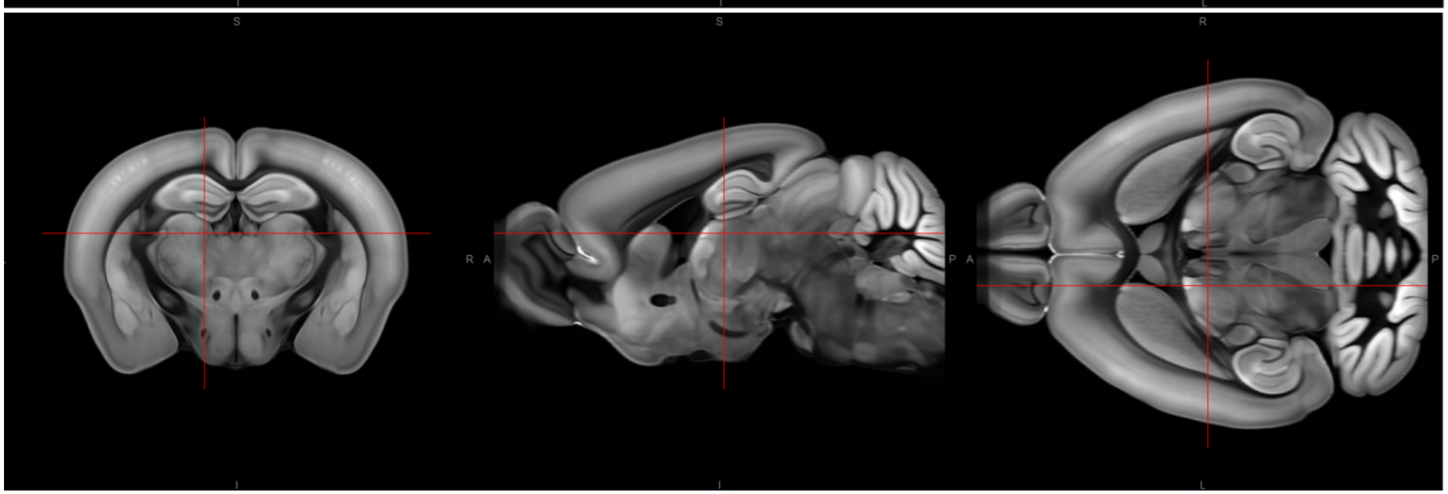


- Each specimen was deformably registered to the template and averaged together
- The average deformation field over all specimens was computed, inverted, and used to deform the average image created in (1).
- This shaped normalized average was then used as the anatomical template in the next iteration.
- For computational efficiency, the method was first applied to the data down sampled to 50μm resolution until convergence was reached.
- This result was then used as input to the 25μm processing round. In the final step, the specimens were resampled at 10μm resolution and averaged to create the final 3-D volume.

