Statistical Modeling of Structural Connectomes Reveal High Genetic Influence on Connectivity

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Summary

- Aimed to define heritability for populations of connectomes using statistical modelling.
- Structural connectomes are heritable without controlling for neuroanatomy.
- Neuroanatomy is also highly heritable
- Connectomes remain heritable after controlling for effects of neuroanatomy on connectomes.
- Provide tools for future analysis on populations of connectomes.

Motivation

- Understanding how brain connectivity is influenced by genetics can improve our understanding of brain function and diseases.
- Current methods of analyzing connectomes or hertability exhibit limitations:
  - Selection Graph theoretic features
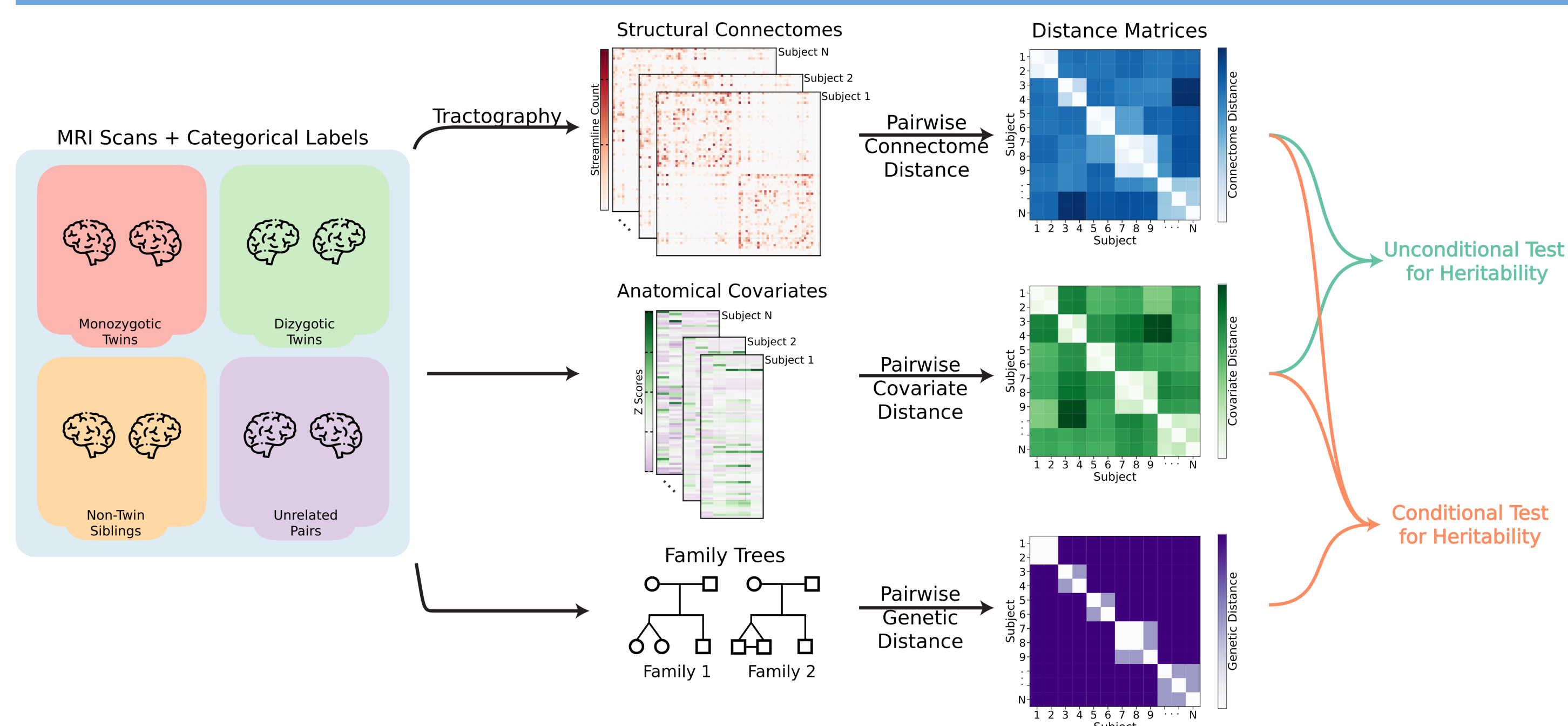 - Multivariate normality assumptions

Overview of Analysis

Fig 1: Overview of the framework for measuring heritability of connectomes.

