Signal propagation dynamics across the Drosophila hemi-brain connectome reveal parallel-hierarchical sensory-cognitive-motor architecture.

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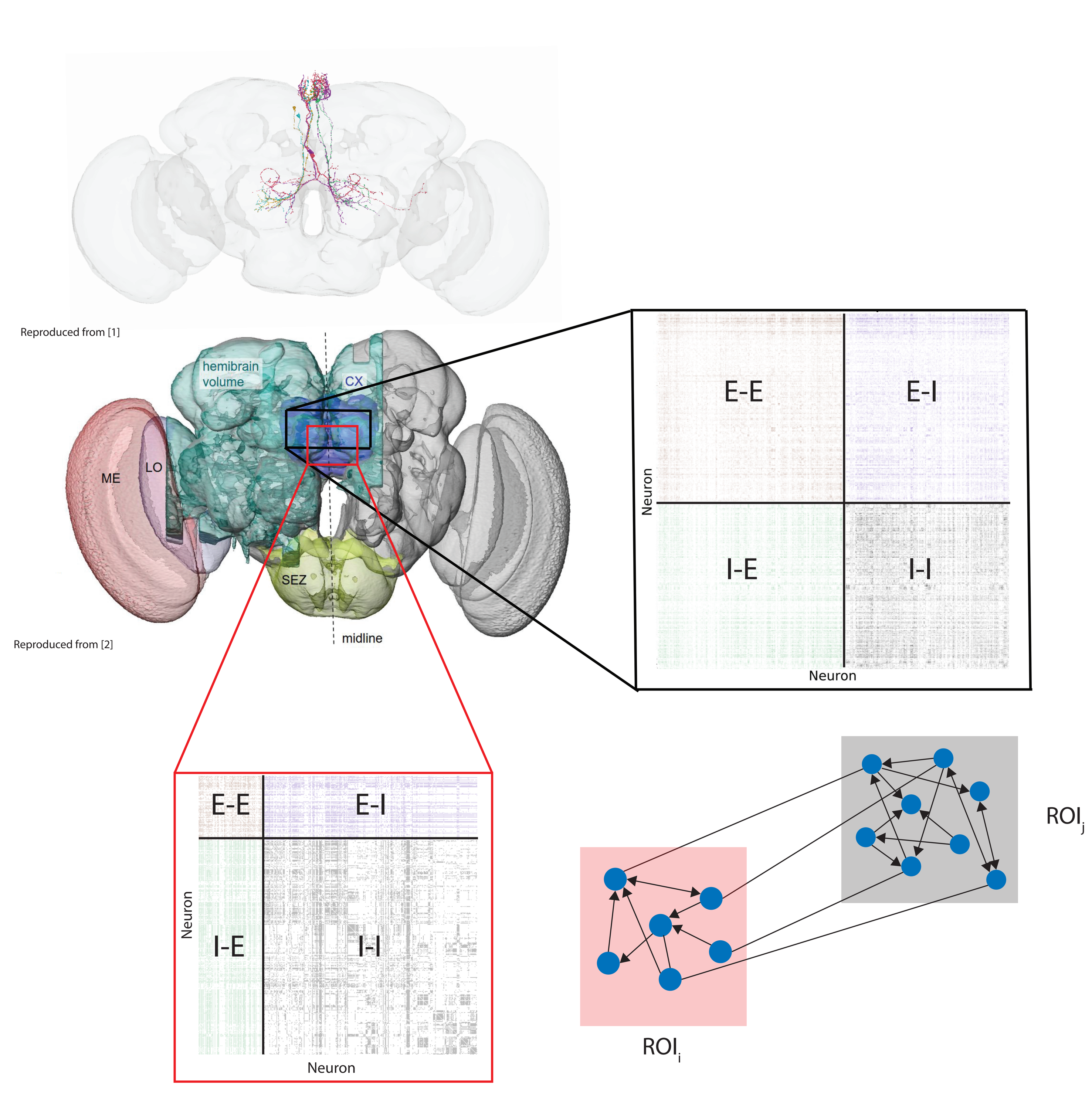
Abstract