VPL

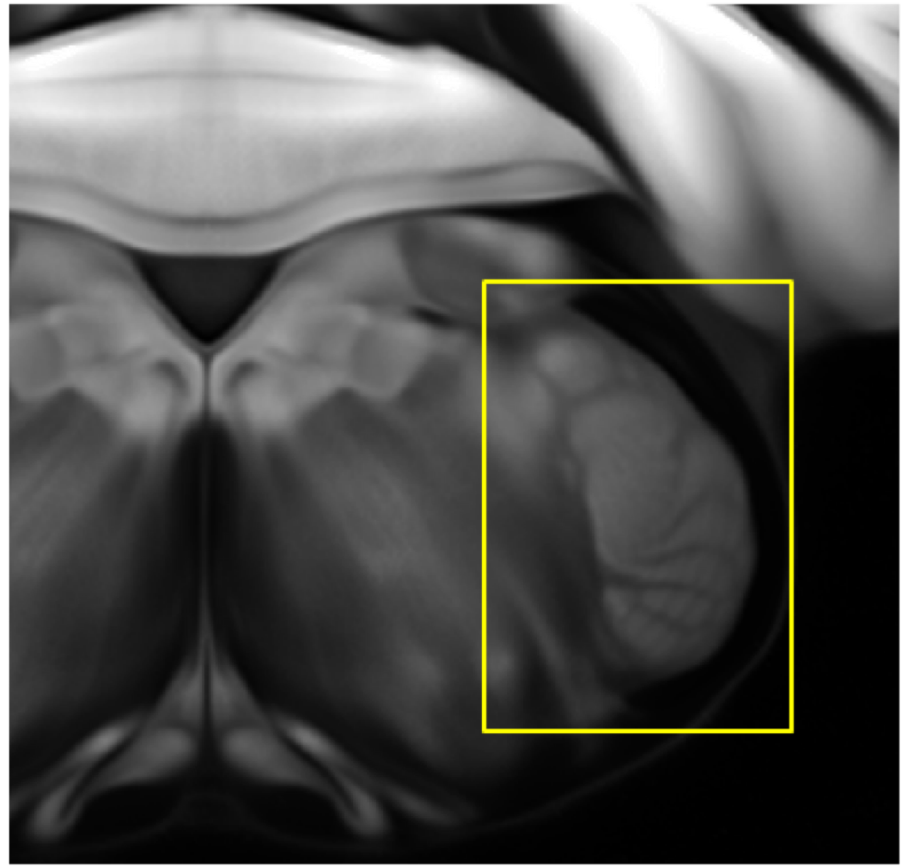


Average of 700+ globally (affine) mapped brains

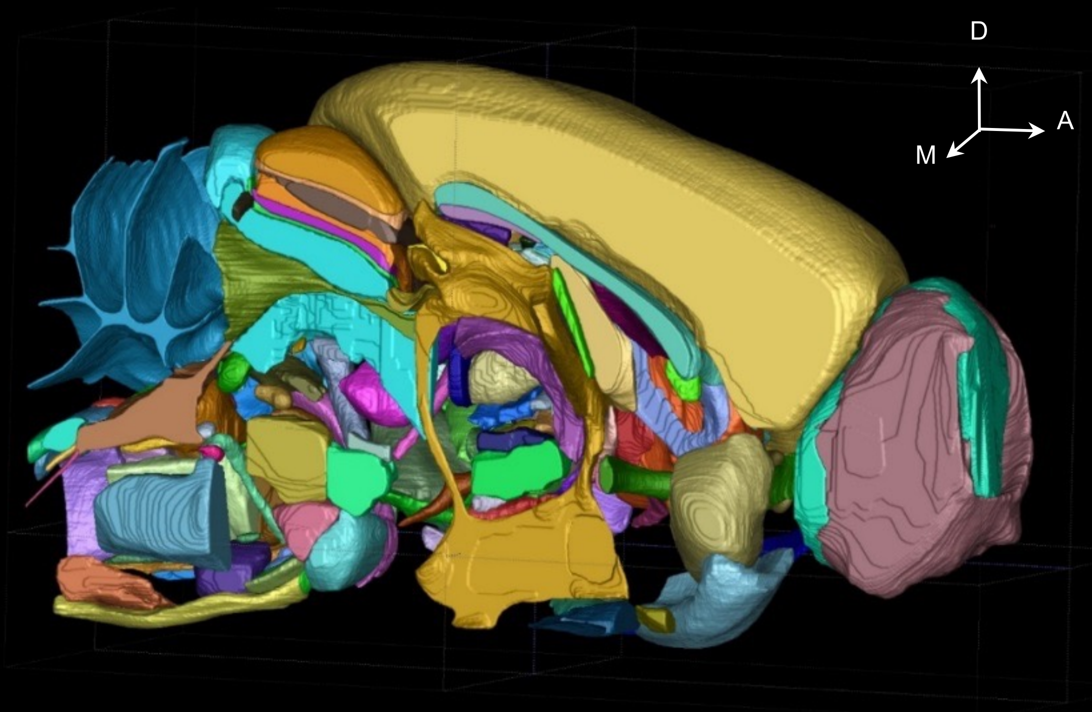


Average of 1200+ brains locally (deformable) mapped after 4 generations

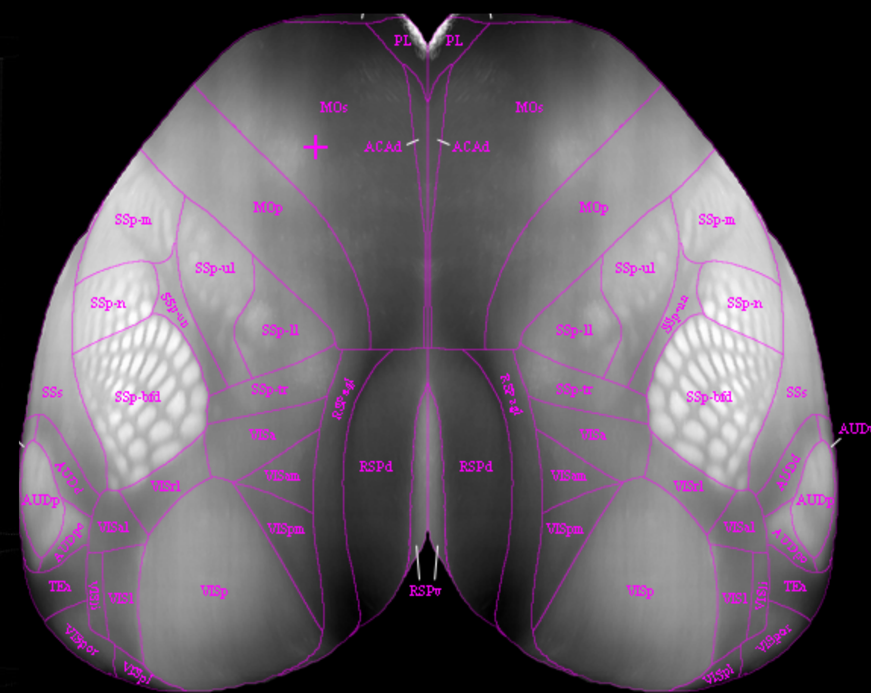
Greater than the sum of its parts



Common Coordinate Framework



