An Examination of Hearing Loss on Memory Formation: A Conductance Model of the Hippocampal CA3 Network

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Introduction

Background

- **Dementia** is a debilitating condition that ruins the well-being of more than 55 million people worldwide.
- **Hearing loss** may be a risk factor for dementia, as reduced auditory input to the **hippocampus** (a brain region responsible for memory) impacts the **firing pattern** of neurons in the CA3 network.
- The **CA3 network** relies on synchronized firing of the excitatory **pyramidal cells (PCs)**, which is modulated by interneurons: **basket cells (BCs)** and **oriens-lacunosum moleculare cells (OLMs)**.
- The neuronal firing contributes to **theta and gamma oscillations**, which are necessary for memory encoding.

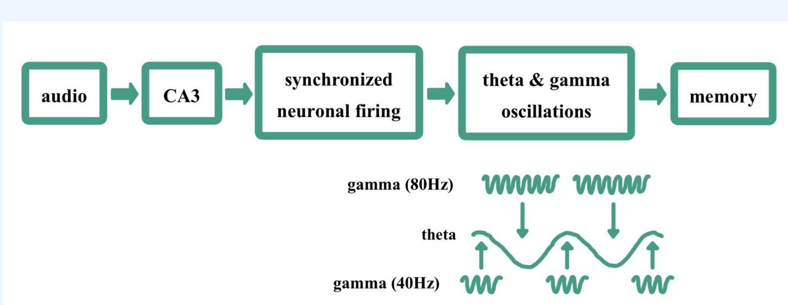


Figure 1: Pathway from audio input to oscillations in the CA3 network

Goal

- Use a **conductance-based neuron model** to simulate various stages of **hearing loss** by altering the **amplitude** of auditory input and investigating **neuronal firing synchronicity**.

Methods

1. **Statistical analysis** of PC spikings: Determines the magnitude and time distribution of multi-neuron synchrony events.
   - **1200 neurons**: 800 PCs, 200 BCs, 200 OLMs.
2. **Raster plots**: Display neuronal activity over time to assess **synchronicity** and **efficacy of memory formation**.
3. **Spike analysis**: Histograms track the number of neuronal spikes per millisecond. To identify **spike clusters** and their **durations**, we extended the timescale before and after the peak spike count until the spike count was under 10% of the peak.

