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

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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 is one such comparison; has been investigated, but not clearly defined as a network hypothesis.

Larval *Drosophila* brain connectome

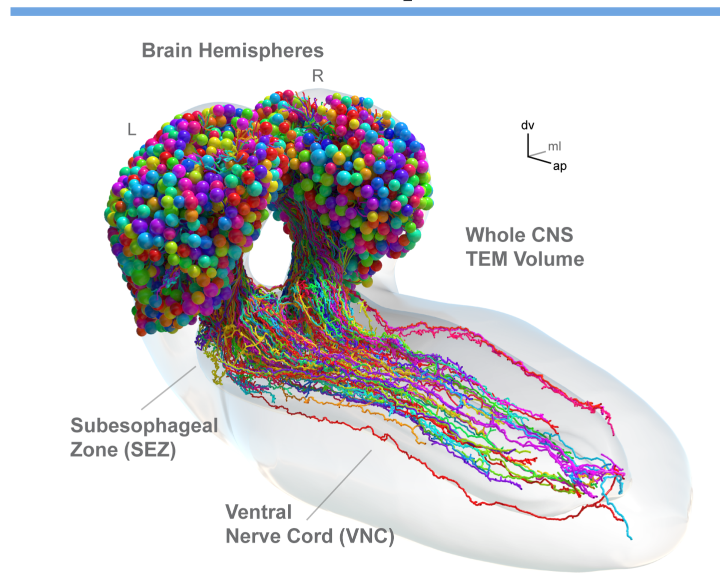

Fig 1A: 3D rendering of a larval *Drosophila* brain connectome [1] comprised of ~3k neurons and ~544k synapses.

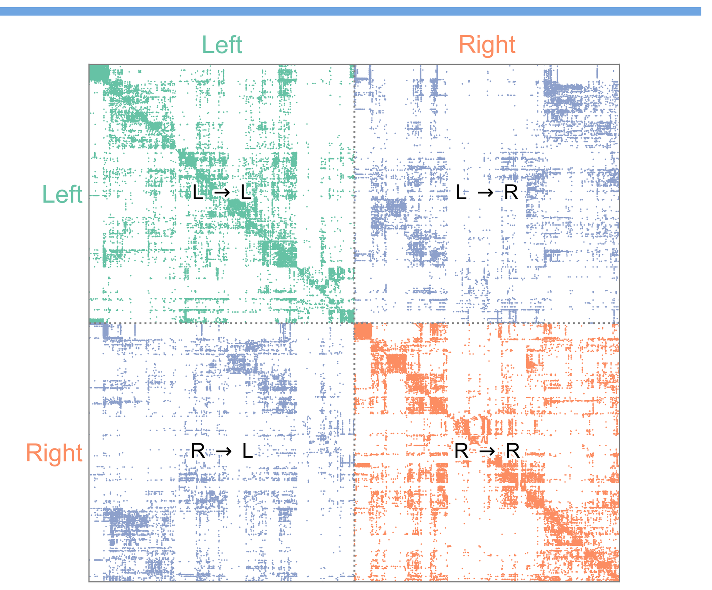

Fig 1B: Directed, binary adjacency matrix sorted by brain hemisphere. We compare $L \rightarrow L$ vs. $R \rightarrow R$ subgraphs.

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)