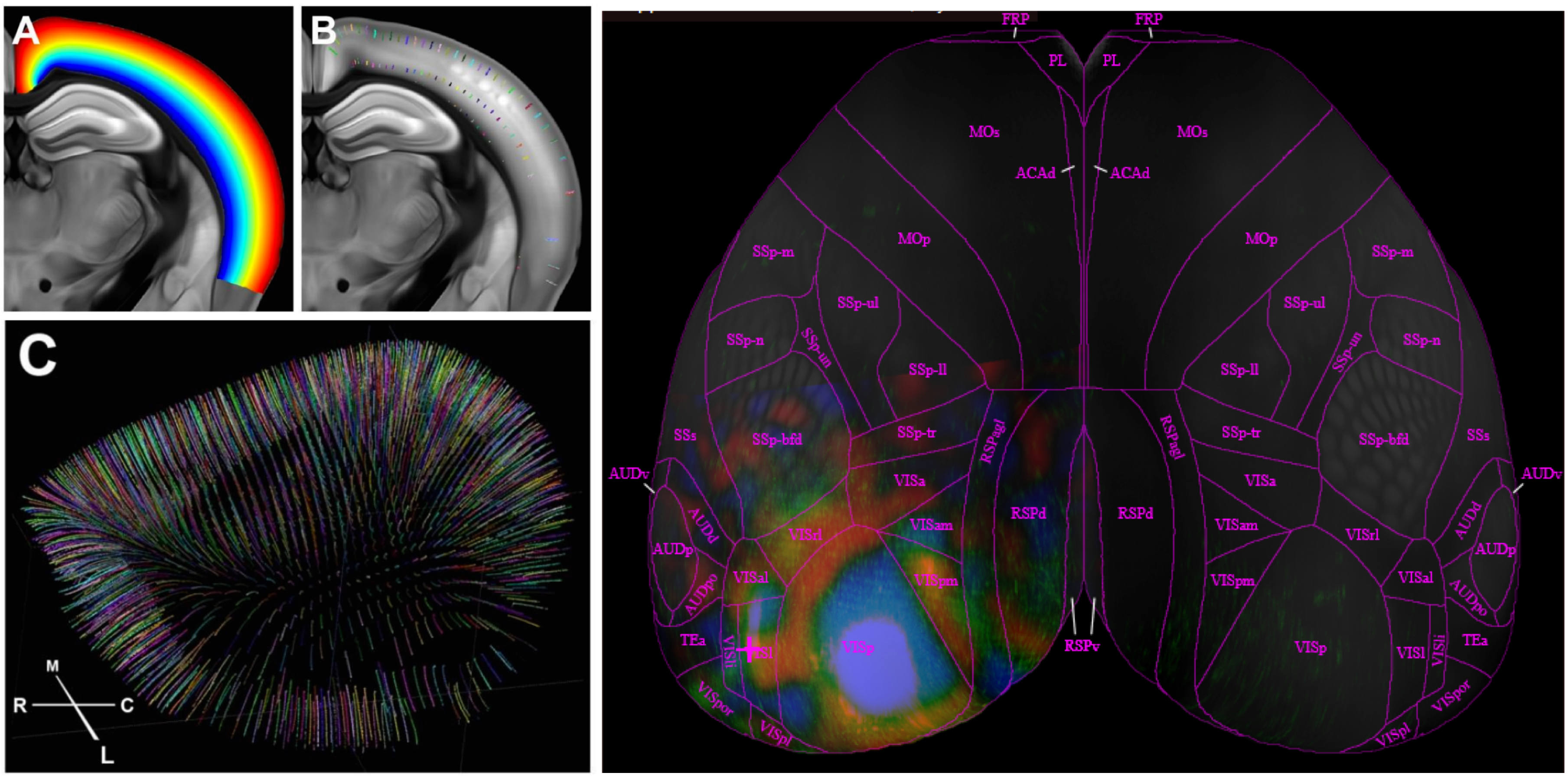
Medial view of subcortical structures and cortical sheet



Dorsal view of cortical areas

CCF: Curved Coordinate System

- As part of the construction of CCF v3, a curved cortical coordinate system was developed to enable the integration of information from different cortical depths.
- Streamlines were used to facilitate the annotation of the entire isocortex, including higher visual areas.



Overview:

- Introduction: Allen Institute for Brain Science
- Allen SDK http://alleninstitute.github.io/AllenSDK/
    - Mouse Connectivity Atlas
    - The Common Coordinate Framework
    - **Allen Cell Types Atlas**
    - Allen Brain Observatory

