Simulated Mechanisms of Gamma Oscillations

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Abstract

Gamma oscillations (25-90 Hz) are important for cognition and are often nested in theta oscillations (4-10 Hz). Two main mechanisms proposed for synchronization in this band are interneuronal network gamma (ING) and pyramidal interneuronal network gamma (PING). The main difference between the two is that ING requires only interneurons to generate gamma oscillations while PING requires both interneurons and pyramidal neurons.

Both ING and PING can be further subdivided based upon the mechanism of oscillation:

- stochastic with subthreshold neurons driven by white noise
- deterministic as a network of coupled oscillators

In addition, the classic PING mechanism has another variant where the excitatory (E) cells (pyramidal cells) are above threshold and drive the subthreshold inhibitory interneuron (I) cells to fire. The interneuron cells then provide an inhibitory feedback which serves to synchronize the pyramidal cells.

To study these different mechanisms of gamma oscillations and network synchronization, two models were implemented in the BRIAN simulation package:

- Theta-modulated grid cell activity in the medial entorhinal cortex (MEC) with 3944 excitatory and 1020 inhibitory exponential integrate and fire neurons (Pastoll et al., 2013)
- Fast oscillations in network of 5000 inhibitory Leaky Integrate and Fire (LIF) neurons with random Gaussian noise (Brunel and Hakim 1999)
- The above model was later modified by replacing the LIF neurons with Izhikevich resonator neurons

Spike raster plots and interspike interval (ISI) histograms were computed and plotted in order to determine the mechanisms.

Introduction

Brain rhythms typically arise from the collective activity of neurons, specifically the interactions between populations of excitatory cells and populations of inhibitory cells. These brain rhythms are commonly divided into several different frequency bands, such as alpha (8-12 Hz), beta (13-30 Hz), and delta (1-4 Hz). Two very important frequency bands are theta (5-10 Hz) and gamma (30-90 Hz).

In rats, theta frequency brain rhythms were observed in the hippocampal formation (a region important for learning and memory) during exploratory locomotion. The gamma frequency brain rhythms were most prominent when they occurred at the peaks of the theta cycles. It is thought that the gamma cycles serve to update the rodent's information regarding location while the theta cycle helps organize the information.

Matthew Nolan's lab tried to understand the basis of theta nested gamma in an in vitro slice preparation of the MEC. They expressed the light sensitive channel rhodopsin in both putative grid cells (excitatory stellate cells) and in the fast spiking inhibitory interneurons. This enabled them to use a sinusoidal light wave to excite the MEC at theta frequency and evoke theta nested gamma rhythms. They found that blocking excitatory connections decreased the individual neuron activity slightly, but almost destroyed the gamma frequency. They published a model that showed how stellate cells, recruited by light oscillating at theta, could synchronize the network at gamma frequencies. However, upon investigation, I found that if excitatory connections are blocked in the model, the interneurons cease firing, and the excitatory cells are left to fire unopposed. (Figure 1; Middle)

