## Allen Institute Data and Resources: An Interactive Tour

### Neurohackademy 2018 UW eScience Institute, Seattle, WA

3 August 2018

Nicholas Cain and Justin Kiggins Allen Institute for Brain Science





- Introduction: Allen Institute for Brain Science
- Allen SDK <u>http://alleninstitute.github.io/AllenSDK/</u>
  - 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 Science2014 – Allen Institute for Cell Science2016 – 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

Data Resources Brain Observatory

Cell Types

API Access

Biophysical

Examples

package allensdk.config package

Github Profile

QUESTIONS Send any questions using the Send Us a Message link below, or submit your question to StackOverflow using with the

'allen-sdk' tag.

allensdk.core package

allensdk.ephys package

allensdk.model package

allensdk.morphology package

allensdk.test\_utilities package

Authors Source Documentation allensdk.api package allensdk.brain\_observatory

Generalized LIF

Models

Mouse Connectivity Reference Space

#### 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)
- · perform summary specific turning unarysis (e.g. unrung gruting uncetion turning)

#### 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 ModelsGeneralized LIF Models

#### ALLEN MOUSE BRAIN CONNECTIVITY ATLAS

If you encounter any problems using the AllenSDK, please create an issue on Github's issue tracker. The Allen Mouse Brain C genetically engineered to throughout the brain. Th

### QUICK SEARCH



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.









# **Python API for RMA:**

ALLEN INSTITUTE BRAIN ATLAS

#### **ALLEN BRAIN ATLAS**

SOFTWARE DEVELOPMENT KIT

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**Data Resources** 

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### QUESTIONS

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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()

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.

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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)





## **Allen Mouse Brain Connectivity Atlas**







## Allen Mouse Brain Connectivity Atlas







### A Single Experiment



hSyn-EGFP-WPRE injection VISp, 21 day survival.

140 serial 100  $\mu m$  vibratome sections, imaged with 2P at 20X, one optical section (z) per slice.

W

TissueCyte1000, TissueVision (Ragan et al., 2012, Nature Methods)

## **Signal detection**



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



### 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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#### **Retinal Projectome**

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





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#### **Targeting of Functional Areas**

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





### **Annotated 3D Reference Space**

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

Allen Reference

Atlas

Common Coordinate Framework: 3D Reference Space

~500 Nissl sections

132 annotated sections

~800 structures





and cortical layers



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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





# **Averaged brain as registration template**

### 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





- 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.



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.





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### **Classifying Cells as a Tool for Discovery**



### **Allen Cell Types Atlas**



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

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.





