EXPLORING INTERNEURON SPECIFIC CONTROL OF ORIENS-LACUNOSUM MOLECULARE (OLM) INTERNEURON RECRUITMENT IN CA1 HIPPOCAMPUS

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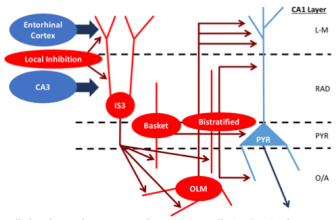
Introduction

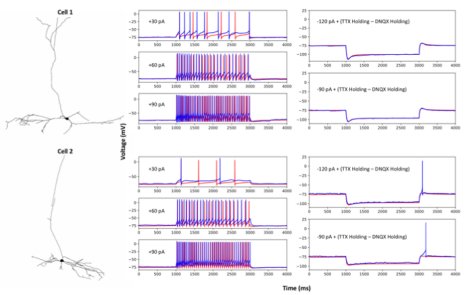
- Interneuron specific 3 (IS3) cells are vasoactive intestinal polypeptide and calretinin positive (VIP+/CR+) cells that only target the dendrites of other inhibitory interneurons, and primarily Oriens-Lacunosum Moleculare (OLM) cells[6].



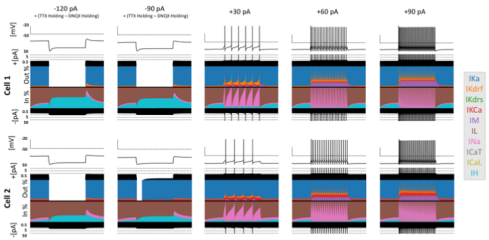
- IS3 cell control over OLM cells has been demonstrated experimentally *in vitro* in the context of theta-timed optogenetic stimulation of CR+ cells[6], however it remains unclear whether this finding is dependent on resultant activity from other interneuron types in CA1 (e.g. feedforward inhibition/excitation), or on contributions of h-current and/or T-type calcium currents to post-inhibitory rebound spiking.
- OLM cells receive inputs from several other populations, including local bistratified (BIS) cells, long range inputs from medial septum (MS), and local CA1 pyramidal (PYR) cells.
- It is also unclear whether OLM cells will display this theta spike resonance *in vivo*, since neurons have been shown to be capable of switching their spike resonance properties when put in *in vivo*-like states[4].
- To test these questions, we perform simulations using recently developed OLM cell multi-compartment models[5], with synaptic inputs constrained to specific inhibitory and excitatory input populations that are known to synapse onto OLM cells.

Models

Multi-Objective Optimization of Spiking Electrophysiology Using BluePyOpt and Neuroscience Gateway (NSG)



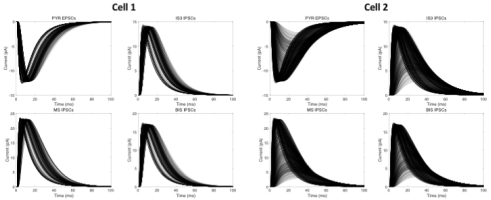
Currentscape Plots Show Current Contribution Profile



Currentscape plotting technique obtained from [1]

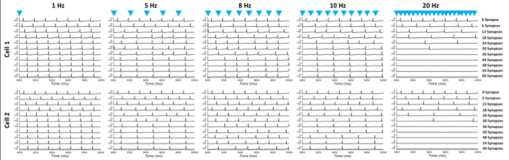
Synaptic Inputs

Literature Values of EPSCs and IPSCs to OLM Cells are Used to Fit Synaptic Parameters to OLM Cell Multi-Compartment Models



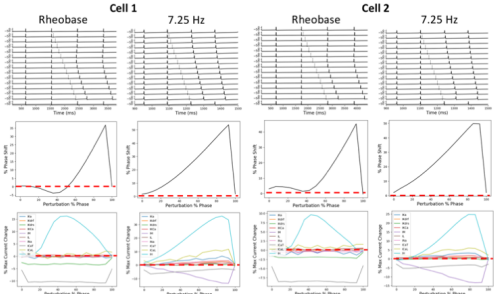
In Vitro-Like Simulations

IS3 Cell Inputs Alone Do Not Elicit Post-Inhibitory Rebound Spiking

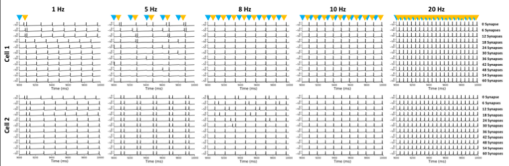


IS3 Cell Perturbations Cause I_H-Dependent Phase Advances Only When Baseline Spike Rate is Low