Figure 1: Pastoll Model Neurons

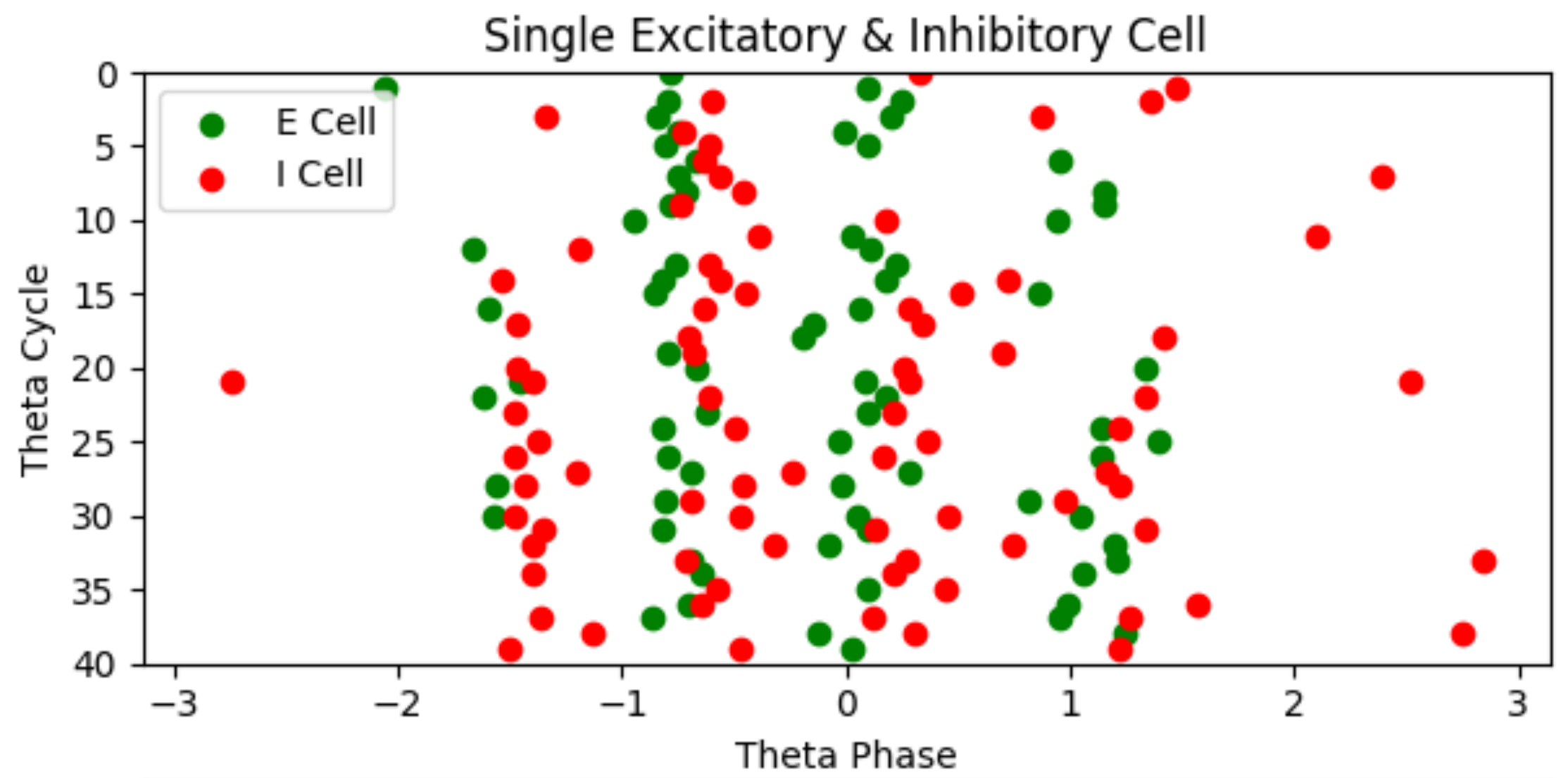

Figure 1a: Single excitatory and inhibitory cell firing data from the Pastoll Model network over 40 theta cycles. E Cell firing occurs at the peaks of theta and is suppressed during the troughs

