Applied math in Neuroscience

Machine learning opportunities

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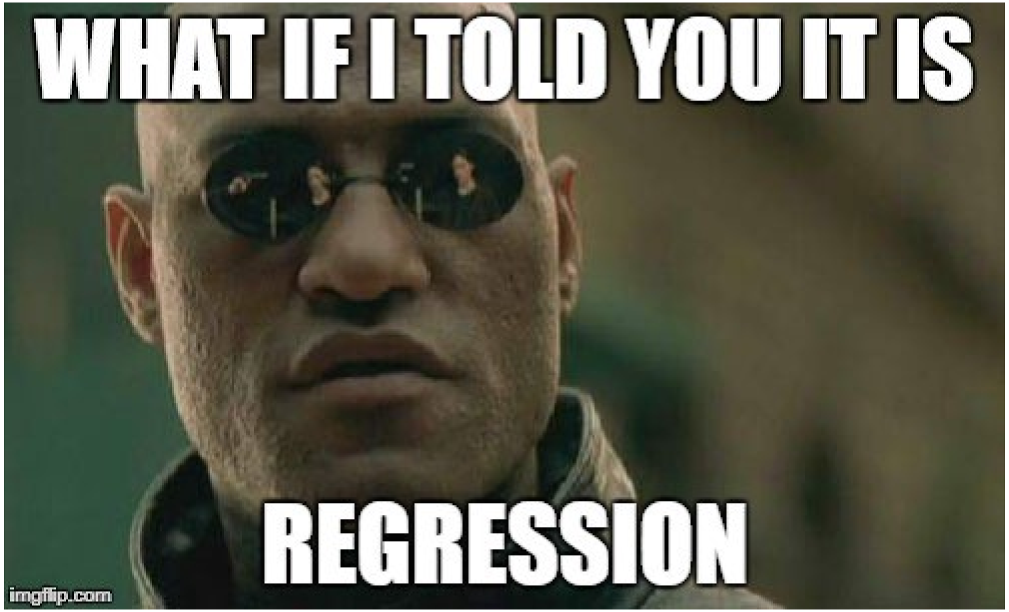
MACHINE LEARNING

(cue hype)



Or a more useful definition…

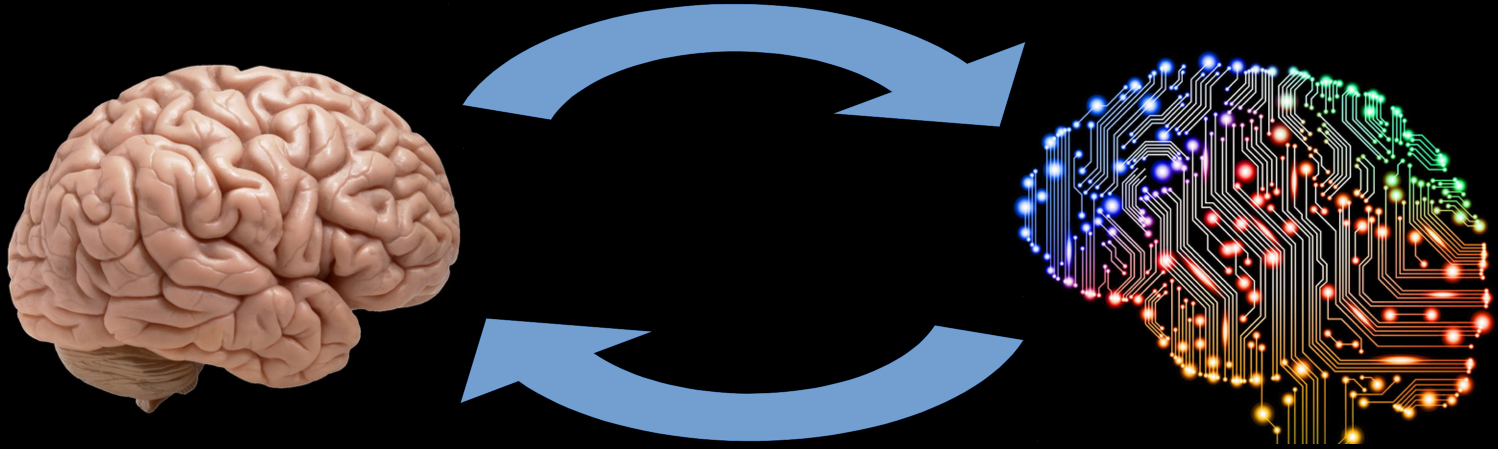
Machine learning = Optimization + Statistics

Data

The ML toolkit

- Optimization
  - Regression
  - Clustering
  - Regularization
  - Linear/quadratic/convex
  - Stochastic optimization (ANN)
- Statistics
  - Likelihoods
  - Bayesian approaches
  - Bias *vs.* variance
  - Generalization bounds
  - Cross-validation, bootstrap

Brain-inspired algorithms
General analysis methods
Alternate models of computation
Emphasis on dynamics



Big data management
Analysis of experiments
Scalable models

slide idea: Guillaume Lajoie, others
images: flickr/_DJ_, neurobanter.com

Plan for today

- Overview of an ML problem or 2 developed for neuro applications
- A short exercise in Jupyter
  - **github.com/kharris/amath50**
  - Please ensure you have `python 3 + jupyter + numpy/scipy`
  - New package: `sklearn` (scikit-learn)
  - You can install as you go

High-resolution data-driven model of the mouse connectome

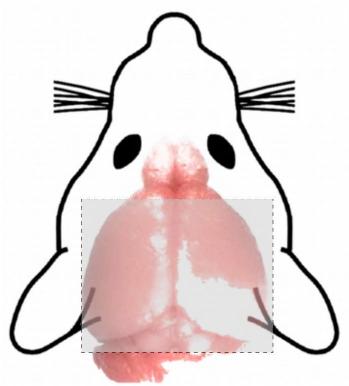
How to go from *networks* to **this**?

Video: Martin Deschênes

What *structural network* is best to compare with **this**?

1 mm
bar

Kim et al. (2016), “Crystal Skull”

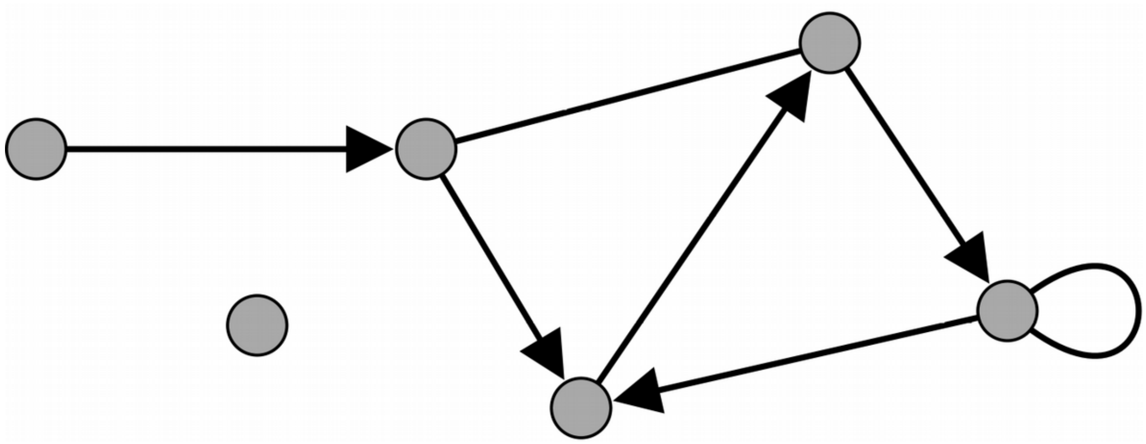


HBP

Table of Contents

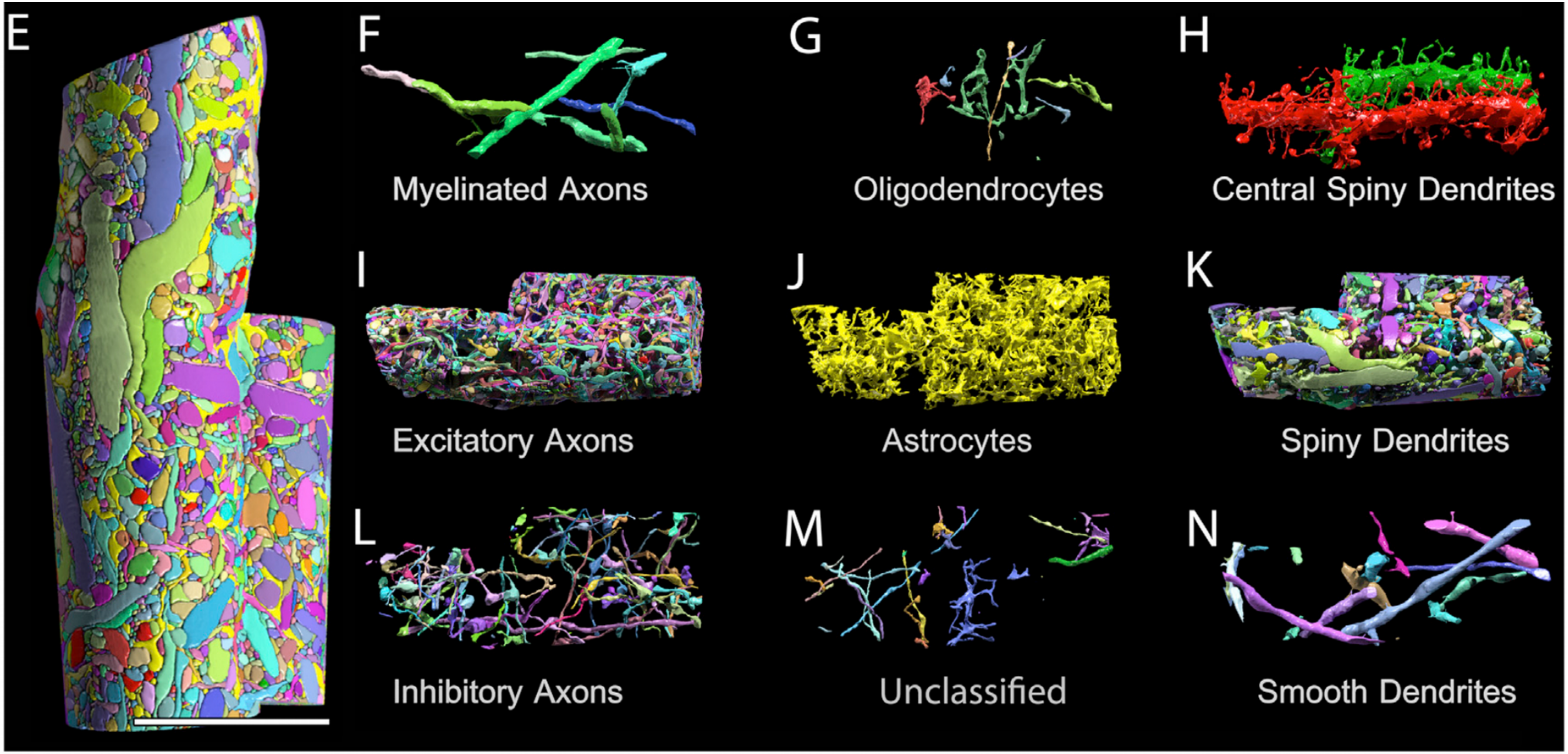
- **Measuring brain structural connectivity**
- Our method:
  - reconstructing mesoscale mouse brain networks
- Analysis of resulting network & future plans