Do changes in genome cause changes in connectomes?

Causal Analysis of Effect of Genome on Connectomes

- Genome directly affects the structural connectome.
- Neuroanatomym (e.g. brain volume) indirectly affects the connectome.
- Participant history, such as the shared and non-shared environmental influences, and traits are potential confounders.
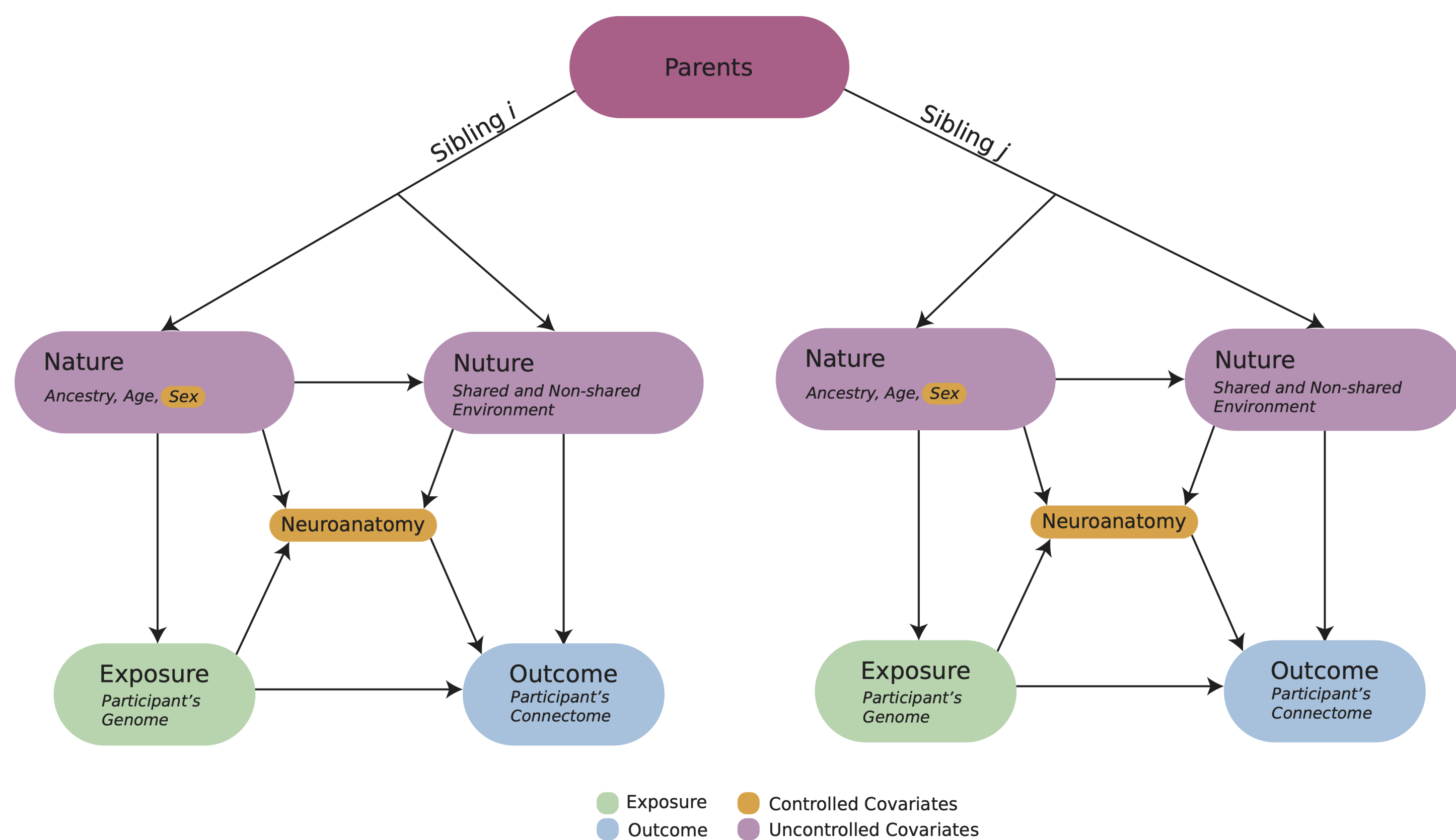- The shared and non-shared environment is controlled by comparing between the same sex individuals.

