Computer Simulation of Synaptic Currents Explain Phenomenon in Drosophila Motoneurons

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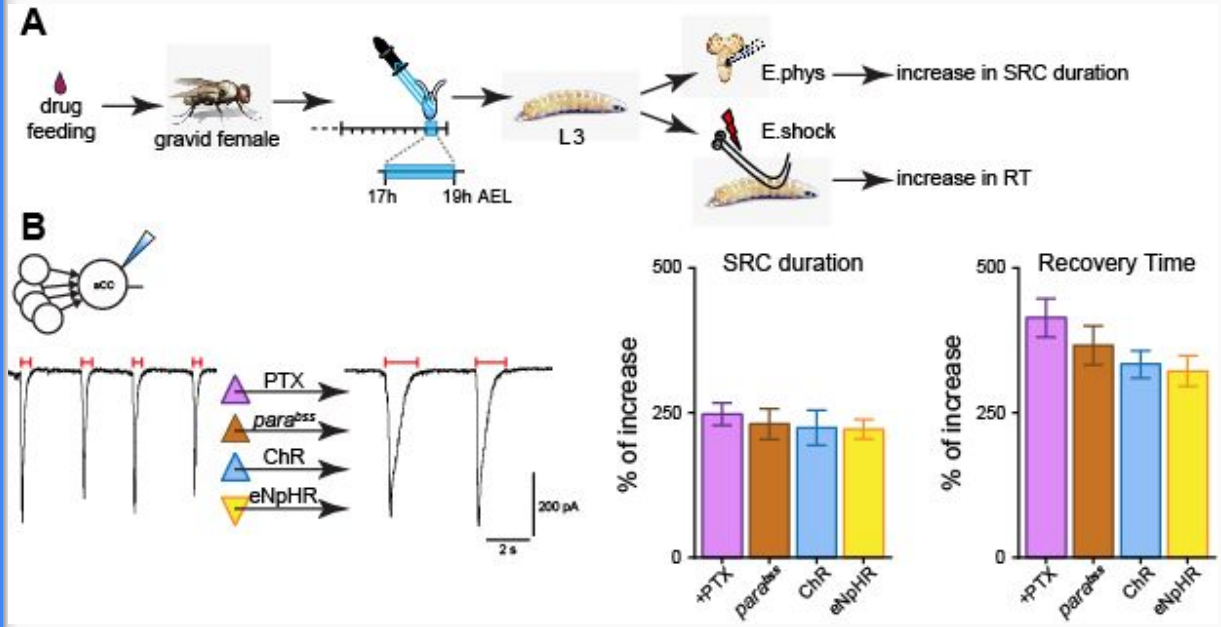
Spontaneous Rhythmic Current (SRC) synaptic inputs widen but does not increase in height, in response to different experimental manipulations against control

