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

Benjamin D. Pedigo[1*], Mike Powell[1], Eric W. Bridgeford[1], Michael Winding[2], Carey E. Priebe[1], Joshua T. Vogelstein[1]

1 - Johns Hopkins University, 2 - University of Cambridge, ∗ - correspondence: bpedigo@jhu.edu @bdpedigo (Github) @bpedigod (Twitter) https://bdpedigo.github.io/

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

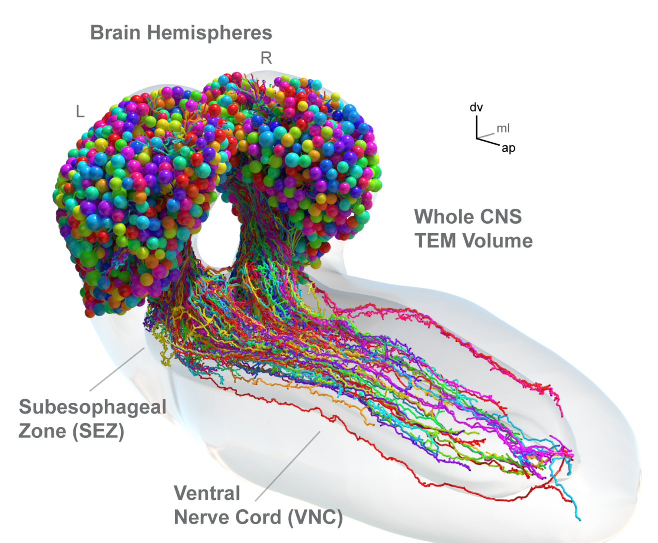

Fig 1A: 3D rendering of larval *Drosophila* brain connectome [1]. Comprised of ~3k neurons and ~544k synapses.

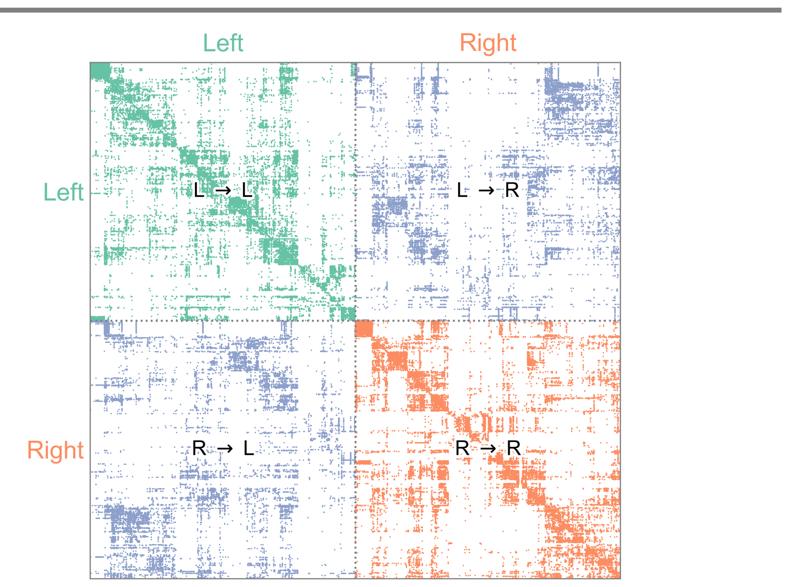

Fig 1B: Adjacency matrix sorted by brain hemisphere. We focus on comparing $L \to L$ vs. $R \to R$ subgraphs.

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 testing (1)

