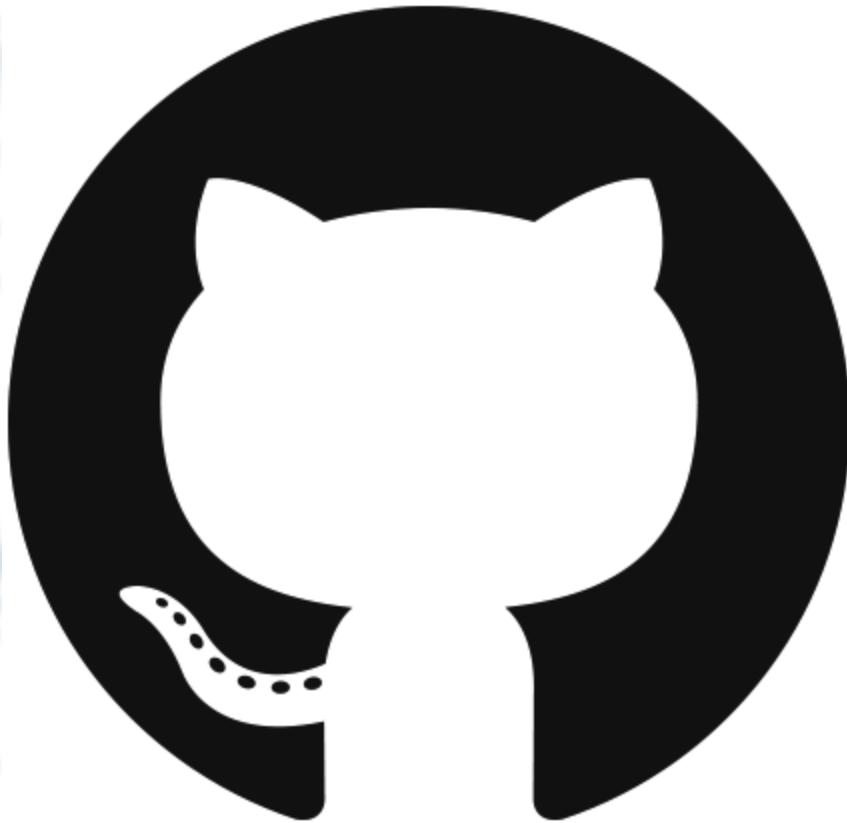


bpedigo@jhu.edu

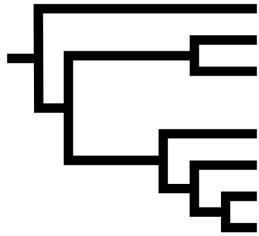


[@bdpedigo \(Github\)](#)

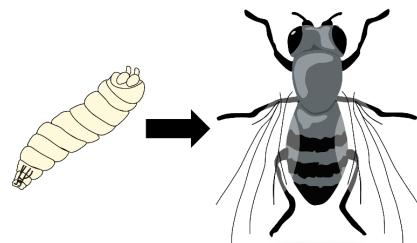


Connectomics is useful...

Many of the stated goals of connectomics rely on linking connectome to other domains...



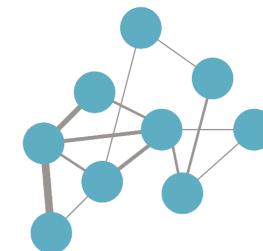
Evolution



Development



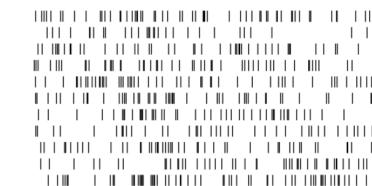
Genome



Connectome



Behavior



Activity

Connectome ↔ memory

...the acquisition of wiring diagrams across multiple individuals will yield insights into
how experiences shape neural connections.

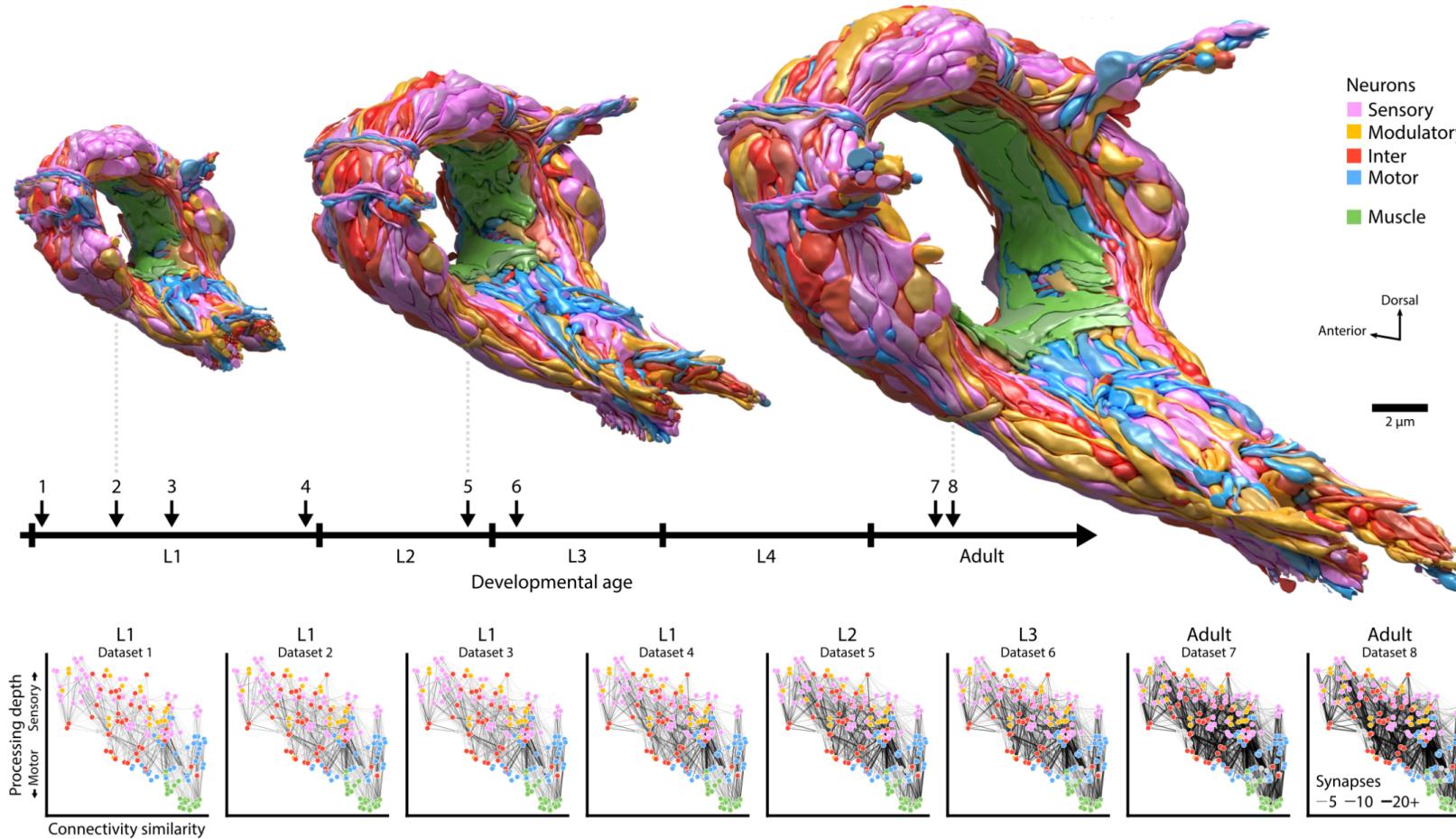
Emphasis added

Connectome ↔ evolution

Comparative connectomics of [...] species across the phylogenetic tree can infer the archetypal neural architecture of each bauplan and identify any circuits that possibly converged onto a shared and potentially optimal, structure.

