Is a whole insect brain connectome bilaterally symmetric?
A case study on comparing two networks

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Summary

- Aimed to define bilateral symmetry for a pair of networks, and formally test this hypothesis.
- Left and right hemispheres are significantly different under even the simplest model of a pair of networks
- Left and right differ significantly in cell type connection probabilities, even when adjusting for the difference in density
- Difference between hemispheres can be explained as combination of network-wide and cell type-specific effects
- 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

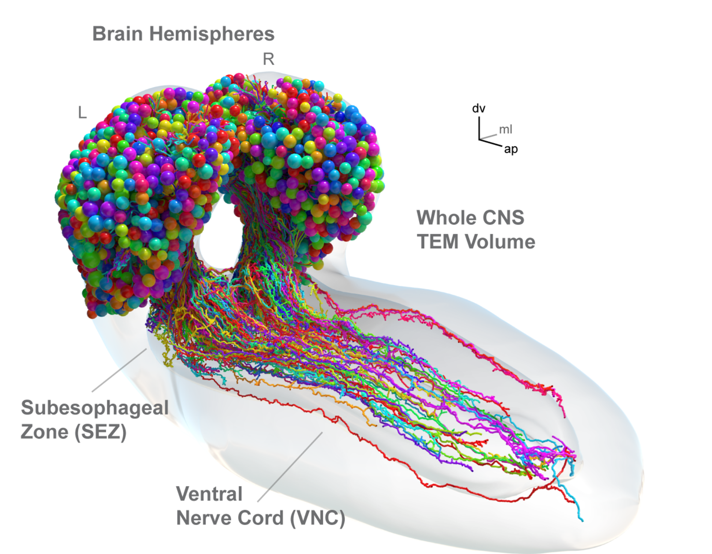

Fig 1A: 3D rendering of larval *Drosophila* brain connectome [1]. Comprised of ~3k neurons and ~544k synapses.

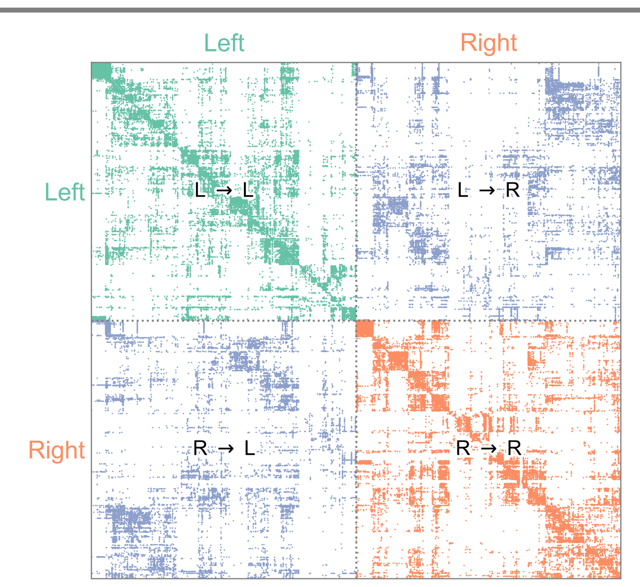

Fig 1B: Adjacency matrix sorted by brain hemisphere. We compare $L \to L$ vs. $R \to R$ subgraphs.

Are the left and right networks "different"?

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

Density test (Model 1)