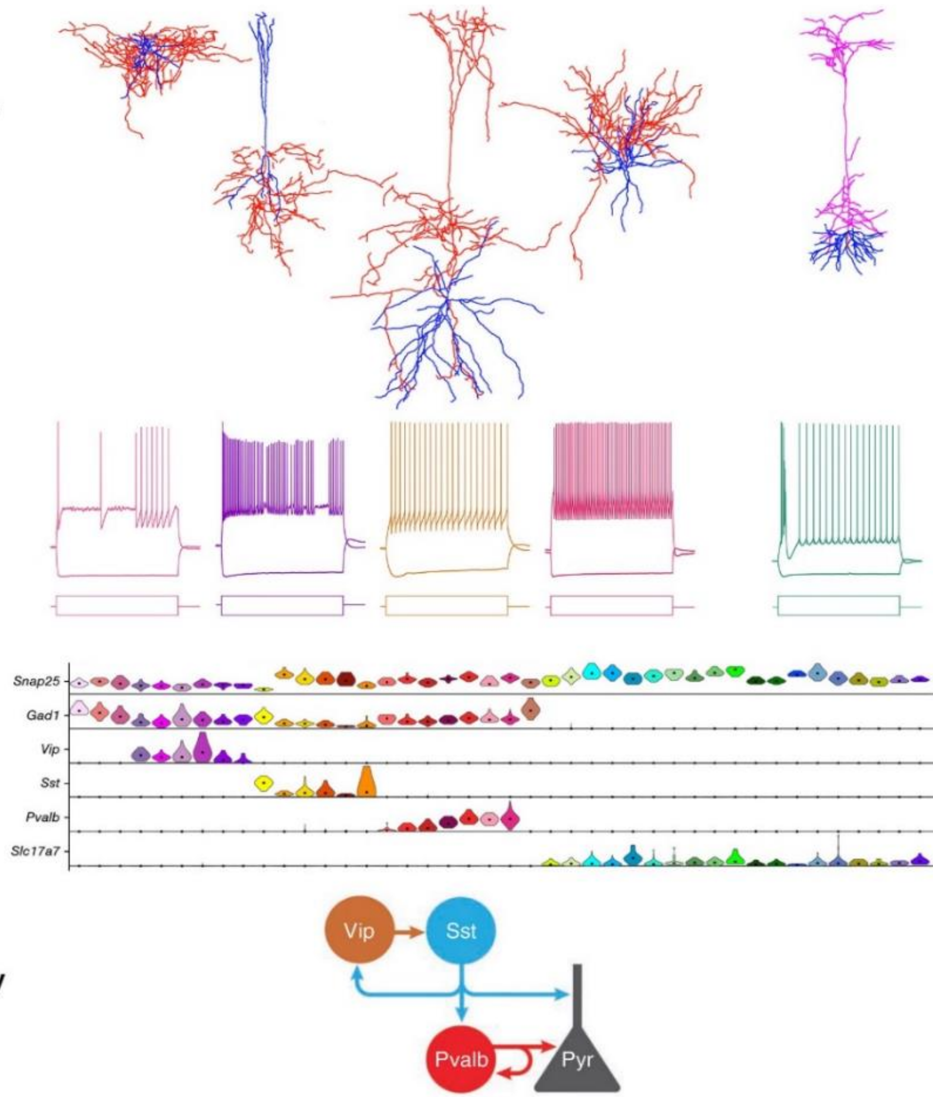
Classifying Cells as a Tool for Discovery

Morphology — **Cell stain and dendritic reconstruction**

Physiology — ***In vitro* slice recording**

Molecular signature — **Transcriptomics (RNA-Seq)**

Connectivity — **Projectional maps & slice physiology**



Allen Cell Types Atlas

ALLEN INSTITUTE | BRAIN ATLAS

ALLEN BRAIN ATLAS
DATA PORTAL

HOME | GET STARTED | CELL TYPES | TOOLS

Search...

OVERVIEW | CELL FEATURE SEARCH | DOWNLOAD | DOCUMENTATION | HELP

Overview

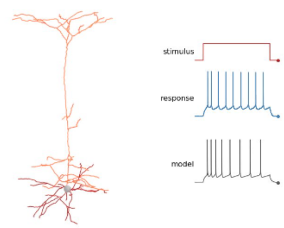
This brain cell database is a survey of biological features derived from single cell data, from human and mouse.

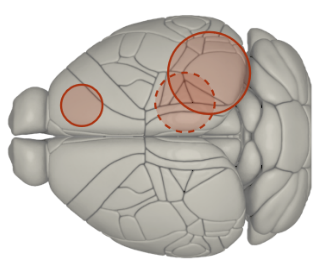
The database contains electrophysiological, morphological, and transcriptomic properties gathered from individual cells, and models simulating cell activity. At this early stage of data generation, survey coverage focused on select areas of cerebral cortex, and thalamic neurons.

Browse electrophysiological response data and reconstructed neuronal morphologies using the Cell Feature Search tool. Transcriptomic data can be accessed through the Download 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 via the Download page, or through the Allen SDK or API.





