Chapter 5

FACILITATING SUB-THRESHOLD SYNAPTIC INPUT USING EPIDURAL STIMULATION TO ACHIEVE NEURON ACTIVATION

After a significant spinal cord injury, the neurons in the spinal cord caudal to the injury often have a decreased amount of connectivity due to the injury and subsequent neural degeneration. But some connectivity and neural activity may remain. Electrical stimulation can of course be used to directly stimulate muscles (Grobelnik and Kralj, 1973; Thrasher, Flett, and Popovic, 2006; Lynch and Popovic, 2008) or activate motor neurons directly (Veraart, W. M. Grill, and Mortimer, 1993), however doing so directly ignores existing neural circuitry in the spinal cord and may also inadvertently activate other undesired neurons. Instead, one hypothesis is to directly facilitate the neuronal activity of existing postural and motor control circuits. Epidural (Edgerton et al., 2008) and transcutaneous (Yury Gerasimenko et al., 2015) electrical stimulation of the spinal cord has proven useful in facilitating the function of existing neural circuitry and even voluntary movement (Harkema et al., 2011; Urban, 2018) in humans and rats with spinal cord injuries.

The experimentally observed facilitation of voluntary movement in subjects with clinically "complete" spinal cord injuries implies that in some of these cases, the brain retains some connectivity with the spinal cord, just not enough to actually move muscles without the aid of spinal stimulation. While there are many existing computational studies of epidural stimulation of the spinal cord (see Section 1.1), to my knowledge there are no existing computational studies exploring how electrical stimulation of the spinal cord could facilitate synaptic input to allow neuron activation. In this chapter, I consider the hypothesis that the electrical stimulation process

somehow facilitates the activation of key neurons in the spinal cord involved in motor control. The anatomical location of these key neurons is still unclear, although recent investigations are shedding light on the possibilities (Asboth et al., 2018; Urban, 2018). It is further unclear how the activity of these neurons is directly facilitated by electrical stimulation. This chapter will consider the possibility that these key neurons are interneurons in the spinal cord that are directly stimulated by the epidural stimulation while being exposed to sub-threshold EPSPs.

The main objective of this chapter is to show that epidural stimulation of a simulated rat spinal cord can facilitate the activation of an interneuron when a sub-threshold EPSP from a synapse on a dendrite is triggered. Of course, in a real biological system, it is possible that multiple EPSPs from sub-threshold synapses in combination with one or more stimulation pulses could result in a facilitated action potential. Understanding single synapse facilitation may lead to principles that are useful in understanding multiple synapse facilitation. Simulations involving multiple stimulation pulses and/or multiple EPSPs could be considered for future work; this thesis will only look at the interaction between a single EPSP and a single stimulation pulse. A number of different synapse weights and stimulation voltages will be used so that the distribution of the number of neurons facilitated vs stimulation voltage and synapse weight can be seen. The properties of this distribution will shed light on the nature of the facilitation process.

Chapter 3 described the interneuron model used in this chapter, and Section 3.4.3 determined the synaptic weights necessary for a single triggered synapse to result in neuron activation without external stimulation. For facilitation, the synaptic weights are required to be less than those thresholds. Chapter 4 explored using epidural stimulation to activate neurons without any triggered synapses. A limited number of neurons were activated by stimulation with a magnitude of less than 5 V, and none were activated using a magnitude of 2.5 V for monophasic stimulation or a

magnitude of 3 V for biphasic stimulation. Chapter 4 also showed that epidural electrical stimulation causes the membrane voltage in the distal tips of the axons and dendrites to have a significantly larger deviation from the resting potential than the proximal parts of the cell. In order to see how this affects the amplitude and propagation of an EPSP from synapses, synapses will be integrated into the model at the distal tips (segment 16) of all dendrites and the middle of the distal section (segment 8) of each dendrite (see locations "A" (segment 8) and "B" (segment 16) in Fig. 3.3). This chapter will consider stimulation magnitudes of 5 V or less, which are biologically relevant. In some of the cases, a few of the neurons will be activated without a synaptic input, but the majority of the neurons will require facilitation by the stimulating field. I found that a synapse triggered within some time window of the stimulation pulse has the greatest opportunity for facilitation. The time window(s) during which the interaction of the stimulation pulse and the synapse response cause neuron activation is referred to as *facilitation window(s)*. After a model neuron is exposed to a subthreshold EPSP (examples seen in Figs. 3.10 and 3.13) the neuron returns to the resting state after some period of time[a]. A subthreshold stimulation pulse (examples shown in Figs. 5.3, 5.3, 5.11 and 5.23) takes less time to return to resting state. Since both the stimulation pulse and the synapse weight are subthreshold by themselves, facilitation cannot occur unless either: (1) a stimulation pulse arrives after a synapse was triggered, but before the neuron's state (V_m, and ion channel state variables) has returned to the resting state, or (2) a synapse is triggered after a stimulation pulse but before the neuron's state has returned to the resting state. Obviously, there are more conditions for facilitation to occur which will be explored a bit in Sections 4.6 and 5.2.

The key finding of this chapter and a contribution of this thesis is that synaptic

[a]For these examples, the neuron takes about 75 ms to 100 ms for the membrane voltage (V_m) and the m ion channel state variables (m_{IKdrSM}, m_{IKaSM}, and m_{INaSM}) to return to the resting state. The h ion channel state variables (h_{IKaSM} and h_{INaSM}) take longer (about 150 ms) to return the resting state.

EPSP inputs that are sub-threshold without stimulation can lead to action potentials with facilitation from epidural stimulation. Prior work (as discussed in Section 1.1) has focused on epidural stimulation of the dorsal roots and myelinated fibers in the white matter. One group of researchers (Capogrosso et al., 2013) have modeled stimulation of interneurons and motor neurons in the spinal cord with epidural stimulation but has not done an intensive study of the interaction of sub-threshold synaptic inputs with epidural stimulation.

Section 5.1 discusses the construction of the simulations and some computational limitations. Section 5.2 shows 8 examples of facilitation using neuron GM1_L_r5_Yn (a neuron in the dorsal horn on the left side under electrode row 5 with an axon pointing in the $-\hat{y}$ direction) and electrode combination A4pA5n (see Section 2.2.1 for electrode combination notation definition) using biphasic and monophasic stimulation. These example sections highlight the facilitation window(s) around a stimulation pulse during which a synaptic input will be facilitated. There is also some evidence that the "least effort" (least magnitude of stimulation and synapse weight) facilitation timing may be dependent on the ion channel states. Section 5.3 summarizes how much facilitation occurs with different stimulation types, synapse locations, stimulation magnitudes, and synapse weights. A significant amount of facilitation occurs when the synapse weight and stimulation magnitude are both large, but sub-threshold. The amount of facilitation decreases as the stimulation magnitude or synapse weight decreases. Section 5.4 finds static voltage features (Section 5.4.1) from static volume conductor simulation and membrane voltage features from stimulation-only (no EPSPs) NEURON simulations (Section 5.4.2) which are useful for separating facilitated neurons (including neurons active with only stimulation) from non-activated neurons. A set of features ($V_{static}^{\text{Synapse}} - V_{static}^{\text{Soma}}$, $V_{static}^{\text{IS}} - V_{static}^{\text{Soma}}$) based on the static volume conductor simulations were better at separating facilitated neurons from

non-activated neurons.

5.1 Modeling of the Facilitation effect

In order to model the mechanism of facilitation, it is necessary to look at the interactions between the effects of a stimulation pulse on a neuron whose synaptic input has been triggered. As shown below, these interactions vary as a function of the time difference between the onset of the stimulation pulse and the onset of synaptic input. In order to study the effect of this time difference, the stimulation pulse onset was fixed in time and the synapse trigger time was varied to include onsets both before and after the stimulation pulse. For each set of parameters (neuron location, orientation, combination, etc.) that would not result in neuron activation without an EPSP, the maximum membrane voltage at the tip of the axon was recorded for each synapse trigger time. A neuron was considered facilitated if the maximum membrane voltage at the axon tip was greater than or equal to $-10\,\text{mV}$, due to the influence of the combined effects of the EPSP and the electrical stimulation and less than $-10\,\text{mV}$ with either alone. The time interval between the onsets that result in facilitation then gives an estimate of how accurately the stimulation pulse must be timed with the existing neuronal activity in order to produce a facilitation effect.

The extracellular voltage was extracted from the volume conductor models and scaled as described in the previous chapter. In addition to the parameters simulated in the last chapter (which yielded 792 simulation configurations for each electrode combination and stimulation type (monophasic or biphasic)), there are 10 synapse locations (distal tip or middle of distal section on 5 dendrites) yielding a total of 7920 simulation parameters. Simulations were conducted using the stimulation voltages and synapse weights in Table 5.1.

In order to understand the temporal interactions between epidural stimulation and the EPSPs, the duration of simulated time was increased from 151 ms to 226 ms,

Table 5.1: Facilitation testing parameters: column $|V_s|$ contains the list of stimulation voltage magnitudes tested, column W_8 contains the list of synapse weights used for the synapse in the middle of the distal section of the dendrite, and W_{16} contains the list of synapse weights used for the synapse of the distal tip of the dendrite.

$\|V_s\|$[mV]	W_8[nS]	W_{16}[nS]
5	3.45	4.783
4	3.443	4.776
3	3.436	4.769
2	3.422	
1	3.394	
0.5	3.337	
	3.225	
	3.0	

and the start of the simulation pulse was moved to $t = 76$ ms to allow for simulation of EPSPs both before, during, and after the stimulation pulse. This time range was believed to be sufficient because the peak of the membrane voltage occurs at a maximum of ~50 ms after synapse trigger, and the maximum membrane voltages due to stimulation pulses occurs within ~25 ms of pulse onset. In each simulation interval, only a single stimulation pulse (at $t = 76$ ms) and a single EPSP (from an Exp2Syn synapse as described in Section 3.3.1) occurred, but the synapse trigger time was selected from the array t_{syn} = [1 ms to 146 ms in steps of 5 ms] (a total of 30 trigger times).

Simulating all of the above parameter configurations would require 792 * (5 dendrites) * (3+8 synapse weights for segments 16 and 8 respectively) * (6 stimulation voltages) * (18 combinations) * (2 stimulation types) * (30 trigger times) =

282,268,800 NEURON simulations, or about 247.5 times the number of simulations required for the previous chapter. Each NEURON simulation for this chapter also can be estimated to take about 1.5 times longer than the simulations in the previous chapter. Since the previous chapter's simulations took on the order of a month to complete, clearly either additional computational resources are required or a smarter sampling algorithm in order to obtain results in a reasonable amount of time. With the goal of reducing computation time while still finding facilitation, a sampling algorithm was written that: (1) avoided simulating synapse firing if the stimulation pulse alone would cause activation, (2) avoided simulations at a particular synapse trigger time if a larger-in-magnitude stimulation voltage or synapse weight did not result in facilitation, unless a neighboring (in time) synapse trigger time did result in facilitation. Using this sampling algorithm, the total number of simulations was reduced to 18,980,825 for monophasic simulations and 10,790,662 for biphasic simulations. The total number of simulations performed (29,771,487) is 10.5% of the number of simulations required to simulate all of the parameter configurations listed earlier. In particular situations, some of the assumptions behind the sampling algorithm could be wrong, and so some facilitation could be missed, but they seem to be true in the cases I specifically examined.

During the NEURON simulations, membrane voltage maxima and minima were recorded at several "probe" locations (axon proper distal tip (seg=16), initial segment ("IS", seg=0), axon hillock ("AH",seg=0), and soma (seg=0). (See Fig. 3.3 for "probe" locations.)

5.2 Examples of facilitation

Before getting to the total amount of facilitation in Section 5.3 or predicting facilitation in Section 5.4, it is necessary to have some understanding of how facilitation occurs and the concept of a facilitation window. A facilitation window is a period

of time near a stimulation pulse during which synaptic input can control the output of the neuron. In this section, I will go through a few examples to help develop a better understanding of the facilitation process.

Consider neuron GM1_L_r5_Yn[b] exposed to stimulation using combination A4pA5n[c] ($V_s^{A4} = V_S G(t)$, $V_s^{A5} = -V_S G(t)$). Based on the data from the last chapter (without synaptic input), biphasic stimulation activates this neuron with stimulation amplitude $V_s = -6\,\text{V}$ or $V_s = 8\,\text{V}$. Using monophasic stimulation it activates using $-4.25\,\text{V}$ of stimulation, and positive monophasic stimulation appears completely ineffective. When synaptic input is present, this situation changes significantly based on the location of the synapse and its synaptic weight. Section 5.2.1 will examine what happens if a synapse is triggered on the distal tip (segment=16) of the distal dendrite pointing in the $+\hat{x}$ direction near the time of a biphasic stimulation pulse. Section 5.2.2 will look at the same situation with 2 polarities of monophasic stimulation. More examples including some with the synapse located in the middle (segment=8) of the distal section are available in Section 5.B.

All of the biphasic examples presented have a "least effort" facilitation window (in terms of least synapse weight and least magnitude of stimulation) for synaptic input ~15-20ms before the stimulation pulse. For the monophasic examples, the facilitation window timing depends on the polarity of the stimulation pulse. With $V_s < 0$, the "least effort" facilitation window for synaptic input is before the stimulation pulse, which is similar to the biphasic examples, but if $V_s > 0$, the facilitation window for synaptic input is mostly after the stimulation pulse.

[b] See Section 4.1 for naming convention. This is a neuron located in the dorsal horn on the left side under electrode row 5 with an axon pointing in the $-\hat{y}$ direction.

[c] See Section 2.2.1 for electrode combination notation definition.

5.2.1 Biphasic stimulation

This section looks an example of facilitation using biphasic stimulation with combination A4pA5n and a negative stimulation ($V_s < 0$) amplitude. Specifically, the facilitation of neuron GM1_L_r5_Yn with a synapse located at segment 16 on the distal dendrite pointing in the $\hat{x}$ direction. Without any synaptic input, the neuron will activate if $V_s = -6\,\mathrm{V}$.

The maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.1. The stimulation pulse starts at 76 ms. The facilitation window(s) for each pairing of stimulation voltage (V_s) and synapse weight consist of any time that the appropriate line indicating the membrane voltage at the axon tip goes above the red line ($-10\,\mathrm{mV}$). In this case, facilitation window(s) exist both before and after the stimulation pulse, but the "least effort" facilitation occurs before the stimulation pulse.

In this case, the window (in time) of facilitation with $V_s = -2\,\mathrm{V}$ is about 40 ms before the middle of the stimulation pulse and 25 ms after the stimulation pulse for all of the tested synapse weights. Note that there is a reduction in the length of the facilitation time window as V_s approaches 0, especially for the lower values of synapse weight. But there is still some facilitation at the higher synapse weights for $V_s = -0.5\,\mathrm{V}$. For $V_s = -0.5\,\mathrm{V}$ and synapse weight 4.776 nS; there is only an ~15 ms window before the stimulation pulse in which the synapse must fire in order to experience facilitation. Anecdotally, all of the biphasic facilitation plots that I have examined exhibit the same pattern: there exists a "least effort" facilitation window before the stimulation pulse.

Figure 5.2 shows the membrane voltage at the axon tip and the synapse location for $V_s = -2\,\mathrm{V}$ and synapse weight 4.783 nS for all the synapse trigger times shown in Fig. 5.1. The periods of neuron activation are shown in orange-red, while the

synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse is depicted as a dotted black line. Any synapse time that results in an activation is part of the facilitation window.

The response of the neuron (membrane voltage and ion-channel state variables) to just the effect of a synaptic input (with synapse weight of 4.783 nS) alone can be found in Fig. 3.13. The response of the neuron to stimulation of level $V_s = -2\,\mathrm{V}$ alone can be found in Fig. 5.3.

When $V_s = -2\,\mathrm{V}$ and the synapse weight takes the value 4.783 nS, a synapse trigger time at $t = 66\,\mathrm{ms}$ maximizes the membrane voltage at the axon tip (compared to other synapse trigger times). Figure 5.4 shows the neuron response to these parameters. Note that this synapse trigger time causes the stimulation pulse to occur when m_{IKdrSM} is at a maximum near the synapse and h_{INaSM} is at a minimum (where m_{IKdrSM} and h_{INaSM} are ion state variables discussed in Section 3.1). These ion channel states may make the neurons more sensitive to biphasic stimulation and explain why the "least effort" facilitation window for biphasic stimulation occurs before the stimulation pulse. Additional examples of biphasic stimulation in Sections 5.B.1 to 5.B.3 show the same behavior.

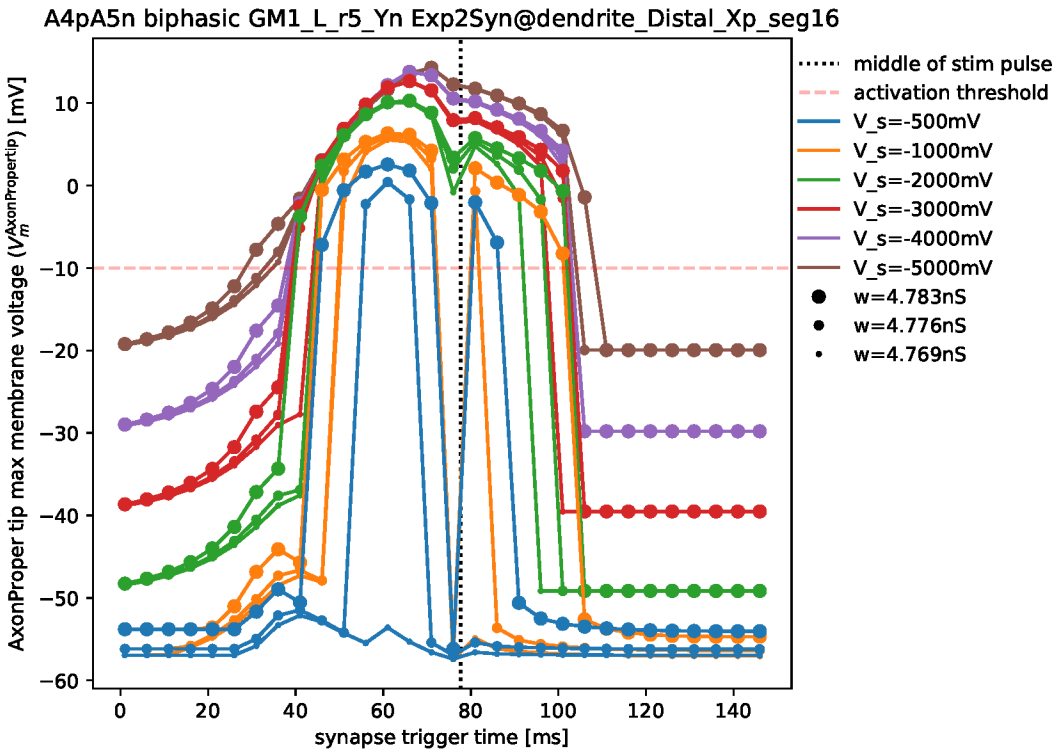


Figure 5.1: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron's synapse is at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to biphasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum pulse amplitudes occur at t=77.66ms ± 0.16ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$), where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above $-10\,\text{mV}$) : (-5.0V, 4.783nS, 10, 6), (-5.0V, 4.776nS, 9, 5), (-5.0V, 4.769nS, 9, 5), (-4.0V, 4.783nS, 8, 5), (-4.0V, 4.776nS, 8, 5), (-4.0V, 4.769nS, 8, 5), (-3.0V, 4.783nS, 8, 5), (-3.0V, 4.776nS, 8, 5), (-3.0V, 4.769nS, 7, 4), (-2.0V, 4.783nS, 8, 5), (-2.0V, 4.776nS, 7, 4), (-2.0V, 4.769nS, 7, 3), (-1.0V, 4.783nS, 6, 5), (-1.0V, 4.776nS, 5, 1), (-1.0V, 4.769nS, 5, 0), (-0.5V, 4.783nS, 6, 2), and (-0.5V, 4.776nS, 3, 0).

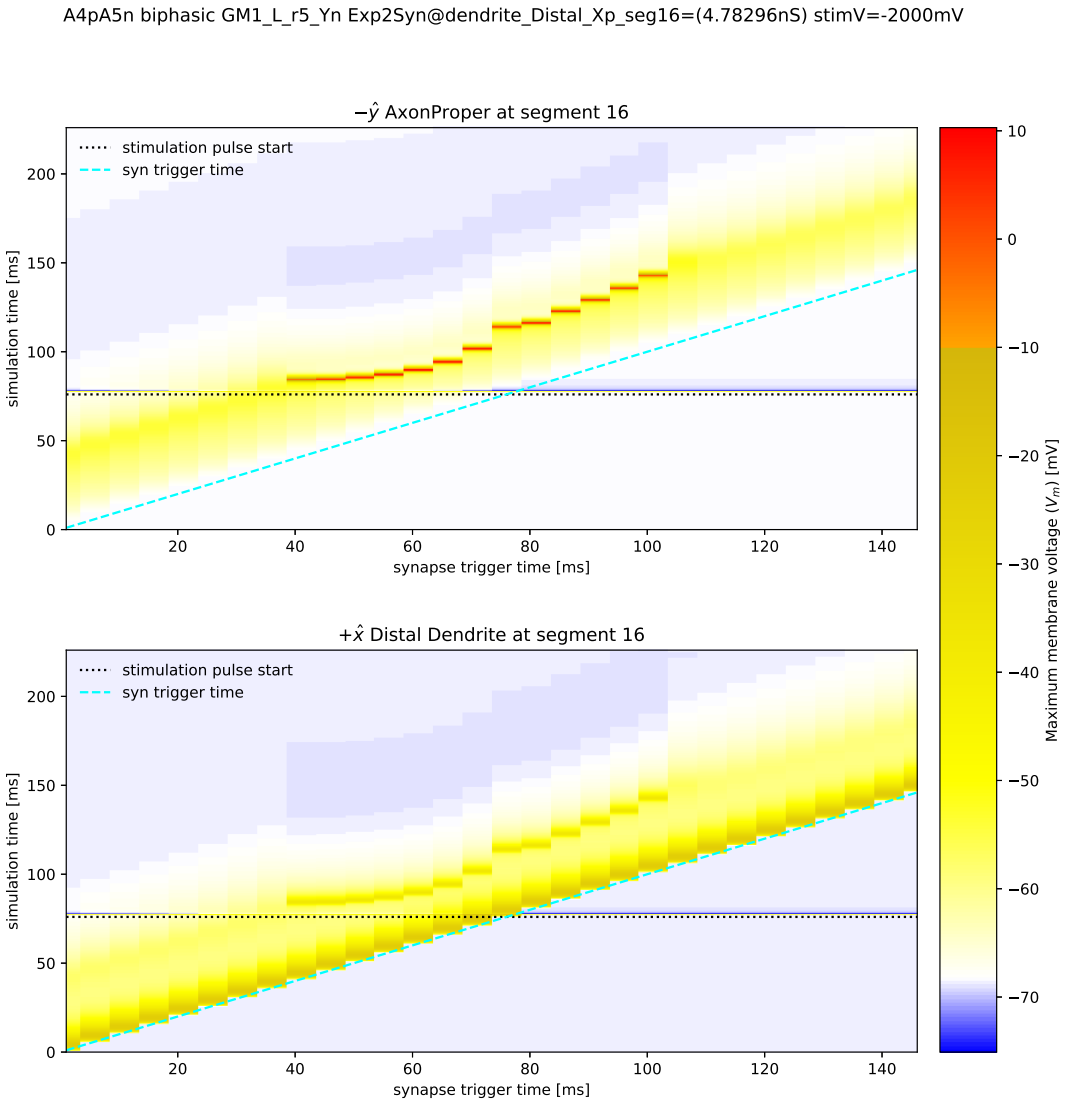
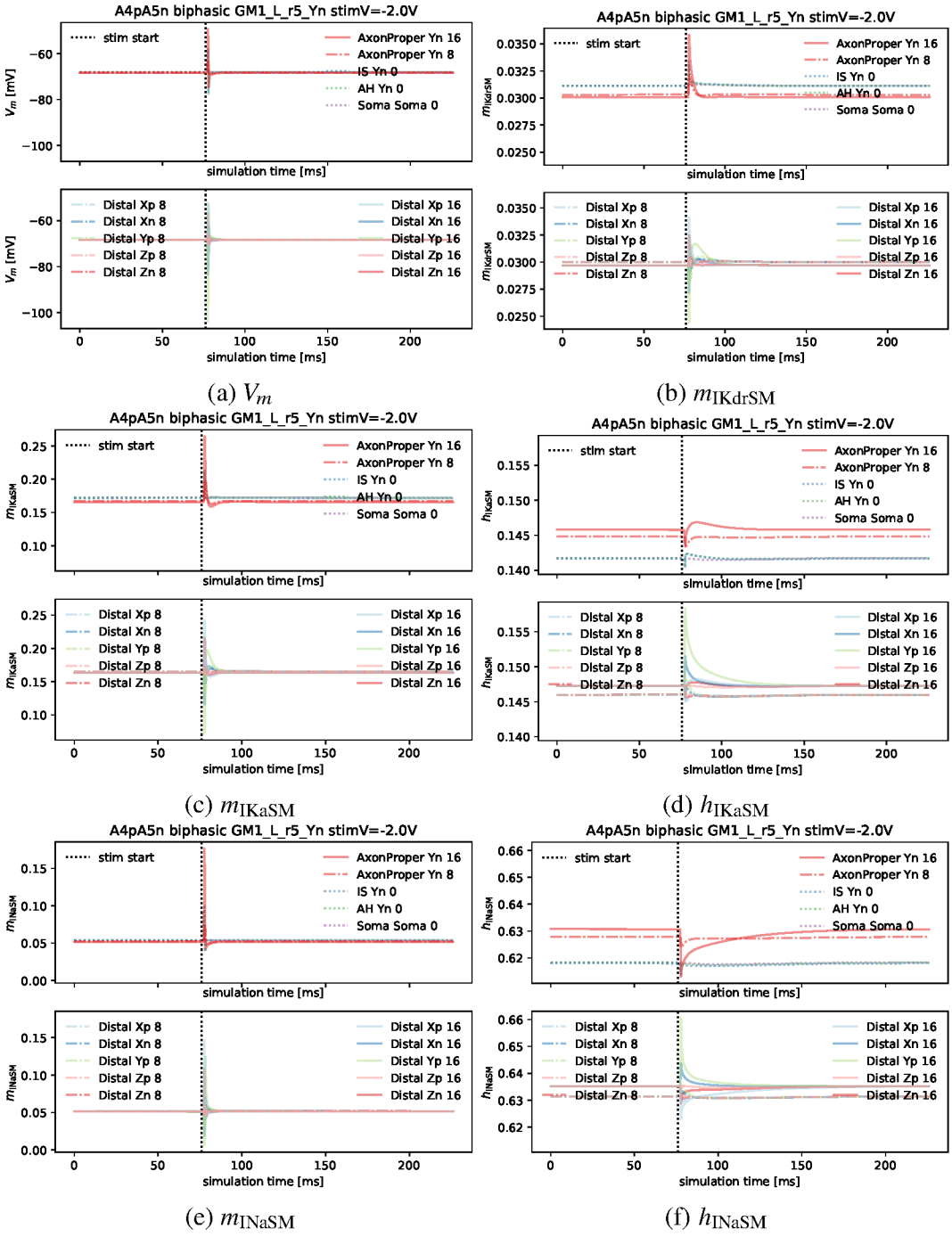


Figure 5.2: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to -2.0 V of biphasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=4.783nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 16. The electrical stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation. Synapse trigger times that have a dark yellow to orange color above them are a part of the "facilitation window."

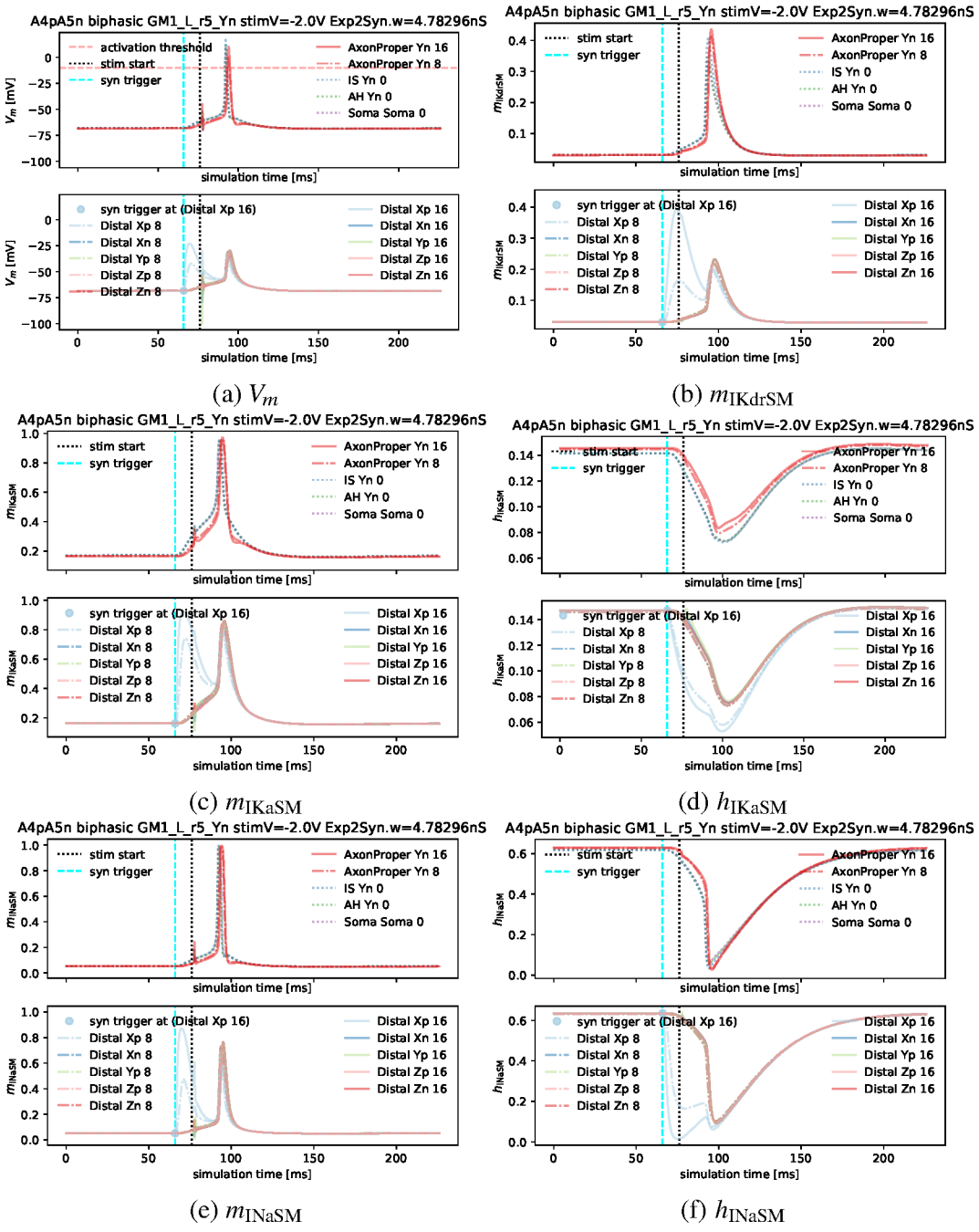


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.3: Stimulation only: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). All data measured using neuron GM1_L_r5_Yn exposed to −2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms.



(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.4: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=66.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.

5.2.2 Monophasic stimulation

This section looks at an example of facilitation using monophasic stimulation with combination A4pA5n with both negative and positive stimulation (V_s). Specifically, the facilitation of neuron GM1_L_r5_Yn with a synapse located at segment 16 on the distal dendrite pointing in the $\hat{x}$ direction. Without any synaptic input, the neuron will activate if $V_s \leq -4.25\,\text{V}$.

The maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.5 for $V_s < 0$ and Fig. 5.9 for $V_s > 0$. Unlike the biphasic stimulation examples, which all have "least effort" facilitation window(s) before the stimulation pulse, in this case if $V_s > 0$, the facilitation window for synaptic input is longer after the stimulation pulse than before the stimulation pulse. The "least effort" facilitation window in this case is when the stimulation pulse occurs. If $V_s < 0$, then the "least effort" facilitation window for synaptic input occurs before the stimulation pulse in the biphasic examples.

With $V_s = -4\,\text{V}$, there are two facilitation windows (one before the stimulation pulse (about 35 ms to 40 ms in width), a gap of about 5 ms to 10 ms of time with no facilitation around the stimulation pulse, and another window after the stimulation pulse with a width of about 35 ms. With $V_s = -3\,\text{V}$, the facilitation window is about 55 ms wide with 40 ms before the stimulation pulse and 15 ms after with no gap in between. For [-2, -1, 0.5]ms, the facilitation windows are all before the stimulation pulse, similar to the biphasic stimulation examples.

Figure 5.6 shows the membrane voltage at the axon tip and the synapse location for $V_s = -2\,\text{V}$ and synapse weight 4.783 nS. Figure 5.10 shows the same for $V_s = 2\,\text{V}$ and the same synapse weight. As in the previous section, the periods of neuron activation are shown in orange-red, while the synapse trigger time is shown as a

dashed cyan line, and the start of the stimulation pulse as a dotted black line.

The response of the neuron (membrane voltage and ion-channel state variables) to just the EPSP (with synapse weight of 4.783 nS) alone can be found in Fig. 3.13. The response of the neuron to $V_s = -2$ V stimulation alone can be found in Fig. 5.7 and $V_s = 2$ V stimulation alone in Fig. 5.11. For $V_s = -2$ V, a synapse trigger time of 71 ms (shown in Fig. 5.8) resulted in the maximum axon tip membrane voltage with a synaptic weight of 4.783 nS. In this case, the stimulation pulse occurs when V_m at the synapse location is a maximum, m_{IKdrSM} is approaching maximum, m_{IKaSM} is close to maximum, m_{INaSM} is near maximum, and h_{INaSM} is approaching minimum. Further study would be required to determine which factors are important for "least effort" timing, but none of the biphasic stimulation examples had "least effort" timing at the maximum of V_m at the synapse.

For the case of $V_s = 2$ V and synapse weight 4.783 nS, the membrane voltage at the axon tip is maximized (compared to other synapse trigger times) when the synapse trigger time coincides with the start of the stimulation pulse. Figure 5.12 shows the neuron response to these parameters.

Additional examples of facilitation with monophasic stimulation and a synapse located in the middle of the distal section of the same dendrite are available in Sections 5.B.4 and 5.B.5. Based on these examples, it appears that the timing of the facilitation window(s) depends on the magnitude, sign, and orientation of the neuron (and likely the orientation of the dendrite with the triggered synapse). There are also differences in the "least effort" facilitation timing between monophasic and biphasic stimulation that should be looked into further.