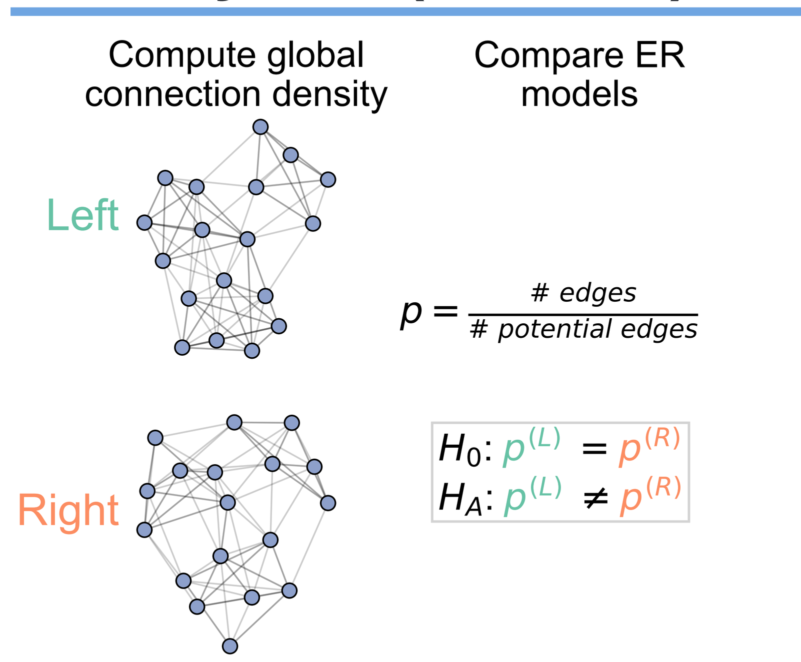

Fig 2A: Testing symmetry under Erdos-Renyi (ER) model [2] compares global connection probability (density), here via Fisher's exact test.

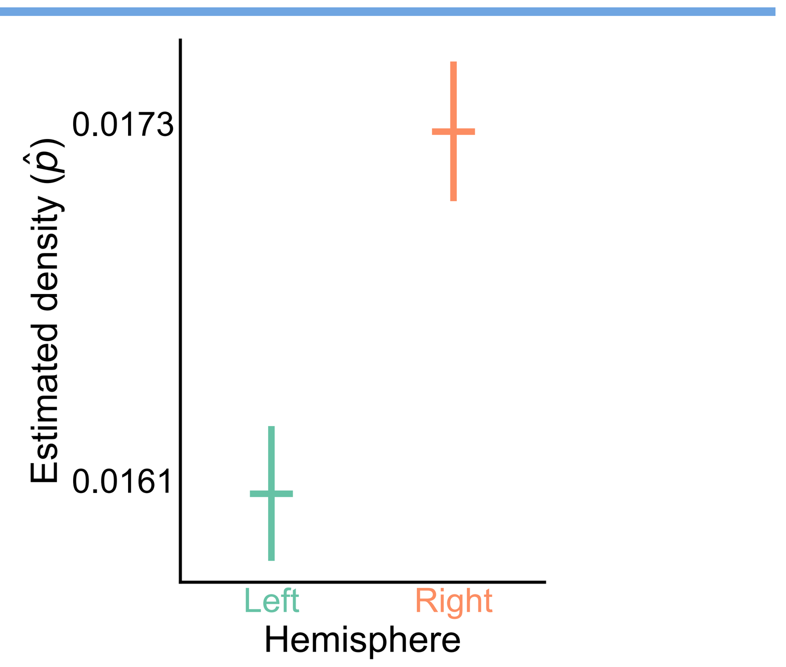

Fig 2B: Test comparing densities rejected $(p{<}10^{-23})$, even the simplest model parameter differs between hemispheres.

Group connection test (Model 2)

