

# Generative network modeling reveals a first quantitative definition of bilateral symmetry exhibited by an whole insect brain connectome

Benjamin D. Pedigo<sup>1\*</sup>, Mike Powell<sup>1</sup>, Eric W. Bridgeford<sup>1</sup>, Michael Winding<sup>2</sup>, Carey E. Priebe<sup>1</sup>, Joshua T. Vogelstein<sup>1</sup>

1 - Johns Hopkins University, 2 - University of Cambridge, \* - correspondence: [@bpedigo \(Github\)](mailto:bpedigo@jhu.edu) [@bpedigod \(Twitter\)](https://github.com/bdpedigo) [bdpedigo.github.io](https://bdpedigo.github.io)

## Summary

- Aimed to define bilateral symmetry for a connectome, and formally test this hypothesis.
- Hemispheres differ in a network-wide parameter under even the simplest model of a network pair.
- Hemispheres differ in neuron group connection probabilities, even when adjusting for the network-wide effect.
- Detect no differences in adjusted group connections after removing a cell type or when only considering strong edges.
- Provided a definition of bilateral symmetry exhibited by this connectome, tools for future connectome comparisons

## Motivation

- Connectomes are rich sources of inspiration for architectures in artificial intelligence.
- Comparing connectomes could help elucidate which structural features are necessary for yielding the capabilities animal intelligences.
- Bilateral symmetry for connectomes has been investigated, but not clearly defined as a network hypothesis.

## Larval *Drosophila* brain connectome

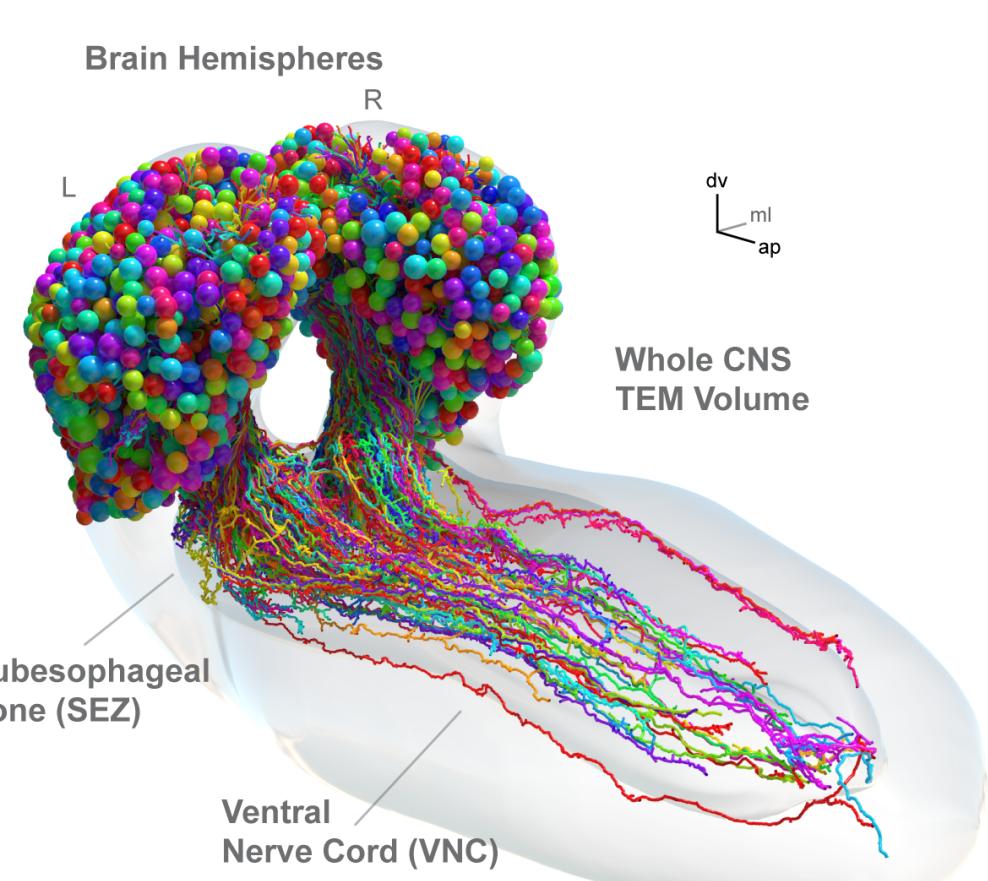


Fig 1A: 3D rendering of a larval *Drosophila* brain connectome [1] comprised of ~3k neurons and ~544k synapses.