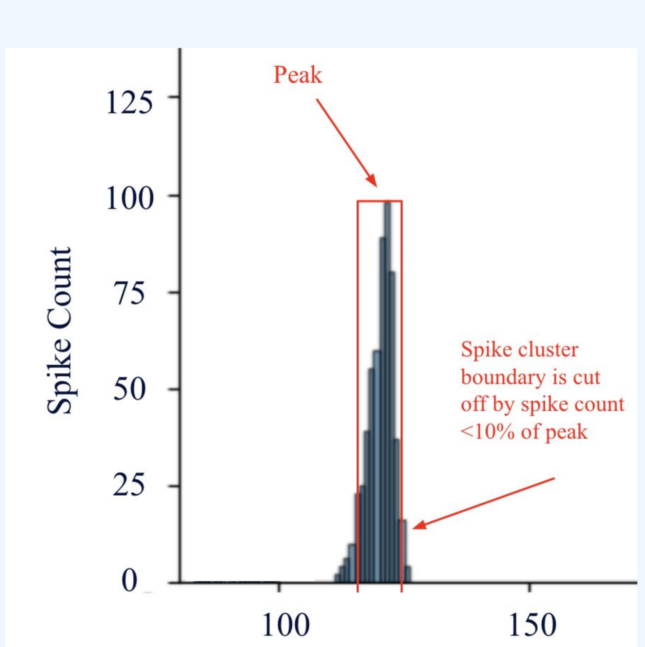


Figure 2: Algorithm used to identify spike clusters