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

#### 33|| alleninstitute.org | brain-map.org

DATA PORTA HOME

OVERVIEW



# 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()

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20.2906596790705	1,23213	496235520	-10.0558316040991	-35.4583358784648	45.8322359764549	215.0	0.105568714428869	3.185075	3 12982906649067	-54.0104204813639		Faise
20.2204349204458	1.18772	\$35732200	-67.4542203322323	-38.71875	35.3541882097892	24.8308900689006	0.155002474784851	11.0210806689067	11.0190320333203	-10.0669079382224	0.410374374782146	False
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22.0690101542392	1.03974	\$77529959	-67.5259038146973	-30.5312519673486	37.35000+5254799		0.0581913310086727	6.3981	6.3937			Faise
17.4747846717279	1.09161	295415495	-67.6406256357829	-37.4581335313533	25.0927080512240	29.7710506685067	0.0635477774143219	6.87009106689067	6.87678166649667		0.163516757909875	Faise
22.931720720319	1.0078	296350718	-42.0859375	-35.9275	93.8904382152557	34.3007142857143	0.12509685268116	3.83708900689067	1 #3602320333205	-51.8541660297982	0.0141153753537825	Faise
4.70420816779076	1.954565	487353194	-48.4875015358789	-32.8229195740153	19.8250011444092	11.1188204545455	0.0348446740982792	15.39686223332223	15.39491166669967		0.00%63635707584602	Faise
10 171803060746	1,25466	44+007300	-17.10106.440048991		11.1404040048891	7.441111111111111111	0 10420022024044	a = (10/9000090007	****************		0.0118003300634077	- man
19.0409301232000	1.0277	475644907	-61.6679190197567	-32.4479170047544	43.7916685741+53	26.07419006491047	0.003/0020602023554	3.400105	3.38945800327000	-10.000002542+5+5	0.0549045832254045	Faise
22.9521001870012	1.17022	509702308	-87.4312507829285	-90.1250025431015	35.4997515254799	103.73777777777	0.137-642618606475	4.23718220332203	4.1200006840067	-60.1686704813639	0.0099574817659216	False
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25.4642457099421	1.091985	482764198	-49.3671094073486	-48.0212512715658	22.8521259534742	75.062272727272727	0.00903304360729609	1.89562106689567	1.865211006669967	-56.5520958764648	0.109990434429967	Faise
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27.58124821273	1.17428	517319795	-42.5187515250789	-35.604 1006640667	32 8500007629395		0.00419125103729067	5.12051222332223	5.0913866686667	-55.3125012715658		Faise
7.54963806288473	1.25476	487585598	-45.817710040682	-27.1458346048091	25.030429082324	16.5120500474576	0.0212017614294426	8.50796200332003	8.52501166649967		0.00680365272305674	Faise
31.531304727814	1.18972	529638314	-43.9218768473486	-37.2083371483366	45.0290709073496	100.765714285714	0.113595296230507	0.89014	3,47324	-04.4791669297982	0.0422461077286602	False
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05 554353445710	1,27013	487064707	-47.4000.02880184	-te-1062512715668	23.76/00/02/54709	191.5281111111111	0.062012230027	1.66091	1.454635		MARKED 70117060800974	- also
5 9959477945994	1,09012	4804 490	-10.22120.0017578	-35.045834004904	00 007000000000000	80.9513836382	0+1500027263775	9.85703102680007	9.64796870017000		0.0453041204549500	- also
5.21202100681405	1482775	480404340	-40.0525015350780	-31.005834004004	23.43000+5254730	41.3011303634344	0.0170604121542104	20.0154900694047	20.4145202322203		0.0167130906274075	Faine
5.925447797272006	17005	2954192022	-42,7052.05		13.8304379764170	Jun cases and	0.0219858920437955					Faise
32.196225423930	1.16102	530098200	-43.4062519073485	-37.9272846248061	35.7656259634743		0.1111412040888262	8,75708	8,72732	-56.6582528146873		Faise
15.0959429699041	1.17961	475234349	-95.0437538146973	-35.5729100840047	41.8952530517578	42.00499906999906	0.0287143194675446	4.250725	4.2206/1006440067	-05.6542512715658		Faise
29.0373642585394	1.108095	480503721	-43.4062522889184	-37.6250325431215	23.1025003014097	52.890555555556	0.0631874379187752	2.35563106689067	2.31306	-54.5419092297982	0.0182063105843093	Faise
10.0723504001151	1.1151	48766-6266	-42.0437519073486	-32.3958339691163	35.0937519073496	61.381	0.0534916235303979	3.730899066699067	3.689845	-57.1689079382334	0.0200560683442852	Faise
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22.0412526685350	1.124285	479508353	-04.1250014305115	-35.354 1996649647	25.0079129768372	80.4504545454545	0.024090737405777	5.35015100689067	5 323903203332003	-52.5729179382324	0.100490290118311	Faise
18.0011372562455	1.094765	482083421	-55.0312528410229	-23.4687519673486	17.0703134534743	5.07975	0.0463106334209442	8.203905	8.2020125		0.0058388572749965	False
110.3408702843265	1 136005	49505-1900		-22.4583346048064	1 45 5500000547570		1.0.000001#3030883406	1.4 \$227882055322055	4 49+695	-50 6723971480385		1 Daine



### **Cell Types Atlas and the AllenSDK**

Code Issues 11 //alleninstitute.github.io/ @ 2,122 commits ch: master • New pull requ	Pull requests 0 Projects 0 Allen P10 branches	Wiki insights	22	, <b>16</b> contributors		
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© 2,122 commits	P 10 branches	<b>17</b> releases	11	16 contributors		
ch: master - New pull requ				416 contributors		
	lest	Create new file	Upload files Find fi	le Clone or download -		
fliss bump version number			Latest co	mmit 61b2c37 24 days ago		
llensdk	bump version number			24 days ago		
oc_template	ABS-146: fixing broken links			25 days ago		
ocker	New GPU Dockerfile			3 months ago		
est-reports	Updates for March Release, AllenSDK	version 0.12.5		8 months ago		
gitignore	updated monitor example with titles or	1 subplots		3 months ago		
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# **Overview:**

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



### **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.

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