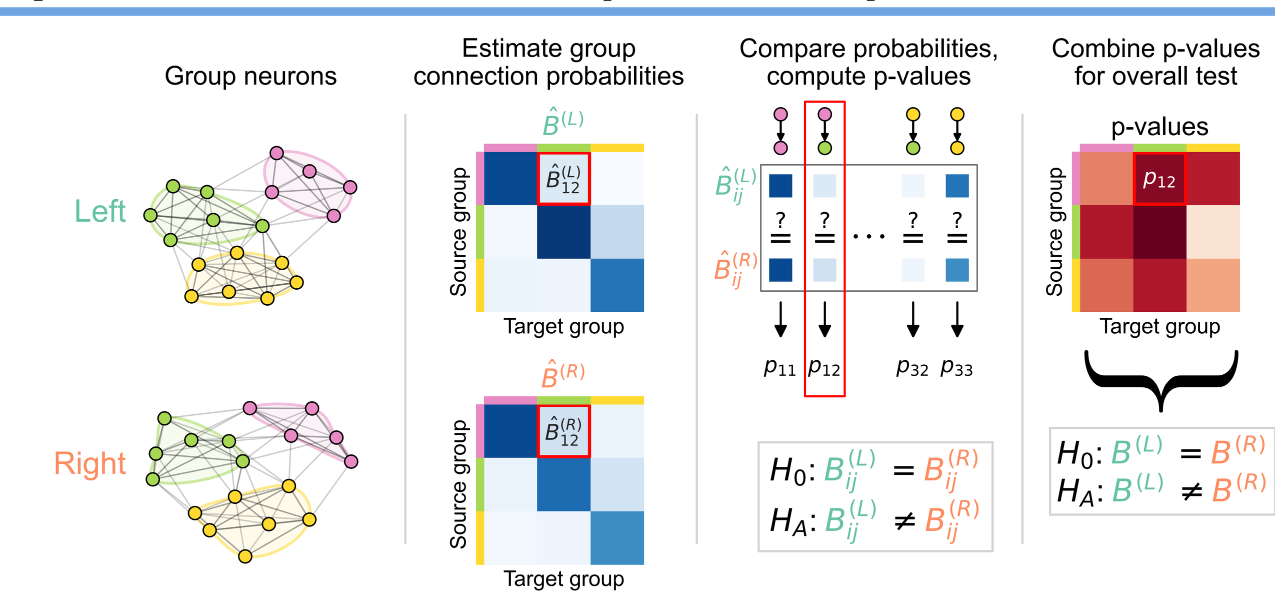

Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types [1]).

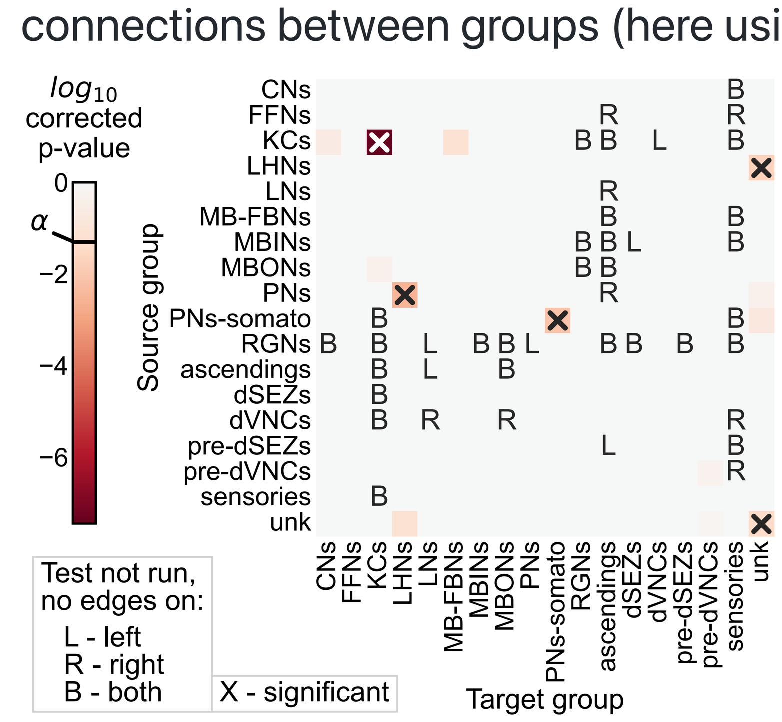

Fig 3B: Test comparing group connections rejected $(p{<}10^{-7})$; five specific connections differ.