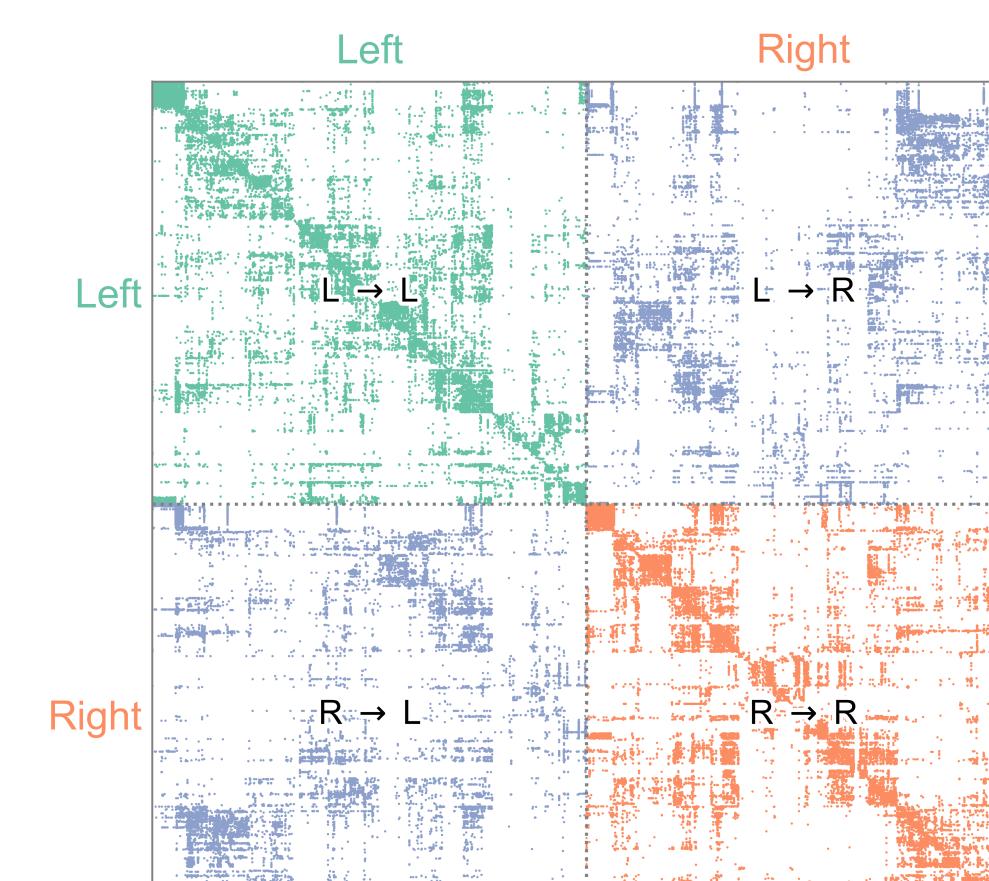


Fig 1B: Directed, binary adjacency matrix sorted by brain hemisphere. We compare  $L \rightarrow L$  vs.  $R \rightarrow R$  subgraphs.

## Are the left and right networks "different"?

Requires that we define what we could mean by "different" for a pair of networks, develop a test procedure for each definition.