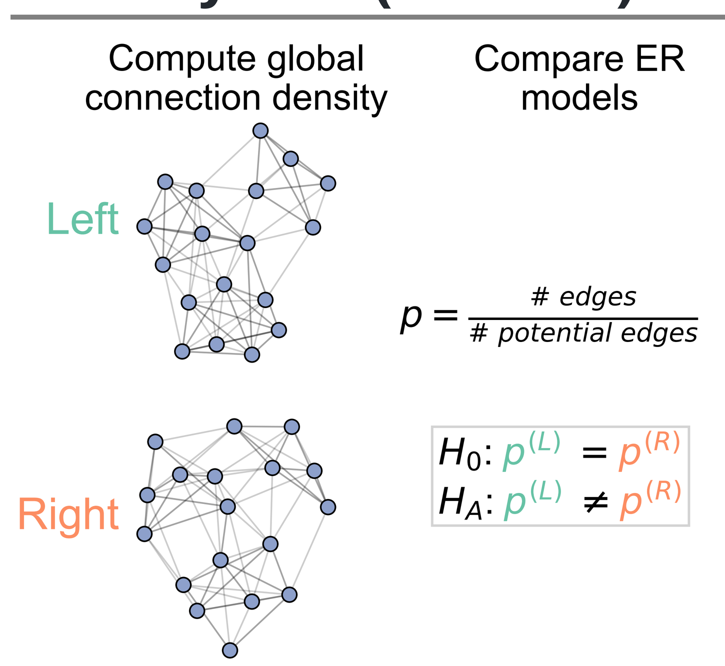

Fig 2A: Testing symmetry under Erdos-Renyi (ER) model [2] amounts to comparing densities (here via Fisher's exact test).

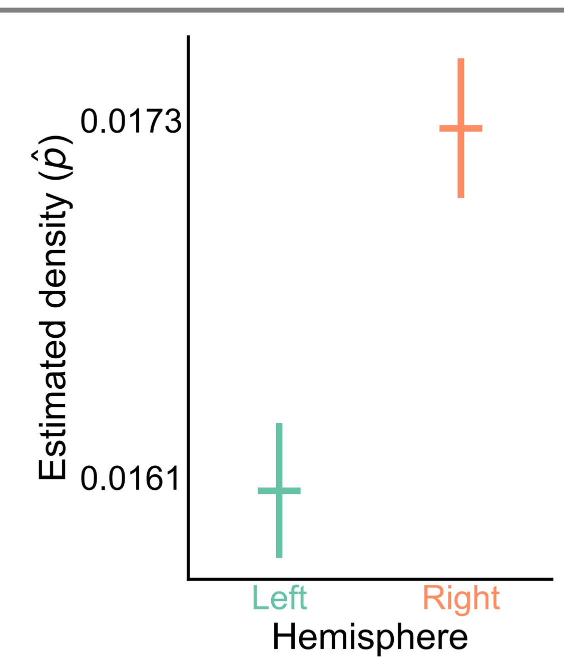

Fig 2B: Densities are significantly different between hemispheres ($p < 10^{-23}$).

Group connection test (Model 2)