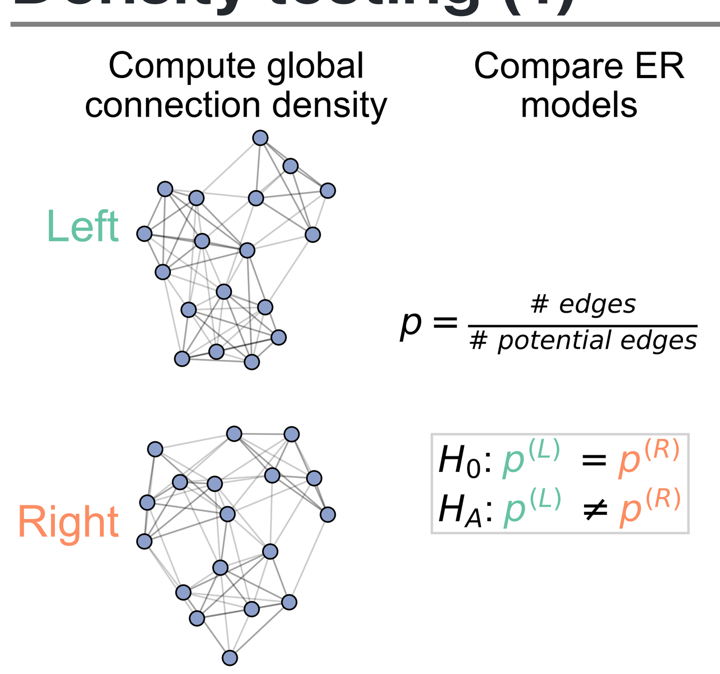

Fig 2A: Testing symmetry under Erdos-Renyi (ER) model [2] amounts to comparing densities (here via Fisher's exact test).

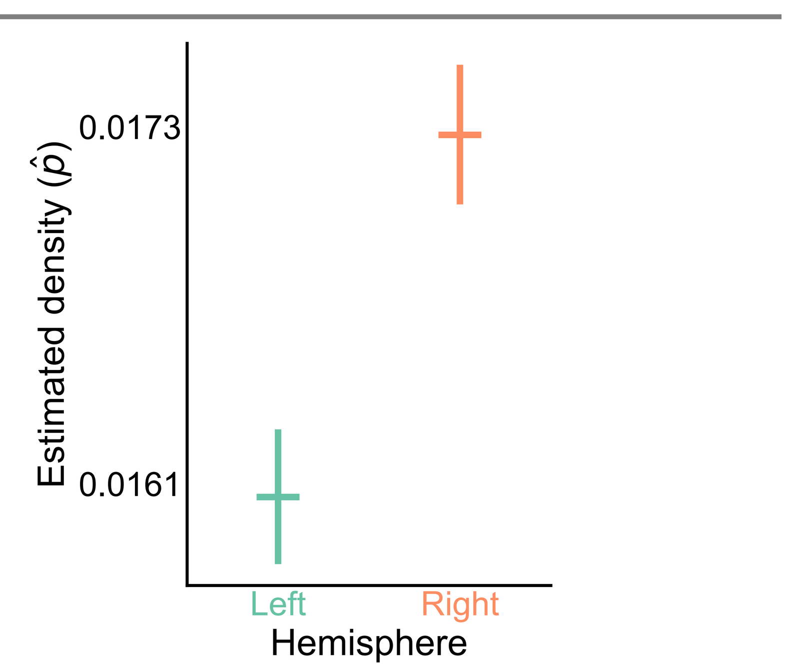

Fig 2B: Densities are significantly different between hemispheres ($p < 10^{-23}$).

Group connection testing (2)