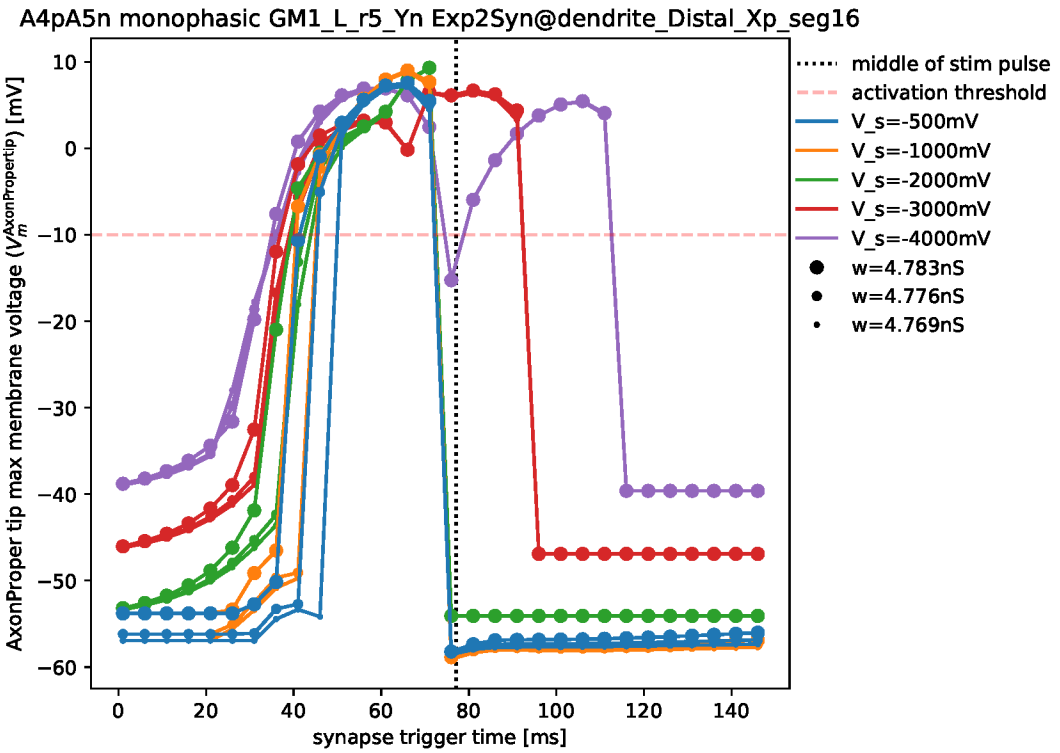


Figure 5.5: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to monophasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. This neuron is active without any EPSPs if exposed to -5.0V of stimulation. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above $-10\,\text{mV}$) : (-4.0V, 4.783nS, 8, 7), (-4.0V, 4.776nS, 8, 7), (-4.0V, 4.769nS, 7, 7), (-3.0V, 4.783nS, 8, 3), (-3.0V, 4.776nS, 8, 3), (-3.0V, 4.769nS, 8, 3), (-2.0V, 4.783nS, 7, 0), (-2.0V, 4.776nS, 6, 0), (-2.0V, 4.769nS, 6, 0), (-1.0V, 4.783nS, 7, 0), (-1.0V, 4.776nS, 6, 0), (-1.0V, 4.769nS, 6, 0), (-0.5V, 4.783nS, 6, 0), (-0.5V, 4.776nS, 6, 0), and (-0.5V, 4.769nS, 5, 0).

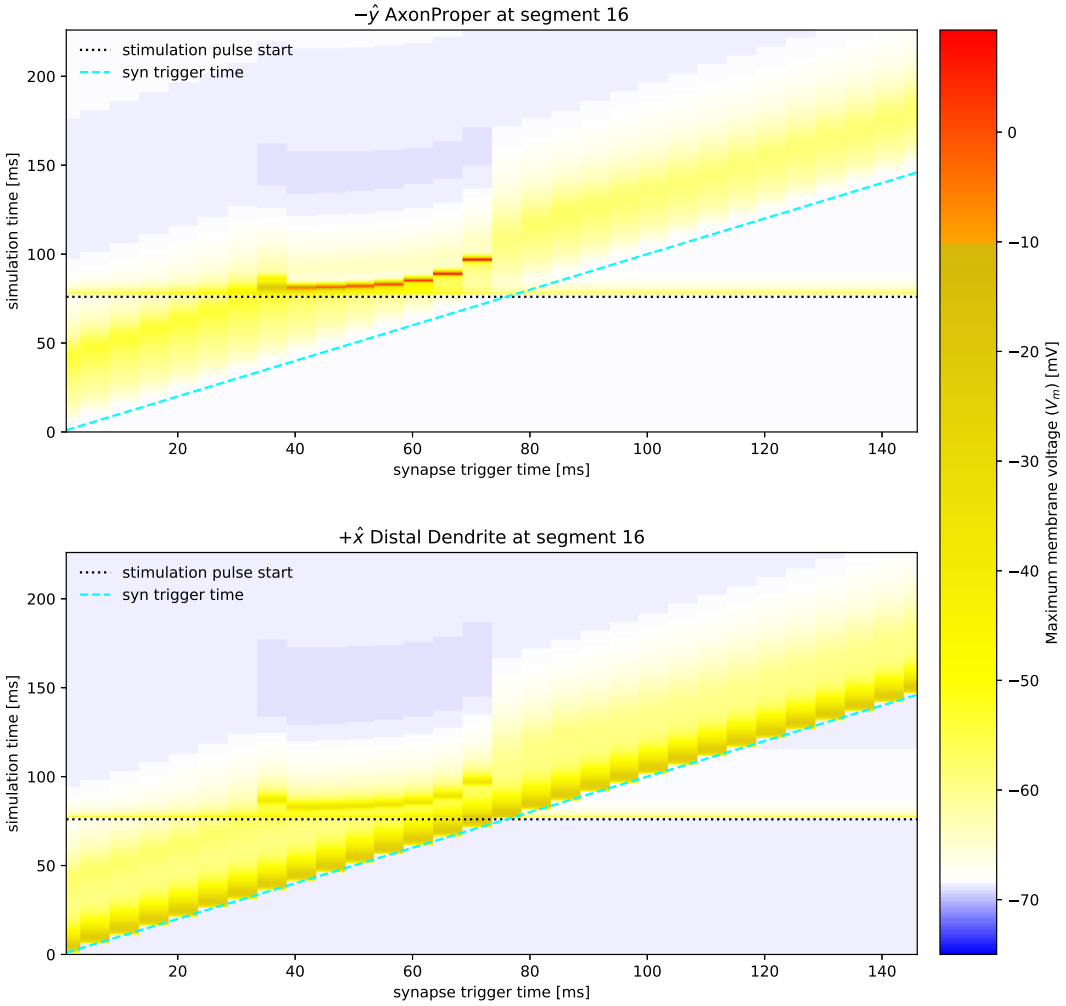
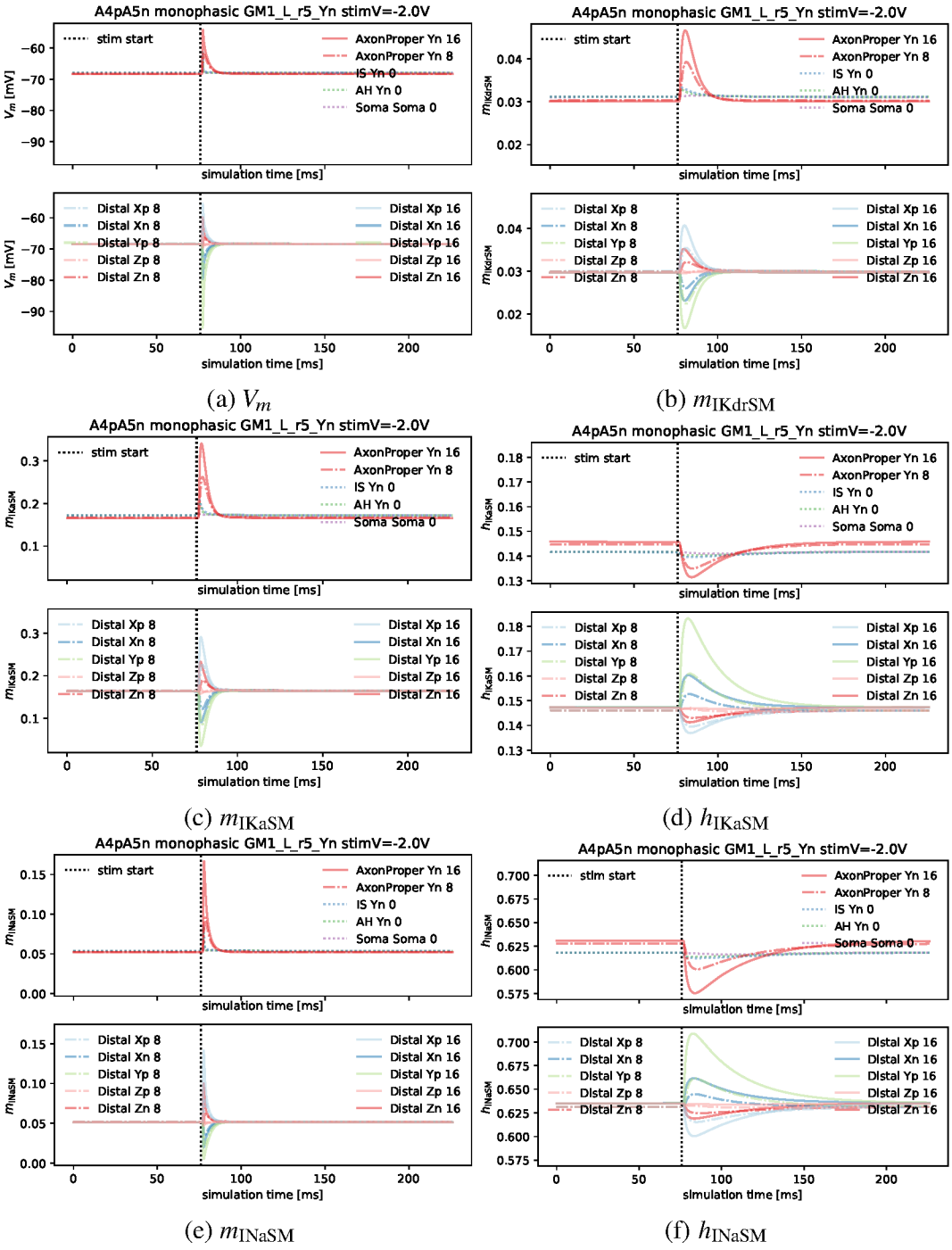


Figure 5.6: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=4.783nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 16. The electrical stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.



(a) V_m

(b) m_{IKdrSM}

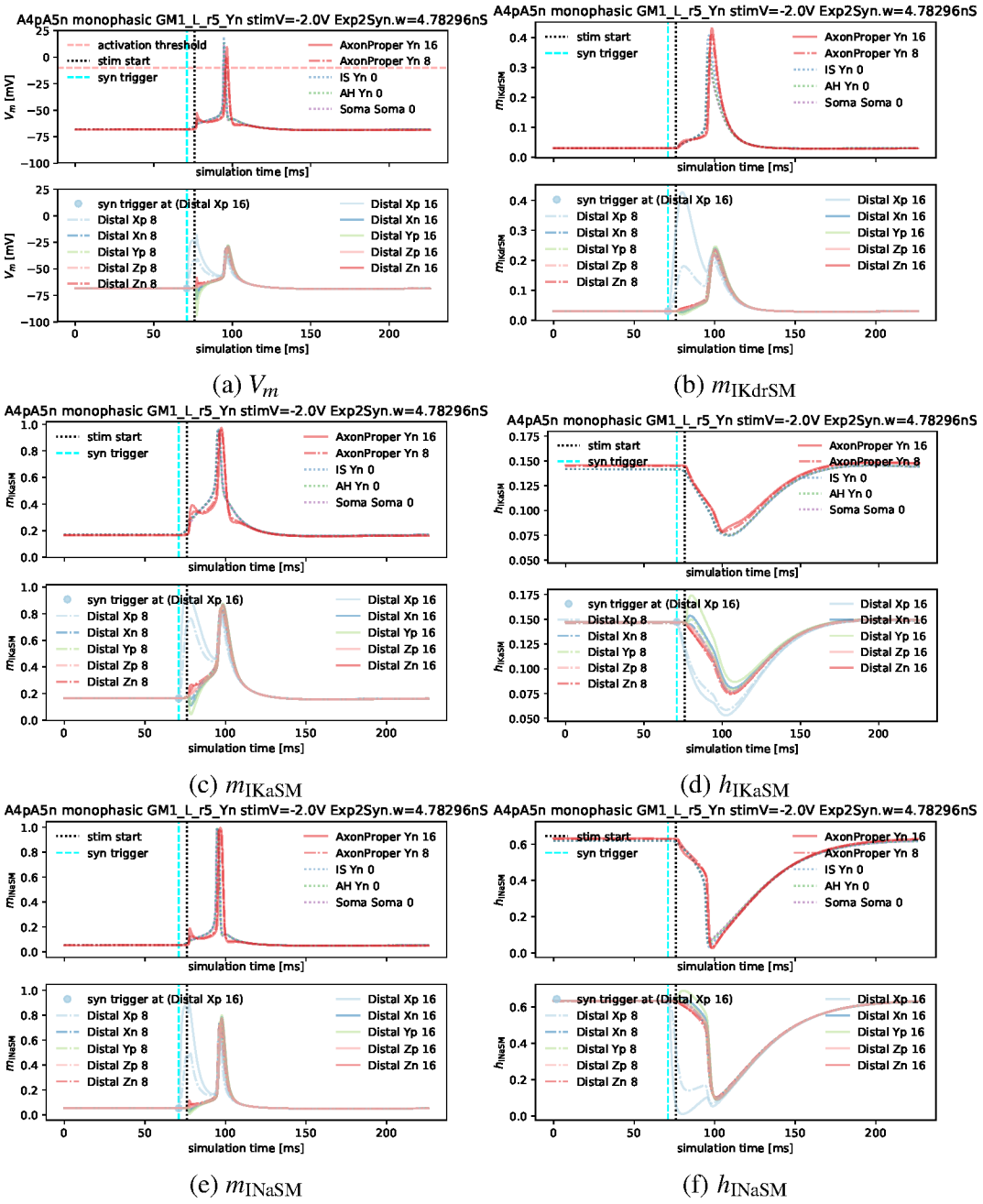
(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.7: Stimulation only: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). All data measured using neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms.



(a) V_m

(b) m_{IKdrSM}

(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.8: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=71.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.

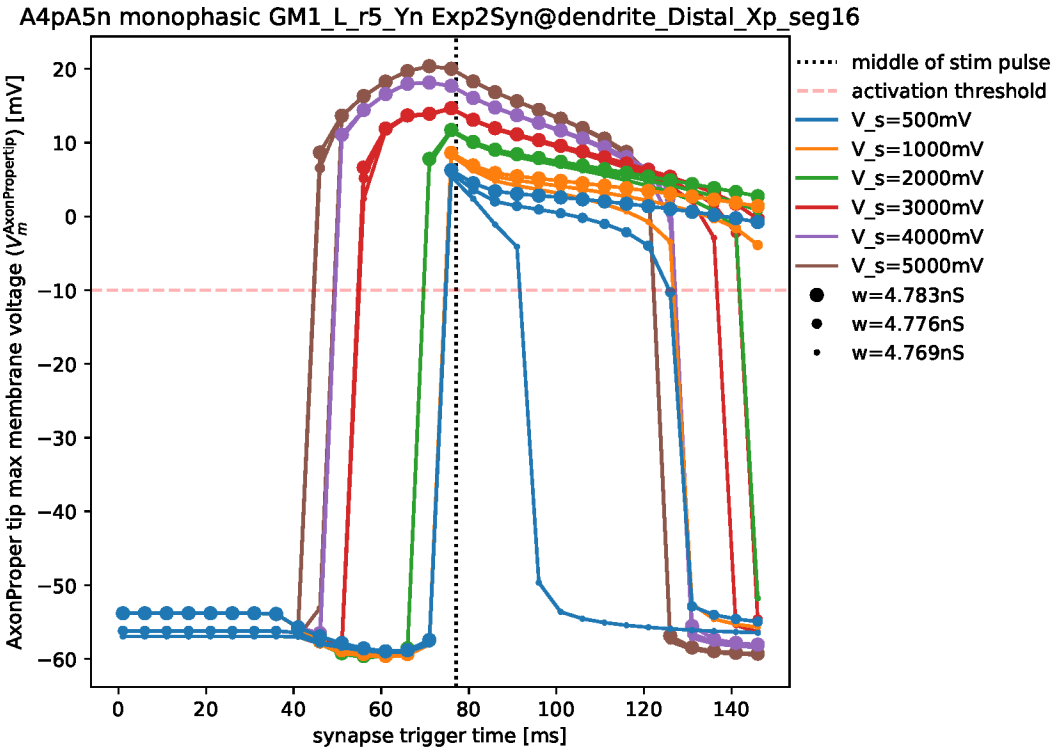


Figure 5.9: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to monophasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above $-10\,\text{mV}$) : (5.0V, 4.783nS, 7, 9), (5.0V, 4.776nS, 7, 9), (5.0V, 4.769nS, 6, 9), (4.0V, 4.783nS, 6, 10), (4.0V, 4.776nS, 6, 10), (4.0V, 4.769nS, 6, 10), (3.0V, 4.783nS, 5, 14), (3.0V, 4.776nS, 5, 13), (3.0V, 4.769nS, 5, 12), (2.0V, 4.783nS, 2, 14), (2.0V, 4.776nS, 2, 14), (2.0V, 4.769nS, 2, 13), (1.0V, 4.783nS, 1, 14), (1.0V, 4.776nS, 1, 14), (1.0V, 4.769nS, 1, 10), (0.5V, 4.783nS, 1, 14), (0.5V, 4.776nS, 1, 9), and (0.5V, 4.769nS, 1, 3).

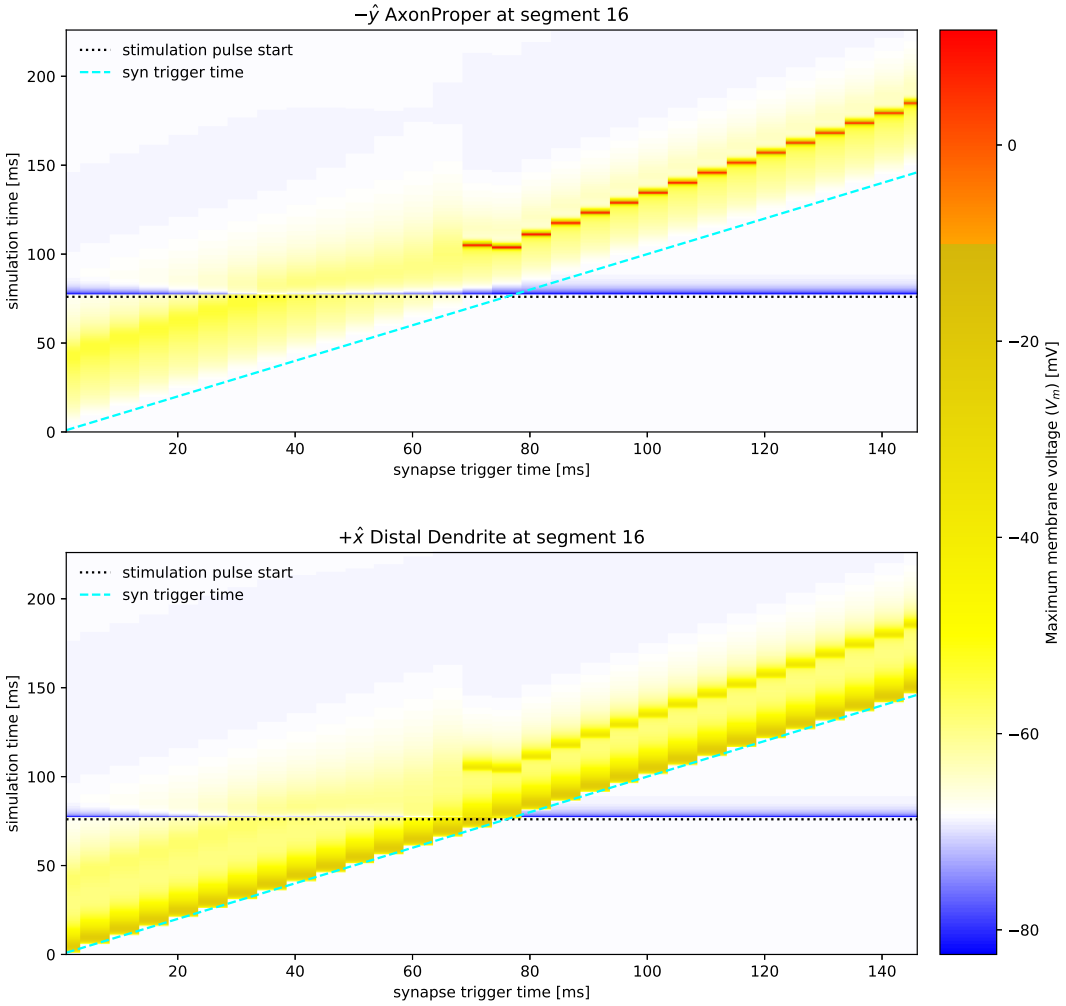
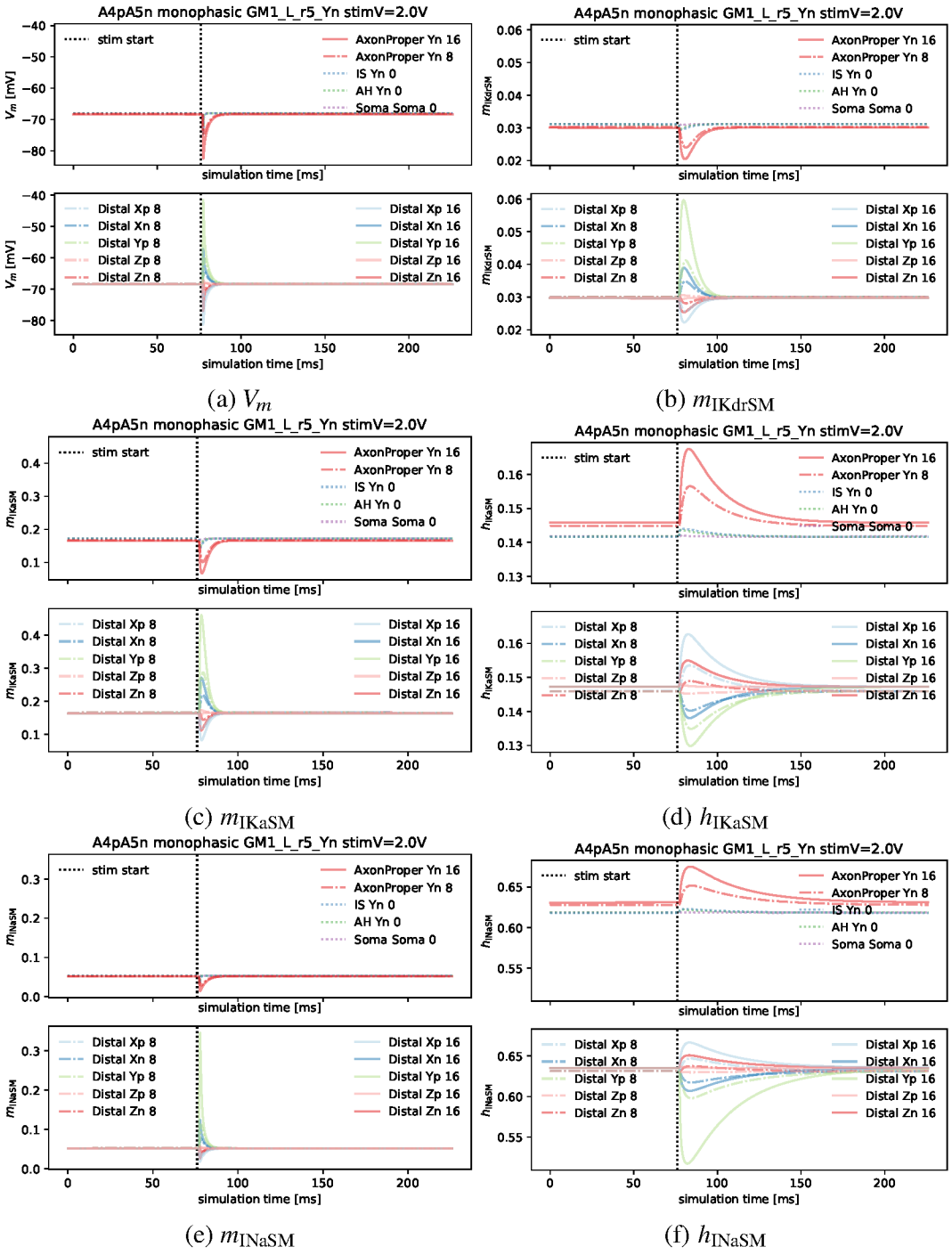


Figure 5.10: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=4.783nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 16. The electrical stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.

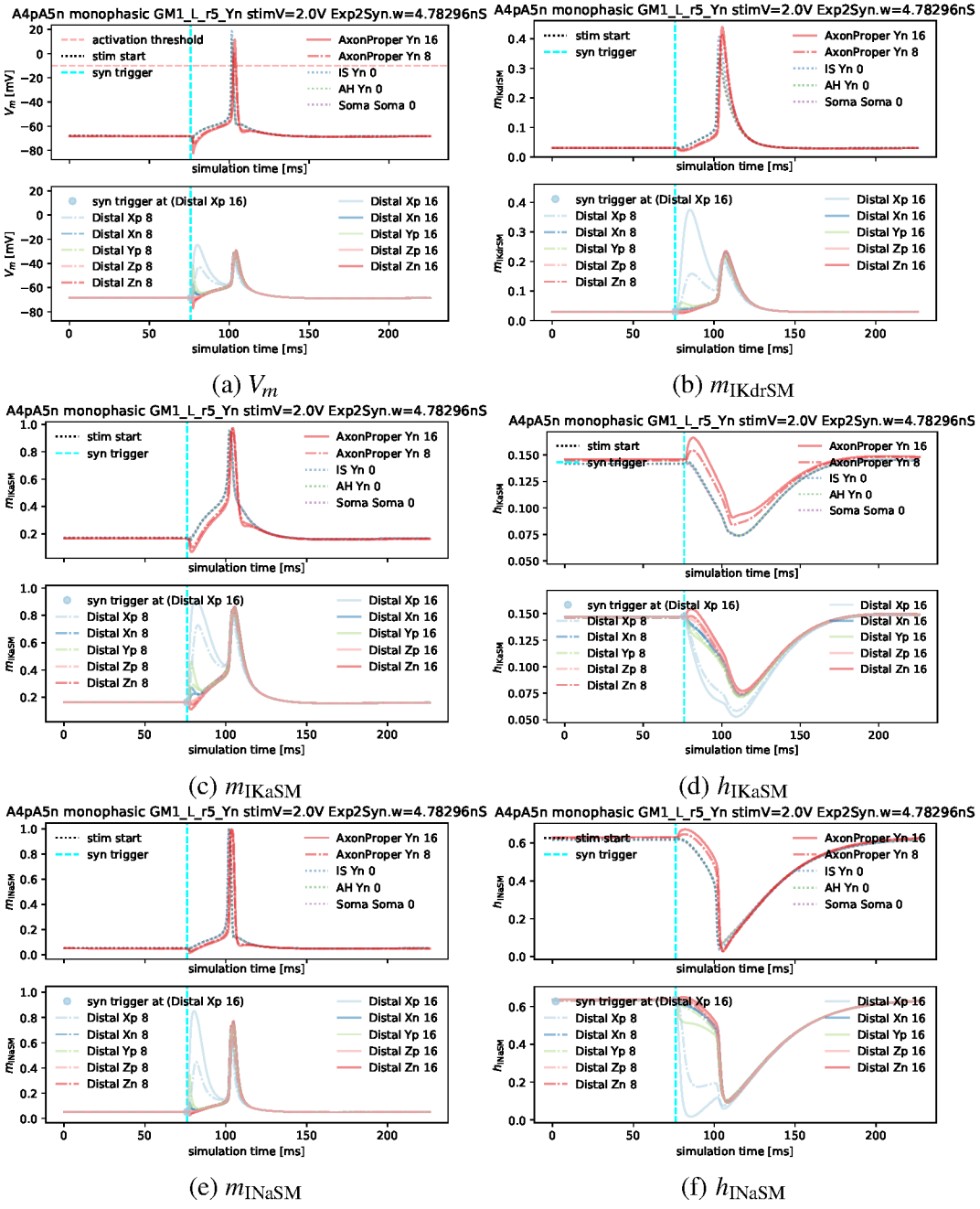


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.11: Stimulation only: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). All data measured using neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms.



(a) V_m

(b) m_{IKdrSM}

(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.12: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=76.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.

5.3 Total facilitated neurons for monophasic and biphasic stimulation

Section 4.3 discussed the total number of active neurons for monophasic and biphasic stimulation without any EPSPs. When a synapse is triggered close enough in time to interact with the stimulation pulse, this interaction may result in facilitation. As seen in Section 5.2, for each synapse weight and stimulation voltage, there may exist one or more facilitation windows (regions of synapse trigger time for a fixed stimulation time) where the interaction of the EPSP from the synaptic input and the stimulation pulse results in facilitation. Larger facilitation windows means that there is a larger probability that a stimulus pulse will facilitate an EPSP and activate a neuron. The number of synapse trigger times which result in facilitation can be used to summarize the facilitation window(s) for each pair of stimulation voltage and synapse weight.

For each type of stimulation (monophasic and biphasic), electrode stimulation voltage ($|V_s|$), synapse weight, and synapse segment (8 or 16), there are: (6 neuron locations for each constant z plane) * (6 geometry types (axon orientations)) * (5+6 z planes (ignoring neurons under rows 1 and 7)) * (2 positive and negative voltage amplitude) * (18 combinations) * (5 dendrites) = 71280 simulated neurons that could be facilitated.

Two-dimensional histograms of the number of simulated neurons vs the duration of the facilitation window(s), as measured using the number of synapse trigger points resulting in activation vs stimulation and synapse weight were generated by combining the number of synapse trigger times resulting in facilitation for all electrode combinations, neuron locations, and neuron orientations. Figure 5.13 shows the 2d histograms (greyscale squares with colorbar just to the right of each histogram indicate the number of neurons) for monophasic (Fig. 5.13a) and biphasic (Fig. 5.13b) stimulation and synapses located in the middle (segment 8) of the distal section of the dendrites. Figure 5.14 shows the 2d histograms (greyscale squares with colorbar

just to the right of each histogram indicate the number of neurons) for monophasic (Fig. 5.14a) and biphasic (Fig. 5.14b) stimulation and synapses located at the distal tips (segment 16) of the distal section of the dendrites. The y-axis of each 2d histogram shows the number of synapse trigger times which result in facilitation (or stimulation only (stimOnly) if no EPSP is required to activate the neuron at that value of V_s). Understanding the x-axis of each 2d histogram requires looking at the background columns behind the histogram. The magnitude of stimulation voltage ($|V_s|$) is represented by the color of each column (see right color bar (virdis[d]) to the right of each plot). The synapse weight of each column is indicated by the hatching of each column (see legend to the far right of each histogram). The grey-scale colorbar indicating the number of neurons facilitated in each square and the viridis colorbar indicating the magnitude of the stimulation voltage ($|V_s|$) are the same in Figs. 5.13a, 5.13b, 5.14a and 5.14b, allowing for direct comparison.

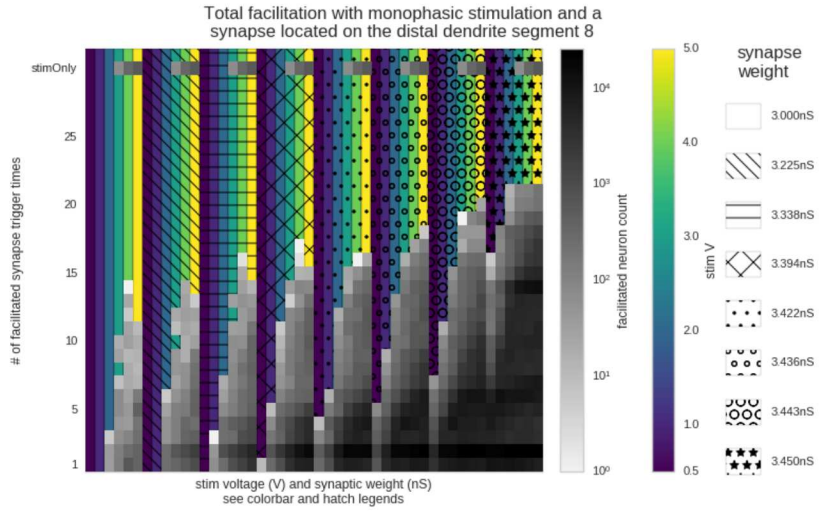
From Figs. 5.13 and 5.14, it appears that monophasic stimulation in general has wider facilitation windows (with a few exceptions) compared with biphasic stimulation. The histograms also show a general expected trend of increasing facilitation with increasing magnitude of stimulation voltage $|V_s|$ and synapse weight. It also appears that the facilitation windows tend to be a bit larger if the synapse is on the distal tip of the distal dendrite compared with the middle of the distal dendrite. Unfortunately, comparisons between synapse locations are not completely accurate because a larger synaptic weight is required to activate the neuron if the synapse is located further from the soma. I have tried to compensate for this effect by choosing synapse weights for each synapse location as an offset from the synapse activation threshold at each location.

Figures 5.15 and 5.16 show the same data using stacked bars indicating the size

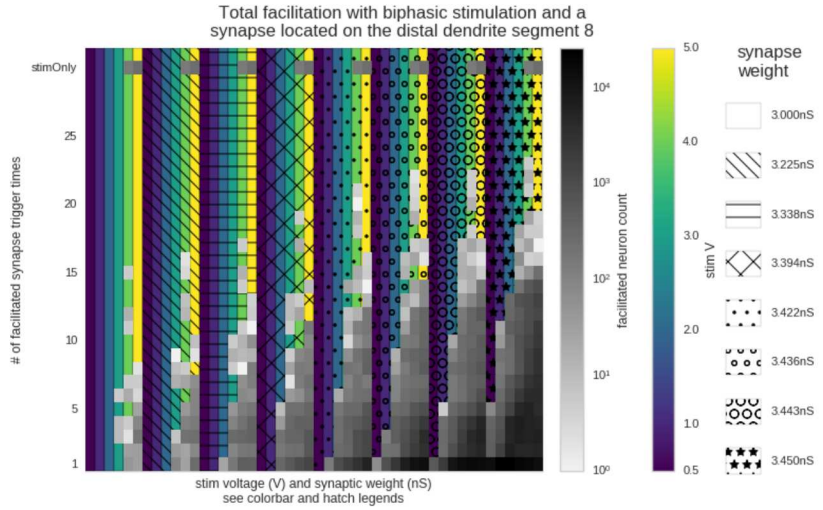
[d]Matplotlib's viridis (yellow-green-blue) colormap is an improvement over traditional rainbow colormaps. See Borland and Ii, 2007 and Liu and Heer, 2018.

of the facilitation windows. The bar charts make it easier to compare the total number of neurons with a facilitation window of various widths. In these plots, the maximum of the y-axis is the total number of neurons so it is easy to see the factions of neurons facilitated. For synapses located in the middle of the distal dendrite (Fig. 5.15), the general trends described above still hold, (monophasic stimulation results in more facilitation than biphasic stimulation, etc.). However, for synapses at the distal tip of the distal dendrite (Fig. 5.15), at the largest synapse weight (4.783 nS), the total number of neurons where at least 1 of the synapse trigger times results in facilitation is actually larger for biphasic than monophasic stimulation if the magnitude of stimulation voltage $|V_s| >= 3$ V.