## Density test (Model 1)

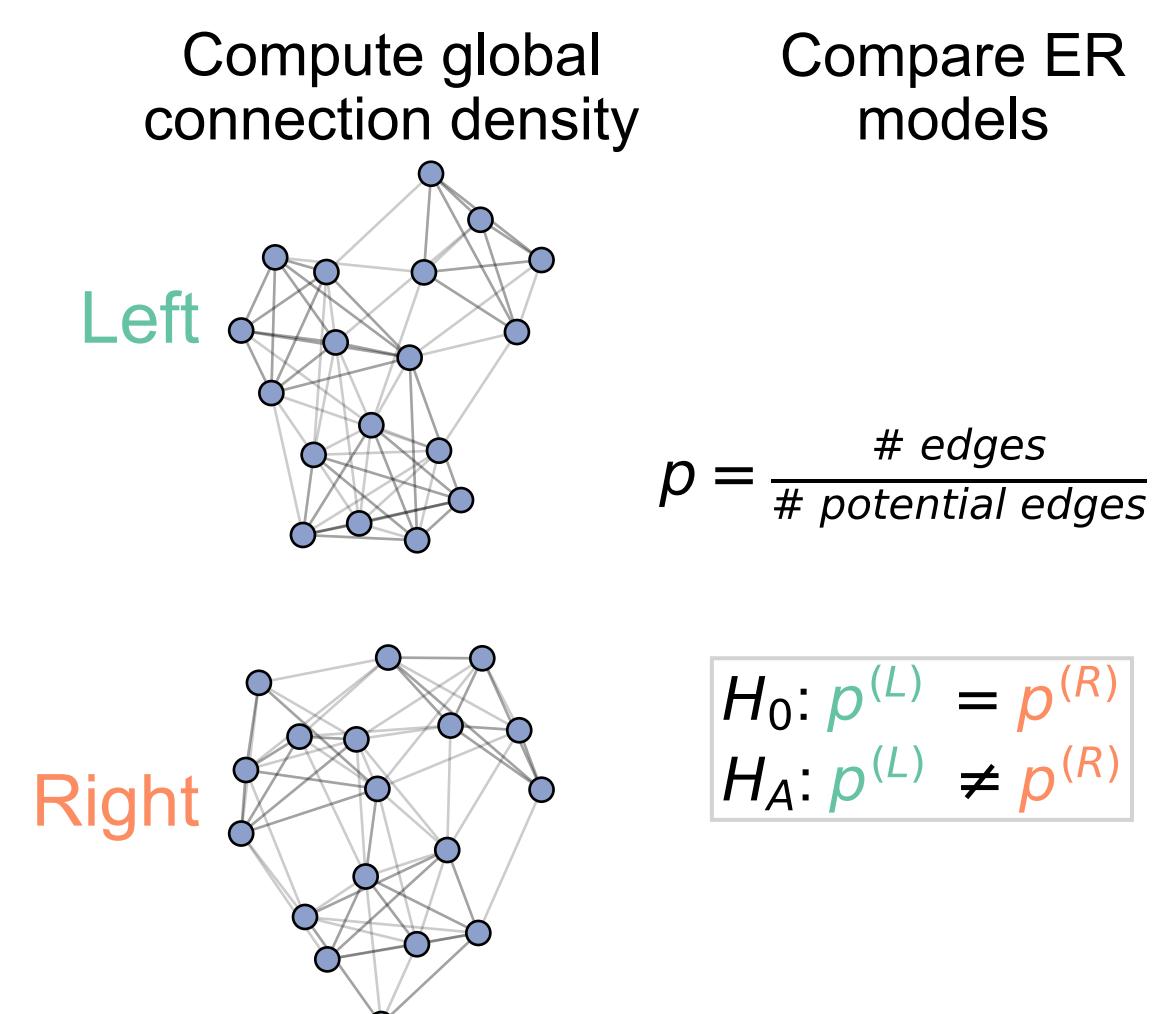


Fig 2A: Testing symmetry under Erdos-Renyi (ER) model [2] compares global connection probability (density), here via Fisher's exact test.

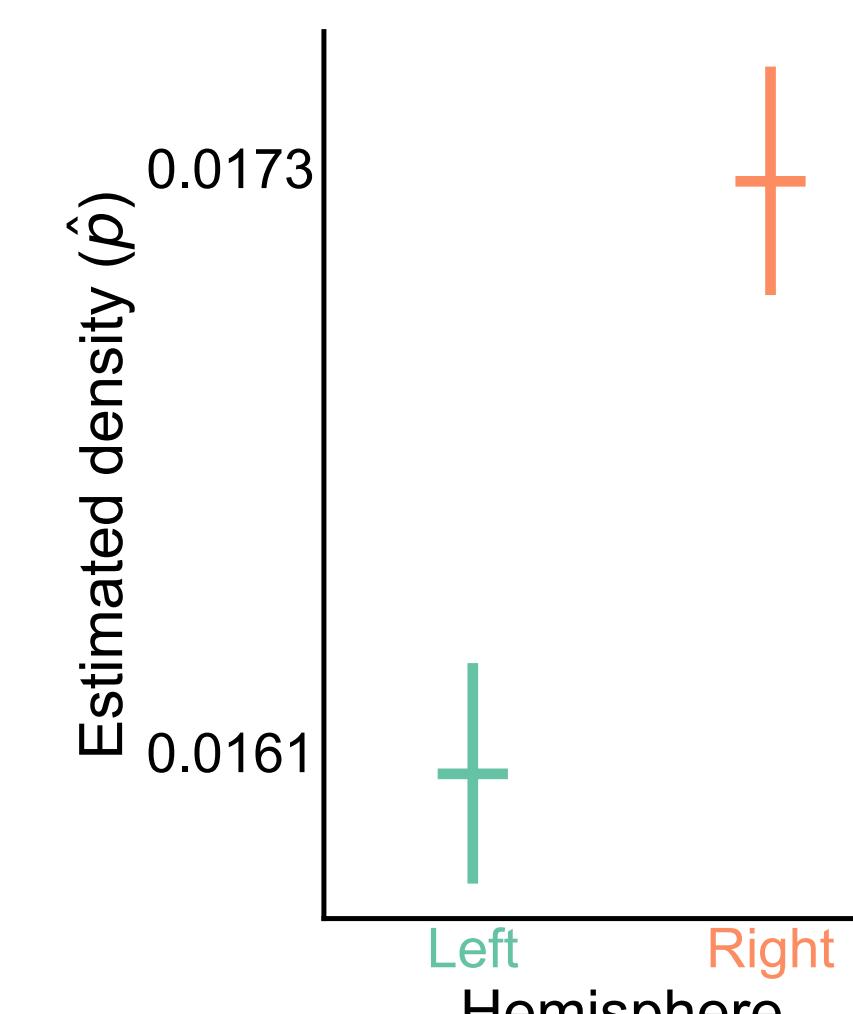


Fig 2B: Test comparing densities rejected ( $p < 10^{-23}$ ), even the simplest model parameter differs between hemispheres.

