Figure 1

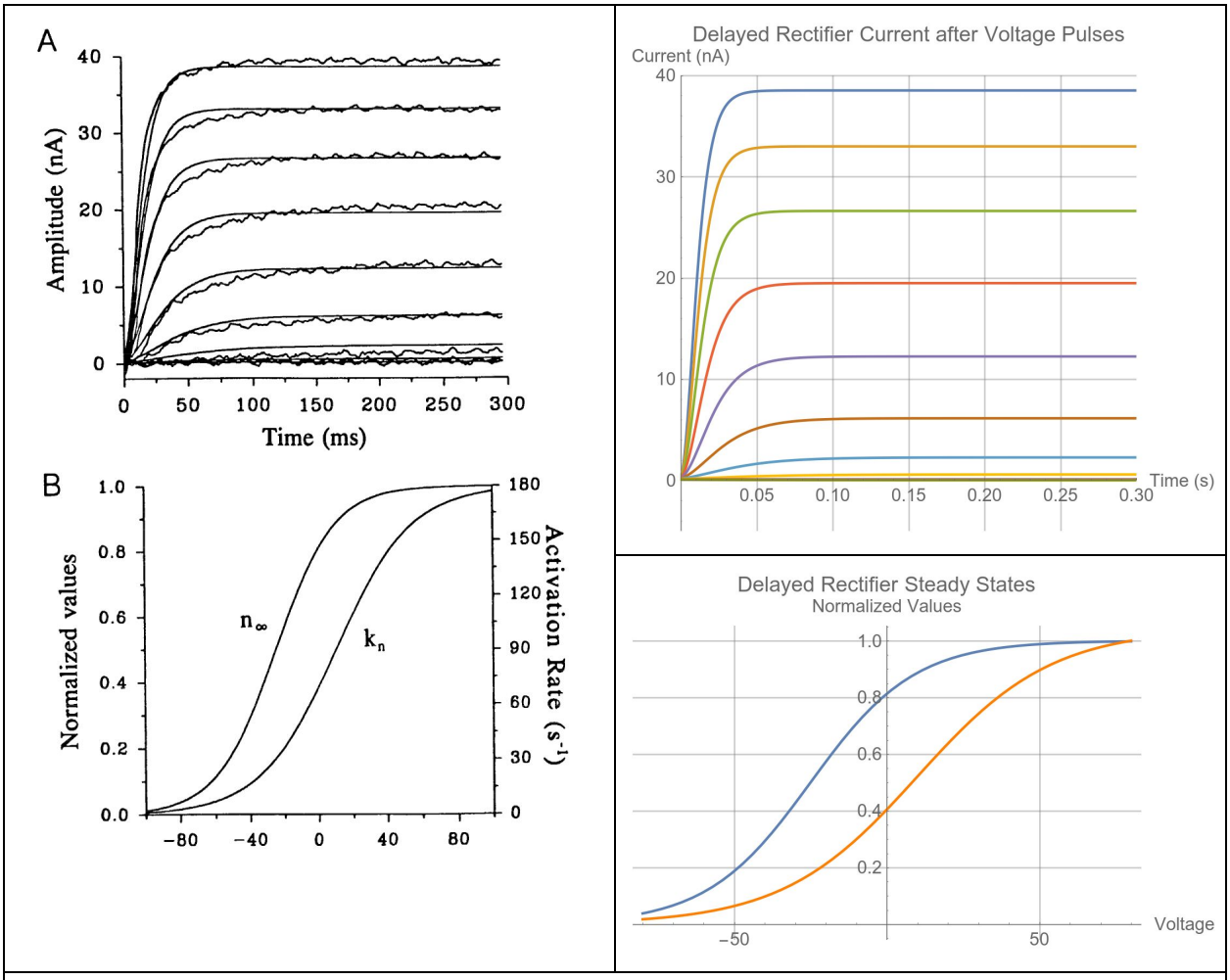

Figure 1, Buccholtz et. al., (1992) *(left)*, and Figure 1 A *(top right)* & B *(bottom right)* my result done in Mathematica (see attached notebook). In 1A of both original and my result, voltages pulses of -50, … 30 mV in steps of 10 mV are arranged top to bottom. The paper's graph includes noisy experimental data overlaid with model results. In my 1B graph, the blue curve represents n_∞ and the orange curve represents k_n.