Naive network scientist picture of a brain



or G(n, p)
or p(k)   ….   + weights

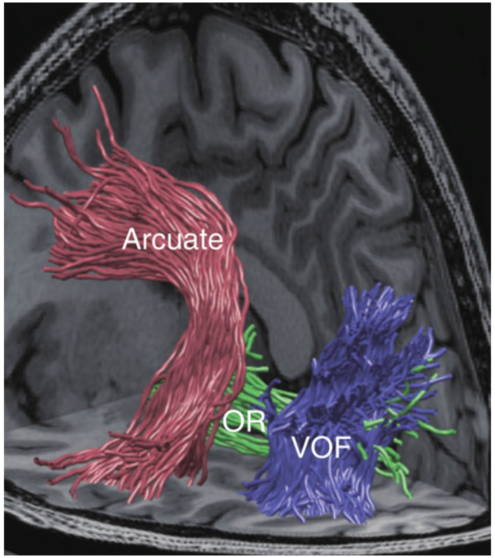
Reality is more complicated



Kasthuri et al. (2015)

Connectivity data exist at multiple scales

Macroscopic
Diffusion MRI

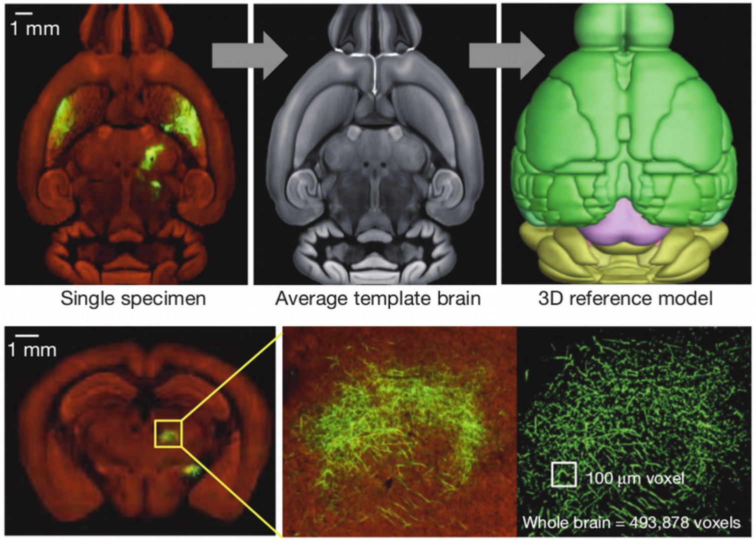


Takemura et al. (2016)

1 – 3 mm

Undirected
Non-destructive

Mesoscopic
Tracing & tomography

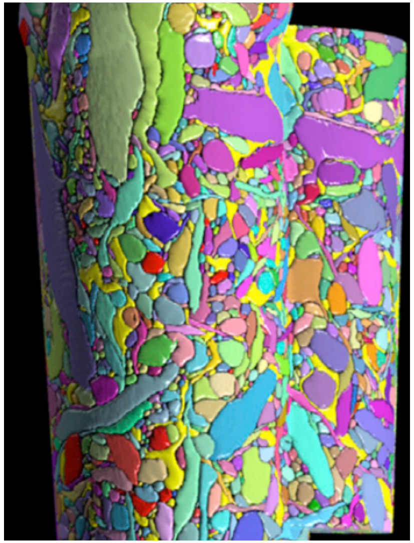


Oh et al. (2014)

10 – 100 μm

Directional
100's of neurons

Microscopic
Electron Microscopy



Kasthuri et al. (2015)

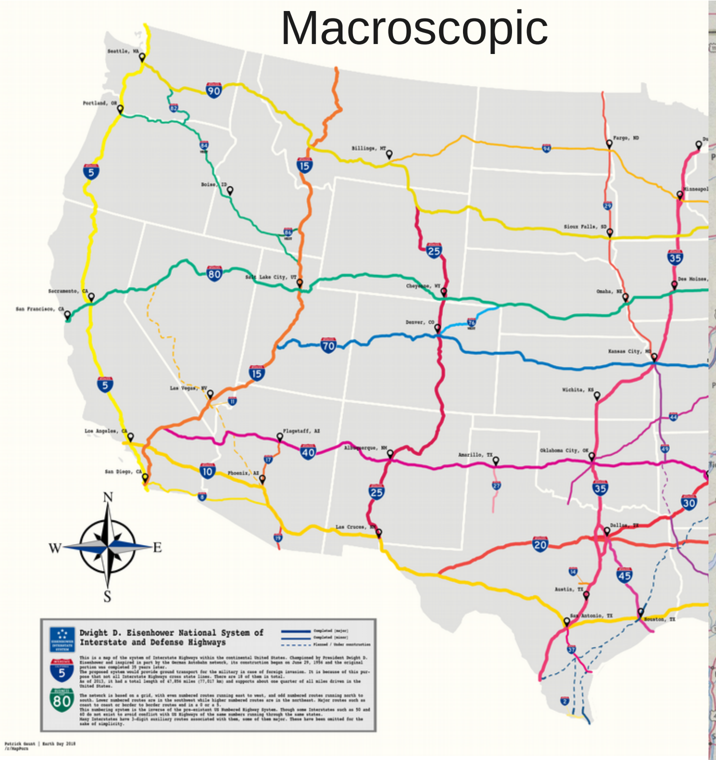
10 nm

Almost everything

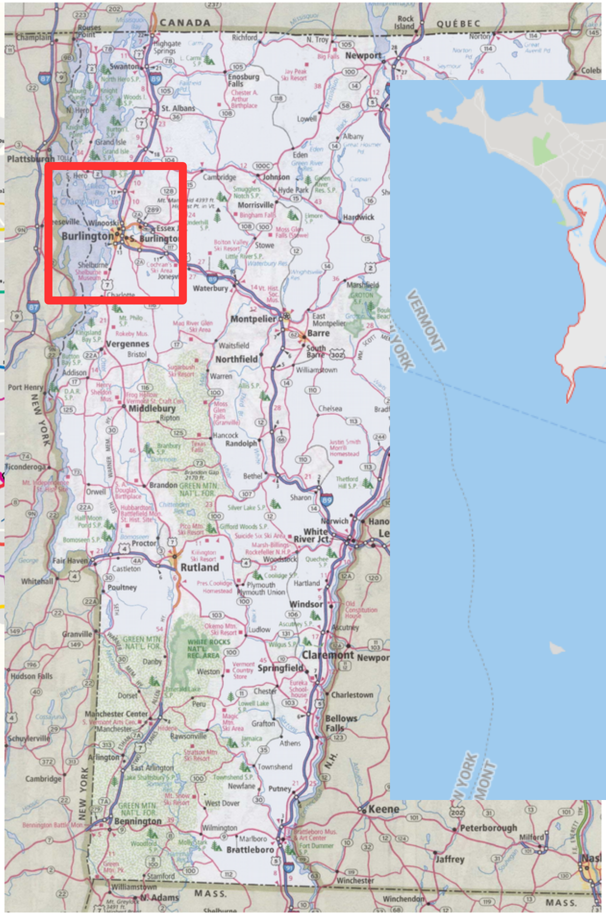
Increasing resolution

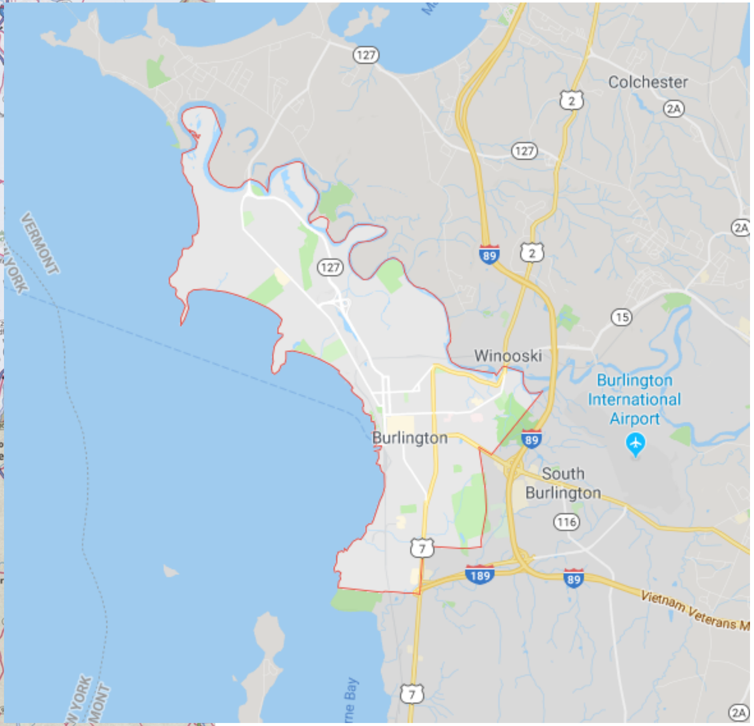
If the brain were the USA...