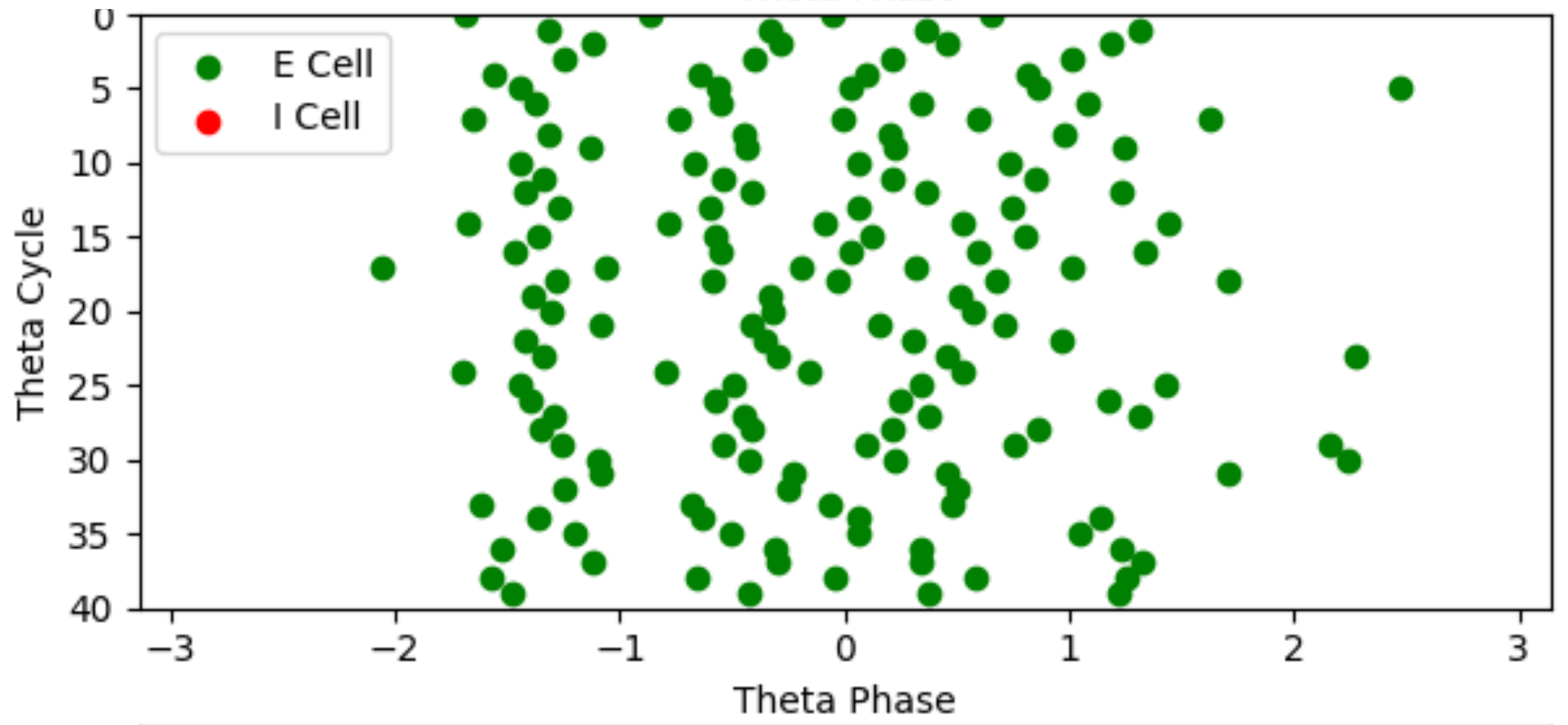

Figure 1b: Same network as in Figure 1a, but the E-I synapses were suppressed, causing uninhibited E Cell firing

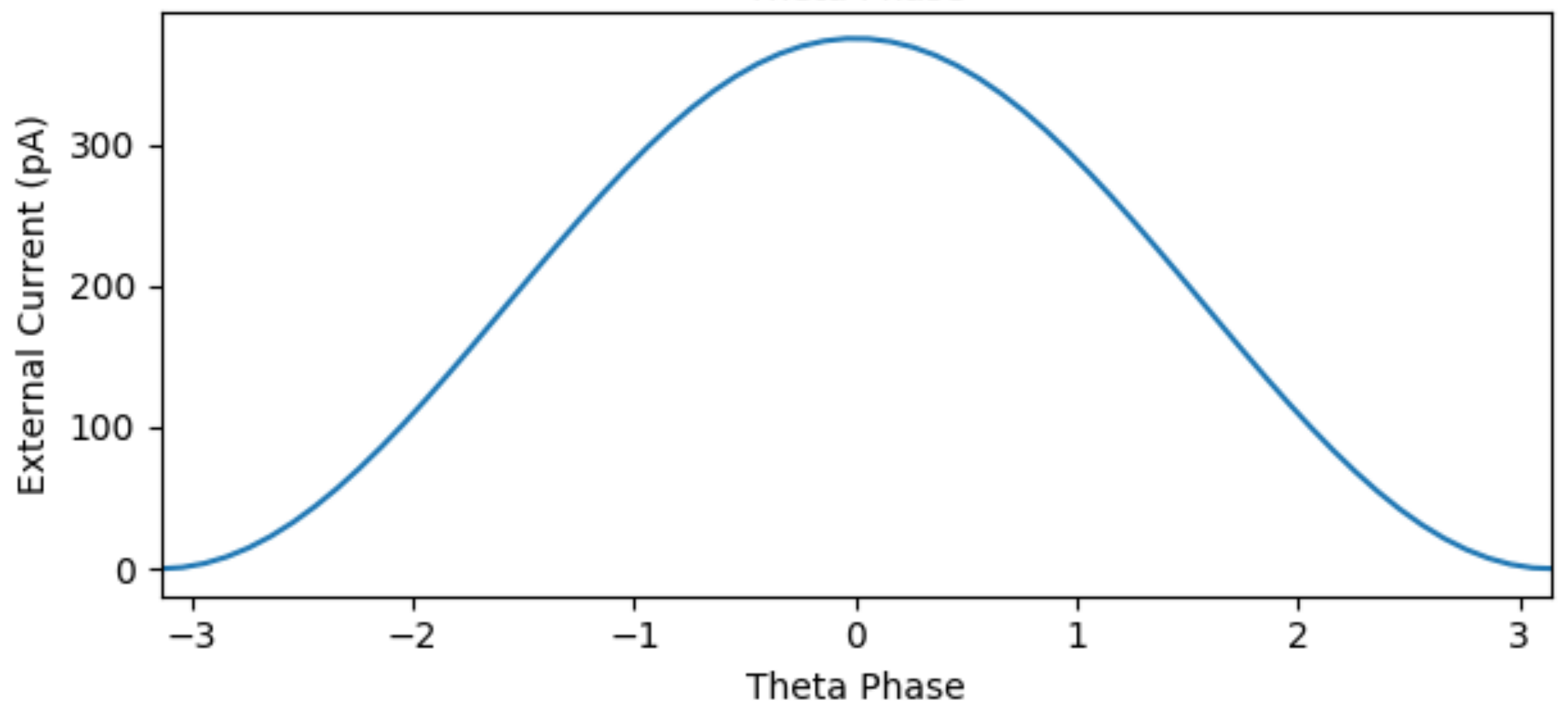

Figure 1c: External current applied to the Pastoll Model network at theta (5-10 Hz) frequency; simulated the sinusoidal light wave used experimentally