For both monophasic and biphasic stimulation, there is also an increase in the number of neurons with greater than 4 trigger points that result in facilitation for synapses at the distal tips of the distal dendrites compared with the synapses in the middle of the distal dendrite as seen in Figs. 5.17 and 5.18. This indicates that facilitation of distal synaptic input may be easier than more proximal (to the soma) synaptic input.

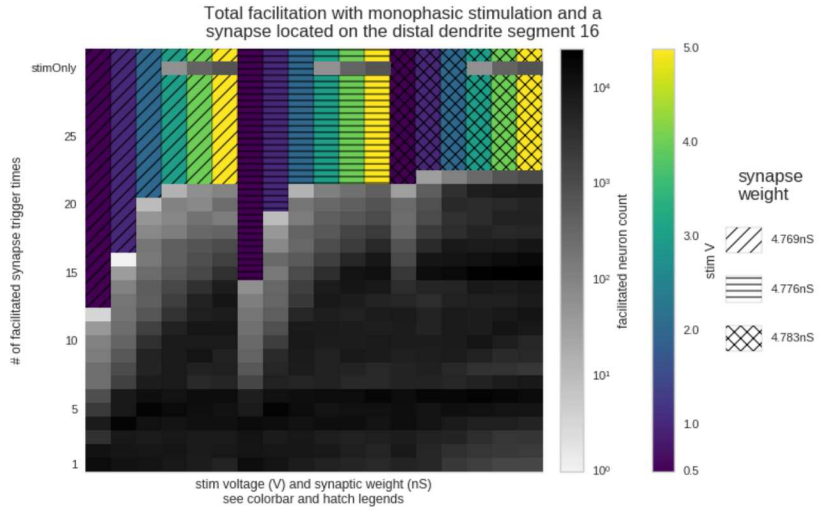


(a) monophasic

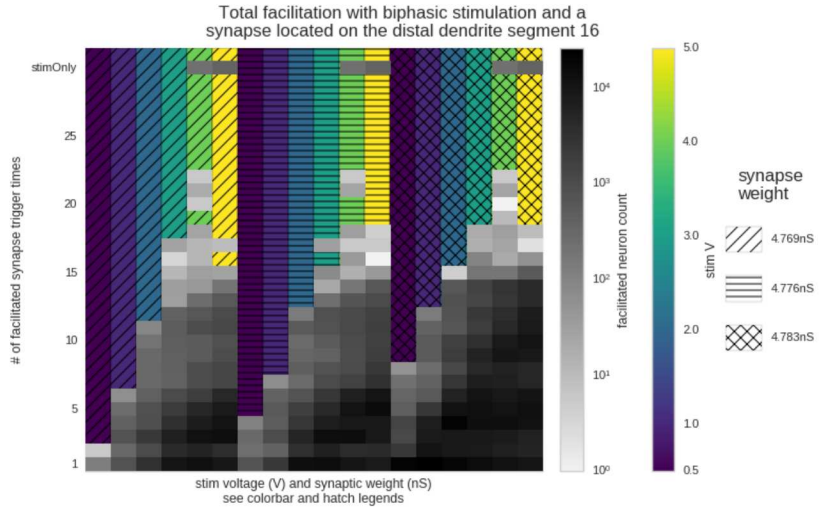


(b) biphasic

Figure 5.13: 2d histogram of the number of facilitated neurons with synapses in the middle (segment 8) of the distal dendrite for: (a) monophasic and (b) biphasic stimulation. The y-axis of each 2d histogram shows the number of synapse trigger times which result in facilitation (or stimOnly if no EPSP is required to activate the neuron at that value of V_s). Understanding the x-axis of each 2d histogram requires looking at the background columns behind the histogram. The magnitude of stimulation voltage ($|V_s|$) is represented by the color of each column (see right color bar to the right of each plot). The synapse weight of each column is indicated by the hatching of each column (see legend to the far right of each histogram). The number of neurons in each square is indicated by the gray-scale colorbar just to the right of the histogram. Each column consists of the results from simulating 71280 neurons under 18 electrode combinations (described in Section 5.3).

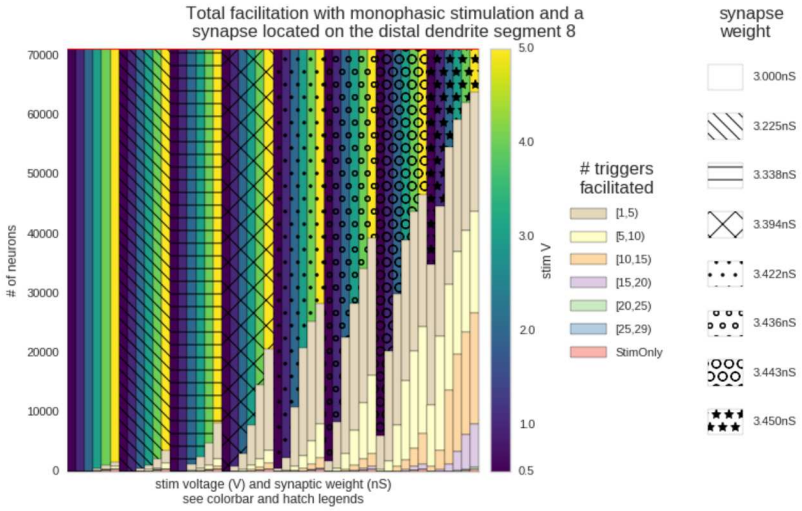


(a) monophasic

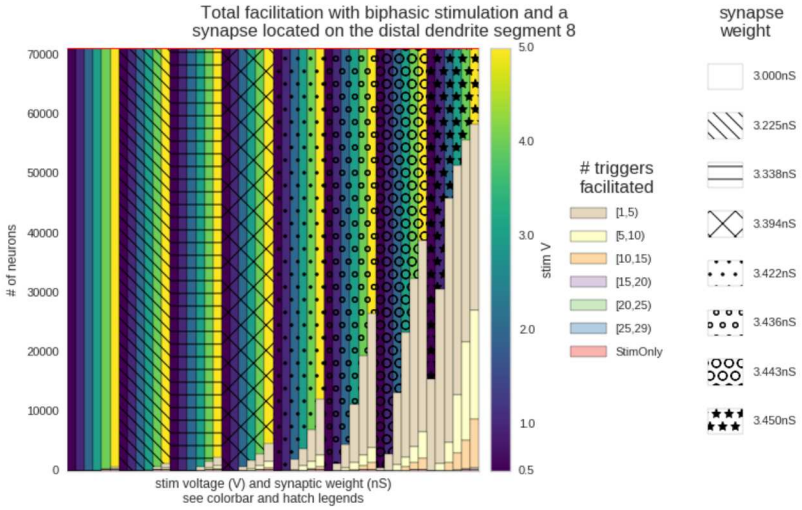


(b) biphasic

Figure 5.14: 2d histogram of the number of facilitated neurons with synapses at the distal tip (segment 16) of the distal dendrite for: (a) monophasic and (b) biphasic stimulation. The y-axis of each 2d histogram shows the number of synapse trigger times which result in facilitation (or stimOnly if no EPSP is required to activate the neuron at that value of V_s). Understanding the x-axis of each 2d histogram requires looking at the background columns behind the histogram. The magnitude of stimulation voltage ($|V_s|$) is represented by the color of each column (see right color bar to the right of each plot). The synapse weight of each column is indicated by the hatching of each column (see legend to the far right of each histogram). The number of neurons in each square is indicated by the gray-scale colorbar just to the right of the histogram. Each column consists of the results from simulating 71280 neurons under 18 electrode combinations (described in Section 5.3).

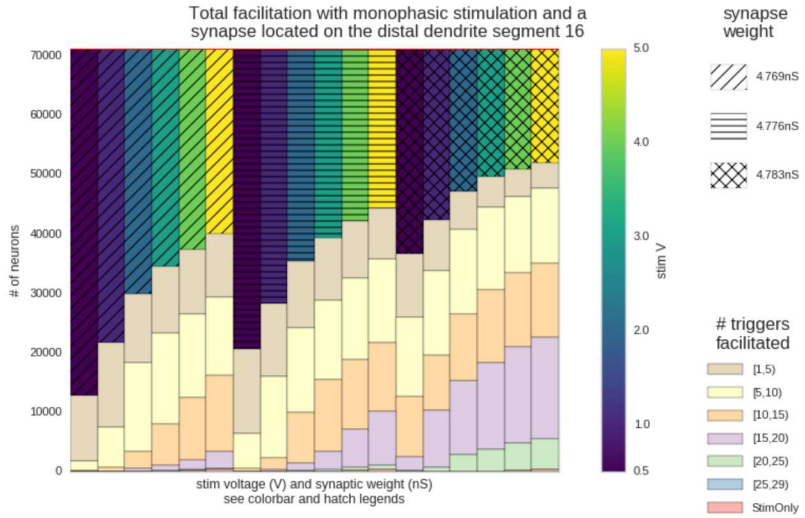


(a) monophasic

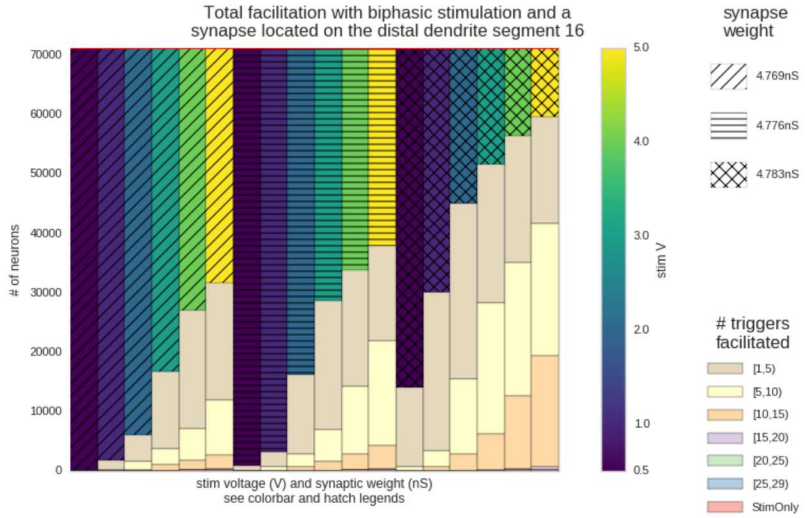


(b) biphasic

Figure 5.15: Stacked bar charts showing the number of active neurons (from facilitation or stimulation-only) where each column corresponds to a different pair of stimulation voltage ($|V_s|$) and synapse weight. These charts are for neurons with synapses in the middle (segment 8) of the distal dendrite and (a) monophasic and (b) biphasic stimulation. Each column consists of the results from simulating 71280 neurons under 18 electrode combinations (described in Section 5.3). Understanding the x-axis of each 2d histogram requires looking at the background columns behind the histogram. The magnitude of stimulation voltage ($|V_s|$) is represented by the color of each column (see virdis (yellow-green-blue color map) color bar to the right of each plot). The synapse weight of each column is indicated by the hatching of each column (see legend to the far right of each histogram). The color of each bar in the stacks (see legend to the right of the colorbar) indicates the number of synapse trigger times which result in facilitation (or stimOnly if the stimulation by itself causes activation). The maximum of the y-axis is the total number of simulated neurons (71280) indicated by a red horizontal line.

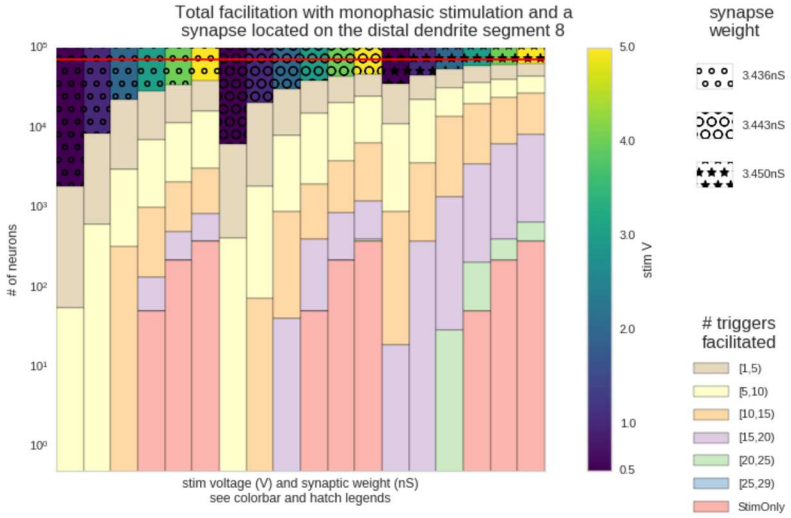


(a) monophasic

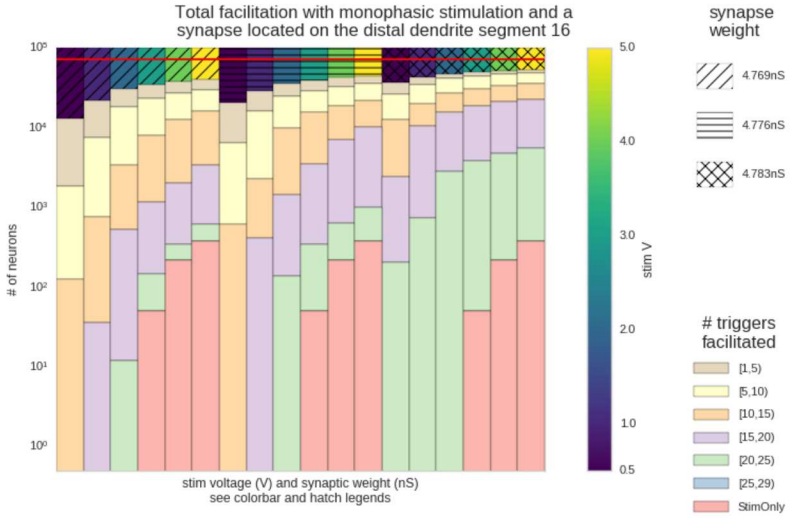


(b) biphasic

Figure 5.16: Stacked bar charts showing the number of active neurons (from facilitation or stimulation-only) where each column corresponds to a different pair of stimulation voltage ($|V_s|$) and synapse weight. These charts are for neurons with synapses at the distal tip (segment 16) of the distal dendrite and (a) monophasic and (b) biphasic stimulation. Each column consists of the results from simulating 71280 neurons under 18 electrode combinations (described in Section 5.3). Understanding the x-axis of each 2d histogram requires looking at the background columns behind the histogram. The magnitude of stimulation voltage ($|V_s|$) is represented by the color of each column (see virdis (yellow-green-blue color map) color bar to the right of each plot). The synapse weight of each column is indicated by the hatching of each column (see legend to the far right of each histogram). The color of each bar in the stacks (see legend to the right of the colorbar) indicates the number of synapse trigger times which result in facilitation (or stimOnly if the stimulation by itself causes activation). The maximum of the y-axis is the total number of simulated neurons (71280) indicated by a red horizontal line.

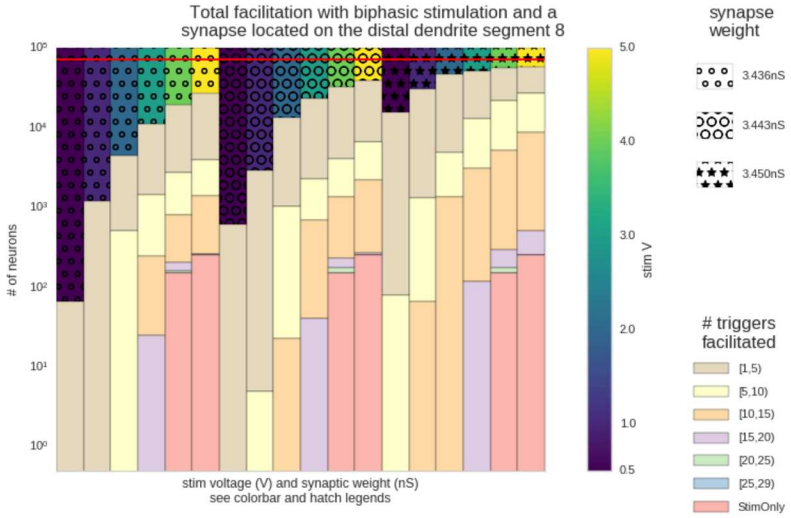


(a) Largest 3 synapse weights with synapse at the middle of the distal dendrite with monophasic stimulation

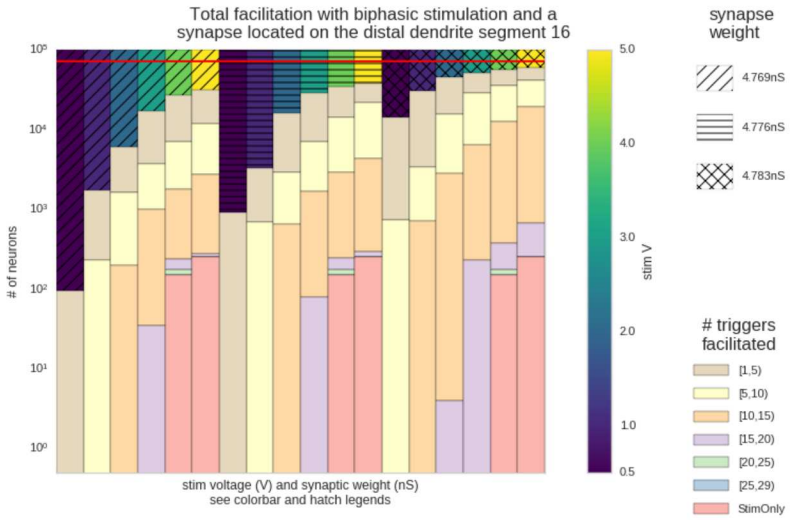


(b) synapse at the distal tip of the distal dendrite with monophasic stimulation

Figure 5.17: These two figures show (a) the largest 3 synapse weights from Fig. 5.15a and (b) Fig. 5.16a. See those figures for detailed description. The y-axis is a $\log_{10}$ scale with the total number of simulated neurons (71280) indicated by a red horizontal line. A greater number of neurons with synapses triggered on the distal tips of the distal dendrites have facilitation windows larger than 2 trigger time samples compared with synapses in the middle of the dendrite for synapse weights that are subthreshold by the same amount.



(a) Largest 3 synapse weights with synapse at the middle of the distal dendrite with biphasic stimulation



(b) synapse at the distal tip of the distal dendrite with biphasic stimulation

Figure 5.18: These two figures show (a) the largest 3 synapse weights from Fig. 5.15b and (b) Fig. 5.16b. See those figures for detailed description. The y-axis is a $\log_{10}$ scale with the total number of simulated neurons (71280) indicated by a red horizontal line. A greater number of neurons with synapses triggered on the distal tips of the distal dendrites have facilitation windows larger than 2 trigger time samples compared with synapses in the middle of the dendrite for synapse weights that are subthreshold by the same amount.

5.4 Predicting neuron facilitation

Section 4.6 showed that $V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}}$ could be useful to estimate if a neuron would be activated by a particular combination of electric fields. Ideally, a similar feature or set of features could be found to estimate neuron facilitation. Additionally, features that are useful for separating facilitated neurons from non-facilitated neurons may indicate which aspects of the neuron's response to stimulation are important.

A dataset including the results from the facilitation simulations, stimulation-only simulations, and static simulations was collected for the 22 facilitation situations (stimulation type, synapse position on the dendrite (middle (iSeg=8) or distal tip (iSeg=16)), and synapse weight). Each of these datasets includes simulations from all 18 bipolar combinations with 6 stimulation voltage levels (0.5V, 1V, 2V, 3V, 4V, 5V). Each data point includes the number of facilitated synapse trigger time samples which, if multiplied by 5 ms (the sampling interval between trigger times), gives an estimate of the width of the facilitation window for that neuron.

In this section, the data is plotted with the number of facilitated synapse trigger time samples vs various features (for illustrative purposes). I have chosen to try to separate the data into three categories referred to by the variable T:

- $T = 0$ or negative – neurons that are not activated by the stimulation, with or without an EPSP,
- $T = 1$ or positive – neurons that are facilitated at 1 or more synapse trigger times or activated with just stimulation, and
- $T = Unknown$ or mixed – neurons cannot be separated or distinguished from others of the opposite category using the current features.

The few neurons that are activated without an EPSP are included in category ($T = 1$) to simplify the analysis.

Attempts to use machine-learning techniques (e.g. random forests) to determine the best features to use and decision boundaries resulted in complicated decision boundaries. These complicated decision boundaries resulted in high true positive rates and low false positive rates using cross-validation. However, the decision boundaries appeared to overfit the data in uncertain regions of the feature space. So a simpler approach (inspired by Fig. 4.22b) was tried with a maximum of 4 decision boundaries.

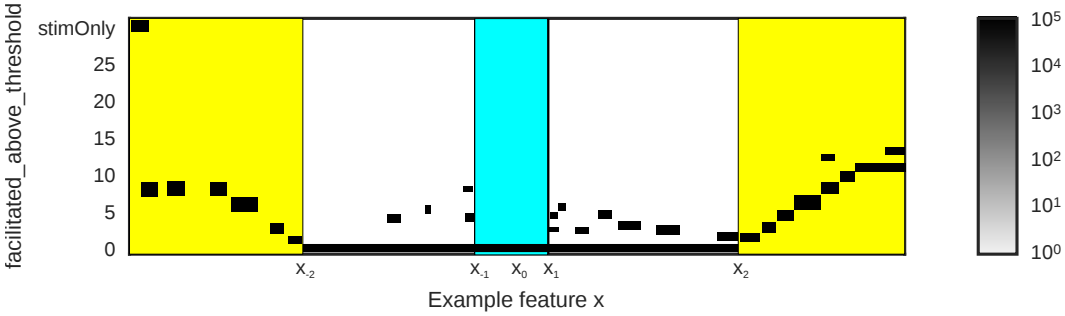


Figure 5.19: Example histogram plot showing the regions of example feature x that can be used for prediction of facilitation. The y-axis is the number of trigger points facilitated above threshold (−10 mV). Each trigger corresponds with about 5 ms of time during which a triggered synapse would cause facilitation. For each feature, active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below for feature value f_0, where T=1 and T=0 indicates that the neuron is active and non-active respectively.
IF ($f_0 < x_{-2}$) THEN (T=1)
ELIF ($x_{-1} < f_0 < x_1$) THEN (T=0)
ELIF ($x_2 < f_0$) THEN (T=1)
ELSE (T=Unknown)

Consider an arbitrary feature x with value x_0 without stimulation voltage. Since all the neurons have no facilitation without stimulation, there might be a region in feature space around x_0 which contains no facilitated neurons. The decision boundaries for this region (if it exists) are referred to as x_{-1} and x_1 where

$$x_{-1} \leq x_0 \leq x_1 \tag{5.1}$$

and all of the neuron simulations with feature values of x such that $x_{-1} \leq x \leq x_1$ have no facilitation. The last two decision boundaries (if they exist) are referred to as x_{-2} and x_2 where $x_{-2} \leq x_{-1} \leq x_0 \leq x_1 \leq x_2$ and all of the neuron simulations with feature values of x such that $x \leq x_{-2}$ or $x_2 \leq x$ have non-zero size facilitation window(s). Figure 5.19 shows a cartoon example of these facilitation decision boundaries for arbitrary feature x. Custom analysis software was written to find the values x_{-2}, x_{-1}, x_1, and x_2 given a feature dataset and the value of x_0 (the value of the feature without stimulation). For many features, one or more of these decision boundaries do not exist, but the remaining decision boundaries (if any) can be used for classification. A greedy cascading search algorithm was written to find which sequence of features is able to separate the largest number of positive ($T = 1$) neurons and negative ($T = 0$) neurons from the rest. This algorithm evaluates how many neurons each single feature is able to classify as positive and negative, picks the best one (sorted by most identified as positive and then most identified as negative if there are ties) and any neuron samples that are still mixed cascade into the next greedy search over the remaining features until the algorithm has reached the feature limit (a sequence of 4 features). In the next section I will define these features and explain how they are chosen.

The results from these searches are summarized in tables and figures in Sections 5.4.1 and 5.4.2. Each figure shows unclassified data in grey scale, and data classified by earlier stages of the cascade in shades of red (facilitated/activated) and blue (no-activation).

5.4.1 Separating facilitated and non-activated neurons using static features

Predicting facilitation from static (rather than time-domain) volume conductor simulations would imply that time-domain volume conductor simulations are unnecessary (once a predictor is built). In Section 4.6, I showed that the 2nd derivative

of static voltage along the axon and static voltage at the axon tip are not useful for separating active neurons from inactive neurons. Similarly, applying a cascade of 4 static voltage features (V^{L}_{static} for locations L, etc) at individual points[e] or a cascade of 4 second derivative features at individual points[f] did not perform well compared to features based on the static voltage differences between individual points and the soma.

The following features were evaluated by the greedy search algorithm:

- $V^{\text{AxonTip}}_{static} - V^{\text{Soma}}_{static}$,
- $V^{\text{AxonMiddle}}_{static} - V^{\text{Soma}}_{static}$,
- $V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$,
- $V^{\text{AH}}_{static} - V^{\text{Soma}}_{static}$,
- $\min_{\forall \text{dendrites}}(V^{\text{DistalDendriteTip}}_{static}) - V^{\text{Soma}}_{static}$,
- $\max_{\forall \text{dendrites}}(V^{\text{DistalDendriteTip}}_{static}) - V^{\text{Soma}}_{static}$,
- $\text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteTip}}_{static}) - V^{\text{Soma}}_{static}$,
- $\min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$,
- $\max_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$,
- $\text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and
- $V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$,

where V^{L}_{static} is the static voltage at location L, $\min_{\forall \text{dendrites}}(V^{\text{L}}_{static})$ is the minimum static voltage at location L across all of the dendrites for that particular neuron and stimulation parameters, $\max_{\forall \text{dendrites}}(V^{\text{L}}_{static})$ is the maximum static voltage at location L across all of the dendrites for that particular neuron and stimulation parameters, and $\text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static})$ is the average static voltage at location L across all of the dendrites for that particular neuron and stimulation parameters.

[e] only able to classify 0.3% to 16% of facilitated neurons over all 22 datasets

[f] only able to classify 0.2% to 20.8% of facilitated neurons over all 22 datasets

The greedy search algorithm was run using the above features for each type of stimulation (biphasic, monophasic), synapse location (distal tip or middle of distal dendrite), and synapse weight. After all those feature sequences were found, they were evaluated on all the datasets and the feature sequence that did best across all datasets was chosen. The best features overall were:

- $f_0 = V_{static}^{\text{Synapse}} - V_{static}^{\text{Soma}}$,
- $f_1 = V_{static}^{\text{IS}} - V_{static}^{\text{Soma}}$,
- $f_2 = \min_{\forall \text{dendrites}}(V_{static}^{\text{DistalDendriteMiddle}}) - V_{static}^{\text{Soma}}$,
- and $f_3 = \text{avg}_{\forall \text{dendrites}}(V_{static}^{\text{DistalDendriteMiddle}}) - V_{static}^{\text{Soma}}$.

With no stimulation voltage, the value of all of these features is 0 mV.

The results of using these features to separate simulations are shown in supplementary figures in Section 5.C. A summary of the results is available in Table 5.2.

These features are interesting:

- Feature $f_0 = V_{static}^{\text{Synapse}} - V_{static}^{\text{Soma}}$ represents the extracellular voltage difference caused by the stimulation between the synapse location and the soma.
- Feature $f_1 = V_{static}^{\text{IS}} - V_{static}^{\text{Soma}}$ is very similar to the feature $(V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}})$ which was used in Fig. 4.22b to predict activation without EPSPs.

In simulations, the initial segment (IS) and the axon hillock (AH) usually have almost the same membrane voltage and the action potential appears to start at both locations almost simultaneously. So, this feature may indicate the amount by which the axon is directly stimulated. The last 2 features likely represent how much other parts of the dendrites are stimulated. The first two features account for most of the

separation of facilitated neurons from the mix of other neurons. In most cases, these features have a low ability to separate non-active neurons from some of the facilitated neurons. This may be because there is a very small difference in feature space between no-activation and a single synapse trigger time that causes facilitation.

Table 5.2: Summary of classification of facilitation for each dataset (labeled by columns stimulation, iSeg, and synapse weight) using features based on the static voltage difference between individual points and the soma at each stage of the cascade. Each stage uses a different feature (f_0, f_1, f_2, and f_3 defined below the table) and has the percent of facilitated neurons identified (id+%) and the percent of non-facilitated neurons identified (id-%) listed. Columns p and n indicate the total number of facilitated and non-facilitated neurons respectively. The Figure column indicates the figure that dataset is plotted in (in the pdf you can click on the figure number to view it).

					Stage f_0		Stage f_1		Stage f_2		Stage f_3		
stimulation	iSeg	synapse weight	p	n	id+%	id-%	id+%	id-%	id+%	id-%	id+%	id-%	Figure
biphasic	8	3.0nS	937	426743	0	4.2	67.24	99.86	67.24	99.86	80.58	99.92	5.47
biphasic	8	3.225nS	2047	425633	4.89	1.26	81.63	22.28	81.63	43.11	88.62	43.57	5.48
biphasic	8	3.337nS	4648	423032	22.16	1.14	84.55	18.4	85.8	35.81	87.74	36.04	5.49
biphasic	8	3.394nS	10070	417610	36.54	1.01	83.82	11.33	87.72	11.42	88.59	11.59	5.50
biphasic	8	3.422nS	24932	402748	51.34	0.47	82.06	4.58	85.24	4.62	85.46	4.73	5.51
biphasic	8	3.436nS	62871	364809	61.96	0.01	84.36	0.79	86.48	0.97	86.65	1.76	5.52
biphasic	8	3.443nS	111204	316476	64.44	0.01	83.94	0.02	85.33	0.05	85.33	0.29	5.53
biphasic	8	3.45nS	257872	169808	79.73	0.01	89.83	0.02	91.05	0.15	91.05	0.15	5.54
biphasic	16	4.769nS	83386	344294	20.66	0.01	75.32	0.03	77.06	0.17	77.34	0.51	5.55
biphasic	16	4.776nS	121016	306664	29.98	0.01	77.98	0.02	79.5	0.1	79.7	0.43	5.56
biphasic	16	4.783nS	257325	170355	40.92	0.01	75.42	0.01	76.67	0.01	76.67	0.03	5.57
monophasic	8	3.0nS	3207	424473	0	0.75	42.25	13.54	42.25	13.78	48.8	13.87	5.58
monophasic	8	3.225nS	7167	420513	28.95	0.66	66.29	1.24	69.02	2.17	73.06	3.77	5.59
monophasic	8	3.337nS	16891	410789	29.93	0.16	67.72	0.52	70.56	0.65	71.36	0.72	5.60
monophasic	8	3.394nS	46967	380713	25.64	0.02	66.05	0.21	68.11	0.26	69.05	0.31	5.61
monophasic	8	3.422nS	88331	339349	33.22	0.01	75.86	0.12	76.9	0.22	77.52	0.24	5.62
monophasic	8	3.436nS	134610	293070	36.38	0.01	74.21	0.08	74.95	0.16	75.8	0.19	5.63
monophasic	8	3.443nS	185932	241748	37.67	0	72.81	0.03	73.4	0.04	73.98	0.06	5.64
monophasic	8	3.45nS	319871	107809	48.17	0	70.56	0	70.87	6.66	70.89	6.66	5.65
monophasic	16	4.769nS	176737	250943	37.15	0	60.03	0.02	60.03	0.02	67.5	0.02	5.66
monophasic	16	4.776nS	210546	217134	40.81	0	60.64	0	60.64	0	70.48	0	5.67
monophasic	16	4.783nS	279199	148481	50.64	0	69.39	0.19	69.39	0.19	72.29	0.21	5.68

$f_0 = V_{static}^{\text{Synapse}} - V_{static}^{\text{Soma}}$
$f_1 = V_{static}^{\text{IS}} - V_{static}^{\text{Soma}}$
$f_2 = \min_{\forall \text{dendrites}}(V_{static}^{\text{DistalDendriteMiddle}}) - V_{static}^{\text{Soma}}$
$f_3 = \text{avg}_{\forall \text{dendrites}}(V_{static}^{\text{DistalDendriteMiddle}}) - V_{static}^{\text{Soma}}$

5.4.2 Separating facilitated and non-activated neurons using stimulation-only membrane voltages

When an electrical stimulation pulse interacts with a neuron, the membrane voltage of the cell deviates from resting potential by different amounts at different locations of the neuron. Predicting whether a neuron would be facilitated based on the membrane voltage changes caused by the stimulation pulse without any EPSP input would reduce the number of NEURON simulations necessary. By using the minimum and the maximum of the membrane voltage at several locations on the neurons as features to separate facilitated neurons from non-activated neurons, I

hope to identify at which locations the membrane voltage changes are most important for facilitation.

The following features were evaluated by the greedy search algorithm:

- $\max_t (V_m^{\text{AxonTip}}(t))$,
- $\max_t (V_m^{\text{AxonMiddle}}(t))$,
- $\max_t (V_m^{\text{IS}}(t))$,
- $\max_t (V_m^{\text{AH}}(t))$,
- $\max_t (V_m^{\text{Soma}}(t))$,
- $\min_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\max_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\text{avg}_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\min_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteMiddle}}(t))$,
- $\max_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteMiddle}}(t))$,
- $\text{avg}_{\forall \text{dendrites}} \max_t (V_m^{\text{DistalDendriteMiddle}}(t))$,
- $\max_t (V_m^{\text{Synapse}}(t))$,
- $\min_t (V_m^{\text{AxonTip}}(t))$,
- $\min_t (V_m^{\text{AxonMiddle}}(t))$,
- $\min_t (V_m^{\text{IS}}(t))$,
- $\min_t (V_m^{\text{AH}}(t))$,
- $\min_t (V_m^{\text{Soma}}(t))$,
- $\min_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\max_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\text{avg}_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteTip}}(t))$,
- $\min_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteMiddle}}(t))$,
- $\max_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteMiddle}}(t))$,
- $\text{avg}_{\forall \text{dendrites}} \min_t (V_m^{\text{DistalDendriteMiddle}}(t))$, and

- $\min_t(V_m^{\text{Synapse}}(t))$,

where $V_m^{\text{L}}(t)$ is the time series of membrane voltage at location L, $\min_t(V_m^{\text{L}}(t))$ is the minimum over time of the membrane voltage at location L, $\max_t(V_m^{\text{L}}(t))$ is the maximum over time of the membrane voltage at location L, and the other functions were defined in Section 5.4.1.

The greedy search algorithm was applied to the above features for each type of stimulation (biphasic, monophasic), synapse location (distal tip or middle of distal dendrite), and synapse weight. After all of those feature sequences were found, they were evaluated on all the datasets, and the feature sequence that had the best minimum performance across all datasets was chosen. The best features overall were:

- $f_0 = \max_t(V_m^{\text{AH}}(t))$,
- $f_1 = \max_t(V_m^{\text{Synapse}}(t))$,
- $f_2 = \min_t(V_m^{\text{Synapse}}(t))$, and
- $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$.

With no stimulation voltage, the value of these features is just the resting membrane voltages found in Fig. 3.5.

The results of using these features to separate simulations are shown in supplementary figures in Section 5.D. A summary of the results is available in Table 5.3.

