Final Report

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Contents

1.1 Introduction

Our work is based on the paper *A detailed anatomical and mathematical model of the hippocampal formation for the generation of sharp-wave ripples and theta-nested gamma oscillations*. The hippocampus exhibits different oscillatory rhythms during the sleep-wake cycle. These rhythms are not yet fully understood. This paper proposes a computational model of the hippocampal formation based on realistic topology and synaptic connectivity built using Brian2.

The main aim of the model is to test three hypotheses:

1. The role of synaptic connectivity and how Acetylcholine concentration affects interactions between regions of the hippocampus.
2. CAN currents and their activation in regards to Acetylcholine concentration.
3. Hippocampal behavior in response to varying oscillatory rhythm inputs.

The model is based on three types of neurons:

- Inhibitory neurons
- Pyramidal CAN (Calcium Activated Nonspecific cationic channel) neurons
- Pyramidal nonCAN neurons

The model investigates the effect of different changes on the network:

- Variation of synaptic conductances
- Variations of the CAN channel conductance
- Variation of inputs

1.2 Models

1.2.1 Neuron Dynamics Model

The model defines equations and creates groups for each neuron type based on hippocampus structure. It adds synapses between groups and then regions of the hippocampus. Input is taken for EEG data for both sleep and awake. This signal then goes through preprocessing to remove noise.

The neurons in our network were simulated using a single compartment conductance-based model derived from Hodgkin-Huxley.

$$C_m \frac{dV_m}{dt} = -I_{\text{leak}} - \sum I_{\text{channel}} - I_{syn_E} - I_{syn_I} + \eta$$

$$I_{\text{leak}} = (g_{\text{leak}} \times A) \times (V_m - E_{\text{leak}})$$

$$I_{\text{channel}} = (g_{\text{channel}} \times A) \times m^k \times (V_m - E_{\text{channel}})$$

The principal excitatory neurons were pyramidal cells modelled with the following ion channels: fast sodium (I_{Na}), potassium (I_K), low-threshold calcium current (I_{Ca}), and potassium M-current (I_M). Some pyramidal cells were also added a Calcium-Activated-Nonspecific (CAN) cationic channel, with corresponding current I_{CAN}.

1.2.2 Synaptic Model

The interactions between neurons were modelled as AMPA and GABA-A synapses, with I_{synE} and I_{synI} currents for excitatory and inhibitory connections respectively. These currents are described by the following bi-exponential differential equations:

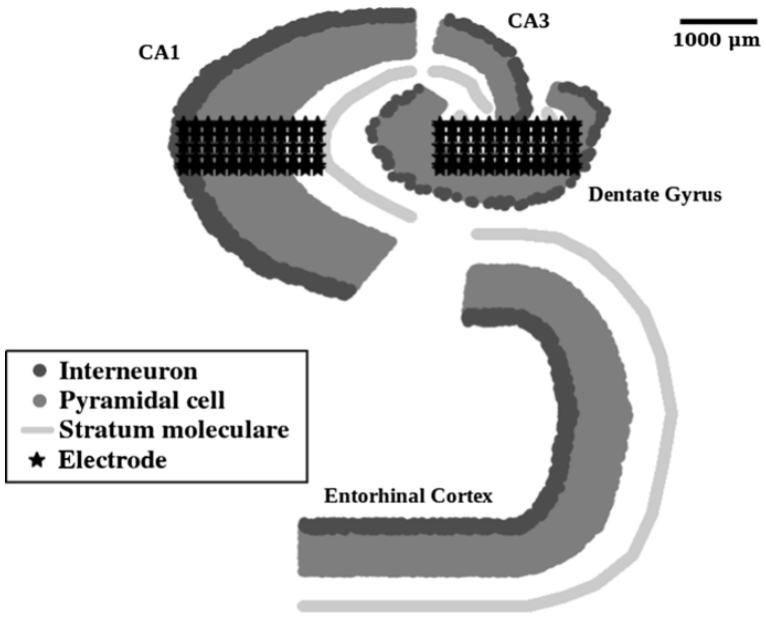
$$\begin{aligned} I_{syn_{I,E}} &= g_{I,E}\left(V_m - E_{I,E}\right), \\ \frac{dg_{I_{I,E}}}{dt} &= \left(-g_{I,E} + h_{I,E}\right)\frac{1}{\tau_{I_{I,E}}}, \\ \frac{dh_{I,E}}{dt} &= -h_{I,E}\frac{1}{\tau_{h_{I,E}}}. \end{aligned}$$