Emphasis added

Connectomes across development

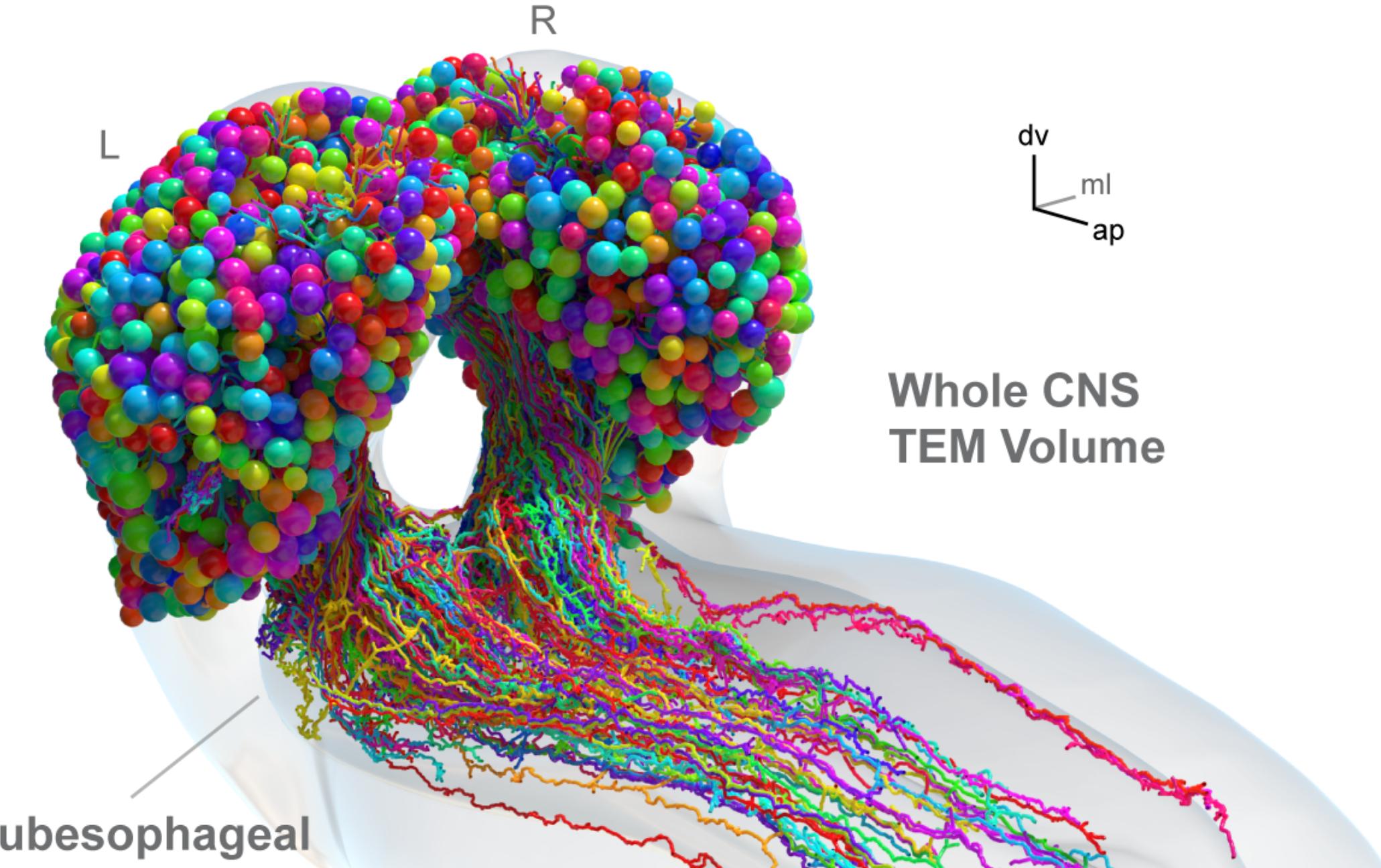


**But it is methodologically hard to compare
connectomes! this is a test**

Outline for today

- Describe a dataset that I'll use for these examples throughout
- Show how connectome comparison can be framed as network hypothesis testing
- Show how we can use automated tools for predicting the correspondence of neurons across datasets
- Mention some extensions to use/combine/extend these tools that we're working on

