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# "**Simulated Mechanisms of Gamma Oscillations**"

**Introduction**: Gamma oscillations (25-90 Hz) are important in cognition and often nested in theta (4-10 Hz). Two main mechanisms proposed for synchronization in this band are interneuronal network gamma (ING) and pyramidal interneuronal network gamma (PING). ING requires only inhibitory interneurons, whereas PING needs both. Either oscillation can be 1) stochastic with subthreshold neurons driven by noise or 2) deterministic as a network of coupled oscillators. In classic PING there is a further variant in which only the excitatory (E) cells (pyramidal cells) are above threshold and drive the subthreshold inhibitory interneuron (I) cells to fire. This inhibitory feedback synchronizes the E cells. Pastoll et al. 2013 showed that optogenetically driven theta-nested gamma in medial entorhinal cortex (MEC) slices required E-I synapses for synchrony but not for firing of the I cells.

**Methods**: Two models implemented in the BRIAN simulation package were used to study mechanisms of gamma oscillations: 1) theta modulated grid cell activity in the MEC (Pastoll et al., 2013) with 68 excitatory and 34 inhibitory exponential integrate and fire neurons.2) fast oscillations in a network of 5000 inhibitory leaky integrate and fire neurons with random Gaussian noise (Brunel and Hakim 1999). Spike rasters and interspike interval (ISI) histograms were plotted to determine mechanism.

**Results**: Simulations of the Pastoll et al 2013 model revealed that during the peaks of theta, E cells were above threshold, and they were subthreshold during the troughs. Moreover, turning off the E to I synapses suppressed all firing in the I cells. Therefore, although it was not stated in the paper, the mechanism for theta-nested gamma was the classic PING mechanism. However, in the experimental study, it is explicitly stated that blocking E-I connections pharmacologically did not stop I cell firing at gamma frequencies, it merely desynchronized the population. Therefore, I showed that the model in their study does not actually account for theta nested gamma synchrony. ISI histograms peaked at additive combinations of multiples of the gamma period, the theta interburst interval, as expected for a deterministic, coupled oscillator model.

It is well-known that leaky integrate and fire (LIF) neurons in the fluctuation-driven regime can produce a stochastic population oscillation. I reproduced these results in the Brunel and Hakim 1999 model, as evidenced by exponential ISI distributions (less a refractory period). Moreover, I extended them by replacing the LIF neurons, which are integrators, with Izhikevich resonator neurons that cannot fire below a cutoff frequency. In the subthreshold, fluctuation driven regime, these resonator neurons preferentially fire bursts at the minimum frequency, resulting in Gaussian uni or multi modal distributions of the interspike intervals; therefore, we have not observed a stochastic population oscillation in model networks of these neurons. On the other hand, a population oscillation can emerge in the mean-driven regime in which 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 network inhibition.

**Conclusions**: I discovered an inconsistency in a published mechanism of theta nested gamma that is now being investigated further in the White/Canavier labs. I also found a novel mechanism for cross frequency modulation.