A. Gravid *Drosophila* were given Picrotoxin(PTX) which inhibits GABA, a inhibitory NT, from reaching synapse

B. Manipulations:
   a. Picrotoxin
   b. Bang Senseless Mutant
   c. Photosensitive ligand channels



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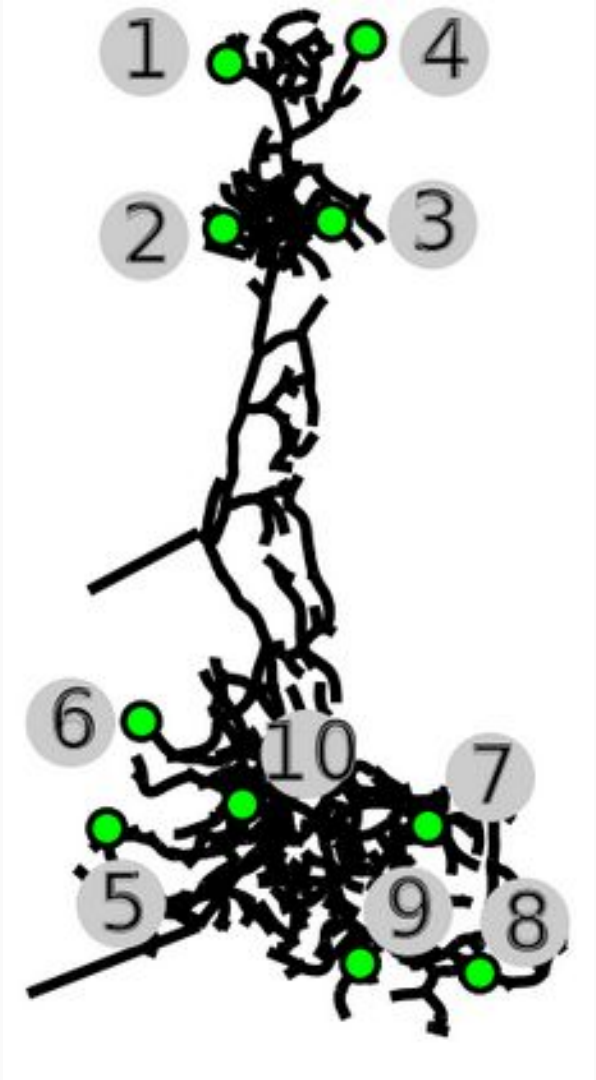
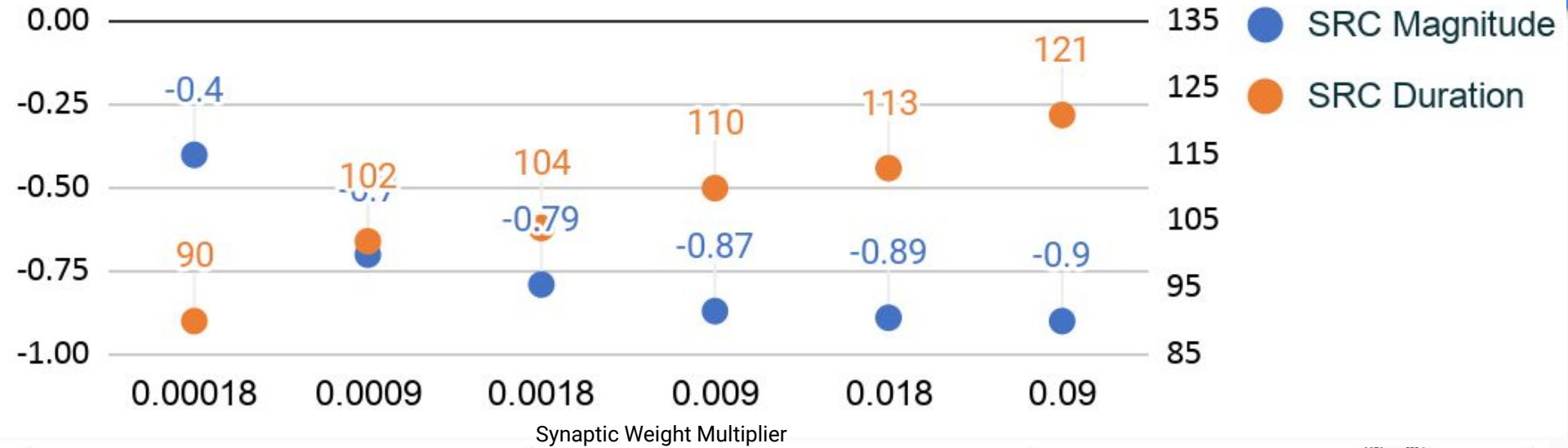
Hypothesis: SRC phenomenon occurs because of membrane biophysics