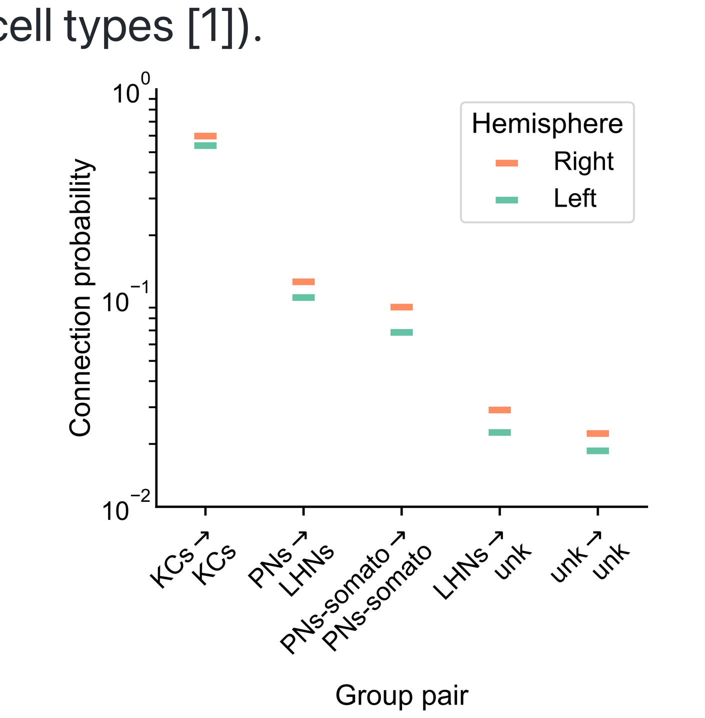

Fig 3C: For significant group connections, denser hemisphere probability is always higher.

Density-adjusted group connection test (Model 3)

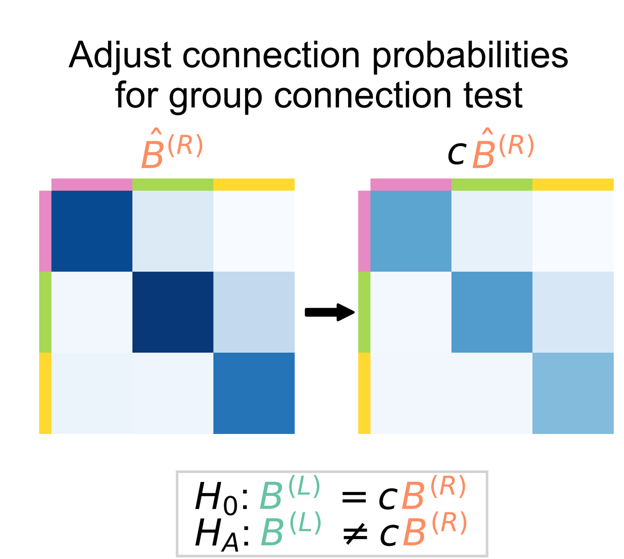

Fig 4A: Hypothesis from Fig 3 modified by a factor c set to make densities equal.

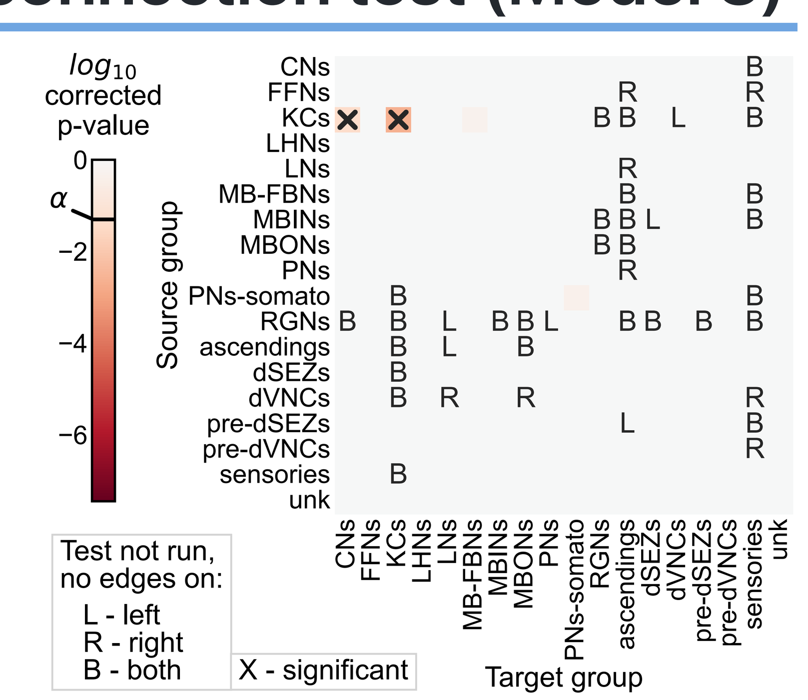

Fig 4B: Test comparing adjusted group connections rejected $(p{<}10^{-2})$; differences from KCs.

