A Deep Dive into the Rat CA1 Network: Insights from Network Science

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Blue Brain Project
Digitally reconstructing and simulating the brain

Abstract

Advancements in large-scale data collection techniques have enabled the integration of network science into neuroscience research. By employing graph-based strategies and utilizing various datasets, such as connectomics and neuronal recordings, researchers have gained valuable insights into the network architecture and information processing mechanisms of the visual cortex and hippocampal formation system.

However, previous studies have often been limited by small sample size or a lack of high-resolution granularity within specific brain regions. In a recent publication [1], we addressed these limitations by developing a comprehensive rat CA1 model that incorporates biophysically authentic dynamics across different scales. In this work, we utilize network science analyses to explore the topological characteristics to dissect the emergent properties of brain networks. We implement scalable tools for analyzing large scale directed weighted graphs which would help bridging the gap between neuroscience and network science.

The Network

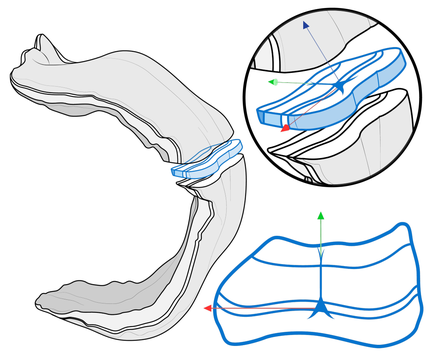

Figure 1: The reconstructed rat CA1 circuit and the slice section used in the experiments and motif calculations.

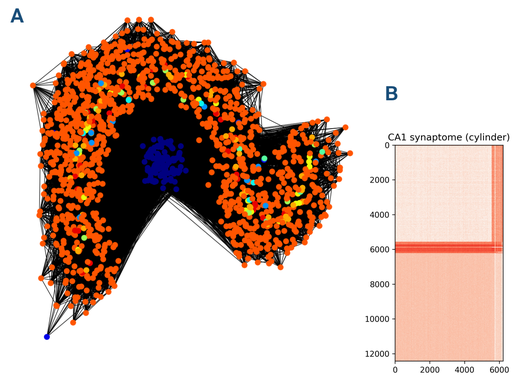

Figure 2: **A.** 400 um slice from the CA1 network with its CA3 projections (blue nodes) represented as graph with spring layout. Colors indicate the cell types.
B. Adjacency matrix of the slice.

Results

Degree Distribution

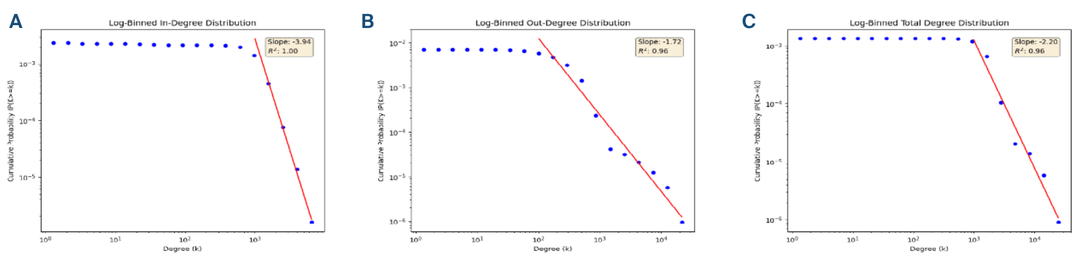

Figure 3: **A**. In- , **B**. Out- and **C**. Total- degree distributions for the network (~460k neurons) plotted in log binned scale to correctly calculate the degree exponent. The directed network shows difference in scale-freenes in this 3 categories.

Hubs & Polarity

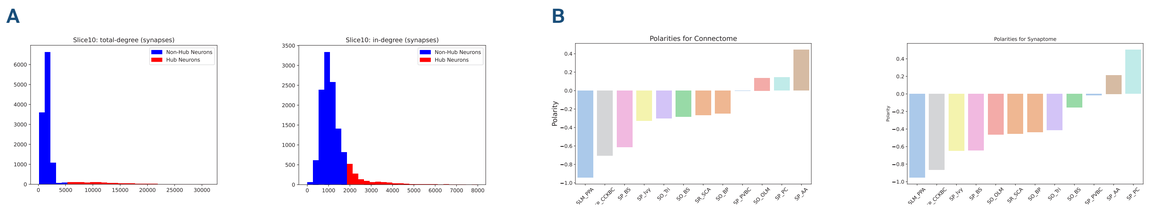

Figure 4: A. Degree distributions for the synaptome for total and indegrees. **B**. Polarity sorted in ascending order for connectome (binary matrix) and synaptome (weigthed matrix) shows difference in graph structure for cell types.