Figure 1 describes the delayed rectifier current identified in the original paper, *Ionic currents of the Lateral Pyloric Neuron of the Stomatogastric Ganglion of the Crab* by Golowasch et. al. A delayed rectifier current is a common feature in neurons, where it's voltage dependence and delay in onset (not showing in experimental data until voltages of -40mV or

higher are clamped) are easily spotted (1992a). In these aspects, our results mirror perfectly those found in the paper. This is an exemplar of the capacity of modeling to isolate current, and since it is obvious in experimental data as well, it makes perfect sense as the first figure in the paper.

Figure 2

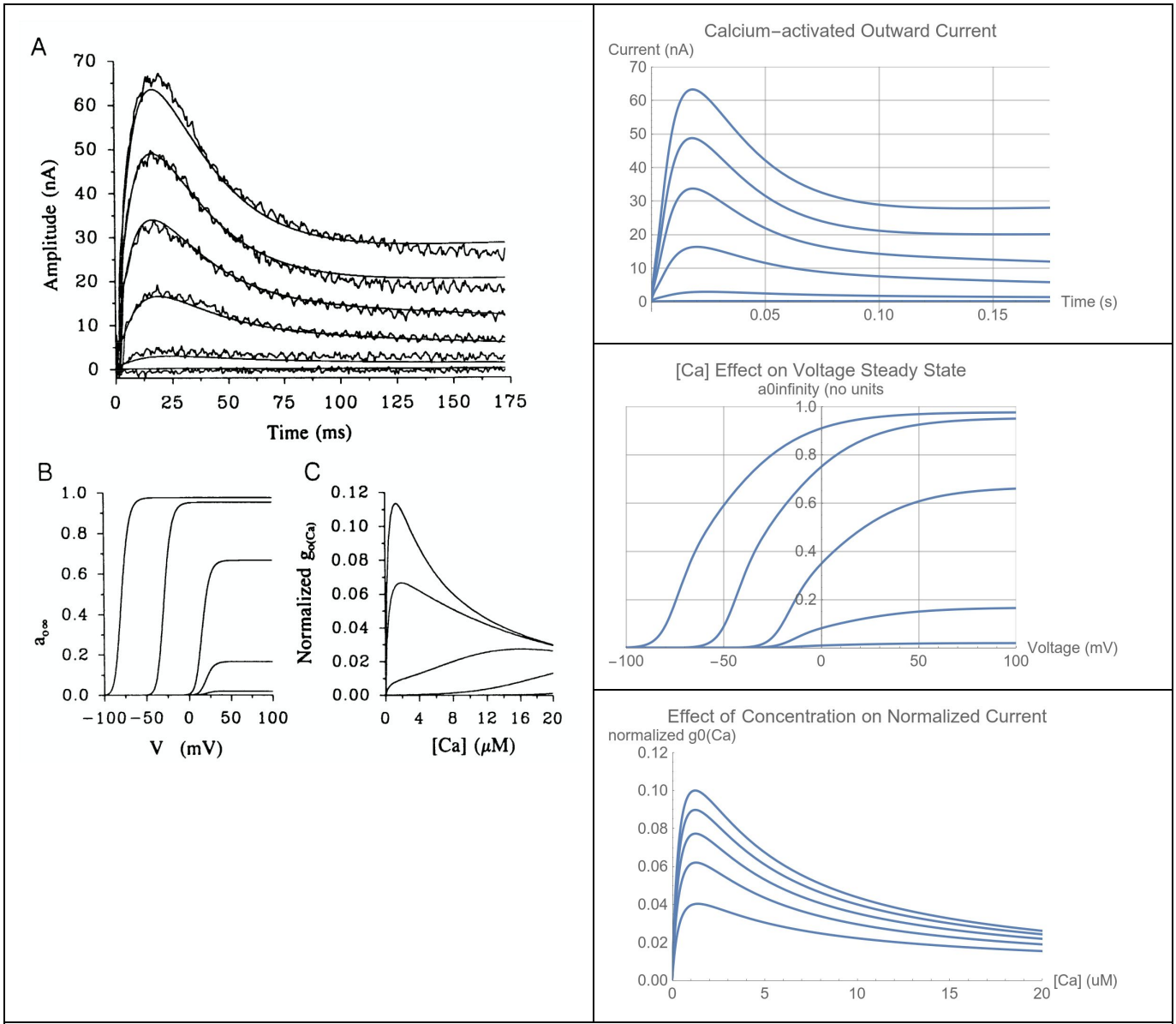

Figure 2, Buchholtz et. al., (1992) *(left)* Figure 2 A *(top right),* B *(middle right)*, C *(bottom right)* my results done in Mathematica. A: Voltage pulses from -30, … 20 mV in steps of 10 mV were applied. Noisy experimental data is overlaid by model output. B: Voltage dependency was calculated at calcium

concentrations of 100, 50, 5, 0.5, and 0.05. C: Voltage is held constant at 30, … -10 mV in steps of 10mV.

The calcium-activated current, calcium current, and calcium buffer system are by far the most interrelated of the elements of the model. Calcium concentration is defined by its own state variable and equation which relies upon the inward calcium current. The calcium-activated current thus depends on both for its Nernst potential.

Interestingly, the graph of the outward current (which relies upon all elements of the calcium system) is identical between our results and those of the author, while the steady state graphs and normalized current as a result of calcium concentration differ greatly. Our graph features a longer initial lag and a much shallower slope compared to those found in the paper. After a thorough examination of parameters and the voltage-dependent equations, we were unable to find discrepancies between our work and that discussed by the authors. By varying the step size of the first activation steady state equation, we are able to rectify the differences noted above, but the altered parameter greatly inflates the value of the current in 2A. Frustratingly (or perhaps amusingly), that reinforces our original observation that we were able to obtain the highest level result, but unable to replicate a much simpler dependency for said result. As noted in the paper, the literature suggests the steepness and shift of the curves is reflected in the literature. We replicate the shifts, but do not see nearly the expected steepness (Buchholtz 334).

Figure 2C shares a similar story. Our results show identical behavior at varying levels of intensity, while the paper shows qualitative changes in behavior at positive, 0-valued, and negative voltages.