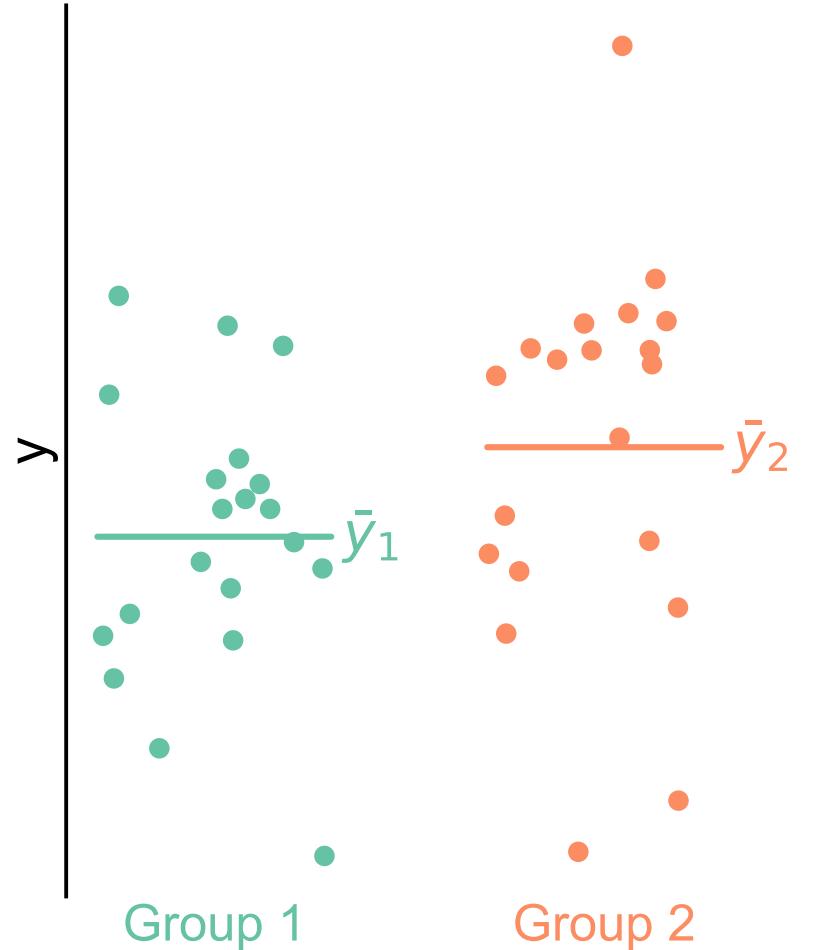
Brain Hemispheres





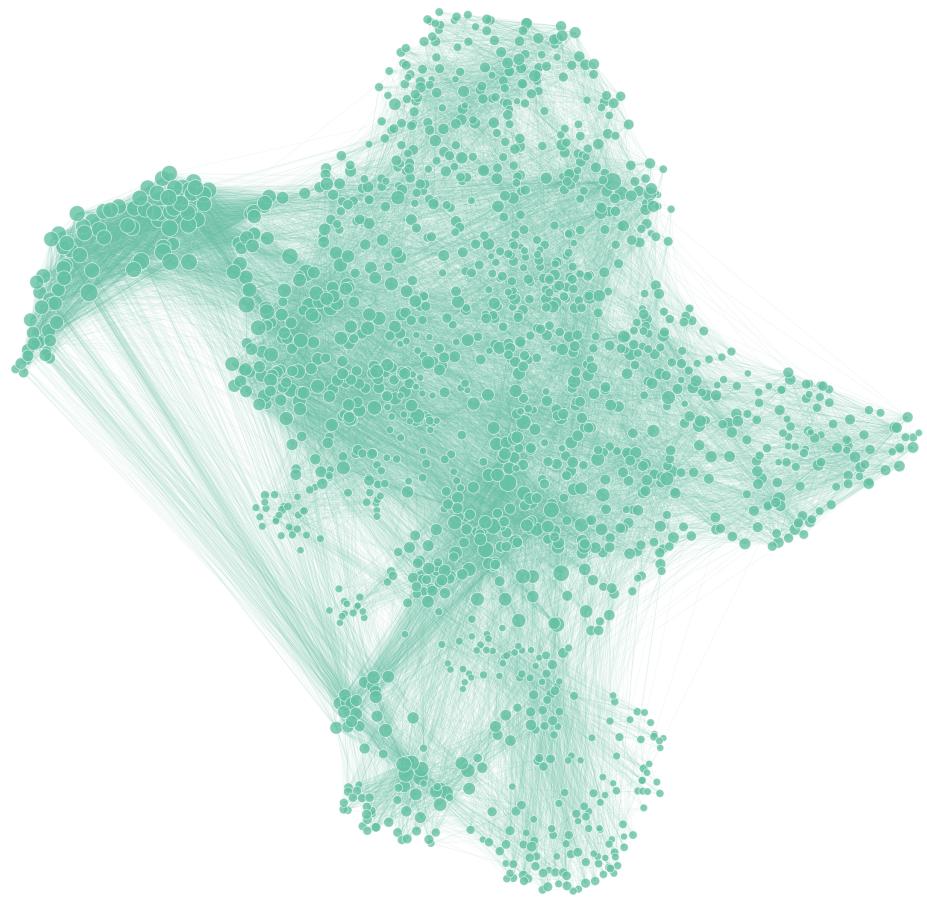
**Are the ` left `
and ` right `
sides of this connectome `<p> </p>` different?**

<div class="columns"> <div>

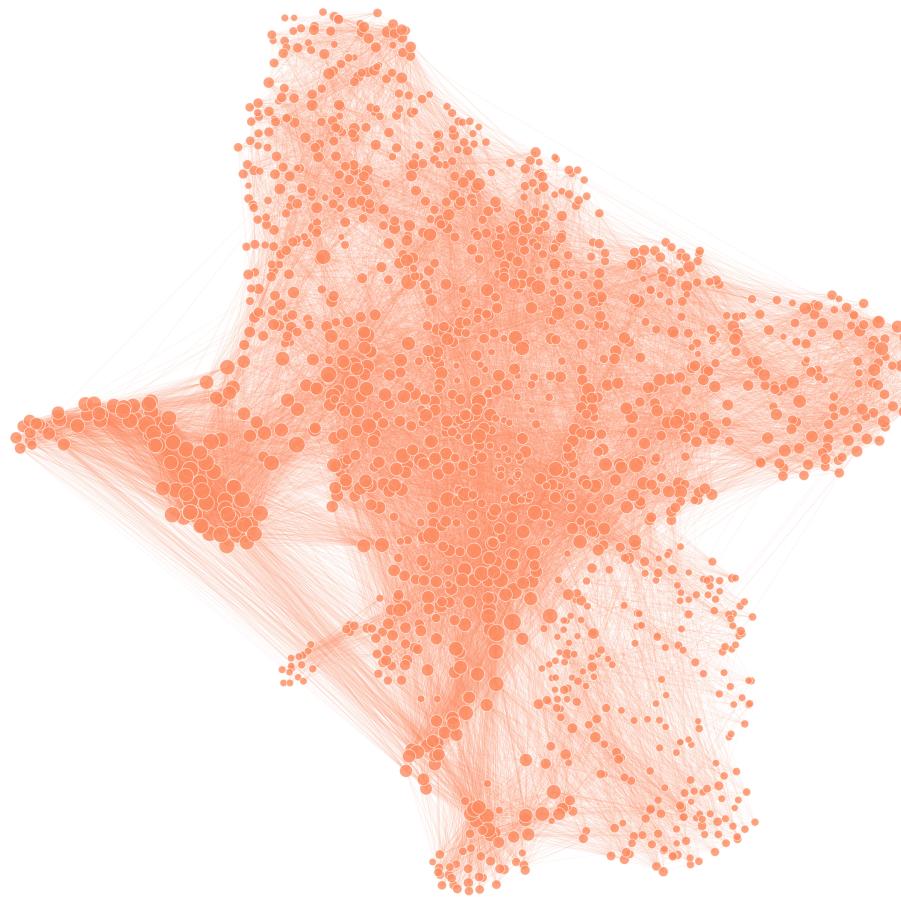


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- Known as two-sample testing
- $Y^{(1)} \sim F^{(1)}$, $Y^{(2)} \sim F^{(2)}$
- $H_0 : F^{(1)} = F^{(2)}$



Left



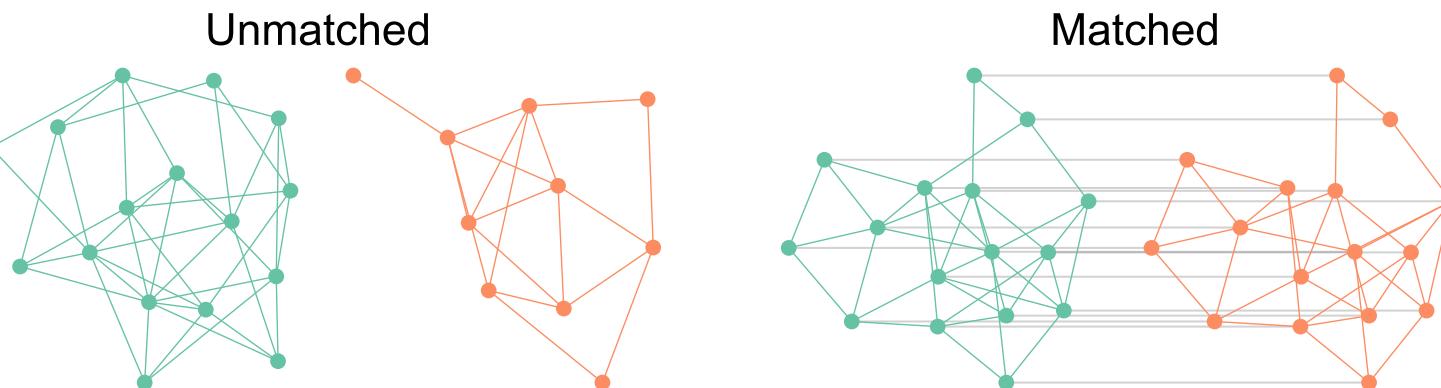
Right

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- Want a two-network-sample test!
- $A^{(L)} \sim F^{(L)}$, $A^{(R)} \sim F^{(R)}$