## Group connection test (Model 2)

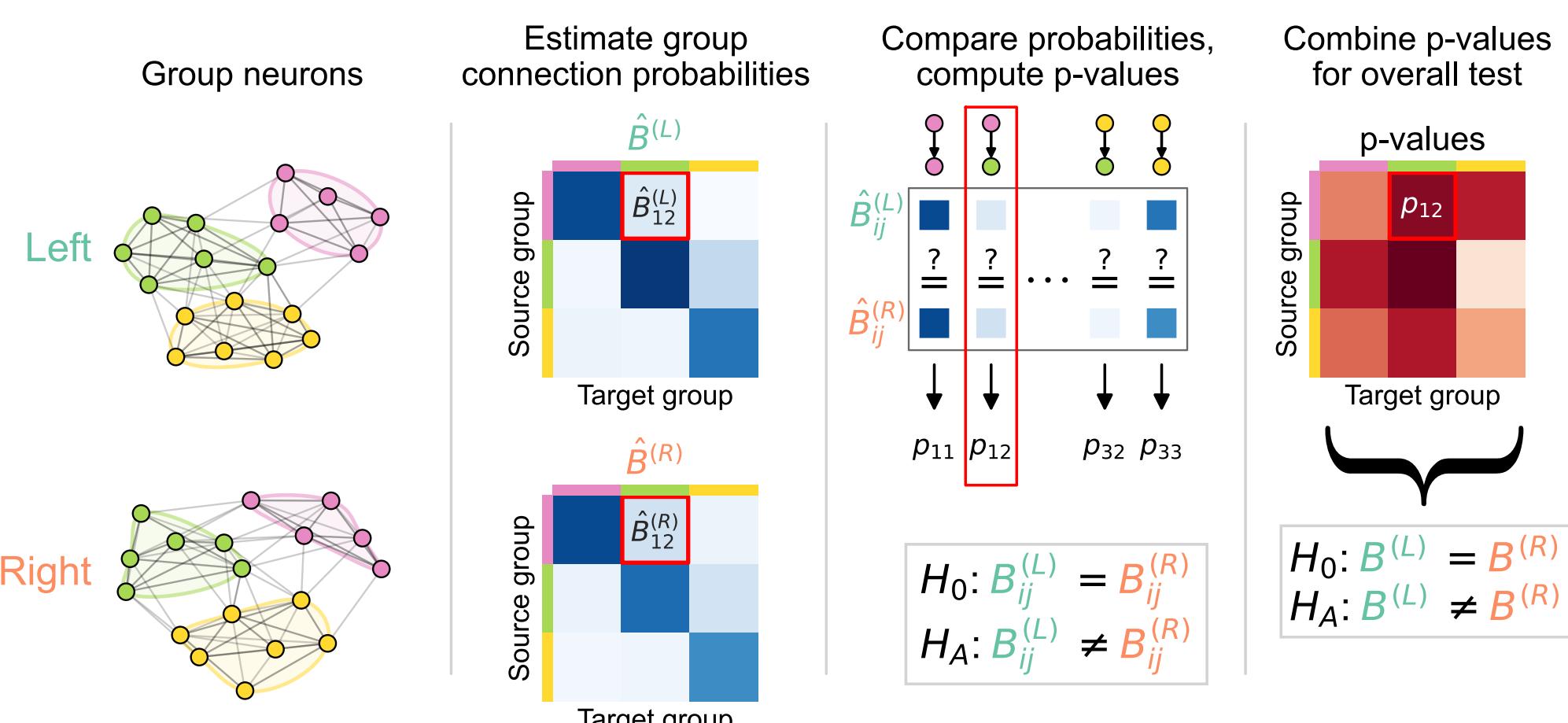


Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types [1]).