Mouse Data

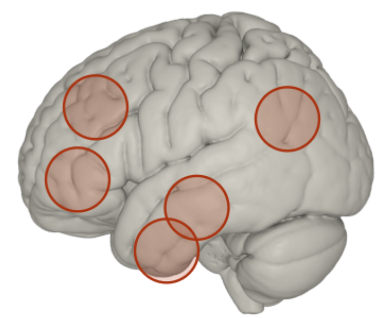
Cells are acquired from selected brain areas in adult mouse. Cells are identified for isolation based on transgenic mouse lines harboring fluorescent reporters driven by cell type specific drivers. For electrophysiological and morphological analyses, excitatory cells with layer-enriched expression and inhibitory cells based on classical markers were selected. Brain areas selected for analysis include subregions from visual cortex, motor cortex and anterior lateral motor cortex (ALM), in the secondary motor area (MOs).

For transcriptomic analysis, regional and laminar dissections were performed on specimens from pan-neuronal, pan-excitatory, and pan-inhibitory transgenic lines, to sample comprehensively. Data from the lateral geniculate nucleus (LGd) is also included.

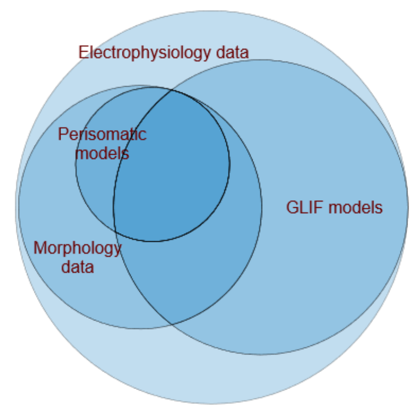
Human Data

Cells are acquired from donated brain tissue in the temporal or frontal lobes based on structural annotations described in The Allen Human Brain Reference Atlas. For electrophysiological and morphological analyses in the cortex, cells are selected based on soma shape and laminar location.

For transcriptomic analysis, individual layers of cortex are dissected, and neuronal nuclei are isolated. Laminar sampling is guided by the relative number of neurons present in each layer.



Donor Profiles



This interactive Venn diagram shows how many cells are available for each data modality (electrophysiology, morphology, transcriptomics) and models. Select a category to view the subset of cells.

