

# Is the maggot brain symmetric? A statistical analysis of bilateral symmetry in an insect connectome

Benjamin D. Pedigo

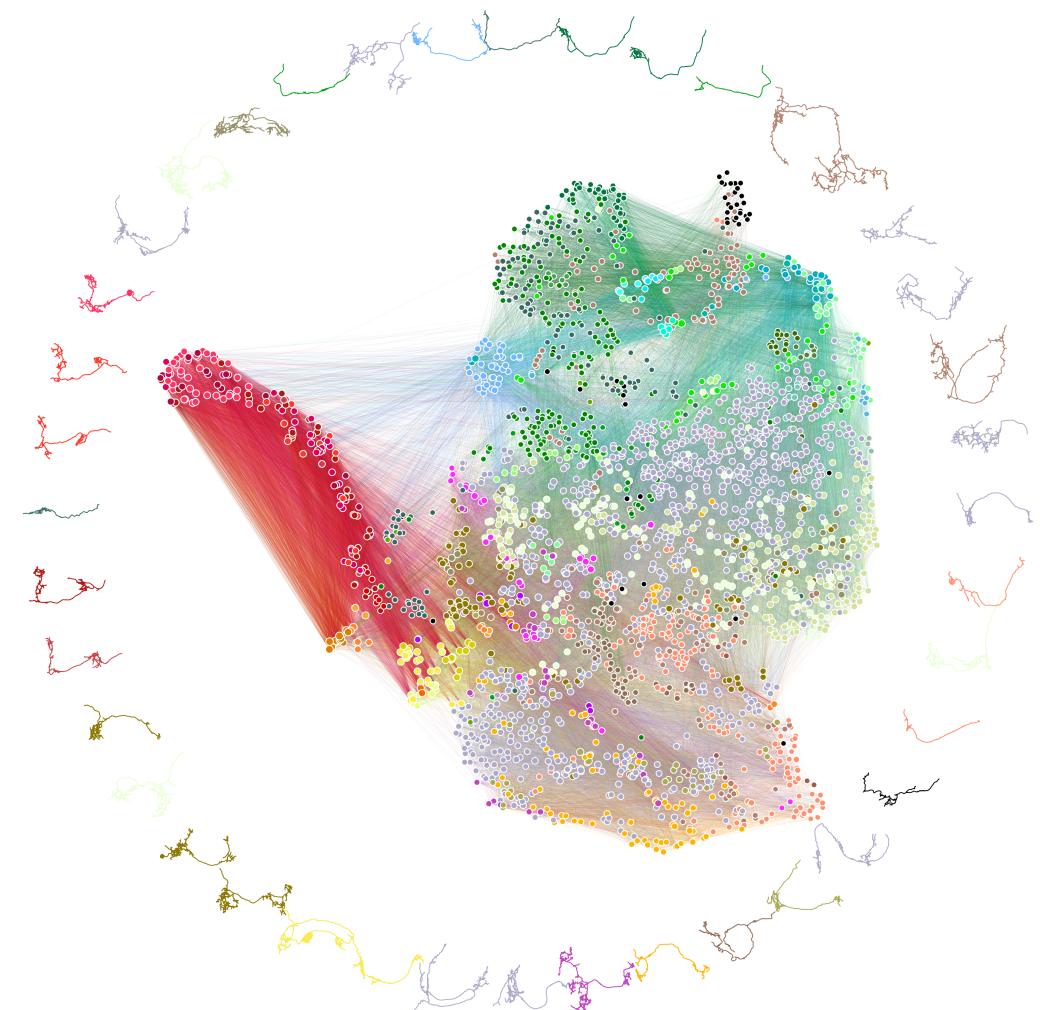
*Johns Hopkins University*

*NeuroData lab*

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

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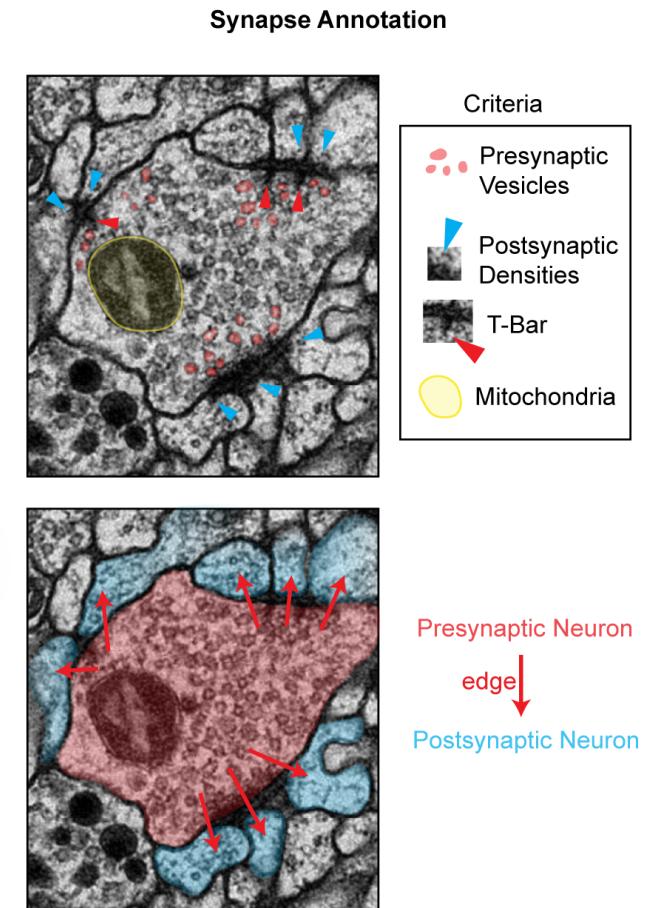
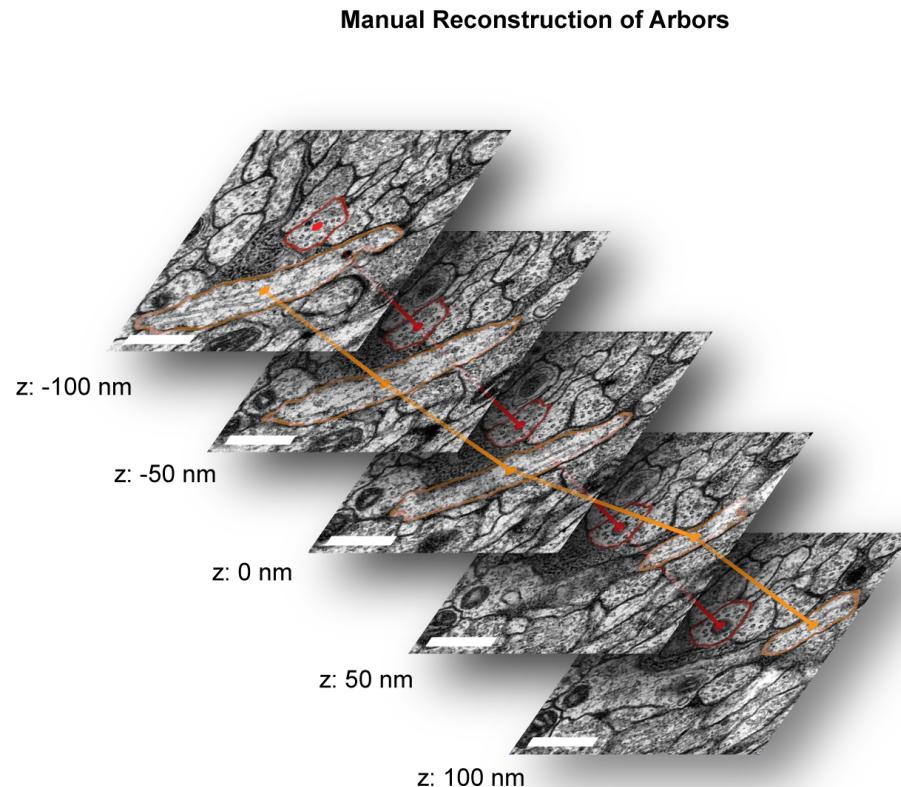
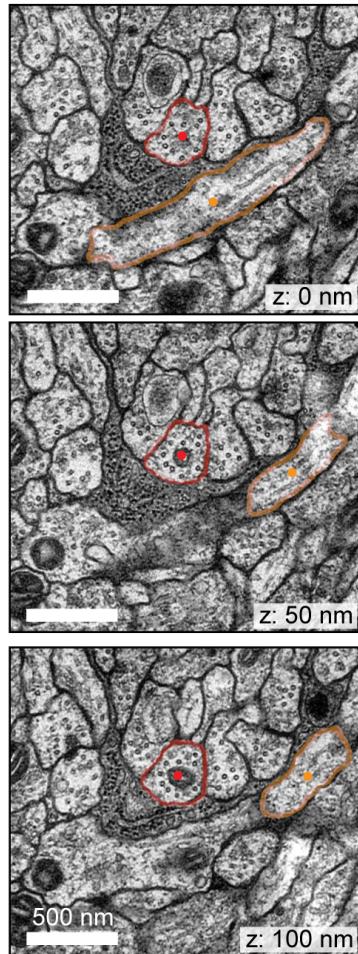
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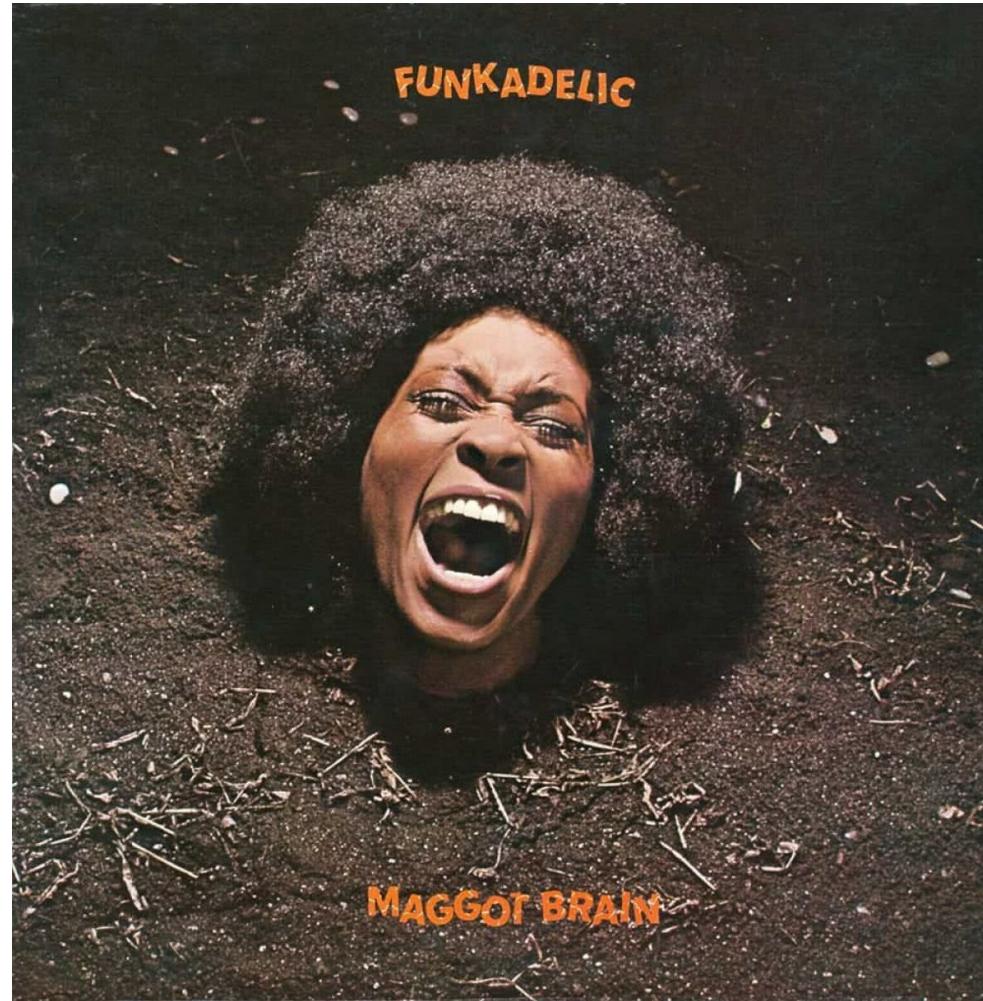
# My requests