Sensory, cognitive, and motor functions rely on transmission/integration of signals across multiple spatiotemporal scales which are fundamentally constrained by neuroanatomy. Uncovering connectivity patterns that shape signal propagation is thus of central importance to understanding brain computations. An organizational principle of the brain is anatomical/functional hierarchy, often conceptualized as signals propagating up from sensory areas to cognitive areas and down to motor areas. However, to determine if such a hierarchy is a sequential (e.g., MLP) or parallel (e.g., U-net) architecture requires consideration of signal propagation dynamics across multiple spatial-temporal scales at full anatomical resolution. Prior work in connectomics has characterized either global connectivity features or single-neuron statistics. To enable rigorous treatment across spatial scales simultaneously, we fit a novel multiplex maximum entropy random graph (MERG) model to the entire directed, weighted Drosophila hemibrain connectome. Structurally, we evaluated the frequency of motifs at various orders. Functionally, we evaluated multi-scale dynamics of signal propagation using Laplacian dynamics. Within individual hemibrain ROIs, we found MERGs with genetic (cell-type) constraints on pairwise connectivity recapitulated low-order motif distributions and short-term propagation dynamics, but failed to account for long-term structure and function. Across the hemibrain, propagation dynamics revealed a robust sensory-cognitive-motor hierarchy that exhibited parallel sensory-motor processing– i.e., a parallel-hierarchical architecture. This hierarchy was not recapitulated by simple anatomical measures (shortest path), but was recapitulated by propagation dynamics on genetically-constrained multiplex-MERGs, indicating that all paths between areas must be considered simultaneously. To further link structure-to-function, we identified the high-order motifs (≤6th-order) that are most important to signal propagation. Our results reveal a parallel-hierarchical architecture of brain function encodable by genetic constraints, while long-time-scale dynamics of signals within an area emerges from high-order motifs not captured by local constraints.

Drosophila anatomy requires a multiplex network model



21,737 Neurons, 25 M synapses, 601 ROI, 101835 multiplex nodes

Probing multiscale, multiplex structure through diffusion dynamics

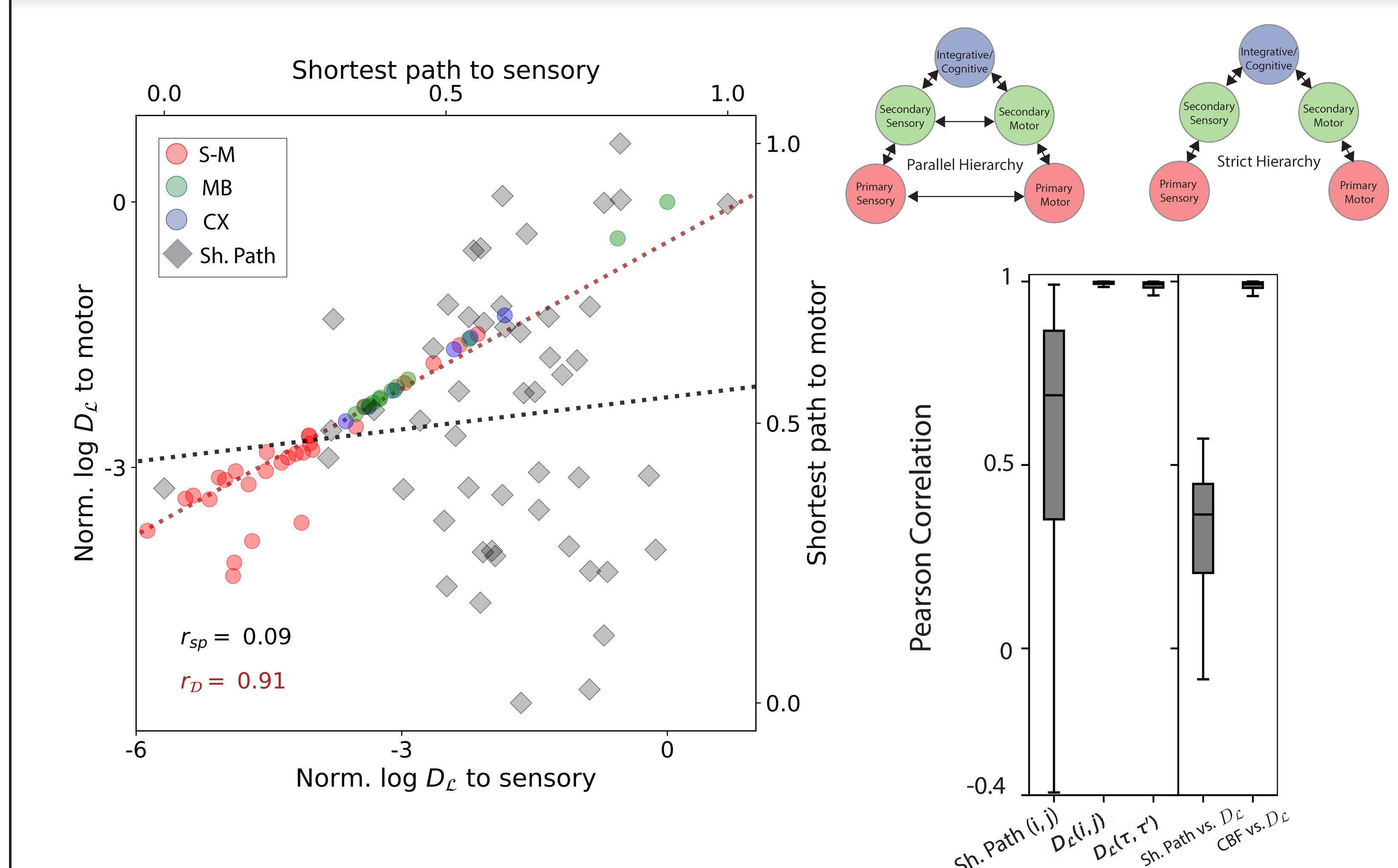
$$A_{\mathrm{mp}} = \oplus_i A_{\mathrm{ROI}_i} + A_{\text{inter-ROI}} \quad \text{(Multiplex Adjacency Matrix)}$$

