



# Comodulation of h- and Na+/K+ Pump Currents Expands the Range of Functional Temporal Bursting Properties in a Central Pattern Generator

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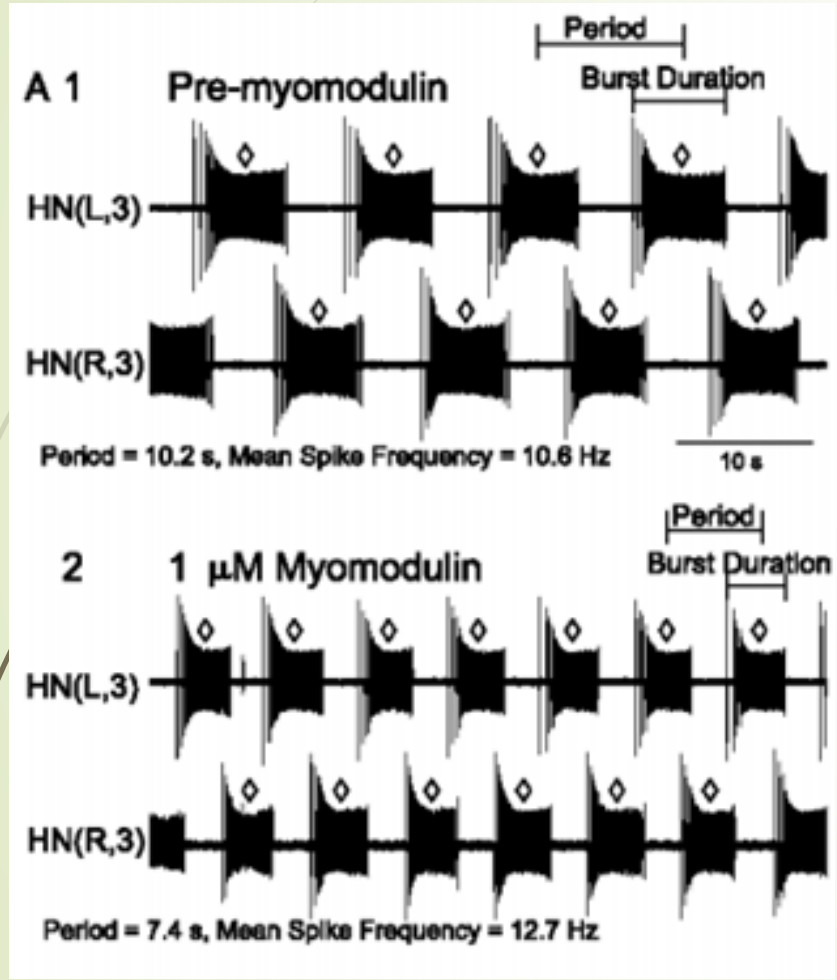
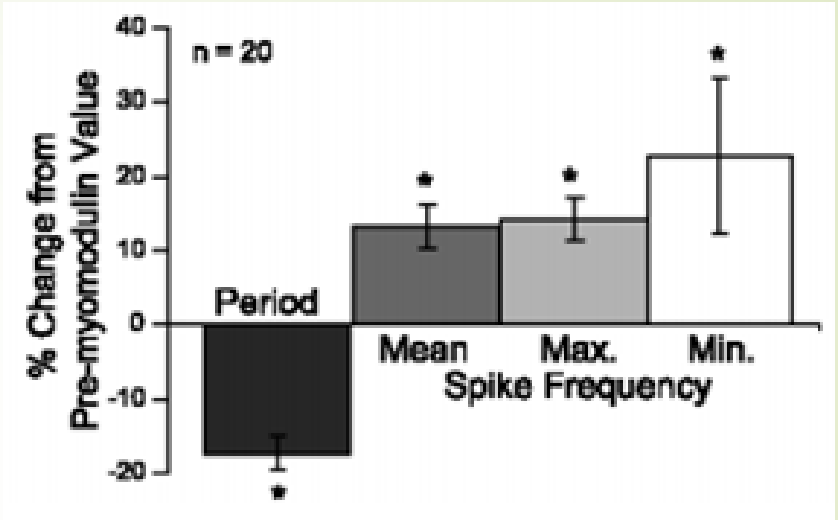
Neuromatch Conference 2020 5/25 – 5/27

# Leech Heart Interneuron Pacing CPG is a Half-Center Oscillator Circuit


- The timing control circuit in the heartbeat CPG of medicinal leeches is well characterized, and ideal for studying questions about rhythm generation from an ion channel level
- Leech heart interneuron (HN) pairs in ganglia 3 and 4 form inhibitory synapses with their contralateral counterparts, assembling a Half Center Oscillator (HCO), and pace activity in the CPG circuit

# Comodulation of h-current and Na/K Pump by Myomodulin



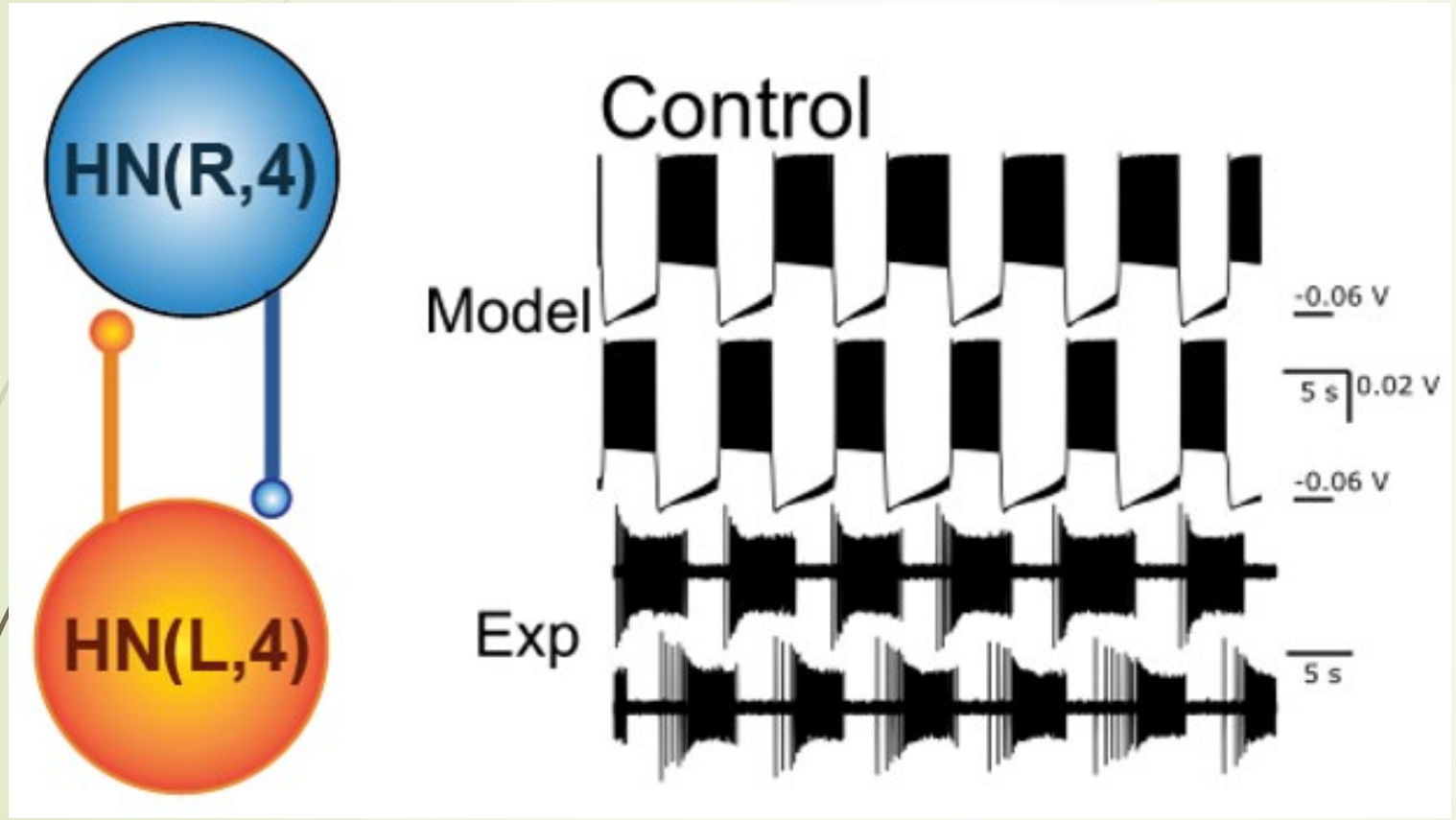




- The Na/K pump is comodulated with h-current under application of 1uM Myomodulin
  - H-current increases
  - Pump current decreases
- Burst period/duration decreases, and spike frequency increases



Tobin A-E, Calabrese RL (2005) Myomodulin Increases Ih and Inhibits the Na/K Pump to Modulate Bursting in Leech Heart Interneurons. J Neurophysiol 94:3938–3950.