- Feedback, feedback, feedback
  - Especially with figures

# Electron microscopy connectomics



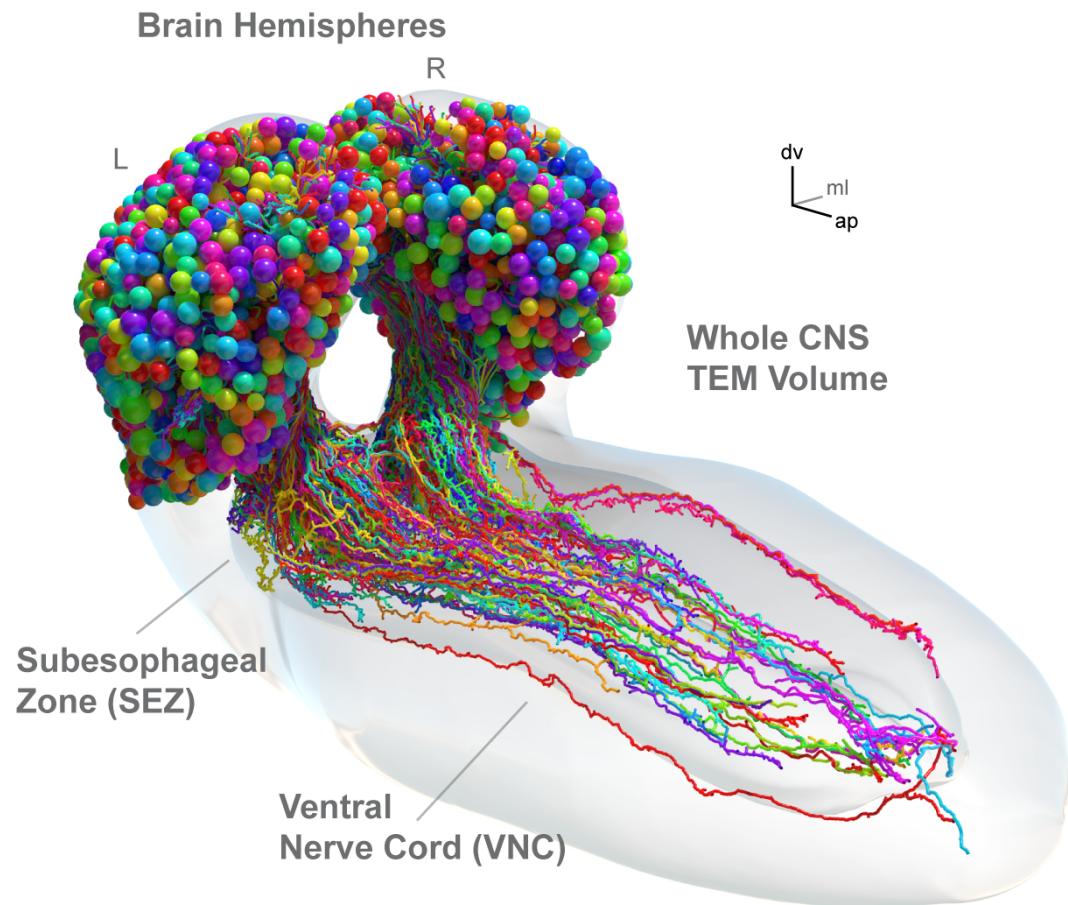
# Why are we talking about maggot brain?



# *Drosophila* larva (AKA a maggot) brain connectome

See [Michael Windings's talk](#)

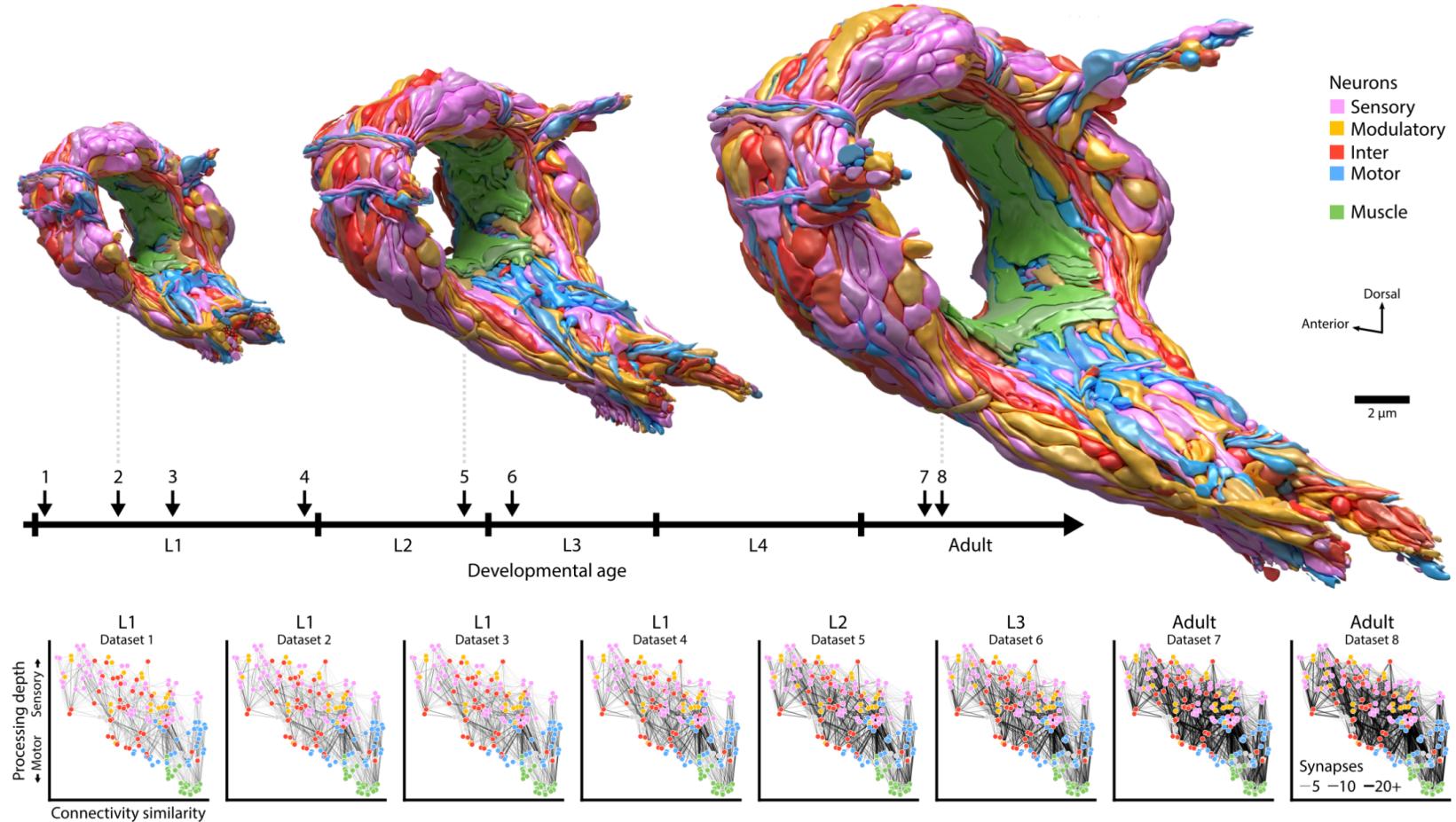
- First whole-brain, single-cell connectome of any insect
- ~3000 neurons, ~544K synapses
- Both hemispheres of the brain reconstructed