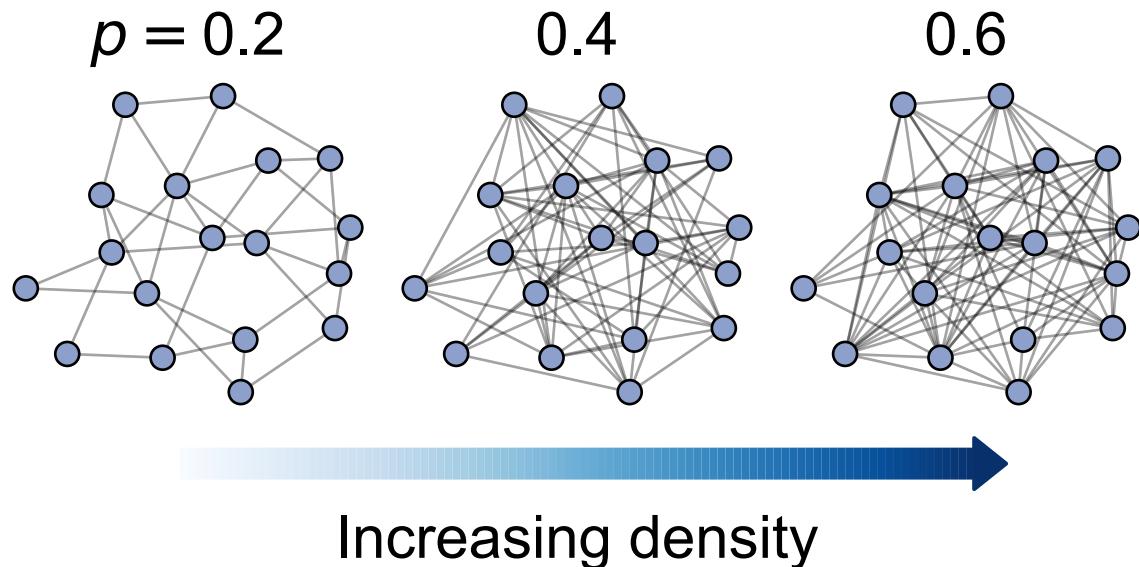
Assumptions

- We know the direction of synapses, so network is *directed*.
- For simplicity (for now), consider networks to be *unweighted*.
- For simplicity (for now), consider the ` left → left ` and ` right → right ` (*ipsilateral*) connections only.
- Not going to assume any nodes are matched



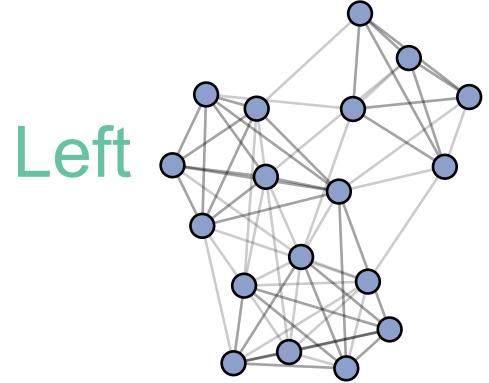
Erdos-Renyi model

- All edges are independent
- All edges generated with the same probability, p



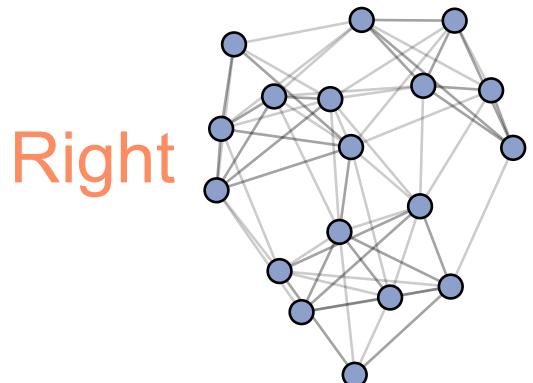
Density-based testing

Compute global connection density



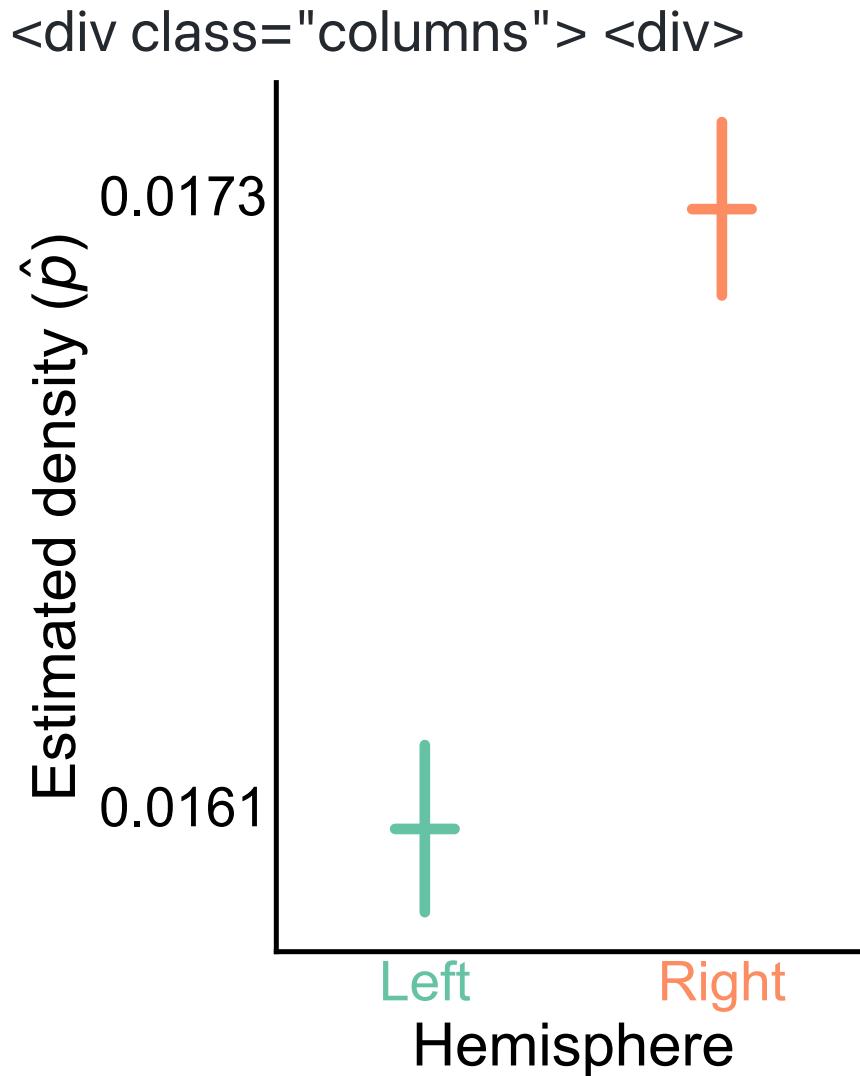
Compare ER models

$$p = \frac{\# \text{ edges}}{\# \text{ potential edges}}$$



$$\begin{aligned} H_0: p^{(L)} &= p^{(R)} \\ H_A: p^{(L)} &\neq p^{(R)} \end{aligned}$$