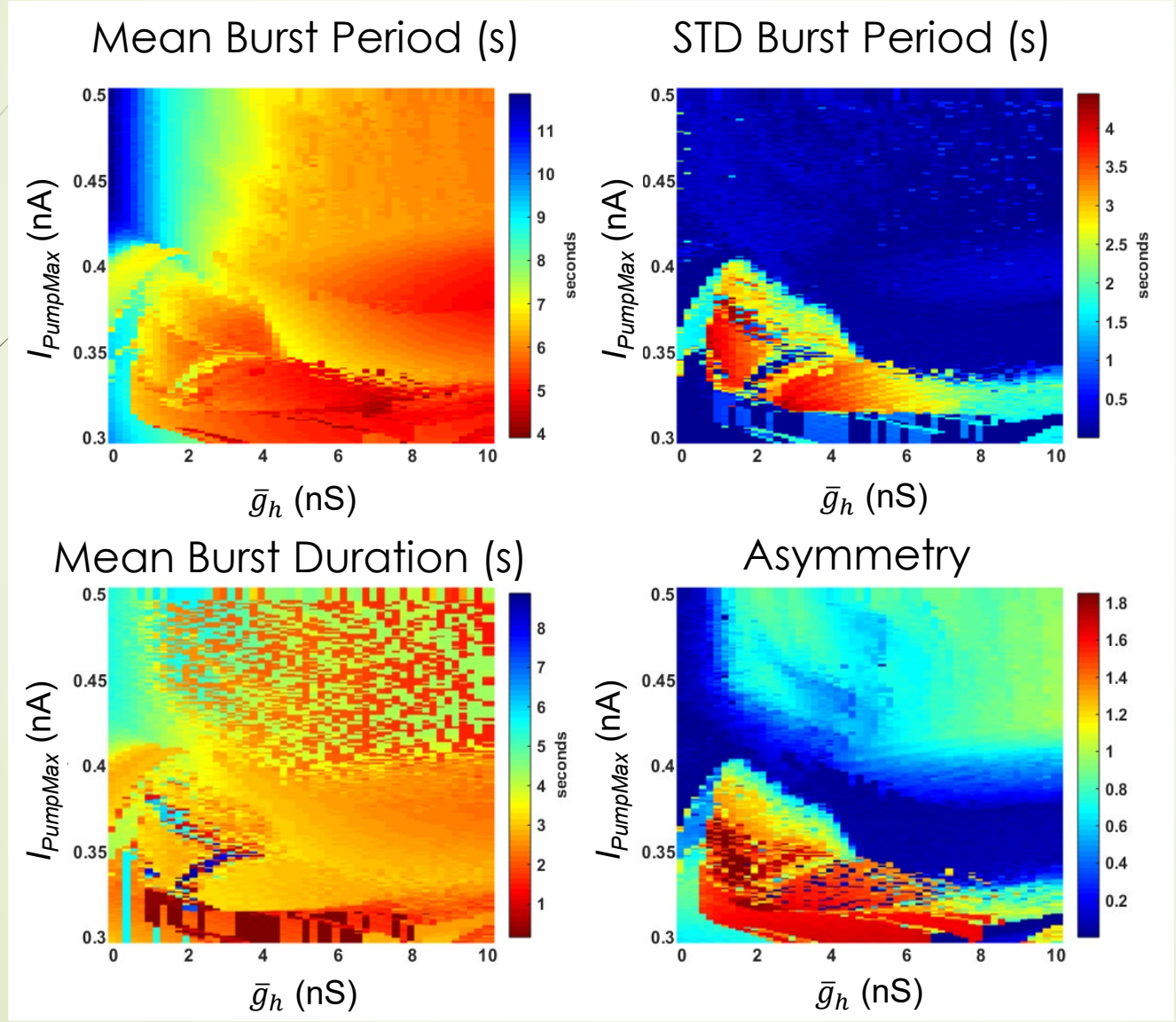
# Tuned Model to experimental data from Leech Heart Interneurons in Myomodulin




- Started with a model from Kueh et. al 2016 (eLife 5:e19322) which was developed for studying the effect of monensin in HN bursting characteristics
- Tuned to more closely align with Tobin/Calabrese 2005 framework using new experimental datasets
- Investigated $\bar{g}_h$ and $I_{PumpMax}$ parameter space

- Extracted temporal burst characteristics at the steady state for each parameter pair to produce a dimensionally reduced map of activity patterns for analysis

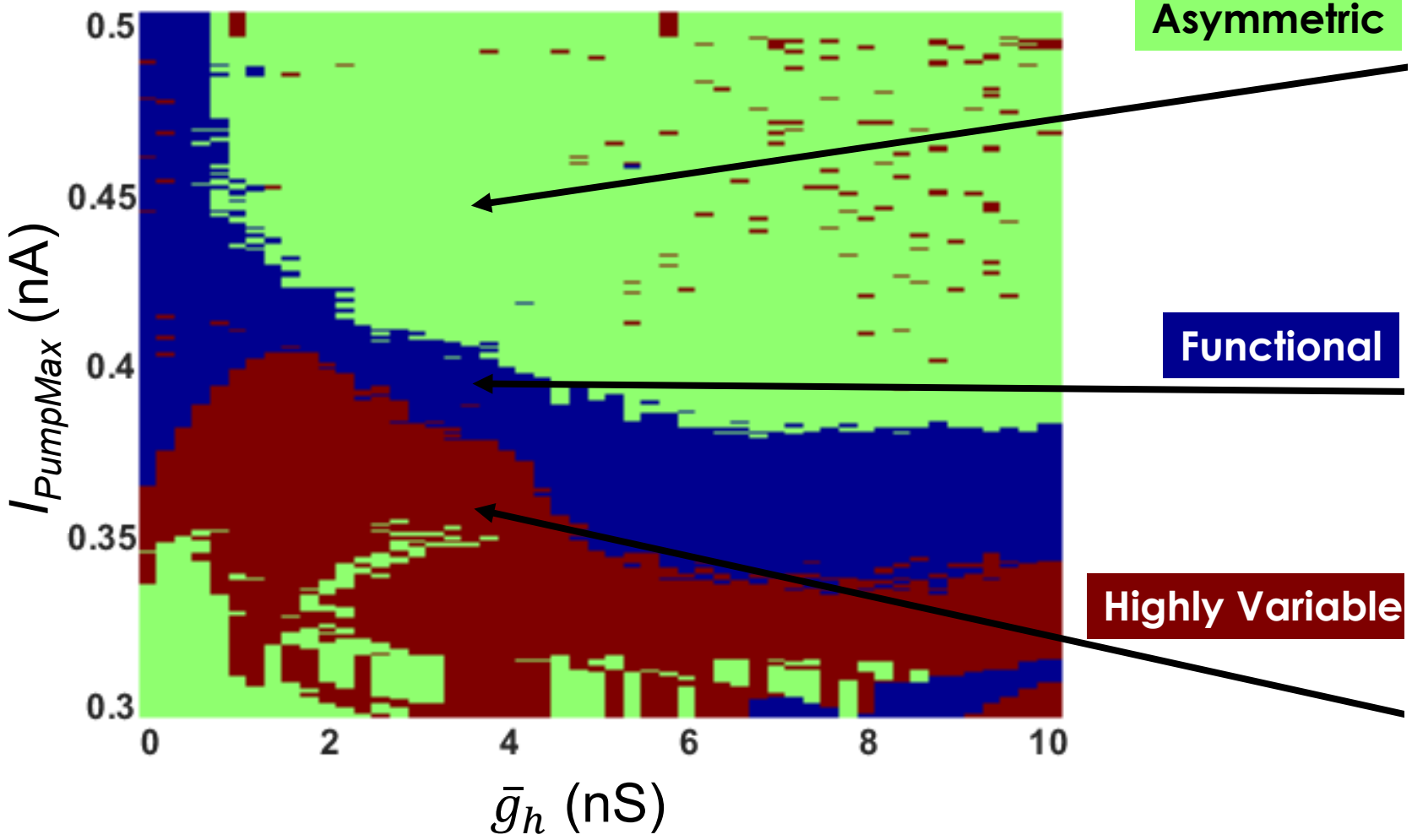
# Half Center Oscillator Model Parameter Sweeps