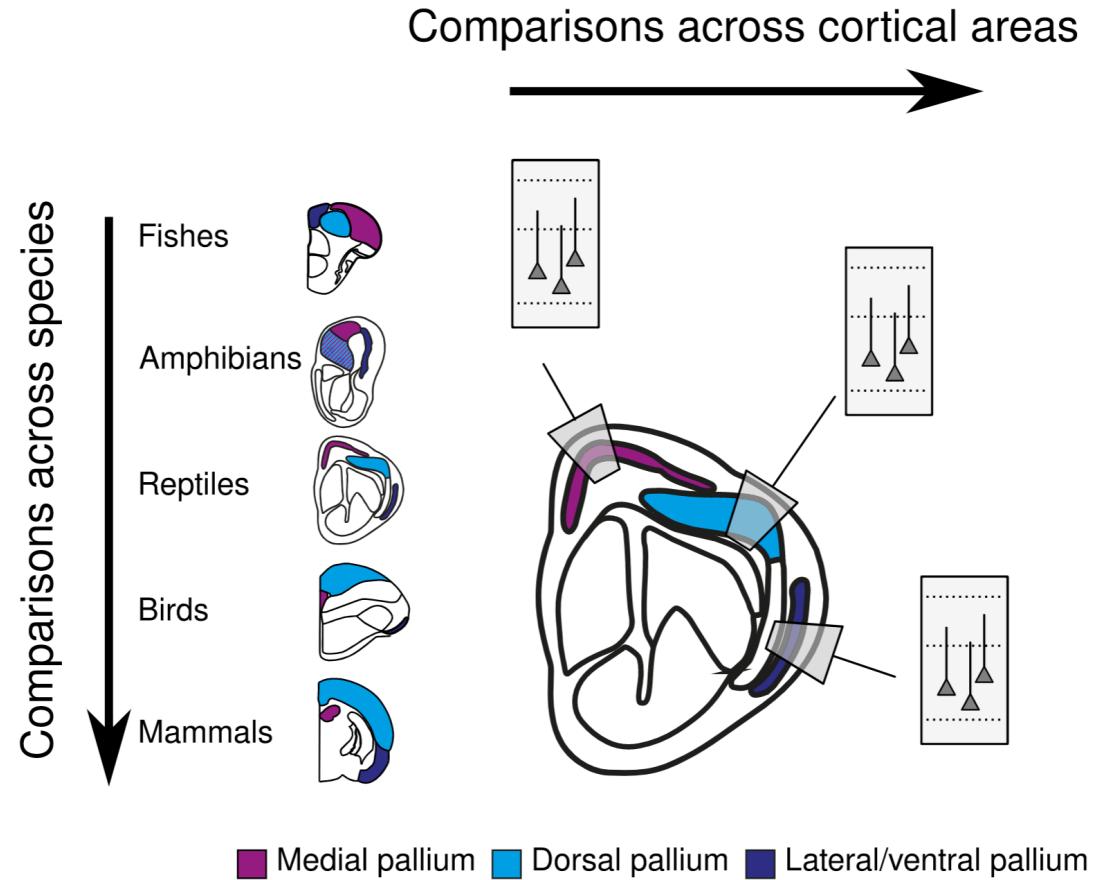
**For us, we're just going to consider this to be a network**

**Many connectomics questions require comparison**

# Connectomes across development



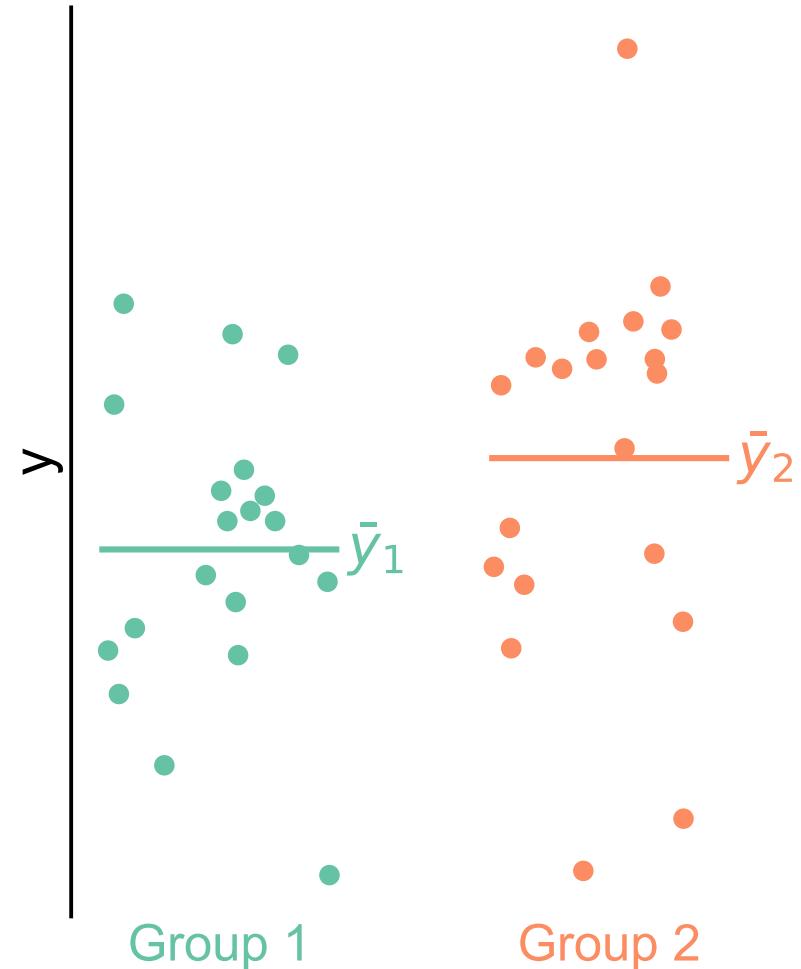
# Connectomes across evolution, cortex



Are the **left** and **right** sides of this connectome  
*the same?*

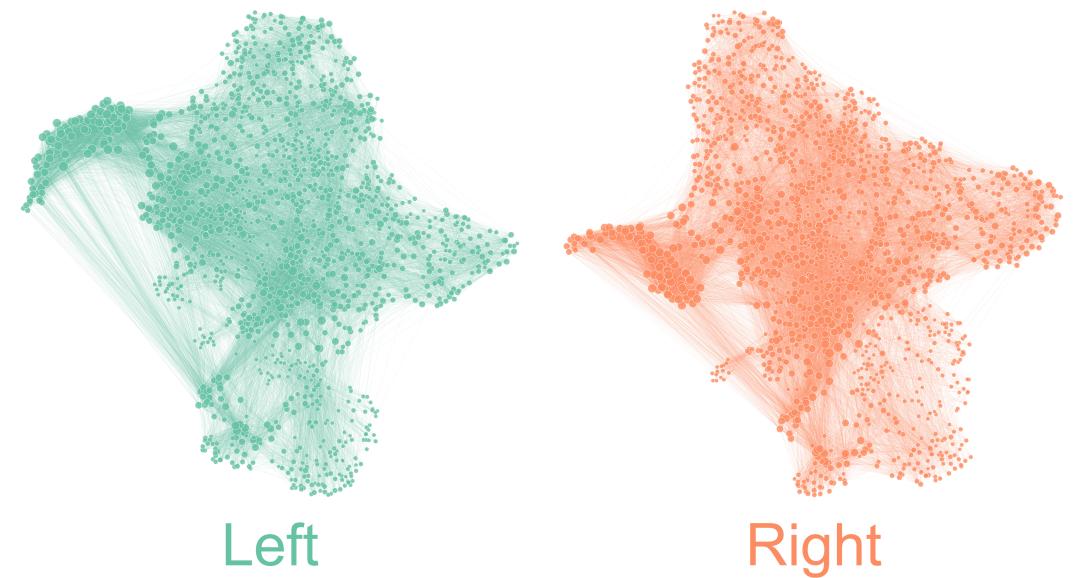
# Are these populations the same?

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



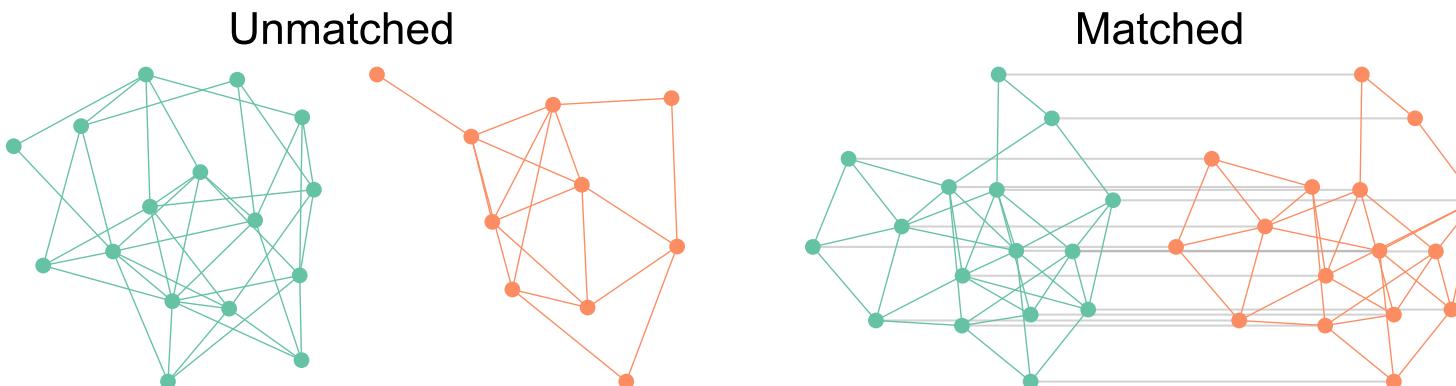
# Are these two *networks* the same?

- Want a two-network-sample test!
- $A^{(L)} \sim F^{(L)}$ ,  $A^{(R)} \sim F^{(R)}$
- $H_0 : F^{(L)} = F^{(R)}$   
 $H_A : F^{(L)} \neq F^{(R)}$