Density

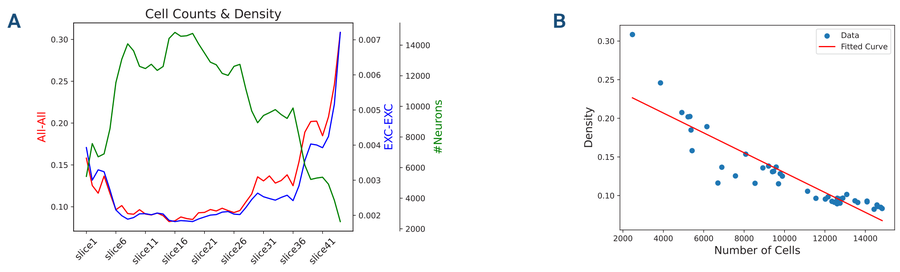

Figure 5: A. Number of neurons and their densities across Dorsoventral (DV) slices of the network for All and for only excitatory (EXC) populations. **B**. Changing density values with respect to number of cells.

Rich Clubs

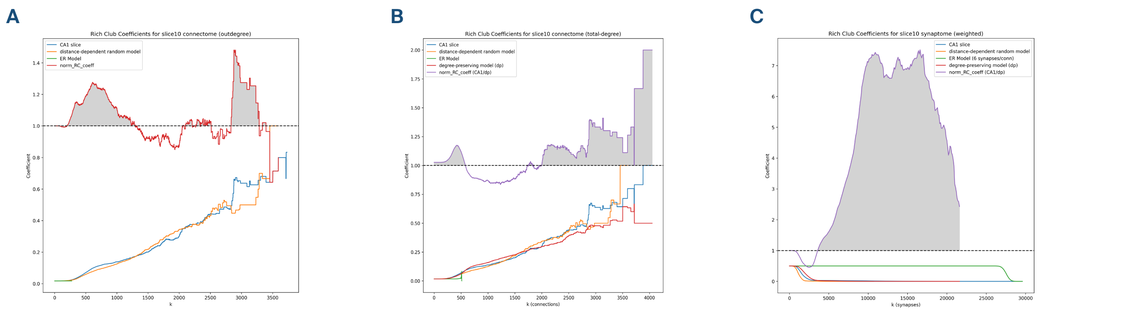

Figure 6: Normalized and non-normalized rich club coefficients (RCCs) for the CA1 connectome and synaptome. RCCs are calculated for directed graphs. **A**. for outdegree (connectome) **B** . total-degree (connectome), and **C** . total-weight (synaptome). For comparisons,Erdos-Renyi graph, distance dependent configurational model, and weight shuffled randomization (for synaptome only) are used as a control with increased complexity.

Triplet Motifs

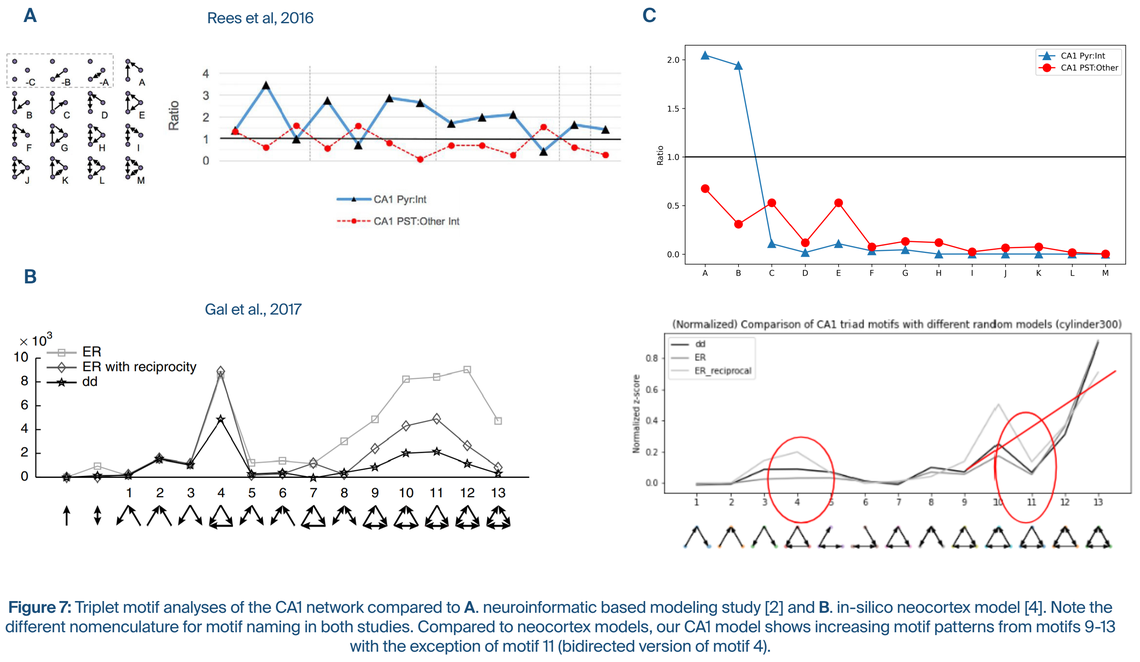

Figure 7: Triplet motif analyses of the CA1 network compared to **A**. neuroinformatic based modeling study [2] and **B**. in-silico neocortex model [4]. Note the different nomenculature for motif naming in both studies. Compared to neocortex models, our CA1 model shows increasing motif patterns from motifs 9-13 with the exception of motif 11 (bidirected version of motif 4).

