Topological properties of a full-scale model of rat hippocampus CA1 and their functional implications

Blue Brain Project
Digitally reconstructing and simulating the brain

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Introduction

Hippocampus has a crucial role in the formation of declarative memories and navigation. Environmental cues from the cortical regions along with the current state of the brain are integrated, diagonalized, and redistributed within hippocampal subregions DG, CA3, CA2, and CA1. This phenomenon is heavily affected by the flow of information defined by the brain's connectome. Therefore, it is imperative to investigate the circuit structure and link it to its function.

In this study, we analyzed the topological features of a data-driven atlas-based rat CA1 model (Romani et al., 2022 [1]) that consists of 456K neurons and 820M intrinsic and 9.1B extrinsic synapses from upstream CA3 region. We observed that our model shows topological properties seen in other biological networks but not in random models with similar connection probabilities.

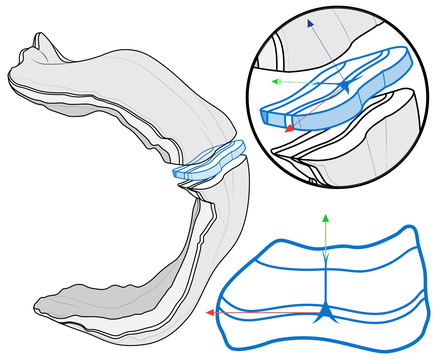
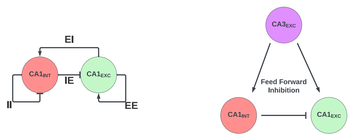


Figure 1: The reconstructed rat CA1 circuit and the slice section used in the experiments and motif calculations.

We then selected a subset of these properties to further investigate the structure-function relationship using the experimental protocol in Sasaki et al. 2006 [2]. Specifically, we randomly removed connections for each pathway in turn (EE,EI,IE,II) [3], and tested how these manipulations affect the network behavior under the influence of Schaffer Collateral stimulation of different strenghts.



Structure

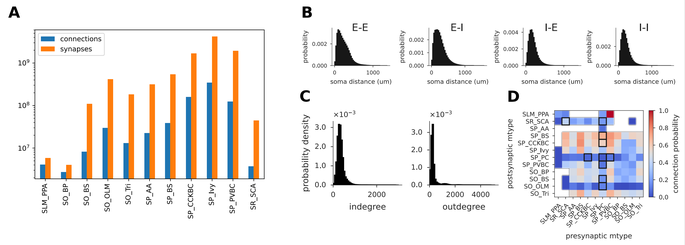


Figure 2: Structural properties of the default circuit. A. Contribution of morphological types to FFI in the original slice. B. Connection probability based on inter somatic distance between synapse classes. C. In- and Out-degree distributions of neurons in the circuit. D. Connection probability matrix for pairs of each morphological type. Black squares indicate the values with experimental counterparts.

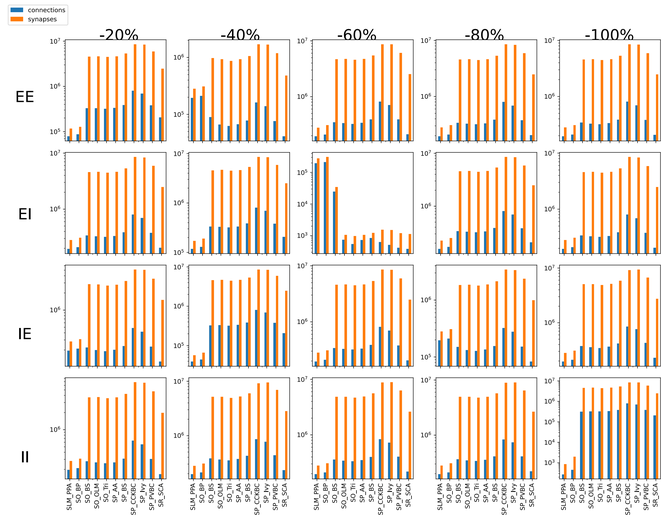


Figure 3: Contributions of individual morphological types to feed-forward inhibition in terms of connections and synapses in different ablation levels.

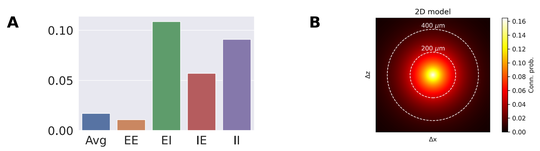


Figure 4: Parameterization of the random models. A. 1st-Order Erdos-Renyi Model use an average connection probability among all connections (Avg) and Stochastic Block Model (SBM) implements a different connection probability depending on the pathways (EE, EI, IE, II). E = Exctitatory, I = Inhibitory. B. 2nd-Order distance dependent exponentially decaying connection probability model.