Figure 2: Pastoll Model Network

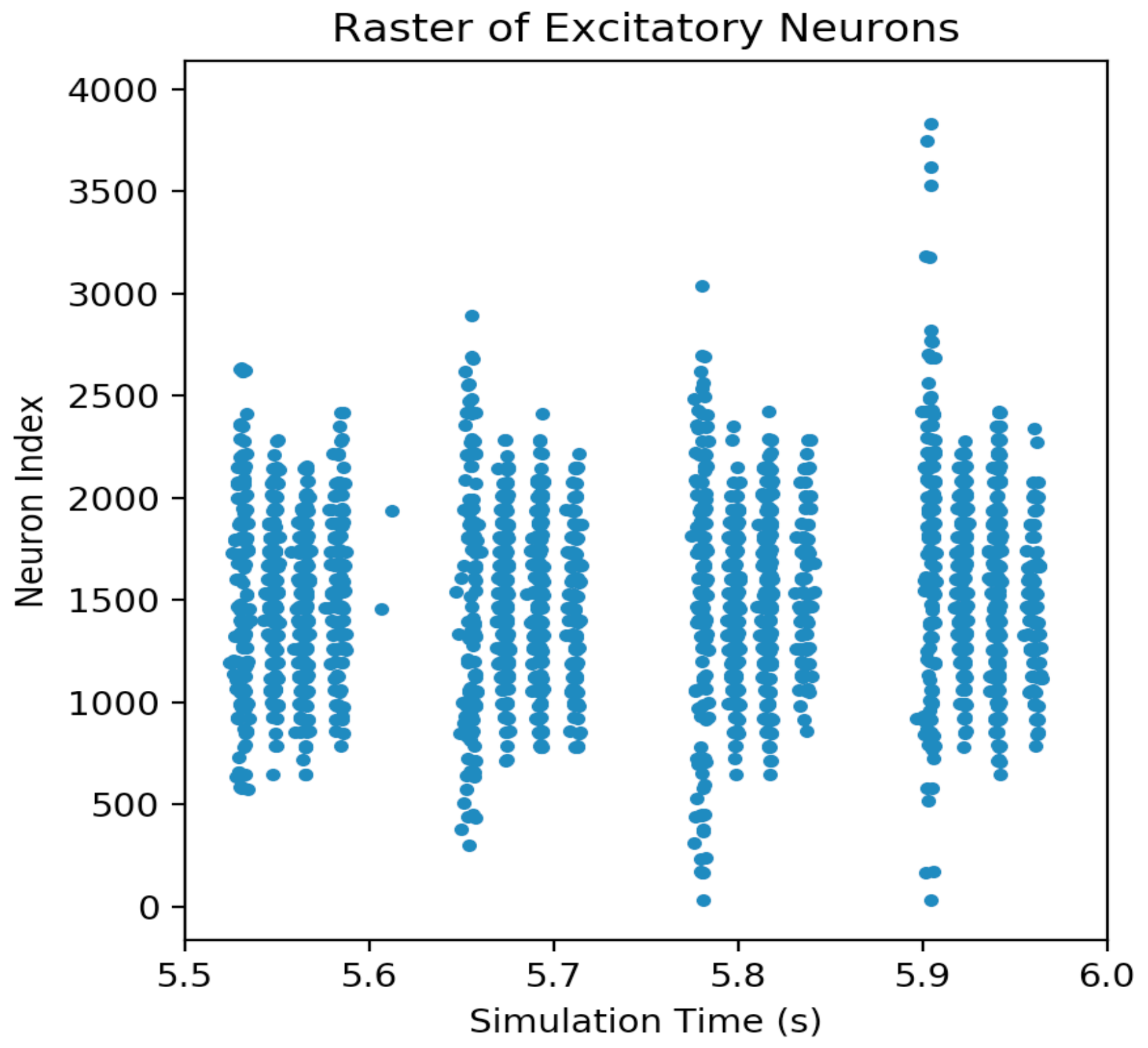

Figure 2a: Raster of all the E Cells in the Pastoll Model network over four consecutive theta cycles showing theta nested gamma waves
(Theta period = 0.125 sec, Gamma period = 0.018 sec)