Macroscopic



Mesoscopic





Microscopic

reddit
http://ontheworldmap.com
Google Maps

Table of Contents

- Measuring brain structural connectivity
- Our method:
  - **reconstructing mesoscale mouse brain networks**
- Analysis of resulting network & future plans

Joseph Knox
Allen Institute
now Facebook data science

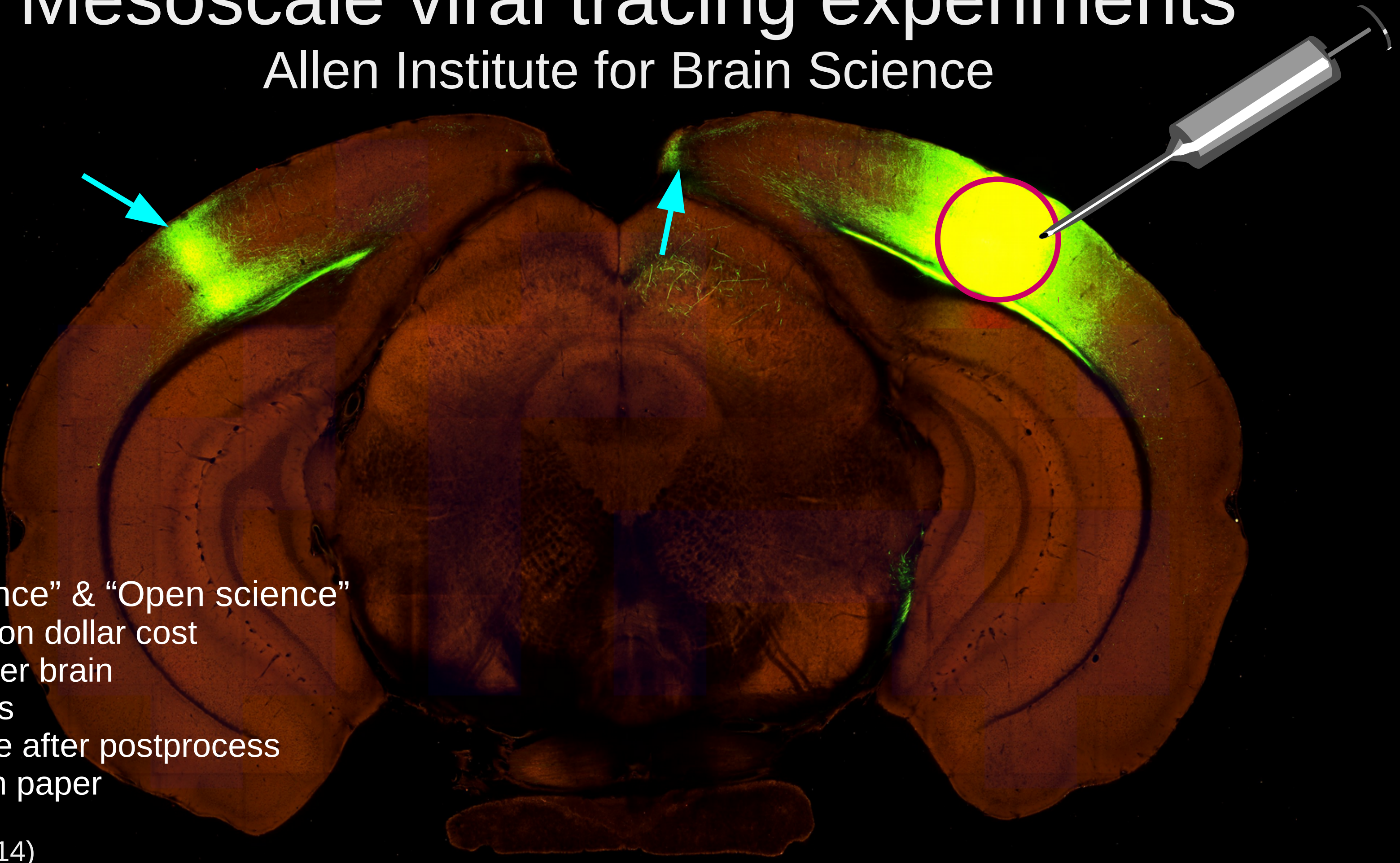
Nile Graddis
Allen Institute
Technology team

- Eric Shea-Brown, UW Applied Math
- Stefan Mihalas, Allen Institute
- Julie Harris, Allen Institute
- plus a large team at the Allen
- Patrick Kürschner (MPI Magdeburg), Sergey Dolgov (Bath), Peter Benner (MPI Magdeburg)

Published as:
- Harris, Mihalas, Shea-Brown. NeurIPS. 2016.
- Knox, Harris, Graddis, et al. Network Neuroscience. 2019.
- Kürschner, Dolgov, Harris, Benner. In review.

Mesoscale viral tracing experiments

Allen Institute for Brain Science

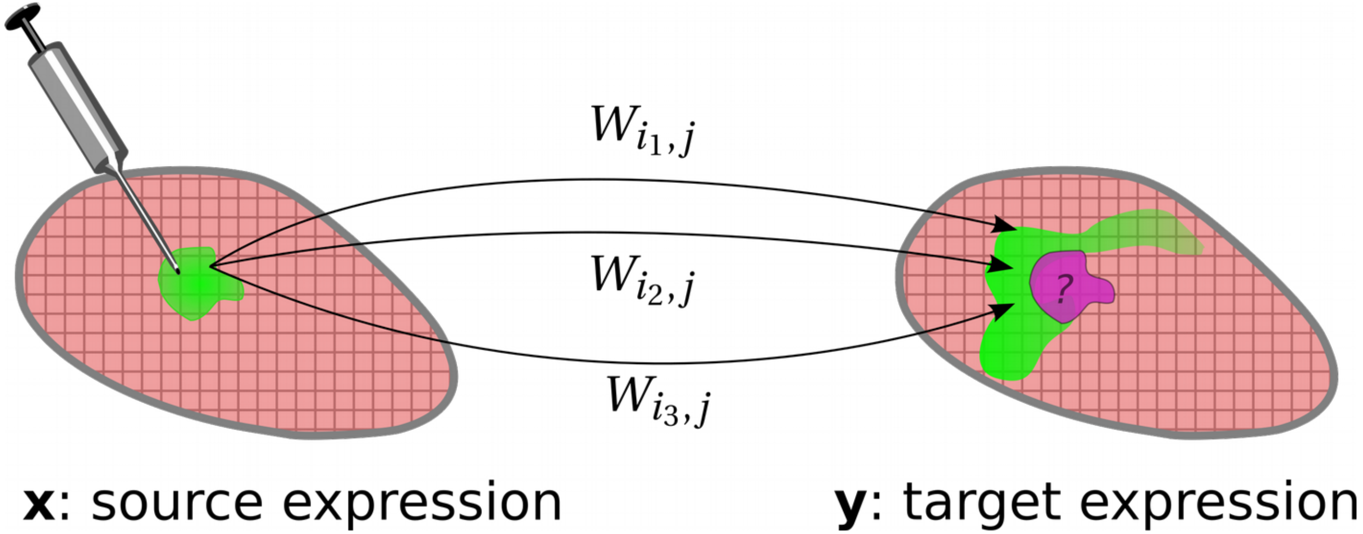


"Team science" & "Open science"

- Multi-million dollar cost
- 750 GB per brain
- 500 brains
- peta-scale after postprocess
- 34 person paper

Oh et al. (2014)

Encode the network as a matrix

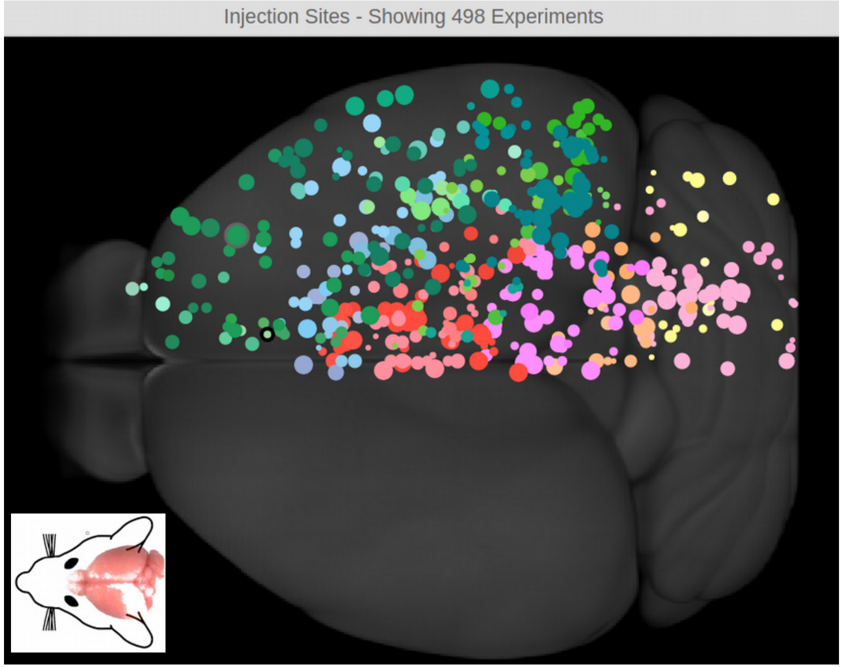


Goal

Find unknown weight matrix *W* so $\mathbf{y} \approx W\mathbf{x}$

Challenges for finding *W*:

1) Injection sites do not cover whole brain
   - severely underdetermined
2) Projection strength unknown at injection site
   - missing data
3) Matrix is huge
   - 5×10^5 by 2×10^5 matrix



Matrix regression model for connectome

- Find *W* **nonnegative** that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Goodness of fit Roughness penalty

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Unknown weight matrix

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\underbrace{\|P(W\overset{\uparrow}{X} - Y)\|^2}_{} + \lambda \|L(W)\|^2$$

Injection data

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\left\| P(WX - Y) \right\|^2 + \lambda \left\| L(W) \right\|^2$$

Projection data

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Mask out holes in data, just like **matrix completion**

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Controls strength of smoothing

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Computes roughness of *W*

Tikhonov regularization using
the Laplace operator

Matrix regression model for connectome

- Find *W* **nonnegative** that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

Goodness of fit,
ignore missing data

Roughness penalty
(regularization/prior)

Matrix regression model for connectome

- Find *W* nonnegative that minimizes the expression

$$\|P(WX - Y)\|^2 + \lambda \|L(W)\|^2$$

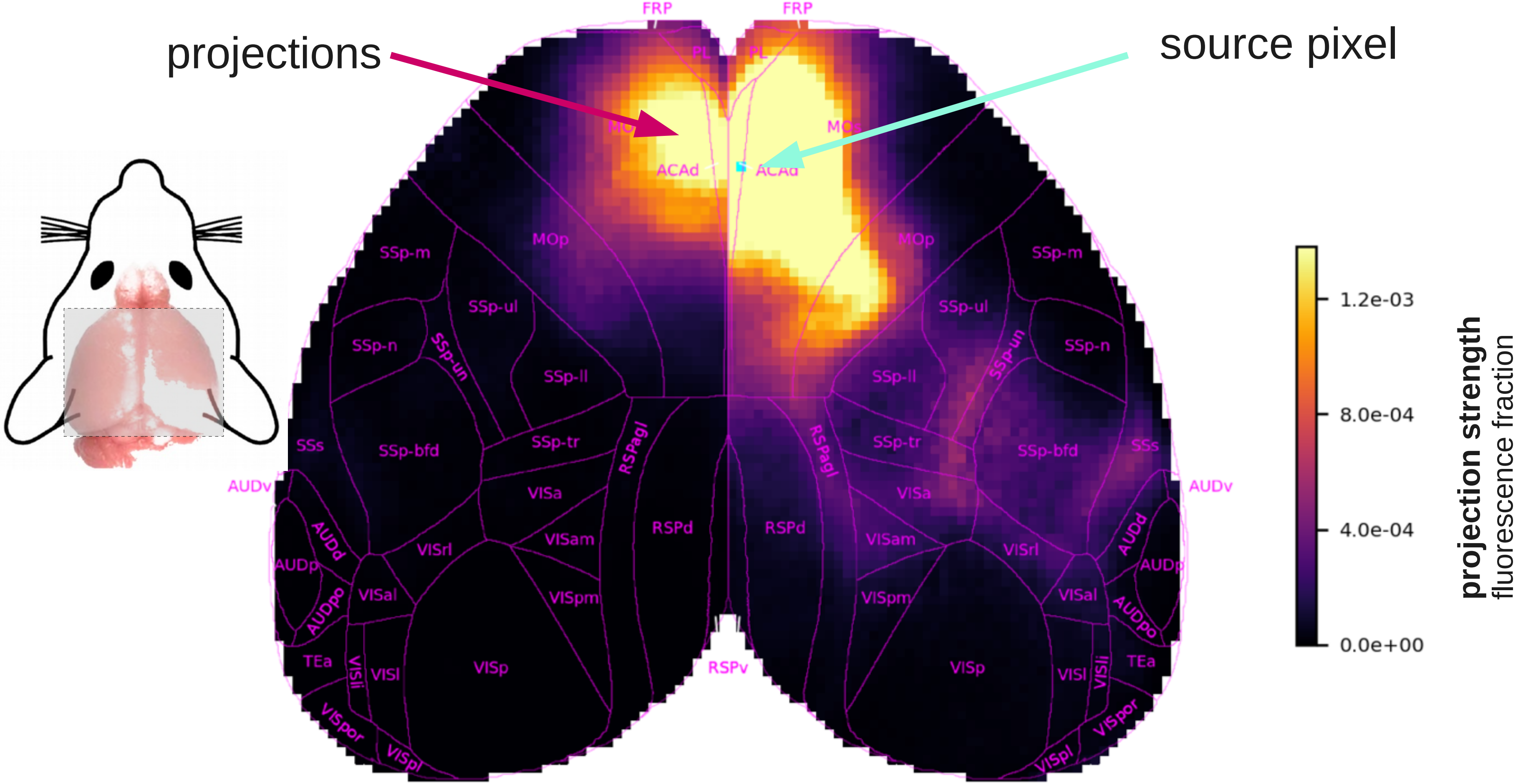
Problem is convex:

- **unique global solution** and **standard methods to find it**
- find λ and evaluate model by cross-validation

Harris, Mihalas, Shea-Brown. NeurIPS. 2016.

*****Actually, enforcing low-rank destroys convexity and makes it harder to solve.
This is an area of active research: Kürschner, Dolgov, Harris, Benner. In revisions.

The network we find



Knox, Harris, Graddis, et al. Network Neuroscience. 2019.

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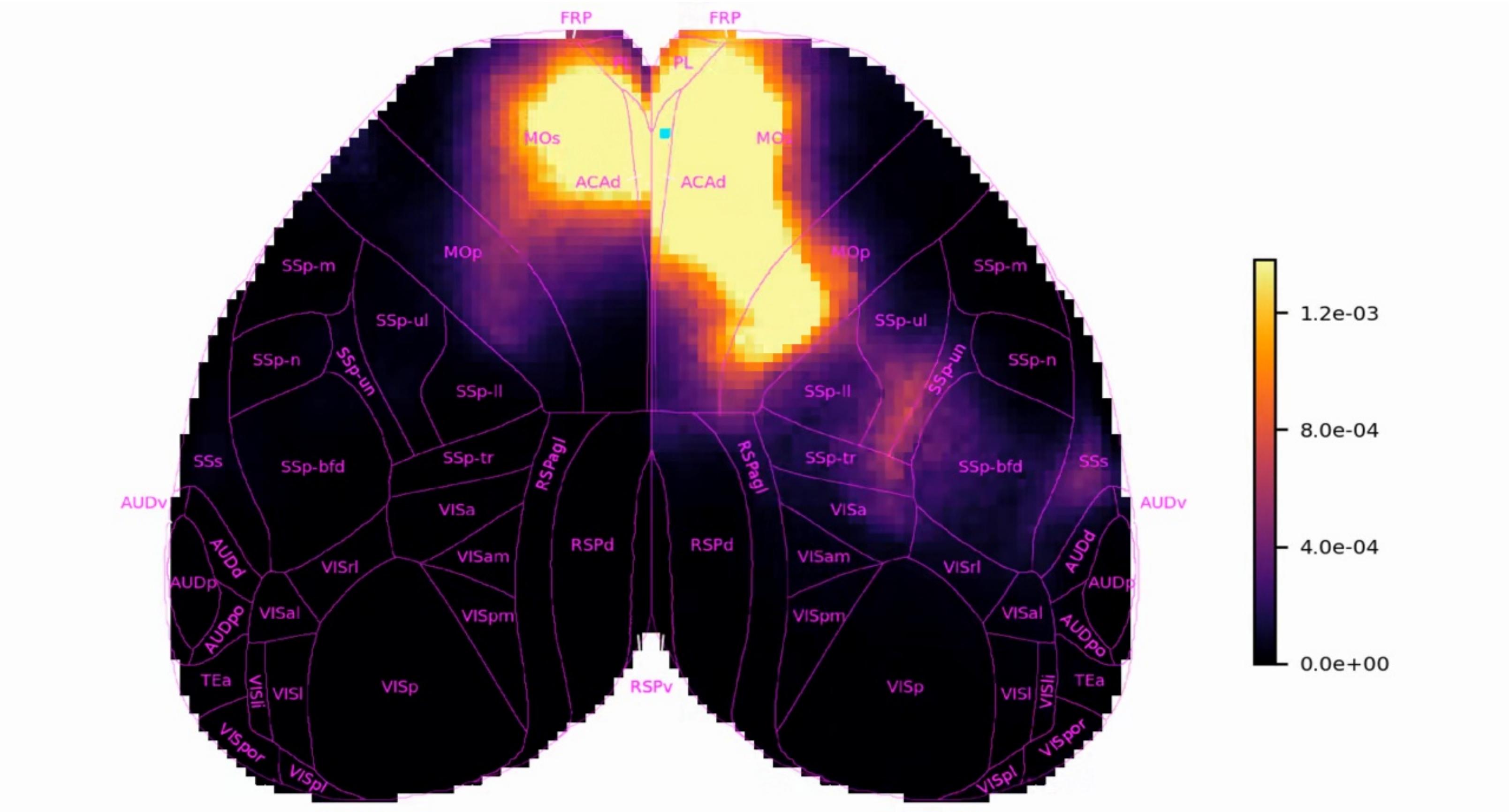

Knox, Harris, Graddis, et al. Network Neuroscience. 2019.