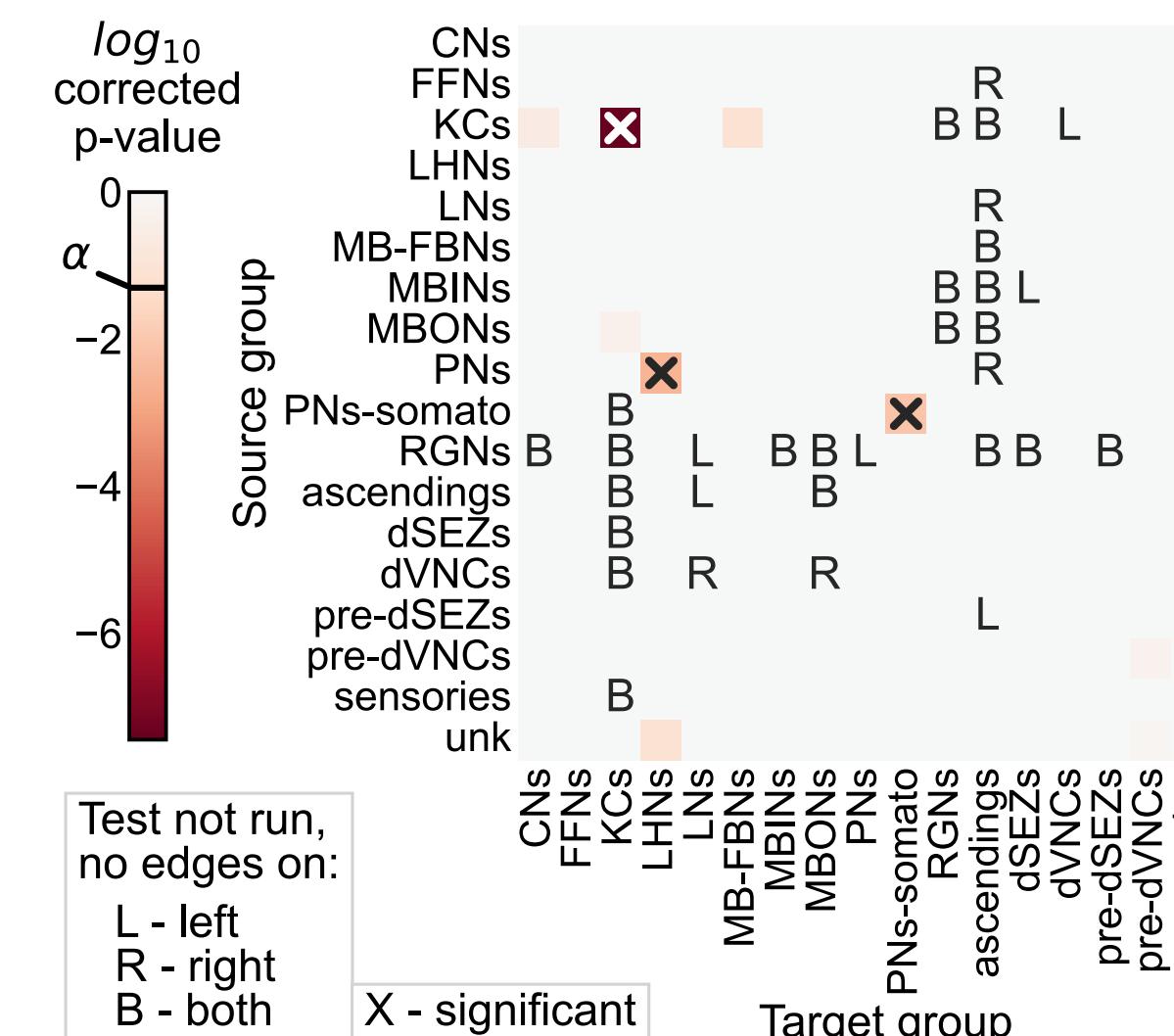


Fig 3B: Test comparing group connections rejected ( $p < 10^{-7}$ ); five specific connections differ.

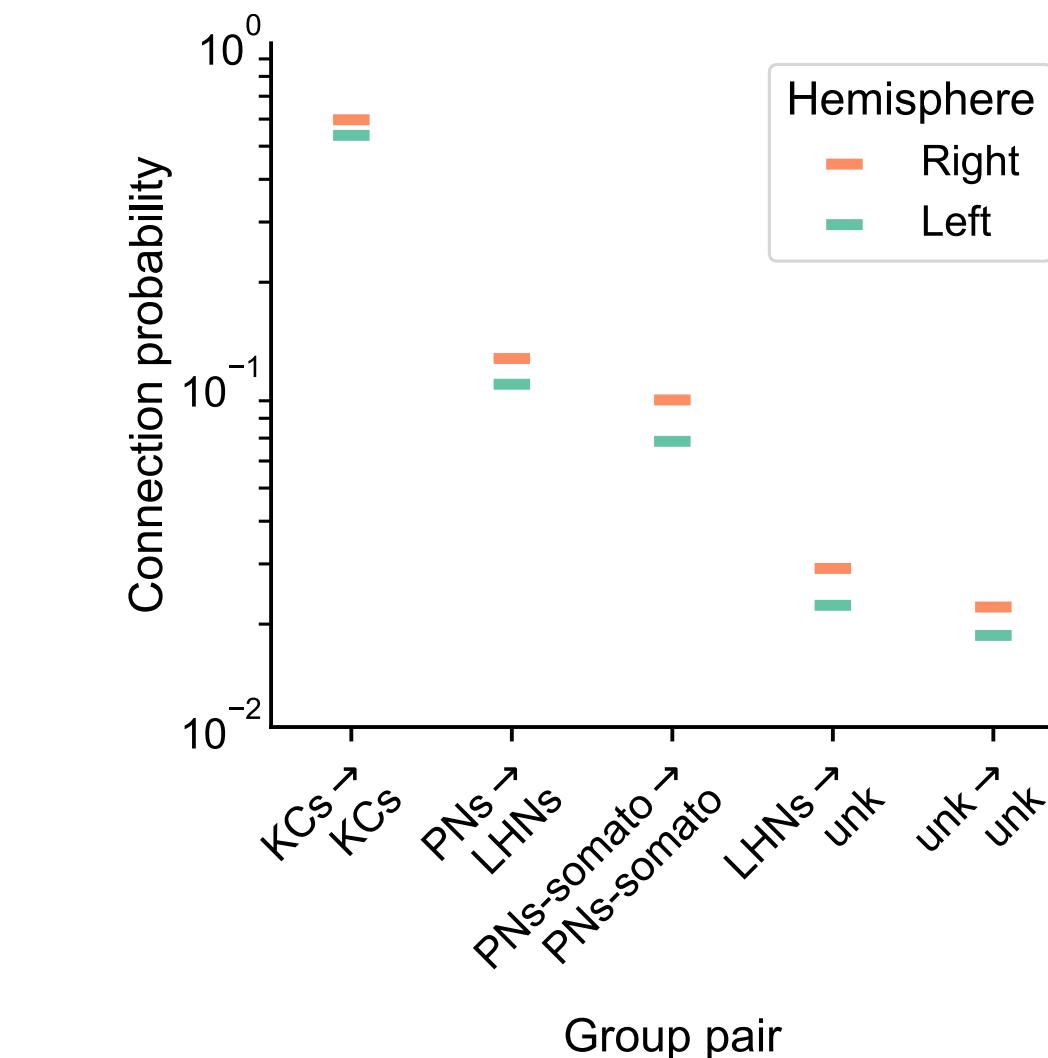


Fig 3C: For significant group connections, denser hemisphere probability is always higher.