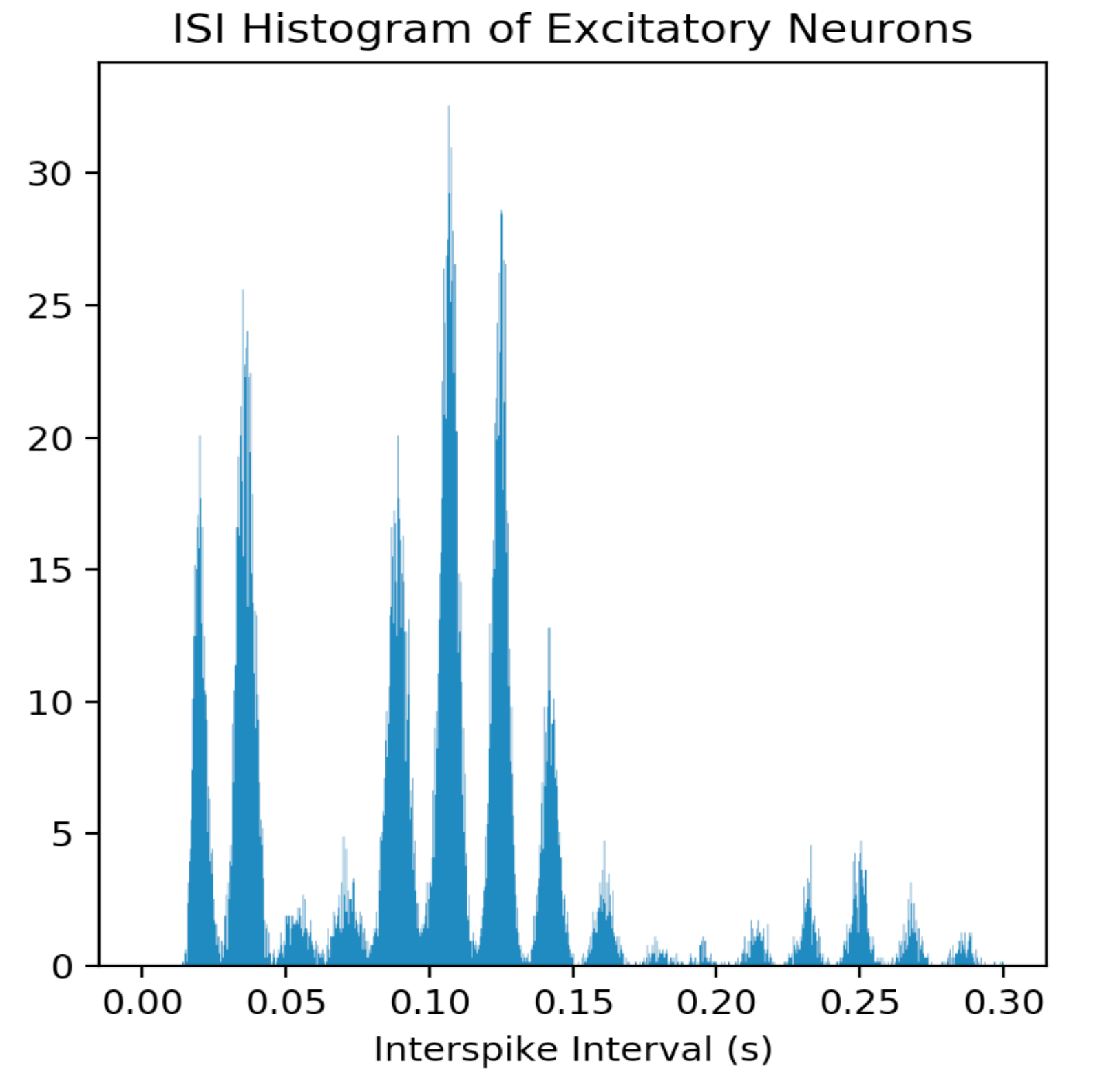

Figure 2b: Interspike Interval (ISI) histogram showing the time between action potentials for each neuron in the network. Peaks occur at linear combinations of the gamma & theta periods