Common Neighbor Bias

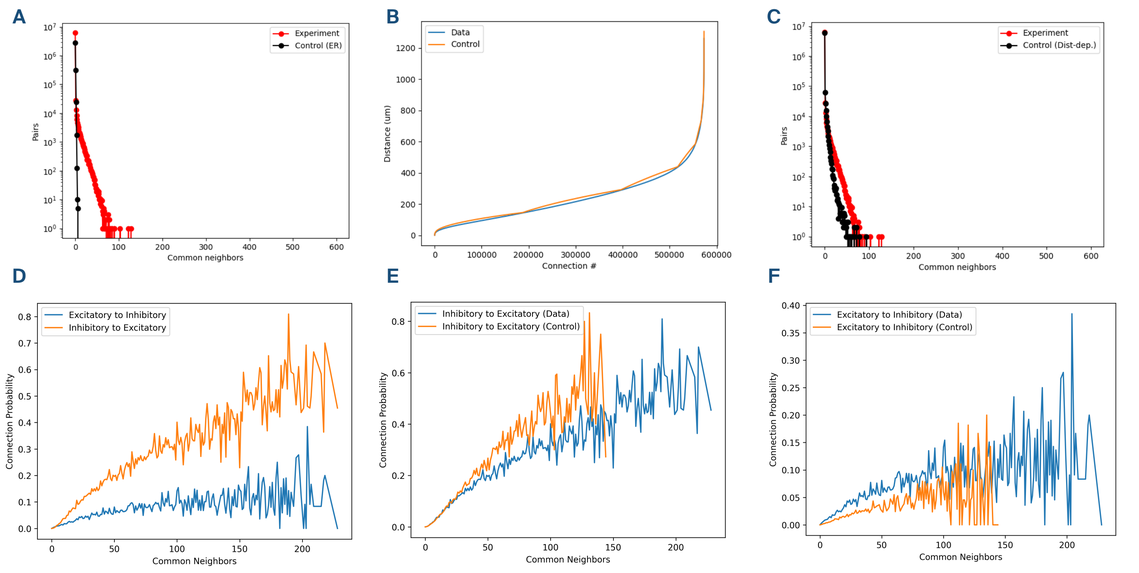

Figure 8: Efferent Common neighbor analysis of the CA1 network. Data is compared to Erdos-Renyi (ER) and degree preserving distance-dependent connection probability (DD) models. **A**. Number of pairs observed with increasing common neighbors with respect to ER shows strong bias in the network. **B**. For a more strong control, number of connections are preserved across varying distances in a degree preserving random model. **C**. With this control, the bias seen in the CA1 model is aprroximated better. **D**. Dependence of connection probability to common neighbors in Exctitatory to Inhibitory (EI) and (IE) connections showing more bias in IE type. **E-F**. Compared to random model (DD) ,the bias is differential across EI and IE pairs, indicating a negative bias in the CA1 network for IE.

Conclusions

- The CA1 model shows scale-free degree distributions for its degree distributions, indicating presence of hubs in the system.
- Connectome and Synaptome level differences in the network analysis show the importance of analyzing weighted graphs rather than binary matrices in brain networks. The synaptome matrix can be further improved into a fully functional connectome with embedded node and edge level features.
- Geometric shape of the region affects the graph features within the local connectome. Assuming this holds in real brain regions as well, this might indicate different computational roles constrained by the bounding structural constraints along with their incoming projection patterns. Further experimental and modeling analyses are needed to validate and inspect the structural and functional differences in these boundaries.
- Rich club structure of this CA1 network model shows highly non-random features across connectome and synaptome level. However, the effects of functionalizing the graph have vast differences in rich club structure, indicating once more the importance of weighted analysis of the networks.
- Certain peaks of weighted rich club indicate modular structure in the network at different connection strenghts, which might be affected by plasticity in the long term.
- Common neighbor analysis across EI pairs indicate a negative bias from inhibitory to excitatory network compared to distance-dependent randomized models and positive bias in the neocortex, indicating an nonrandom anti-rich club structure for this connection type.
- Triplet structures shows diverging fingerprints compared to neocortical motifs, highlighting more increased local connectivity within its structure except for motif 11, which is consistent with negative efferent common neighbor bias from IE pairs.

References

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