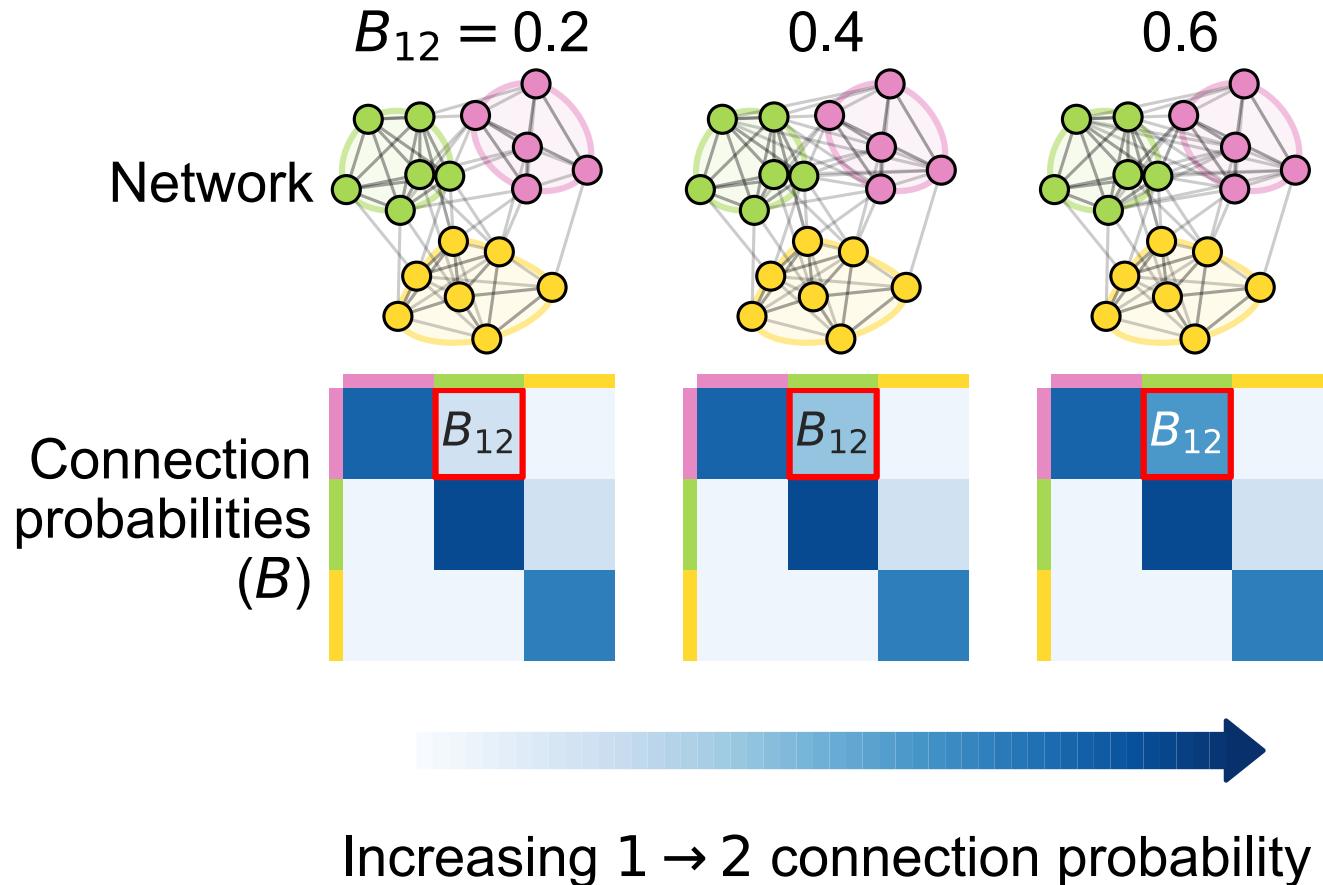
We detect a difference in density

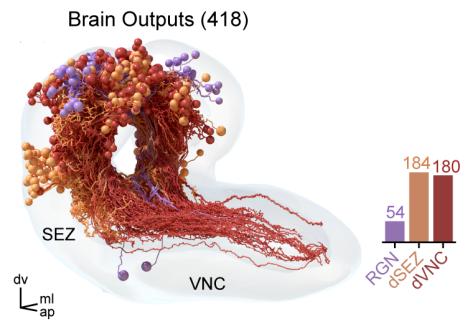
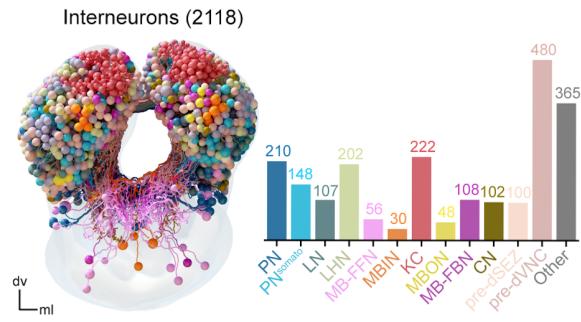
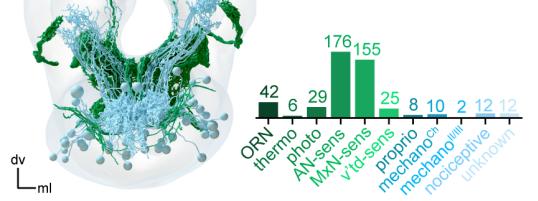


- p-value $< 10^{-22}$

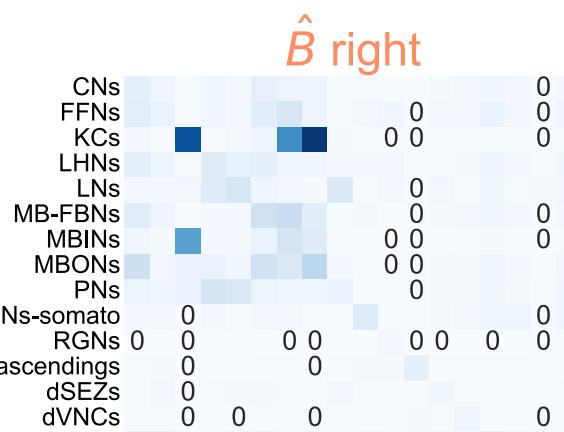
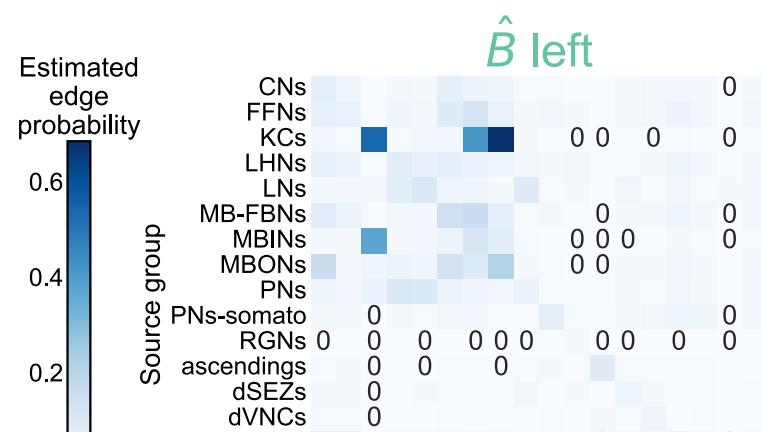
Stochastic block model

- Edge probabilities are a function of a neuron's group



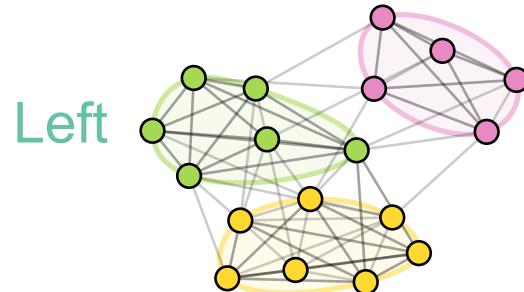


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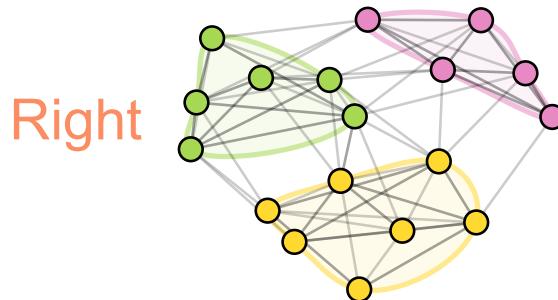