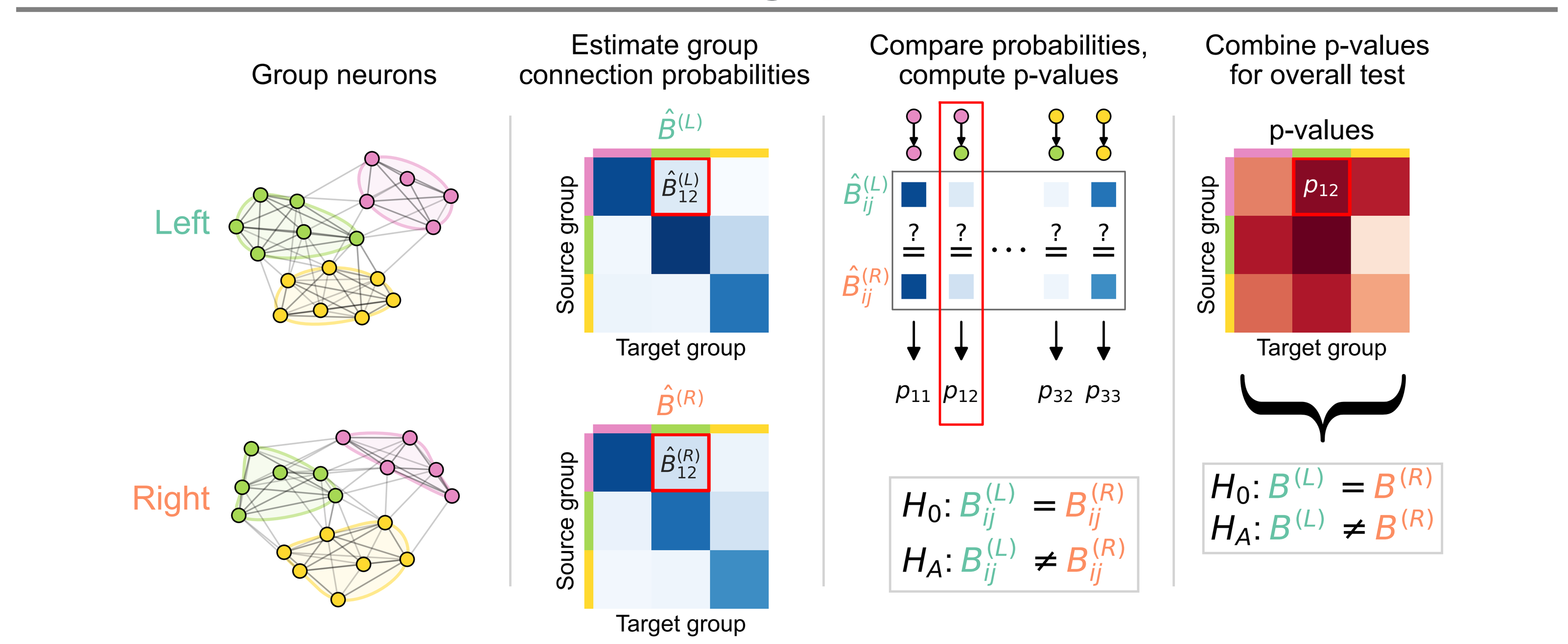

Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types).

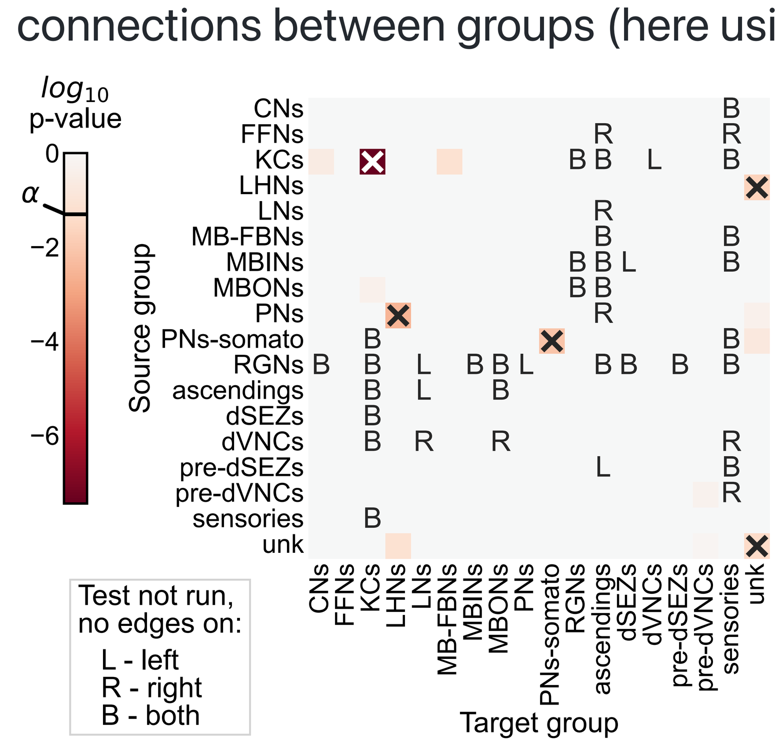

Fig 3B: Corrected p-values for each group connection. P-value test of equal group connections is $< 10^{-8}$.