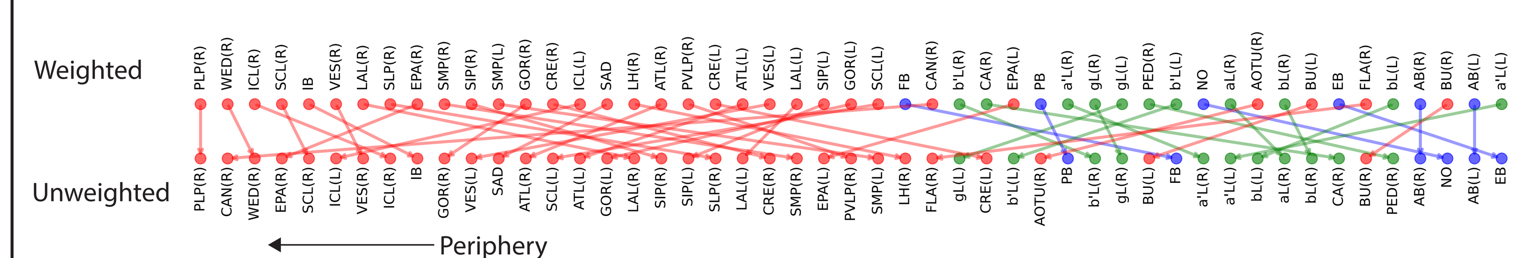
$$\mathcal{L} = I - A_{\mathrm{mp}} D_{\mathrm{mp}}^{-1} \quad D_{\mathrm{mp}} = \mathrm{diag}\left(\sum_i [A_{\mathrm{mp}}]_{ij}\right) \quad \text{(Multiplex Laplacian)}$$

$$\dot{v} = -\mathcal{L}v \quad v(\tau) = e^{-\mathcal{L}\tau} v(0) = \sum_{k=0}^{\infty} \frac{\tau^k e^{-\tau}}{k!} \left(A_{\mathrm{mp}} D_{\mathrm{mp}}^{-1}\right)^k \quad \text{(Diffusion Dynamics)}$$