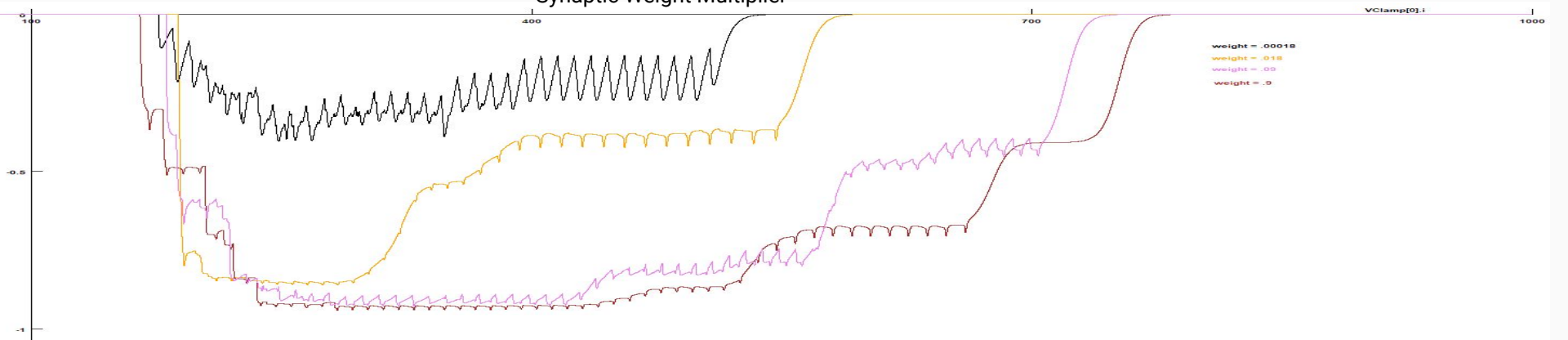
Method: Simulate SRC input in computer model

- Simulating SRCs by applying a train of spikes in multiple synapses on aCC motoneuron
- 15 spikes are applied at fixed intervals at same 10 synaptic locations
- Each synapse receives spikes at different starting times drawn from a normal random distribution, but same start times maintained across experiments
- EPSCs share common strength or **weight** parameter that we increased exponentially



In the model, magnitude of SRC begins to saturate while duration continues to increase with no sign of saturation as we increase the synaptic drive



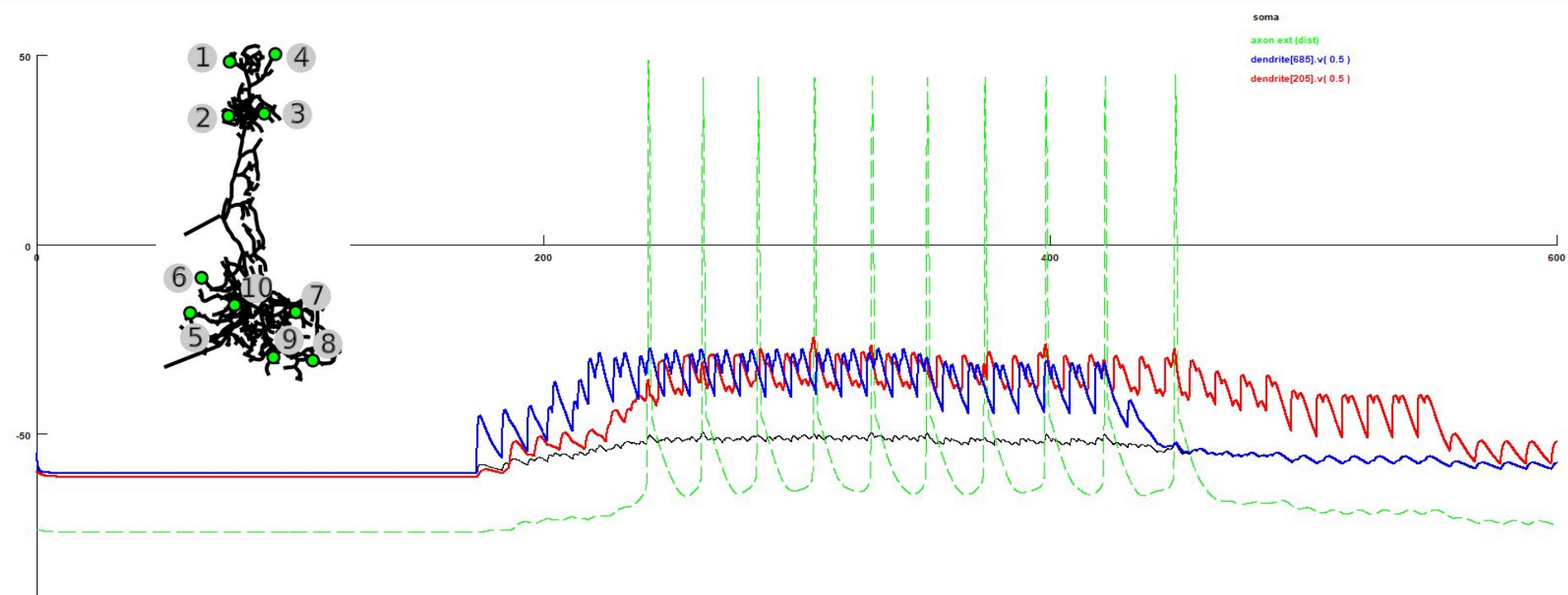


What is the mechanism?