Figure 3

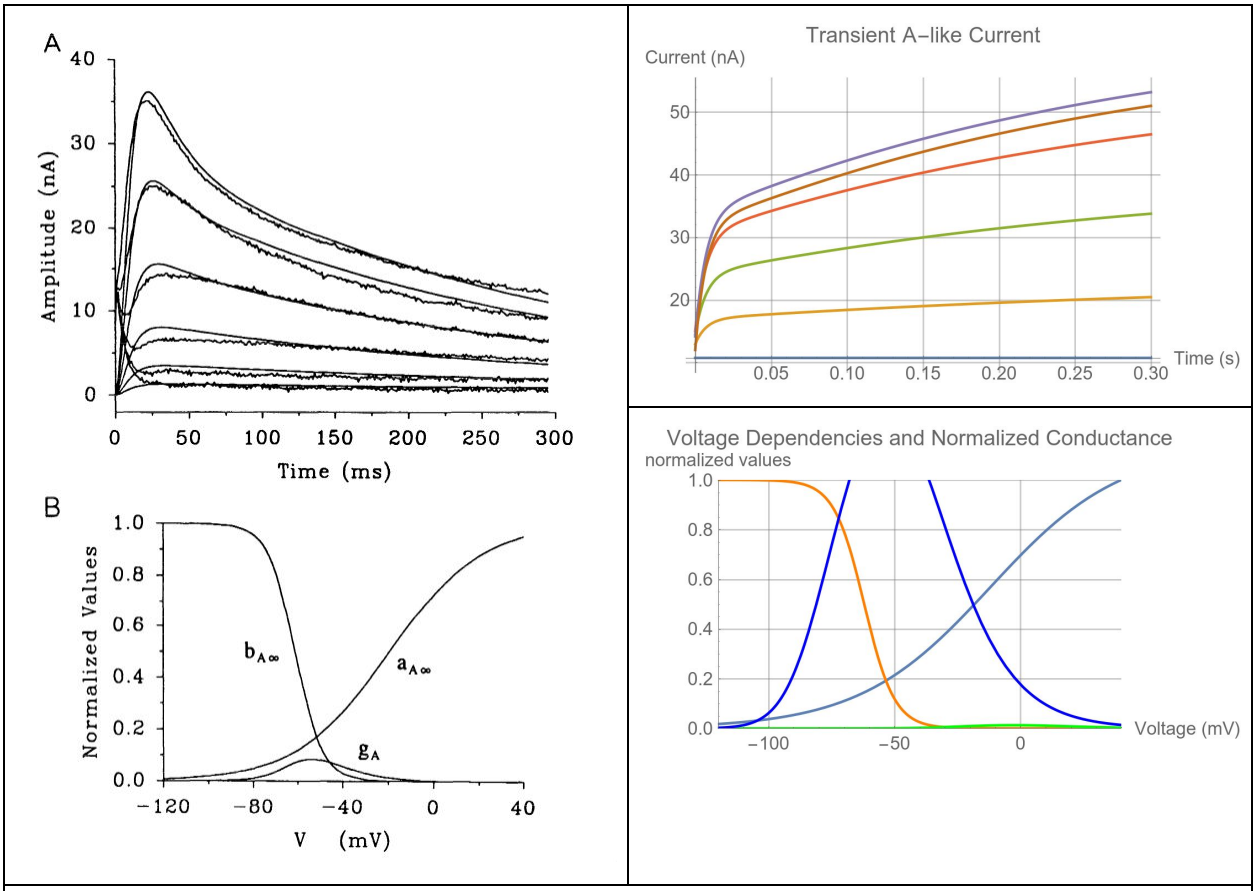

Figure 3, Buchholtz et. al. (1992) *(left)*, Figure 3 A *(top right)* & B *(bottom right)* from my results. A: a plot of the A-like potassium current against time. From bottom to top within the graph, voltage pulses of -40, … 10 mV in steps of 10 mV are plotted. Noisy experimental data is overlaid with model results in the paper. B: Voltage dependency steady states are graphed, along with normalized conductance. The orange line indicates the first inactivation, the light blue line activation, and the green and dark blue lines attempts at the normalized conductance curve.

The transient A-like current is a fast potassium current found in the cell. It is notable for its unconventional inactivation, in which two separate processes are weighted against each other, allowing for differing behaviors at depolarized and hyperpolarized voltages. This is shown well by the paper's graph, in which positive and negative voltage pulses have qualitatively different

results as would be expected. Unfortunately, these results proved irreproducible from the paper's equations and parameters. Following a suggestion from Dr. Chiel, we attempted to lower the power of the activation from three to one. This led to an increase in the magnitude of our graph (note the different y-axes in order to show the data more fully) -- an understandable change since the scalar activation value always falls between zero and one.