Group-based testing

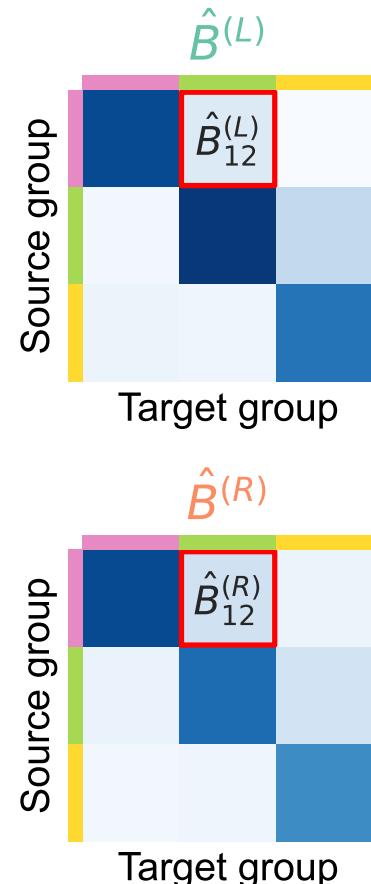
Group neurons



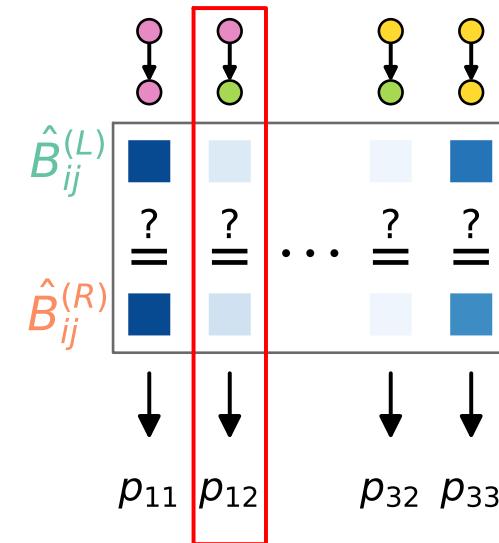
Right



Estimate group
connection probabilities

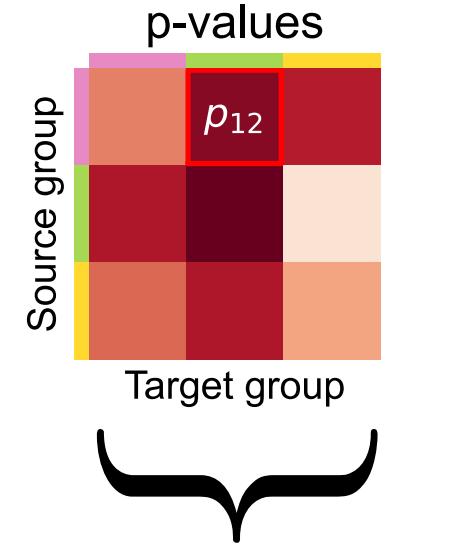


Compare probabilities,
compute p-values



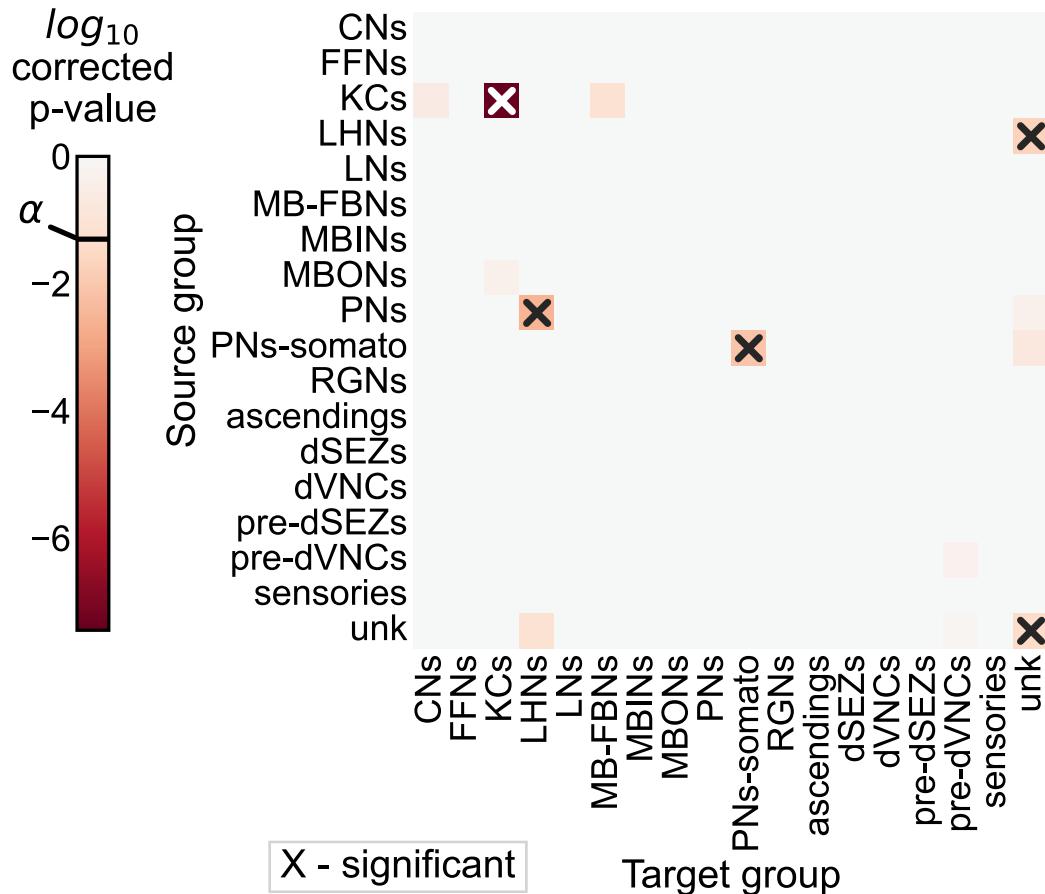
$$\begin{aligned} H_0: B_{ij}^{(L)} &= B_{ij}^{(R)} \\ H_A: B_{ij}^{(L)} &\neq B_{ij}^{(R)} \end{aligned}$$

Combine p-values
for overall test



$$\begin{aligned} H_0: B^{(L)} &= B^{(R)} \\ H_A: B^{(L)} &\neq B^{(R)} \end{aligned}$$

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X - significant

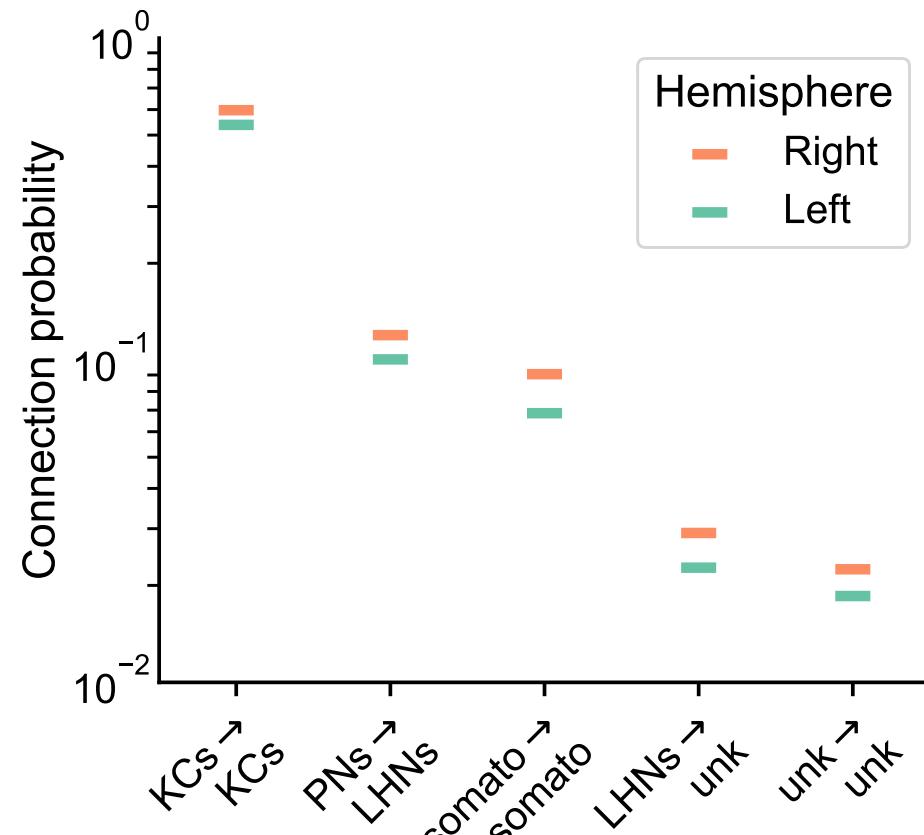
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- After multiple comparison, find 5 group-to-group connections which are significantly different
- Combine (uncorrected) p-values (like a meta-analysis), leads to p-value for overall