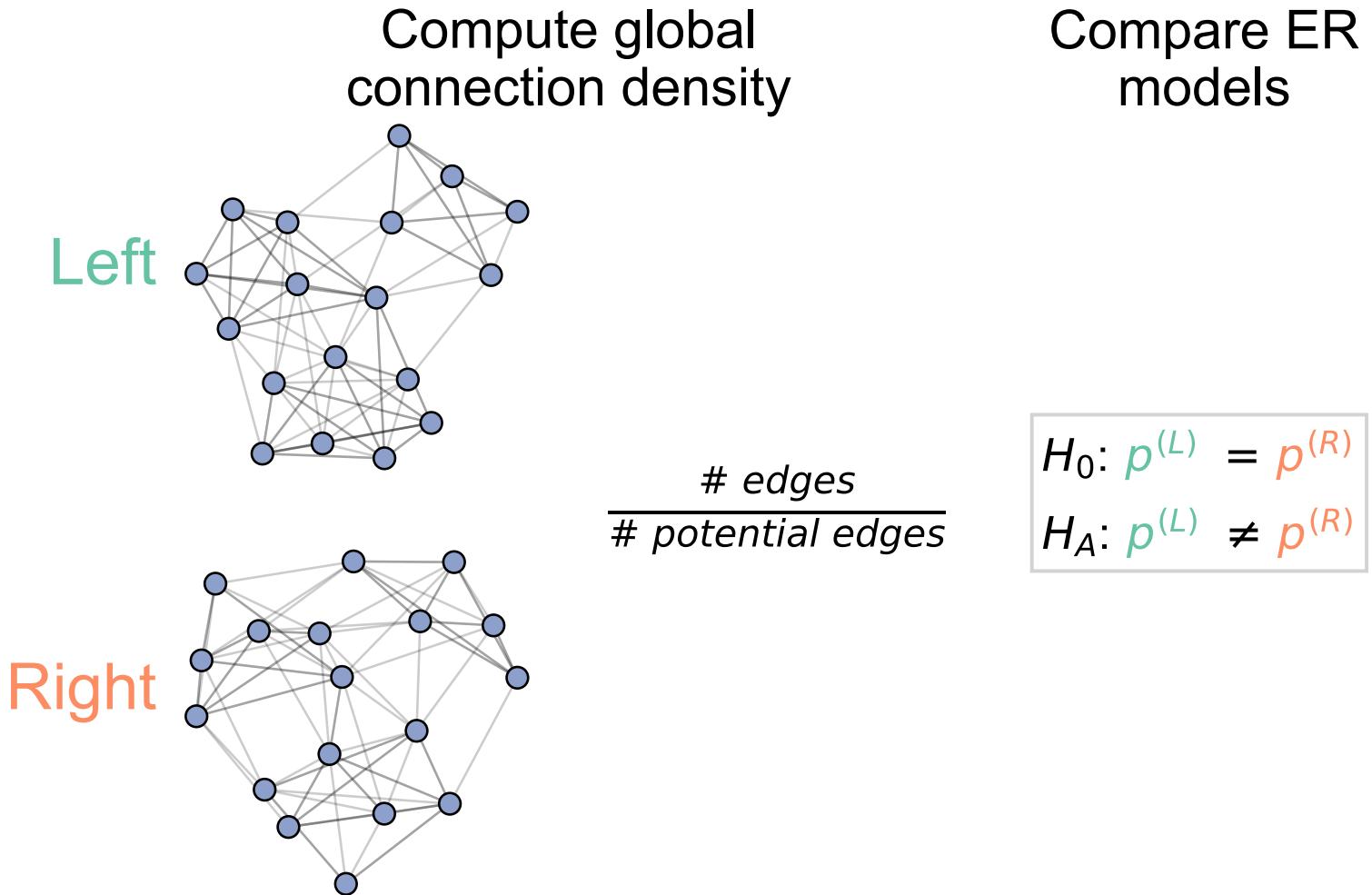


# Assumptions

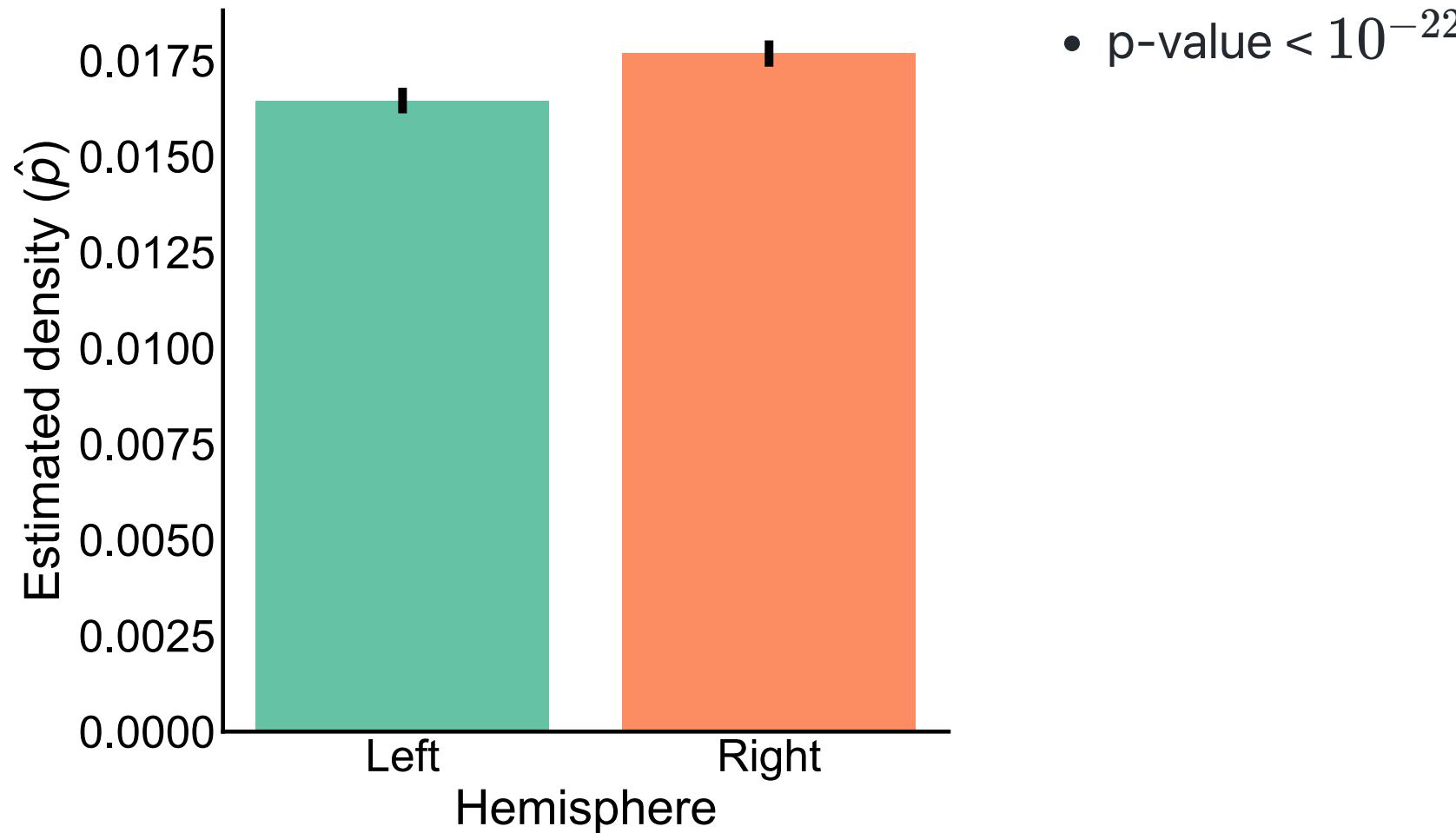
- We know the direction of synapses, so network is *directed*.
- For simplicity (for now), consider networks to be *unweighted*.
- For simplicity (for now), consider the **left** → **left** and **right** → **right** (*ipsilateral*) connections only.
- Not going to assume any nodes are matched



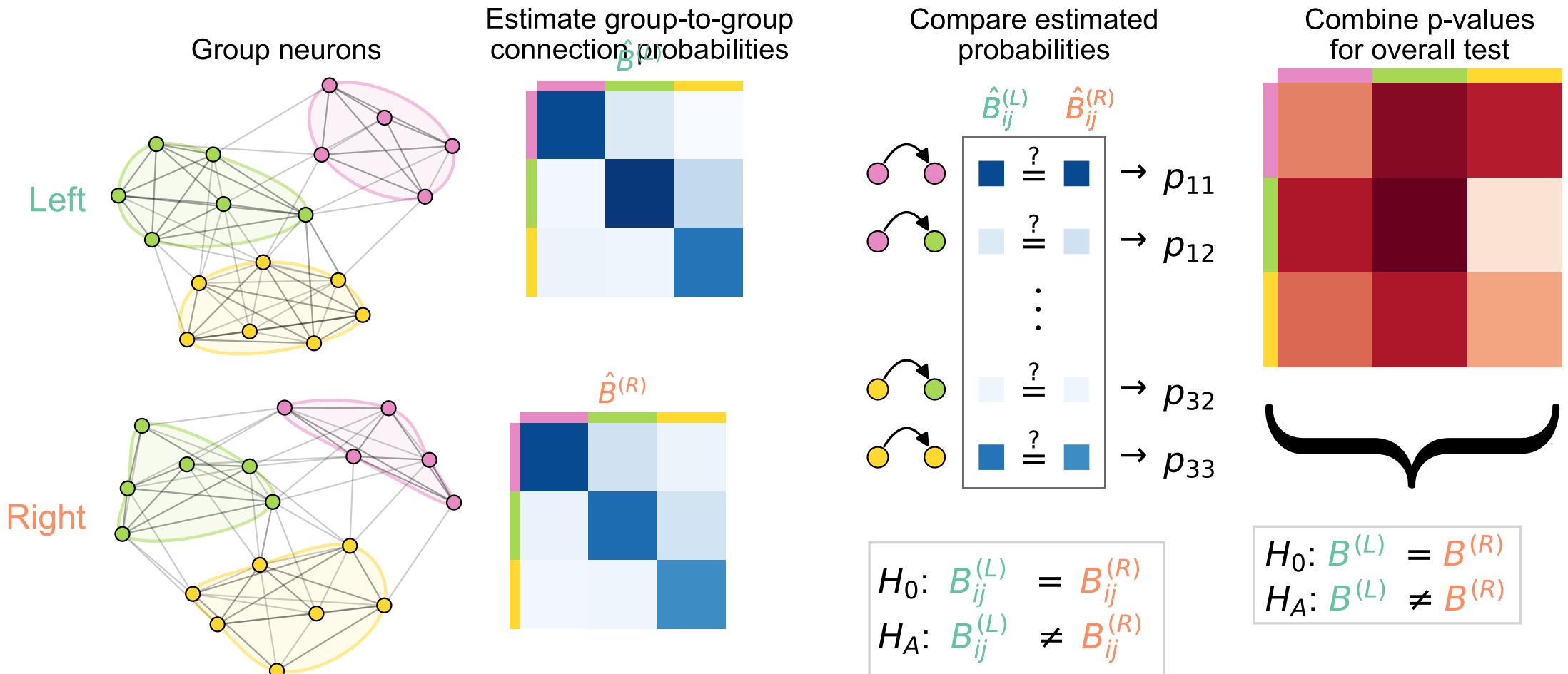
# Density-based testing: Erdos-Renyi (ER) model