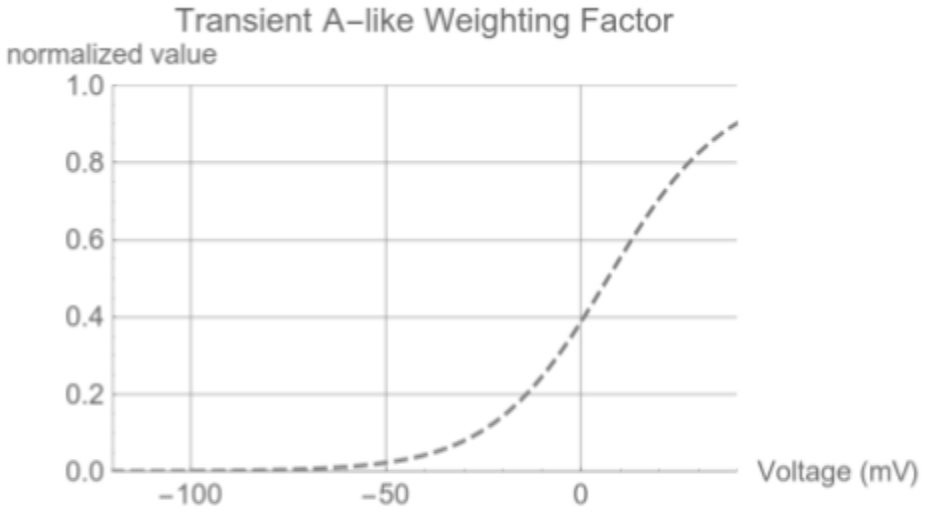

Figure I. This is not a result shown explicitly in the paper, but rather one generated during our research to explain the function of the weighting factor. Since the second inactivation is multipled by 1-x(V), where x(V) is the weighting factor, at positive voltages it is suppressed, but at negative voltages it is allowed to dominate.

Upon graphing, it was revealed that the second inactivation process behaved more similarly to an activation than an inactivation; namely, it was high at hyperpolarized values and low at depolarized values. This behavior is suppressed by the weighting factor as described above in the caption of figure I, allowing the first, more traditional inactivation, to dominate. This allows for the behavior seen in the paper's figure 2A, where negative voltage pulses generate large spikes and positive pulses cause little perturbation. This can be likened to the relevant gates remaining closed under similar experimental conditions in the neuron.