Results

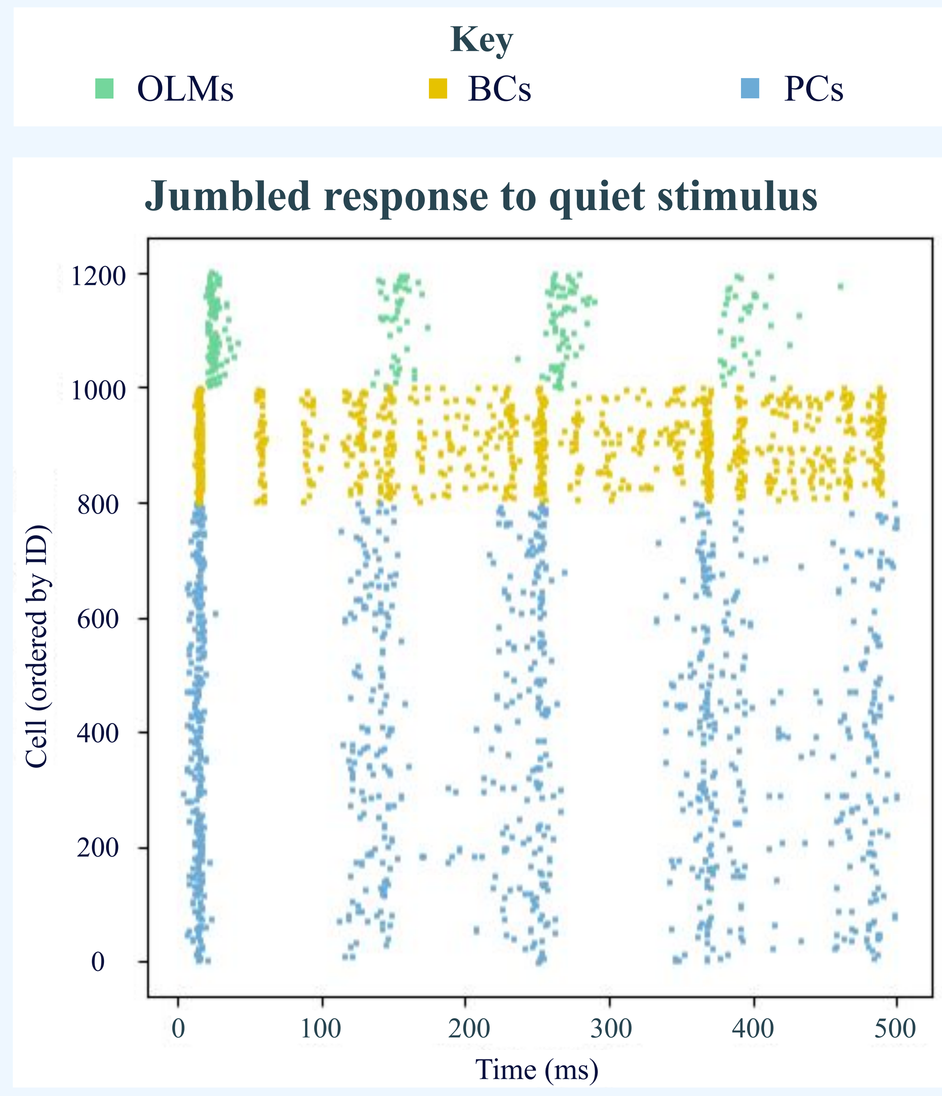


Figure 3a: Raster plot with 10 pA input current