## Density-adjusted group connection test (Model 3)

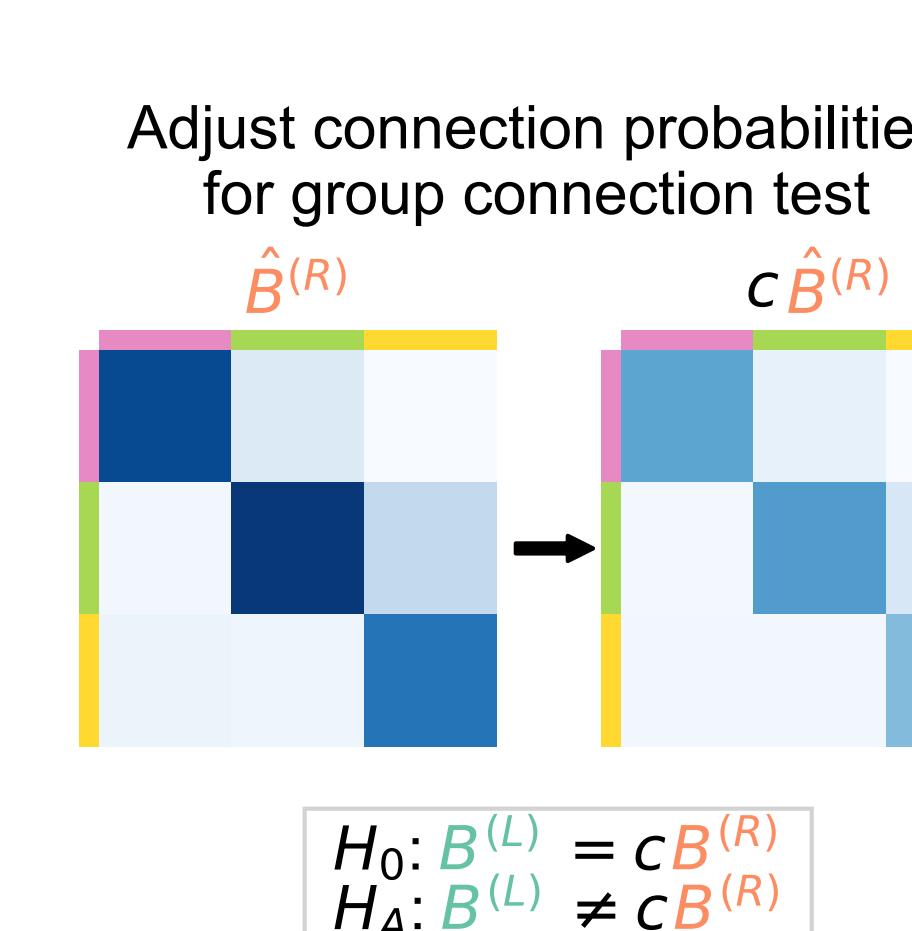


Fig 4A: Hypothesis from Fig 3 modified by a factor  $c$  set to make densities equal.