Figure 3: LIF Network

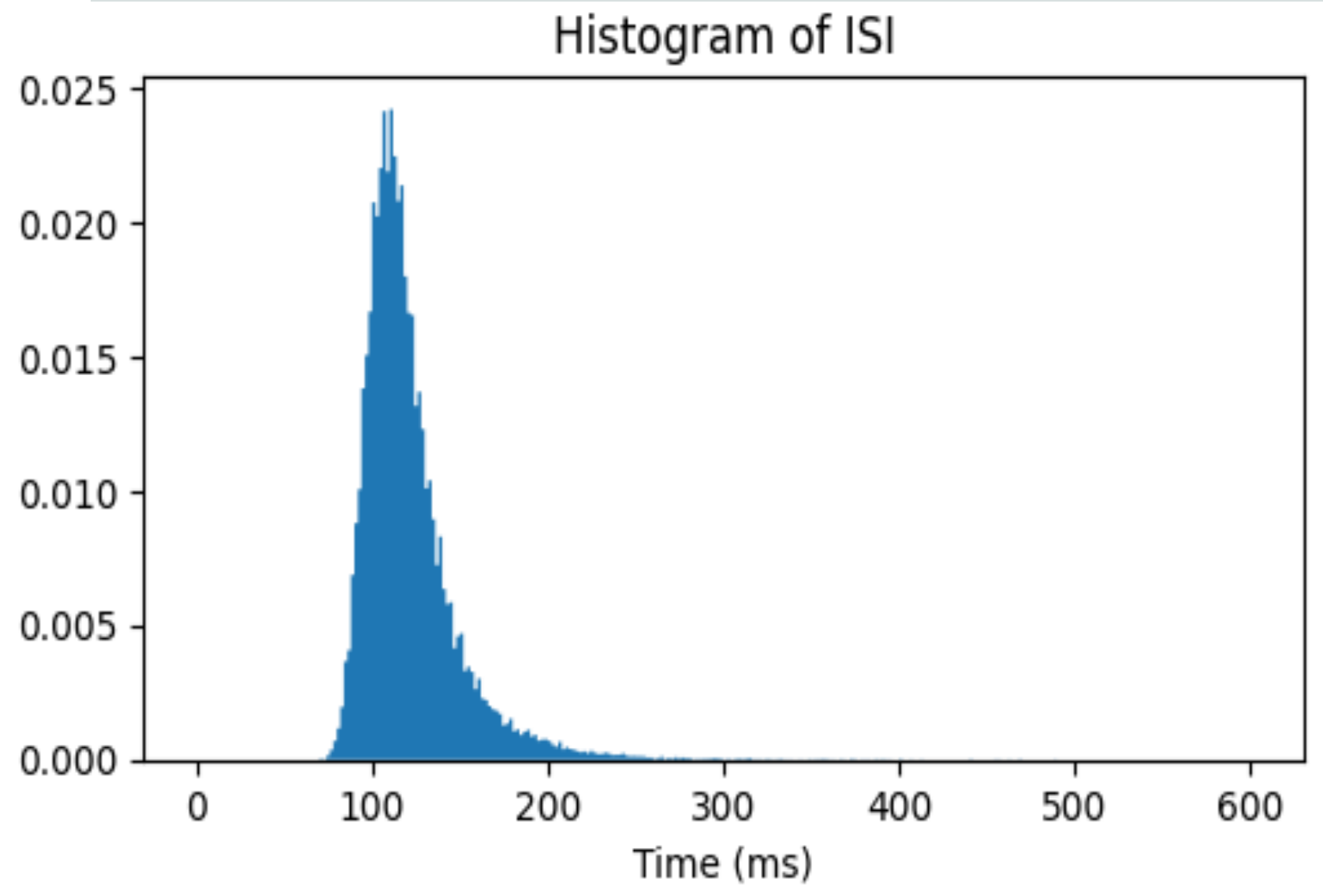

Figure 3a: ISI histogram for the 5000 LIF neuron network. This is an exponential ISI distribution vs the multimodal Gaussian ISI distribution seen in Figures 2b and 4a