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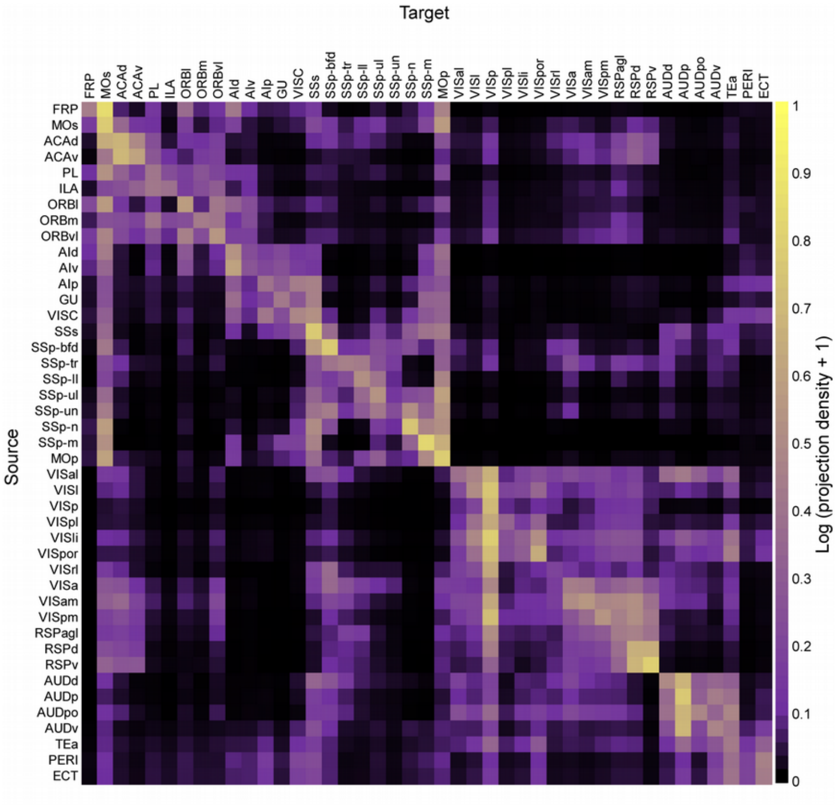
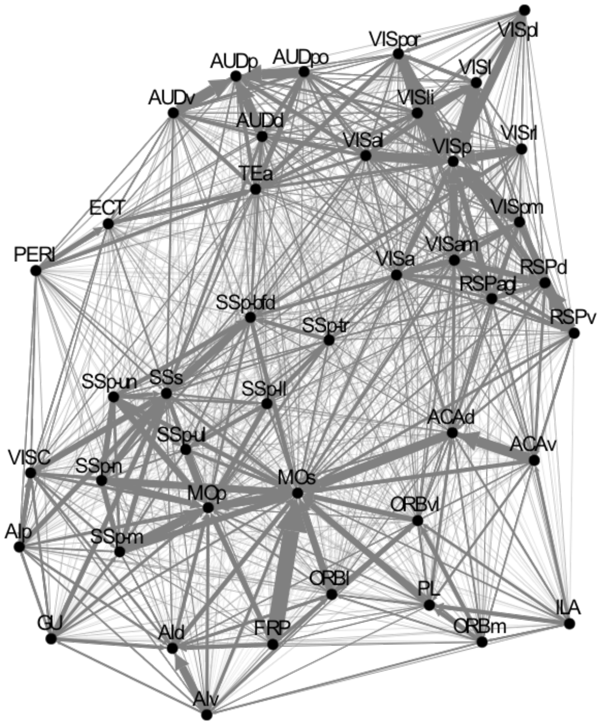
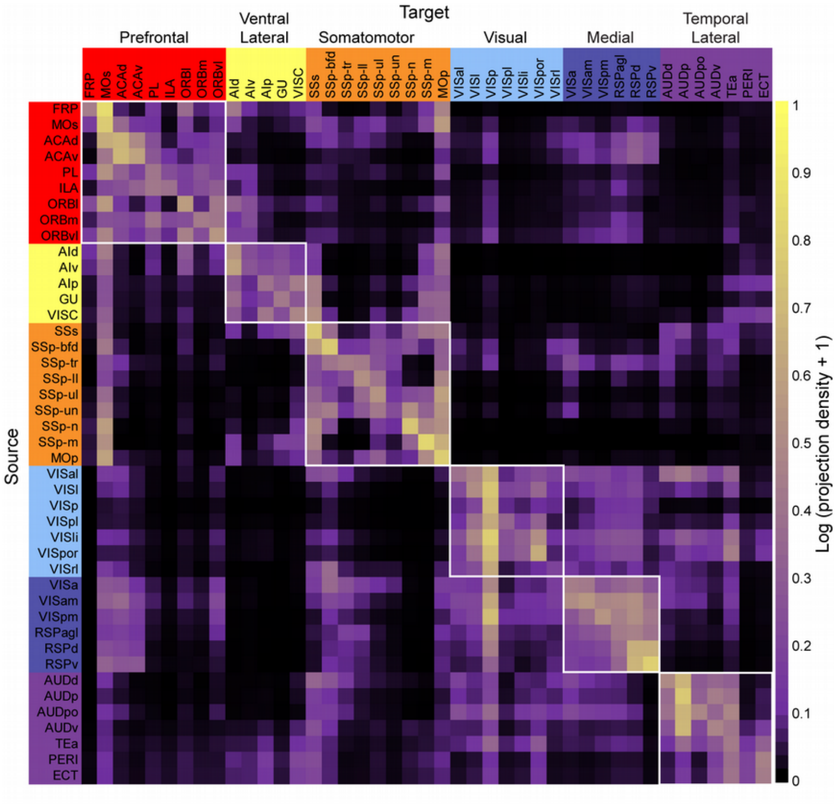
Our spatial network enables new science

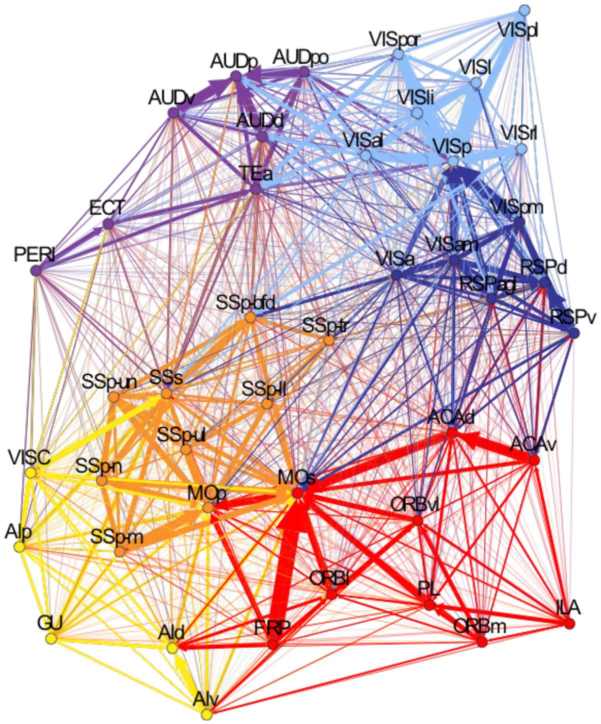


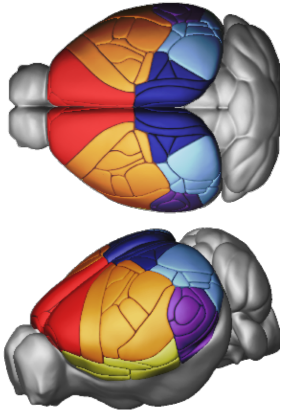


Harris JA, Mihalas S, Hirokawa KE, Whitesell JD, Knox J, Bernard A, Bohn P, Caldejon S, Casal L, Cho A, Feng D, Gaudreault N, Gerfen C, Graddis N, Groblewski PA, Henry A, Ho A, Howard R, Kuan L, Lecoq J, Luviano J, McConoghy S, Mortrud M, Naeemi M, Ng L, Oh SW, Oullette B, Sorensen S, Wakeman W, Wang Q, Williford A, Phillips J, Jones A, Koch C, Zeng H. (2018) bioRxiv [preprint] 292961

Our spatial network enables new science







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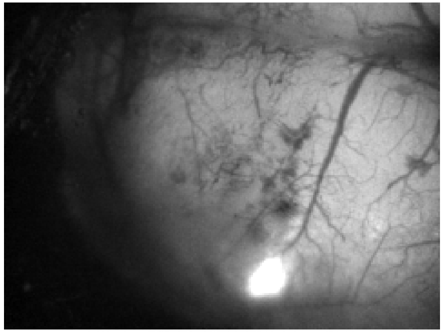
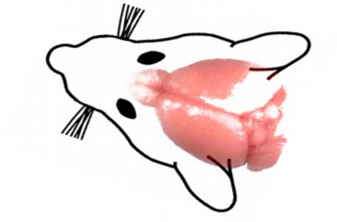
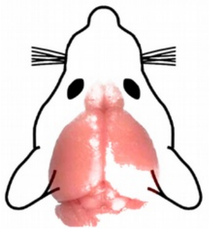
Next steps: comparing activity