Phase Advance = Phase Shift < 0 Phase Delay = Phase Shift > 0



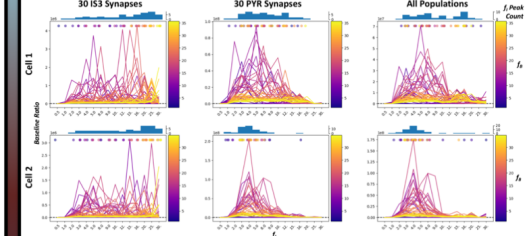
Adding 3 PYR Cell Synapses Allows Robust Recruitment



In Vitro Spike Resonance is Dependent on the Baseline Spike Rate

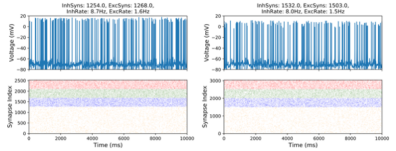
S_{XX} = Spike Train Power Spectrum f_i = Input Frequency f_B = Baseline Frequency

Baseline Ratio = $S_{XX}(f_i)_{\text{Modulated}} / S_{XX}(f_i)_{\text{No Modulation}}$

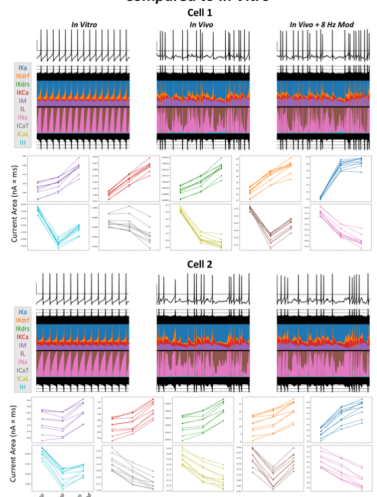


In Vivo-Like[2] Simulations

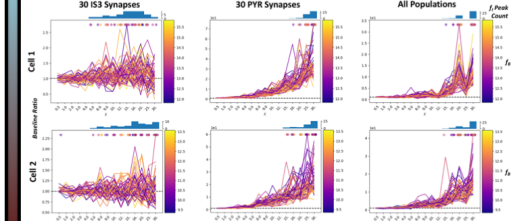
Synaptic Bombardment Generates In Vivo-Like States in OLM Cells



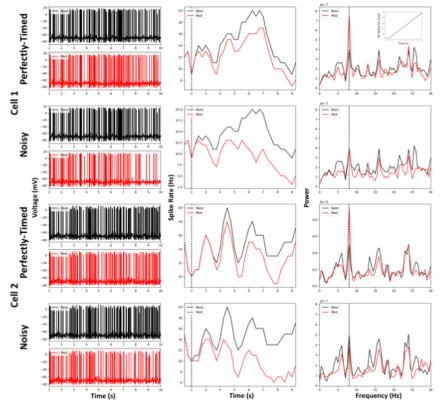
In Vivo-Like States Enhance Intrinsic Current Contributions Compared to In Vitro



In Vivo Spike Resonance is Shifted to Higher Frequencies



Ramping Up IS3 Cell Inputs During 8Hz Modulation Suppresses OLM Cell Spiking & Enhances 8 Hz Recruitment if Perfectly-Timed



Conclusions and Future Work

- IS3 cells can recruit OLM cells through disinhibition of PYR cells *in vitro*
- IS3 cells can also recruit OLM cells *in vivo* if they show a high degree of phase locking to its endogenous spike resonance frequency.
- If IS3 cell inputs are not phase-locked enough, OLM cell spiking will mainly just be suppressed, which may be beneficial for behavioral state transitions[3].
- The effects of inhibitory perturbations *in vivo* will also be modulated by their interactions with the various channel currents present in OLM cells, which show different contributions *in vivo* and at different spike rates

References

[1] Alonso & Marder. (2019). Elife. pii: e42722.
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[4] Prescott, *et al*, (2008). *J Neurophysiol*. 100: 3030–3042
[5] Sekulić, *et al*, (2019). *BioRxiv*. doi: https://doi.org/10.1101/633941.
[6] Tyan, *et al*. (2014). *J Neurosci*. 34(13):4534-47.

Acknowledgements

NSERC CRSNG
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