$$Asymmetry = \frac{2|BD_1 - BD_2|}{BD_1 + BD_2}$$

# Regime Classification of HCO model

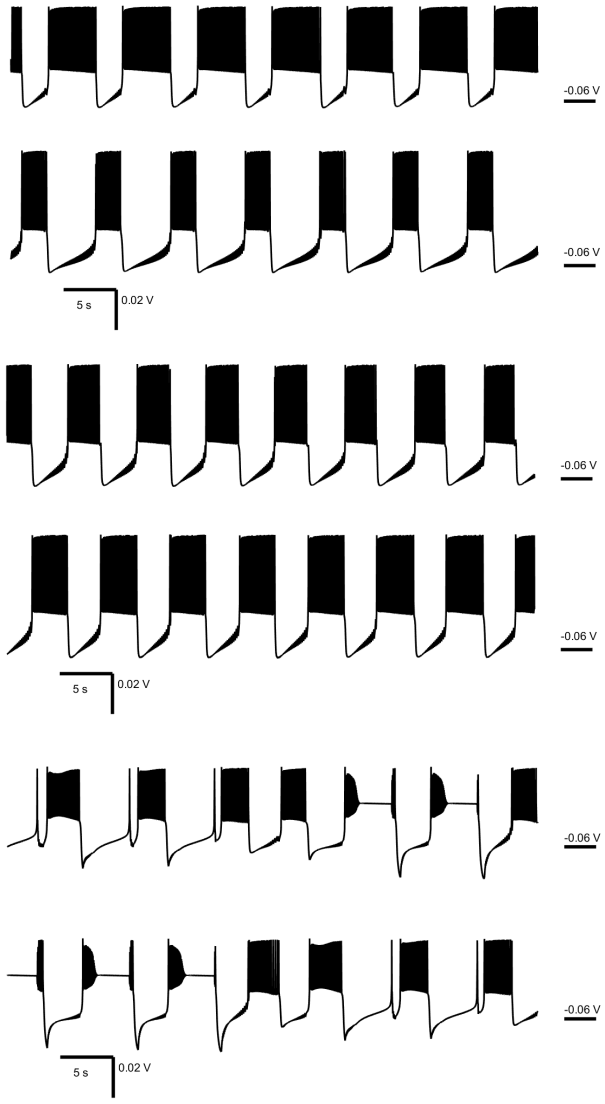




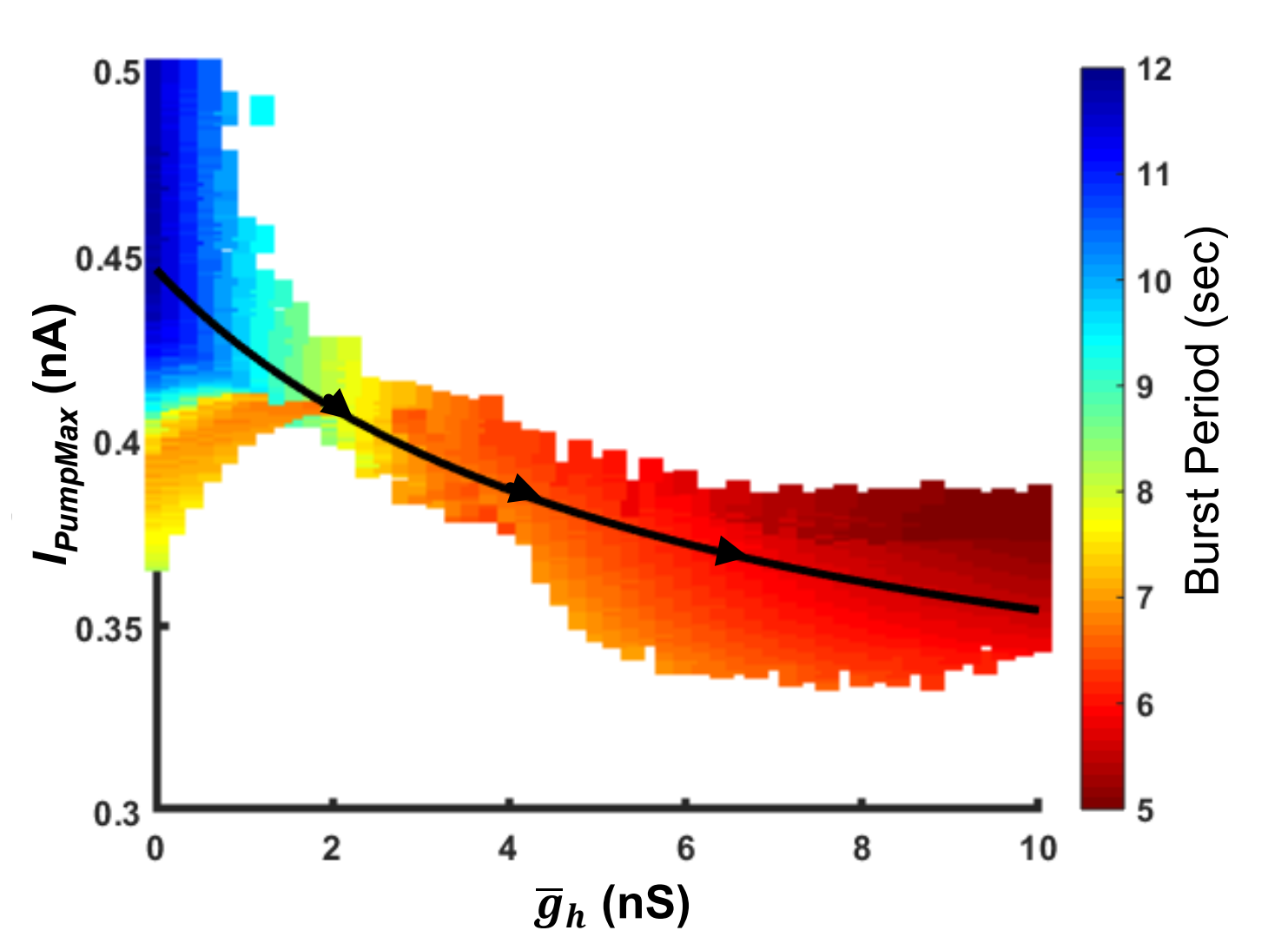

Asymmetric

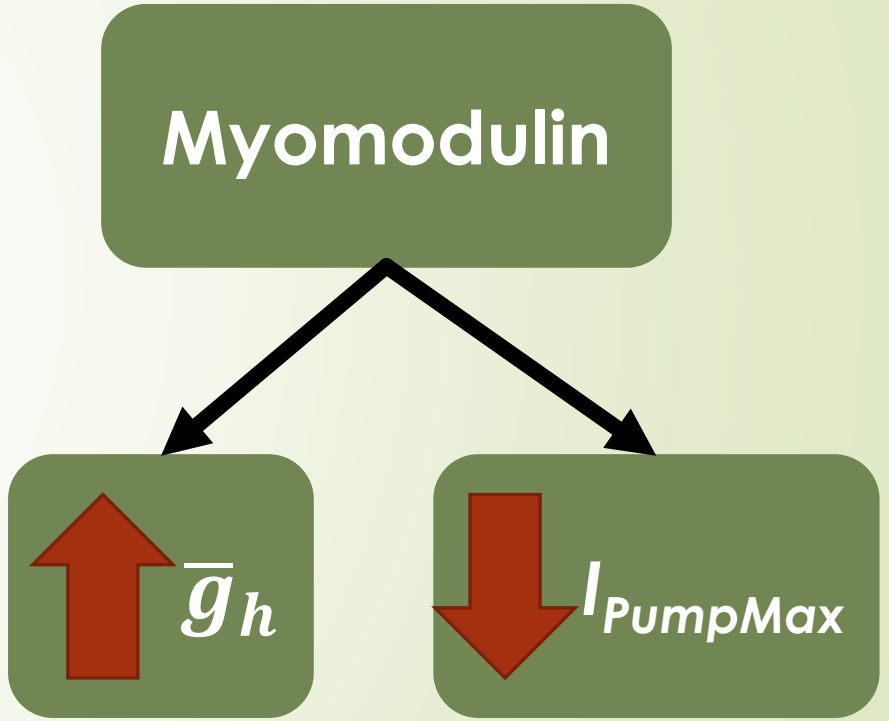