As discussed briefly in Section 5.4.1, there is minimal membrane voltage difference between the axon hillock (AH) and the initial segment (IS). So, the first feature ($f_0 = \max_t(V_m^{\text{AH}}(t))$) is almost identical to $\max_t(V_m^{\text{IS}}(t))$, which would correspond with feature $V_{static}^{\text{IS}} - V_{static}^{\text{Soma}}$ from Section 5.4.1. The next two features

($f_1 = \max_t(V_m^{\text{Synapse}}(t))$ and $f_2 = \min_t(V_m^{\text{Synapse}}(t))$) deal with the membrane voltage at the synapse location and would correspond with feature $V_{static}^{\text{Synapse}} - V_{static}^{\text{Soma}}$ from Section 5.4.1. The last feature in the cascade is the maximum membrane voltage in the middle of any dendrite, which seems to measure how much the dendrites in general are stimulated. Compared to the static voltage difference features used in Section 5.4.1, the membrane voltage features tested here seem less able to separate facilitated (and active) neurons from the non-active neurons. These membrane voltage features are better at separating non-active neurons from the rest. The reduced performance on separating facilitated and active neurons from non-active neurons remains even if the cascade is allowed to use 8 features. This seems to indicate that the minimum and maximum of the membrane voltage are not the best choice of features. This may be because of sharp transients in the membrane voltage caused by the stimulation pulse.

Table 5.3: Summary of classification of facilitation for each dataset (labeled by columns stimulation, iSeg, and synapse weight) using membrane voltage features at each stage of the cascade. Each stage uses a different feature (f_0, f_1, f_2, and f_3 defined below the table) and has the percent of facilitated neurons identified (id+%) and the percent of non-facilitated neurons identified (id-%) listed. Columns p and n indicate the total number of facilitated and non-facilitated neurons respectively. The Figure column indicates the figure that dataset is plotted in (in the pdf you can click on the figure number to view it).

					Stage f_0		Stage f_1		Stage f_2		Stage f_3		
stimulation	iSeg	synapse weight	p	n	id+%	id-%	id+%	id-%	id+%	id-%	id+%	id-%	Figure
biphasic	8	3.0nS	937	426743	66.7	99.65	66.7	99.67	66.7	99.67	66.7	99.67	5.69
biphasic	8	3.225nS	2047	425633	76.94	35.88	78.85	36.25	78.85	60.57	78.85	77.17	5.70
biphasic	8	3.337nS	4648	423032	69.6	10.6	81.15	52.38	81.63	71.33	82.98	77.25	5.71
biphasic	8	3.394nS	10070	417610	60.58	4.11	77.41	20.46	81.01	45.8	83.58	61.48	5.72
biphasic	8	3.422nS	24932	402748	42.88	1.43	66.31	22.77	74.41	44.33	76.97	52.13	5.73
biphasic	8	3.436nS	62871	364809	34.4	0.56	64.08	7.2	72.63	16.57	74.09	33.1	5.74
biphasic	8	3.443nS	111204	316476	36.01	0.2	58.95	6.72	70.69	14.09	71.87	26.01	5.75
biphasic	8	3.45nS	257872	169808	43.96	0	58.29	0.19	70.98	4.38	72	13.72	5.76
biphasic	16	4.769nS	83386	344294	60.09	0.59	62.52	0.59	62.56	2.61	63.99	31.45	5.77
biphasic	16	4.776nS	121016	306664	58.65	0.39	61.21	0.4	61.25	1.97	62.74	24.01	5.78
biphasic	16	4.783nS	257325	170355	58.58	0	61.35	0.07	61.43	0.85	62.67	12.07	5.79
monophasic	8	3.0nS	3207	424473	48.8	63.9	48.8	70.95	48.8	92.18	48.8	92.29	5.80
monophasic	8	3.225nS	7167	420513	35.3	42.66	35.82	42.66	62.83	77.44	70.18	78.26	5.81
monophasic	8	3.337nS	16891	410789	32.68	29.38	34.73	29.38	59.22	67.59	64.44	68.49	5.82
monophasic	8	3.394nS	46967	380713	31.93	20.96	34.57	20.96	49.24	61.5	52	62.4	5.83
monophasic	8	3.422nS	88331	339349	37.77	12.27	40.71	12.27	58.21	36.26	59.78	37.31	5.84
monophasic	8	3.436nS	134610	293070	42.74	7.23	47.38	7.23	63.85	25.01	64.89	25.67	5.85
monophasic	8	3.443nS	185932	241748	40.65	3	48.18	3.31	63.92	18.11	64.63	18.49	5.86
monophasic	8	3.45nS	319871	107809	38.11	1.04	50.89	1.73	63.21	9	63.56	13.15	5.87
monophasic	16	4.769nS	176737	250943	20.99	0.99	51.29	0.99	51.29	5.95	51.29	6.18	5.88
monophasic	16	4.776nS	210546	217134	17.62	0.67	47.14	0.67	47.14	4.34	47.14	4.64	5.89
monophasic	16	4.783nS	279199	148481	13.29	0.43	47.92	0.43	47.92	1.44	47.92	1.97	5.90

$f_0 = \max_t(V_m^{\text{AH}}(t))$
$f_1 = \max_t(V_{gt}^{\text{Synapse}}(t))$
$f_2 = \min_t(V_m^{\text{Synapse}}(t))$
$f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$

5.5 Discussion

Simulations of a sub-threshold synaptic input combined with a sub-threshold stimulation pulse showed that time windows where synaptic input would be facilitated existed both before and after a stimulation pulse for a significant number of neurons if the synapse weight and/or the stimulation pulse magnitude is large enough. The location and orientation of both the neuron and the synaptic input also has an effect. As either the stimulation magnitude or the synapse weight is decreased, the size of the facilitation windows (time range that a synapse triggered relative to a fixed stimulation pulse causes neuron activation) is reduced and the number of facilitated neurons is also reduced. For larger synapse weights ([3.45, 3.443, 3.436]nS associated with synapses in the middle of the distal dendrite and [4.783, 4.776, 4.769]nS for synapses located on the distal tip of a dendrite), facilitation is possible for both monophasic and biphasic stimulation pulses of magnitude 0.5 V. With stimulation magnitudes of 5 V or less, monophasic stimulation clearly causes more facilitation compared to biphasic stimulation, with the exception of synapses on the distal tips of dendrites and the largest synapse weight (4.783 nS). However, monophasic stimulation also causes more neuron activation without synaptic input, as seen in Chapter 4, which might be counterproductive for purely facilitating existing circuits.

Based on the examples in Section 5.2, it appears that it takes less magnitude of biphasic stimulation to facilitate a synaptic input if the stimulation pulse occurs within a time window of about 20 ms after the synapse is triggered. For monophasic stimulation, some stimulation combinations and neuron locations show the same behavior as described for biphasic stimulation, but reversing the polarity on those examples caused the facilitation window to be after the stimulation pulse rather than before. For some of the neurons and synapse locations, less magnitude of monophasic stimulation was needed to cause facilitation if the stimulation pulse

occurred at the same time as the synaptic input. These cases also showed a large facilitation window of possibly greater than 75 ms for synaptic input after the stimulation pulse. The exact size of the actual facilitation window in some of these cases is unknown because I underestimated the maximum size of the facilitation window.

The timing of the synaptic input and a biphasic stimulation pulse that results in "least effort" facilitation (lowest magnitude stimulation, and lowest synapse weight) results in the stimulation pulse occurring when m_{IKdrSM} is at a maximum near the synapse and h_{INaSM} is at a minimum. For monophasic stimulation, the "least effort" facilitation timing for the examples shown is either that the synaptic input and the stimulation pulse occur at the same time, or the stimulation pulse occurs after the synaptic input when V_m is at a maximum at the synapse location, m_{IKdrSM} is approaching maximum, m_{IKaSM} is close to maximum, m_{INaSM} is near maximum, and h_{INaSM} is approaching minimum. A more comprehensive study of the facilitation windows and "least effort" facilitation timing could be considered for future work. In particular, the interaction of the ion channel dynamics, synapse dynamics, and stimulation pulses should be examined further.

A method of predicting the probability of facilitation for a given neuron without computing large numbers of time-domain volume conductor simulations and/or NEURON simulations would allow consideration of more complicated electrode patterns and stimulation types. While I have not built a detailed predictor in this thesis, I have found that the features ($V_{static}^{\mathrm{Synapse}} - V_{static}^{\mathrm{Soma}}$, $V_{static}^{\mathrm{IS}} - V_{static}^{\mathrm{Soma}}$) based on the static volume conductor simulations were able to separate many of the facilitated (and activated by stimulation-only) neurons from non-activated neurons. Features based on the minima and maxima of the membrane voltage at various points were also able to separate many of the facilitated neurons from the rest; however, they were not able to separate as many of the neurons as the features based on the difference of static voltage between locations on the neuron and the soma. Features

based on the second derivative of the static voltage were not useful for separating facilitated neurons from non-facilitated neurons.

Additional facilitation simulations using the neurons listed in Tables 4.2 and 4.3 were carried out using passive dendrites instead of active dendrites. When the synapse weights from Table 5.1 were used with the passive dendrite model, I found a significant reduction in the amount of facilitation. This supports the hypothesis that ion channels in the dendrites are important to the facilitation of synaptic input using electrical stimulation.

The next chapter will summarize the main contributions of thesis and discuss possible future work.

5.A Appendix: Position of facilitated neurons

This appendix contains tables of figures showing the width of the facilitation windows (in 5 ms size intervals) for biphasic and monophasic stimulation using electrode combination A3pC5n with synaptic input in the middle (segment 8) of the distal section of each dendrite.

When plotting the activation thresholds in Section 4.A, there was only one number (the activation threshold) for each axon orientation. To plot the width of the facilitation windows for each pair of stimulation voltage and synapse weight, there are 5 dendrites that the synapse could be located on for each axon orientation. The following scheme was used to plot the additional information:

- If the neuron with an axon in that orientation would be activated by stimulation at that voltage without synaptic input, plot the axon as a red line.
- If synaptic input of any of the dendrites (at segment 8) has non-zero facilitation windows then plot the axon as a gray line.
- For each of the synapse locations that have a non-zero facilitation window, plot a cone (colored according to the width of the facilitation window) with a base at the distal tip of the axon and the tip of the cone pointing in the same Euclidean direction as the dendrite the synapse is on.

This scheme allows one to quickly see the amount of facilitation in each location. Figure 5.20 shows an example with biphasic stimulation with combination A3pC5n, a stimulation magnitude of V_s=2 V, and a synapse weight of 3.436 nS.

Tables 5.4 to 5.7 show tiny figures similar to Fig. 5.20 for each pairing of stimulation voltage and synapse weight. All figures in this section have positive electrode voltage indicated by a blue label and negative electrode voltage with a red label.

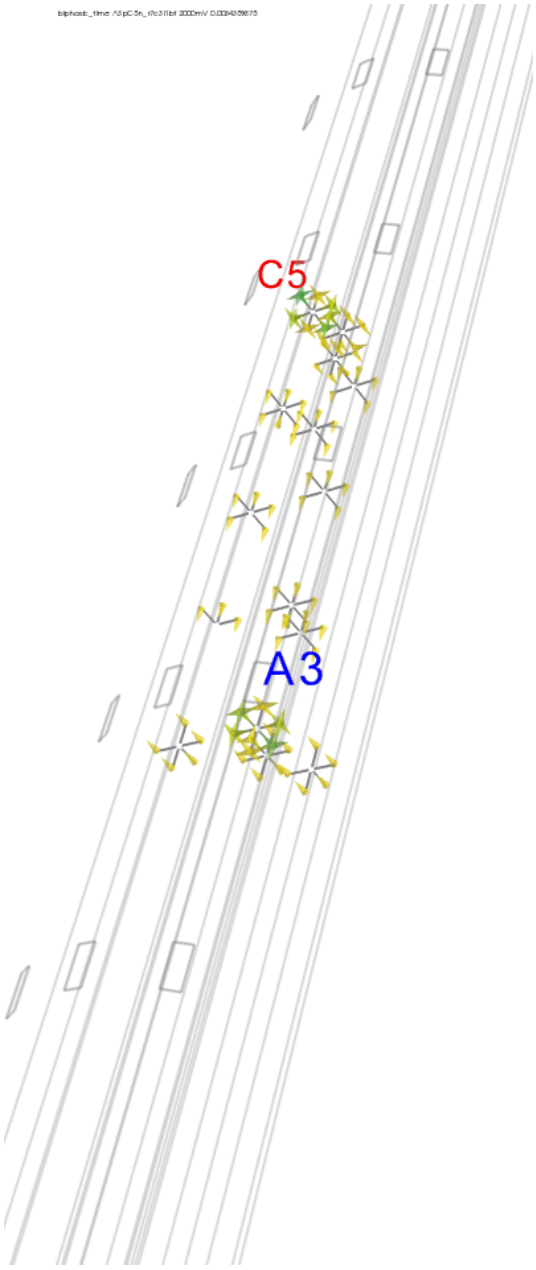


Figure 5.20: Stimulation type: Biphasic, combination: A3pC5n, stimulation magnitude: V_s =2 V. Synapses are on segment 8 of each dendrite with a synapse weight of 3.436 nS. See Section 5.A for more description. Colormap indicating facilitation width can be found in Table 5.4. Darker colors indicate wider facilitation windows.

Table 5.4: Stimulation type: Biphasic, combination: A3pC5n.

Table 5.5: Stimulation type: Biphasic, combination: -A3pC5n.

Table 5.6: Stimulation type: Monophasic, combination: A3pC5n.

Table 5.7: Stimulation type: Monophasic, combination: -A3pC5n.

5.B Appendix: More examples of facilitation

This appendix contains supplementary examples of facilitation similar to those in Section 5.2. Sections 5.B.1 to 5.B.3 contain detailed descriptions of facilitation with biphasic stimulation and Sections 5.B.4 and 5.B.5 for monophasic stimulation. These examples serve to show some of the ways that facilitation can occur. Some interesting findings from these sections are summarized in Section 5.5.

5.B.1 Biphasic stimulation with $V_s > 0$ and a distal tip synapse

For biphasic stimulation using A4pA5n with $V_s > 0$ of neuron GM1_L_r5_Yn with a synapse located at segment 16 on the distal dendrite pointing in the $\hat{x}$ direction, the maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.21. Without any synaptic activity, the neuron will activate if $V_s = 8\,\text{V}$. As with $V_s < 0$ (described in Section 5.2.1), the duration of the facilitation window is larger for synaptic input occurring before the stimulation pulse. But facilitation also happens for synaptic input occurring after the stimulation pulse. As $|V_s|$ and synapse weight decrease, the facilitation window is only before the stimulation pulse. Even though the baseline stimulation-only membrane voltage at the axon tip is less than with $V_s < 0$ (for the same $|V_s|$), there is a similar amount of facilitation. For $V_s = 0.5\,\text{V}$, all of the facilitation occurs before the stimulation pulse and there is some facilitation with all three tested synapse weights. Figure 5.22 shows the membrane voltage at the axon tip and the synapse location for $V_s = 2\,\text{V}$ and synapse weight $4.783\,\text{nS}$ for all the synapse trigger times shown in Fig. 5.21. The neuron is active in plot regions which are orange-red, while the synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse as a dotted black line. The time at which the neuron becomes active generally increases with increasing synaptic trigger time (after an initial decrease).

The response of the neuron (membrane voltage and ion-channel state variables) to just the synaptic input (with synapse weight of 4.783 nS) alone can be found in Fig. 3.13. The response of the neuron to $V_s = 2\,\mathrm{V}$ stimulation alone can be found in Fig. 5.23. Figure 5.24 shows the facilitated response to a synapse triggered before the stimulation pulse. Figure 5.26 shows the facilitated response to a synapse triggered after the stimulation pulse.

As in Section 5.2.1, Figs. 5.24 and 5.26 show many similarities if the synapse trigger times are lined up. The stimulation pulse causes what appear to be minor deviations in the state of the neuron compared to the EPSP by itself, but these deviations are enough to cause activation when combined with the presence of an EPSP.

For the case of $V_s = 2\,\mathrm{V}$ and synapse weight 4.783 nS, a synapse trigger time of $t = 66\,\mathrm{ms}$ (same as with $V_s = -2\,\mathrm{V}$) maximizes the membrane voltage at the axon tip (compared to other synapse trigger times). Figure 5.25 shows the neuron response to these parameters. Note that this synapse trigger time causes the stimulation pulse to occur when m_{IKdrSM} is at a maximum near the synapse and h_{INaSM} is at a minimum. This was also seen in Section 5.2.1.

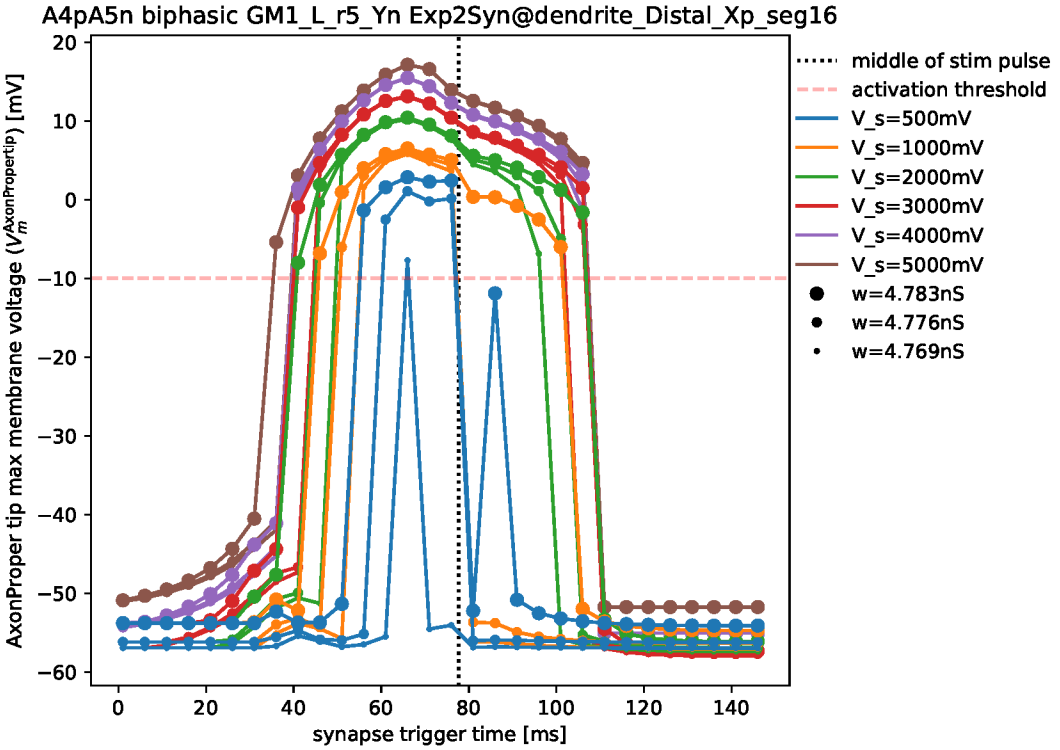


Figure 5.21: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to biphasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above -10 mV) : (5.0V, 4.783nS, 9, 6), (5.0V, 4.776nS, 8, 6), (5.0V, 4.769nS, 8, 6), (4.0V, 4.783nS, 8, 6), (4.0V, 4.776nS, 8, 6), (4.0V, 4.769nS, 8, 6), (3.0V, 4.783nS, 8, 6), (3.0V, 4.776nS, 7, 6), (3.0V, 4.769nS, 7, 5), (2.0V, 4.783nS, 8, 6), (2.0V, 4.776nS, 7, 5), (2.0V, 4.769nS, 6, 4), (1.0V, 4.783nS, 7, 5), (1.0V, 4.776nS, 6, 0), (1.0V, 4.769nS, 5, 0), (0.5V, 4.783nS, 5, 0), (0.5V, 4.776nS, 4, 0), and (0.5V, 4.769nS, 1, 0).

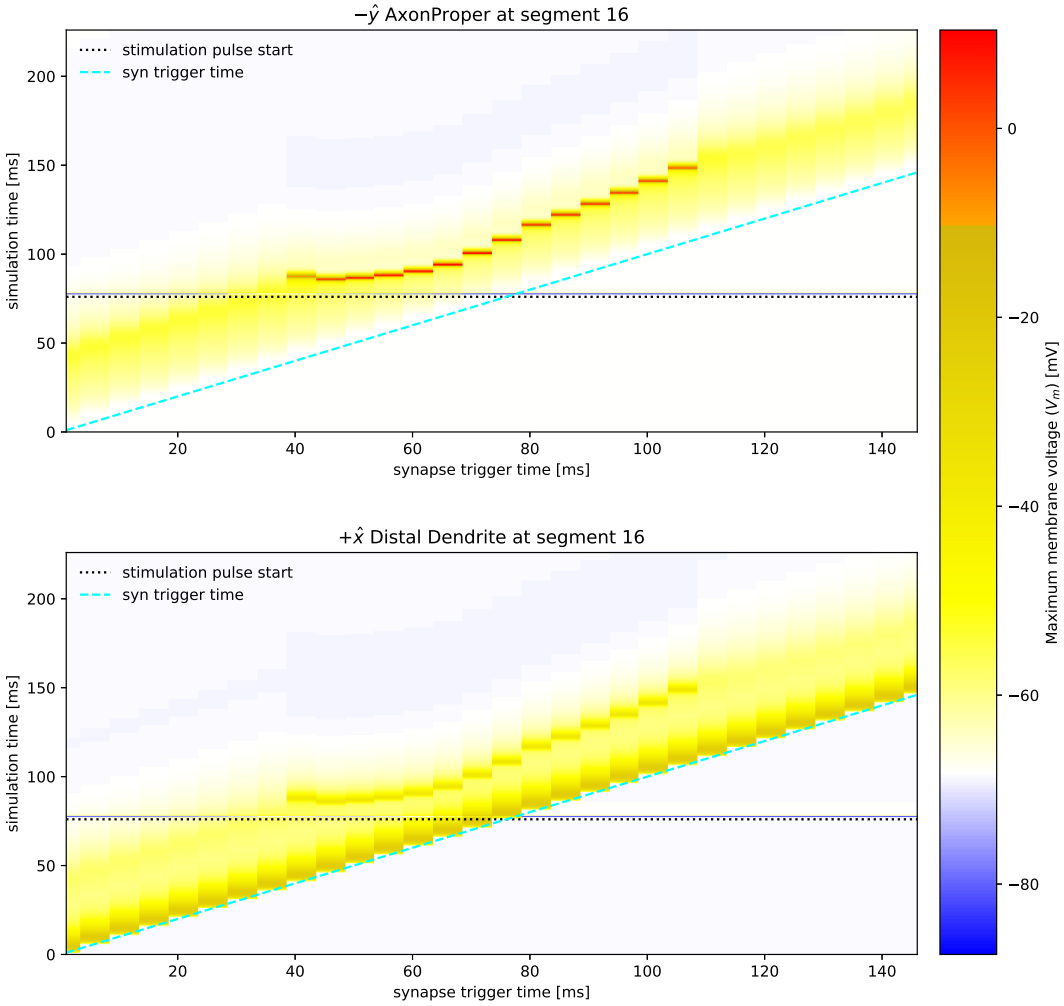
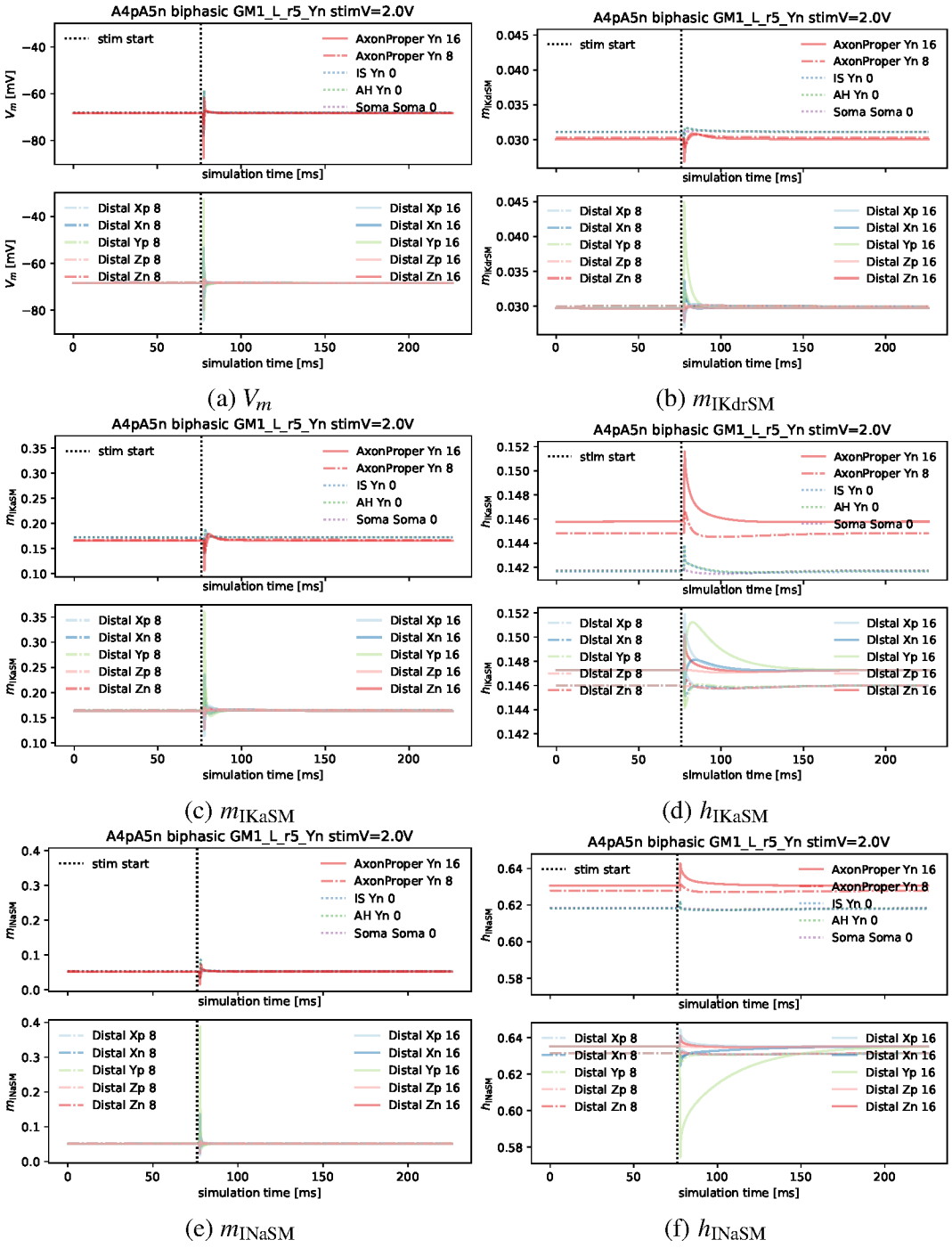


Figure 5.22: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=4.783nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 16. The electrical stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.



(a) V_m

(b) m_{IKdrSM}

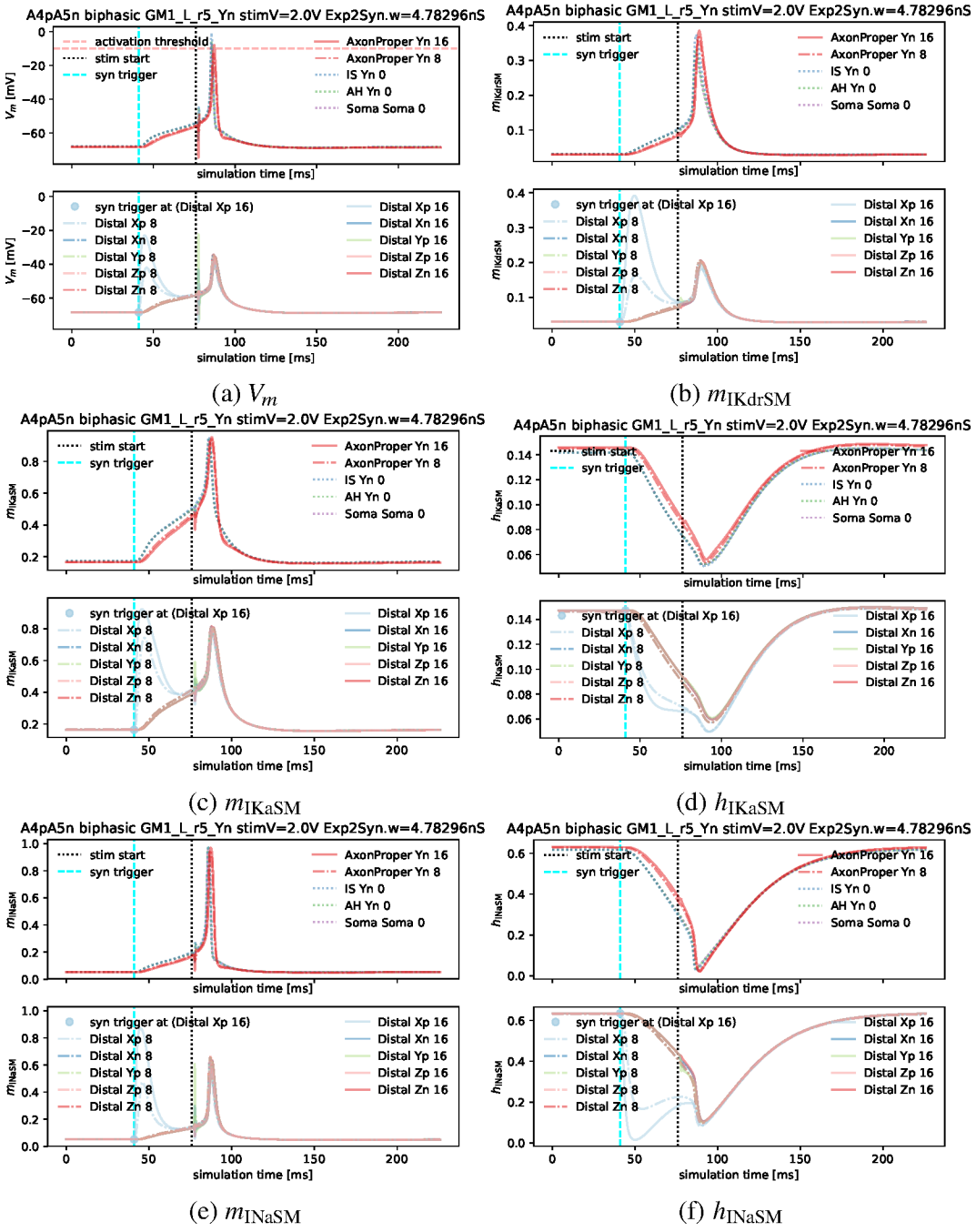
(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.23: Stimulation only: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). All data measured using neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms.

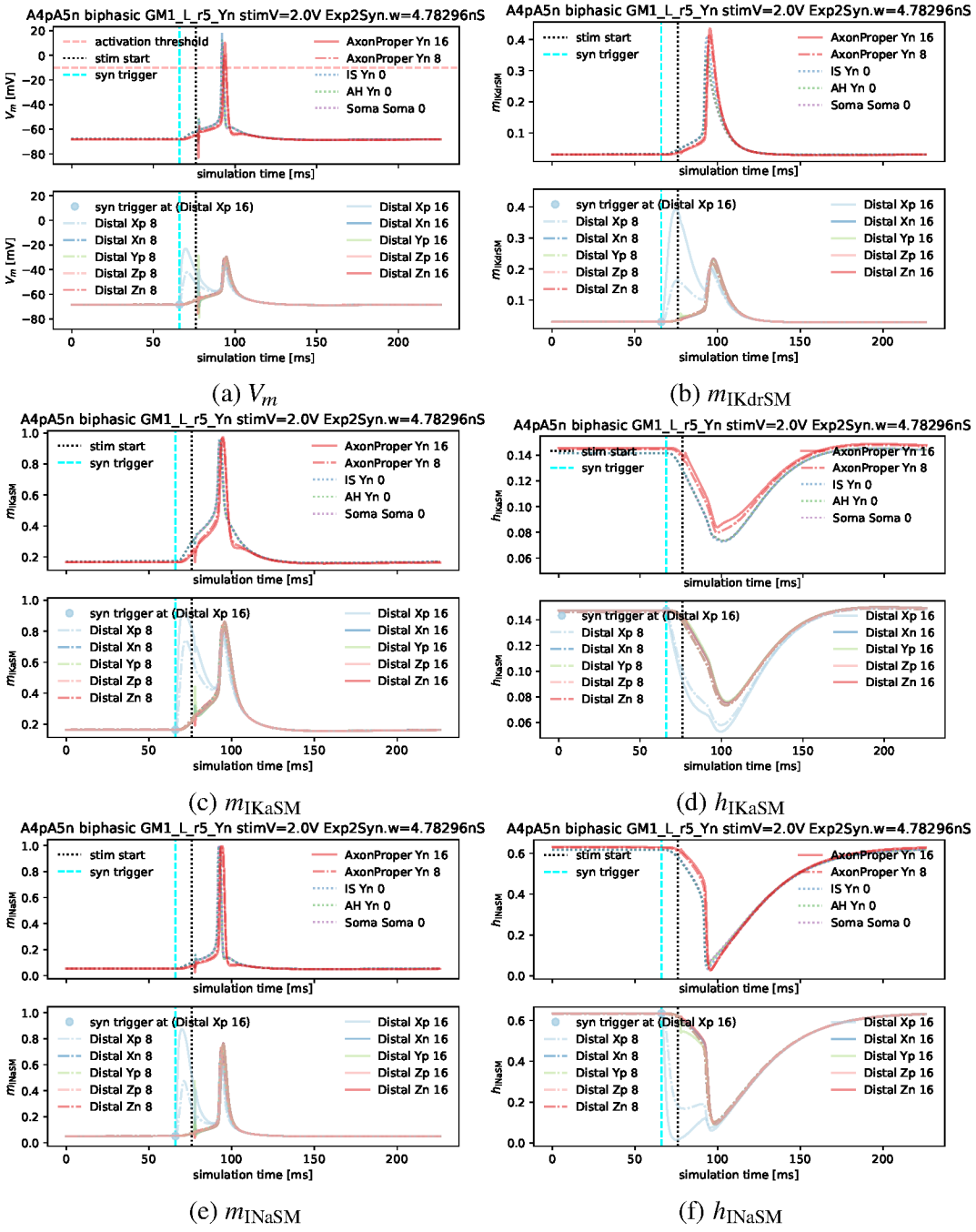


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.24: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=41.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.