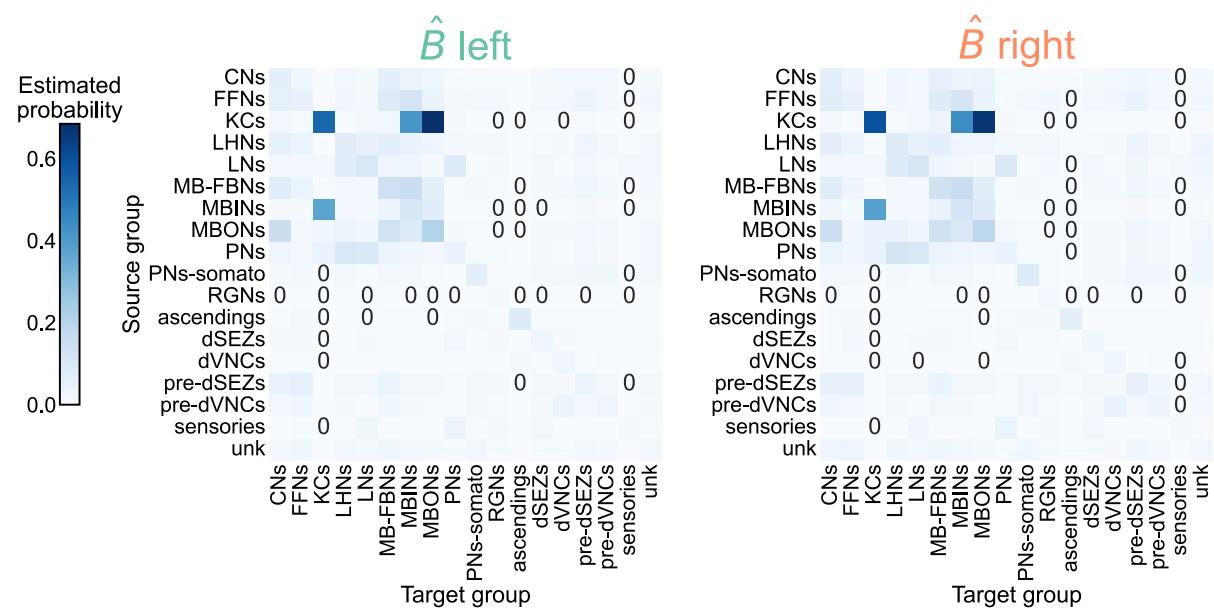
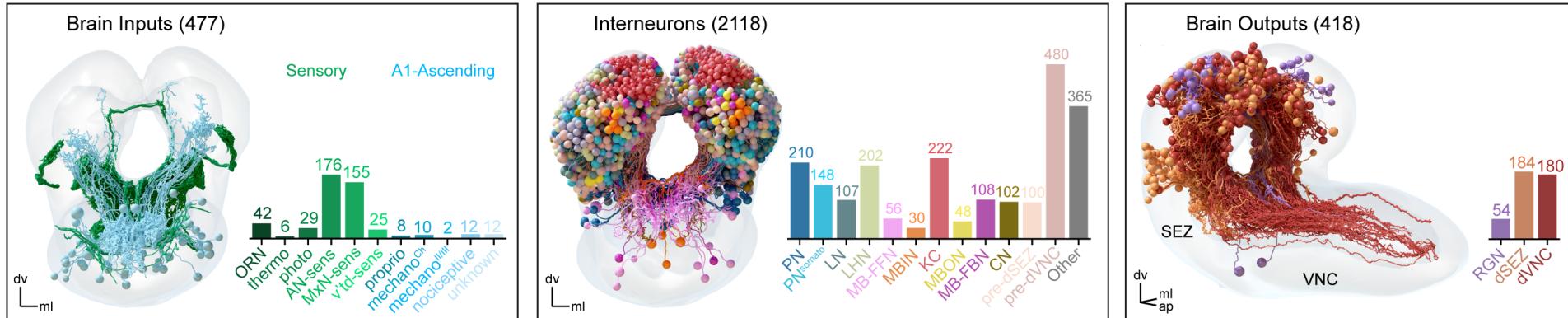
# We detect a difference in density



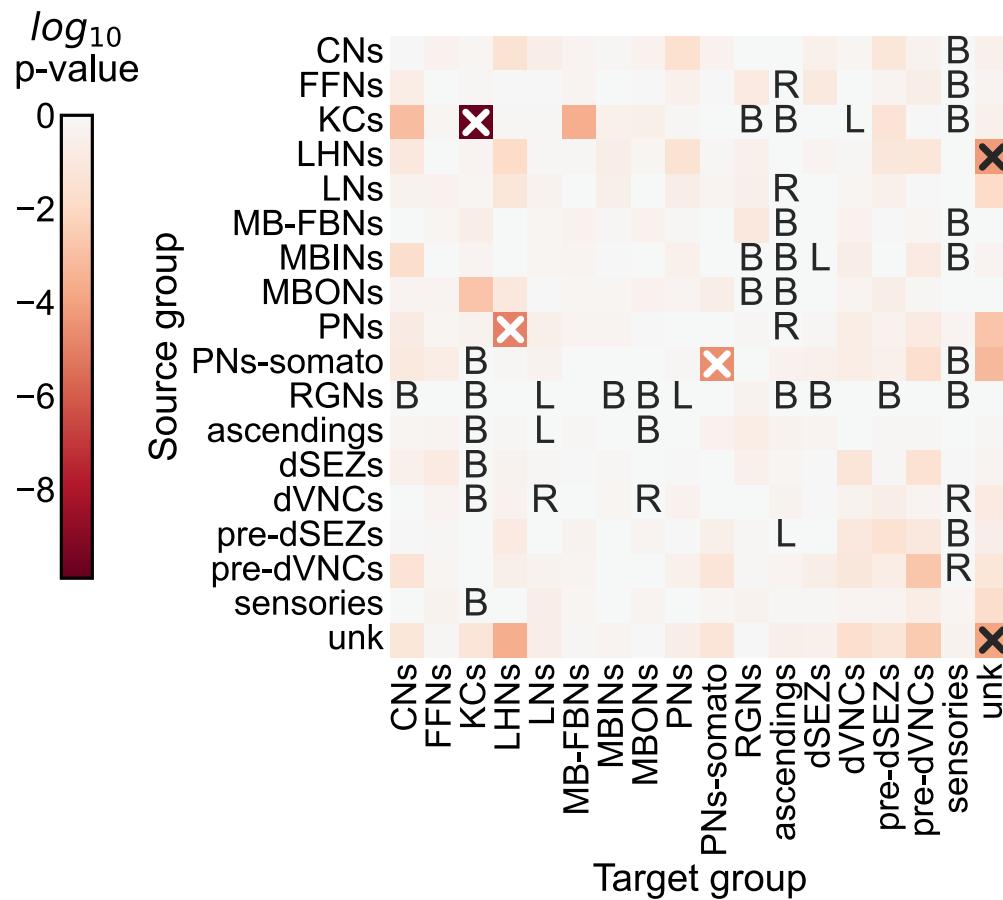
# Group-based testing: stochastic block model (SBM)



# Connection probabilities between groups



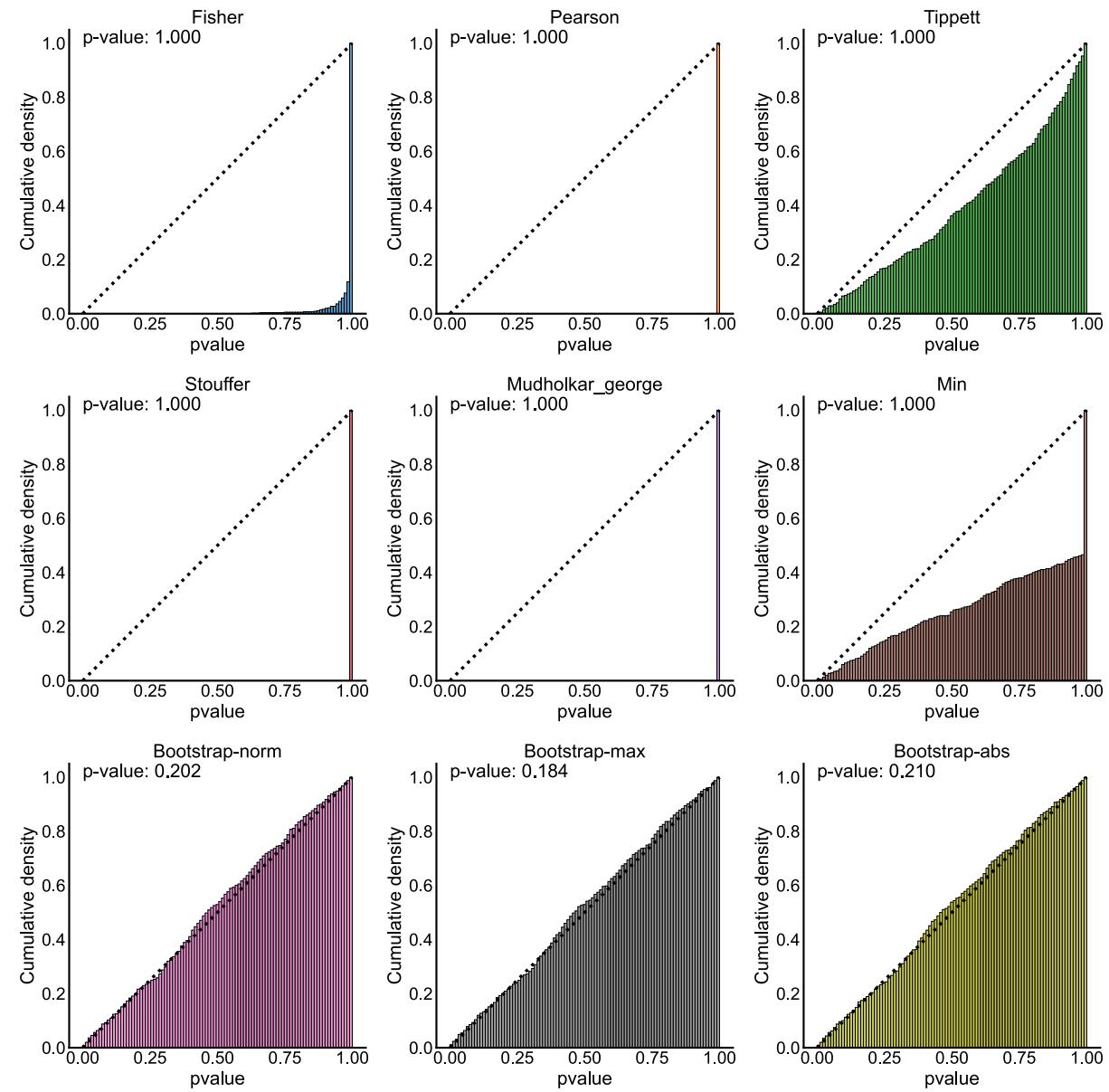
# We detect a difference in group-to-group connection probabilities