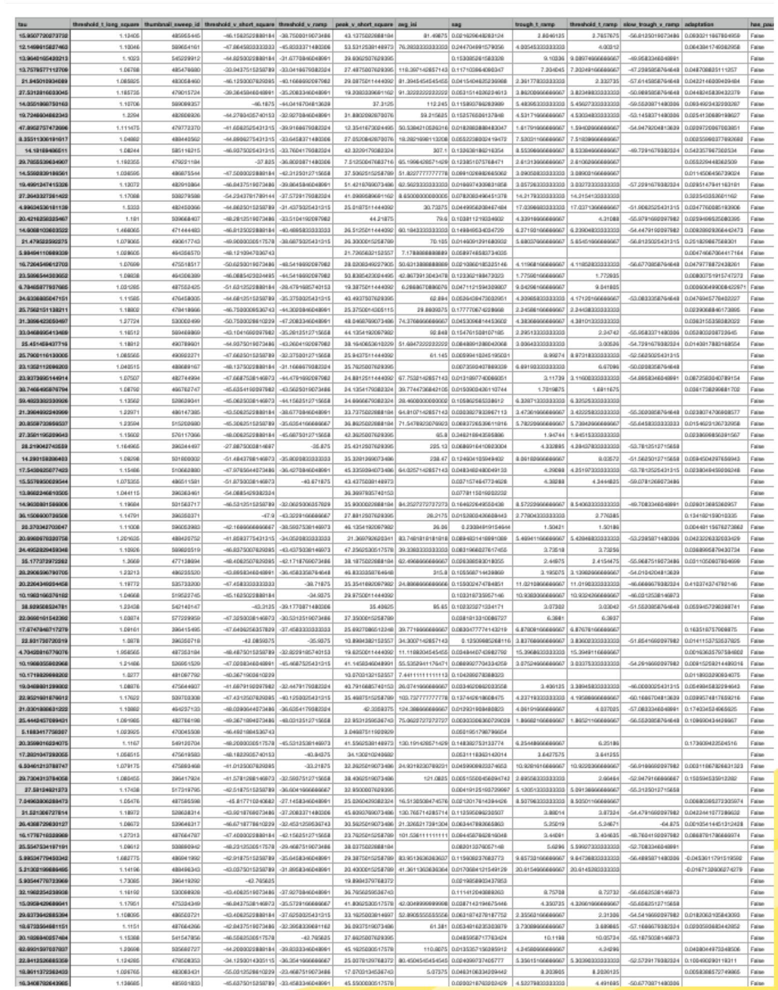
Include Transcriptomic Data

alleninstitute.org | brain-map.org

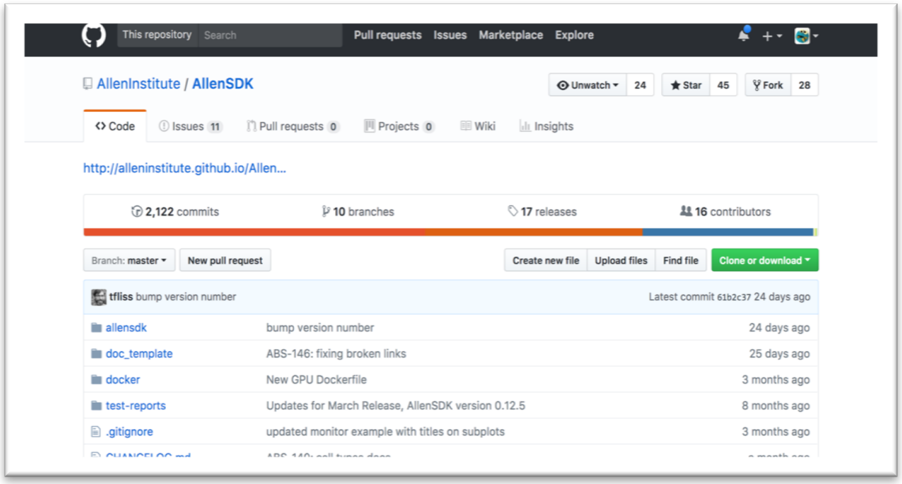
Motivation

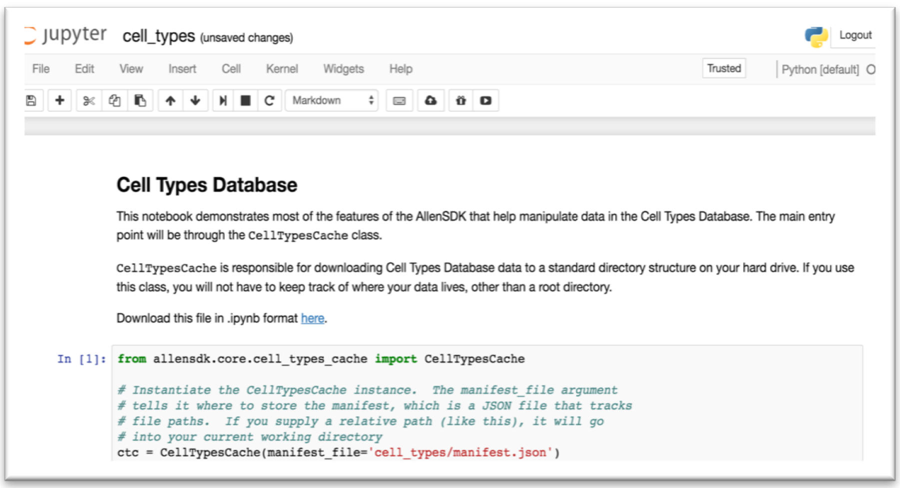
- 1337 cells…
- 55 electrophysiological features…
- 5 lines of code (including installation!)…