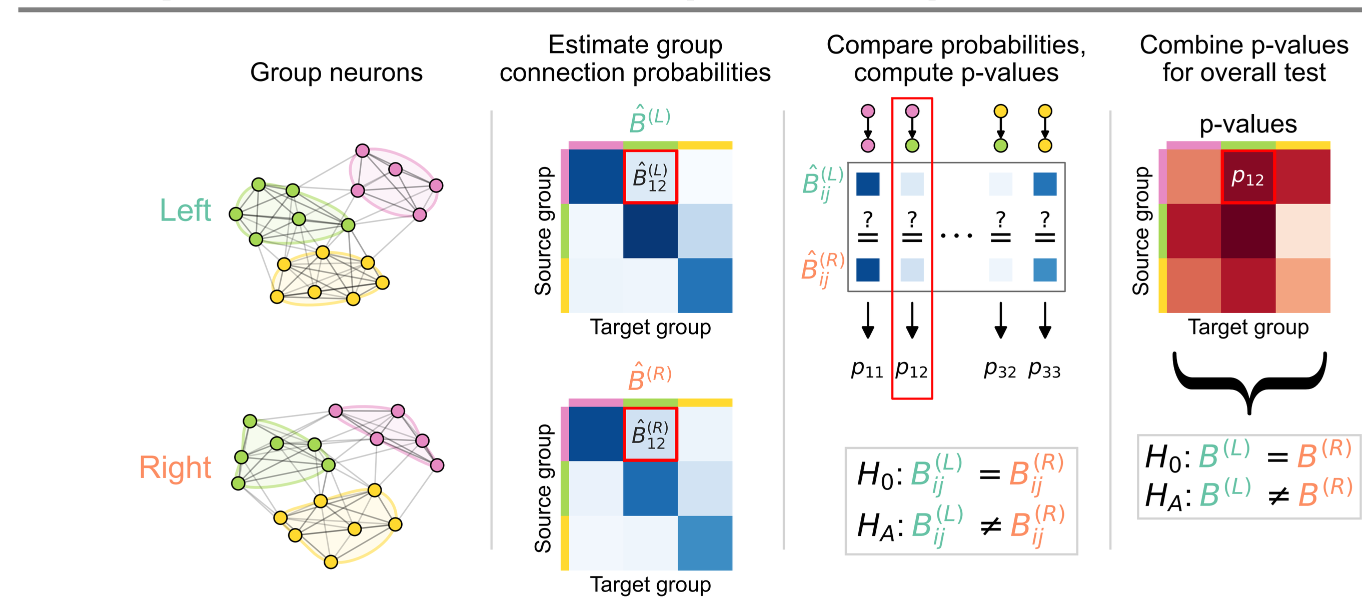

Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types).

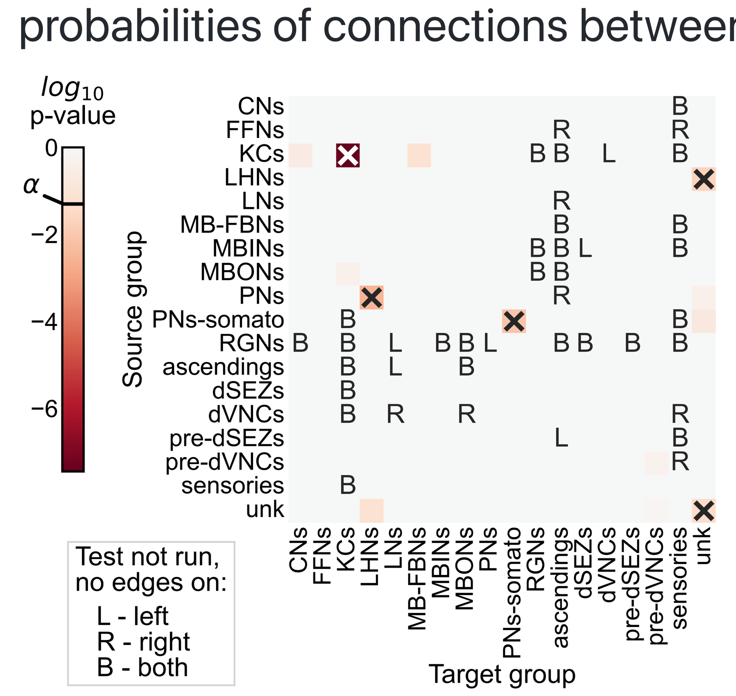

Fig 3B: Test comparing group connections rejects ($p < 10^{-7}$); five specific connections differ.

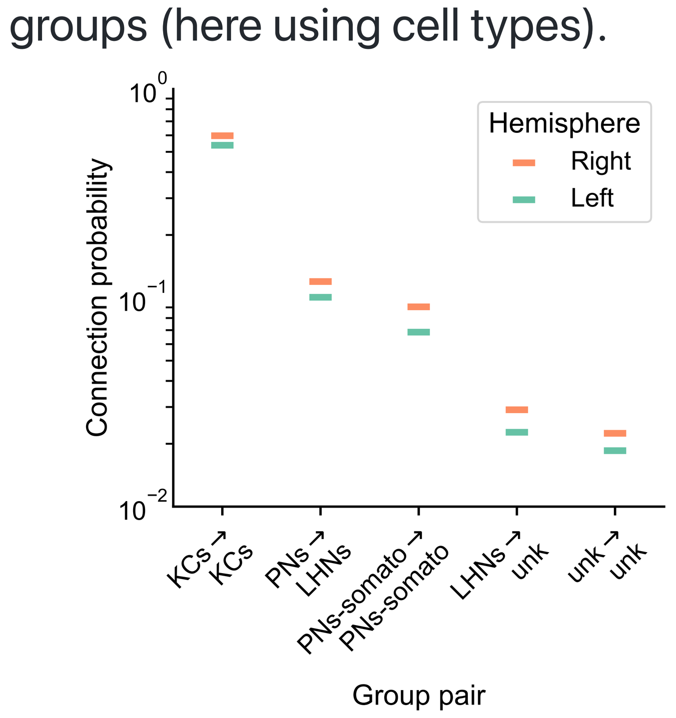

Fig 3C: For significant group connections, denser hemisphere probability is always higher.