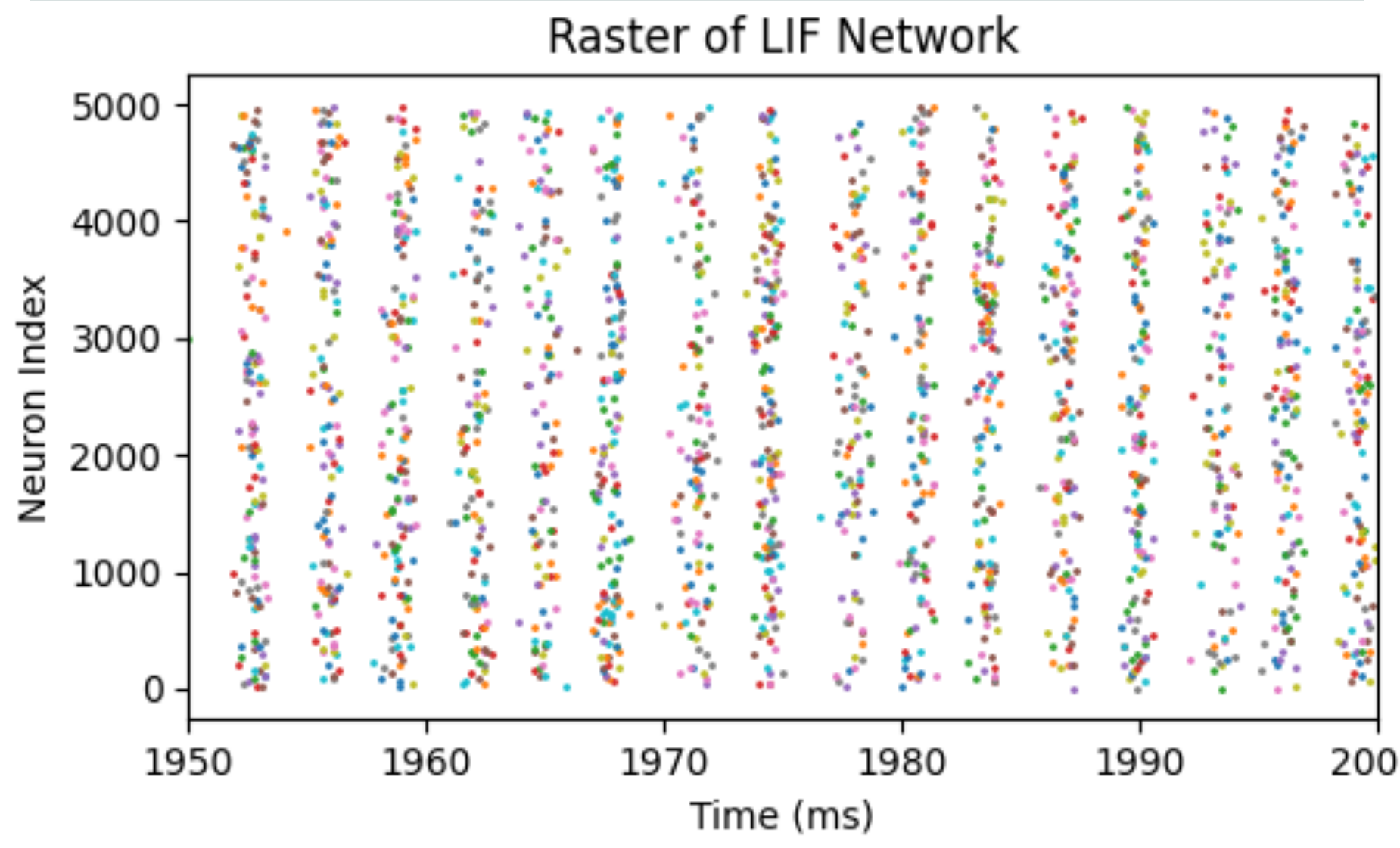

Figure 3b: Firing data of all neurons in the LIF network. While the population is firing rhythmically, individual cells are firing in a more random manner

Figure 4: Izhikevich Network

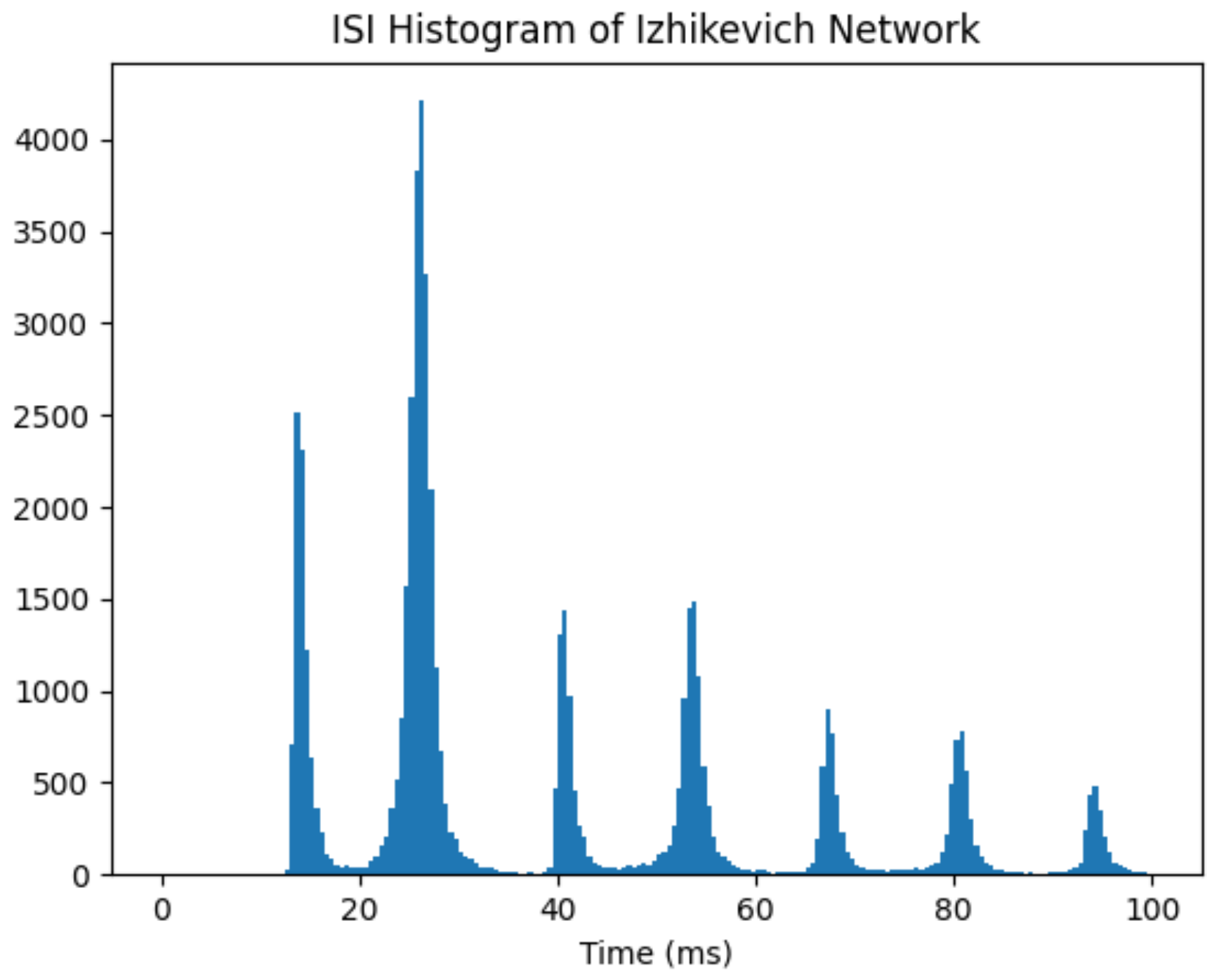

Figure 4a: ISI histogram for the Izhikevich network. This is a multimodal Gaussian ISI distribution, similar to the one in Figure 2b, shifted by the neuron's refractory period