Functional

Highly Variable

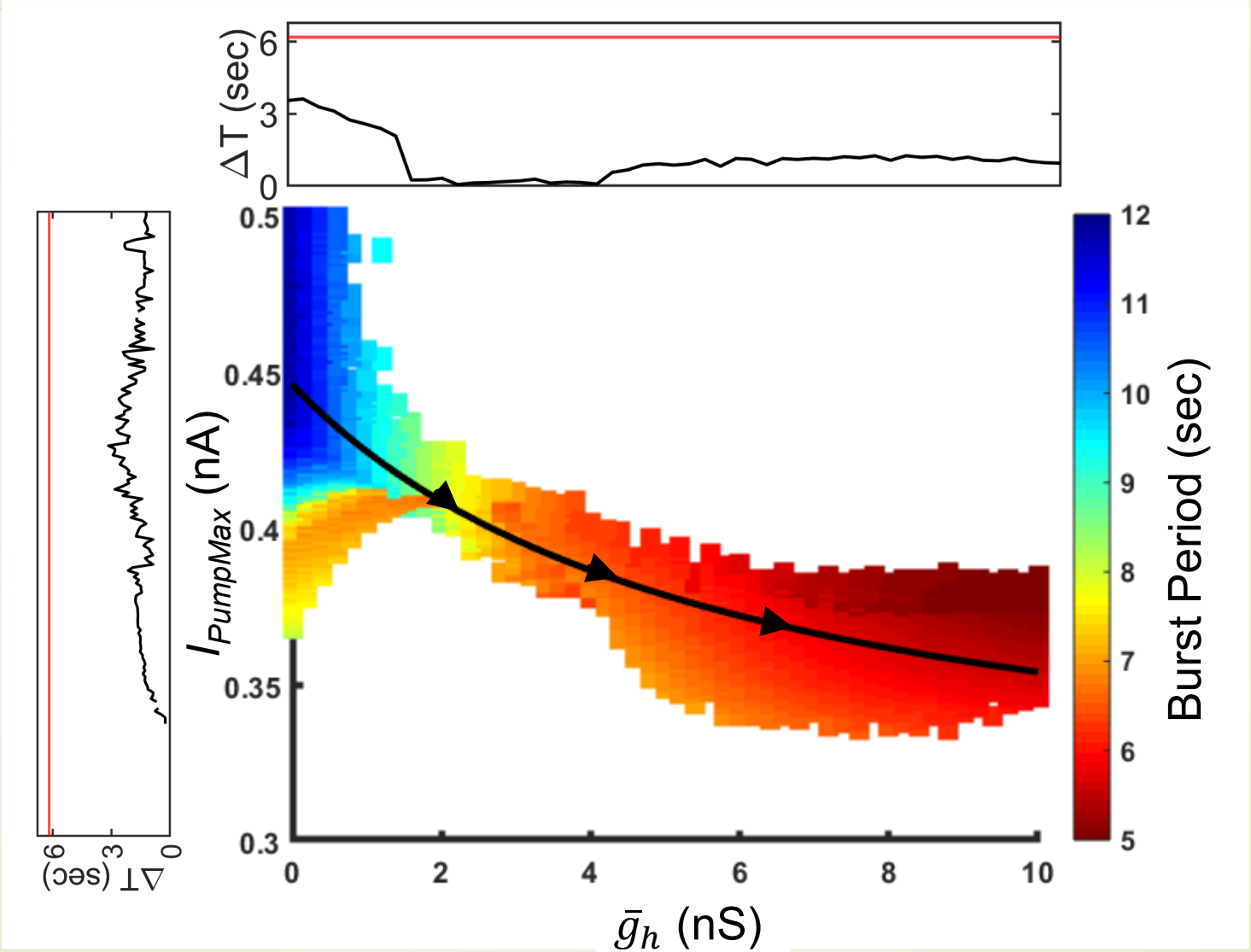


# Comodulation Avoids Asymmetric and Highly Variable Regimes

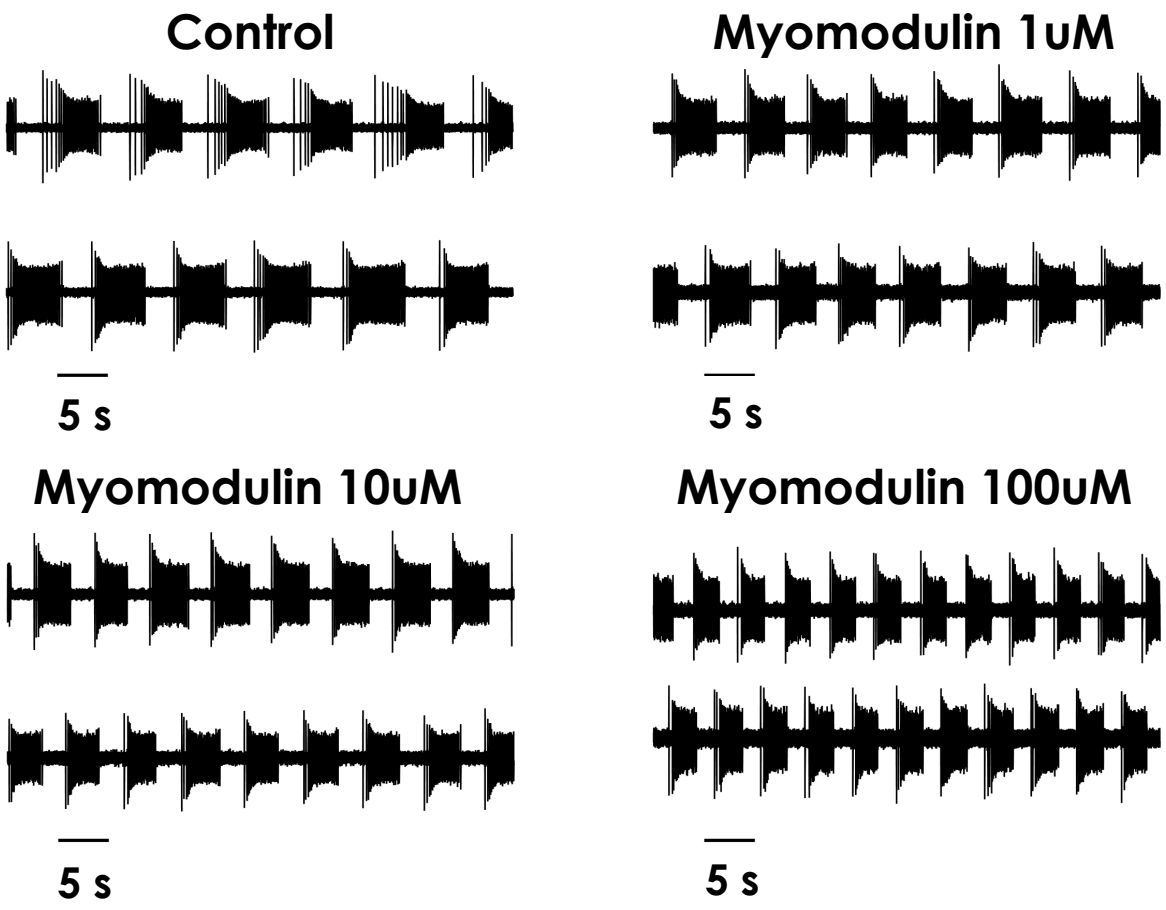


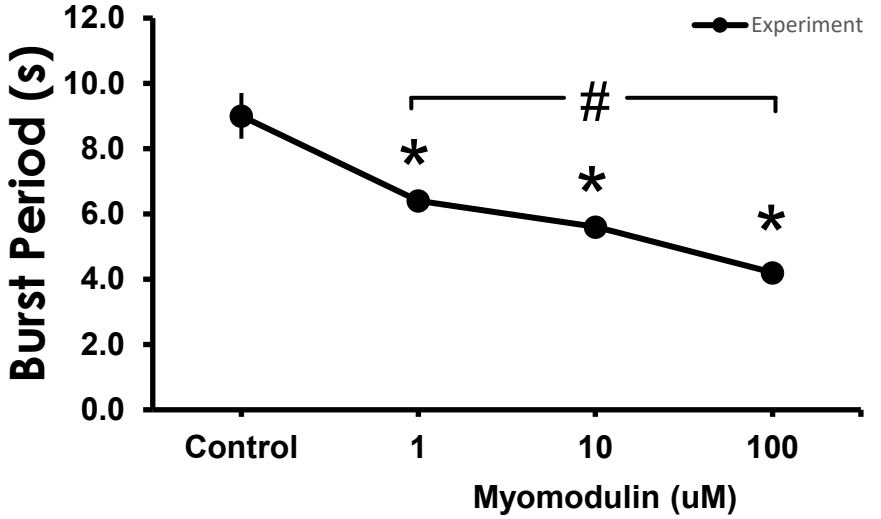