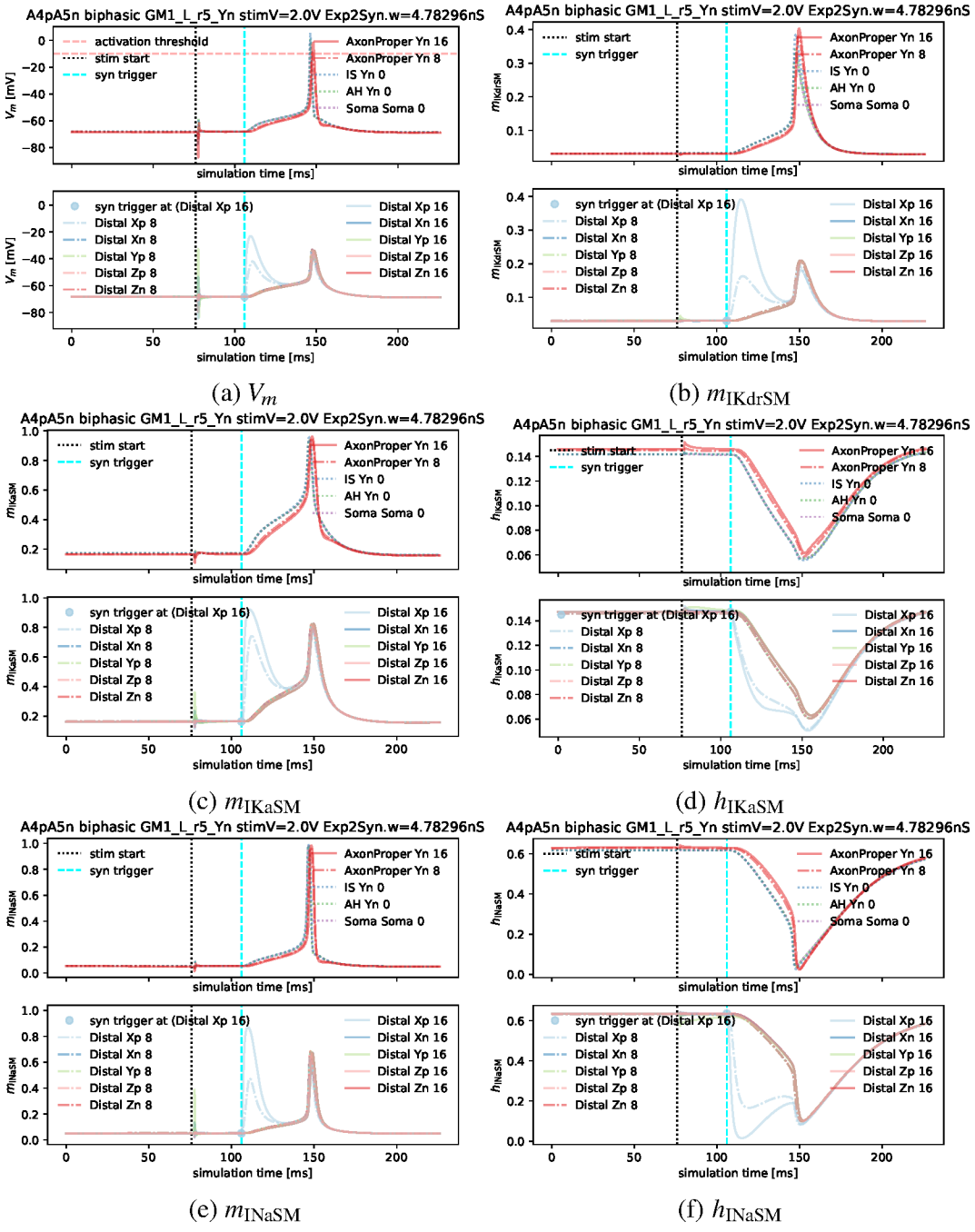


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.25: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=66.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.26: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=106.0 ms with a synaptic weight of 4.783nS. The synapse was located at segment 16 on the distal dendrite that points in the $+\hat{x}$ direction.

5.B.2 Biphasic stimulation with $V_s < 0$ and a mid-dendrite synapse

For biphasic stimulation using A4pA5n with $V_s < 0$ of neuron GM1_L_r5_Yn with a synapse triggered on the distal dendrite pointing in the $\hat{x}$ direction at segment 8, the maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.27. Without any EPSPs, the neuron will activate if $V_s = -6\,\text{V}$. As with the previous biphasic stimulation examples, the window of facilitation is larger before the stimulation pulse. As $|V_s|$ and synapse weight decrease, the facilitation window is only before the stimulation pulse. This implies that it takes less biphasic stimulation and/or synapse weight to facilitate the neuron if the synapse is triggered first and the biphasic stimulation pulse occurs within about 20 ms after.

Figure 5.28 shows the membrane voltage at the axon tip and the synapse location for $V_s = -2\,\text{V}$ and synapse weight 3.45 nS for all the synapse trigger times shown in Fig. 5.27. The neuron activations are shown in orange-red, while the synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse as a dotted black line. The time of the neuron activations generally increases with increasing synaptic trigger time (with a gap of no facilitation in the middle), and each of the activations travels back to the synapse location.

The response of the neuron (membrane voltage and ion-channel state variables) to just the EPSP (with synapse weight of 3.45 nS) alone can be found in Fig. 3.10. The response of the neuron to $V_s = 2\,\text{V}$ stimulation alone can be found in Fig. 5.23. Figure 5.29 shows the facilitated response to a synapse triggered before the stimulation pulse. Figure 5.31 shows the facilitated response to a synapse triggered after the stimulation pulse.

As in Sections 5.2.1 and 5.B.1, Figs. 5.29 and 5.31 show many similarities if the synapse trigger times are lined up. The stimulation pulse causes what appear to be

minor deviations in the state of the neuron compared to the EPSP by itself, but these deviations are enough to cause activation when combined with the EPSP.

For the case of $V_s = 2\,\mathrm{V}$ and synapse weight 3.45 nS, a synapse trigger time of $t = 66\,\mathrm{ms}$ (same as with $V_s = -2\,\mathrm{V}$) maximizes the membrane voltage at the axon tip (compared to other synapse trigger times). Figure 5.30 shows the neuron response to these parameters. Note that this synapse trigger time causes the stimulation pulse to occur when m_{IKdrSM} is at a maximum near the synapse and h_{INaSM} is at a minimum. This behavior was also seen in Sections 5.2.1 and 5.B.1.

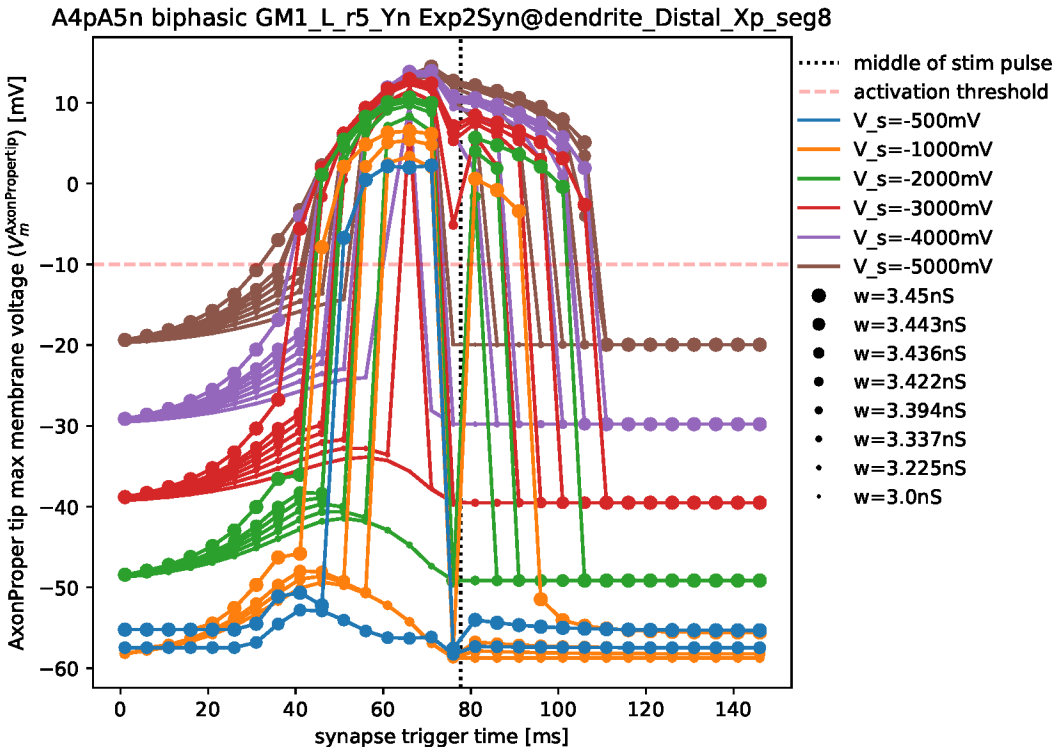


Figure 5.27: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to biphasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above -10 mV) : (-5.0V, 3.45nS, 9, 6), (-5.0V, 3.443nS, 8, 6), (-5.0V, 3.436nS, 8, 6), (-5.0V, 3.422nS, 7, 5), (-5.0V, 3.394nS, 7, 4), (-5.0V, 3.337nS, 7, 3), (-5.0V, 3.225nS, 6, 1), (-5.0V, 3.0nS, 4, 0), (-4.0V, 3.45nS, 8, 6), (-4.0V, 3.443nS, 7, 5), (-4.0V, 3.436nS, 7, 5), (-4.0V, 3.422nS, 7, 4), (-4.0V, 3.394nS, 6, 2), (-4.0V, 3.337nS, 6, 1), (-4.0V, 3.225nS, 4, 0), (-4.0V, 3.0nS, 2, 0), (-3.0V, 3.45nS, 8, 6), (-3.0V, 3.443nS, 7, 4), (-3.0V, 3.436nS, 7, 3), (-3.0V, 3.422nS, 6, 2), (-3.0V, 3.394nS, 5, 0), (-3.0V, 3.337nS, 4, 0), (-3.0V, 3.225nS, 1, 0), (-2.0V, 3.45nS, 6, 5), (-2.0V, 3.443nS, 5, 2), (-2.0V, 3.436nS, 5, 1), (-2.0V, 3.422nS, 4, 0), (-2.0V, 3.394nS, 3, 0), (-1.0V, 3.45nS, 6, 3), (-1.0V, 3.443nS, 4, 0), (-1.0V, 3.436nS, 3, 0), and (-0.5V, 3.45nS, 5, 0).

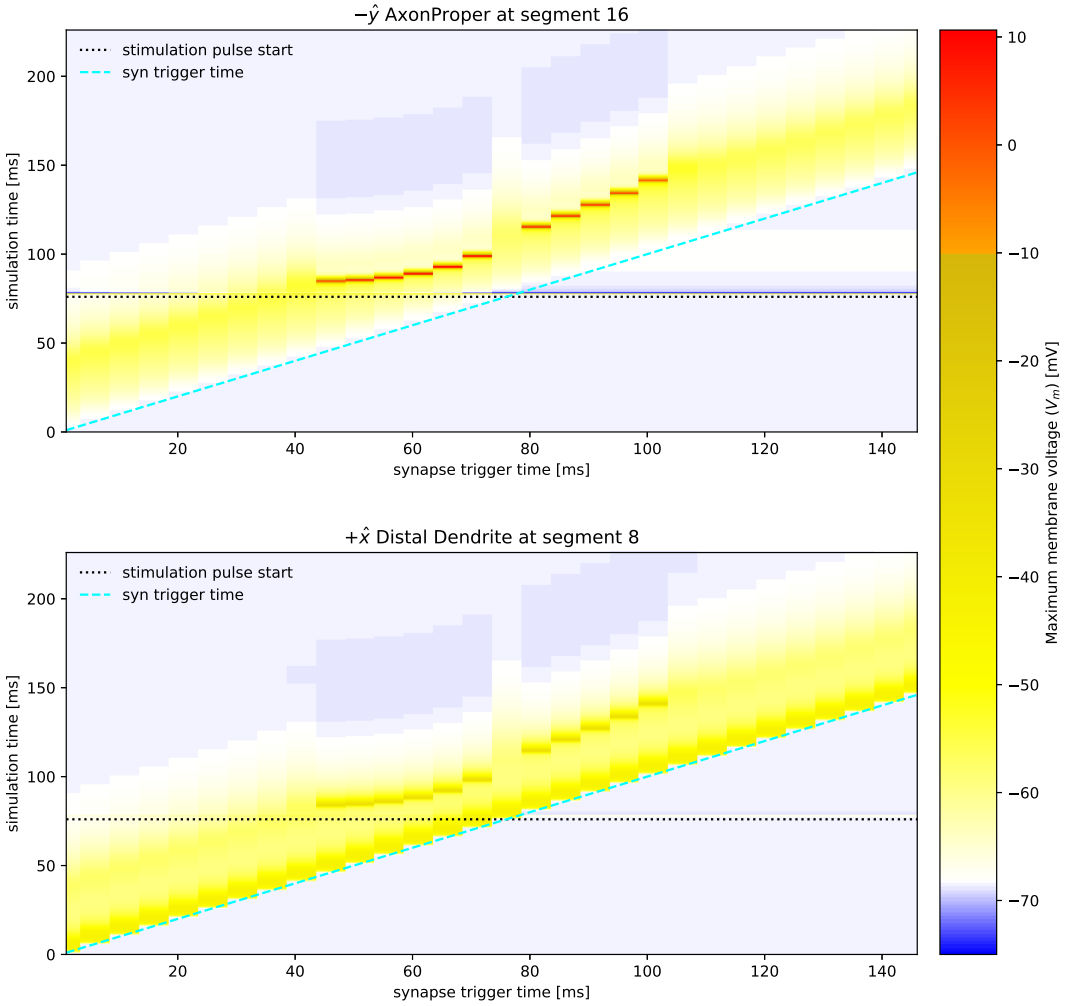
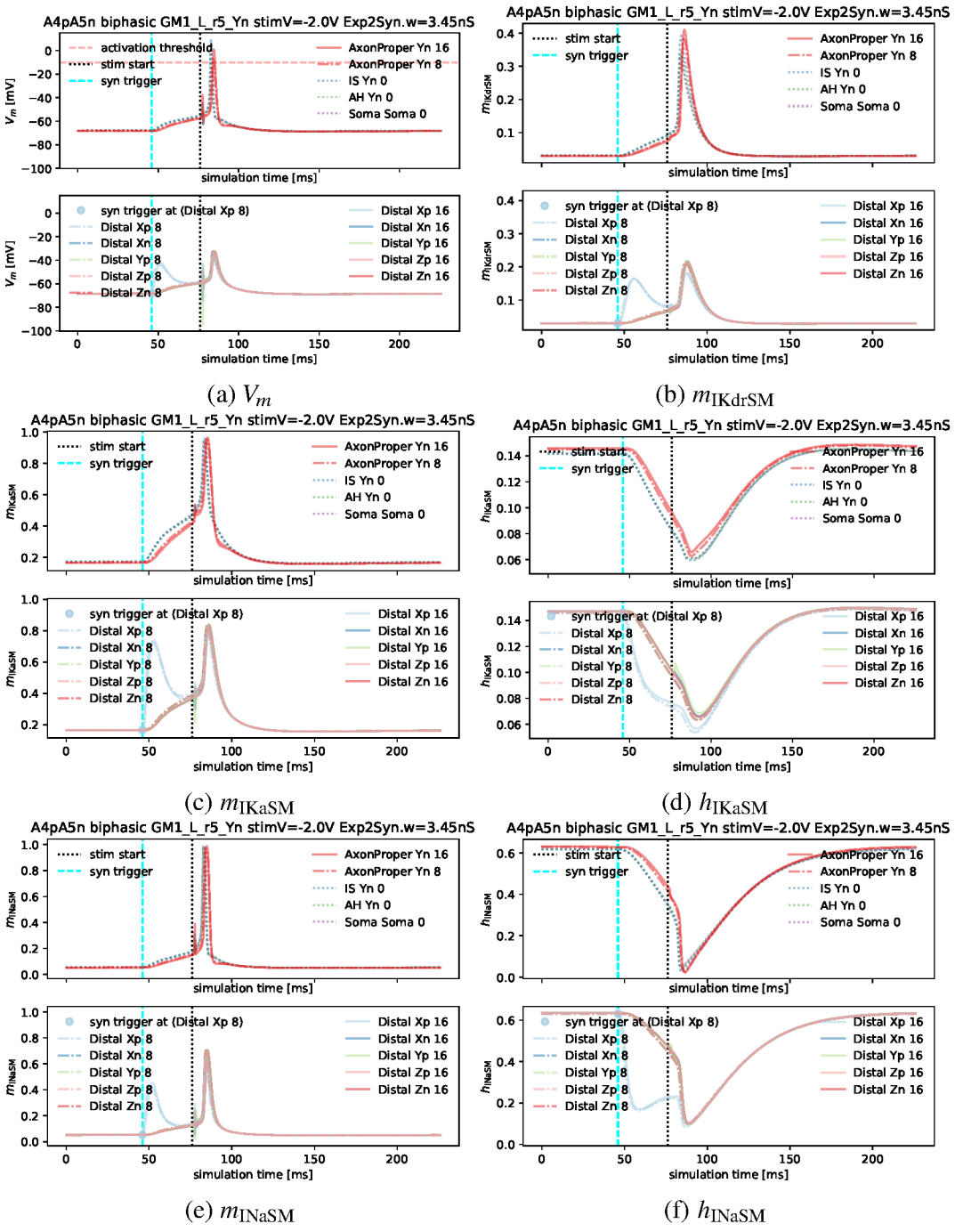


Figure 5.28: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of biphasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=3.45nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 8. The electrical stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.

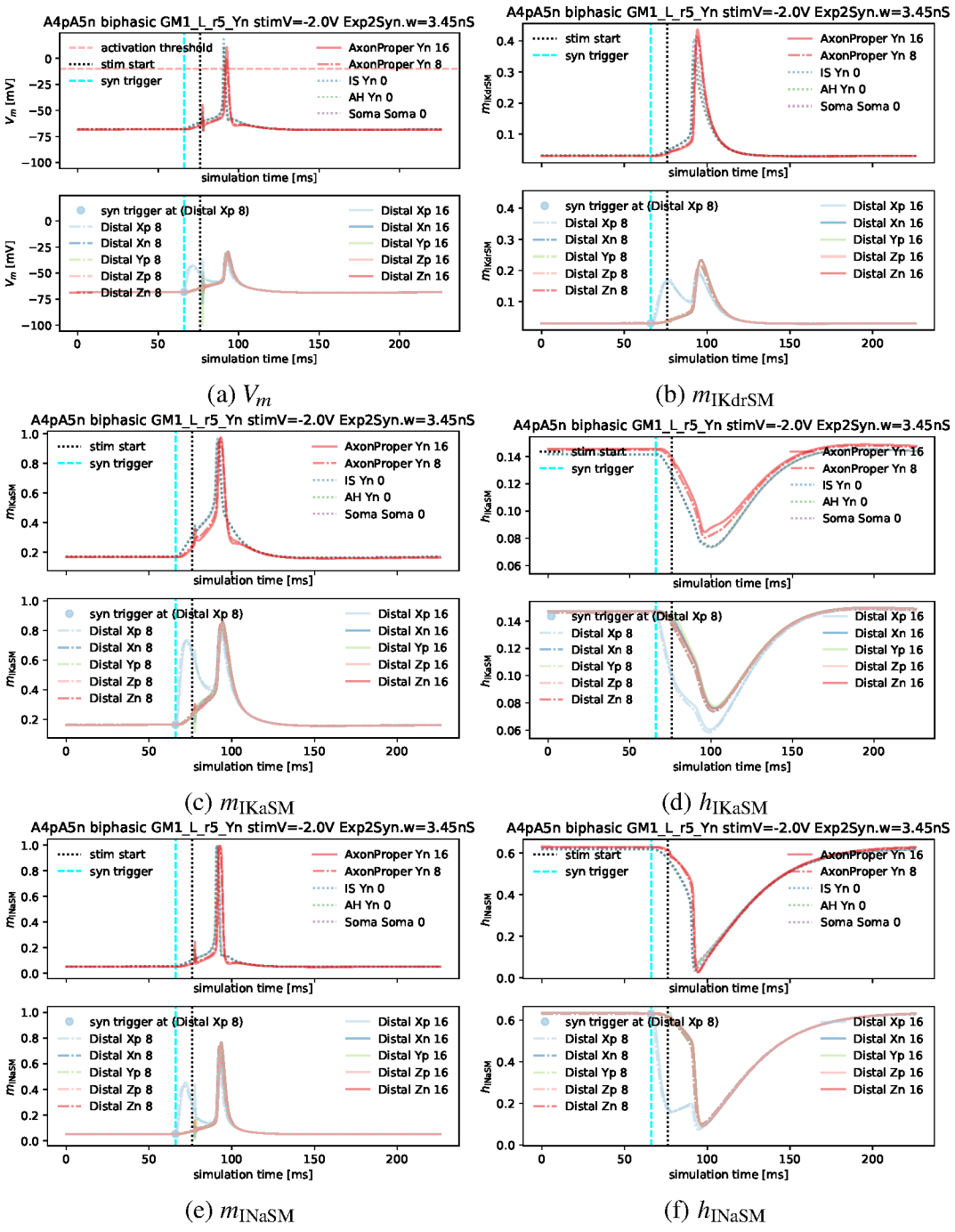


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.29: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=46.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

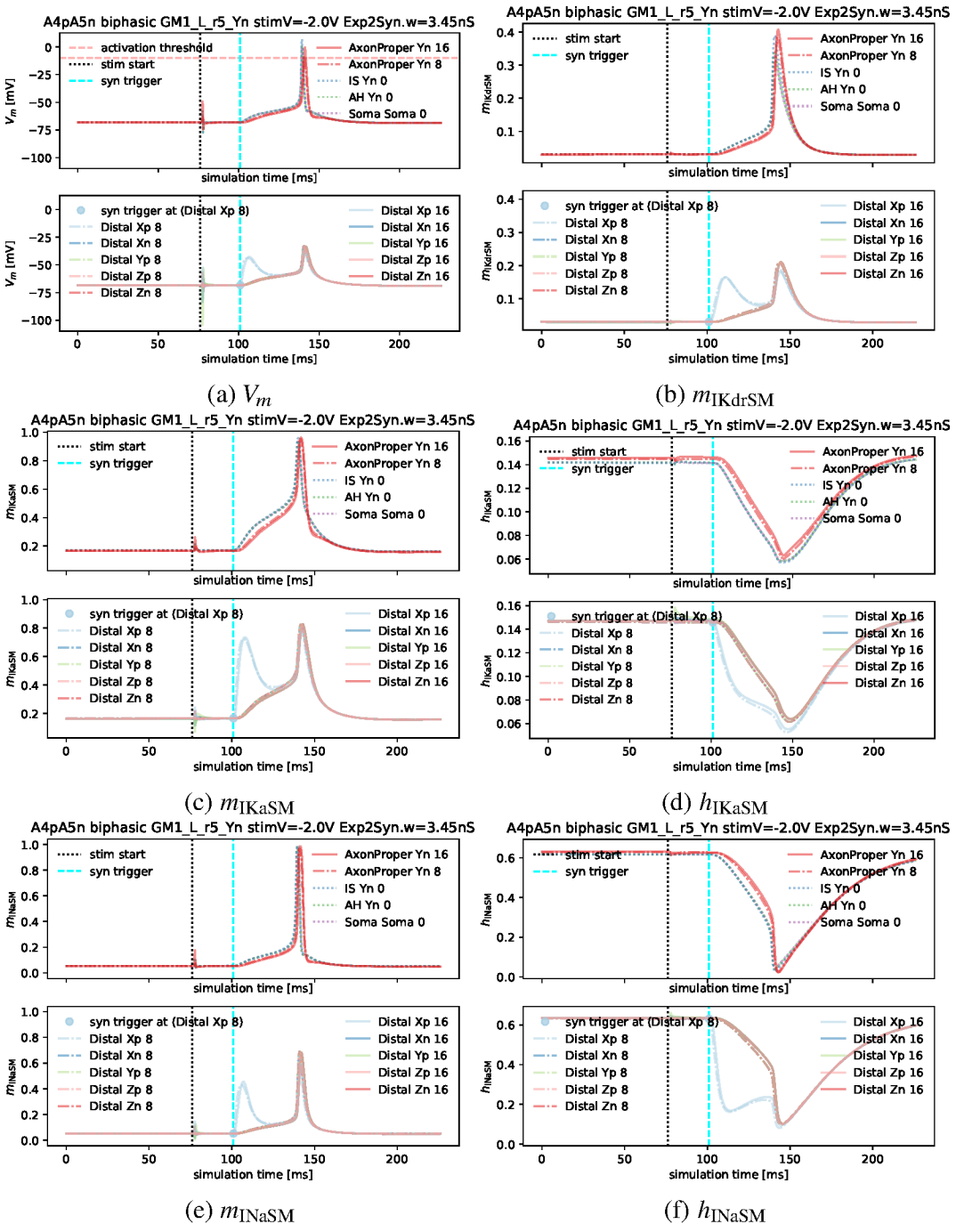


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.30: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to -2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=66.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.31: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=101.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

5.B.3 Biphasic stimulation with $V_s > 0$ and a mid-dendrite synapse

For biphasic stimulation using A4pA5n with $V_s > 0$ of neuron GM1_L_r5_Yn with a synapse triggered on the distal dendrite pointing in the $\hat{x}$ direction at segment 8, the maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.32. Without any EPSPs, the neuron will activate if $V_s = 8\,\mathrm{V}$. As with the previous biphasic stimulation examples, the window of facilitation is larger before the stimulation pulse. As $|V_s|$ and synapse weight decrease, the facilitation window is only before the stimulation pulse. This implies that it takes less biphasic stimulation and/or synapse weight to facilitate the neuron if the synapse is triggered first and the biphasic stimulation pulse occurs within about 20 ms after.

Figure 5.33 shows the membrane voltage at the axon tip and the synapse location for $V_s = 2\,\mathrm{V}$ and synapse weight 3.45 nS for all the synapse trigger times shown in Fig. 5.32. The neuron activations are shown in orange-red, while the synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse as a dotted black line. The time of the neuron activations generally increases with increasing synaptic trigger time and each of the activations travels back to the synapse location.

The response of the neuron (membrane voltage and ion-channel state variables) to just the EPSP (with synapse weight of 3.45 nS) alone can be found in Fig. 3.10. Figure 5.34 shows the facilitated response to a synapse triggered before the stimulation pulse. Figure 5.36 shows the facilitated response to a synapse triggered after the stimulation pulse.

As in Sections 5.2.1 to 5.B.2, Figs. 5.34 and 5.36 show many similarities if the synapse trigger times are lined up. The stimulation pulse causes what appear to be minor deviations in the state of the neuron compared to the EPSP by itself, but these deviations are enough to cause activation when combined with the EPSP.

For the case of $V_s = 2\,\mathrm{V}$ and synapse weight 3.45 nS, a synapse trigger time of $t = 66\,\mathrm{ms}$ (same as with $V_s = -2\,\mathrm{V}$) maximizes the membrane voltage at the axon tip (compared to other synapse trigger times). Figure 5.35 shows the neuron response to these parameters. Note that this synapse trigger time causes the stimulation pulse to occur when m_{IKdrSM} is at a maximum near the synapse and h_{INaSM} is at a minimum. The same behavior was also seen in Sections 5.2.1 to 5.B.2.

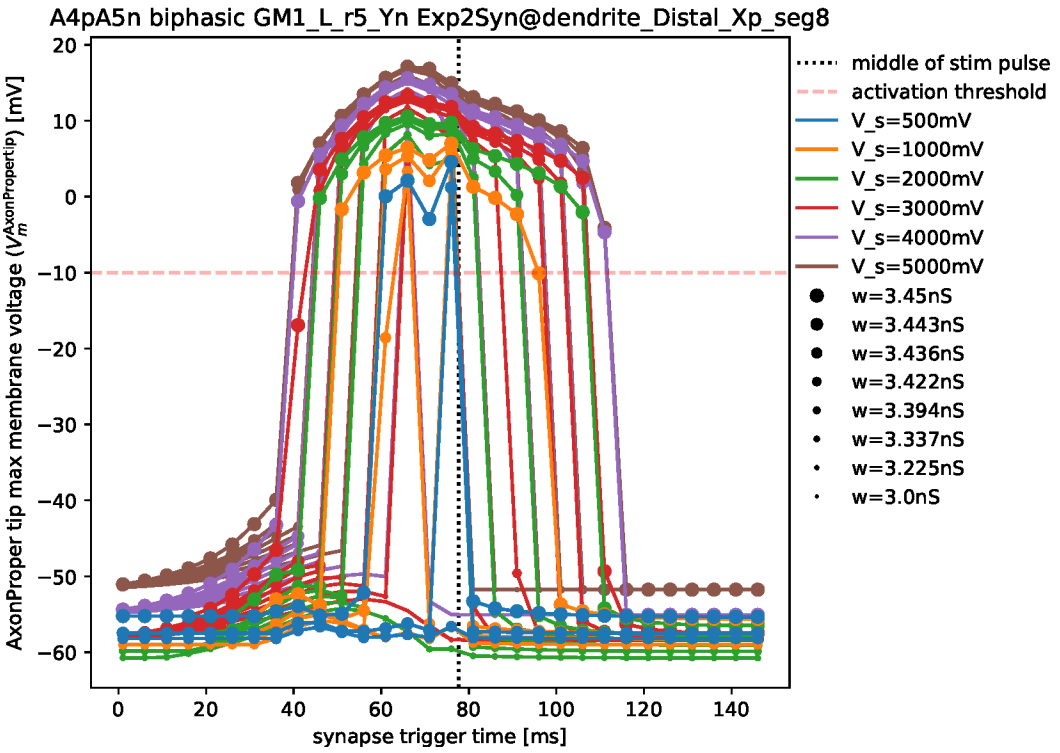


Figure 5.32: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to biphasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above -10 mV) : (5.0V, 3.45nS, 8, 7), (5.0V, 3.443nS, 8, 6), (5.0V, 3.436nS, 8, 6), (5.0V, 3.422nS, 7, 5), (5.0V, 3.394nS, 7, 4), (5.0V, 3.337nS, 7, 3), (5.0V, 3.225nS, 6, 1), (5.0V, 3.0nS, 5, 0), (4.0V, 3.45nS, 8, 7), (4.0V, 3.443nS, 7, 6), (4.0V, 3.436nS, 7, 5), (4.0V, 3.422nS, 7, 4), (4.0V, 3.394nS, 6, 3), (4.0V, 3.337nS, 6, 1), (4.0V, 3.225nS, 5, 0), (4.0V, 3.0nS, 1, 0), (3.0V, 3.45nS, 7, 6), (3.0V, 3.443nS, 7, 5), (3.0V, 3.436nS, 6, 4), (3.0V, 3.422nS, 6, 2), (3.0V, 3.394nS, 5, 0), (3.0V, 3.337nS, 4, 0), (3.0V, 3.225nS, 1, 0), (2.0V, 3.45nS, 7, 6), (2.0V, 3.443nS, 6, 3), (2.0V, 3.436nS, 5, 1), (2.0V, 3.422nS, 5, 0), (2.0V, 3.394nS, 4, 0), (1.0V, 3.45nS, 6, 3), (1.0V, 3.443nS, 4, 0), (1.0V, 3.436nS, 2, 0), (0.5V, 3.45nS, 4, 0), and (0.5V, 3.443nS, 1, 0).

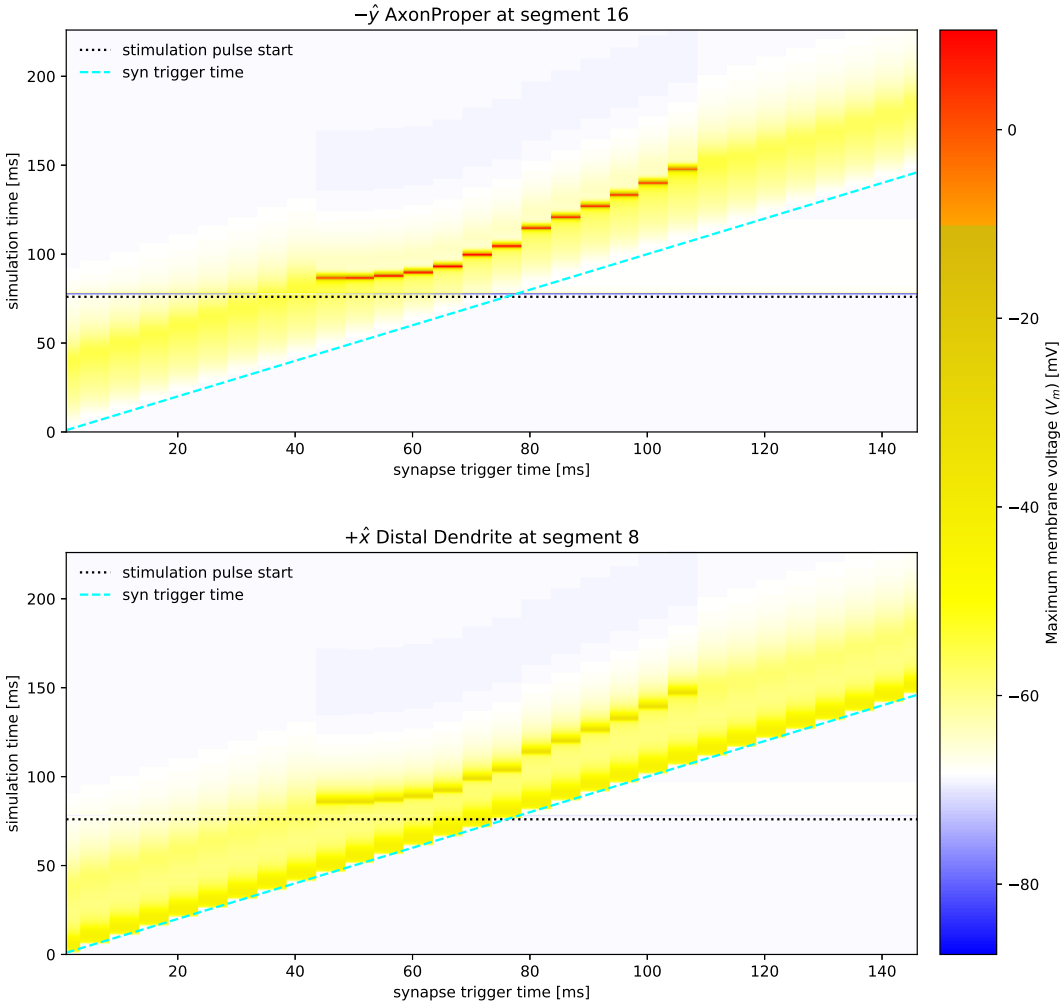
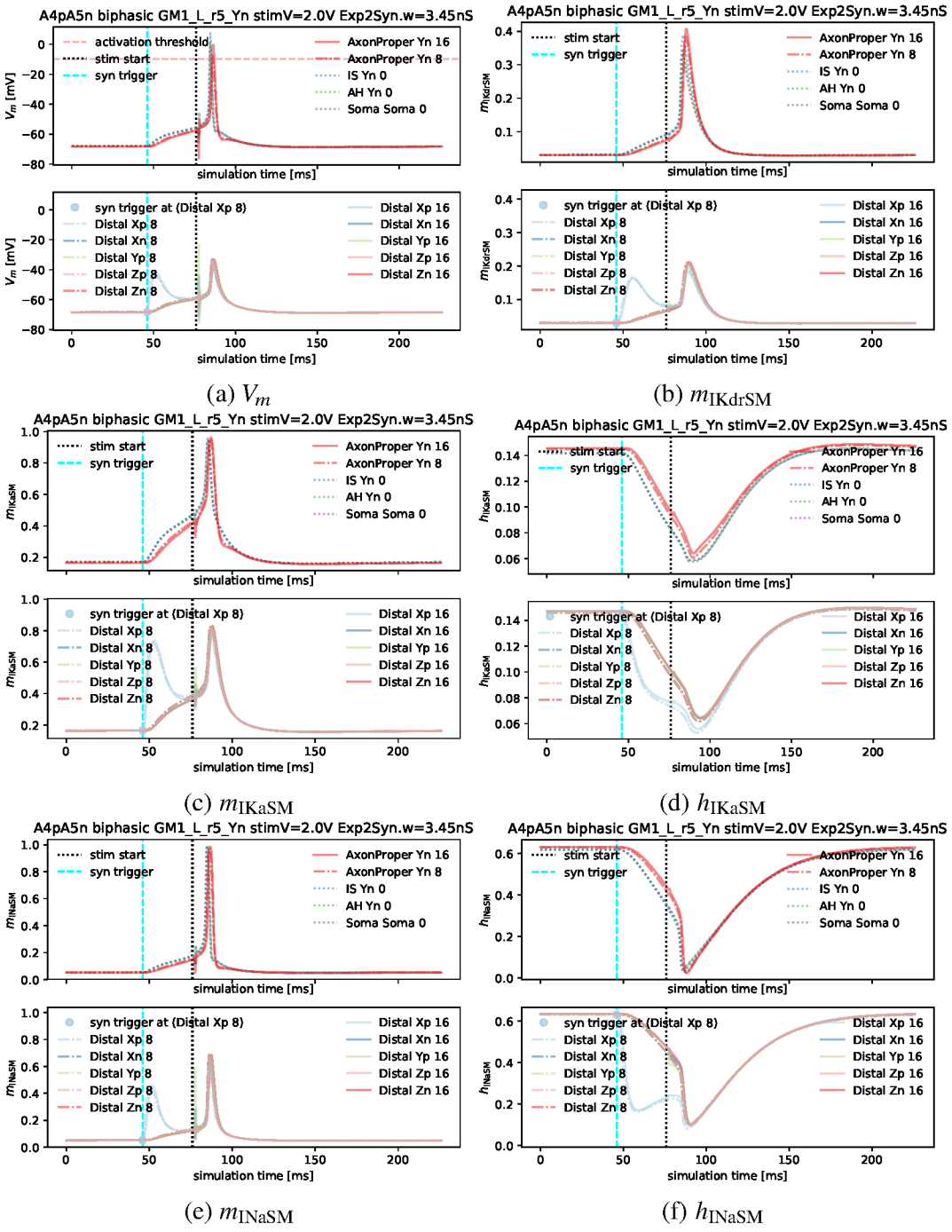


Figure 5.33: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=3.45nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 8. The electrical stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.