1.2.3 Anatomical Model

The network consists of the hippocampus and the entorhinal cortex. The hippocampus is divided into 3 substructures, each with different ratios and different types of neurons, and the ratio of neurons between CA1 and CA3 is 10:1:

- Dentate Gyrus: 100:1 ratio for pyramidal vs interneurons, non-CAN neurons
- CA3: 10:1 ratio for pyramidal vs interneurons, CAN pyramidal neurons
- CA1: 10:1 ratio for pyramidal vs interneurons, CAN pyramidal neurons

The Entorhinal Cortex has CAN pyramidal neurons as well.



1.3 Experiments

We devised a few experiments with the given model to understand its behaviour under different conditions better. To do this, we have taken 3 approaches-

1. Vary the input data- To this end we have used random inputs sampled from a Poisson distribution and have tried using step inputs and graphed the results.

2. Effects of different neuron types- Similar to the paper where the authors tested the impact of topology, we have simulated the model with the existing topology but by changing the types of neurons simulated in the model. We observed model behaviour when we changed all neurons to Pyramidal Non-CAN neurons.

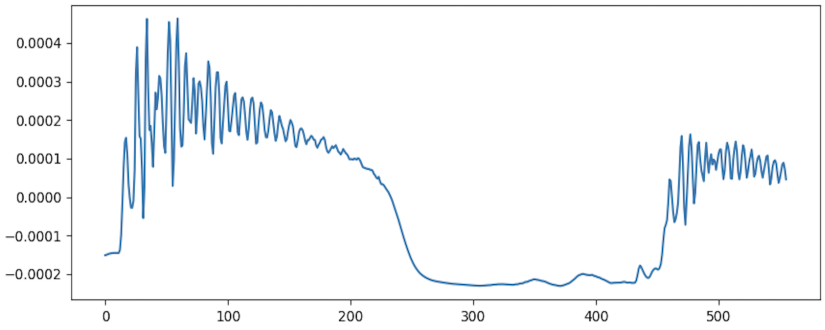
3. Neuron activation visualisation- Using brian2's SpikeMonitor, we have tried to visualise how different parts of the hippocampus activate under our inputs.

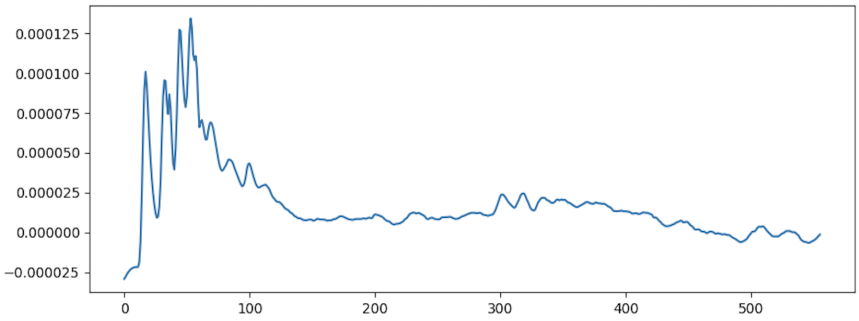
In all experiments we have simulated the hippocampus for 0.5 seconds. Running this on our system takes over 6 minutes. This is in part because we have had to resort to not use cython for on-the-fly code generation which results in severe slowdowns in brian2 simulations. The given code does not work otherwise due to changes in brian2 since the model debut in 2018.

