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

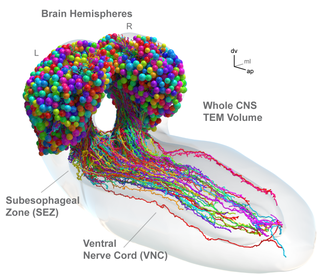

Fig 1A: 3D rendering of larval *Drosophila* brain connectome [1]. Comprised of ~3k neurons and ~544k synapses.

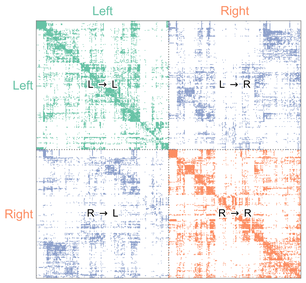

Fig 1B: Adjacency matrix sorted by brain hemisphere. We focus on comparing $L \to L$ vs. $R \to R$ subgraphs.

Are the left and right networks "different"?

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

Density testing

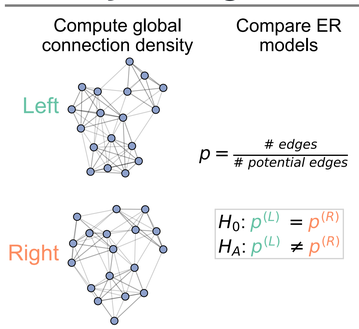

Fig 2A: Testing symmetry under Erdos-Renyi (ER) model [2] amounts to comparing densities (here via Fisher's exact test).

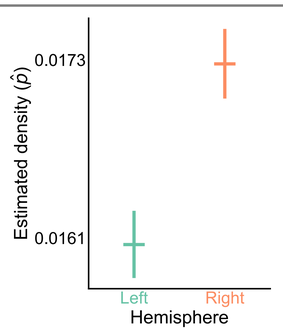

Fig 2B: Densities are significantly different between hemispheres ($p < 10^{-23}$).

Group connection testing

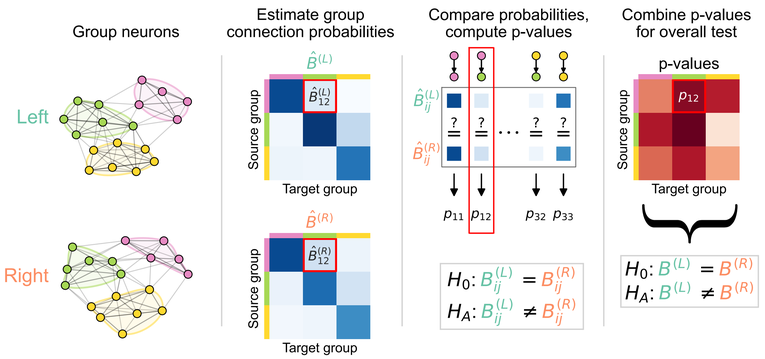

Fig 3A: Testing under stochastic block model (SBM) compares probabilities of connections between groups (here using cell types).

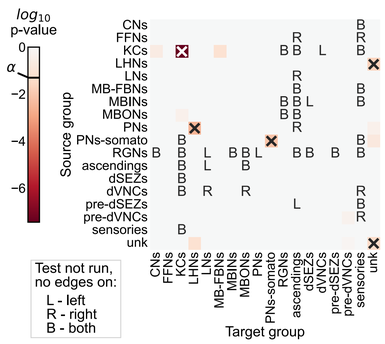

Fig 3B: Corrected p-values for each group connection.

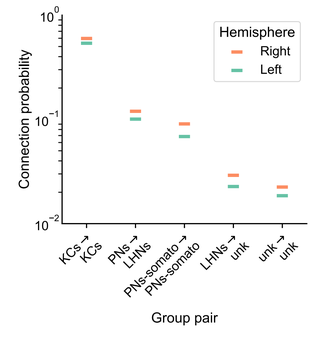

Fig 3C: Comparison of probabilities for significant connections.

Density-adjusted group connection testing

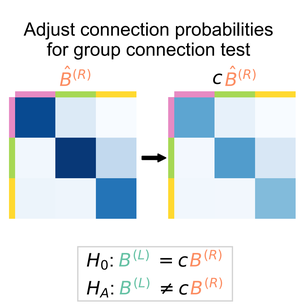

Fig 4A: Density-adjusted hypothesis, modified from Fig 3.

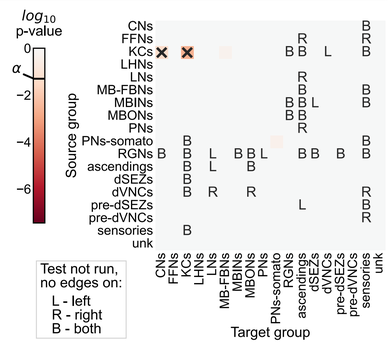

Fig 4B: Corrected p-values for group connections w/ density adjustment.

Removing Kenyon cells

Reran all tests after removing the asymmetric cell type (see below)

Notions of bilateral symmetry

Model	H_0 (vs. $H_A \neq$)	KCs	p-value	Interpretation
ER	$p^{(L)} = p^{(R)}$	+	$< 10^{-23}$	Reject equal densities
SBM	$B^{(L)} = B^{(R)}$	+	$< 10^{-7}$	Reject equal group connection probabilities
aSBM	$B^{(L)} = cB^{(R)}$	+	≈ 0.002	Reject above even w/ density adjustment
ER	$p^{(L)} = p^{(R)}$	-	$< 10^{-26}$	Reject equal densities
SBM	$B^{(L)} = B^{(R)}$	-	≈ 0.003	Reject equal group connection probabilities
aSBM	$B^{(L)} = cB^{(R)}$	-	≈ 0.43	Fail to reject above after density adjustment

Edge weight thresholds

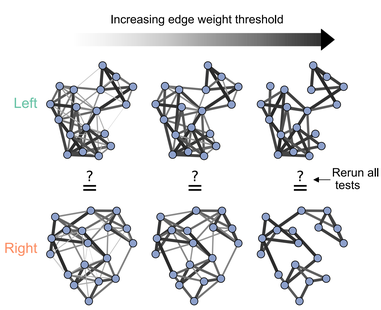

Fig 5A: Removed edges below some edge weight (synapse count or proportion of input to downstream neuron) threshold, testing bilateral symmetry for each resulting pair of networks.

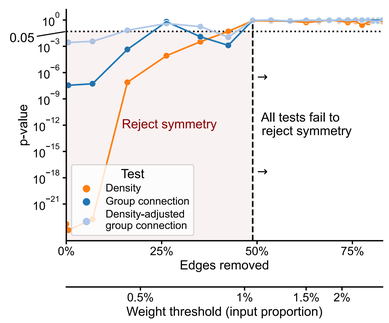

Fig 5B: Higher edge weight thresholds generally make networks more symmetric. Less apparent when using synapse counts as edge weights (not shown).

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)