- Already saw that even the overall densities were different
- For all significant comparisons, probabilities on the right hemisphere were higher
- Maybe the right is just a "scaled up" version of the left?
 - $H_0 : B^{(L)} = cB^{(R)}$

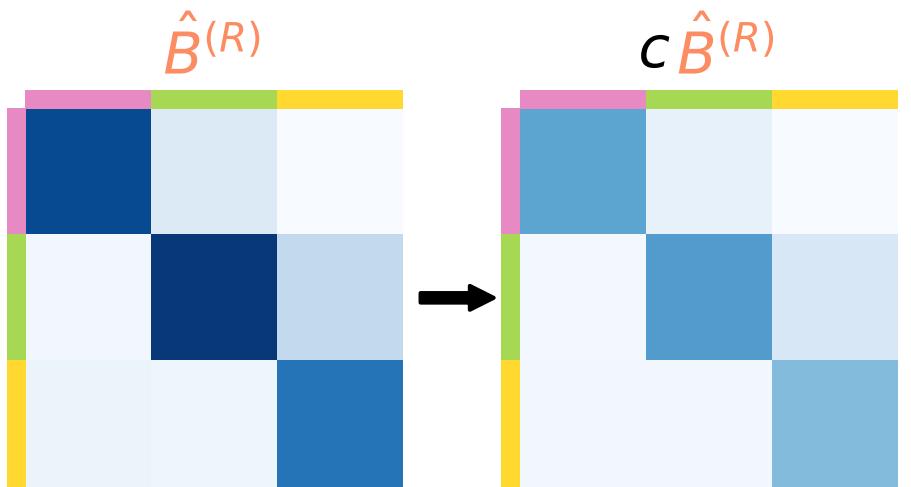
where c is a density-adjusting constant, $\frac{p^{(L)}}{p^{(R)}}$

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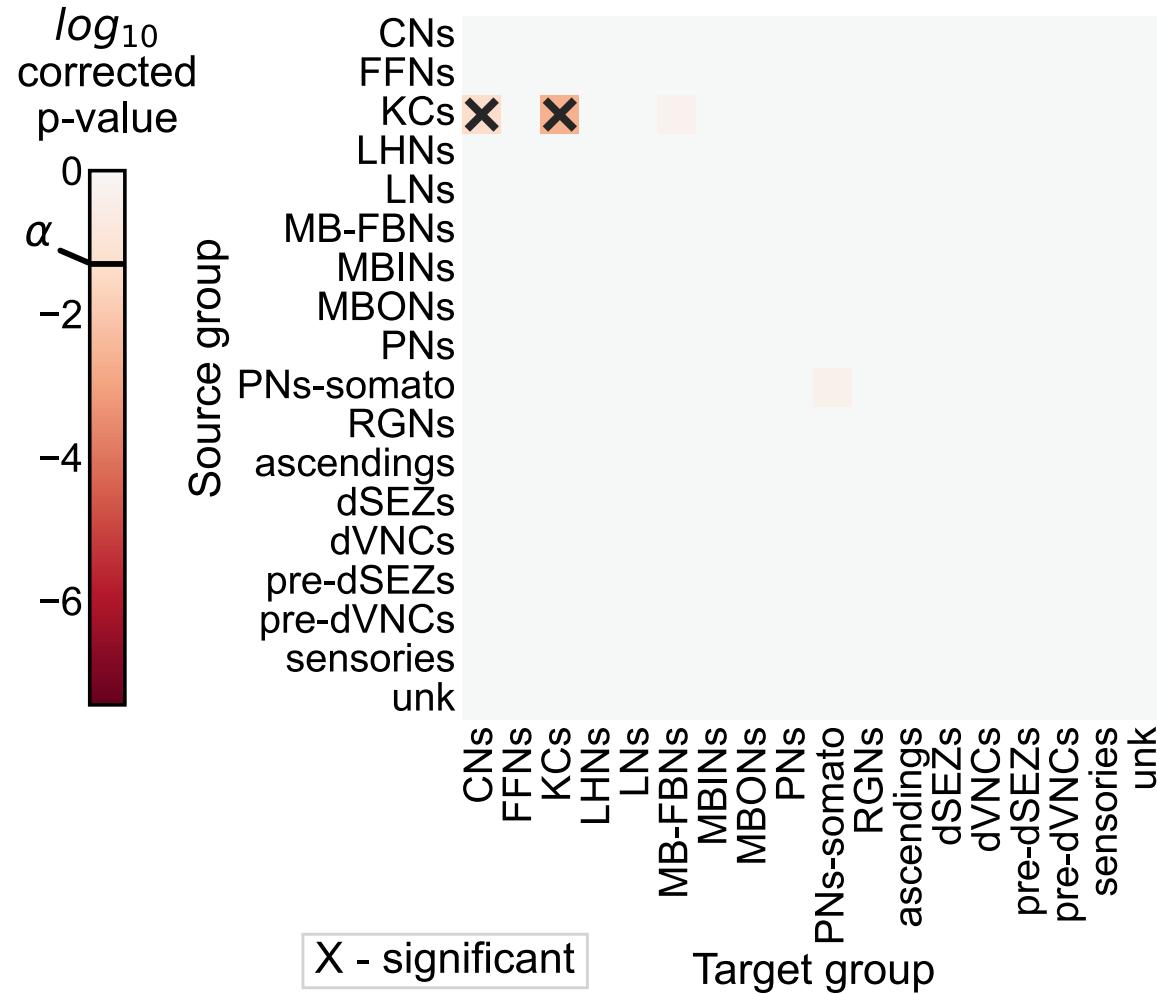
Adjusting for a difference in density

Scale connection probabilities
to match densities



$$\begin{aligned} H_0: B^{(L)} &= cB^{(R)} \\ H_A: B^{(L)} &\neq cB^{(R)} \end{aligned}$$

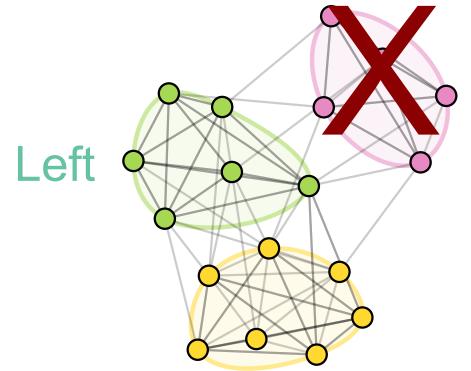
Remaining differences are isolated to KCs



we detect remaining differences...

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Remove Kenyon cells



Re-run all tests

Density

$$\begin{aligned} H_0: p^{(L)} &= p^{(R)} \\ H_A: p^{(L)} &\neq p^{(R)} \end{aligned}$$

Group connection

$$\begin{aligned} H_0: B^{(L)} &= B^{(R)} \\ H_A: B^{(L)} &\neq B^{(R)} \end{aligned}$$



Density-adjusted group connection

$$\begin{aligned} H_0: B^{(L)} &= cB^{(R)} \\ H_A: B^{(L)} &\neq cB^{(R)} \end{aligned}$$

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- ER test: $p < 10^{-26}$
- SBM test: $p \approx 0.003$

To sum up...

Model	H_0 (vs. $H_A \neq$)	KCs	p-value	Interpretation
ER	$p^{(L)} = p^{(R)}$	+	$< 10^{-23}$	Reject densities the same
SBM	$B^{(L)} = B^{(R)}$	+	$< 10^{-7}$	Reject group connection probabilities the same
aSBM	$B^{(L)} = cB^{(R)}$	+	≈ 0.002	Reject above even after accounting for density
ER	$p^{(L)} = p^{(R)}$	-	$< 10^{-26}$	Reject densities the same (w/o KCs)
SBM	$B^{(L)} = B^{(R)}$	-	≈ 0.003	Reject group connection probabilities the same (w/o KCs)
aSBM	$B^{(L)} = cB^{(R)}$	-	≈ 0.43	Don't reject above after density adjustment (w/o KCs)

Matching neurons

Extensions and ongoing work

matched versions of our tests

- we think greater power, basically

testing for a significant matching

- evaluate stereotypy at a single neuron level, basically

the value of pairs - looking at models

- show the hierarchical clustering
- SBM cross validation curve

Summary

How to use these tools?

graspologic

bilateral repo

bgm

get in touch!