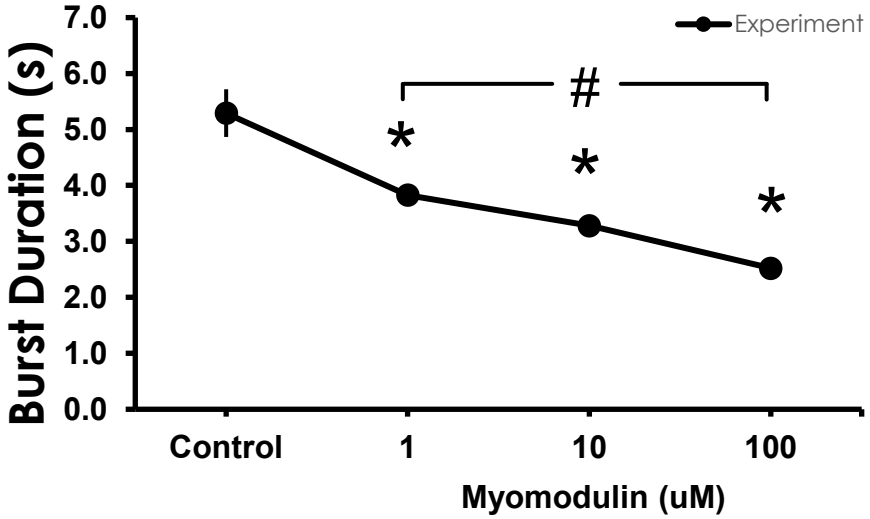
# Comodulation Expands the Range of Functional Temporal Burst Characteristics



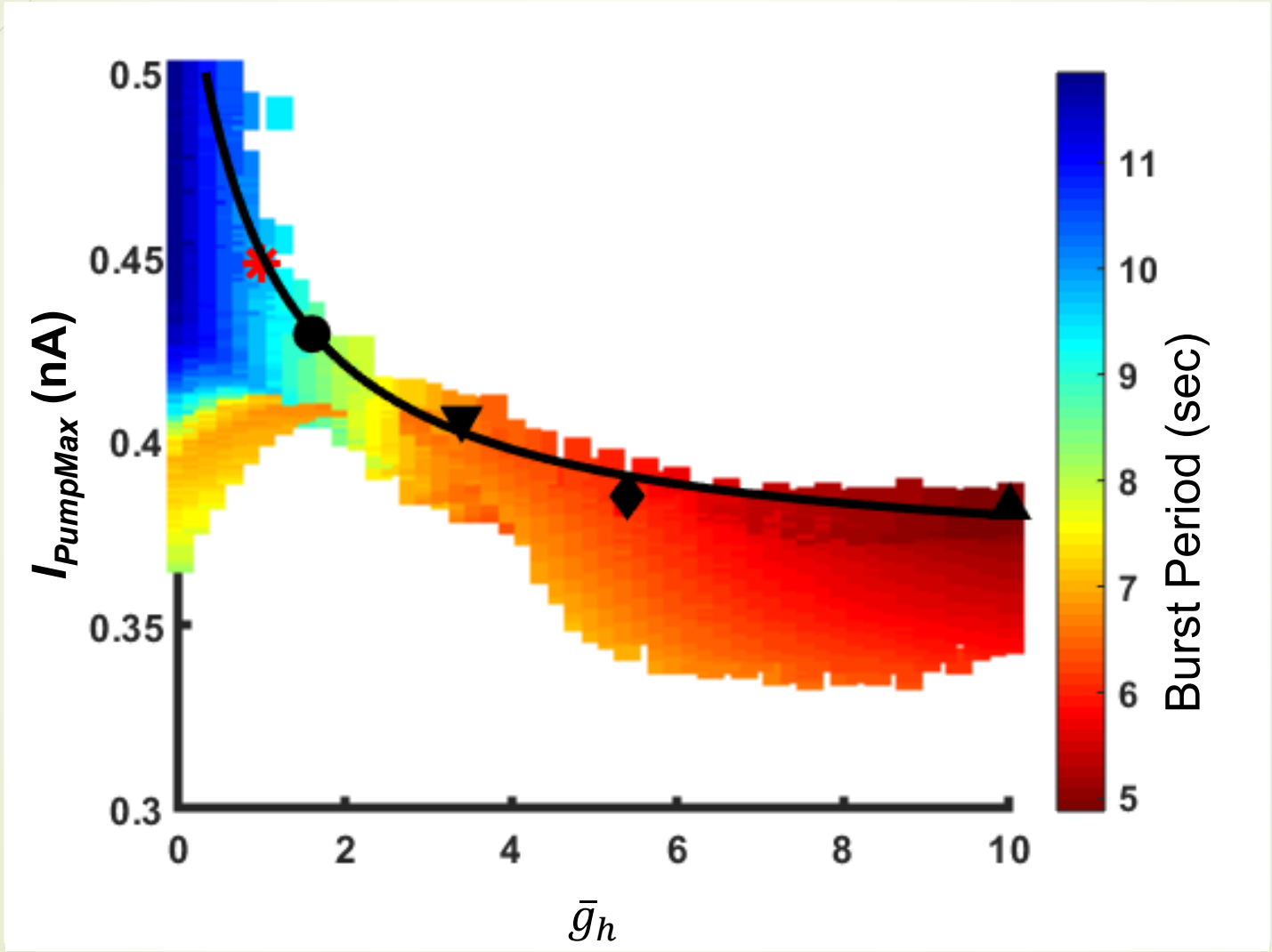
# Experimental Data Display a Dose-Response to Myomodulin