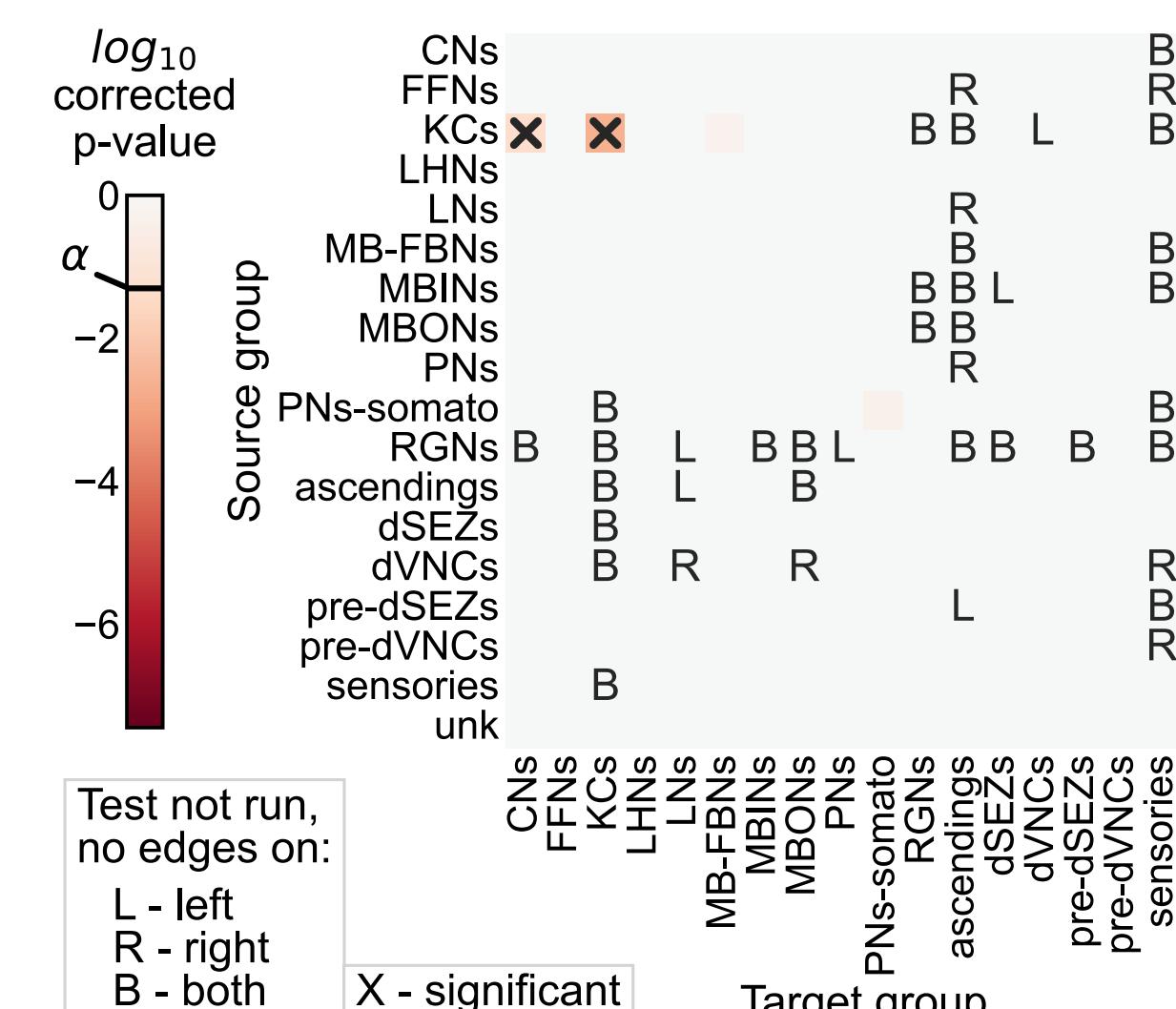


Fig 4B: Test comparing adjusted group connections rejected ( $p < 10^{-2}$ ); differences from KCs.

## Notions of bilateral symmetry

### With Kenyon cells

Model	$H_0$ (vs. $H_A \neq$ )	p-value
1	$p^{(L)} = p^{(R)}$	$< 10^{-23}$
2	$B^{(L)} = B^{(R)}$	$< 10^{-7}$
3	$B^{(L)} = cB^{(R)}$	$< 10^{-2}$

### Without Kenyon cells

Model	$H_0$ (vs. $H_A \neq$ )	p-value
1	$p^{(L)} = p^{(R)}$	$< 10^{-26}$
2	$B^{(L)} = B^{(R)}$	$< 10^{-2}$
3	$B^{(L)} = cB^{(R)}$	0.51

## Edge weight thresholds

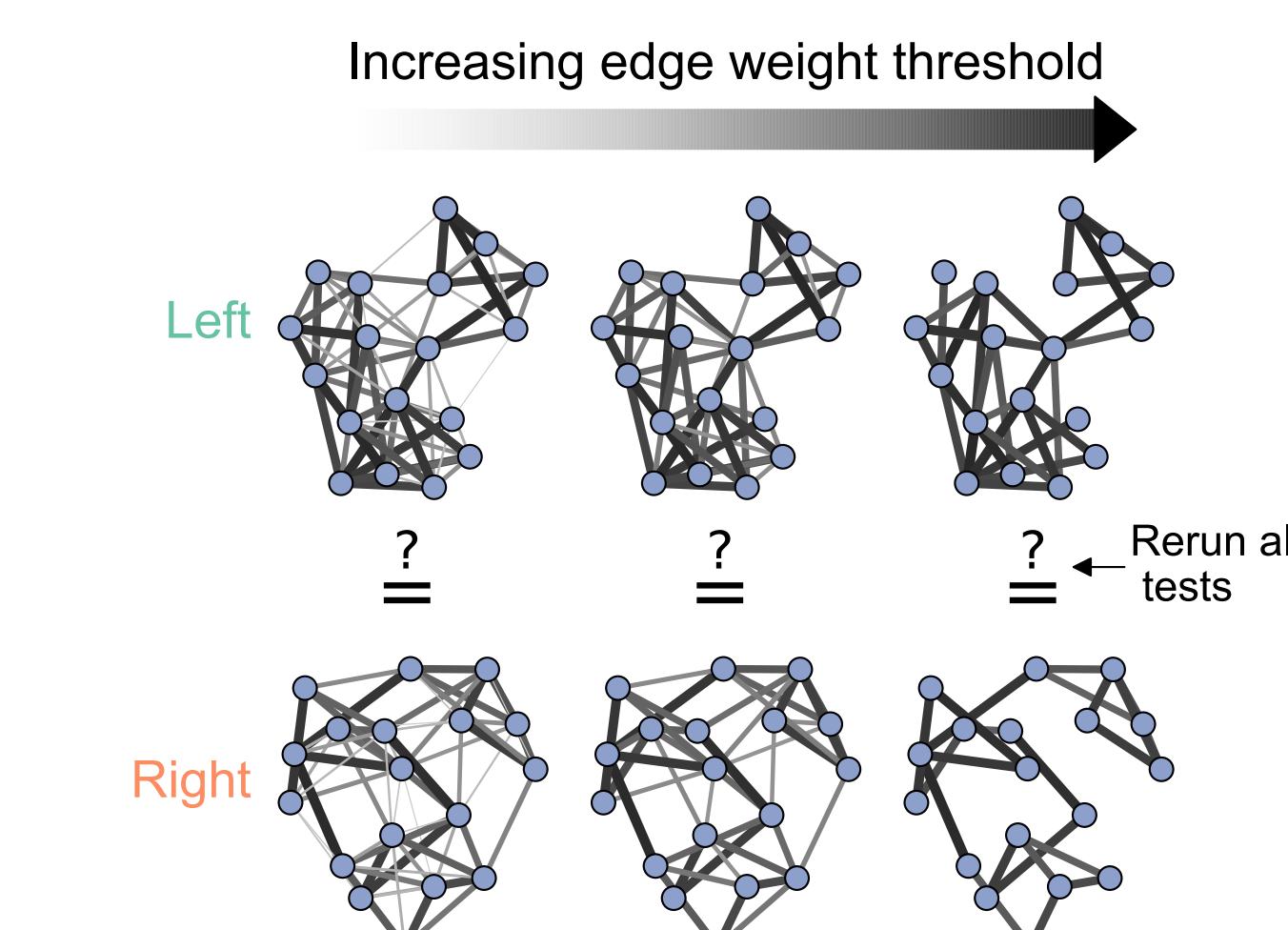


Fig 5A: Removed edges w/ weight (synapse count or percentage of input to downstream neuron) below some threshold, tested symmetry for each pair of networks.