Eric Bridgeford

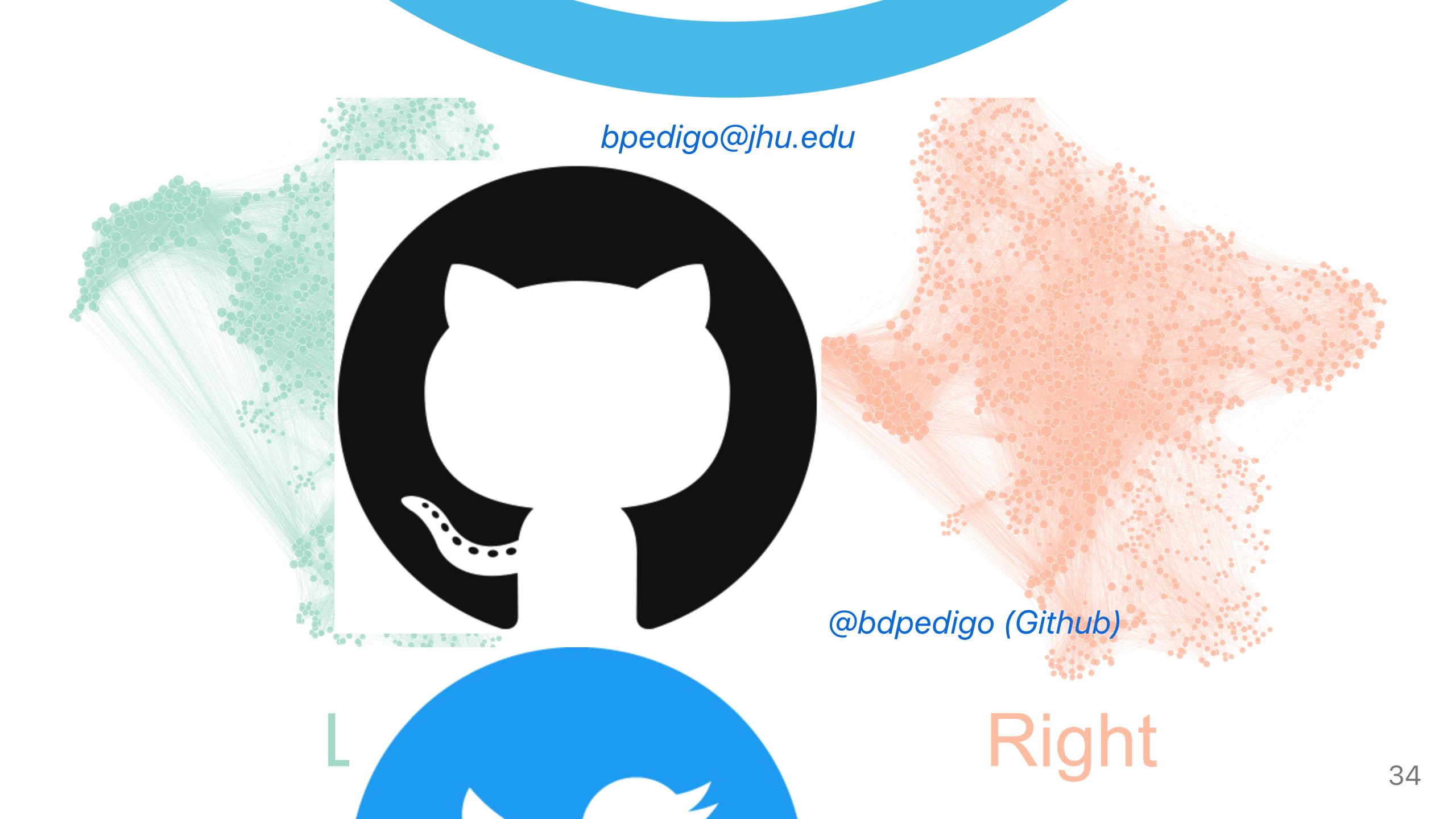
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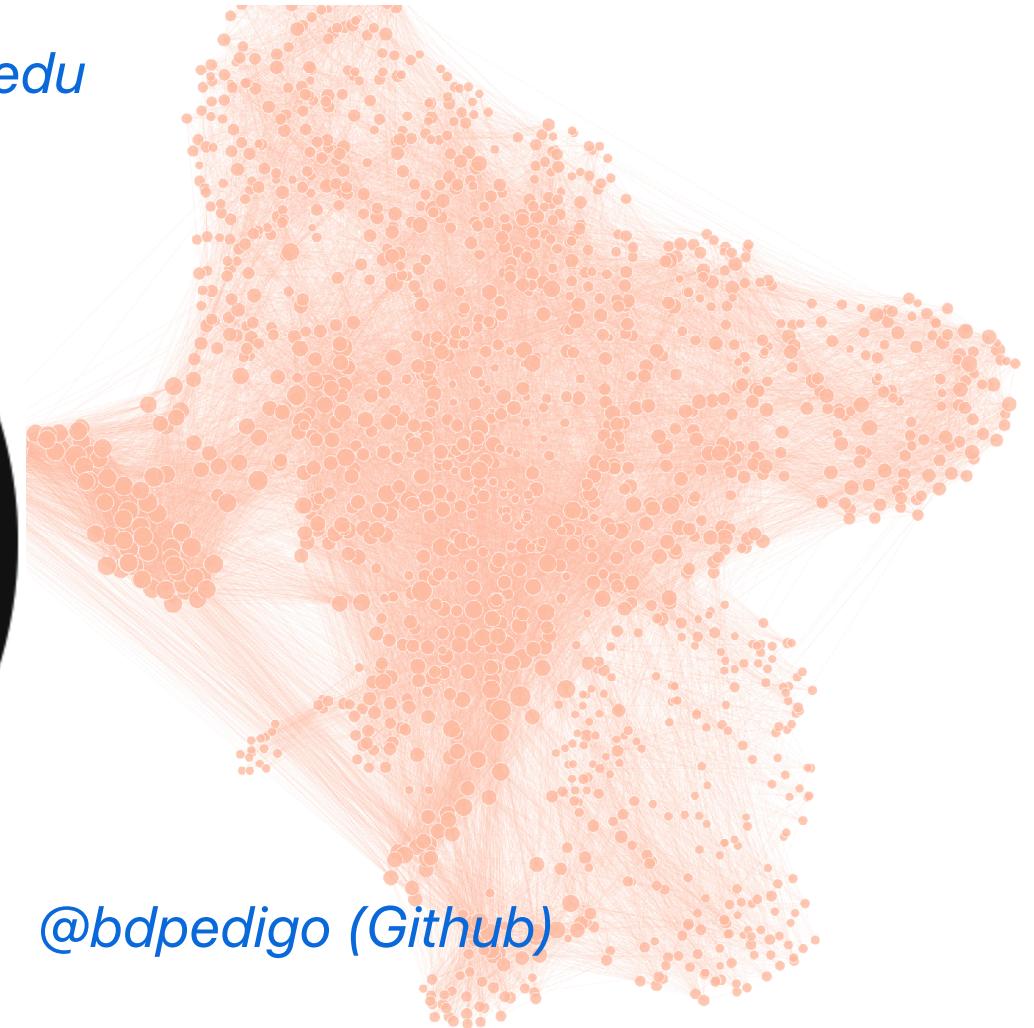
Ali
Saad-Eldin

</div> <div>





bpedigo@jhu.edu



Right