# Experimental Data Maps Well to Model Parameter Space



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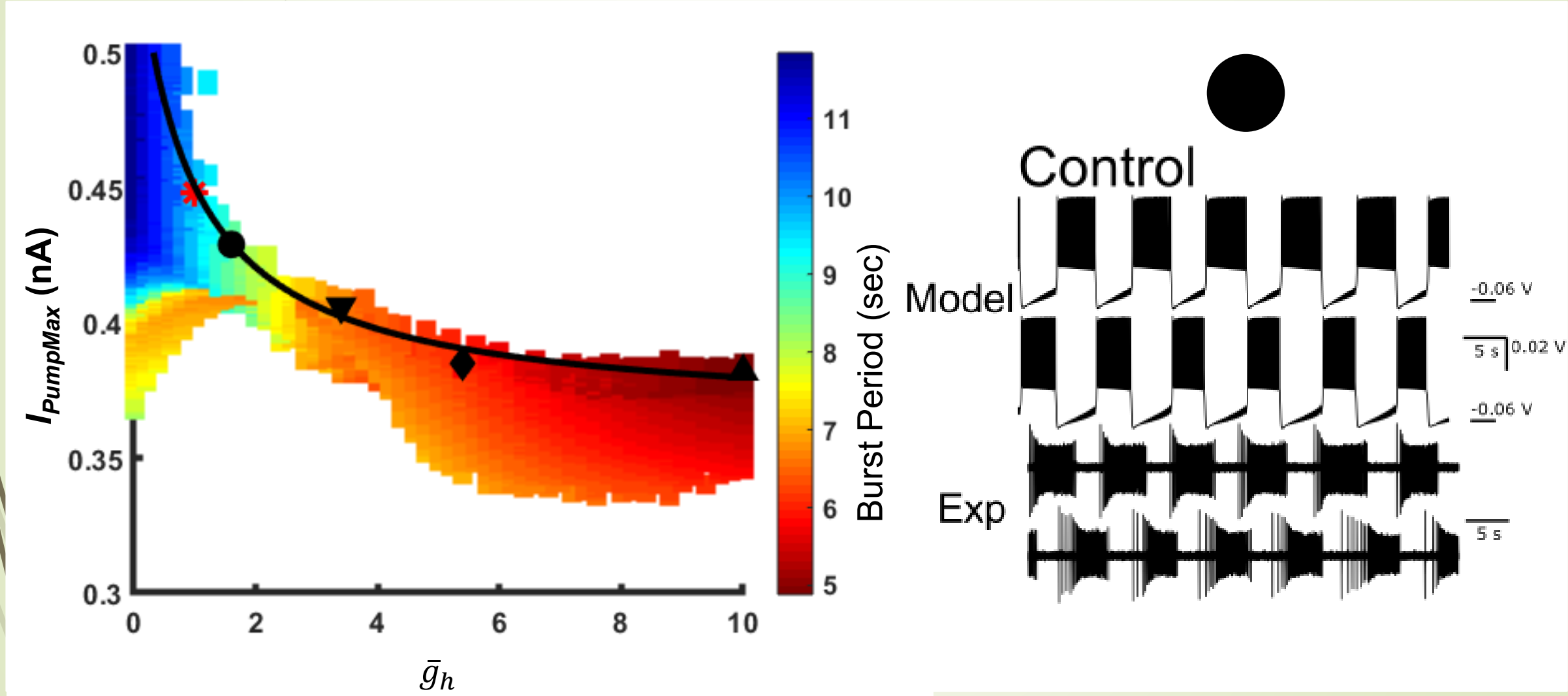

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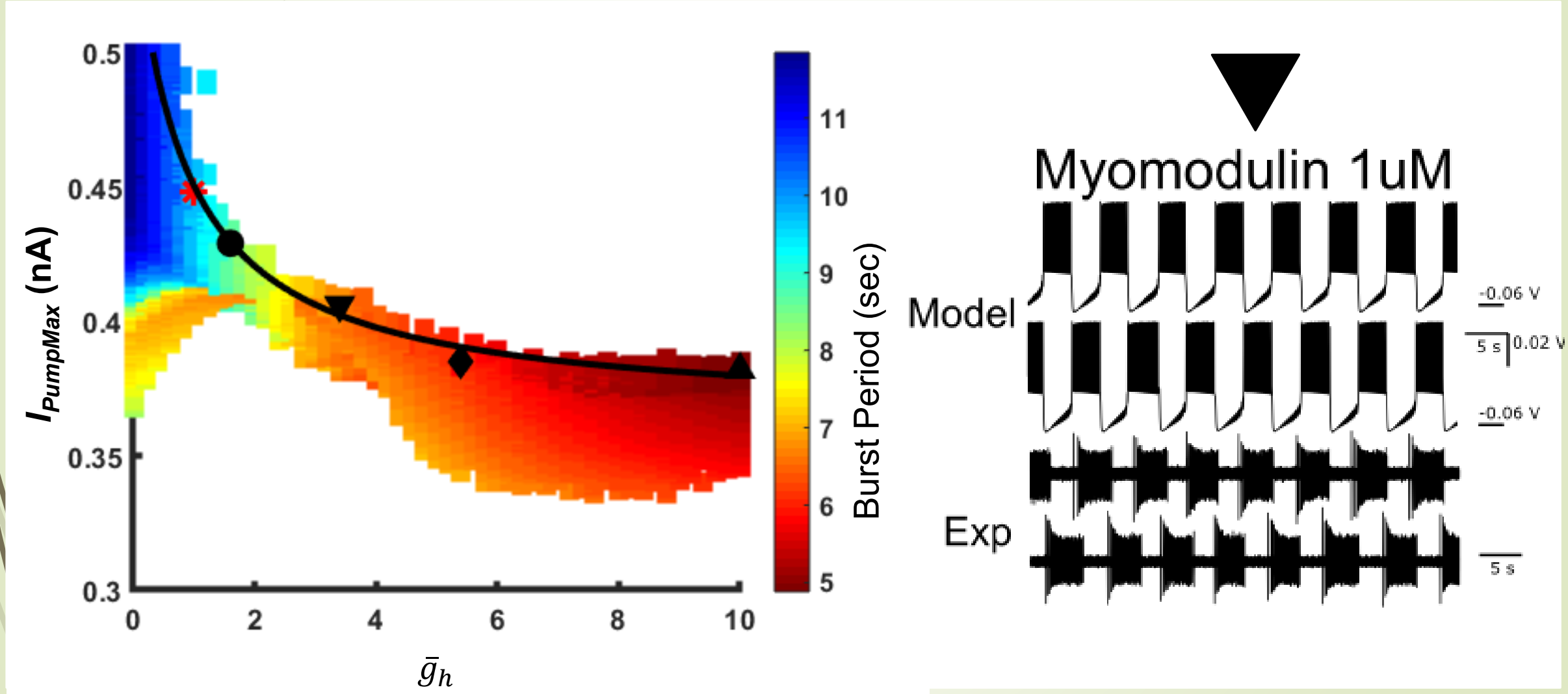