Measuring voltage at the synapses: Control

Setting: weight=0.00018, tau=5, interval=10, magepsc=20

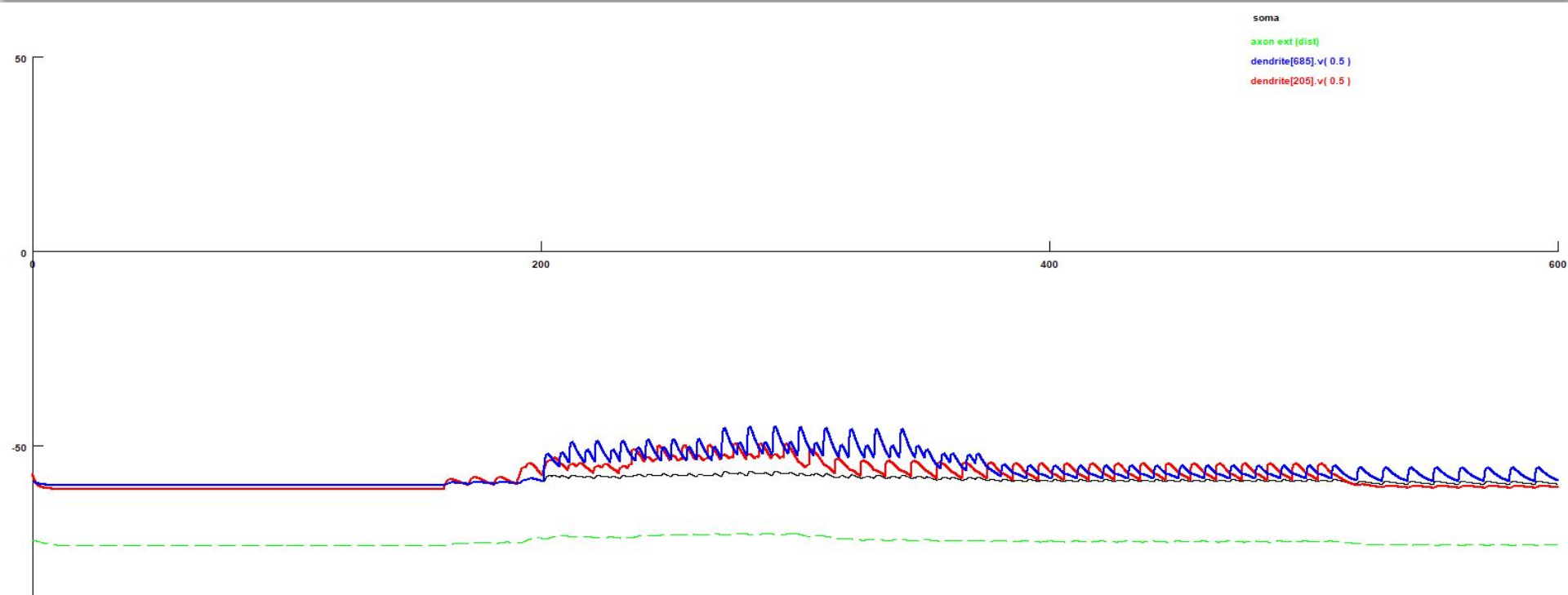
Results: dendrite[685].v(0.5) = -27mV, dendrite[205].v(0.5) = -24mV, action potentials = 10