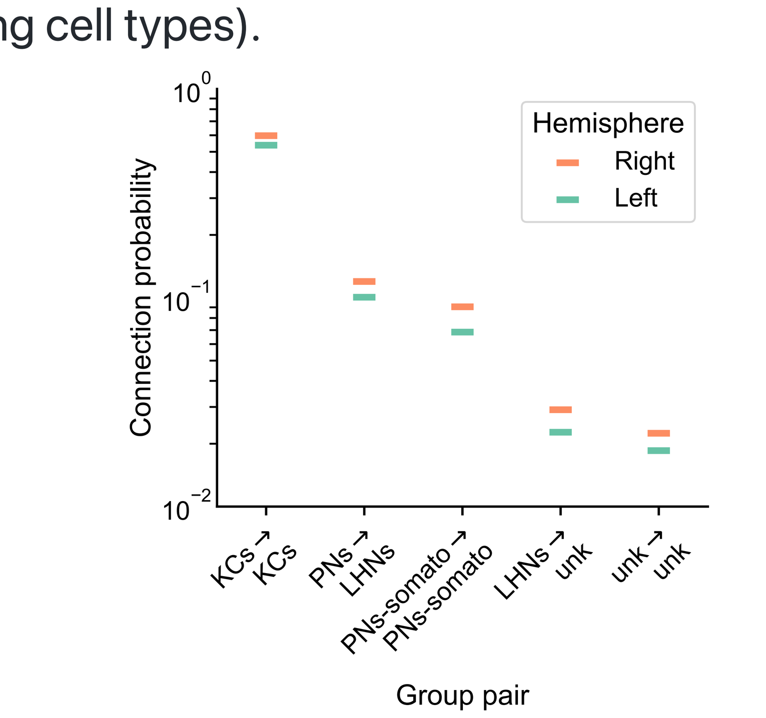

Fig 3C: Comparison of probabilities for significant connections: denser hemisphere probability always higher.

Density-adjusted group connection testing (3)

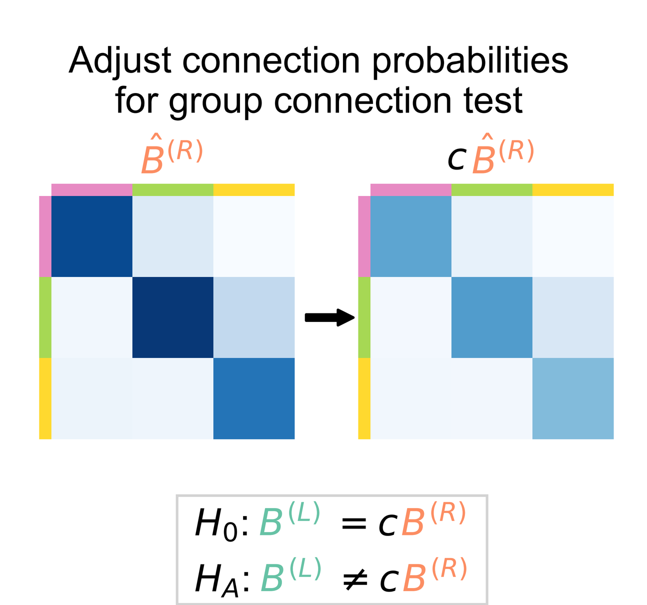

Fig 4A: Density-adjusted hypothesis, modified from Fig 3.

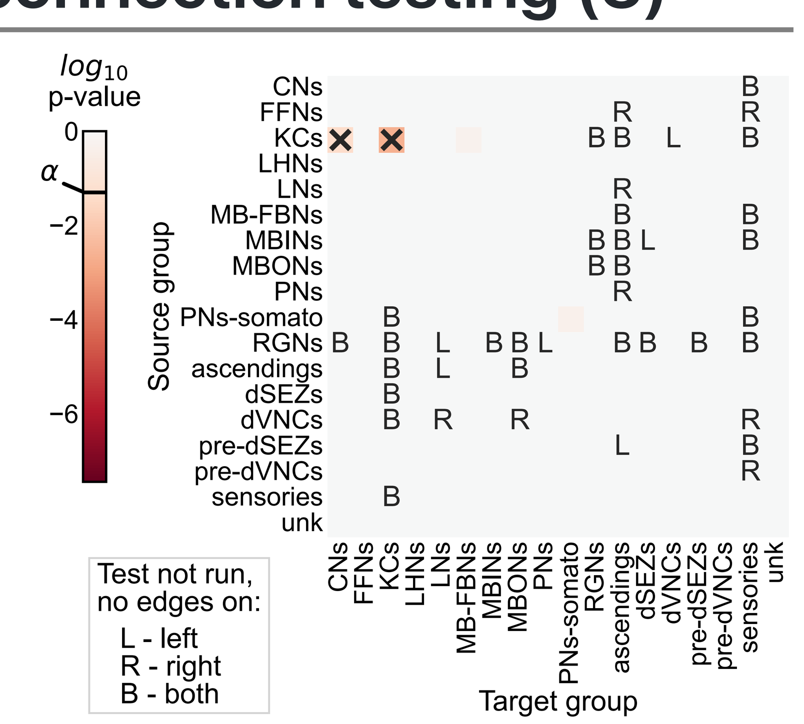

Fig 4B: Corrected p-values for group connections w/ density adjustment.