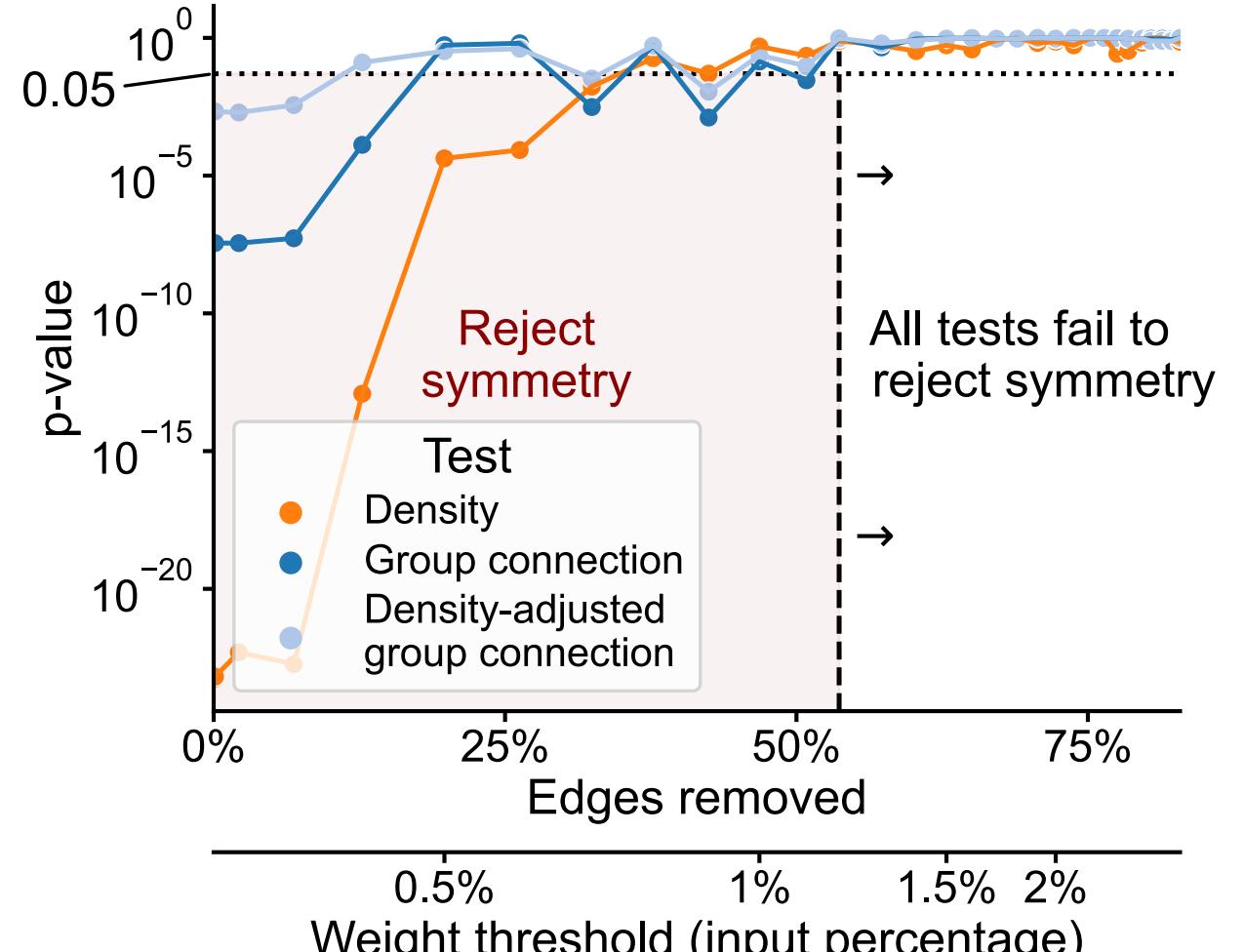


Fig 5B: Did not detect asymmetry in networks of only top ~50% of edges (by input percentage) under models studied here. Not true using synapse counts edge weights (not shown).

## Limitations and extensions

- Other models to consider (e.g. random dot product graph [3])
- Other sensible neuron groupings for group connection test
- Matching nodes across networks leads to new models, likely more power

## Code



## This work



## References

- [1] Winding, Pedigo et al. "The complete connectome of an insect brain," In preparation (2022)
- [2] Chung et al. "Statistical connectomics," Ann. Rev. Statistics and its Application (2021)
- [3] Athreya et al. "Statistical inference on random dot product graphs: a survey," JMLR (2017)

## Funding

B.D.P. supported by the NSF GRFP (DGE1746891). J.T.V. supported by NSF CAREER Award (1942963). J.T.V + C.E.P. supported by NIH BRAIN Initiative (RF1MH123233). Findings and conclusions expressed are those of the authors and not necessarily those of the funders.

## Acknowledgements

Marta Zlatic's lab, Albert Cardona's lab and all tracers for the amazing dataset and many ideas. NeuroData lab for feedback. Many at Microsoft Research for w/ graspologic.