Fig 2: Directed acyclic graph (DAG) illustrating potential relationships between the genome and connectome.

Human Connectome Project 1200

- Structural connectomes are estimated using structural (sMRI) and diffusion magnetic resonance imaging (dMRI).
- Processed with *m2g* pipeline, which uses Constrained Spherical Deconvolution (CSD) model and deterministic tractography.

	Monozygotic	Dizygotic	Non-twin siblings
N	322	212	490
Sex	196 F, 126 M	125 F, 87 M	237 F, 253 M
Age (mean)	29.6 (3.3)	28.9 (3.4)	28.3 (3.9)

Table 1: Participants and their demographics of HCP1200 Dataset.

Three Models of Connectomes

- **Exact:** Are the generative models of connectomes the same?
- **Global scale:** Are the generative models same after considering global scaling?
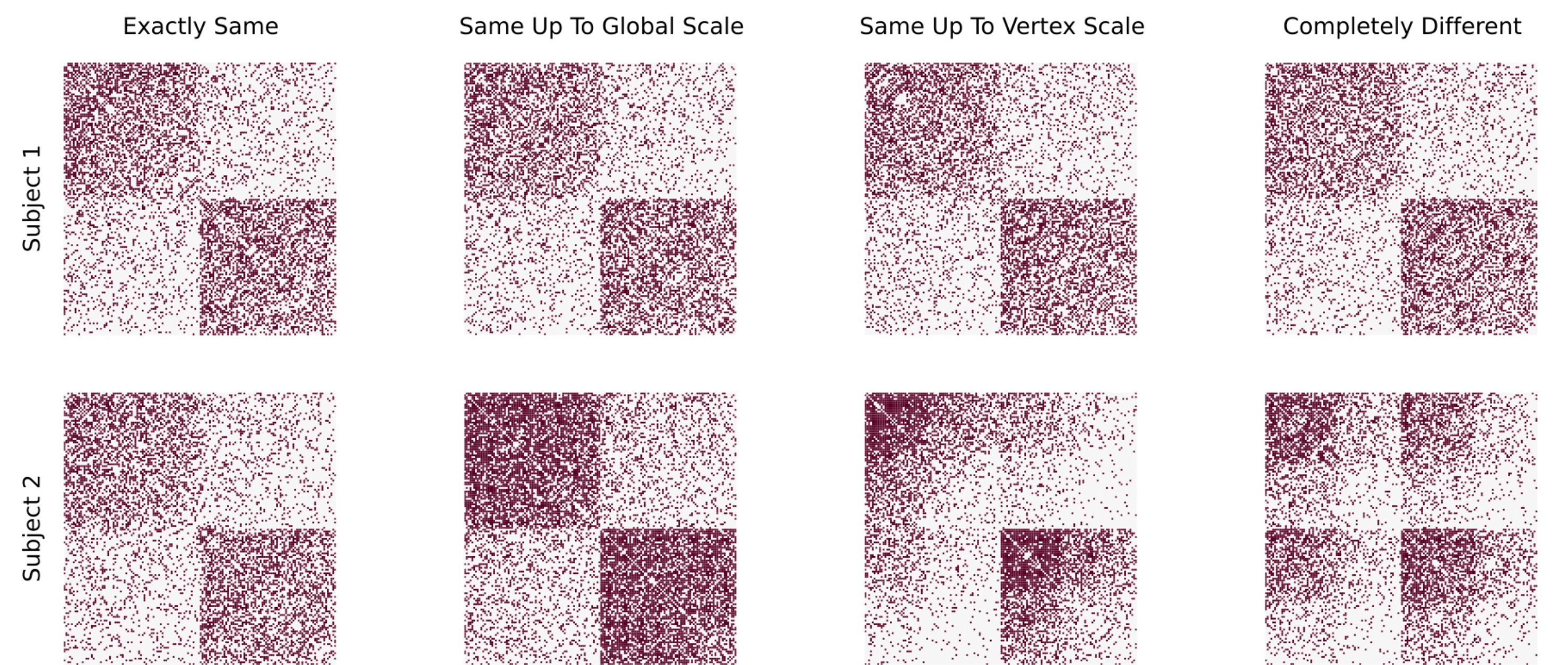- **Vertex scale:** Are the generative models same after considering vertex wise scaling?