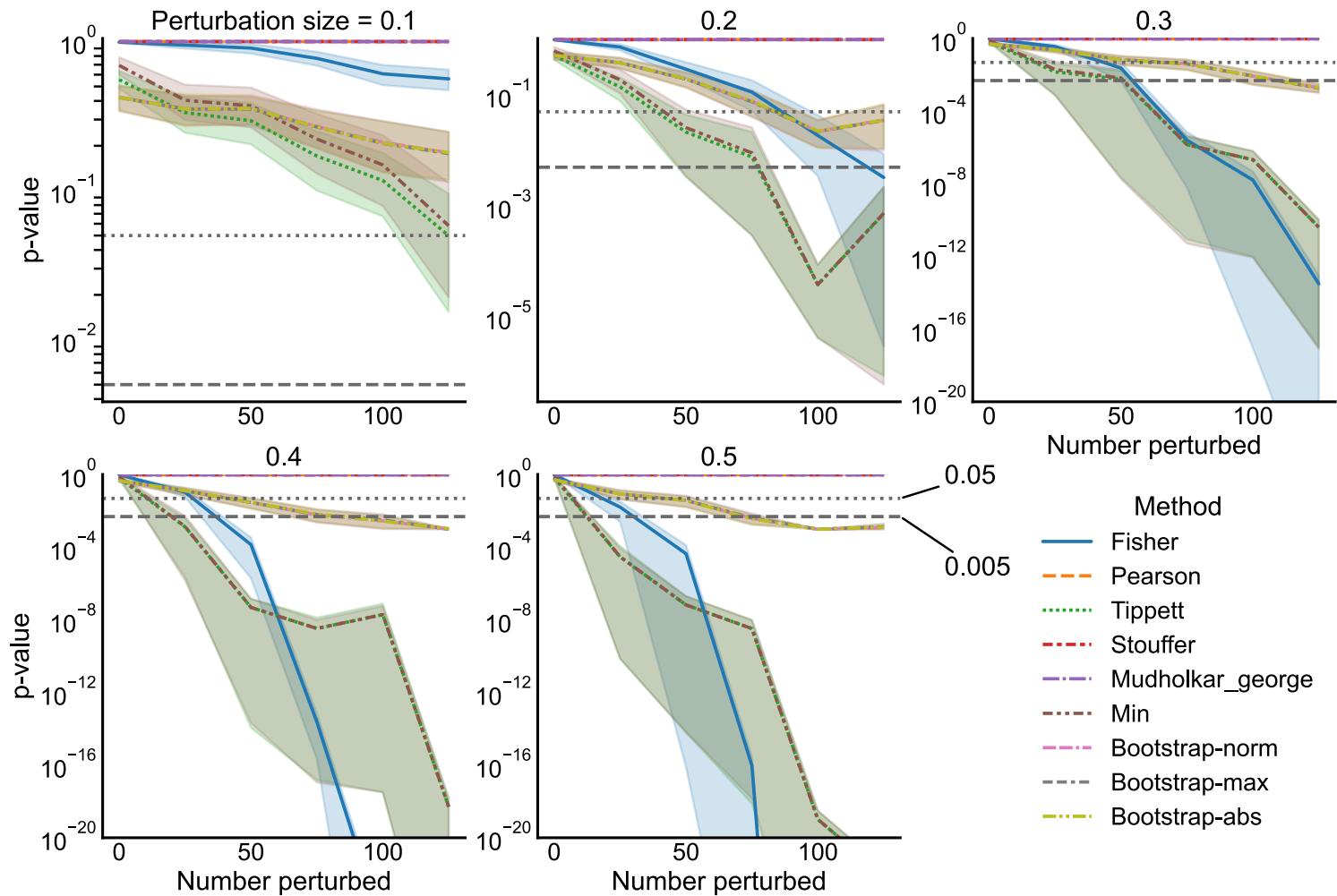
- After multiple comparison, find 5 group-to-group connections which are significantly different
- Combine (uncorrected) p-values (like a meta-analysis), leads to p-value for overall test of  $< 10^{-7}$

# A massive aside

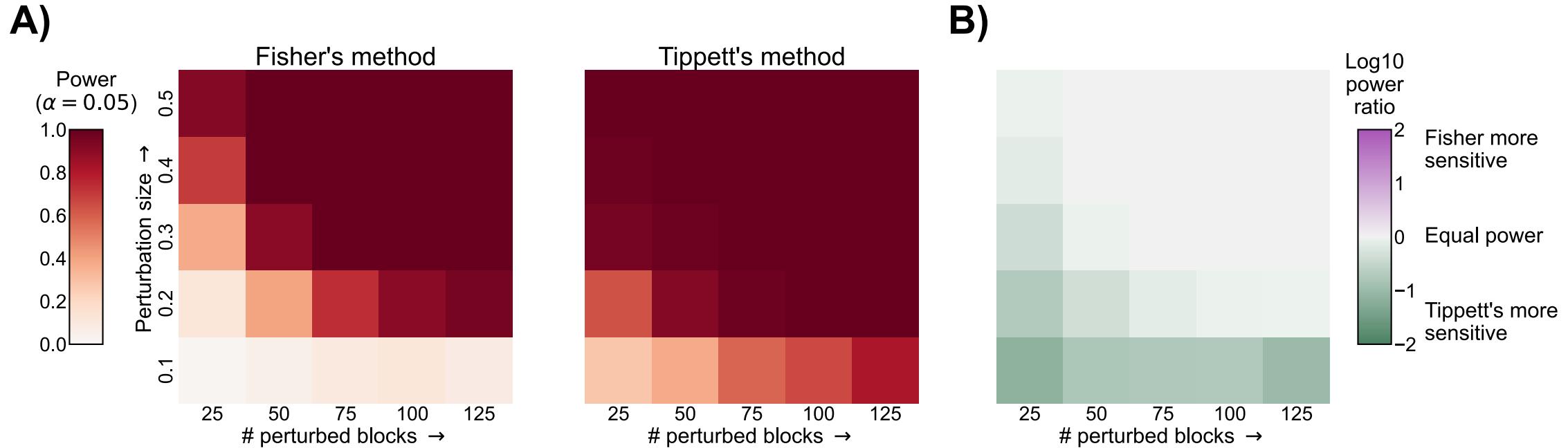
# Distribution under the null for combine pvalues



# Power for combine p-values



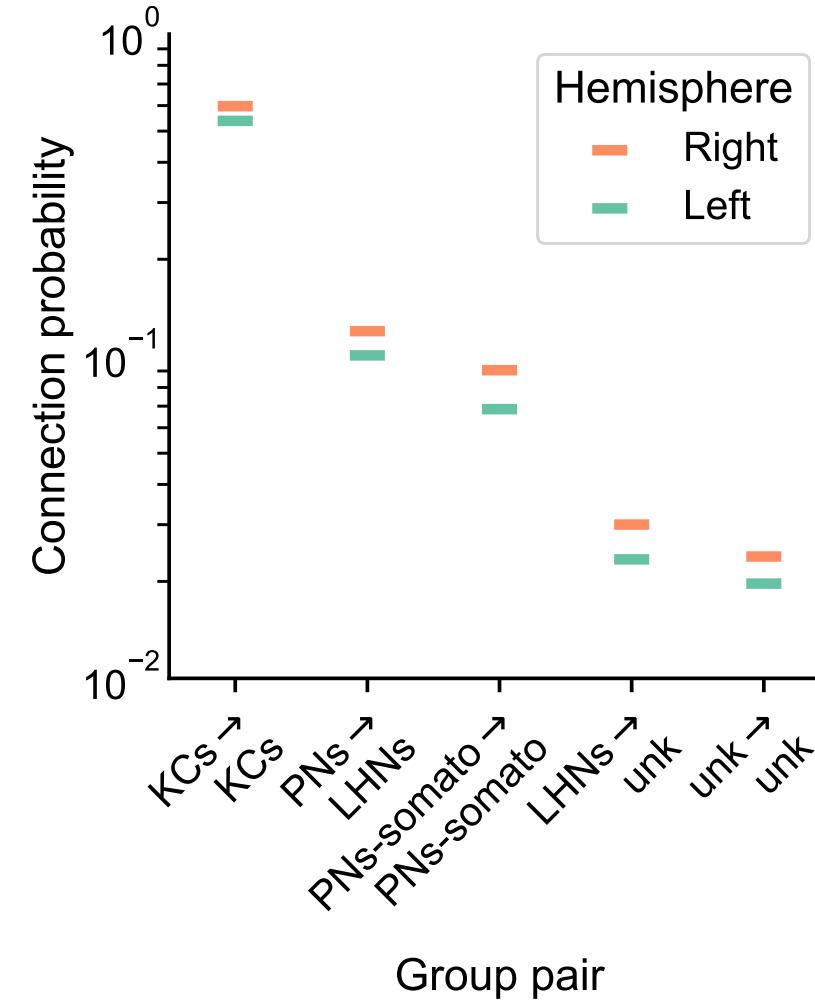
# Relative power (Fisher's vs Tippett's)