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

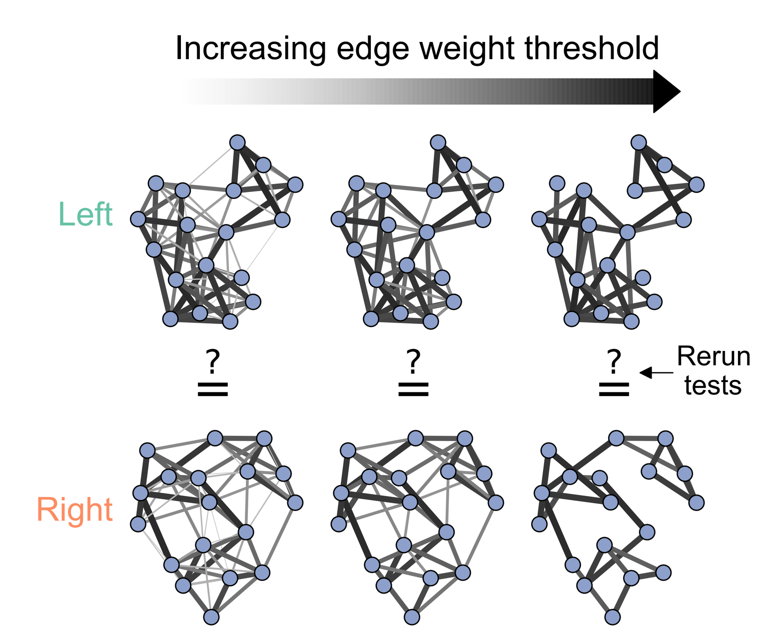

Fig 5A: Removed edges w/ weight (synapse count or percentage of input to downstream neuron) below some threshold, tested symmetry for each pair of networks.

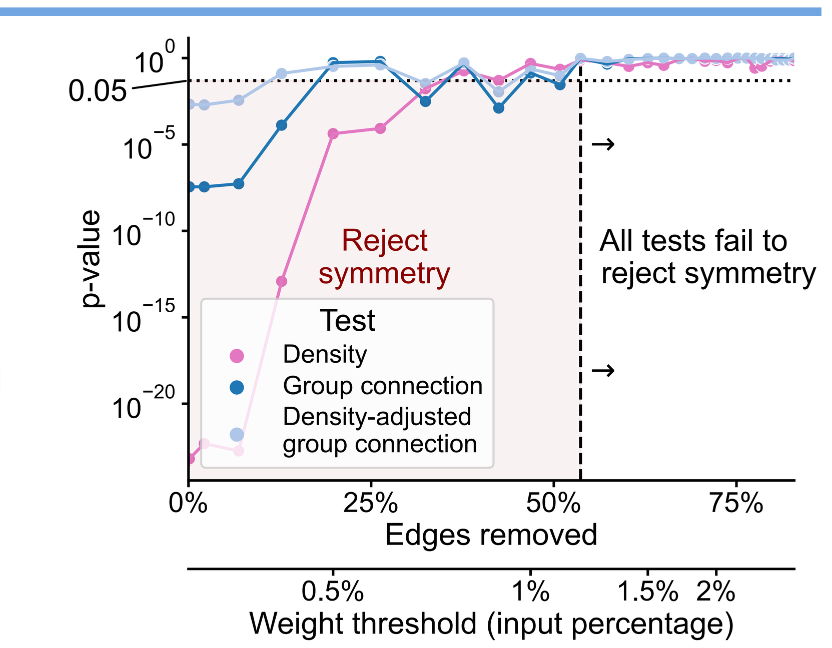

Fig 5B: Did not detect asymmetry in networks of only top ~50% of edges (by input percentage) under models studied here. Not true using synapse counts edge weights (not shown).

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

graspologic downloads 116k Stars 245

This work jupyter book

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)

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