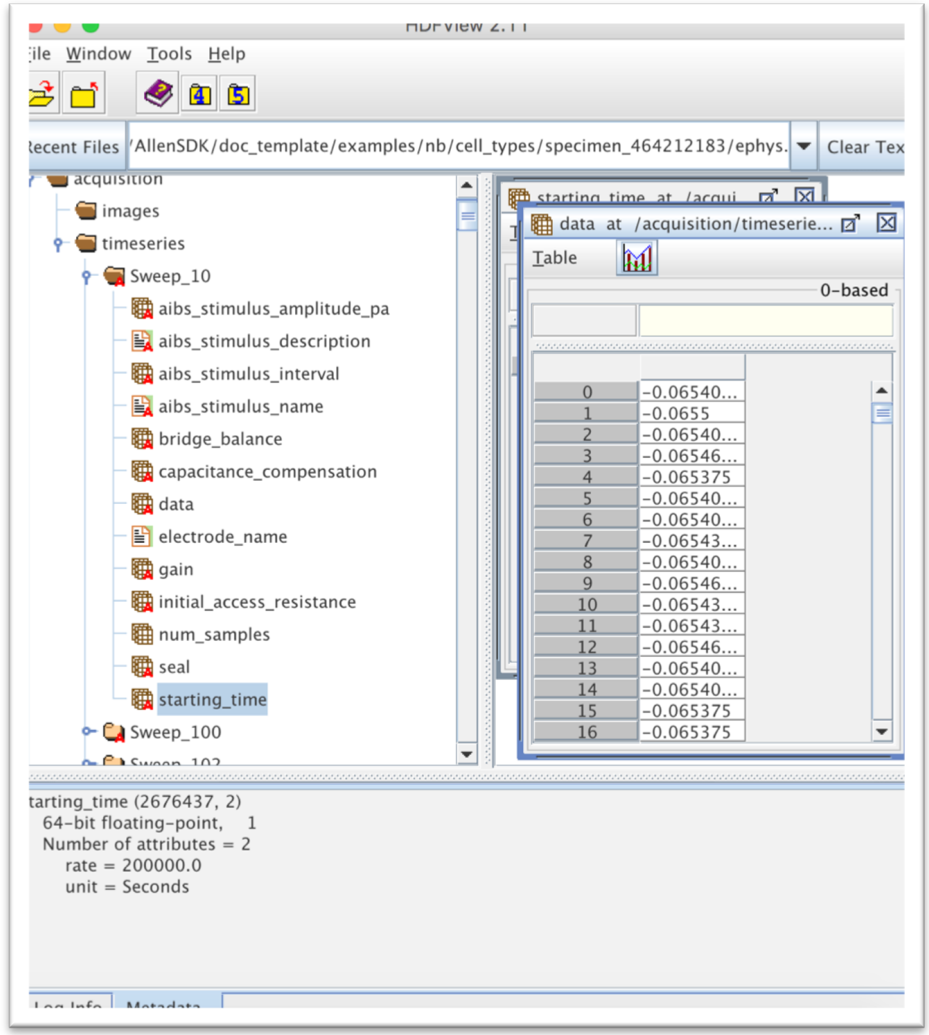
```
[nicholasc@nicholasc-mac]$ pip install allensdk
[nicholasc@nicholasc-mac]$ ipython

In [1]: from allensdk.core.cell_types_cache import CellTypesCache

In [2]: ctc = CellTypesCache(manifest_file='cell_types/manifest.json')

In [3]: data = ctc.get_ephys_features()
```



Cell Types Atlas and the AllenSDK







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THANK YOU

We wish to thank the Allen Institute for Brain Science founders,
Paul G. Allen and Jody Allen, for their vision, encouragement and support.

ALLENINSTITUTE.ORG
BRAIN-MAP.ORG

ALLEN INSTITUTE *for* BRAIN SCIENCE