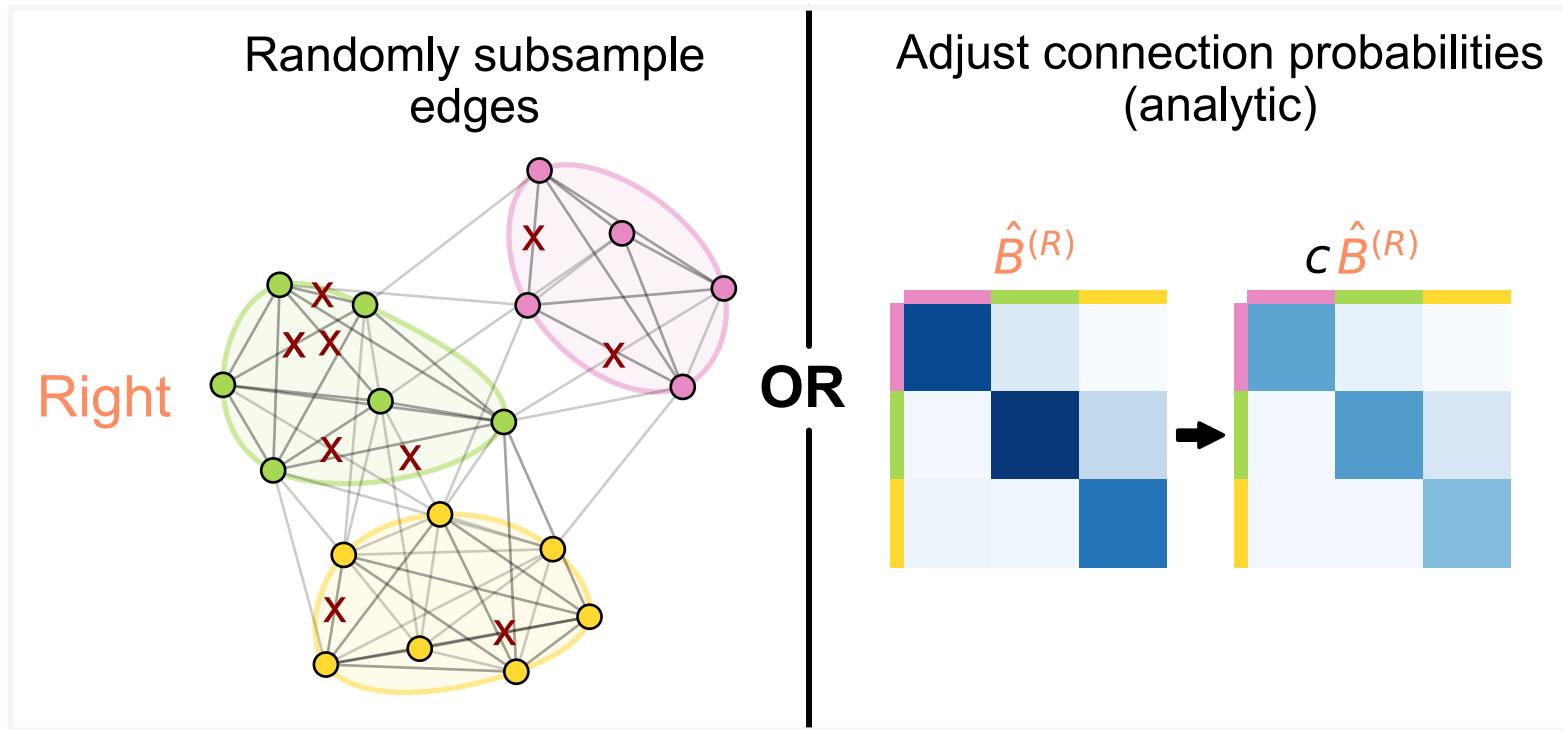
**Back to the main thread...**

# Should we be surprised?

- 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,  $\frac{p^{(L)}}{p^{(R)}}$



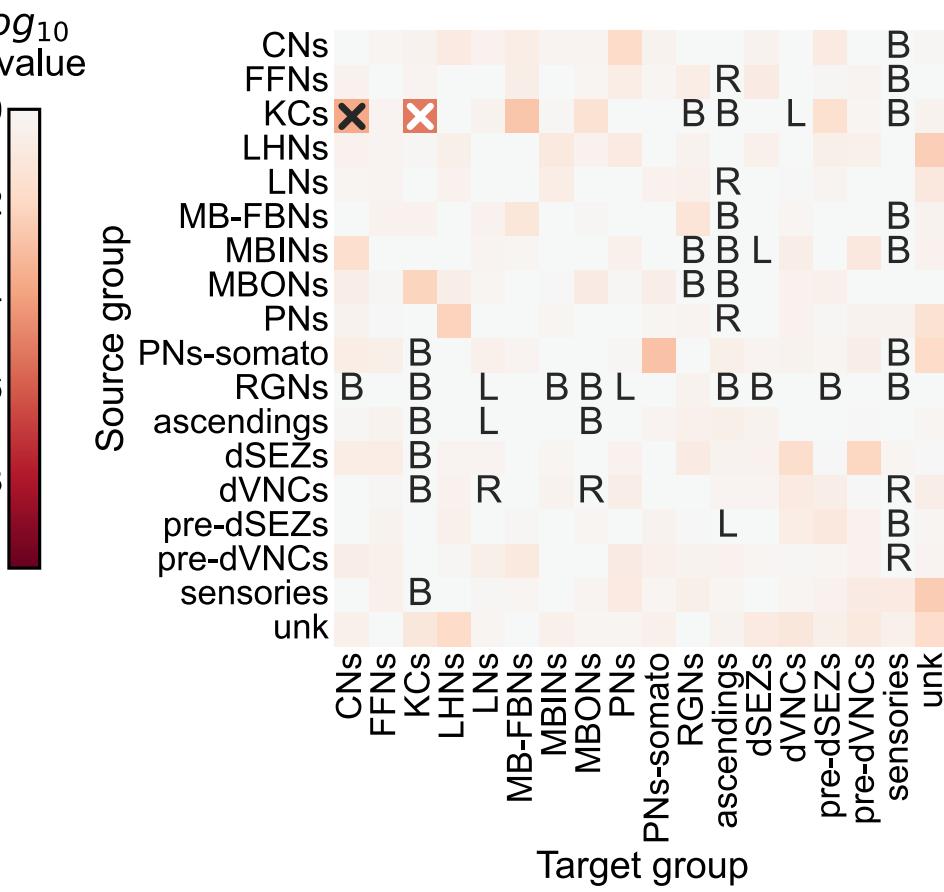
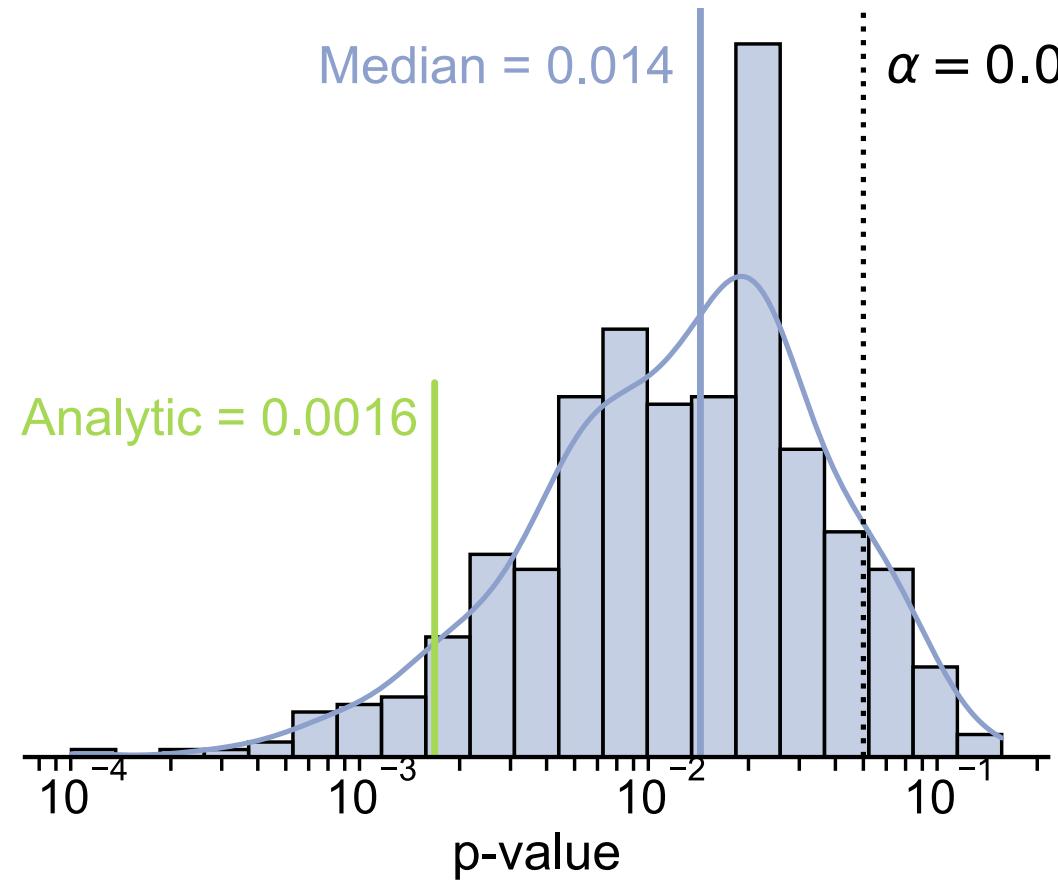
# Adjusting for a difference in density