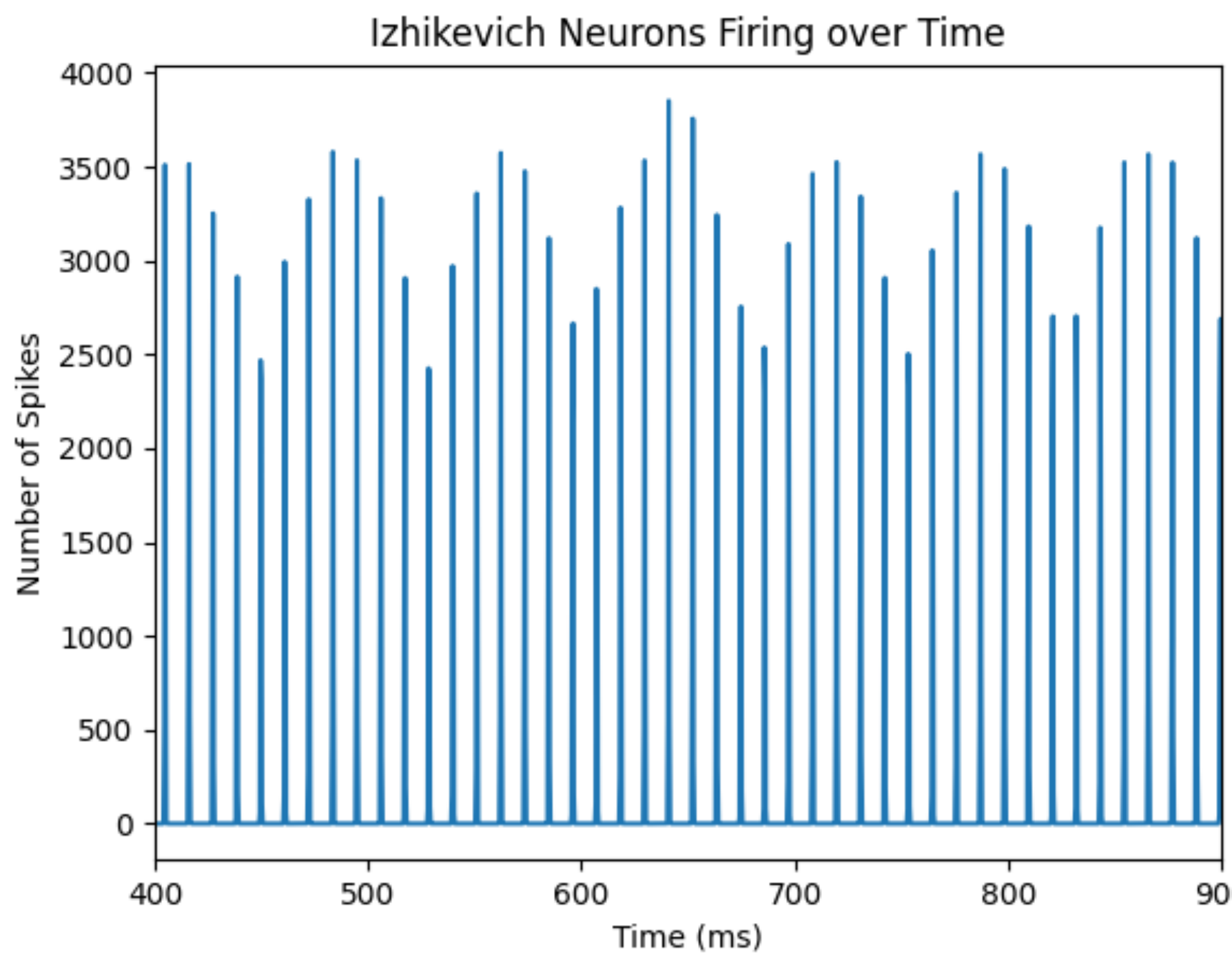

Figure 4b: Izhikevich network activity shown over time. The rhythmic firing of the population causes a slower oscillation to emerge

Results

Pastoll Model Network:

- Simulations of the model revealed that the E cells were above threshold during the peaks of the external theta current and were subthreshold during the troughs (Figure 1a)
- Turning off the E-I connections suppressed all I cell firing, indicating that the mechanism for the theta-nested gamma oscillations was the classic PING mechanism (Figure 1b)
- However, experimental data shows I cells should still fire even with blocked E-I synapses
- This inconsistency in a published mechanism of theta-nested gamma oscillations is currently being investigated further in the White/Canavier labs

LIF & Izhikevich Networks:

- Reproducing results from the Brunel and Hakim 1999 model, I found the LIF network in the subthreshold fluctuation-driven regime produced a stochastic population oscillation, evidenced by the exponential ISI distribution (Figure 3a)
- Replacing the LIF neurons with Izhikevich resonator neurons, I tried to find a corresponding stochastic population oscillation in the new Izhikevich network but was unable to
- However, changing the regime to mean-driven caused a new population oscillation to emerge where the fraction of neurons firing on each population cycle oscillates at a tenth the frequency of the faster population oscillation due to waxing and waning inhibition (Figure 4b)
- This novel mechanism for cross frequency modulation will be investigated in the future