Simulated Amnesia in a Model Hippocampal CA1 Microcircuit
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Introduction
The human hippocampus has long been associated with the encoding and storage of long-term memory. While much of the detail surrounding the biological mechanisms underlying this essential function remains unknown, its structure has been well-studied. A particularly salient network in the hippocampus is the CA1 region.

Entorhinal Cortex
CA1 Region
CA3 Region
(Sketch by neuroscientist-artist Ramon y Cajal)

In this poster, we study the effect of damage on both the retrograde (referring to memories formed prior to a traumatic event) and anterograde (referring to memories formed subsequent to a traumatic event) in this same CA1 microcircuit model. Specifically, we consider recall performance of the model network as a function of its cell population in order to better understand the mechanisms underlying affections such as amnesia (often associated with hippocampal damage). We also assess the claim that neural networks may respond in relatively significant ways behaviorally when subjected to what amount physically to fairly small alterations (2) in the specific case of this model hippocampal microcircuit. This assertion is of particular interest as it could indicate deep underlying connections between the underlying neuromorphological causes of a diverse family of conditions ranging from schizophrenia to dementia.

Methods
Simulations were run on a model CA1 microcircuit consisting of 100 pyramidal cells, 4 inhibitory inputs—each corresponding to a different inhibitory cell type—and excitatory inputs from the Medial Septum, Entorhinal Cortex, and CA3 microcircuit (1). Neurons in the network are modeled individually in the NEURON language and are configured according to empirically-determined electrophysiological parameters. A theta rhythm of 4 hertz was used in all experiments. Each simulation kept the following general procedure:

- **Pattern Selection:** Initial cell connectivities are determined by a set of five “pre-learned” patterns in accordance with a Hebbian learning paradigm: cells that are stimulated simultaneously in at least one pattern undergo increased synaptic connectivity (with all connections being symmetric). In total, 3 different sets of patterns were employed, with one being taken from (1) and the other two being chosen uniformly and at random from the space of all admissible “Patterns.”

- **Cell Death:** A randomly chosen subset of the pyramidal cells in the neuron is “killed off”, in practice by setting all incident connectivities to 0. For each of the six pattern-retrograde/anterograde pairs we ran simulations removing 0, 10, 30, 50, 70, and 90 cells.

- **Network Stimulation:** The CA1 network receives repeatedly as input one specific pattern in order to simulate the “learning”/“retention” process. In the retrograde case the stimulating pattern is selected from those involved in the “Pattern Selection” step whereas in the anterograde case the pattern is entirely novel.

- **Performance Evaluation:** All neuronal spiking activity is then compiled into a single file and is analyzed for recall performance using the metric given in (1), which in a sense computes the correlation between the input and the resulting spike profile.

Results
Each pattern induces a graph of connections on the 100-pyramidal-cell subnetwork of the microcircuit which we analyze below by means of degree distribution, i.e. the number of nodes with a given amount of neighbors plotted against said number of neighbors. Note the significant deviation of Pattern 1’s distribution from those of Patterns 2 and 3, with the latter two being chosen uniformly and at random from the space of all admissible “Patterns.”

**Degree Distribution of Pattern-Generated Networks**

<table>
<thead>
<tr>
<th>Number of Neighbors</th>
<th>Pattern 1</th>
<th>Pattern 2</th>
<th>Pattern 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.015</td>
<td>0.015</td>
<td>0.015</td>
</tr>
<tr>
<td>1</td>
<td>0.153</td>
<td>0.147</td>
<td>0.153</td>
</tr>
<tr>
<td>2</td>
<td>0.286</td>
<td>0.286</td>
<td>0.286</td>
</tr>
<tr>
<td>3</td>
<td>0.331</td>
<td>0.331</td>
<td>0.331</td>
</tr>
<tr>
<td>4</td>
<td>0.168</td>
<td>0.168</td>
<td>0.168</td>
</tr>
<tr>
<td>5</td>
<td>0.056</td>
<td>0.056</td>
<td>0.056</td>
</tr>
<tr>
<td>6</td>
<td>0.015</td>
<td>0.015</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Where $B_i$ are vectors representing expected and actual network spiking respectively.

**Simulated Amnesia in a Model Hippocampal CA1 Microcircuit**

![CA1 Microcircuit Architecture implemented by Cutsuridis et al. (1)](image)

**Surviving Pyramidal Cell Population**

**Anterograde Recall Performance**

**R²=0.920 (linear regression)**

**R²=0.854 (linear regression)**

Discussion/Conclusions
There, as expected, a strong observed correlation between cell population and recall acuity. More interestingly, this correlation is strongly linear, especially when the Pattern 1, Retrograde is viewed as an outlier. To assess whether a “gradual transition” model of memory vs. cell count is more applicable to the results obtained than a “sudden shift” characterization, we perform least-squares regressions of the data to the following two functions:

$$f(p) = ap^b + \beta$$

Where $p$ is the number of surviving cells in the simulated microcircuit. The results from all six simulations may be compiled as

**Step Function Model**

<table>
<thead>
<tr>
<th>$c_r$</th>
<th>$c_l$</th>
<th>$c_l$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrograde</td>
<td>0.2892</td>
<td>0.7393</td>
<td>0.7893</td>
</tr>
<tr>
<td>Anterograde</td>
<td>0.4000</td>
<td>0.7999</td>
<td>0.8000</td>
</tr>
</tbody>
</table>

In the linear model, the anterograde simulations have an average a higher $\beta$ coefficient, and this difference is statistically significant ($p<0.00375$). In other words, the ability of the simulated microcircuit to encode new memories is more affected by a decrease in cell population than said microcircuit’s ability to surmount various obstacles we encountered.

Acknowledgements
This project would not have been possible without the significant contributions, financial and otherwise, of the RISE program at BU. Particular thanks goes to the RISE Practicum instructors, whose guidance proved invaluable in designing and executing our research. We are also greatly indebted to the course assistants, and in particular Wonyl Choi, with whom we had the great fortune to discuss our project at length, and whose insight allowed us to surmount various obstacles we encountered.

References

All p-values are reported as given by a unpaired one-tailed Student’s t-test.