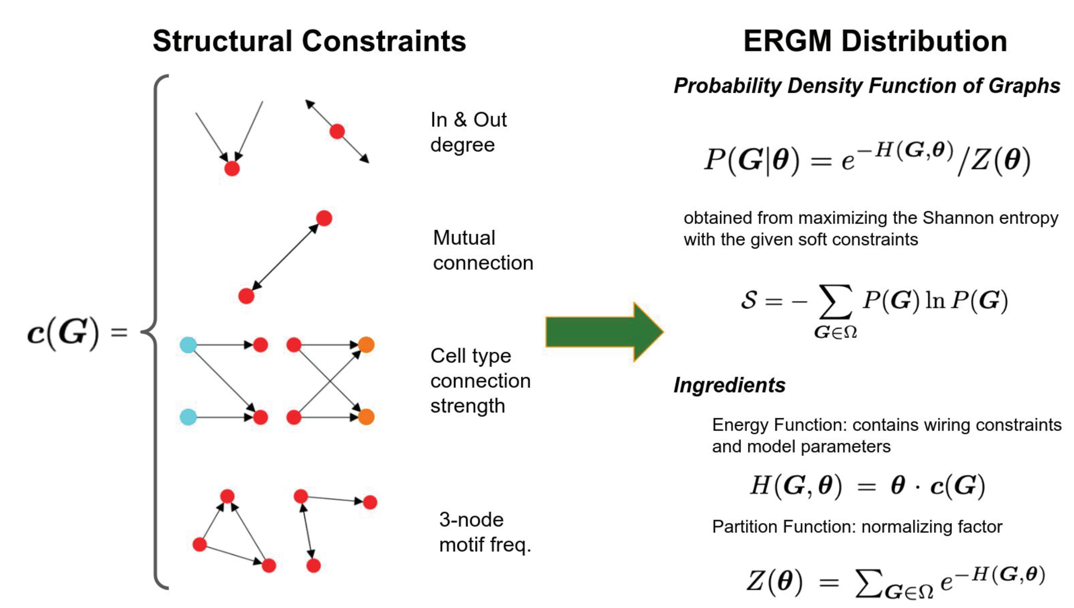
$$[D_{\mathcal{L}}(\tau)]_{ij} = ||e^{-\mathcal{L}\tau} v_i - e^{-\mathcal{L}\tau} v_j|| \quad \text{(Diffusion Distance)}$$

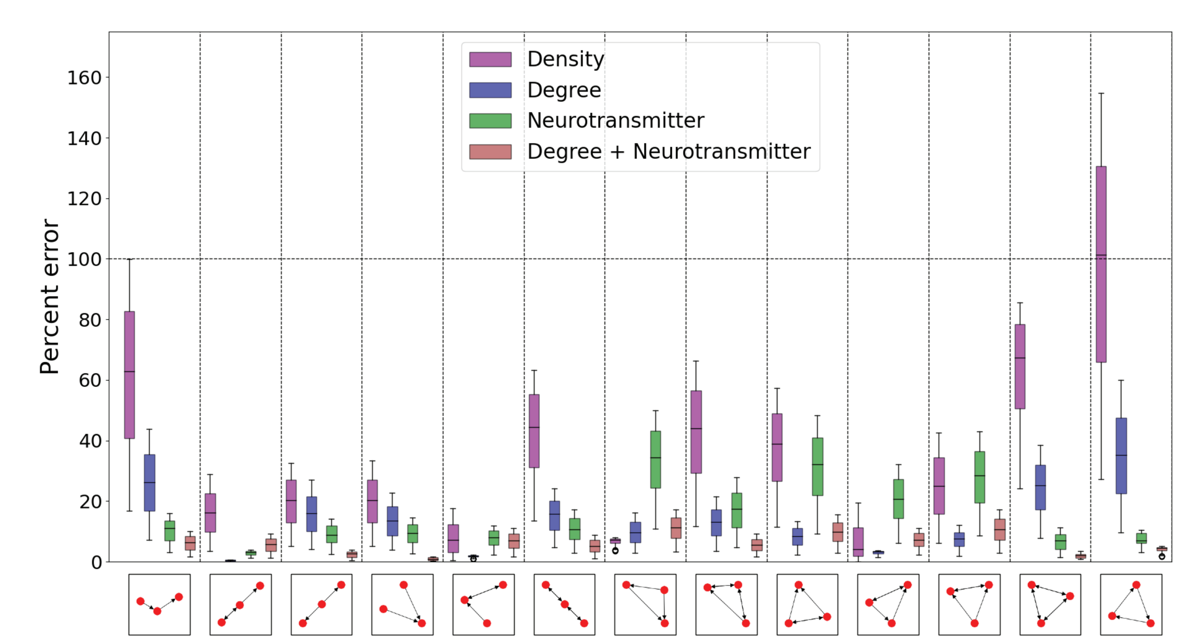
Diffusion dynamics reveal parallel-hierarchical architecture