The Low

Setting: weight= .000045, tau=5, interval=10, magepsc=20

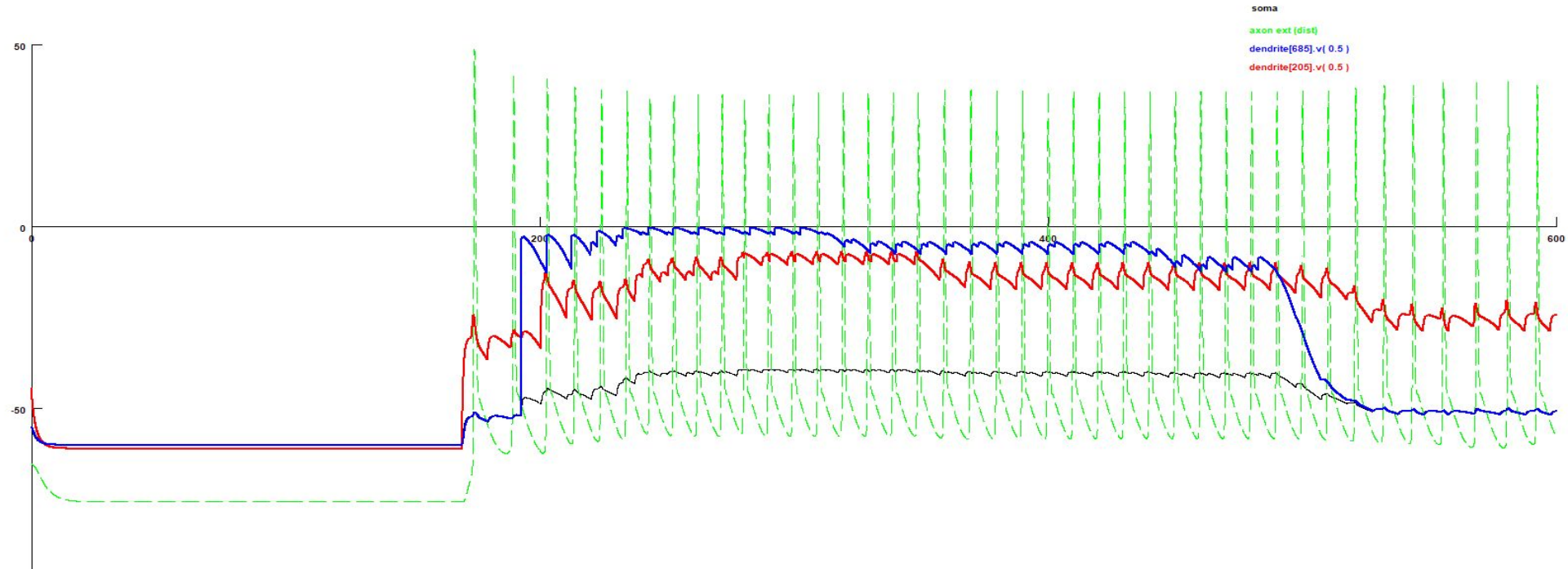
Results: dendrite[685].v(0.5) = -45mV, dendrite[205].v(0.5) = -49mV, action potentials = 0