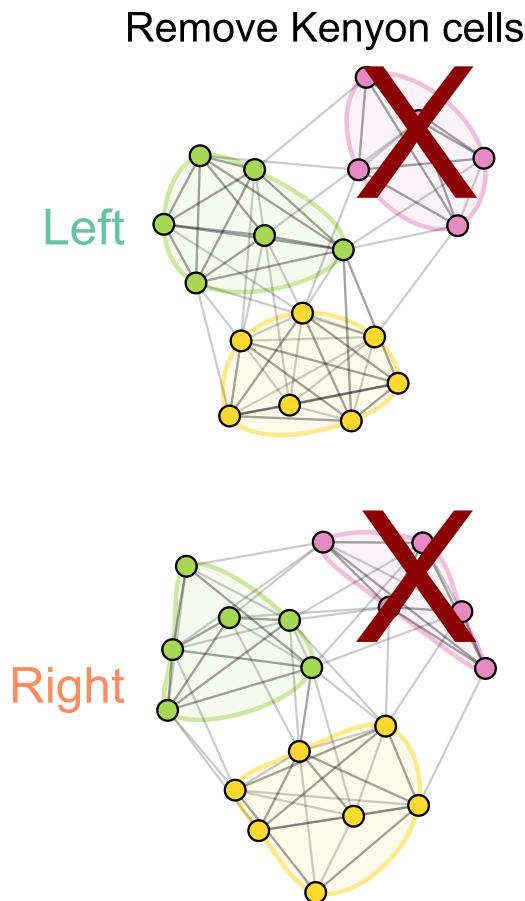
Rerun SBM testing

$$H_0: B^{(L)} = c B^{(R)}$$
$$H_A: B^{(L)} \neq c B^{(R)}$$

# Even with density adjustment, we detect a difference



# So the Kenyon cells are the only group with remaining differences...



Re-run all tests

ER

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

SBM

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

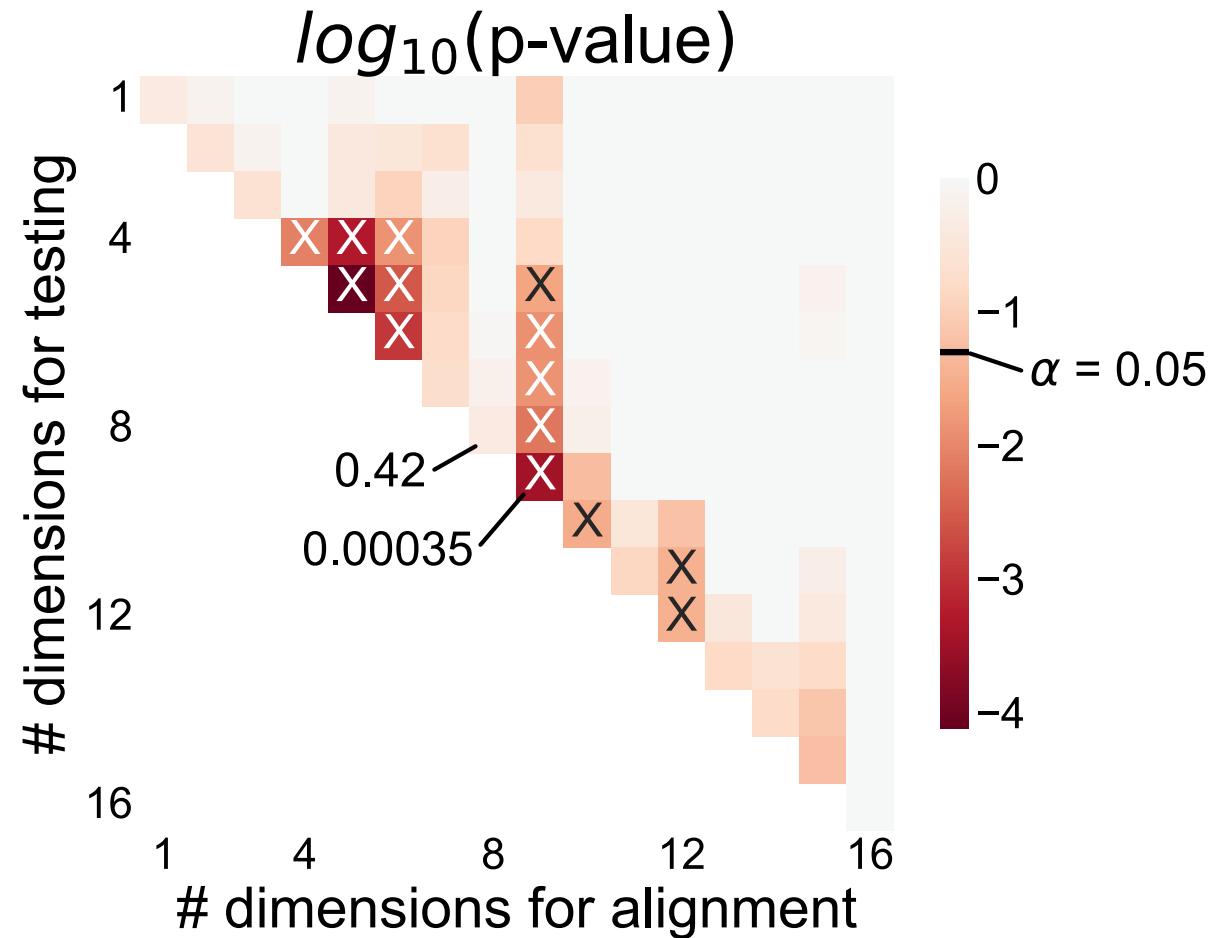
aSBM

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

- ER test:  $p < 10^{-26}$
- SBM test:  $p \approx 0.0027$
- Adjusted SBM test:  $p \approx 0.43$

**But wait, there's more (tests one could run)!**

# Latent distribution test (RDPG)



# To sum up...

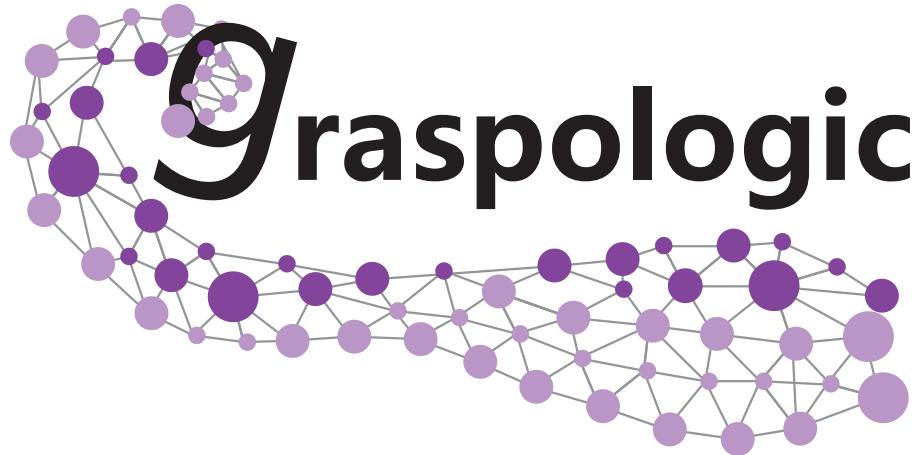
| Model | $H_0$ (vs. $H_A \neq$ ) | KC | p-value          | Interpretation   |
|-------|-------------------------|----|------------------|--|
| ER    | $p^{(L)} = p^{(R)}$     | +  | $< 10^{-23}$     | Reject densities the same                                |
| SBM   | $B^{(L)} = B^{(R)}$     | +  | $< 10^{-7}$      | Reject group connection probabilities the same           |
| aSBM  | $B^{(L)} = cB^{(R)}$    | +  | $\approx 0.0016$ | Reject above even after accounting for density           |
| ER    | $p^{(L)} = p^{(R)}$     | -  | $< 10^{-26}$     | Reject densities the same (w/o KCs)                      |
| SBM   | $B^{(L)} = B^{(R)}$     | -  | $\approx 0.0027$ | Reject group connection probabilities the same (w/o KCs) |
| aSBM  | $B^{(L)} = cB^{(R)}$    | -  | $\approx 0.43$   | Don't reject above after density adjustment (w/o KCs)    |

## More generally

- We studied simple ways of framing a network two sample test
- We found that it can be important to "mod out" by other simple network statistics if you don't care about them (like density)
- We provide recommendations for what to run for you future connectome comparisons

# graspologic:

[github.com/microsoft/graspologic](https://github.com/microsoft/graspologic)



downloads 104k



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contributors 46

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# This work:

[github.com/neurodata/bilateral-connectome](https://github.com/neurodata/bilateral-connectome)

The Erdos-Renyi (ER) model

The [Erdos-Renyi \(ER\) model](#) is one of the simplest network models. This model treats the probability of each potential edge in the network occurring to be the same. In other words, all edges between any two nodes are equally likely.

**Math**

Let  $n$  be the number of nodes. We say that for all  $(i, j)$ ,  $i \neq j$ , with  $i$  and  $j$  both running from  $1 \dots n$ , the probability of the edge  $(i, j)$  occurring is:

$$P[A_{ij} = 1] = p_{ij} = p$$

Where  $p$  is the global connection probability.

Each element of the adjacency matrix  $A$  is then



# Acknowledgements

## **Johns Hopkins University**

Mike Powell, Eric Bridgeford, Carey Priebe, Joshua Vogelstein, Kareef Ullah, Diane Lee, Sambit Panda, Jaewon Chung, Ali Saad-Eldin, NeuroData lab

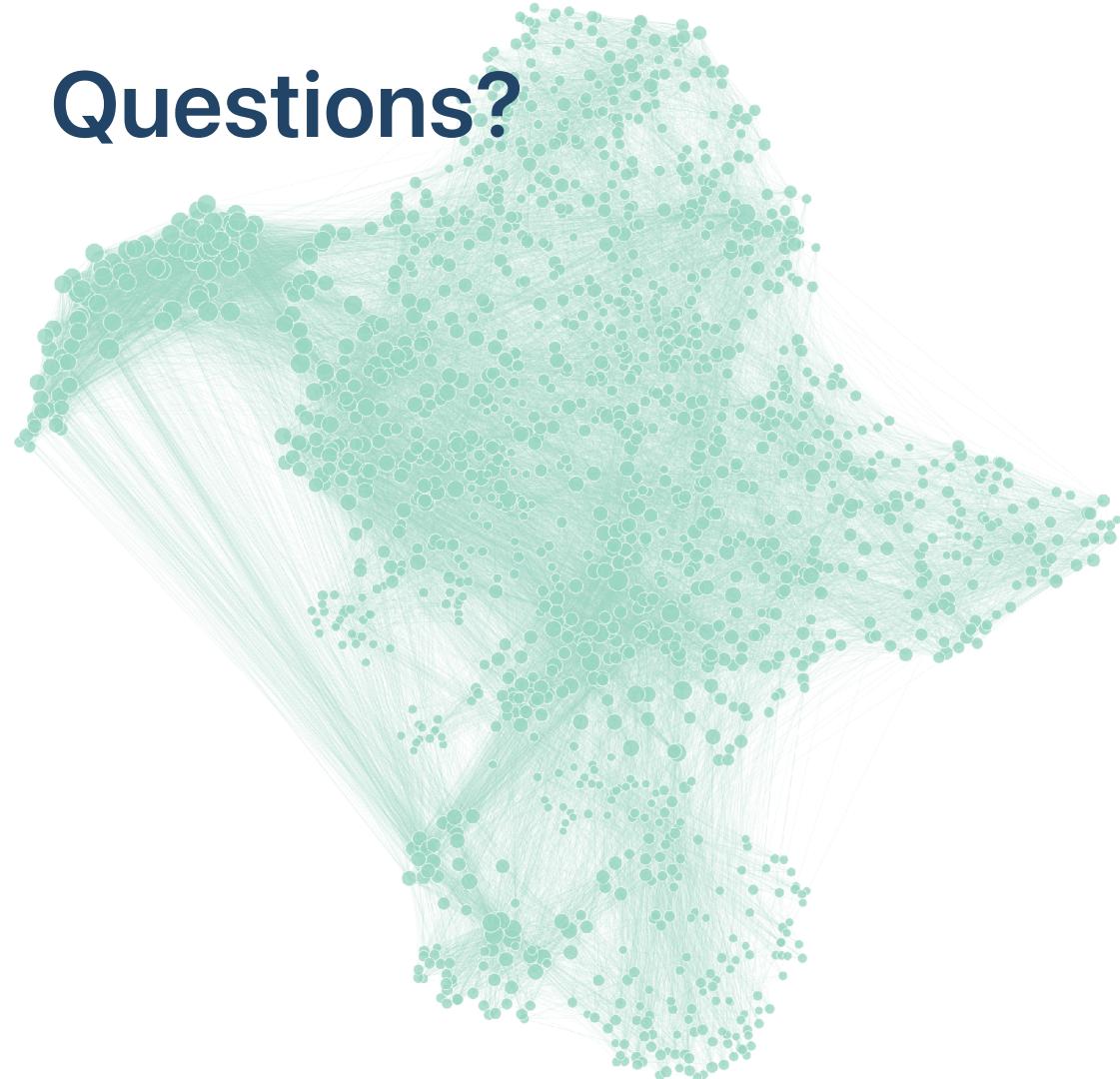
## **University of Cambridge / MRC Laboratory of Molecular Biology**

Michael Winding, Albert Cardona, Marta Zlatic, Chris Barnes

## **Microsoft Research**

Hayden Helm, Dax Pryce, Nick Caurvina, Bryan Tower, Patrick Bourke, Jonathan McLean, Carolyn Buractaon, Amber Hoak

# Questions?



Left



Right