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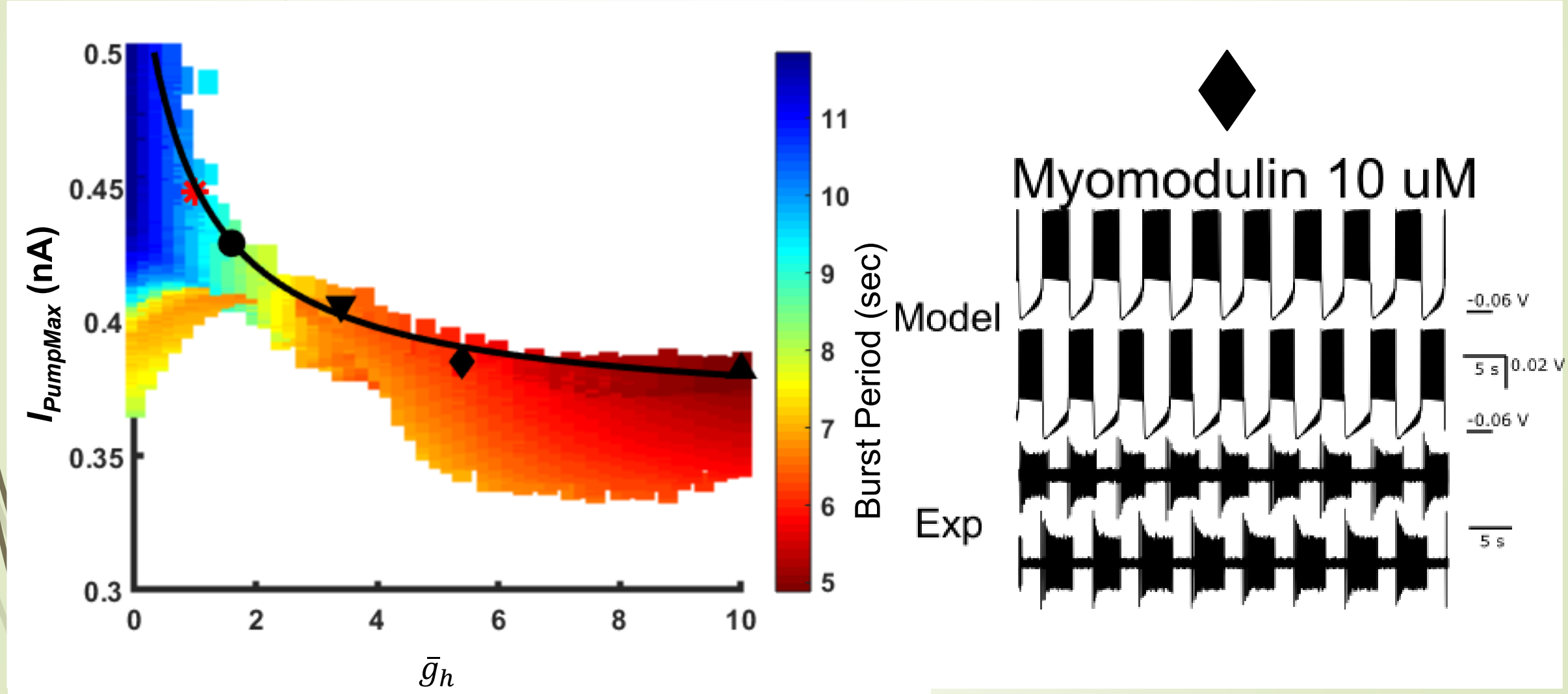

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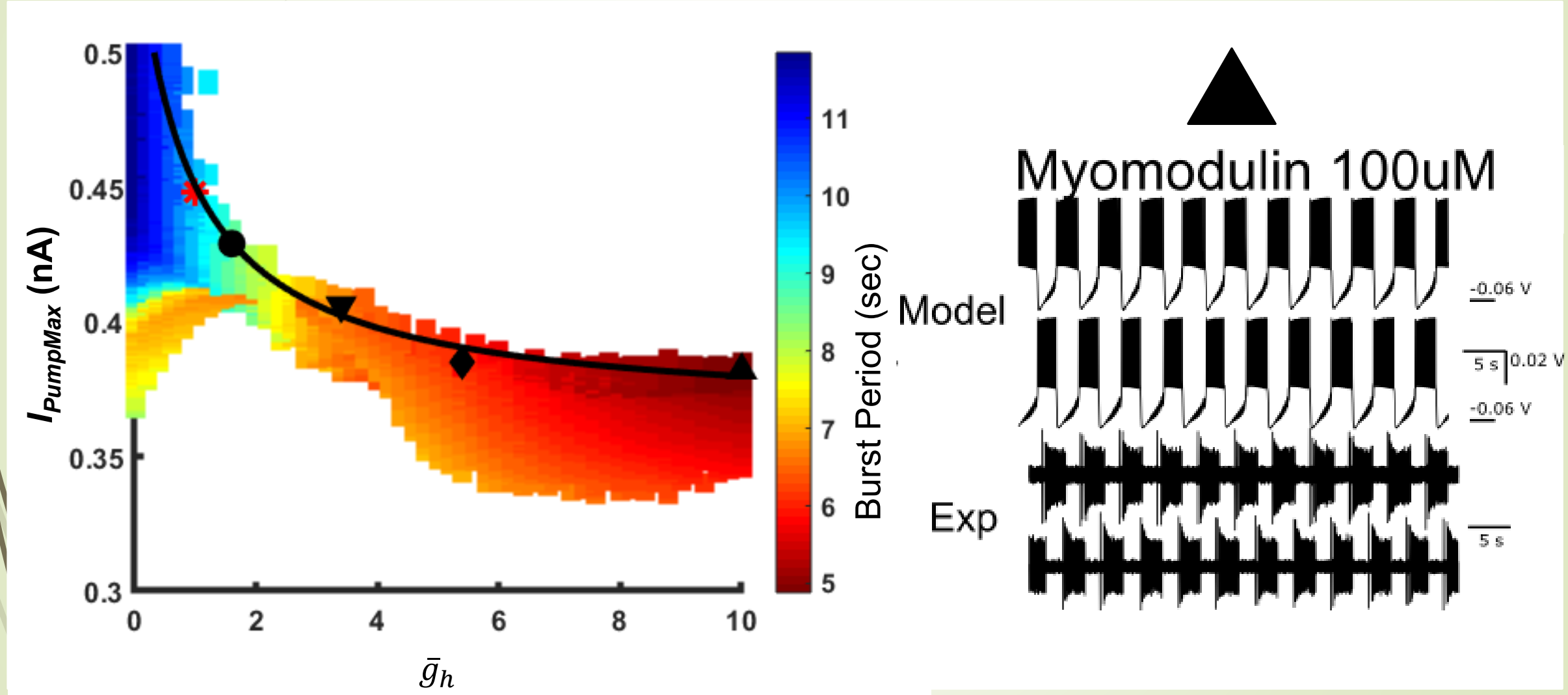

