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/

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

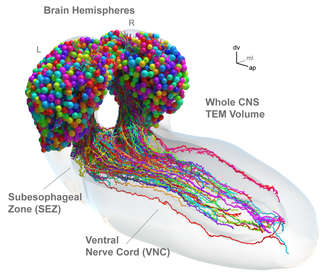

Fig 1A: 3D rendering of larval *Drosophila* brain connectome [1]. Comprised of ~3k neurons and ~544k synapses.

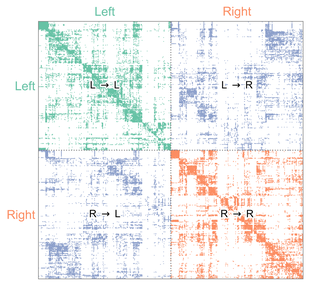

Fig 1B: Adjacency matrix sorted by brain hemisphere. We focus on comparing $L \to L$ vs. $R \to R$ subgraphs.

Are left and the right networks "different"?

Requires that we define what we mean by "different" for a network, and develop a test procedure for any definition.

Density testing

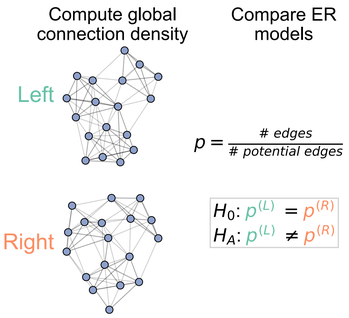

Fig 2A: Testing symmetry under Erdos-Renyi (ER) model amounts to comparing densities (here via Fisher's exact test).

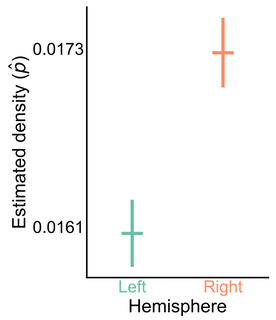

Fig 2B: Densities are significantly different between hemispheres ($p < 10^{-23}$).

this is some overflow here i

Group connection testing

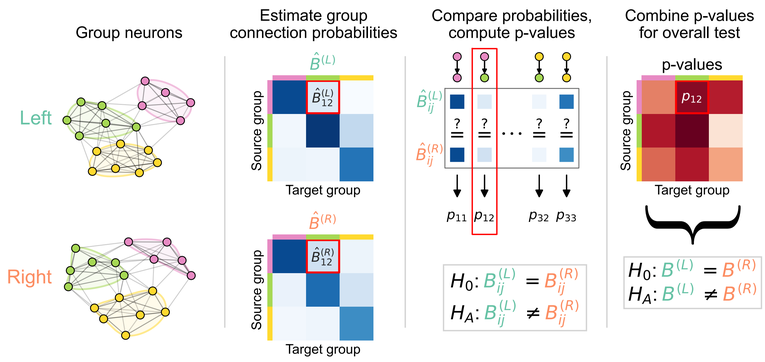

Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types).

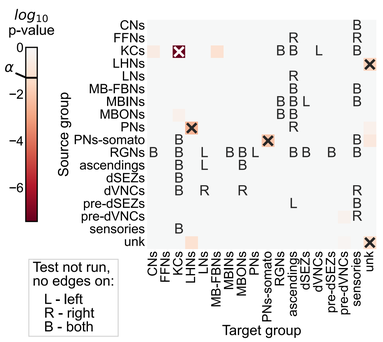

Fig 3B: Corrected p-values for each group connection.

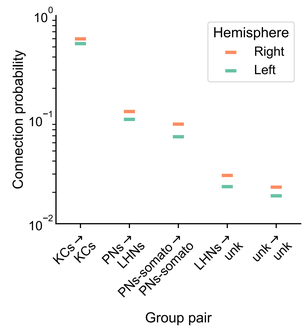

Fig 3C: Comparison of probabilities for significant connections.

Density-adjusted group connection testing

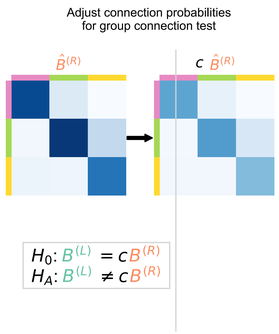

Fig 4A: Density-adjusted hypothesis from Fig 3.

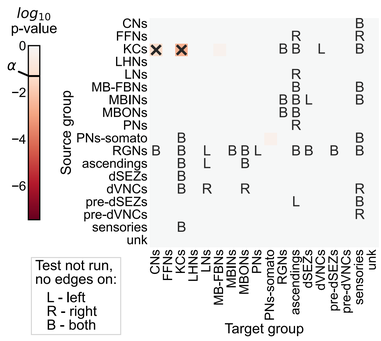

Fig 4B: Corrected p-values for group connections w/ density adjustment.

Notions of bilateral symmetry

Model	H_0 (vs. $H_A \neq$)	KCs	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	$B^{(L)} = cB^{(R)}$	+	≈ 0.002	Reject above even after accounting for density
ER	$p^{(L)} = p^{(R)}$	-	$< 10^{-26}$	Reject densities the same (w/o KCs)
SBM	$B^{(L)} = B^{(R)}$	-	≈ 0.003	Reject group connection probabilities the same (w/o KCs)
aSBM	$B^{(L)} = cB^{(R)}$	-	≈ 0.43	Don't reject above after density adjustment (w/o KCs)

Edge weight thresholds

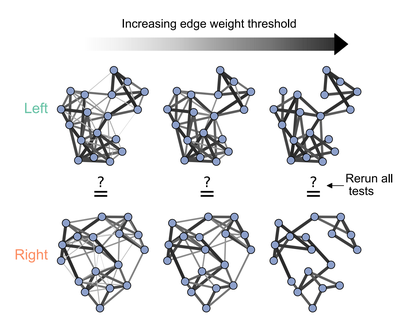

Fig 5A: Removed edges below some edge weight threshold, examining bilateral symmetry for each resulting pair of networks.

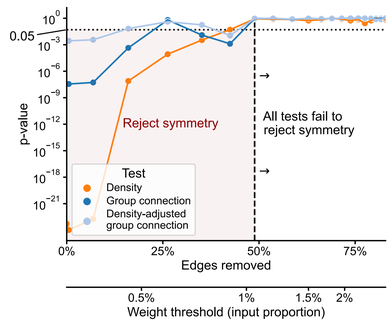

Fig 5B: Higher edge weight thresholds generally make networks more symmetric. Less apparent when using synapse counts as edge weights (not shown).

Limitations and extensions

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

Code

graspologic

downloads 115k

Stars 245

github.com/microsoft/graspologic

jupyter book

github.com/neurodata/bilateral-connectome

References

[1]: Winding, Pedigo et al. *The complete connectome of an insect brain* In prep. (2022)