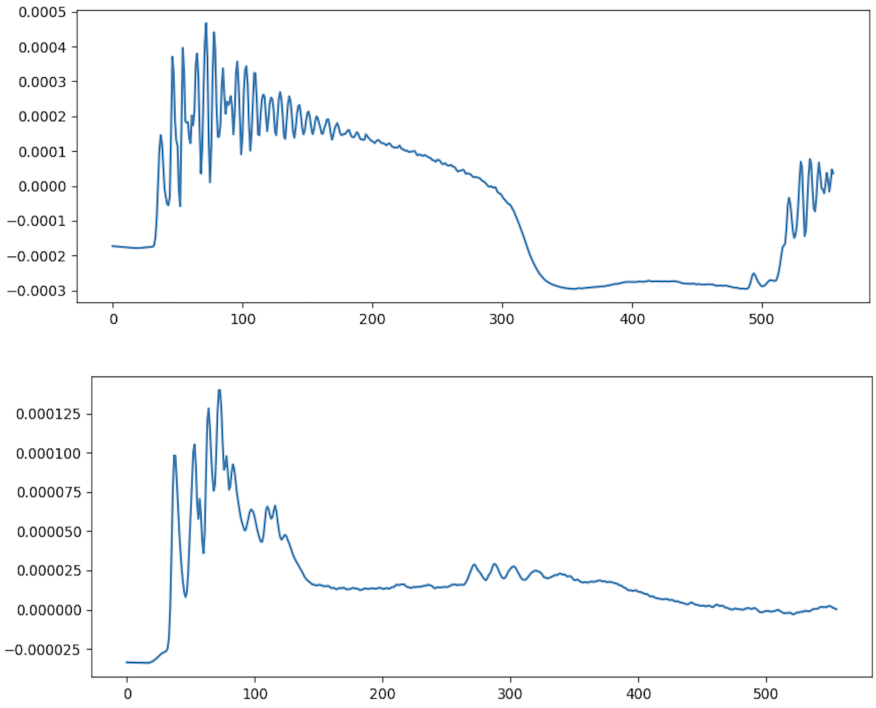
1.4 Results

1.4.1 Input Variation

For both Poisson and step input we see Sharp waves and ripples for sleep mode and a tapering off in wake mode. The oscillations are present at a greater frequency with the Poisson input. Given below are the results for Poisson input sleep & wake, and for Step input sleep & wake respectively.

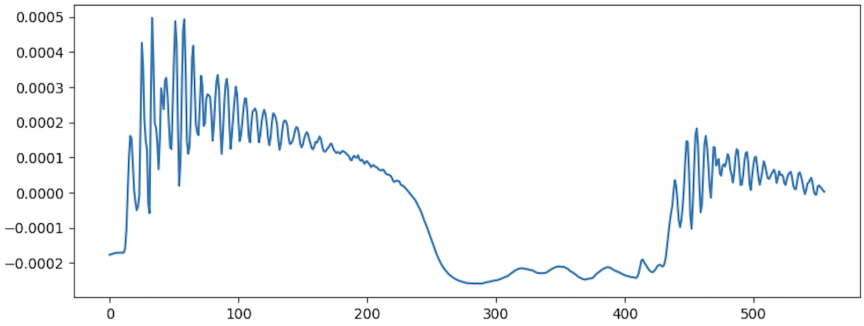


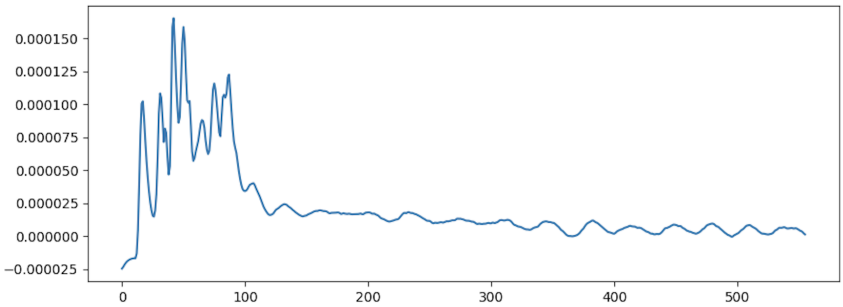




1.4.2 Changing Neuron Types

Using inputs sampled from Poisson distribution, we observe results with the model as made of only as only non-CAN neurons under both sleep and wakefulness conditions. The images are presented in the same order.





1.4.3 Visualisation of neuron activity

We have plotted neuron activity for every type of neuron cluster in the model. Since there are 12 of these, we have not included these images in this report, but these are present in 'neuronSpikes' folder of code submission. Unfortunately, it has proven too difficult to render the neuron spikes in an anatomically accurate manner. These plots can be generated for any type of model input and condition.