Figure 4

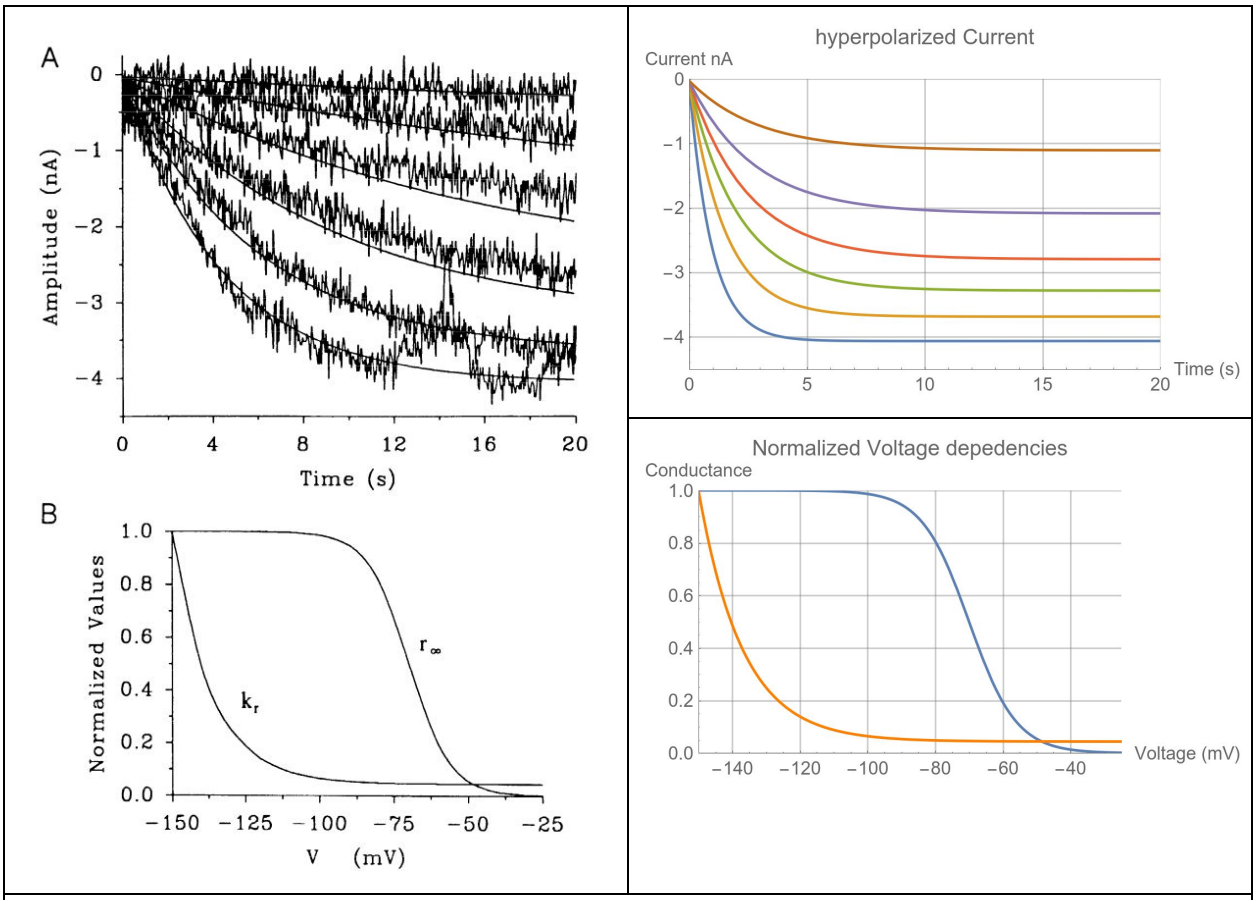

Figure 4, Buchholtz et. al., (1992) *(left)* and Figure 4 A *(top right)* & B *(bottom right)* from my results done in Mathematica. A: voltage was stepped to -120, … -70 mV in steps of 10 mV from top to bottom. On the left, noisy experimental data is overlaid. B: normalized steady state values. On my graph, the orange curve represents relaxation rate k_r and the blue curve represents activation r_∞.

The slow, inward i_h current activates at voltages more hyperpolarized than the resting potential, -45 mV. In figure 4B this becomes apparent by the low relaxation value at that potential. Note the length of the axes compared to the other figures: the current is orders of magnitude smaller and slower. This reflects the rather minor effect that i_h has on the overall function of the cell.

Compared to the paper's graph, our results in figure 4A appear to reach maximal amplitude earlier, and show more strongly asymptotic behavior. Minimal explanation of the

current is given in the original paper, making diagnosis of our issues particularly difficult. Ultimately we do not expect this slight discrepancy to have a large effect on the cell as a whole due to its slight magnitude and the common end behavior.

Missing Figures

The paper produces three additional figures from their experimental and model full cell data. As we were unable to produce correct behavior out of several of our currents at this time, it proved impossible to create meaningful data from the full model. Note that the model relies on a summation of currents to determine the rate of change in potential. Thus when some currents misbehave, the model refuses to provide insightful results.

Hypothesis

The clarity of the experimental data in the isolated currents allows a simple check for individual currents. Indeed, the simplistic i_{dr} and i_h are easily reproduced to match perfectly the paper's model and the approximately experimental data. The calcium is much more interesting; here it seems we are able to model the current rather well, but unable to model it's normalized conductance or steady states. This quirk demands further investigation.

References

Buchholtz, F., Golowasch, J., Epstein, I. R., & Marder, E. (1992). Mathematical model of an identified stomatogastric ganglion neuron. *Journal of Neurophysiology, 67*(2), 332-340. doi:10.1152/jn.1992.67.2.332

Golowasch, J., & Marder, E. (1992). Ionic currents of the lateral pyloric neuron of the stomatogastric ganglion of the crab. *Journal of Neurophysiology, 67*(2), 318-331. doi:10.1152/jn.1992.67.2.318