Network Model of Nociceptive Processing in the Superficial Spinal Dorsal Horn Reveals Mechanisms of Hyperalgesia, Allodynia, and Spinal Cord Stimulation

Abbreviated Title: Network model of the superficial dorsal horn

John E. Gilbert¹, Tianhe Zhang², Rosana Esteller², Warren M. Grill¹,³,⁴,⁵*

¹- Department of Biomedical Engineering, Duke University, Durham, NC
²- Neuromodulation Research and Advanced Concepts, Boston Scientific Neuromodulation, Valencia, CA
³- Department of Electrical and Computer Engineering, Duke University, Durham, NC
⁴- Department of Neurobiology, Duke University School of Medicine, Durham, NC
⁵- Department of Neurosurgery, Duke University School of Medicine, Durham, NC.
* Correspondence and requests for materials should be addressed to W.M.G. (email: warren.grill@duke.edu)

Supplemental Figs. S1–S3
Figure S1. Changes in PKCγ neuron firing behavior with different biophysical properties. A, Example PKCγ neuron firing behaviors as the value of $V_h$ (shift in the Boltzmann equations for the slow inactivation gate, Equations 4-5, (Aguiar et al., 2010)) and $g_{K_A}$ (the conductance of the A-Type potassium current) are varied in the model. B, Changes in the neuron responses with increasing current inputs.
Figure S2. Combined model responses were generated by adding existing deep dorsal horn model to the superficial dorsal horn model. A, Network architecture of existing deep dorsal horn model (Zhang et al., 2014). B, Additional network connections added to connect the superficial dorsal horn model (See Figure 1A) and the deep dorsal horn model.
Figure S3. Example model WDR neuron responses to 5 seconds of SCS at 10 Hz and 50 Hz. A, WDR neuron activity without any changes to the model architecture, and with a 50% reduction in the strength of glycinergic synapses, a 50% reduction in the strength of GABAergic synapses or a +8mV shift in reversal potential of both GABAergic and glycinergic synapses. B, Absolute and normalized in median model WDR neuron median firing rates with different pain models. The right plot firing rates are normalized to the baseline firing rate without SCS (FR (norm) = 1). Bars show the median and error bars show 25th and 75th percentile. Dots show individual responses across simulations.