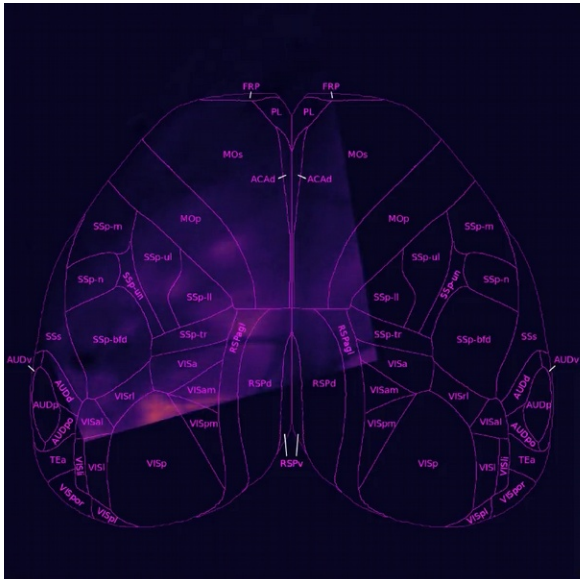
Image captured
by lab camera







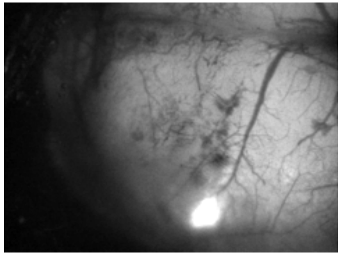
transform to
connectivity
coordinates



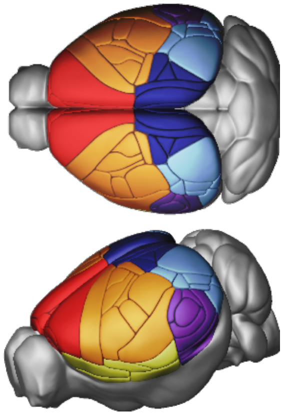
Yuchen Wang
CSE & neurosci senior

Bing Brunton
Bill Moody
Dennis Tabuena

Conclusions: spatial connectivity enables

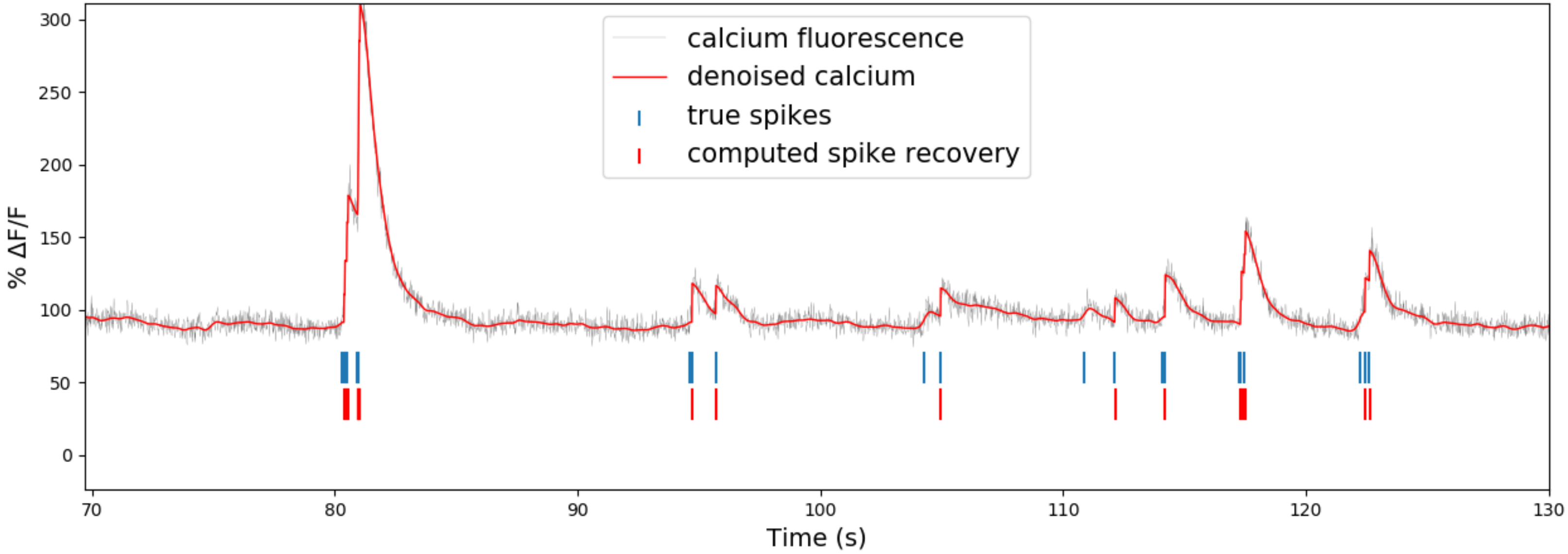


- **Comparisons with brain-wide activity data**
- **Network analyses**
- Unknown maps between regions?
- Connectivity-defined regions
- Extend to cell-type specific networks



Related data analysis problems

Spike deconvolution from Ca^{2+} imaging

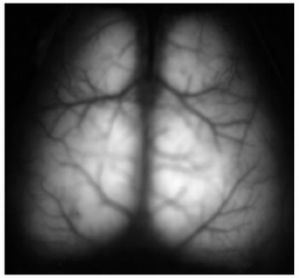


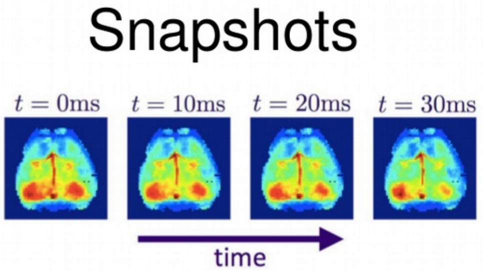
Nathan Lee
AMATH PhD student

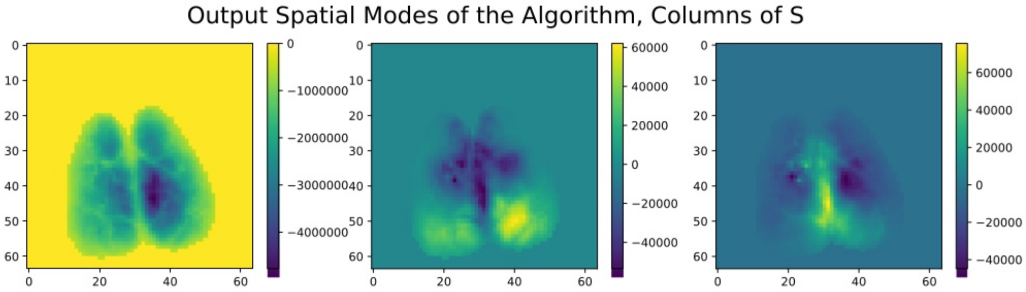
Sasha Aravkin (Applied Math)
Daniela Witten (Statistics)

More with Bing Brunton, Rajesh Rao, & students

Wide-field Ca^{2+} imaging models



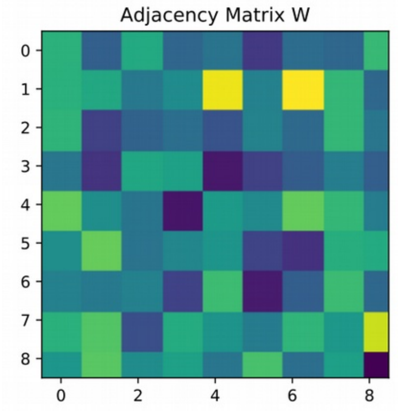




$$\min_{S,T,r \text{ of rank } \nu; W} \|D - ST\|_F^2$$

$$s.t. \;\; T_t = \gamma T_{t-1} + r_t$$

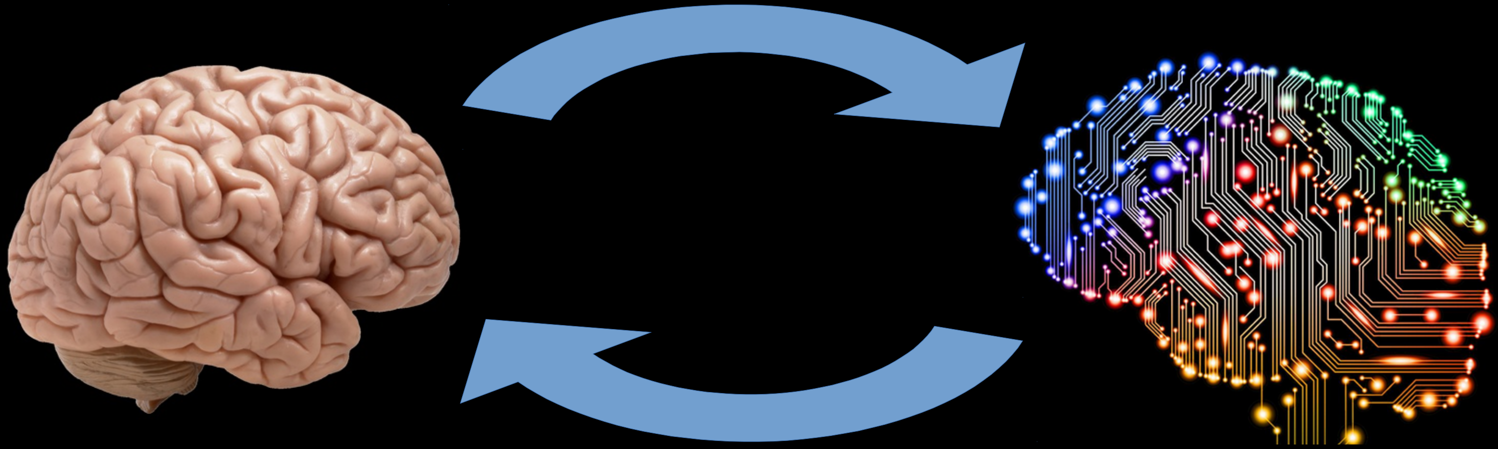
$$\dot{r}_t = -r_t + W f(r_t)$$



Roman Levin
(AMATH PhD student)

Merav Stern
Sasha Aravkin
Eric Shea-Brown

Thank you!



images: flickr/_DJ_, neurobanter.com

Acknowledgements

<u>Mentees:</u>

Joseph Knox
Allen Institute
now Facebook data science

Nile Graddis
Allen Institute
Technology team

Yuchen Wang
CSE & neurosci senior

Positions available in Bing Brunton's lab!