Density-adjusted group connection test (Model 3)

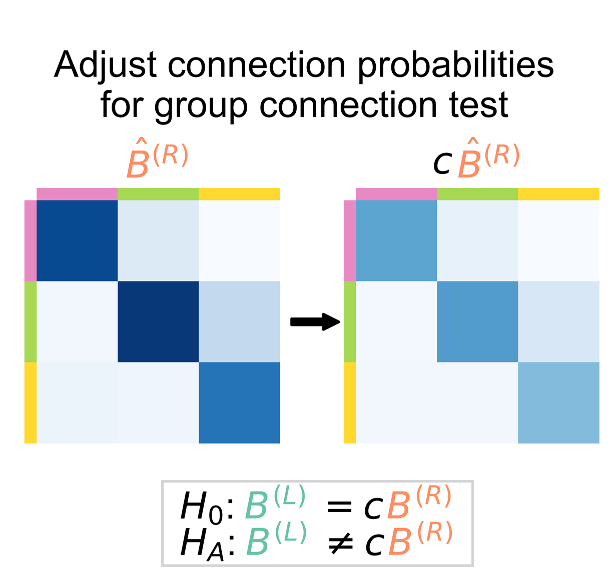

Fig 4A: Hypothesis from Fig 3 modified by a factor c set to make densities equal.

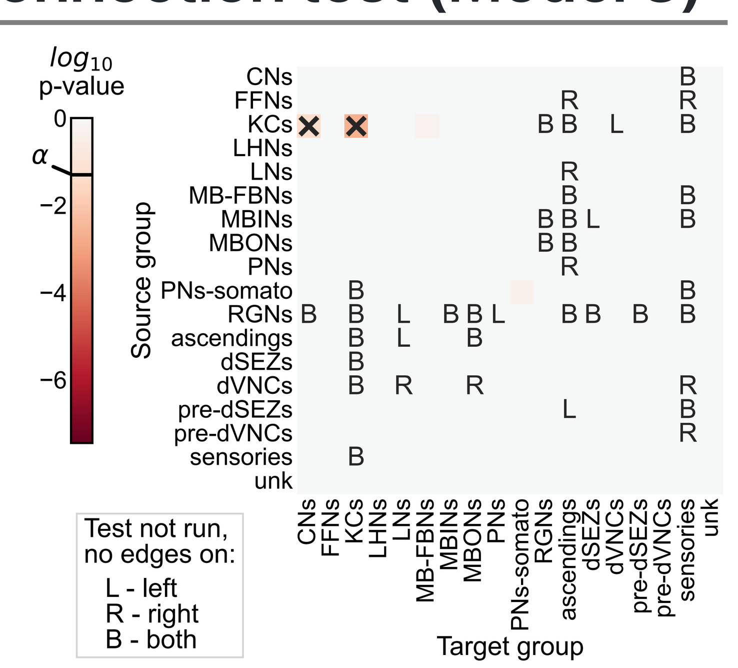

Fig 4B: Test comparing adjusted group connections rejects ($p < 10^{-2}$); two differing connections from KCs.