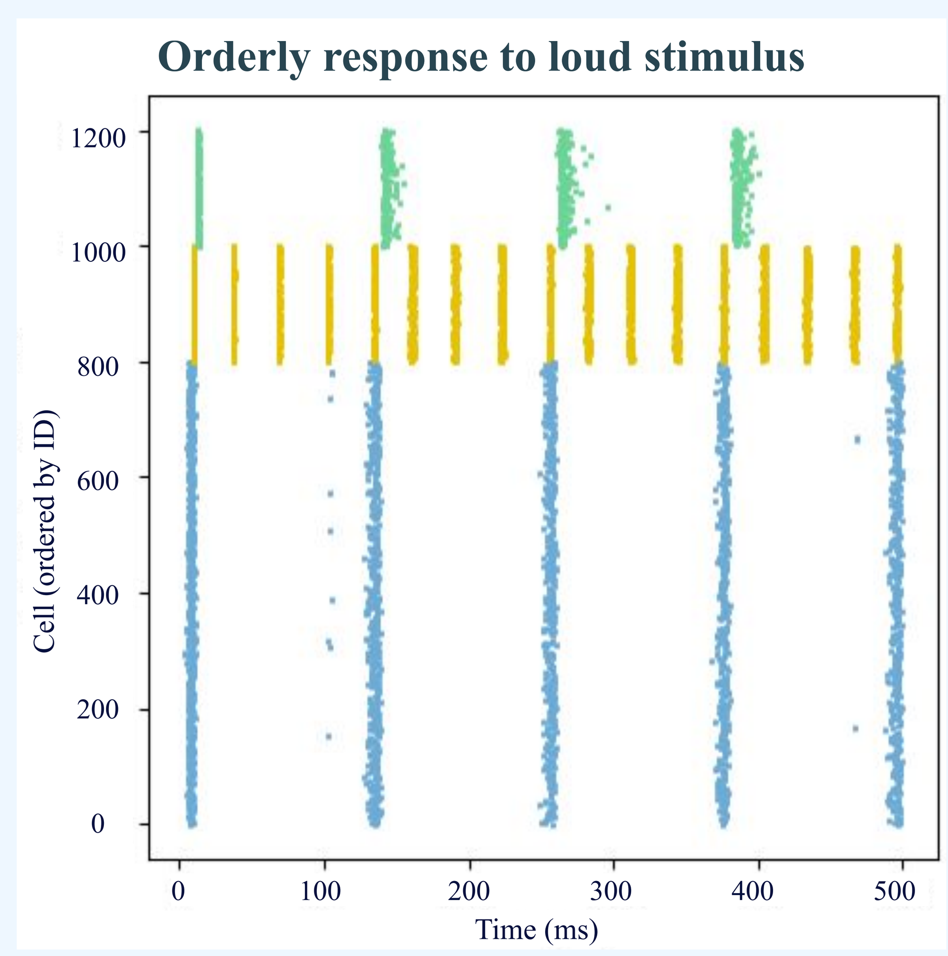
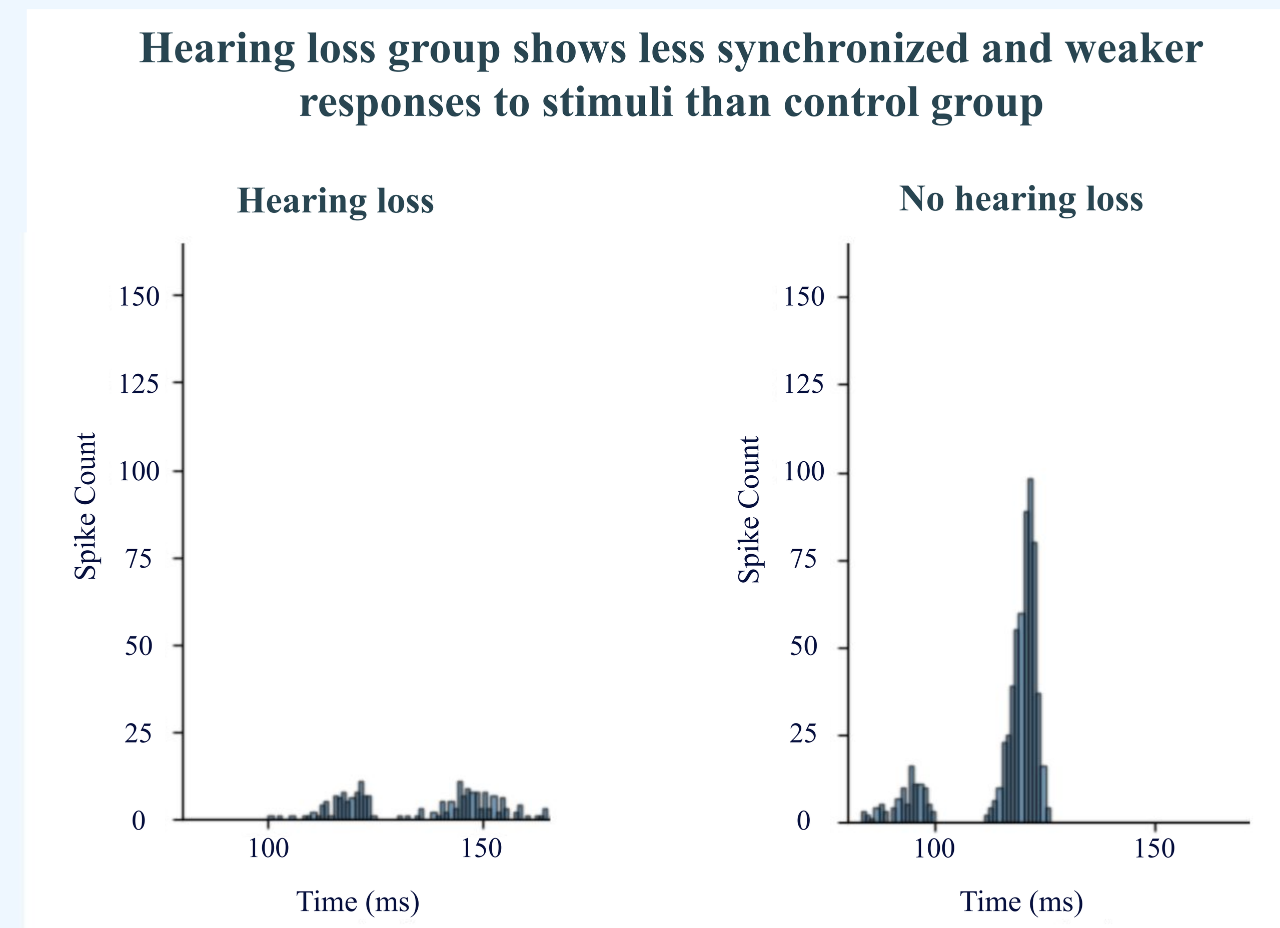