- Collaborators
  - Eric Shea-Brown (Applied Math)
  - Stefan Mihalas (Allen Institute)
  - Julie Harris (Allen Institute)
  - Bill Moody (Biology)
  - Dennis Tabuena (Bio student)
  - Bing Brunton (Biology)

Research Awards: Washington Research Foundation Postdoctoral Fellowship, NIH Big Data for Genomics & Neuroscience Training Grant, Boeing Fellowship

Other Funding: DARPA award FA8750-18-2-0259, NSF CNS award 1630178

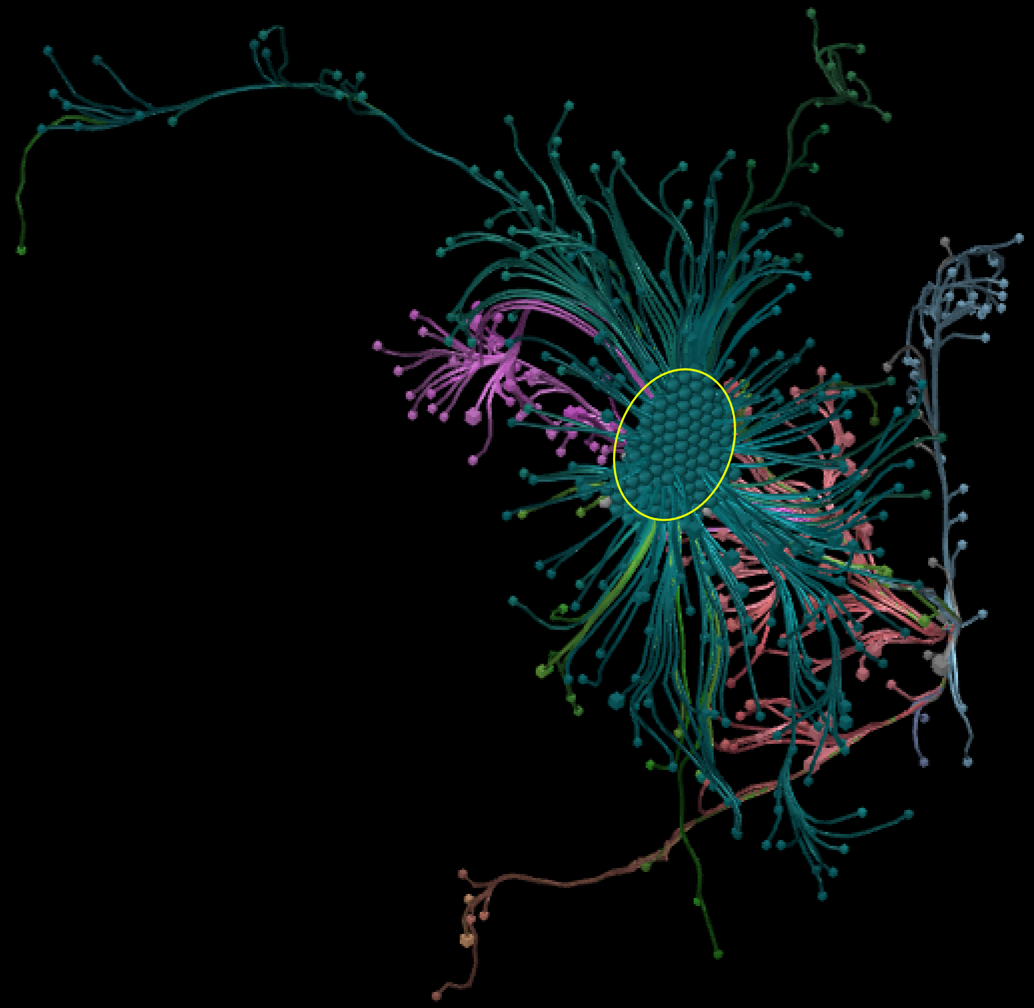
Exercise: spike deconvolution

- A short exercise in Jupyter
  - **github.com/kharris/amath50**
  - **`python 3 + jupyter + numpy/scipy`**
  - New package: **`sklearn`** (scikit-learn)

(Extra slides)

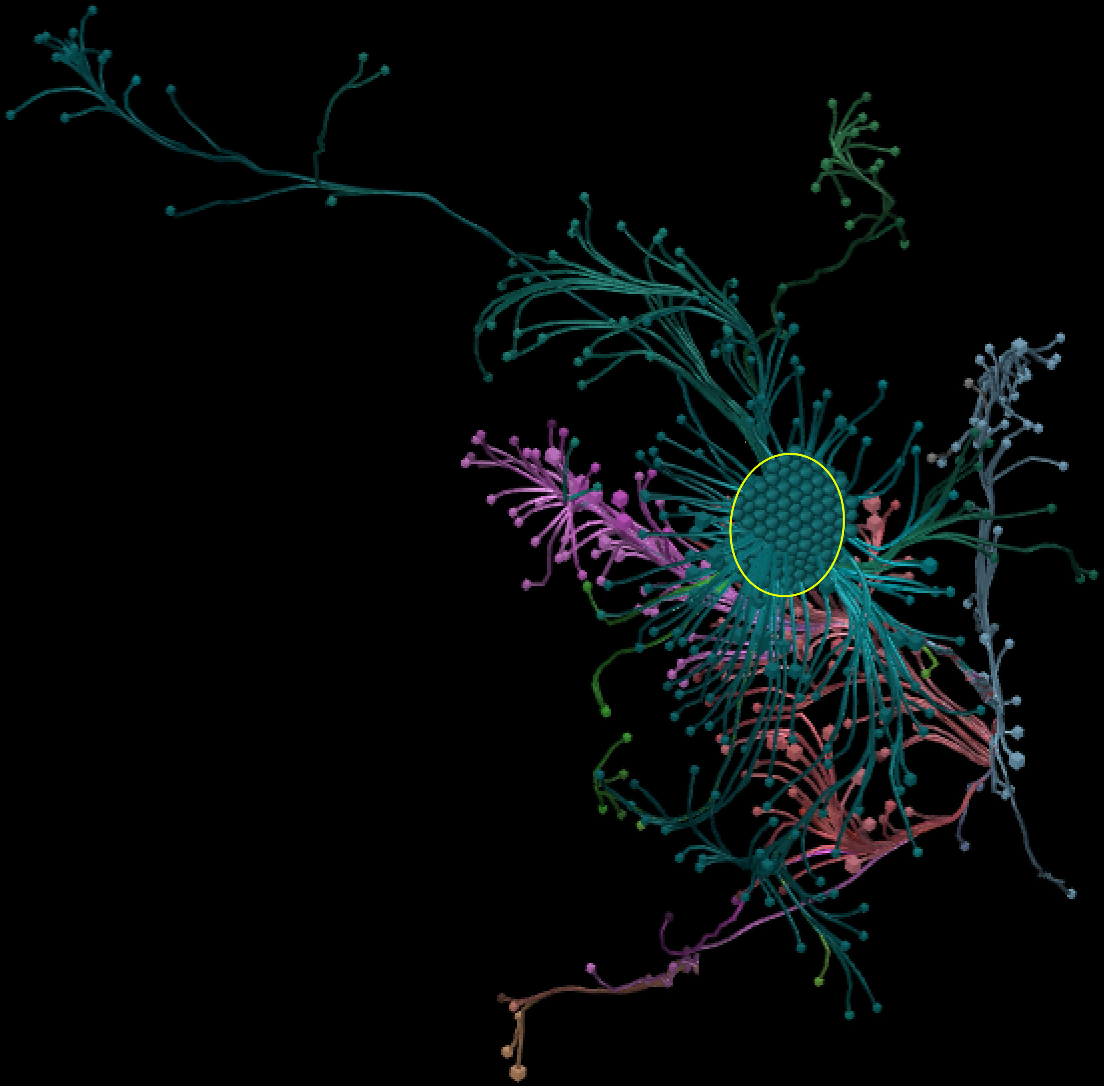
Is smoothing a good idea?