(a) V_m

(b) m_{IKdrSM}

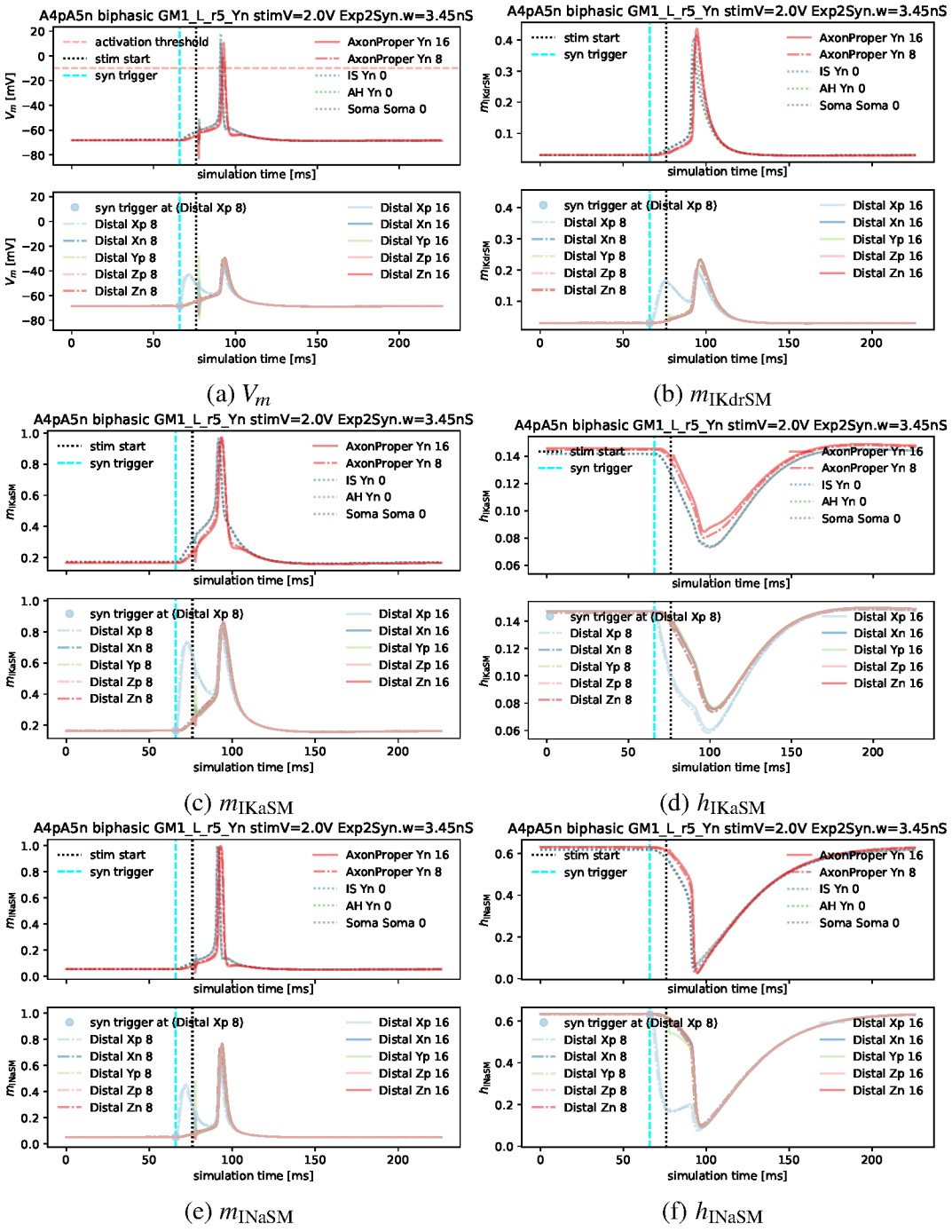
(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.34: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=46.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.35: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=66.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

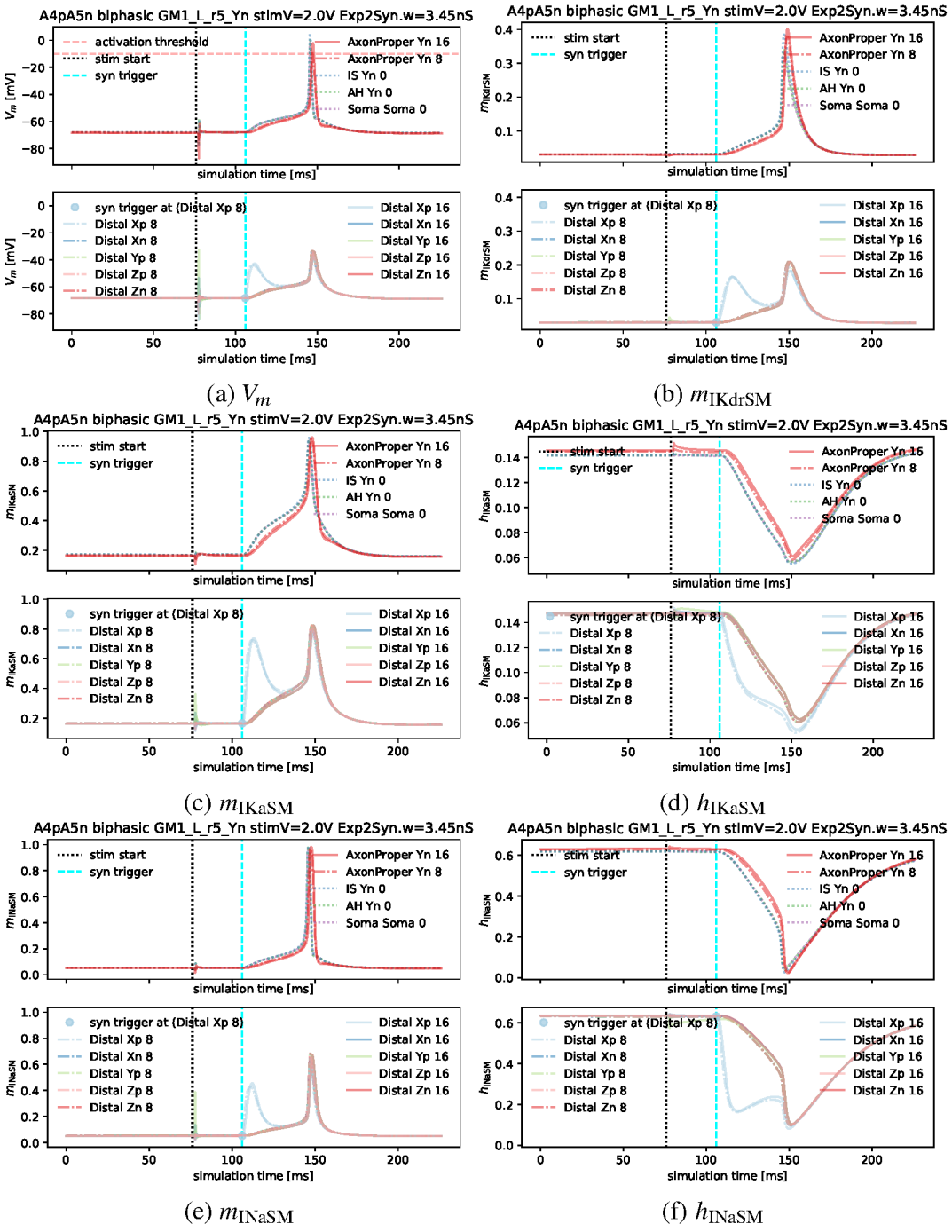


Figure 5.36: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of biphasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and the maximum amplitudes of the pulse occur at t=77.66ms ± 0.16ms. An Exp2Syn synapse was triggered at t=106.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

5.B.4 Monophasic stimulation with $V_s < 0$ and a mid-dendrite synapse

For monophasic stimulation using A4pA5n with $V_s < 0$ of neuron GM1_L_r5_Yn with a synapse triggered on the distal dendrite pointing in the $\hat{x}$ direction at segment 8, the maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.37. Without any EPSPs, the neuron will activate if $V_s = -4.25\,\text{V}$. The window of facilitation is fairly balanced between before and after the stimulation pulse if $V_s = -4\,\text{V}$. If V_s is [0.5, 1, 2, 3]V, there is clearly more facilitation if the synapse is triggered before the stimulation pulse.

Figure 5.38 shows the membrane voltage at the axon tip and the synapse location for $V_s = -2\,\text{V}$ and synapse weight 3.45 nS for all the synapse trigger times shown in Fig. 5.27. The neuron activations are shown in orange-red, while the synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse as a dotted black line. The time of the neuron activations generally increases with increasing synaptic trigger time and each of the activations travel back to the synapse location.

The response of the neuron (membrane voltage and ion-channel state variables) to just the EPSP (with synapse weight of 3.45 nS) alone can be found in Fig. 3.10. The response of the neuron to $V_s = -2\,\text{V}$ stimulation alone can be found in Fig. 5.6. Figure 5.39 shows the facilitated response to a synapse triggered before the stimulation pulse. Figure 5.41 shows the facilitated response to a synapse triggered after the stimulation pulse.

For the case of $V_s = -2\,\text{V}$ and synapse weight 3.45 nS, the membrane voltage at the axon tip is maximized (compared to other synapse trigger times) if synapse trigger time is the same as the start of the stimulation pulse ($t = 76\,\text{ms}$). Figure 5.40 shows the neuron response to these parameters.

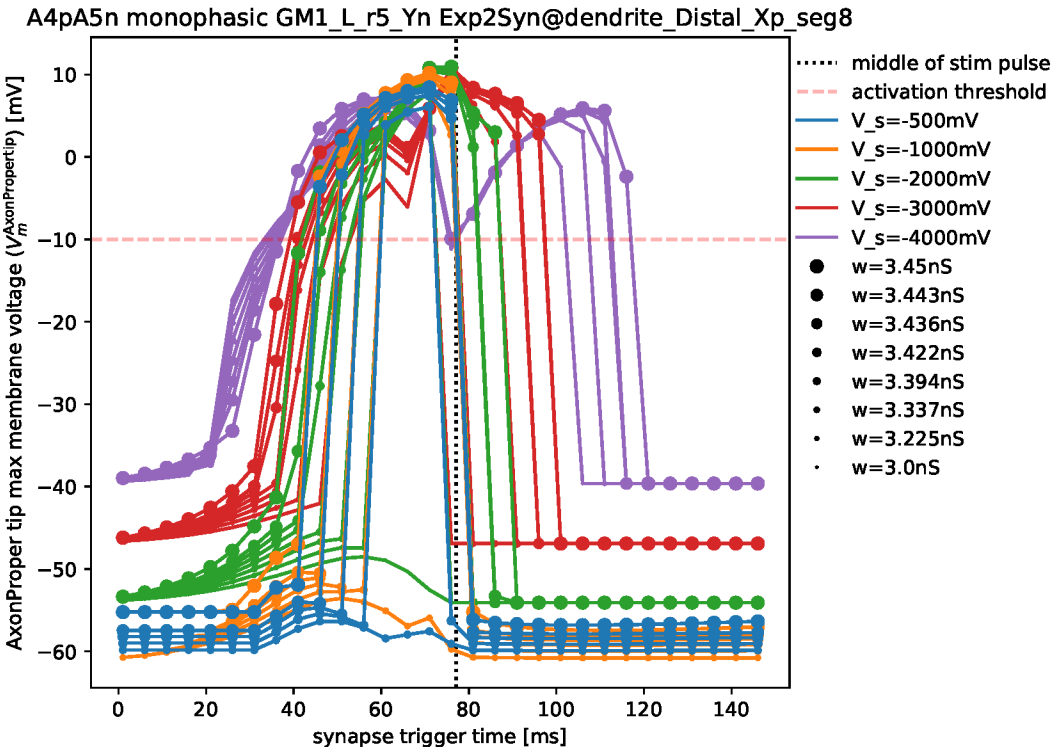


Figure 5.37: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to monophasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. This neuron is active without any EPSPs if exposed to -5.0V of stimulation. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above $-10\,\text{mV}$) : (-4.0V, 3.45nS, 8, 8), (-4.0V, 3.443nS, 8, 7), (-4.0V, 3.436nS, 8, 7), (-4.0V, 3.422nS, 7, 7), (-4.0V, 3.394nS, 8, 7), (-4.0V, 3.337nS, 8, 7), (-4.0V, 3.225nS, 8, 6), (-4.0V, 3.0nS, 8, 5), (-3.0V, 3.45nS, 8, 4), (-3.0V, 3.443nS, 8, 4), (-3.0V, 3.436nS, 7, 3), (-3.0V, 3.422nS, 7, 3), (-3.0V, 3.394nS, 7, 2), (-3.0V, 3.337nS, 7, 0), (-3.0V, 3.225nS, 6, 0), (-3.0V, 3.0nS, 4, 0), (-2.0V, 3.45nS, 7, 2), (-2.0V, 3.443nS, 7, 1), (-2.0V, 3.436nS, 6, 1), (-2.0V, 3.422nS, 6, 0), (-2.0V, 3.394nS, 5, 0), (-2.0V, 3.337nS, 5, 0), (-2.0V, 3.225nS, 3, 0), (-1.0V, 3.45nS, 7, 0), (-1.0V, 3.443nS, 6, 0), (-1.0V, 3.436nS, 6, 0), (-1.0V, 3.422nS, 5, 0), (-1.0V, 3.394nS, 4, 0), (-0.5V, 3.45nS, 7, 0), (-0.5V, 3.443nS, 6, 0), (-0.5V, 3.436nS, 5, 0), and (-0.5V, 3.422nS, 3, 0).

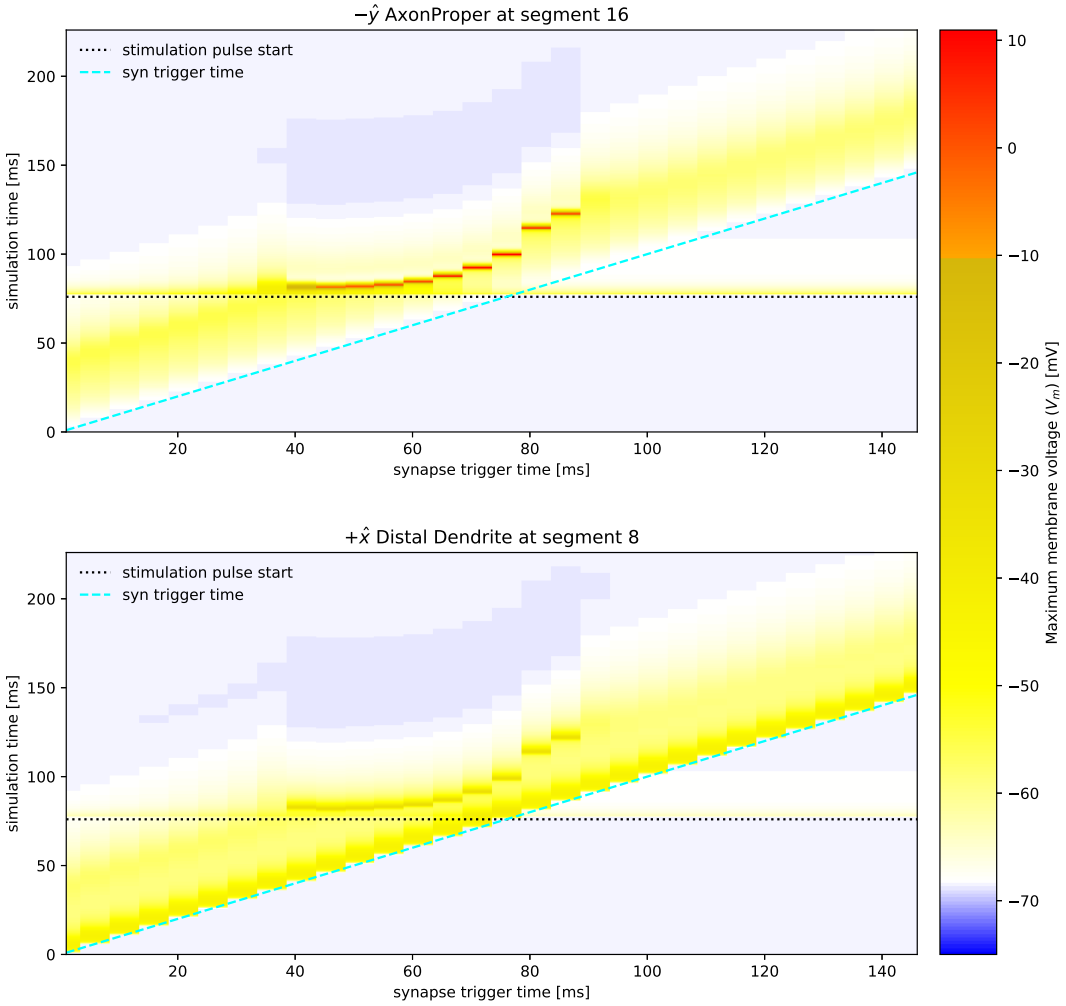


Figure 5.38: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=3.45nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 8. The electrical stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.

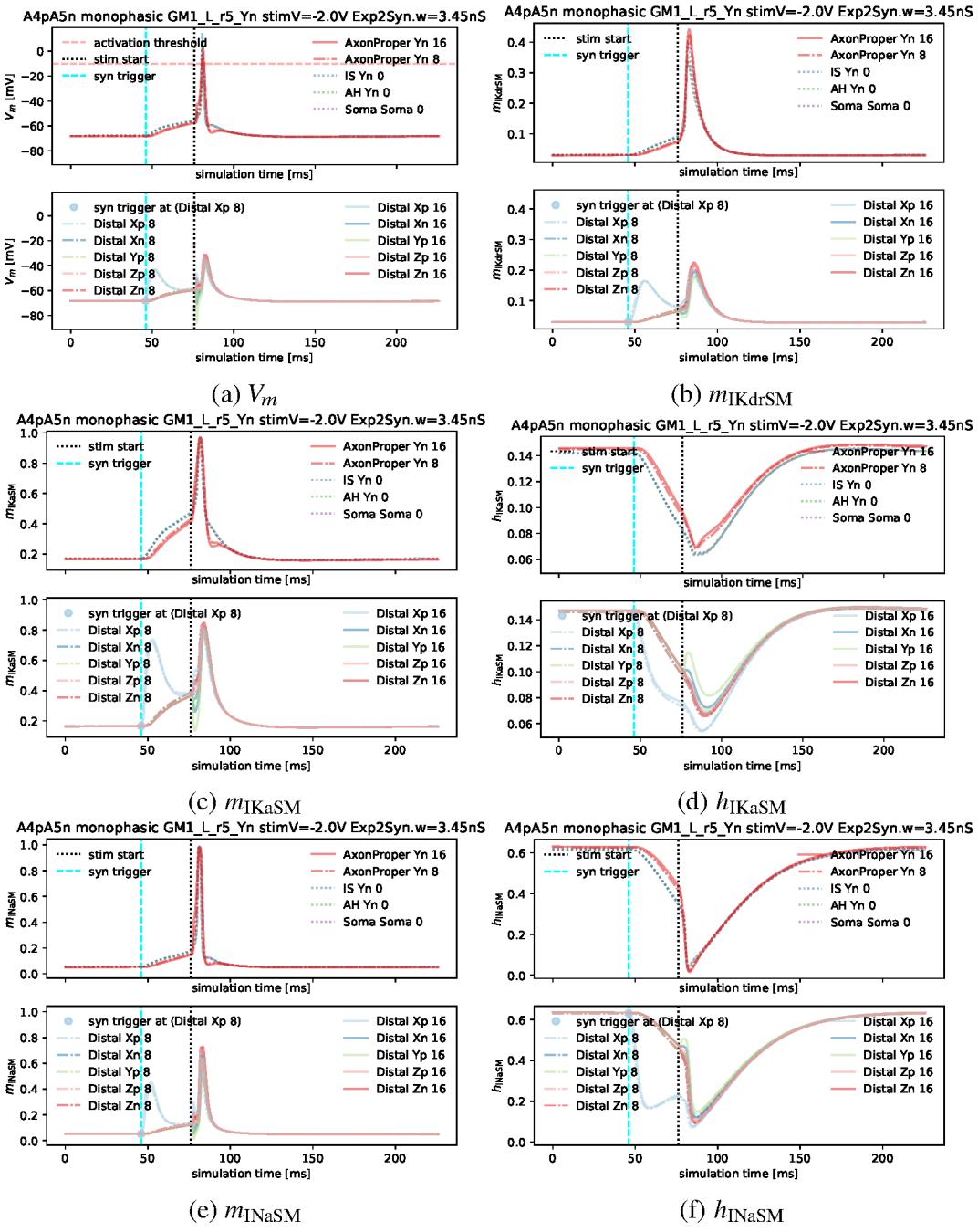
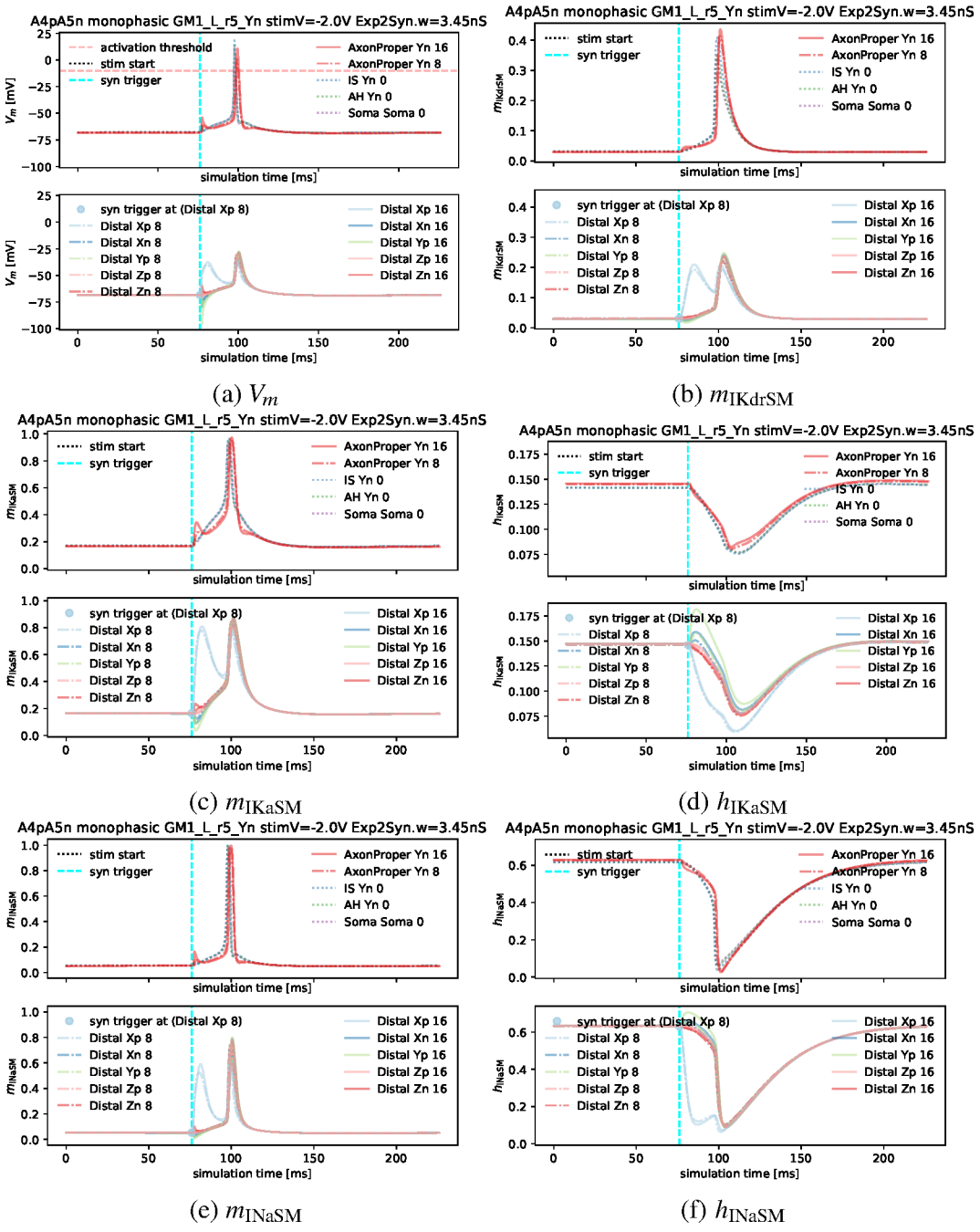


Figure 5.39: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=46.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m

(b) m_{IKdrSM}

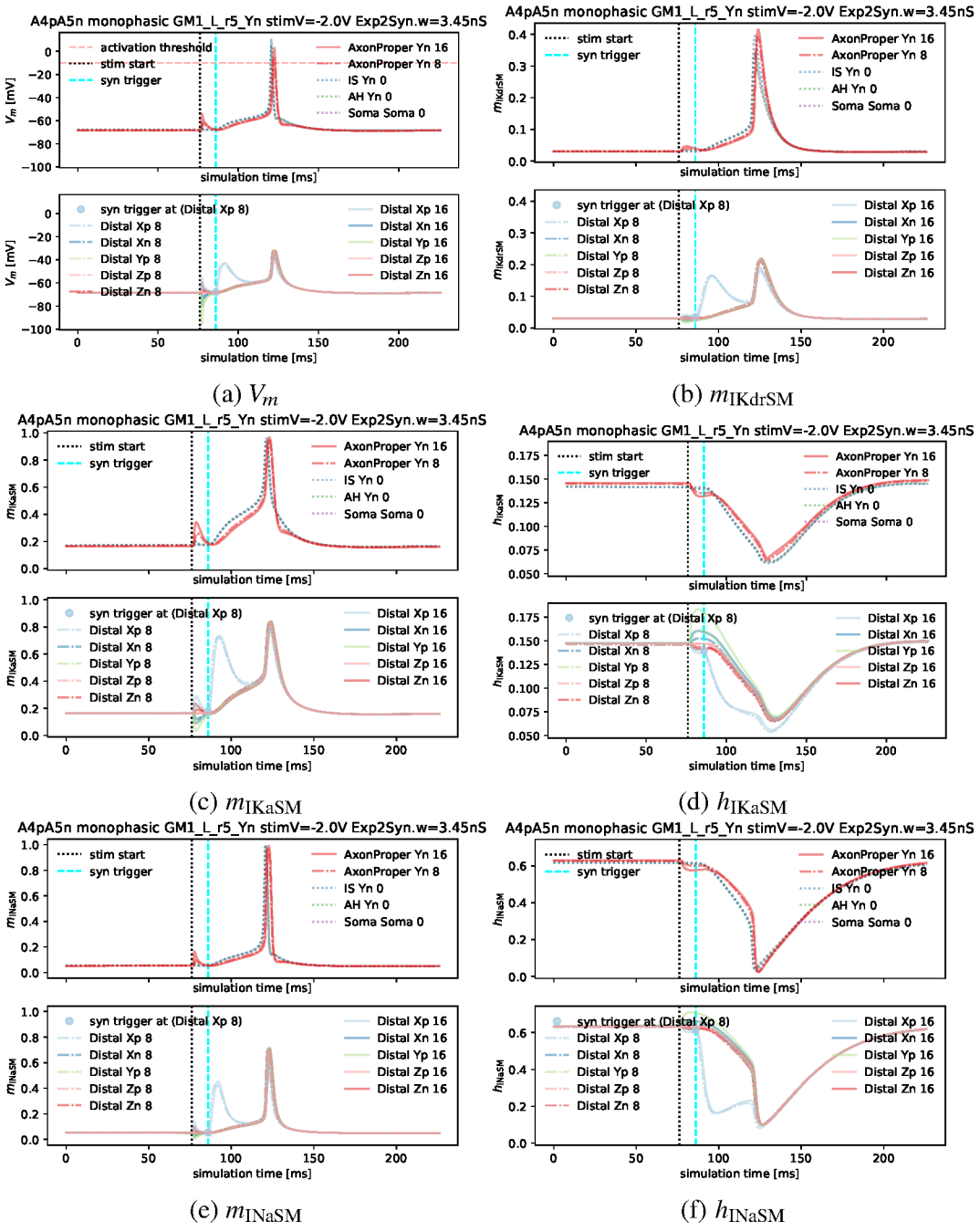
(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.40: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=76.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m

(b) m_{IKdrSM}

(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.41: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to −2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=86.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

5.B.5 Monophasic stimulation with $V_s > 0$ and a mid-dendrite synapse

For monophasic stimulation using A4pA5n with $V_s > 0$ of neuron GM1_L_r5_Yn with a synapse triggered on the distal dendrite pointing in the $\hat{x}$ direction at segment 8, the maximum membrane voltage at the axon tip for the synapse weights, trigger times, and stimulation voltages listed in Section 5.1 can be seen in Fig. 5.42. Without any EPSPs, it appears that this neuron will not activate with monophasic stimulation if $V_s > 0\,\text{V}$. Unlike the biphasic stimulation examples and the previous example, the facilitation window for the synapse trigger time is clearly larger after the stimulation pulse. If V_s is [2, 1, 0.5]V, the facilitation window is completely after the stimulation pulse starts and goes all the way to the last synapse trigger time tested for the maximum synapse weight (3.45 nS).

Figure 5.43 shows the membrane voltage at the axon tip and the synapse location for $V_s = 2\,\text{V}$ and synapse weight 3.45 nS for all the synapse trigger times shown in Fig. 5.42. The neuron activations are shown in orange-red, while the synapse trigger time is shown as a dashed cyan line, and the start of the stimulation pulse as a dotted black line. The time of the neuron activations increases with increasing synaptic trigger time (after the small decrease in time when the synaptic trigger time coincides with the stimulation pulse start time) and each of the activations travel back to the synapse location.

The response of the neuron (membrane voltage and ion-channel state variables) to just the EPSP (with synapse weight of 3.45 nS) alone can be found in Fig. 3.10. The response of the neuron to $V_s = 2\,\text{V}$ stimulation alone can be found in Fig. 5.11. Figure 5.45 shows the response to the earliest synapse trigger time (t=81 ms) that caused facilitation with $V_s = 2\,\text{V}$ and synapse weight 4.783 nS. A synapse trigger time of 81 ms also maximizes the membrane voltage at the axon tip (compared to other synapse trigger times). Fig. 5.46 shows the response to the latest tested synapse trigger time (t=146 ms) that caused facilitation.

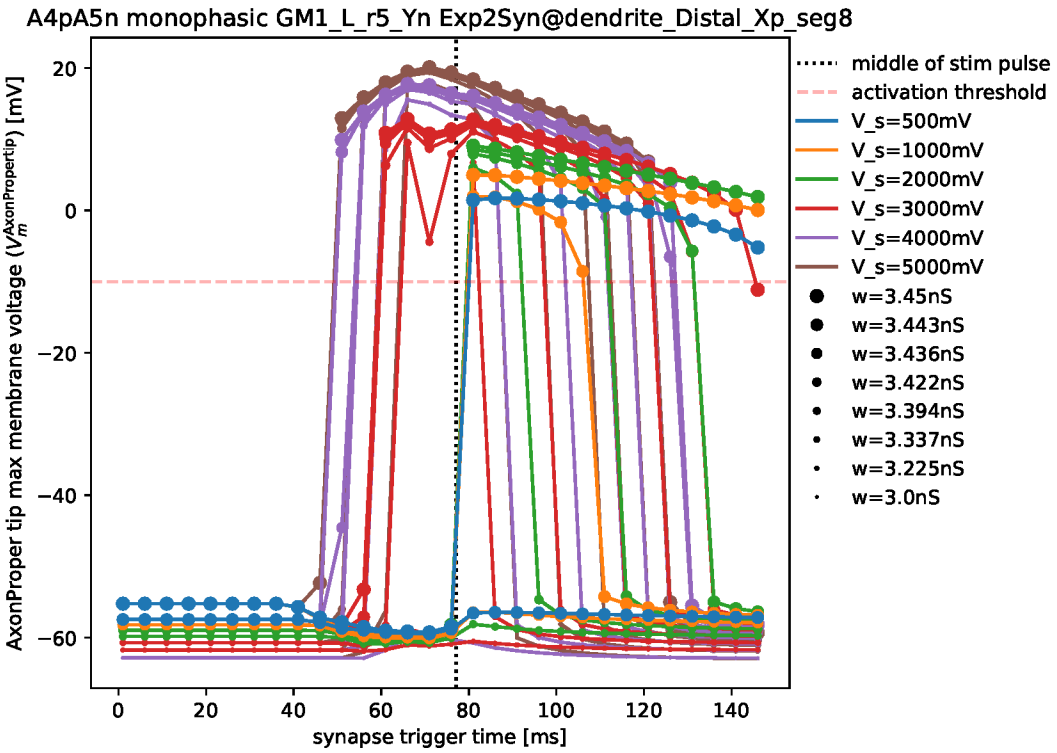


Figure 5.42: Membrane voltage at the axon tip (V_m^{axontip}) vs synapse trigger time for a neuron whose axon points in the $-\hat{y}$ direction located at GM1_L_r5. This neuron has a synapse triggered at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction and is exposed to monophasic epidural stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The following list contains tuples of the form (V_s, w, $\#T_B$, $\#T_A$) where V_s is the stimulation voltage, w is the synapse weight, and ($\#T_B$, $\#T_A$) is the number of synapse trigger time samples (x-axis samples in the above graph) before or after the stimulation pulse, respectively, given the values of V_s and w that result in neuron activation (a value of V_m^{axontip} above $-10\,\text{mV}$) : (5.0V, 3.45nS, 6, 9), (5.0V, 3.443nS, 6, 9), (5.0V, 3.436nS, 6, 9), (5.0V, 3.422nS, 6, 8), (5.0V, 3.394nS, 5, 7), (5.0V, 3.337nS, 5, 6), (5.0V, 3.225nS, 4, 4), (5.0V, 3.0nS, 3, 2), (4.0V, 3.45nS, 6, 10), (4.0V, 3.443nS, 6, 10), (4.0V, 3.436nS, 5, 9), (4.0V, 3.422nS, 5, 8), (4.0V, 3.394nS, 5, 7), (4.0V, 3.337nS, 4, 5), (4.0V, 3.225nS, 4, 2), (3.0V, 3.45nS, 4, 13), (3.0V, 3.443nS, 4, 11), (3.0V, 3.436nS, 4, 9), (3.0V, 3.422nS, 4, 7), (3.0V, 3.394nS, 3, 4), (3.0V, 3.337nS, 0, 1), (2.0V, 3.45nS, 0, 14), (2.0V, 3.443nS, 0, 11), (2.0V, 3.436nS, 0, 7), (2.0V, 3.422nS, 0, 3), (1.0V, 3.45nS, 0, 14), (1.0V, 3.443nS, 0, 6), and (0.5V, 3.45nS, 0, 14).