Function

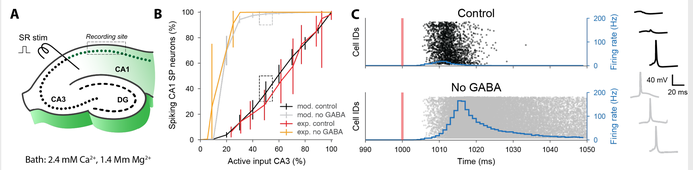


Figure 5: Experimental Results in Sasaki et al. 2006 [2] and default CA1 model. A. Illustration of the stimulation and recording sites. B. Spiking rate of neurons in SP layer with an increasing CA3 stimulation. Yellow and Red: Results from experiment with and without Gabazine, respectively [2]. Light and Dark Gray: Results from the default model [1].

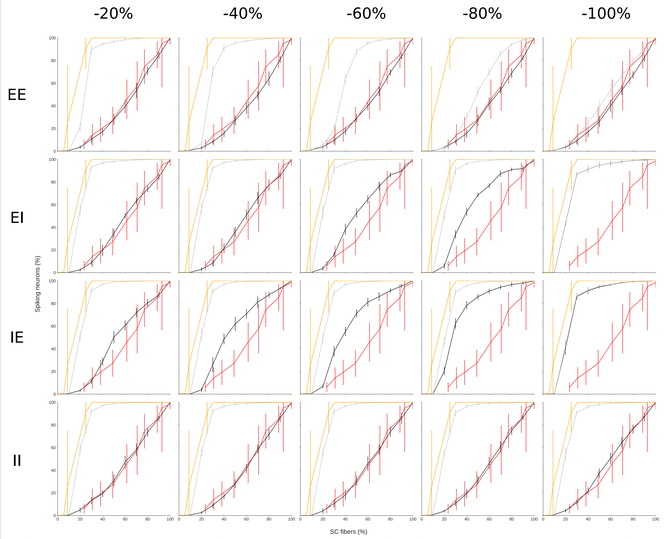


Figure 6: IO responses from manipulated circuits with increasing rate of ablation (x axis) and in different synaptic pairs (y axis).

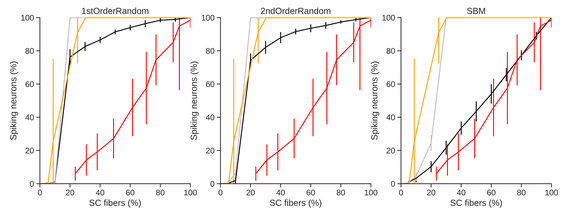


Figure 7: IO responses from randomly rewired circuits. The linearization phenomenon is not observed until the Stochastic Block Model.

Conclusions

- EE connections are necessary to see the saturation behavior in the IO plot.
- Gradually decreasing the EE connections linearizes the IO response, which behaves as a disconnected circuit.
- CA1 circuit can accomplish this without having to disconnect the cells while achieving other circuit level phenomenona.
- Changing EI or IE connections have a similar effect but in different rates.
- 1st and 2nd Order Random Models can't achieve such phenomenon here since they do not have the capability to linearize the IO curve.
- Linearization phenomenon starts to emerge at SBM.

Future Plans

- Examine the susceptibility of the linearization phenomenon observed in random models with the ablation studies.
- Investigate the contributions of individual morphological types to simulation outputs.
- Extend the ablation studies to examine the robustness of other circuit level phenomena.
- Examine if this phenomenon generalizes to other brain regions.

References

1. Romani A, et al. (2022). Reconstruction and Simulation of a Full-scale Model of Rat Hippocampus CA1. Manuscript in Preparation.
2. Sasaki T, Kimura R, Tsukamoto M, Matsuki N, Ikegaya Y (2006) Integrative spike dynamics of rat CA1 neurons: a multineuronal imaging study. J Physiol (Lond) 574:283–290.
3. Pokorny C et al. Impact of simplified network structure on cortical activity. Poster presented at: Bernstein Conference 2022; Sept 15 2022; Berlin.

Funding

This study was supported by funding to the Blue Brain Project, a research center of the École polytechnique fédérale de Lausanne (EPFL), from the Swiss government's ETH Board of the Swiss Federal Institutes of Technology.