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

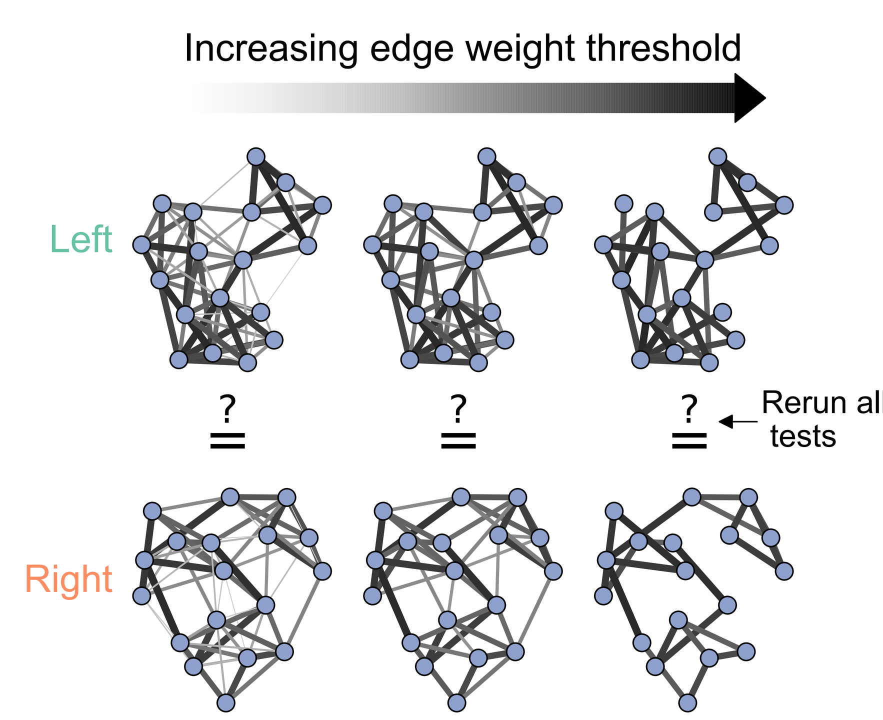

Fig 5A: Removed edges w/ weight (synapse count or percentage of input to downstream neuron) below some threshold, tested symmetry for each pair of networks.

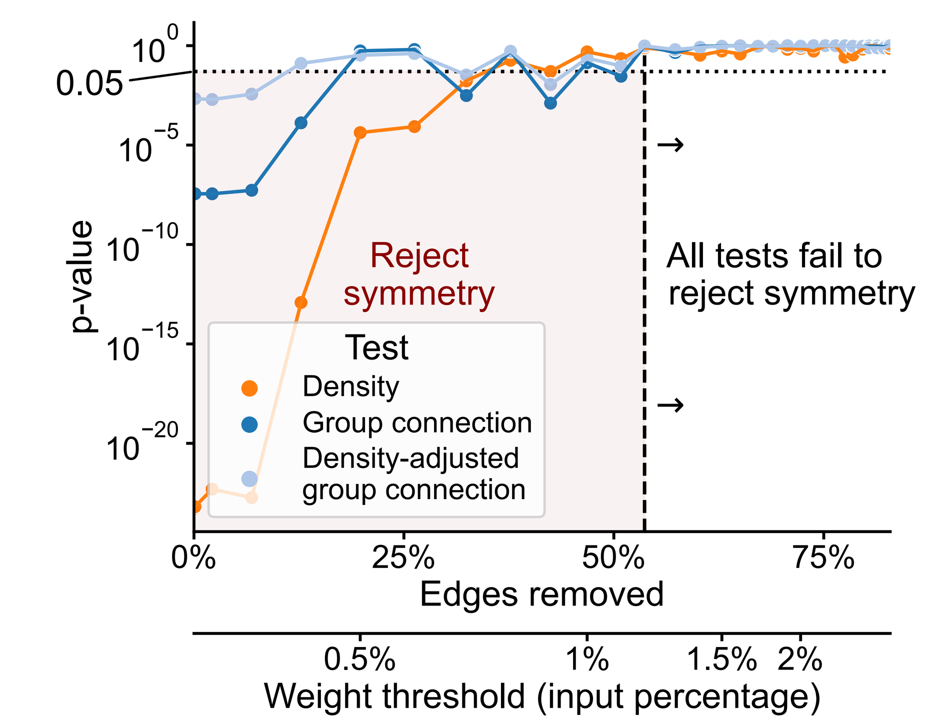

Fig 5B: Higher edge weight thresholds generally made networks more symmetric. Less apparent when using synapse counts as edge weights (not shown).

Limitations and extensions

- Many other models to consider (e.g. random dot product graph [3])
- Many other potential neuron groupings for group connection testing
- Matched nodes between networks

Code

graspologic downloads 116k Stars 245

This work jupyter book

References

[1] Winding, Pedigo et al. "The complete connectome of an insect brain," In prep. (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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