Fig 3: Examples of the three different models (exact, global scale, and vertex scale) of connectome heritability visualized as adjacency matrices.

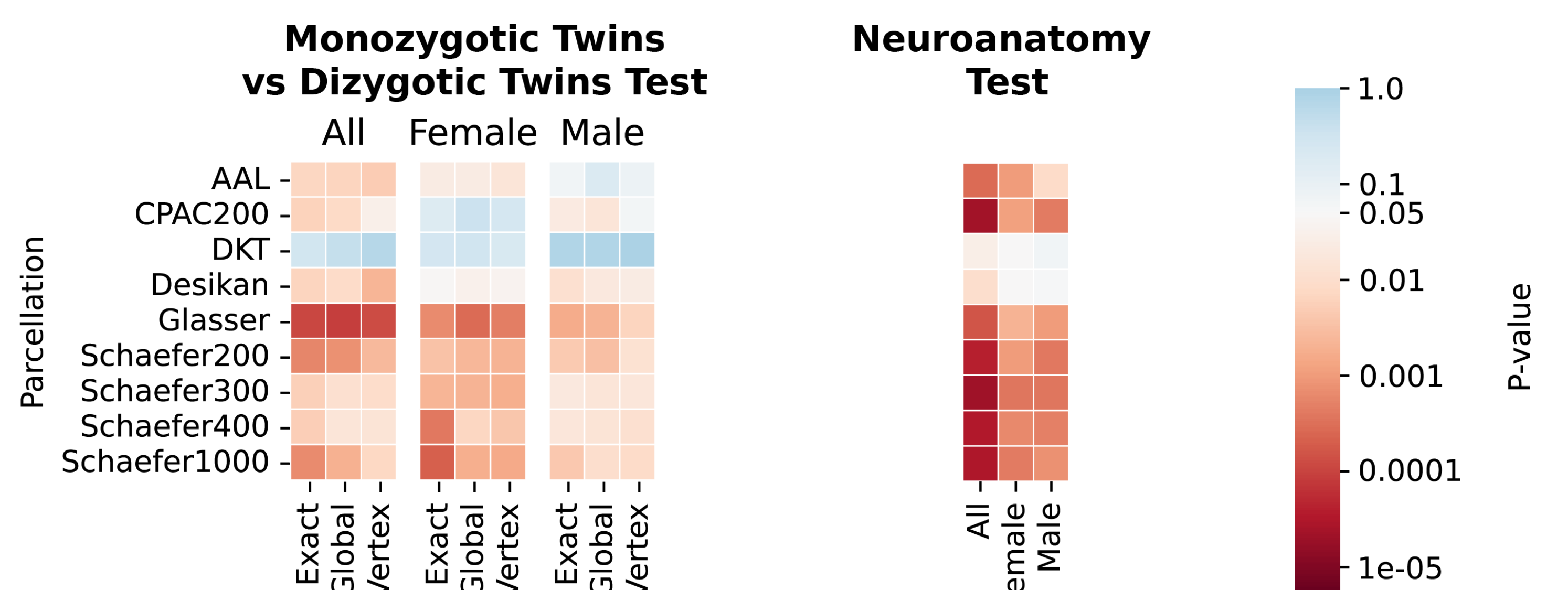## Connectome Validation and Heritability of Neuroanatomy