Notions of bilateral symmetry

With Kenyon cells

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

Without Kenyon cells

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

Edge weight thresholds

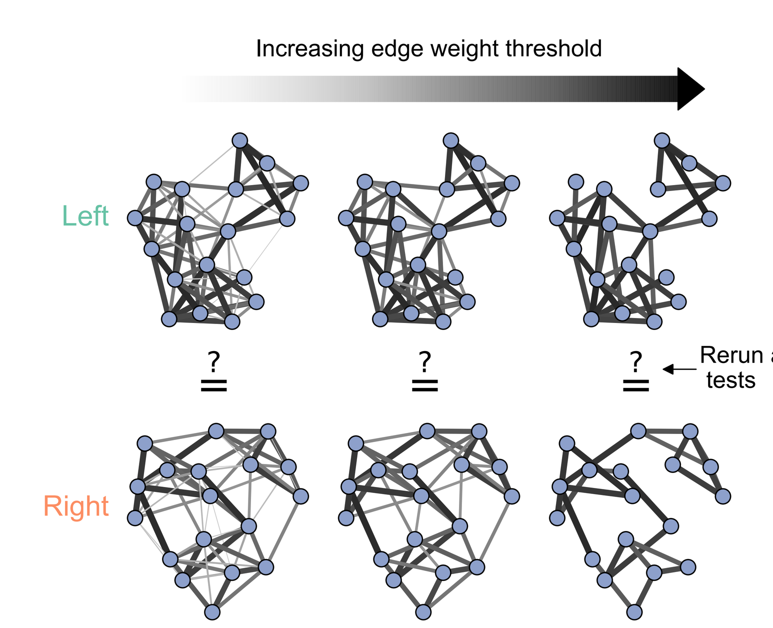

Fig 5A: Removed edges w/ weight (synapse count or proportion of input to downstream neuron) below some threshold, testing bilateral symmetry for each resulting pair of networks.

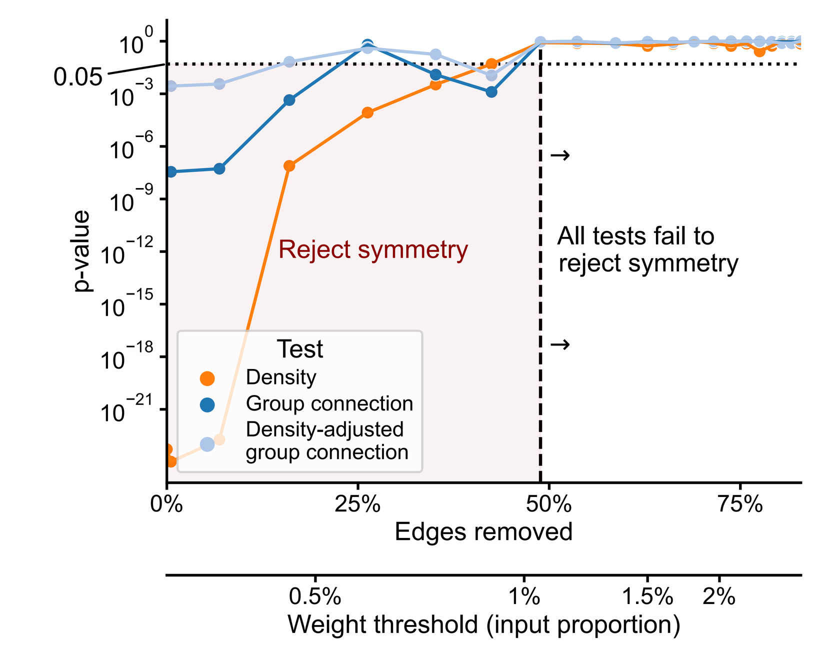

Fig 5B: Higher edge weight thresholds generally make networks more symmetric. Less apparent when using synapse counts as edge weights (not shown).

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 and references

graspologic downloads 115k Stars 245

github.com/microsoft/graspologic

jupyter book

github.com/neurodata/bilateral-connectome

[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)