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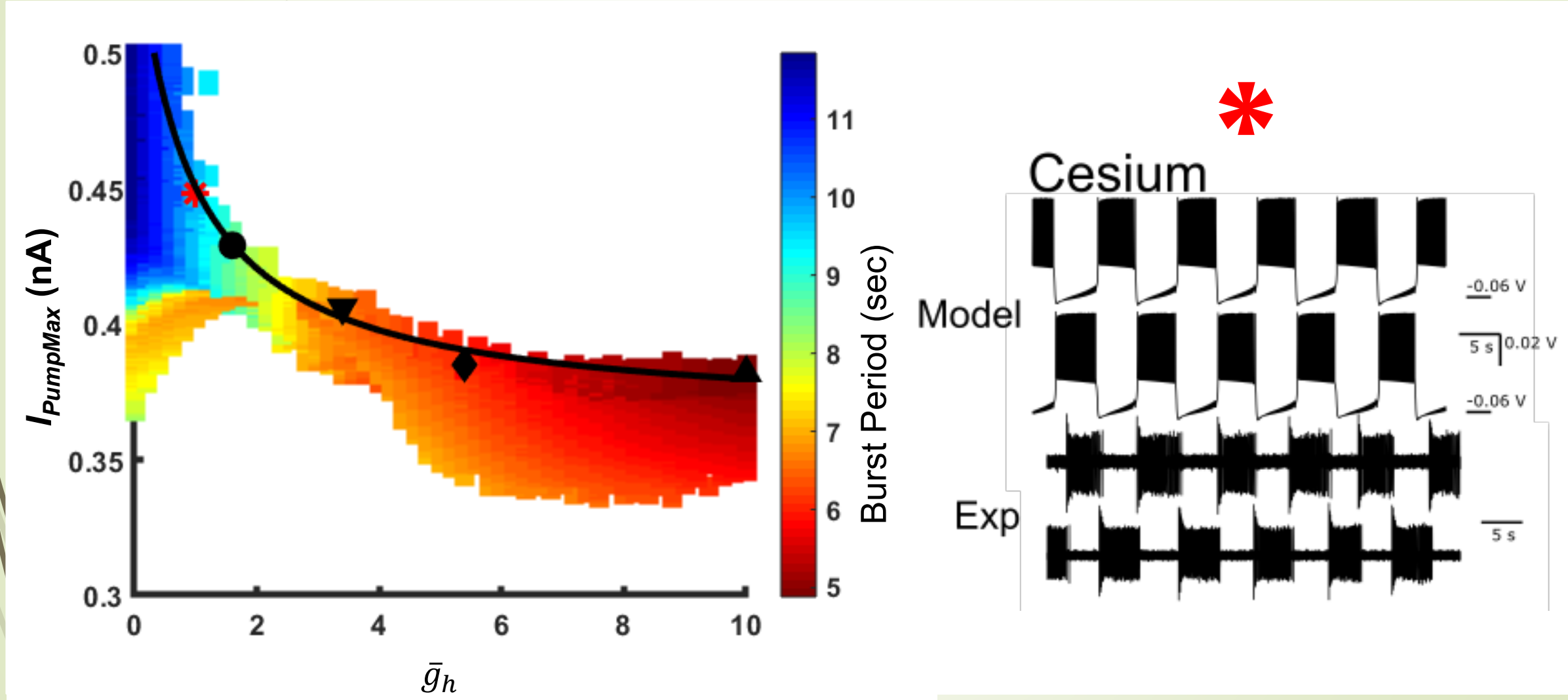
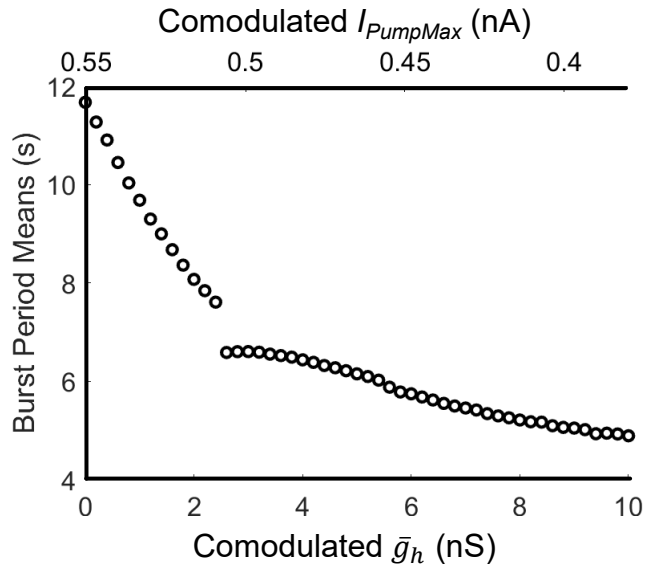
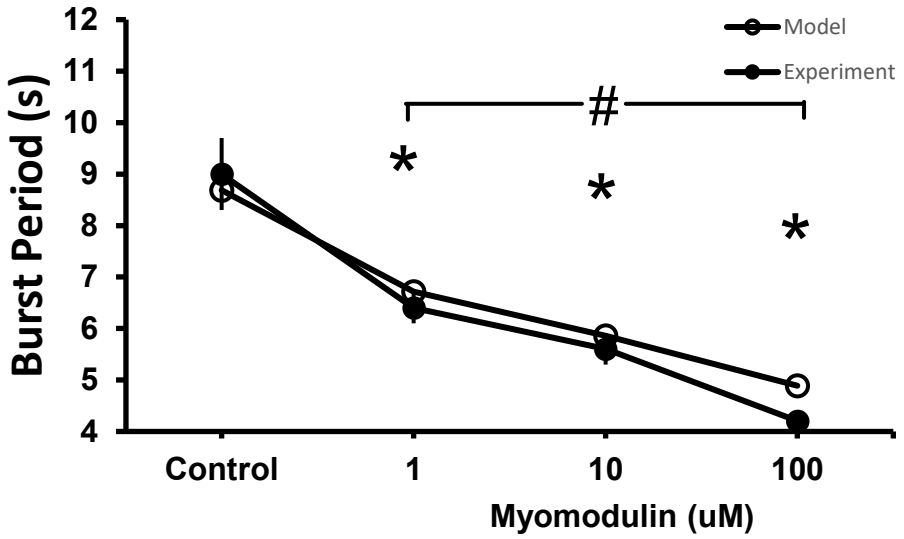
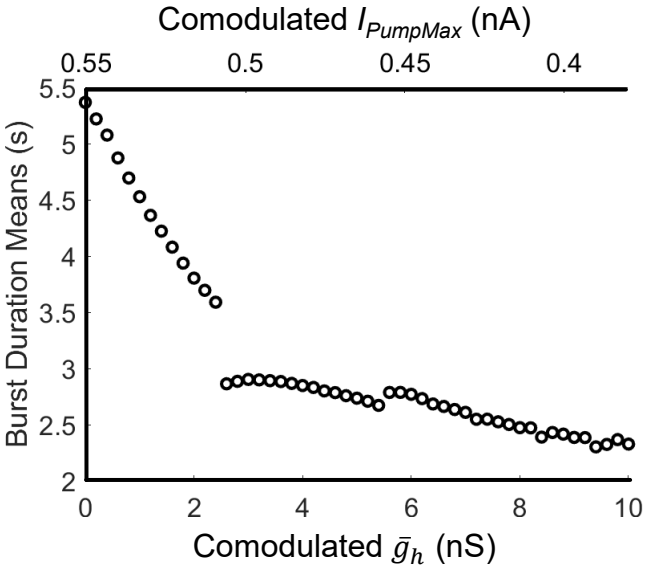
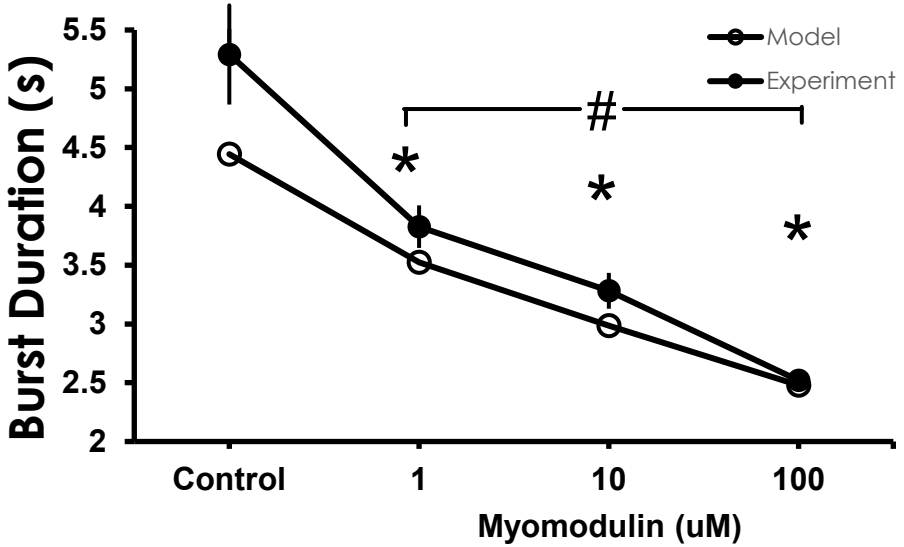


# Simulation Along the Axis of Comodulation Compares Well to Experimental Results



# Conclusions



- We developed a model of the Leech heartbeat central pattern generator pacing circuit.
- Investigation of the parameter space associated with the action of the neuropeptide myomodulin and subsequent regime classification revealed a channel of functional activity within parameter space which corresponds to the action of myomodulin.
- Comodulation in this system allows the CPG to retain functional activity, while expanding the range of possible shifts in temporal bursting characteristics by 75% compared to modulation of $I_{PumpMax}$ alone or by nearly 90% compared to modulation of $\bar{g}_h$ alone
- We validated the model by fitting experimental conditions within the model parameter space.

# Acknowledgements


- GSU Brains and Behavior Fellowship
  - Funding me
- NIH Grant 1 R21 NS111355 issued to GC and RC
  - Project funding, and funding for me for Fall 2020


- Please feel free to contact me at pellingson3@gmail.com
- Thank you for listening