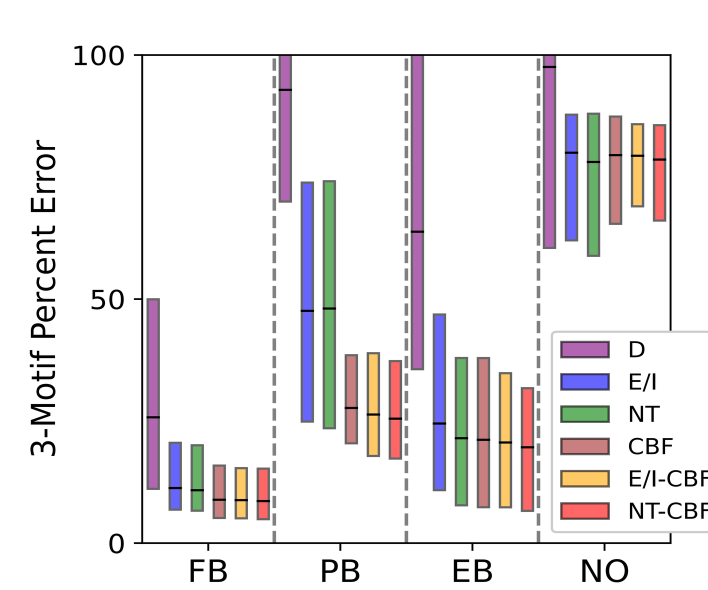


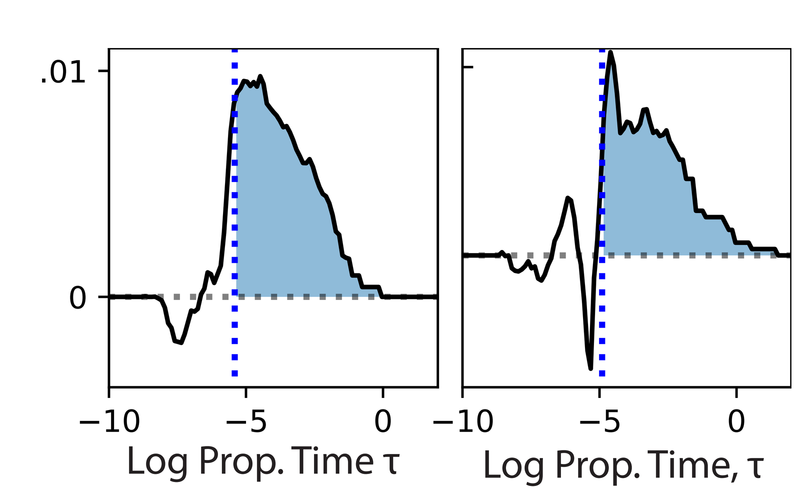


Maximum entropy null models capture low order motifs statistics









Identifying structural motifs important for the diffusion distance

Given a linear dynamical system over adjacency matrix A: $\dot{v} = f(A)v$ and a scalar observable $g(A)$,

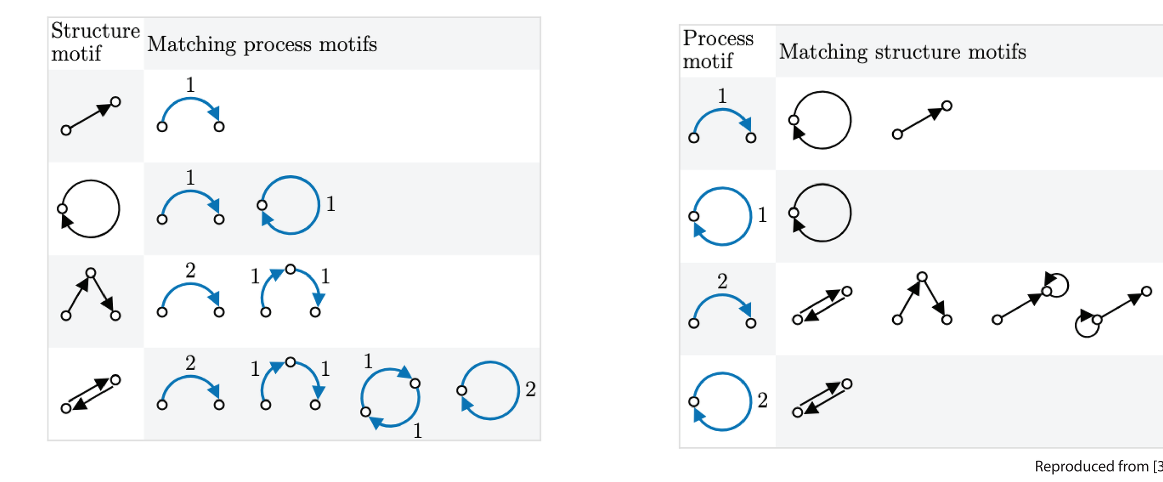
$$g(A) = \sum_i b_{\mathrm{p}_i} n_{p_i}$$