Observed Truncation: Starting Point

weight=0.00576, tau=5, interval=10, magepsc=20

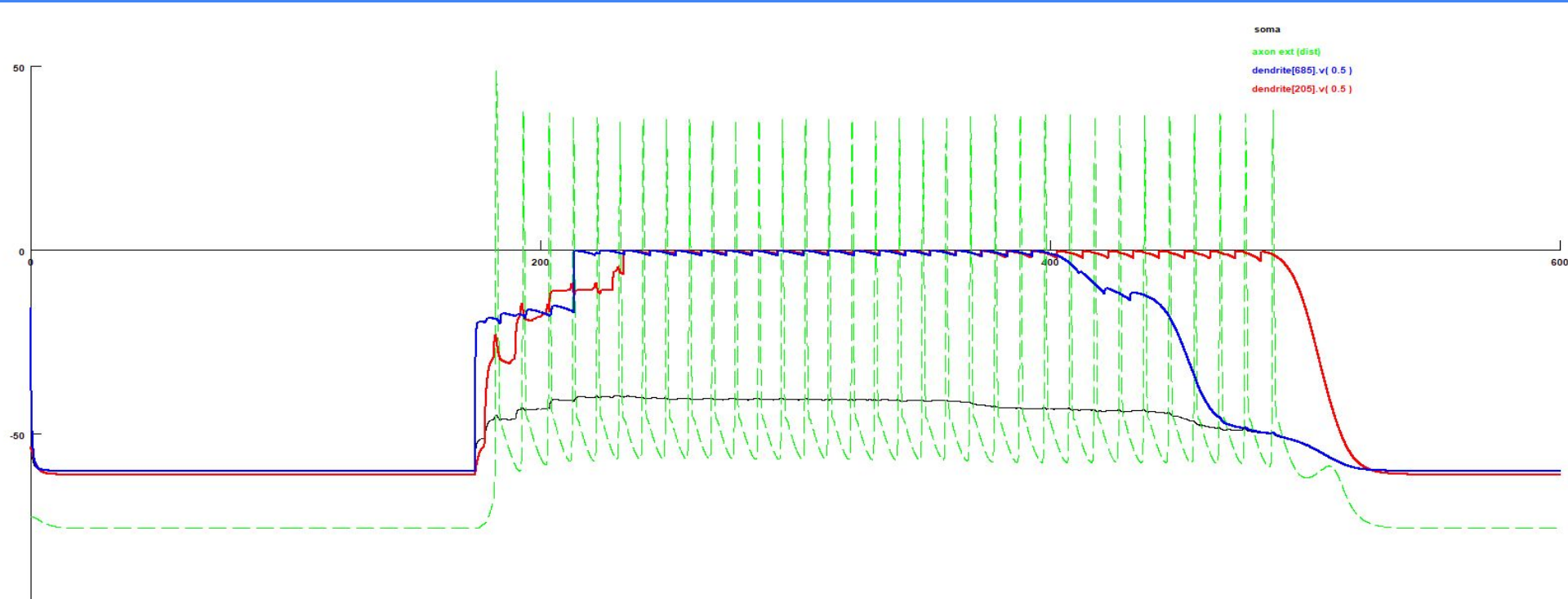
Results: dendrite[685].v(0.5) = -0.5mV, dendrite[205].v(0.5) = -7mV, action potentials = 41



Observed Truncation cont.

Setting: weight=0.02304, tau=5, interval=10, magepsc=20

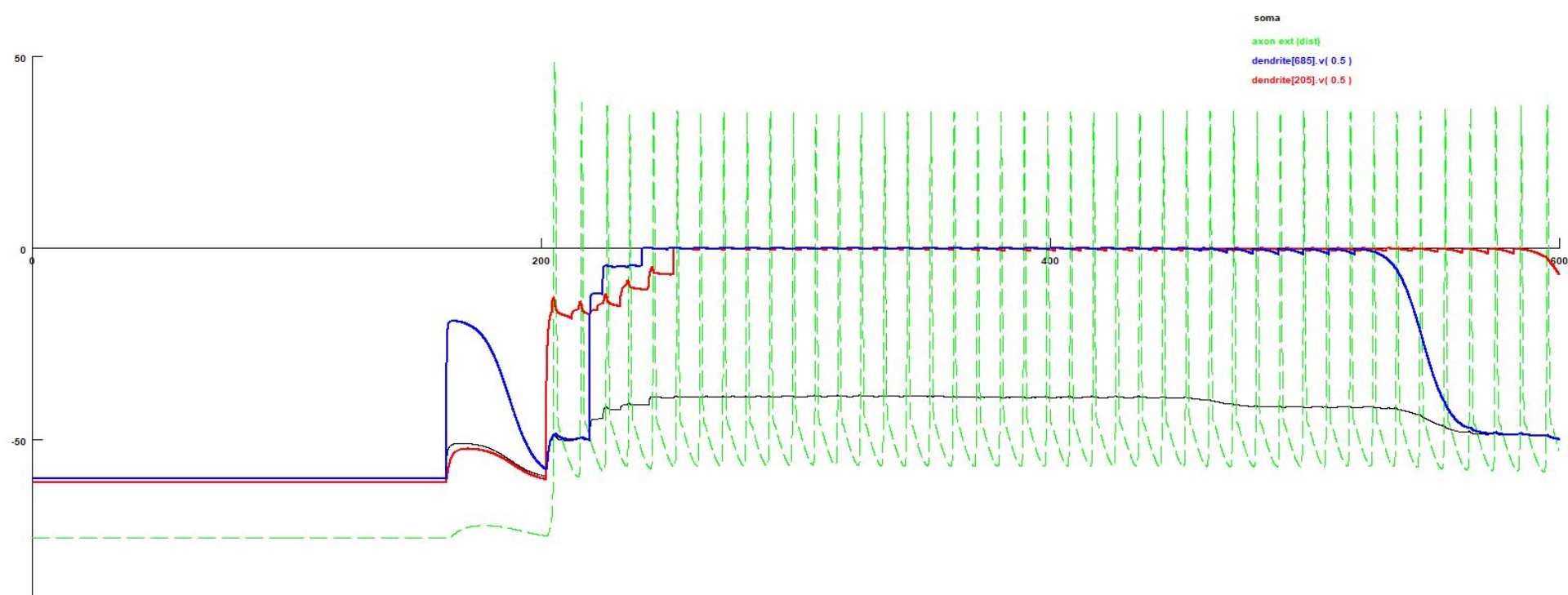
Results: dendrite[685].v(0.5) = -0.2mV, dendrite[205].v(0.5) = -0.2mV, action potentials = 33