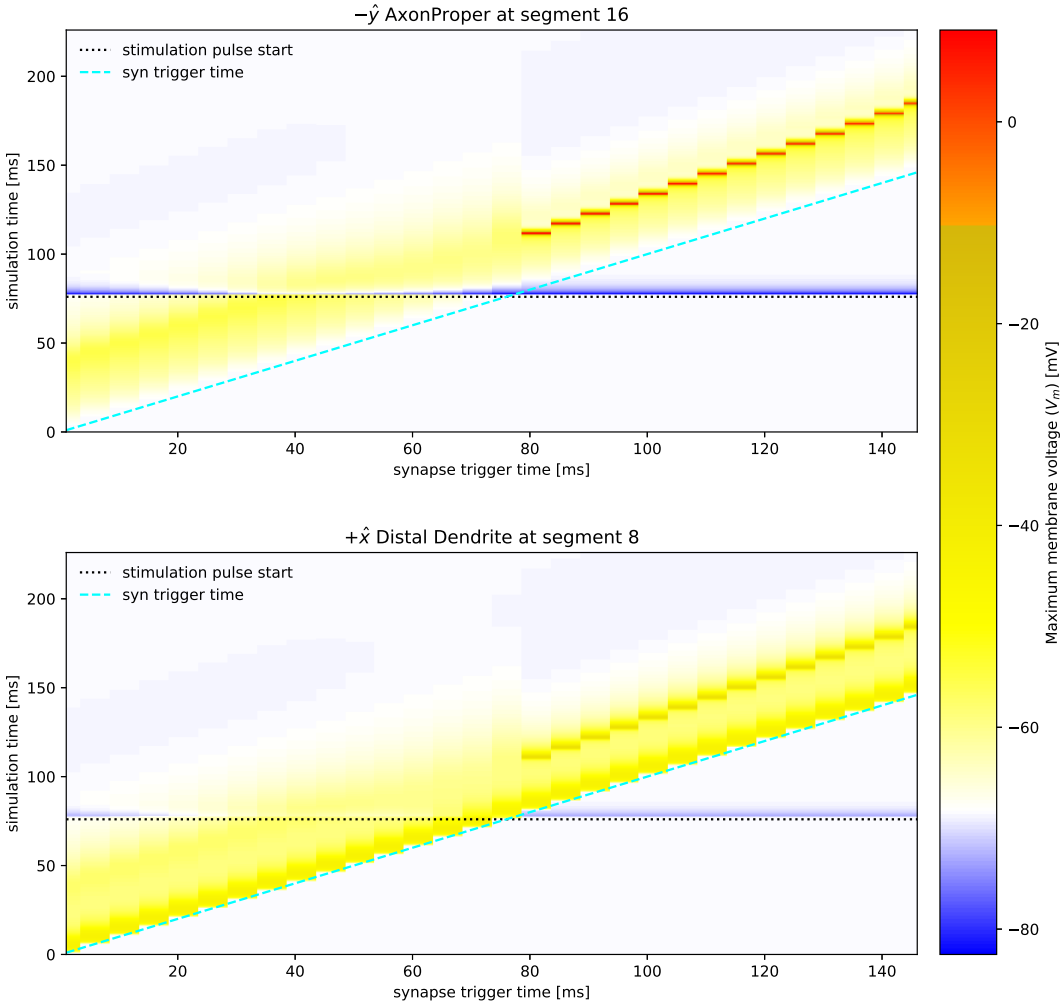
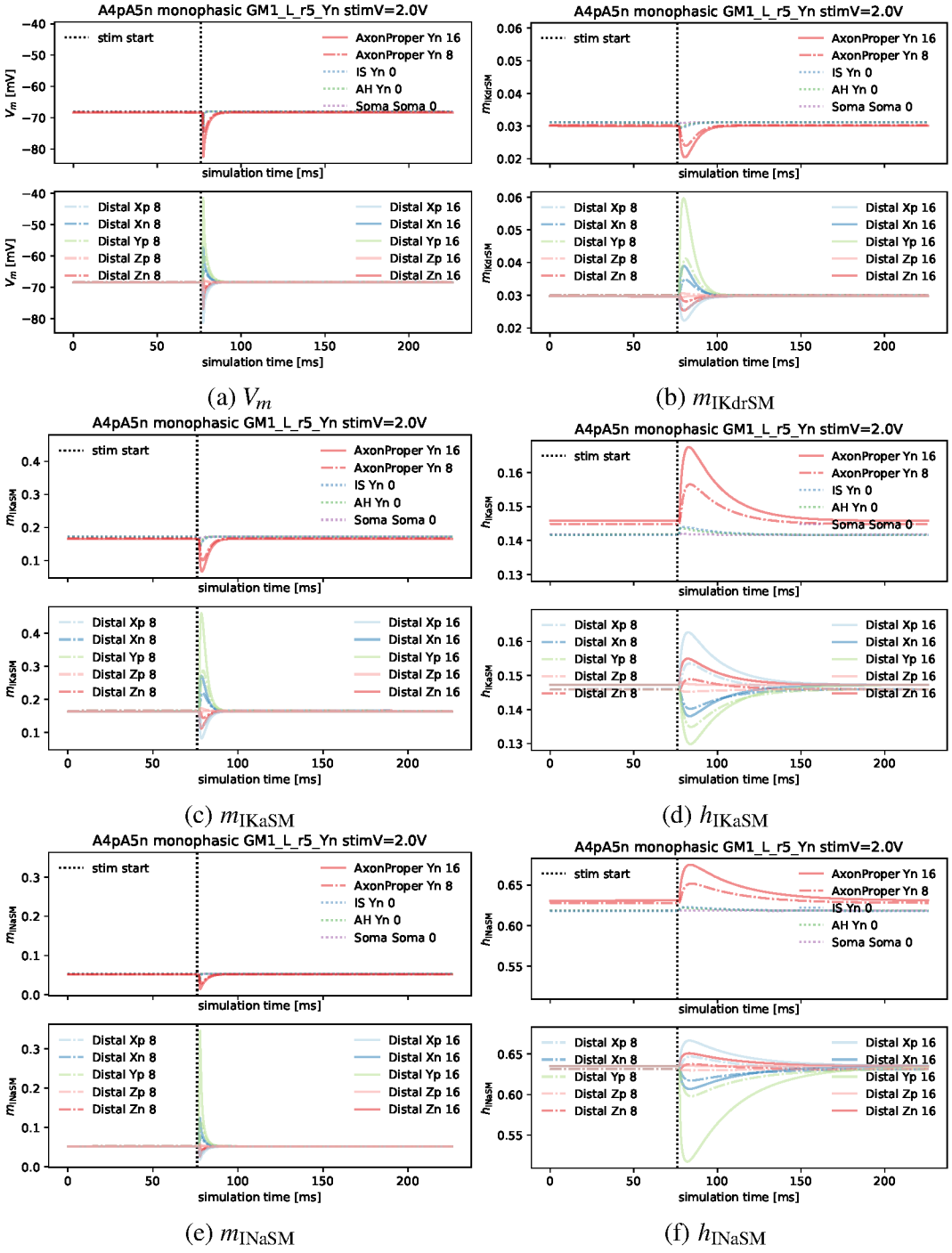


Figure 5.43: Membrane voltage (V_m) (see colormap) at the axon tip (top figure) and at the synapse location (bottom figure) as a function of synapse trigger time (x-axis) and simulation time (y-axis). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic epidural stimulation using stimulating electrode combination A4pA5n while a synaptic input with synapse weight=3.45nS is triggered at varying times on the distal dendrite that points in the $+\hat{x}$ direction at segment 8. The electrical stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. The colormap is white when $V_m = -68.31$ mV (the resting membrane voltage for the distal axon tip) and changes from dark yellow to orange at $V_m = -10$ mV to indicate neuron activation.

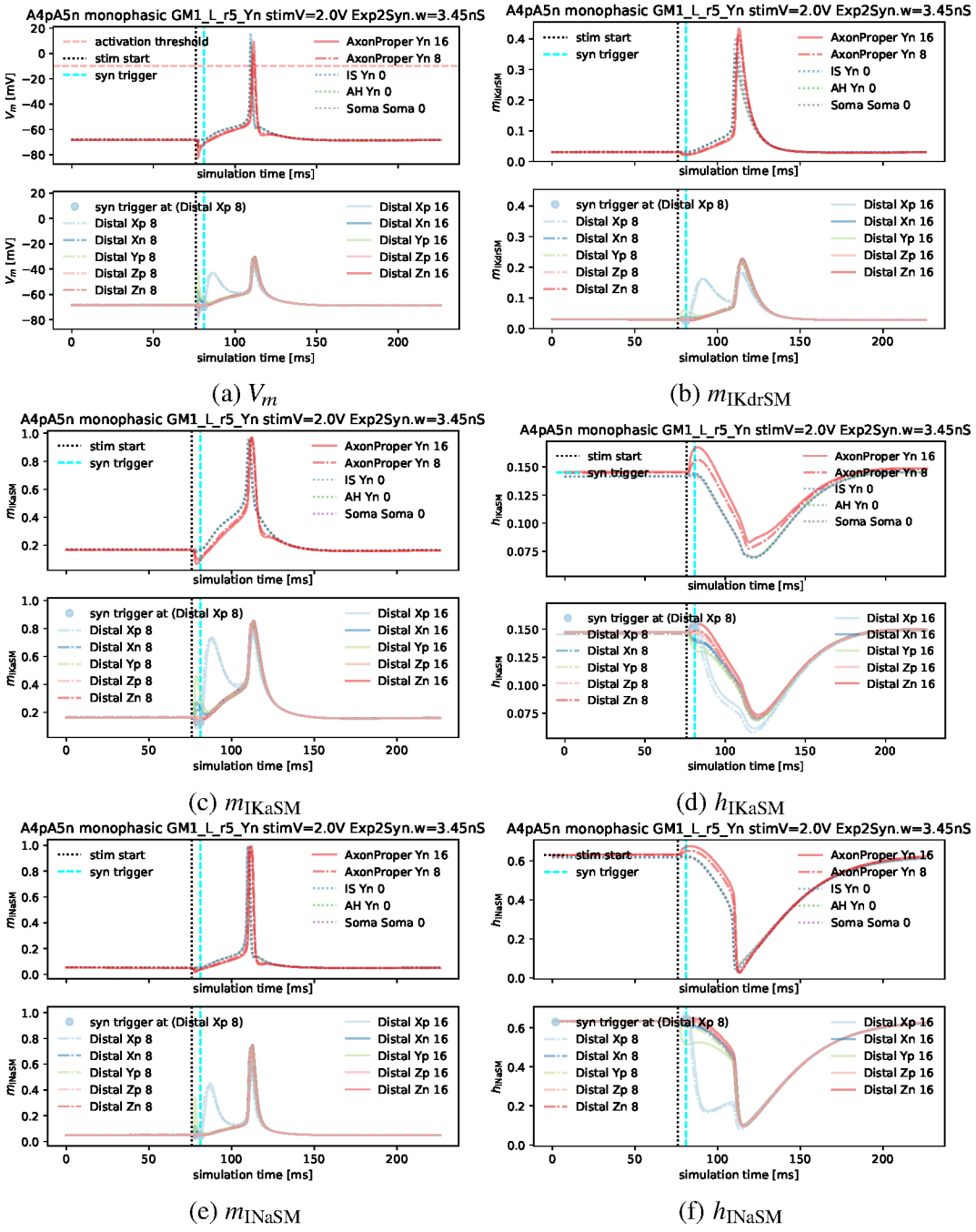


(a) V_m (b) m_{IKdrSM}

(c) m_{IKaSM} (d) h_{IKaSM}

(e) m_{INaSM} (f) h_{INaSM}

Figure 5.44: Stimulation only: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). All data measured using neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms.



(a) V_m

(b) m_{IKdrSM}

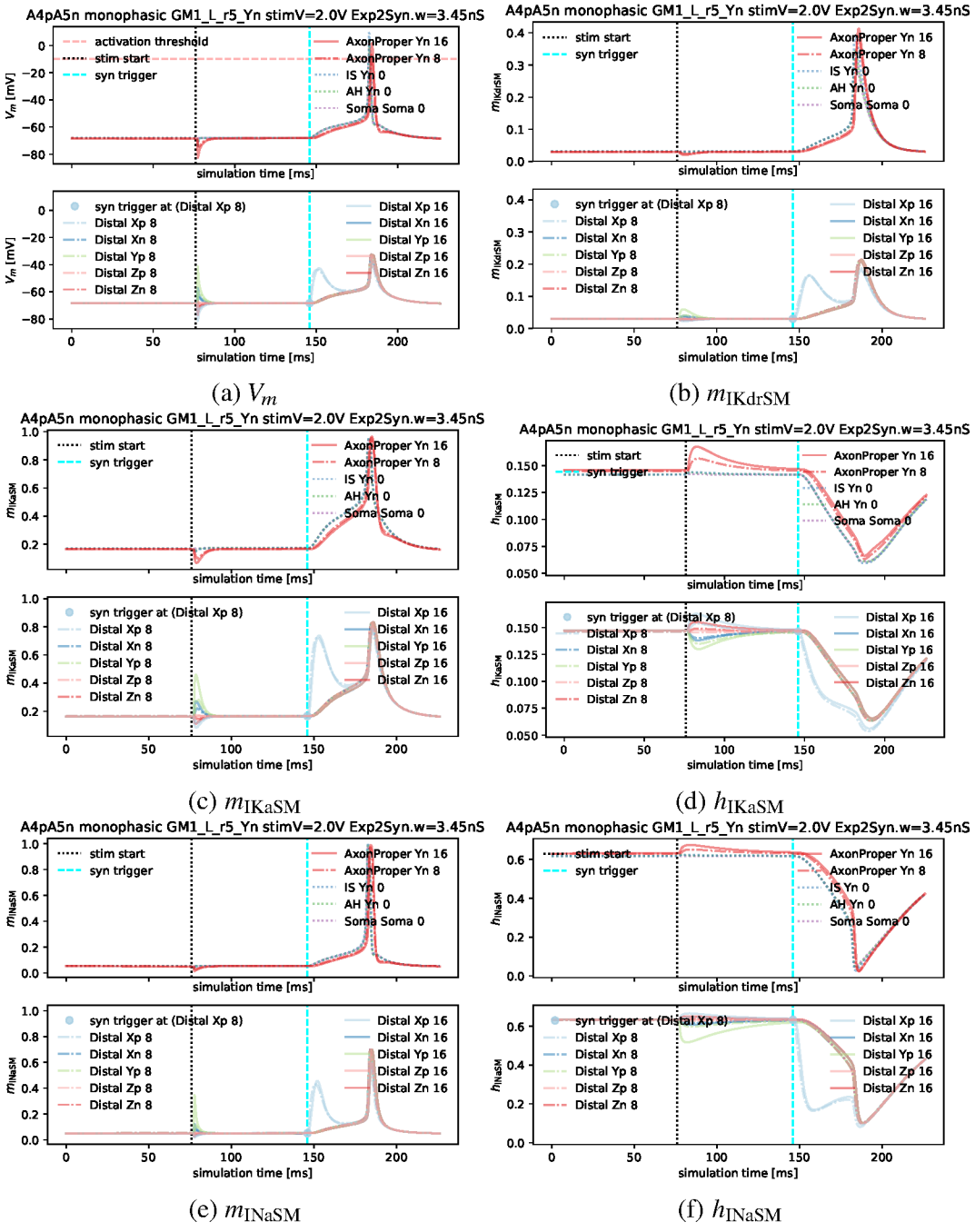
(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.45: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=81.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.



(a) V_m

(b) m_{IKdrSM}

(c) m_{IKaSM}

(d) h_{IKaSM}

(e) m_{INaSM}

(f) h_{INaSM}

Figure 5.46: Stimulation + EPSP: Each subplot plots a different variable ((a) V_m, (b) m_{IKdrSM}, (c) m_{IKaSM}, (d) h_{IKaSM}, (e) m_{INaSM}, and (f) h_{INaSM}) against simulation time (ms) for probes on axon-soma (sub-top) and dendrites (sub-bottom). Measured on neuron GM1_L_r5_Yn exposed to 2.0 V of monophasic stimulation using stimulating electrode combination A4pA5n. The stimulation pulse starts at t=76.0ms and has a maximum amplitude at t=77.13ms. An Exp2Syn synapse was triggered at t=146.0 ms with a synaptic weight of 3.45nS. The synapse was located at segment 8 on the distal dendrite that points in the $+\hat{x}$ direction.

5.C Appendix: Supplementary figures for separating facilitated and non-activated neurons using static features

This appendix contains supplementary figures for Section 5.4.1.

The results of using the best features found in Section 5.4.1 to separate simulations of biphasic stimulation with EPSPs are shown in Figs. 5.47-5.57 and corresponding monophasic stimulation results are displayed in Figs. 5.58-5.68. A summary of these results is available in Table 5.2.

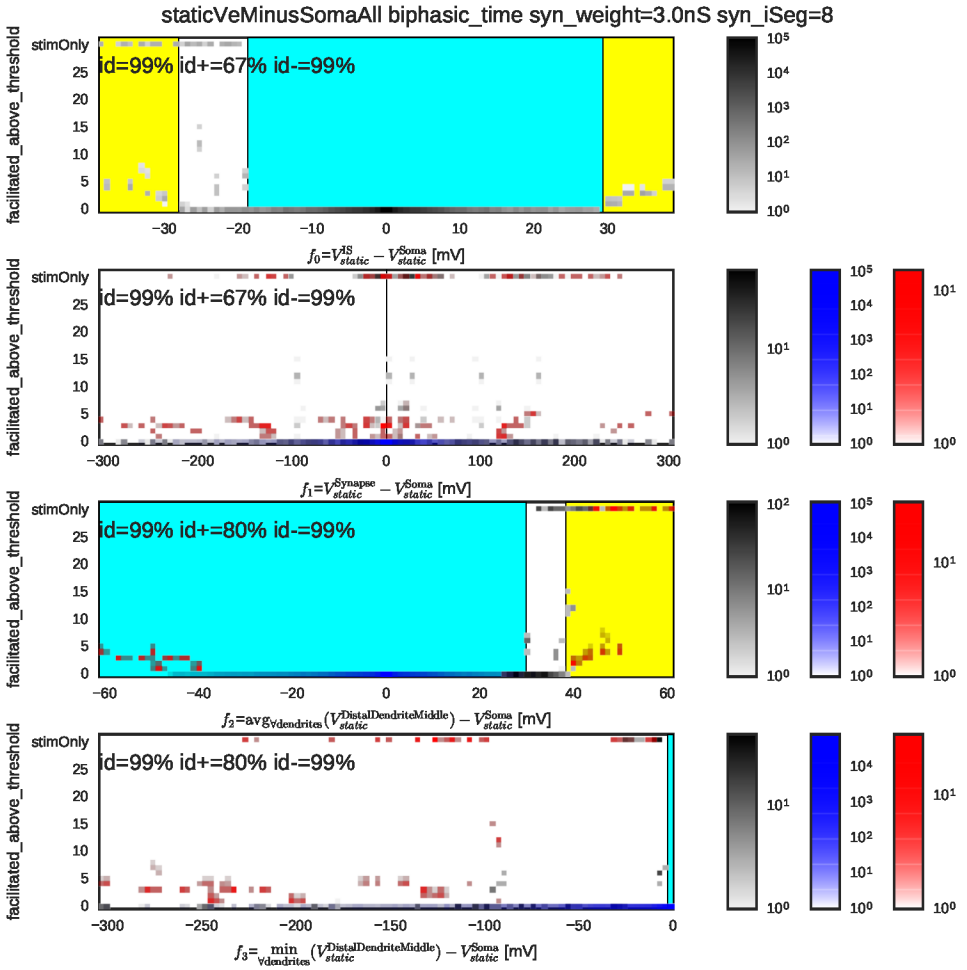


Figure 5.47: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.0 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 537 are facilitated, and 426743 are non-active.

IF (f_0 < −28.08 mV) THEN (T=1) /* 330 samples */
ELIF (−18.75 mV < f_0 < 29.32 mV) THEN (T=0) /* 426115 samples */
ELIF (29.32 mV < f_0) THEN (T=1) /* 300 samples */
ELIF (−0.045 14 mV < f_1 < 0.5408 mV) THEN (T=0) /* 29 samples */
ELIF (f_2 < 29.8 mV) THEN (T=0) /* 272 samples */
ELIF (38.29 mV < f_2) THEN (T=1) /* 125 samples */
ELIF (−3.031 mV < f_3) THEN (T=0) /* 3 samples */
ELSE (T=Unknown) /* 506 samples */

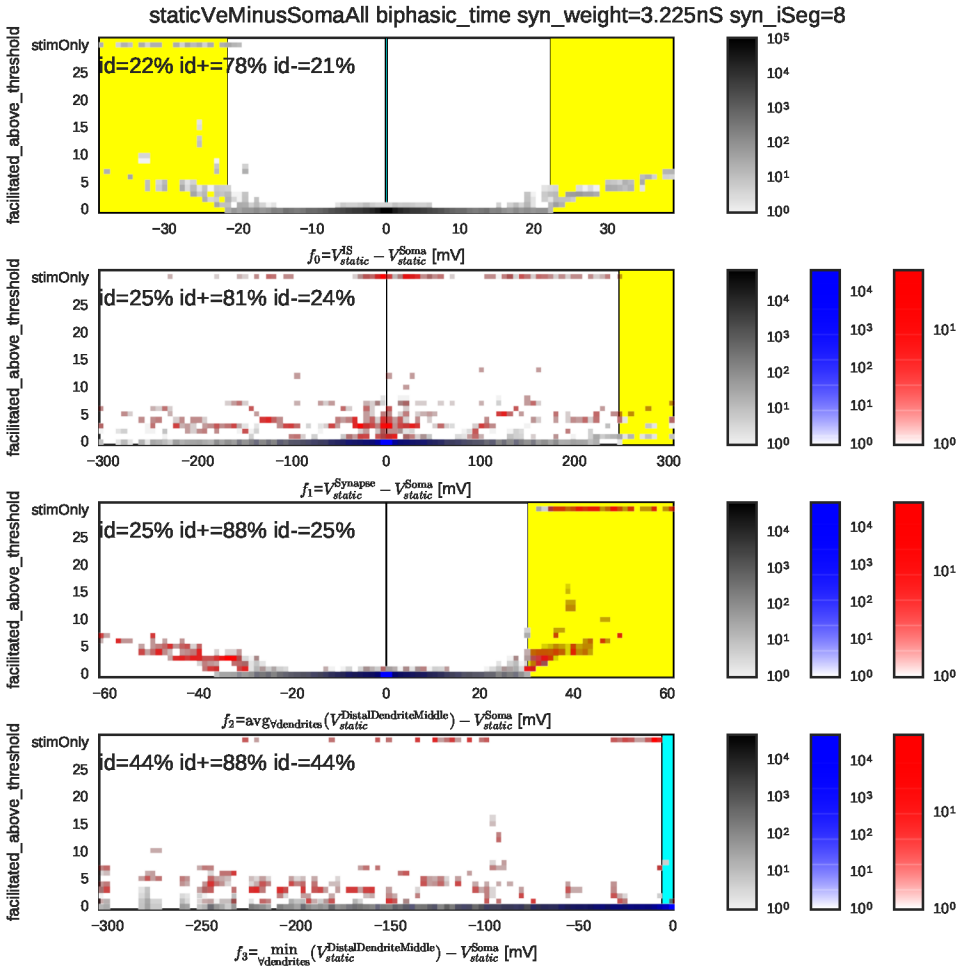


Figure 5.48: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.225 nS using features $f_0 = V^{IS}_{static} - V^{Soma}_{static}$, $f_1 = V^{Synapse}_{static} - V^{Soma}_{static}$, $f_2 = \text{avg}_{\forall dendrites}(V^{DistalDendriteMiddle}_{static}) - V^{Soma}_{static}$, and $f_3 = \text{min}_{\forall dendrites}(V^{DistalDendriteMiddle}_{static}) - V^{Soma}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 1647 are facilitated, and 425633 are non-active.

IF (f_0 < −21.47 mV) THEN (T=1) /* 830 samples */
ELIF (−0.1284 mV < f_0 < 0.1284 mV) THEN (T=0) /* 92790 samples */
ELIF (22.17 mV < f_0) THEN (T=1) /* 775 samples */
ELIF (−0.035 48 mV < f_1 < 0.4075 mV) THEN (T=0) /* 12850 samples */
ELIF (246.6 mV < f_1) THEN (T=1) /* 66 samples */
ELIF (−0.1063 mV < f_2 < 0.022 74 mV) THEN (T=0) /* 1935 samples */
ELIF (30.19 mV < f_2) THEN (T=1) /* 143 samples */
ELIF (−5.949 mV < f_3) THEN (T=0) /* 81810 samples */
ELSE (T=Unknown) /* 236481 samples */

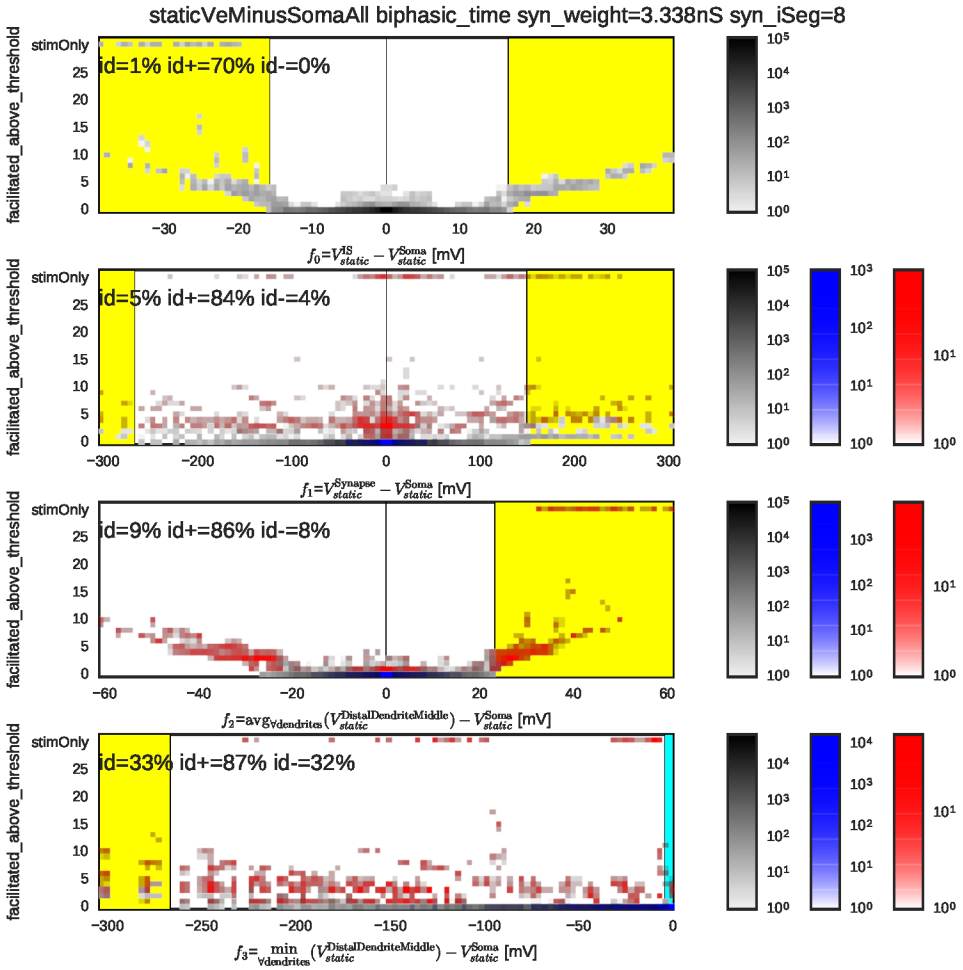


Figure 5.49: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.338 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 4248 are facilitated, and 423032 are non-active.

IF (f_0 < −15.77 mV) THEN (T=1) /* 1690 samples */
ELIF (−0.000 354 2 mV < f_0 < 0.000 354 2 mV) THEN (T=0) /* 2990 samples */
ELIF (16.49 mV < f_0) THEN (T=1) /* 1600 samples */
ELIF (f_1 < −266.9 mV) THEN (T=1) /* 24 samples */
ELIF (−0.047 31 mV < f_1 < 0.047 31 mV) THEN (T=0) /* 14992 samples */
ELIF (148.8 mV < f_1) THEN (T=1) /* 616 samples */
ELIF (−0.022 93 mV < f_2 < 0.018 34 mV) THEN (T=0) /* 17988 samples */
ELIF (23.16 mV < f_2) THEN (T=1) /* 90 samples */
ELIF (f_3 < −266.9 mV) THEN (T=1) /* 58 samples */
ELIF (−4.462 mV < f_3) THEN (T=0) /* 101971 samples */
ELSE (T=Unknown) /* 285661 samples */

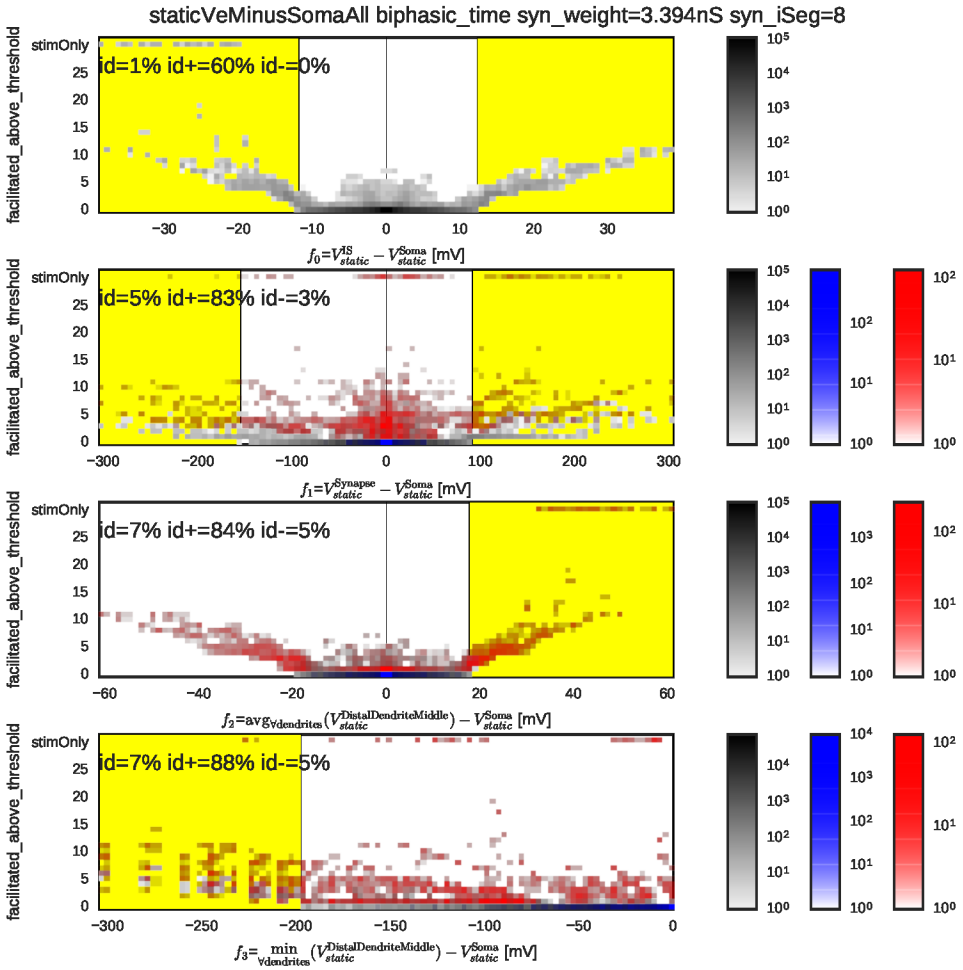


Figure 5.50: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.394 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 9670 are facilitated, and 417610 are non-active.

IF (f_0 < −11.81 mV) THEN (T=1) /* 3160 samples */
ELIF (−0.000 210 2 mV < f_0 < 0.000 210 2 mV) THEN (T=0) /* 2170 samples */
ELIF (12.3 mV < f_0) THEN (T=1) /* 2975 samples */
ELIF (f_1 < −154.5 mV) THEN (T=1) /* 482 samples */
ELIF (−0.035 48 mV < f_1 < 0.035 48 mV) THEN (T=0) /* 13064 samples */
ELIF (91.31 mV < f_1) THEN (T=1) /* 1824 samples */
ELIF (−0.013 76 mV < f_2 < 0.002 251 mV) THEN (T=0) /* 7826 samples */
ELIF (17.67 mV < f_2) THEN (T=1) /* 88 samples */
ELIF (f_3 < −197.3 mV) THEN (T=1) /* 392 samples */
ELIF (−0.000 796 3 mV < f_3 < 0.0155 mV) THEN (T=0) /* 170 samples */
ELSE (T=Unknown) /* 395529 samples */

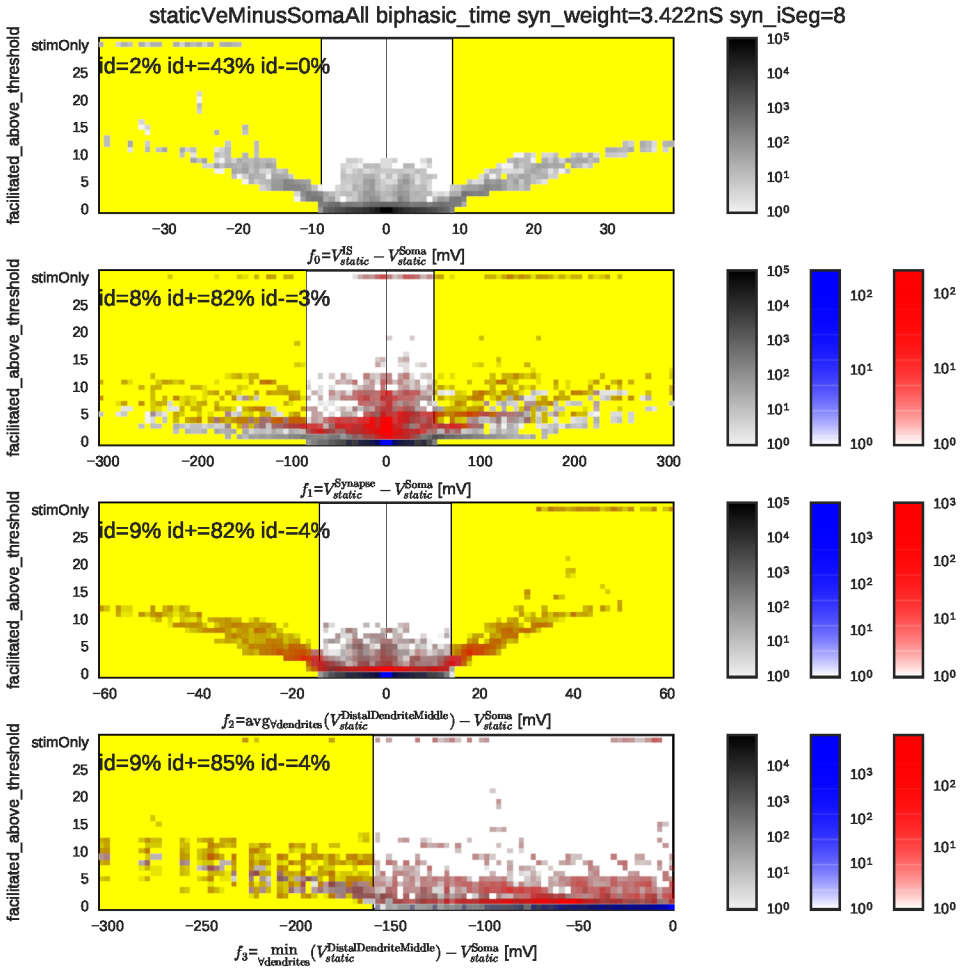


Figure 5.51: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.422 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 24532 are facilitated, and 402748 are non-active.