Fig 4: Validating connectomes by comparing monozygotic and dizygotic twins using Kolmogrov-Smirnov test. Heritability of neuroanamy is tested using unconditional test framework. Red squares indicate significant tests; blue indicate non-significant tests.
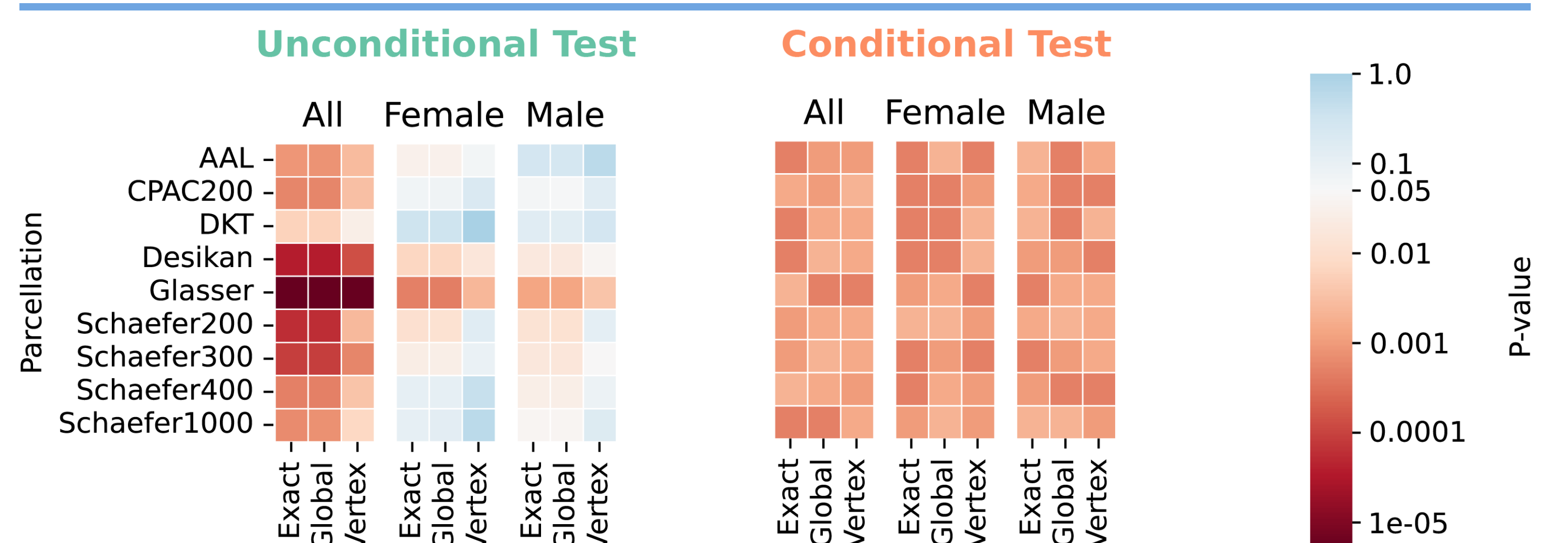
Tests for Heritability of Connectomes

Fig 5: Testing for unconditional and conditional heritability of connectomes. Red squares indicate significant tests; blue indicate non-significant tests.

Limitations and extensions

- Other staitsical models to consider (e.g. COSIE [3])
- Repeated analysis on functional MRI or in other twin study datasets.

Code

graspologic — downloads 131k — ○ Stars 255

hyppo — downloads 88k — ○ Stars 126

Acknowledgements

References

[1] Chung et al. "Connectomic Heritability," In preparation (2022)
[2] Chung et al. "Statistical connectomics," Ann. Rev. Statistics and its Application (2021)
[3] Arroyo et al. "Inference for multiple heterogeneous networks with a common invariant subspace," JMLR (2021)

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