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Abstract

Network rhythmic oscillations result from the cooperative activity of the participating neurons and synaptic connectivity. Several neuron types exhibit subthreshold (membrane potential) resonance (a peak in the voltage amplitude response to oscillatory current inputs at a preferred, resonant, frequency). Whether and how subthreshold preferred frequency responses translate to the spiking regimes in single cells and networks (spiking and network resonance) are still open questions. We use mathematical modeling and simulations to address these issues in the context of in vivo experimental results where pyramidal cells (PYR) and parvalbumin immunoreative interneurons (INT) were optogenetically stimulated using wide-band (WB) oscillatory signals (Stark et al., Neuron, 2013). Dependence of spiking activity on input frequency was measured by the spectral coherence between the input and output signals. While PYR have been shown to exhibit theta subthreshold resonance in vitro (Hu et al., J Physiol, 2002), in vivo responses of individual directly stimulated PYR were not predominantly at theta, but WB as INT were. In contrast, PYR exhibited theta band-limited rebound spiking induced through direct stimulation of INT, which exhibited a WB response. We present a minimal biophysical (conductance-based) model of a CA1 hippocampal network that captures these experimental results. The basic model includes PYR and INT. The extended model includes also OLM (orients-lacunosum moleculare cells). PYR and OLM included h-currents. The presence of subthreshold resonance in isolated PYR is not communicated to the spiking regime mainly due to the strong effect of the oscillatory input amplitude. PYR theta-band response results from a combination of rebound spiking and a timing mechanism. Rebound spiking is responsible for the generation of spikes at input frequencies that are low enough for the voltage response to be above threshold. The timing mechanisms are responsible for ”erasing” spikes generated by input frequencies lower than theta. We implemented two such mechanisms: (i) network-mediated inhibition from OLM or (ii) synaptic depression of INT synapses. Overall, these results provide a mechanistic understanding of network resonance at theta frequencies.