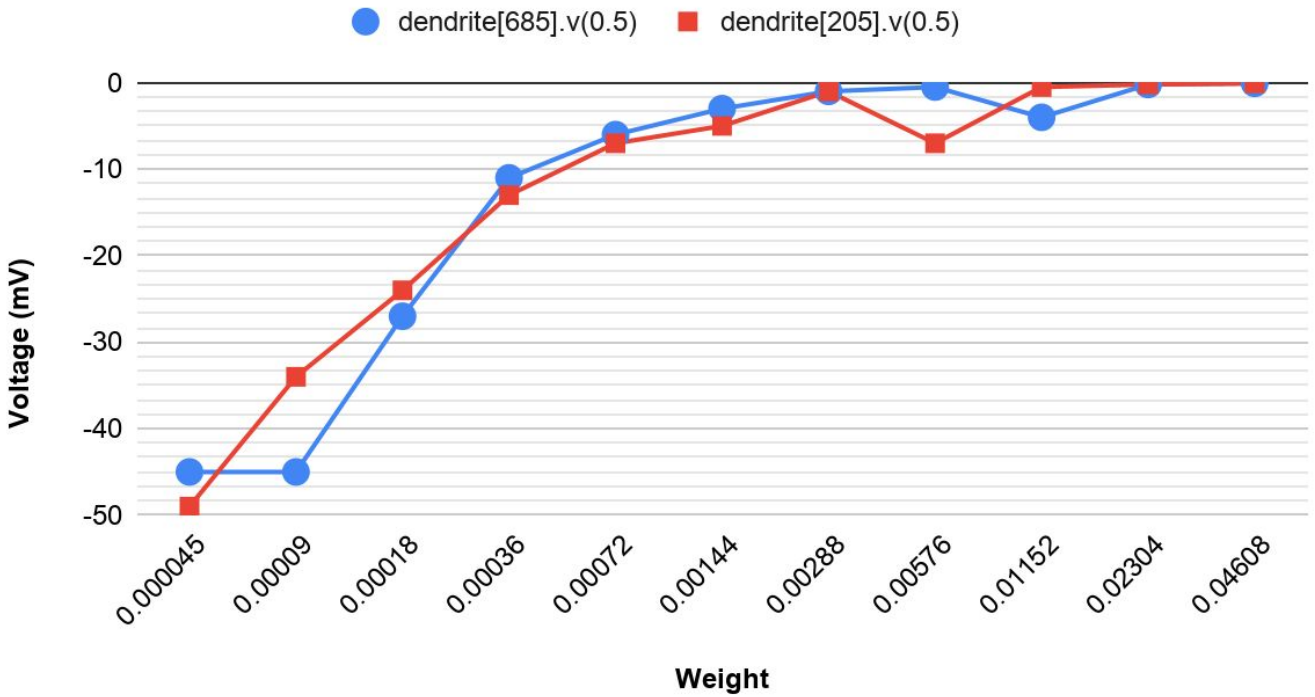
The Phenomenon

Setting: weight=0.04608, tau=5, interval=10, magepsc=20

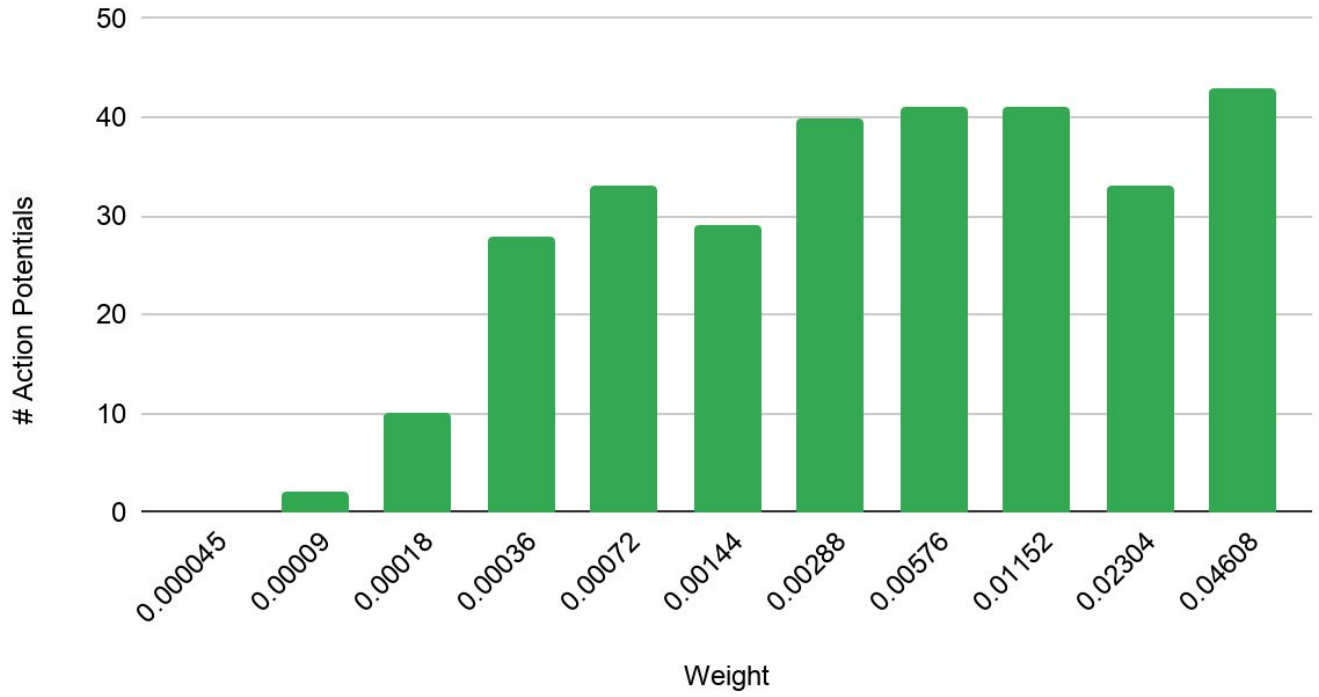
Results: dendrite[685].v(0.5) = -0.07mV, dendrite[205].v(0.5) = -0.07mV, action potentials = 43



Summary of Truncation Effect



Postsynaptic Spikes are Also Saturated



Why?

Synaptic driving force saturates at the reversal potential of E_{syn} = 0 mV

$$I_{syn} = g_{syn}(V_m - E_{syn})$$

How?

1. *Membrane potential depolarizes and approaches 0mV*
2. *Driving force (V_m-E_{syn}) is reduced*
3. *Resulting current I_{syn} is smaller*
4. *Membrane never exceeds 0 mV*

Discussion and Future Directions

- We replicated a previously unexplained, experimentally observed phenomenon with computer modeling and proposed a mechanism
- Saturation effect stems from depolarizing neurites reaching synaptic current reversal potential

Future Directions:

- Are there any other explanations of the phenomenon? Receptor saturation or vesicle depletion?
- Are there other synaptic placements that avoid this outcome in model?

Acknowledgments

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