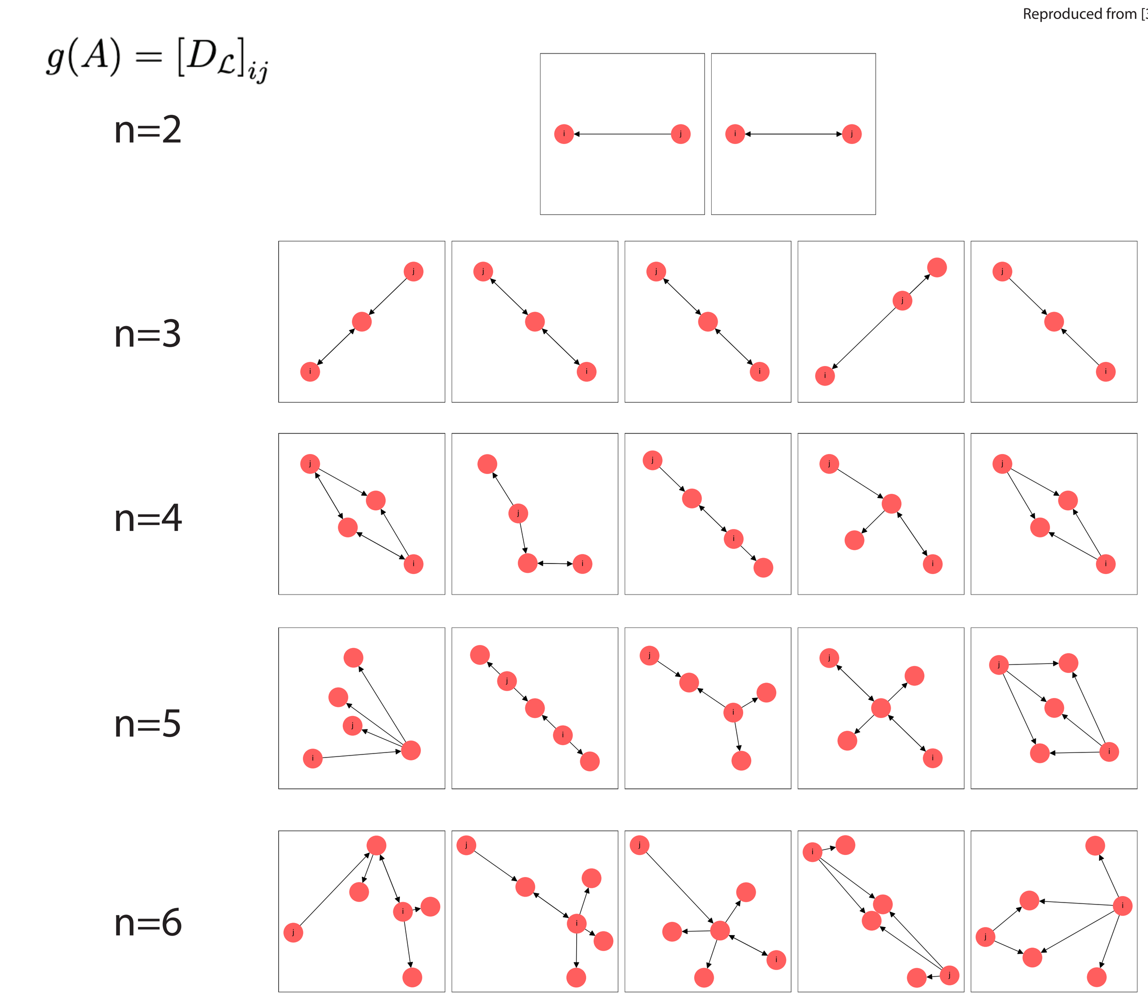
$$g(A) = \sum_i \hat{c}_{s_i} n_{s_i}$$

$$c_s = \sum_{p \in P_s} b_p = g(c_s)$$

$$\hat{c}_s = c_s - \sum_{s' \subset s} c_{s'}$$

p_i : Process Motif
c_i : Structure Motif





Ongoing Work

1. Null models for interlayer connectivity to assess origin of parallel hierarchical structure.
2. Effects of coupling constraints across ROIs in the multiplex ERGM model.
3. Connectivity derived cell typing.
4. Assessing null model motif counts of functionally important motifs.
5. Alternative Approaches to motif importance (e.g. Shapely subgraph scores, [4])

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