Injection 1
VISp



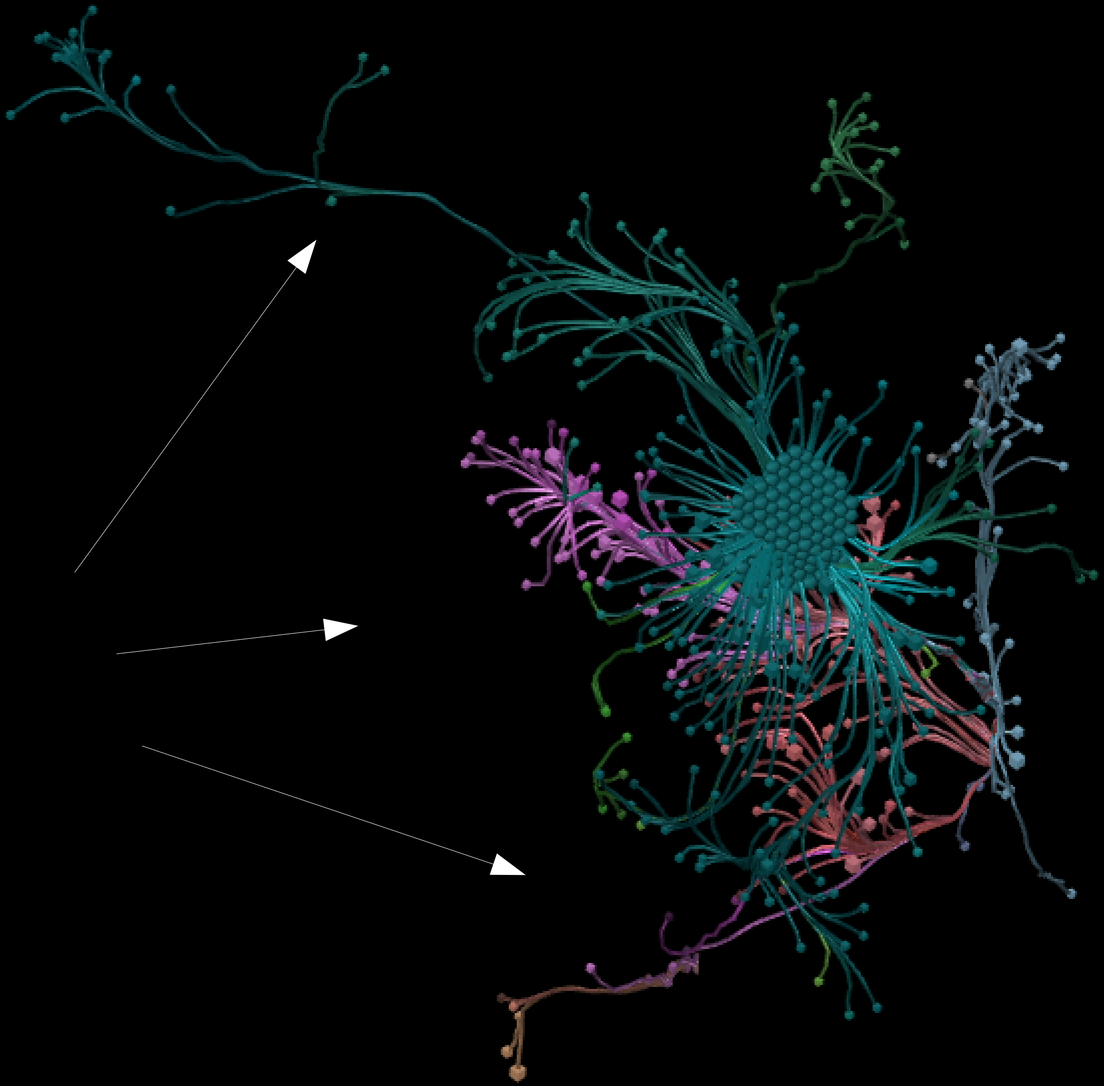
Images made with
Allen Brain Explorer

Injection 2
VISp

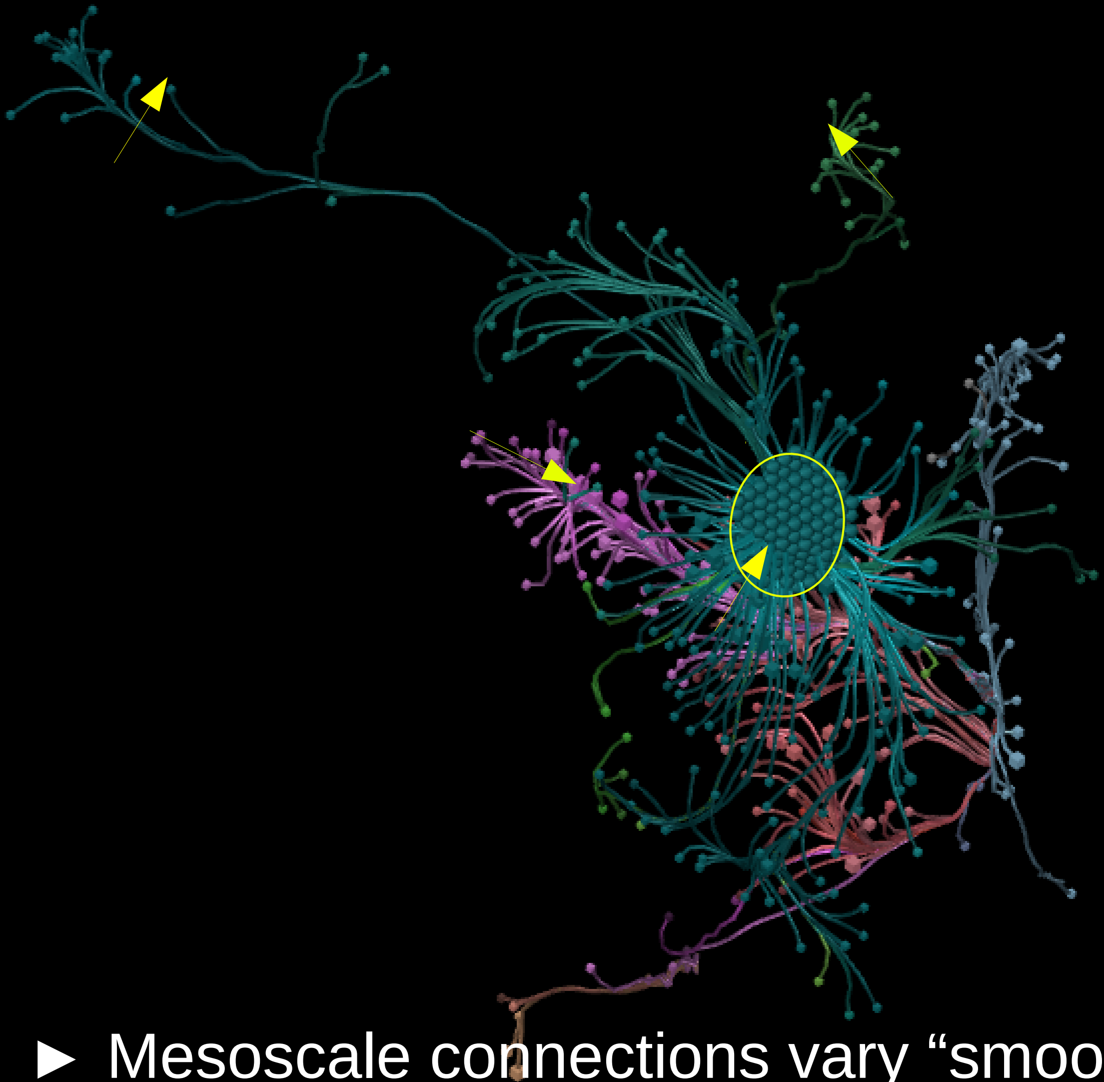


Injection 2
VISp

Same long-range clusters of projections (region specificity)



Injection 2
VISp

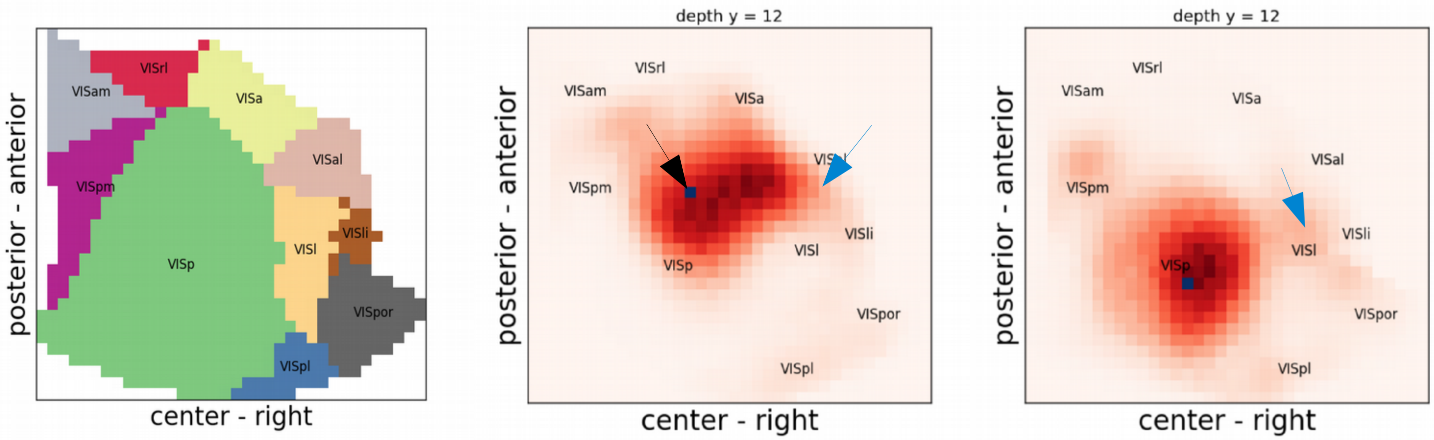


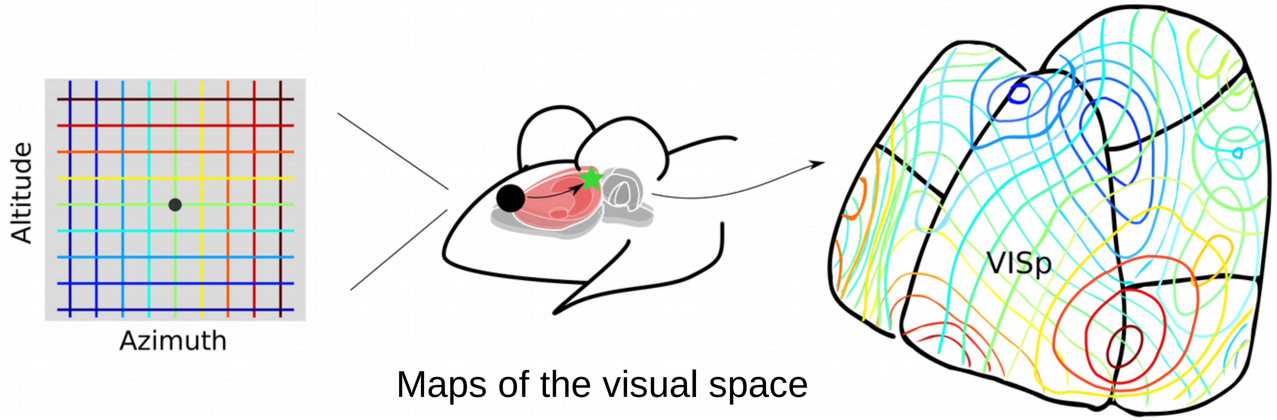
Long-range connections have shifted centers of mass

► Mesoscale connections vary "smoothly"

What do you mean by “maps between areas?”

In visual cortex, we see hints of retinotopy





Maps of the visual space