Figure 3b: Raster plot with 90 pA input current



Figures 4a & 4b: Spiking clusters (periods of high neuronal firing) of 10 pA (left) and 90 pA (right) input current

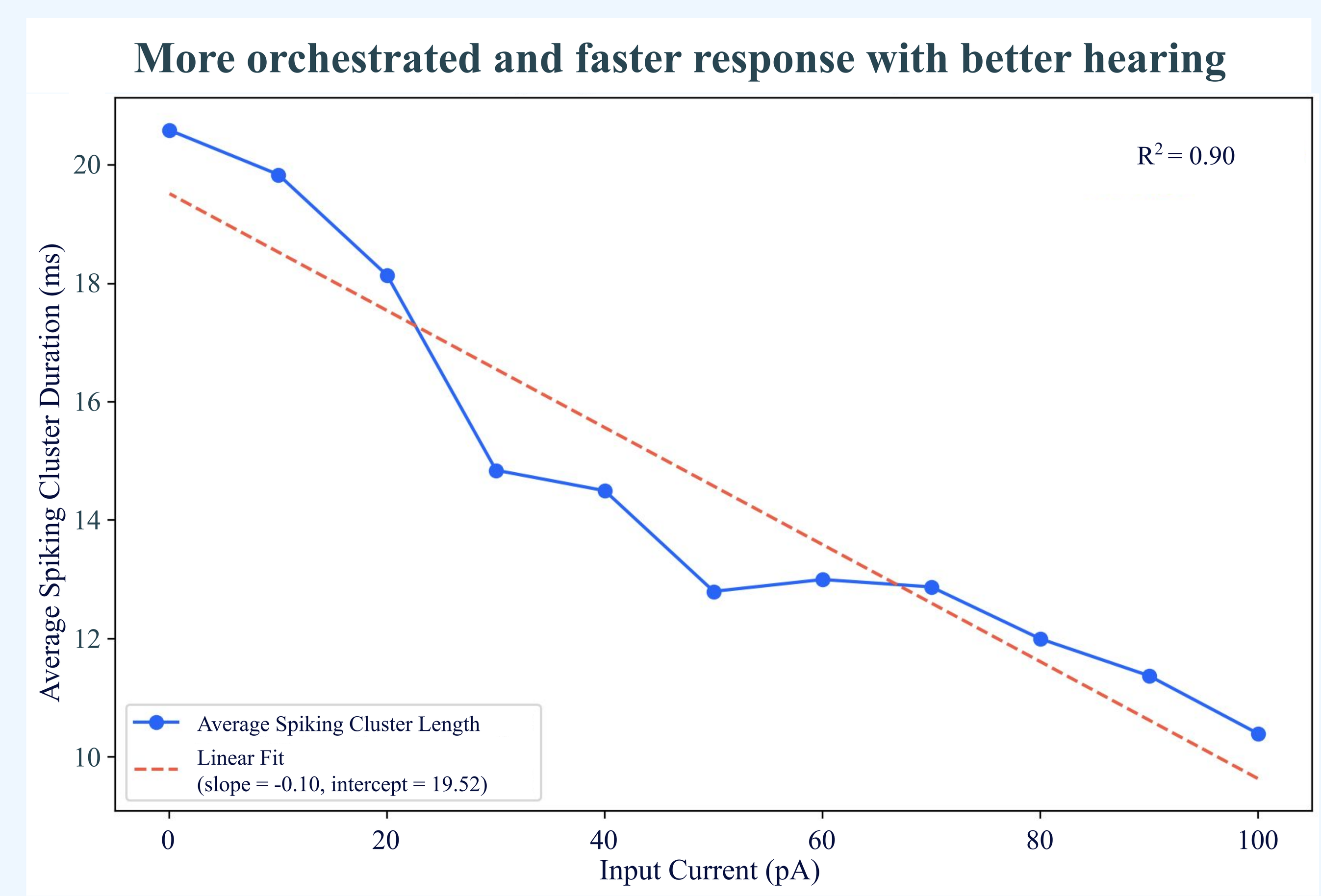


Figure 5: Average spiking cluster duration vs. input current

Discussion

Analysis

- Spike cluster durations are **shorter** with more inputted current (Figures 4a, 4b, and 5), indicating **higher synchronicity** of neuronal firing.
- Lack of input resulted in more **ground activity** (consistent, non-synchronized firing); current input resulted in synchronized bursts of activity.
- **Negative linear relationship** ($R^2 = 0.90$) between input current and synchronicity of neurons.

Applications

- Demonstrates how reduced hearing impairs **formation of auditory memories**.
- Highlights the synchronicity of neuronal firing as closely dependent on **strength of signal** from the auditory cortex.
- Reveals importance of **sensory input** in cognitive functions such as memory.

Limitations

- **Scale-down**: our model contains only **1200 cells**.
- **Time-scale**: our simulation only runs for **500 ms**, whereas memory formation occurs on the scale of **seconds**.
- Rather than occurring in spikes to simulate sustained signals from another neuron, our input current is **continuous over time**.
- **Plasticity**: our model does not account for changes in synaptic plasticity during memory formation.

Future Research

- **Expand the network** to encapsulate the auditory pathway to elucidate the impacts of different types of auditory stimulus on memory formation.
- Explore the role of **neuroplasticity** in mitigating the effects of hearing loss.
- Investigate how **varying levels** of sensory information alters how auditory memory is encoded in **engrams**.

References

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