IF ($f_0 < -8.774$ mV) THEN (T=1) /* 5475 samples */
ELIF (-2.809×10^{-5} mV $< f_0 < 2.809 \times 10^{-5}$ mV) THEN (T=0) /* 620 samples */
ELIF (8.953 mV $< f_0$) THEN (T=1) /* 5285 samples */
ELIF ($f_1 < -84.92$ mV) THEN (T=1) /* 2086 samples */
ELIF (−0.035 48 mV $< f_1 <$ 0.047 31 mV) THEN (T=0) /* 14898 samples */
ELIF (50.4 mV $< f_1$) THEN (T=1) /* 7613 samples */
ELIF ($f_2 < -14.26$ mV) THEN (T=1) /* 39 samples */
ELIF (−0.002 49 mV $< f_2 <$ 0.002 49 mV) THEN (T=0) /* 2941 samples */
ELIF (13.87 mV $< f_2$) THEN (T=1) /* 16 samples */
ELIF ($f_3 < -159.1$ mV) THEN (T=1) /* 792 samples */
ELIF (−0.000 481 2 mV $< f_3 <$ 0.000 711 5 mV) THEN (T=0) /* 66 samples */
ELSE (T=Unknown) /* 387849 samples */

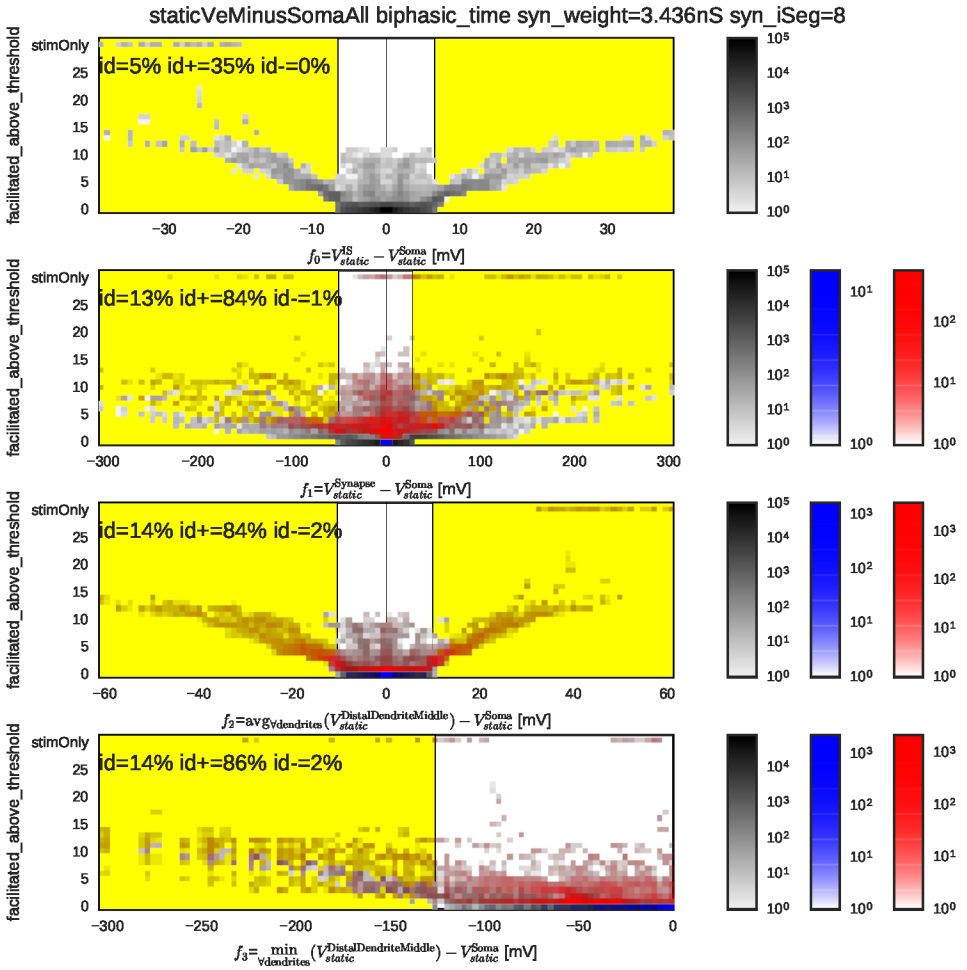


Figure 5.52: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.436 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \text{min}_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 62471 are facilitated, and 364809 are non-active.

IF (f_0 < −6.521 mV) THEN (T=1) /* 11095 samples */
ELIF (−4.193 × 10^{-7} mV < f_0 < 4.193 × 10^{-7} mV) THEN (T=0) /* 40 samples */
ELIF (6.521 mV < f_0) THEN (T=1) /* 11095 samples */
ELIF (f_1 < −50.57 mV) THEN (T=1) /* 6487 samples */
ELIF (−0.004 668 mV < f_1 < 0.004 668 mV) THEN (T=0) /* 4788 samples */
ELIF (27.75 mV < f_1) THEN (T=1) /* 24361 samples */
ELIF (f_2 < −10.48 mV) THEN (T=1) /* 39 samples */
ELIF (−0.001 801 mV < f_2 < 0.002 49 mV) THEN (T=0) /* 3306 samples */
ELIF (9.894 mV < f_2) THEN (T=1) /* 114 samples */
ELIF (f_3 < −126.2 mV) THEN (T=1) /* 1288 samples */
ELIF (−0.000 881 3 mV < f_3) THEN (T=0) /* 249 samples */
ELSE (T=Unknown) /* 364818 samples */

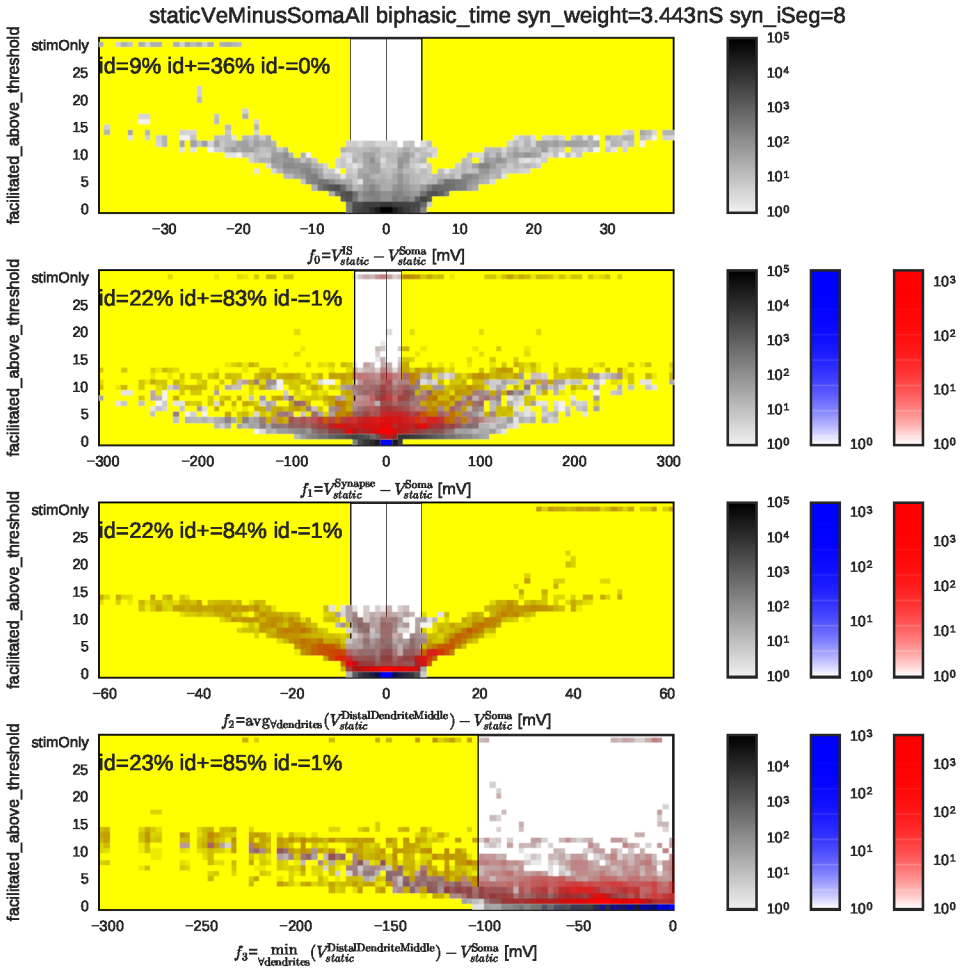


Figure 5.53: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.443 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 110804 are facilitated, and 316476 are non-active.

IF (f_0 < −4.844 mV) THEN (T=1) /* 20460 samples */
ELIF (−1.797 × 10^{-7} mV < f_0 < 1.797 × 10^{-7} mV) THEN (T=0) /* 20 samples */
ELIF (4.823 mV < f_0) THEN (T=1) /* 20600 samples */
ELIF (f_1 < −33.67 mV) THEN (T=1) /* 14472 samples */
ELIF (−0.003 747 mV < f_1 < 0.003 747 mV) THEN (T=0) /* 4186 samples */
ELIF (16.35 mV < f_1) THEN (T=1) /* 37812 samples */
ELIF (f_2 < −7.604 mV) THEN (T=1) /* 59 samples */
ELIF (−0.000 267 9 mV < f_2 < 0.000 267 9 mV) THEN (T=0) /* 396 samples */
ELIF (7.523 mV < f_2) THEN (T=1) /* 89 samples */
ELIF (f_3 < −103.6 mV) THEN (T=1) /* 1476 samples */
ELIF (−0.000 140 4 mV < f_3 < 0.000 202 9 mV) THEN (T=0) /* 20 samples */
ELSE (T=Unknown) /* 328090 samples */

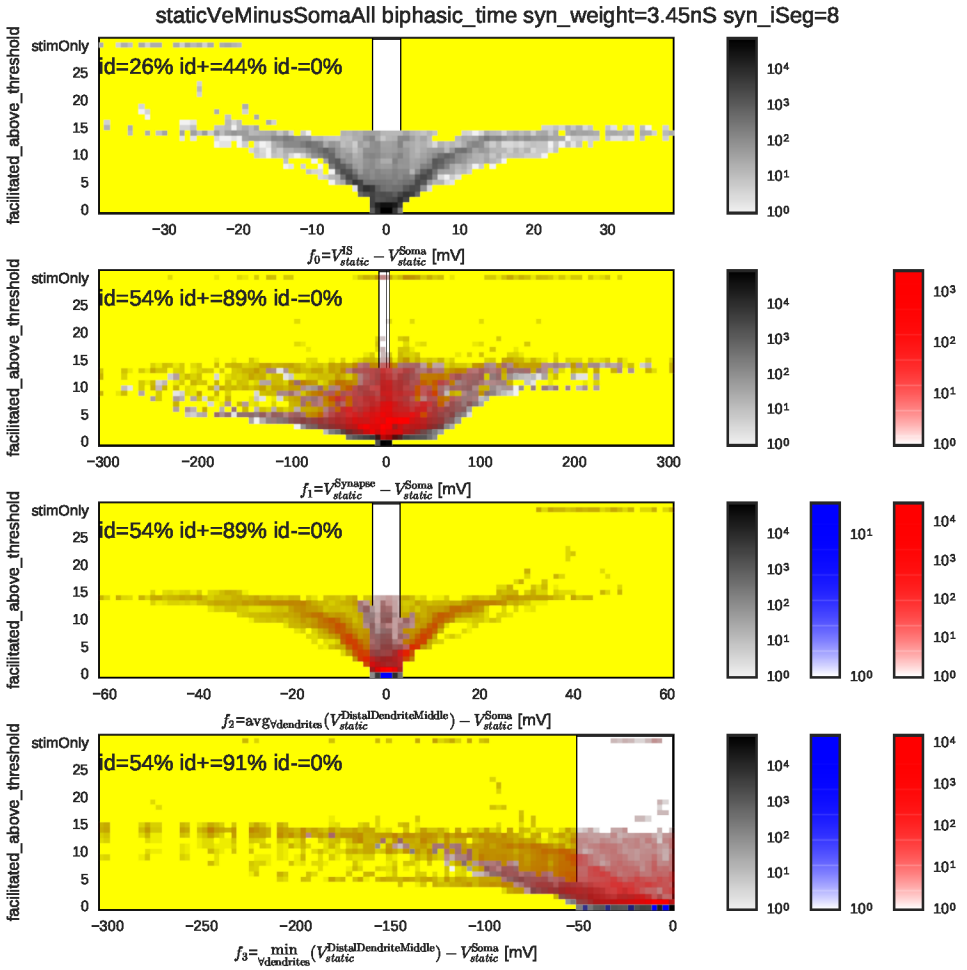


Figure 5.54: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.45 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 257472 are facilitated, and 169808 are non-active.

IF ($f_0 < -1.848$ mV) THEN (T=1) /* 57880 samples */
ELIF (1.921 mV $< f_0$) THEN (T=1) /* 56210 samples */
ELIF ($f_1 < -7.948$ mV) THEN (T=1) /* 41784 samples */
ELIF (-1.038×10^{-6} mV $< f_1 < 1.038 \times 10^{-6}$ mV) THEN (T=0) /* 38 samples */
ELIF (3.337 mV $< f_1$) THEN (T=1) /* 75768 samples */
ELIF ($f_2 < -2.894$ mV) THEN (T=1) /* 182 samples */
ELIF (2.895 mV $< f_2$) THEN (T=1) /* 86 samples */
ELIF ($f_3 < -51.15$ mV) THEN (T=1) /* 2905 samples */
ELIF ($-0.000\,634\,3$ mV $< f_3$) THEN (T=0) /* 223 samples */
ELSE (T=Unknown) /* 192604 samples */

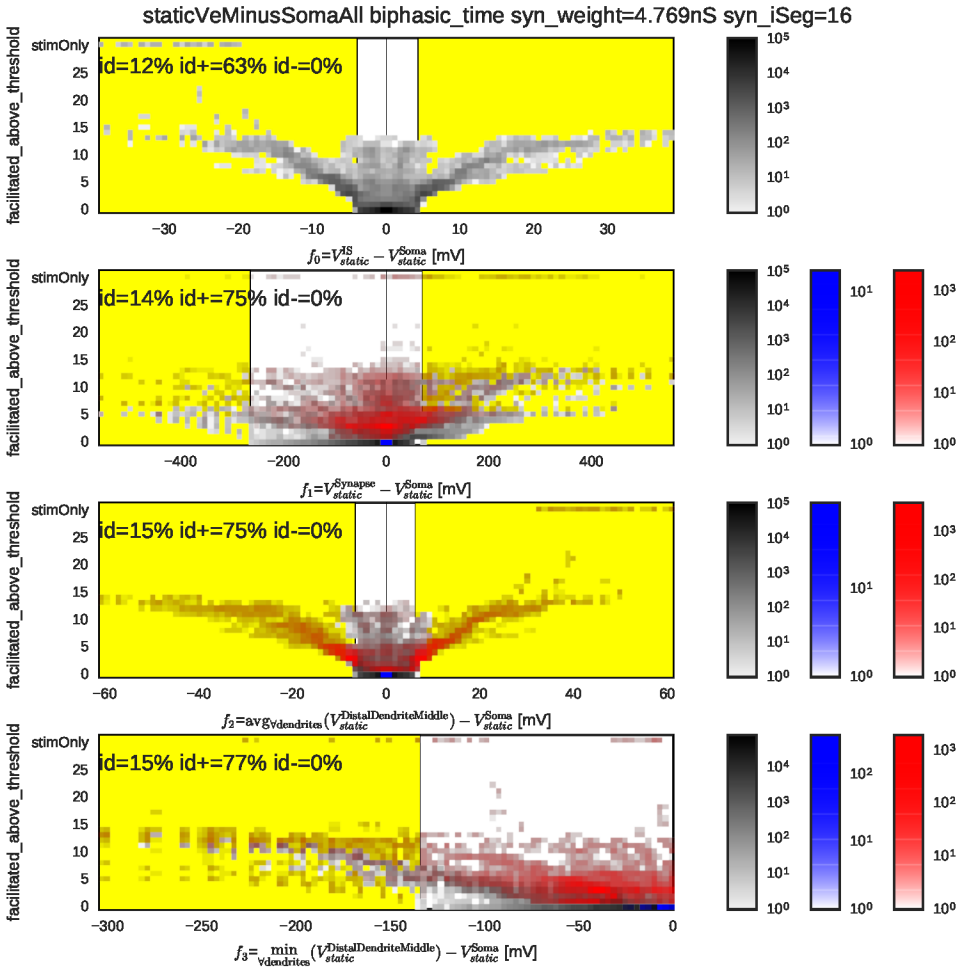


Figure 5.55: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.769 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 82986 are facilitated, and 344294 are non-active.

IF (f_0 < −3.96 mV) THEN (T=1) /* 28110 samples */
ELIF (−4.193 × 10^{-7} mV < f_0 < 4.193 × 10^{-7} mV) THEN (T=0) /* 40 samples */
ELIF (4.294 mV < f_0) THEN (T=1) /* 24770 samples */
ELIF (f_1 < −265 mV) THEN (T=1) /* 404 samples */
ELIF (−0.000 174 9 mV < f_1 < 0.000 174 9 mV) THEN (T=0) /* 178 samples */
ELIF (69.75 mV < f_1) THEN (T=1) /* 9522 samples */
ELIF (f_2 < −6.581 mV) THEN (T=1) /* 223 samples */
ELIF (−0.000 459 6 mV < f_2 < 0.000 459 6 mV) THEN (T=0) /* 1088 samples */
ELIF (6.126 mV < f_2) THEN (T=1) /* 183 samples */
ELIF (f_3 < −134.2 mV) THEN (T=1) /* 1279 samples */
ELIF (−0.000 881 3 mV < f_3) THEN (T=0) /* 491 samples */
ELSE (T=Unknown) /* 361392 samples */

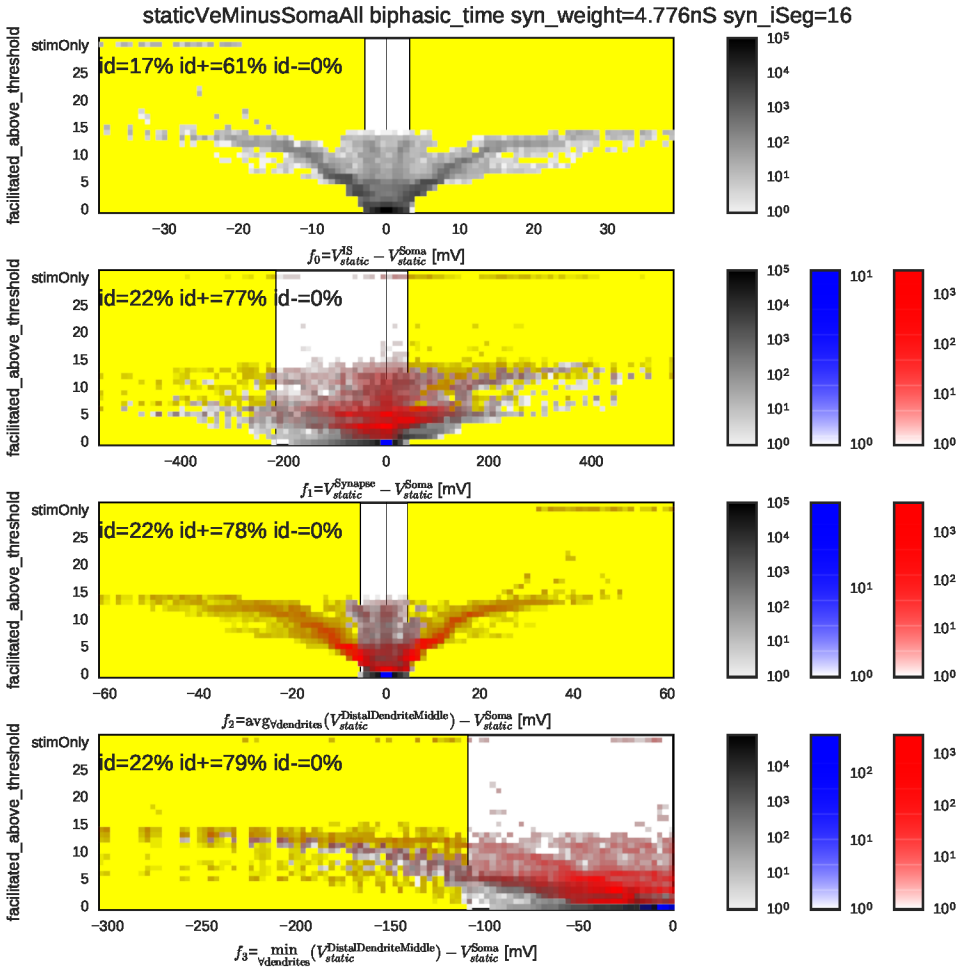


Figure 5.56: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.776 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \text{min}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 120616 are facilitated, and 306664 are non-active.

IF (f_0 < −2.916 mV) THEN (T=1) /* 38670 samples */
ELIF (−2.995 × 10^{-7} mV < f_0 < 2.995 × 10^{-7} mV) THEN (T=0) /* 30 samples */
ELIF (3.136 mV < f_0) THEN (T=1) /* 35855 samples */
ELIF (f_1 < −214.6 mV) THEN (T=1) /* 637 samples */
ELIF (−0.000 189 1 mV < f_1 < 0.000 189 1 mV) THEN (T=0) /* 186 samples */
ELIF (41.85 mV < f_1) THEN (T=1) /* 19211 samples */
ELIF (f_2 < −5.537 mV) THEN (T=1) /* 111 samples */
ELIF (−0.000 404 8 mV < f_2 < 0.000 404 8 mV) THEN (T=0) /* 952 samples */
ELIF (4.493 mV < f_2) THEN (T=1) /* 479 samples */
ELIF (f_3 < −109 mV) THEN (T=1) /* 1493 samples */
ELIF (−0.000 140 4 mV < f_3 < 0.003 868 mV) THEN (T=0) /* 223 samples */
ELSE (T=Unknown) /* 329833 samples */

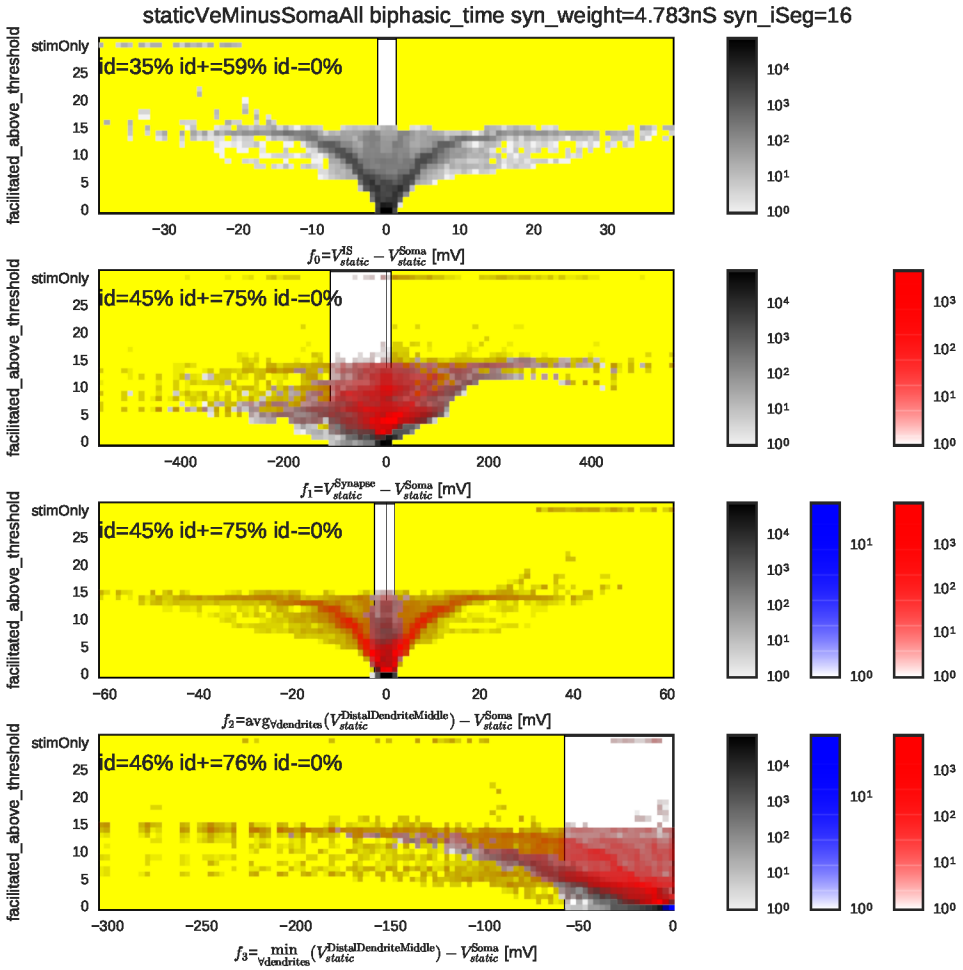


Figure 5.57: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.783 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 256925 are facilitated, and 170355 are non-active.

IF ($f_0 < -1.142$ mV) THEN (T=1) /* 80350 samples */
ELIF (1.354 mV $< f_0$) THEN (T=1) /* 72055 samples */
ELIF ($f_1 < -108.8$ mV) THEN (T=1) /* 1203 samples */
ELIF (-3.725×10^{-5} mV $< f_1 < 3.725 \times 10^{-5}$ mV) THEN (T=0) /* 42 samples */
ELIF (9.507 mV $< f_1$) THEN (T=1) /* 40467 samples */
ELIF ($f_2 < -2.521$ mV) THEN (T=1) /* 113 samples */
ELIF (-6.694×10^{-5} mV $< f_2 < 6.694 \times 10^{-5}$ mV) THEN (T=0) /* 46 samples */
ELIF (1.789 mV $< f_2$) THEN (T=1) /* 455 samples */
ELIF ($f_3 < -57.61$ mV) THEN (T=1) /* 2912 samples */
ELSE (T=Unknown) /* 230037 samples */

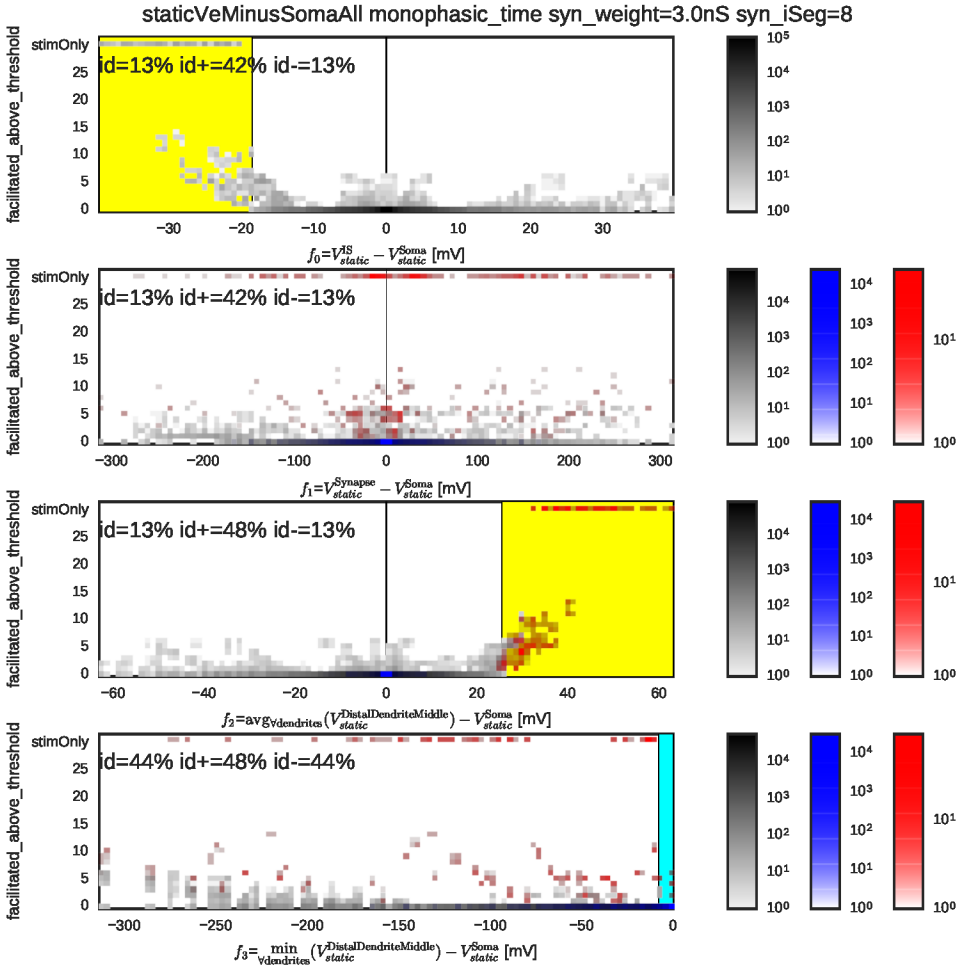


Figure 5.58: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.0 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 2562 are facilitated, and 424473 are non-active.

IF (f_0 < −18.55 mV) THEN (T=1) /* 1355 samples */
ELIF (−0.074 81 mV < f_0 < 0.0561 mV) THEN (T=0) /* 56200 samples */
ELIF (−0.002 051 mV < f_1 < 0.002 051 mV) THEN (T=0) /* 1276 samples */
ELIF (−0.061 48 mV < f_2 < 0.041 36 mV) THEN (T=0) /* 390 samples */
ELIF (25.42 mV < f_2) THEN (T=1) /* 210 samples */
ELIF (−7.963 mV < f_3) THEN (T=0) /* 131049 samples */
ELSE (T=Unknown) /* 237200 samples */

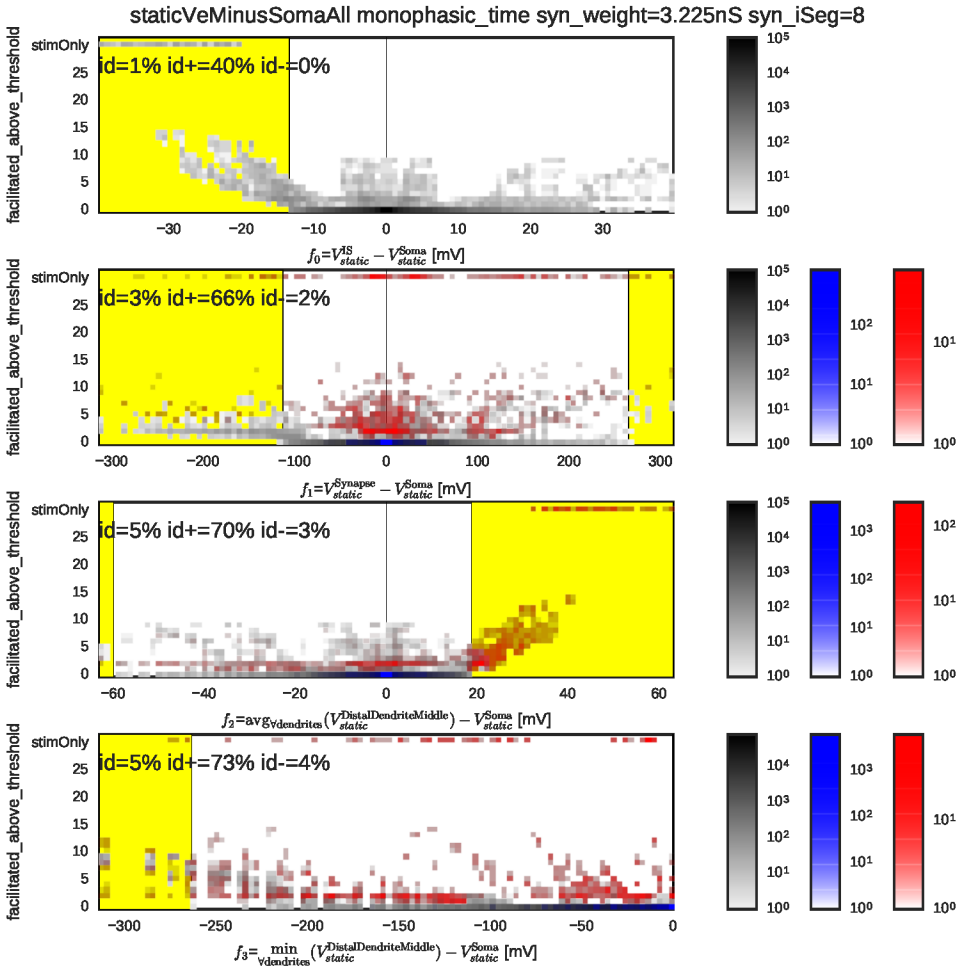


Figure 5.59: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.225 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 6522 are facilitated, and 420513 are non-active.

IF (f_0 < −13.4 mV) THEN (T=1) /* 2870 samples */
ELIF (−0.000 301 1 mV < f_0 < 0.000 301 1 mV) THEN (T=0) /* 2510 samples */
ELIF (f_1 < −113.1 mV) THEN (T=1) /* 1836 samples */
ELIF (−0.019 84 mV < f_1 < 0.019 84 mV) THEN (T=0) /* 8320 samples */
ELIF (264.6 mV < f_1) THEN (T=1) /* 45 samples */
ELIF (f_2 < −59.92 mV) THEN (T=1) /* 15 samples */
ELIF (−0.007 248 mV < f_2 < 0.007 248 mV) THEN (T=0) /* 5848 samples */
ELIF (18.73 mV < f_2) THEN (T=1) /* 274 samples */
ELIF (f_3 < −263.2 mV) THEN (T=1) /* 196 samples */
ELIF (−0.097 63 mV < f_3) THEN (T=0) /* 2157 samples */
ELSE (T=Unknown) /* 403609 samples */

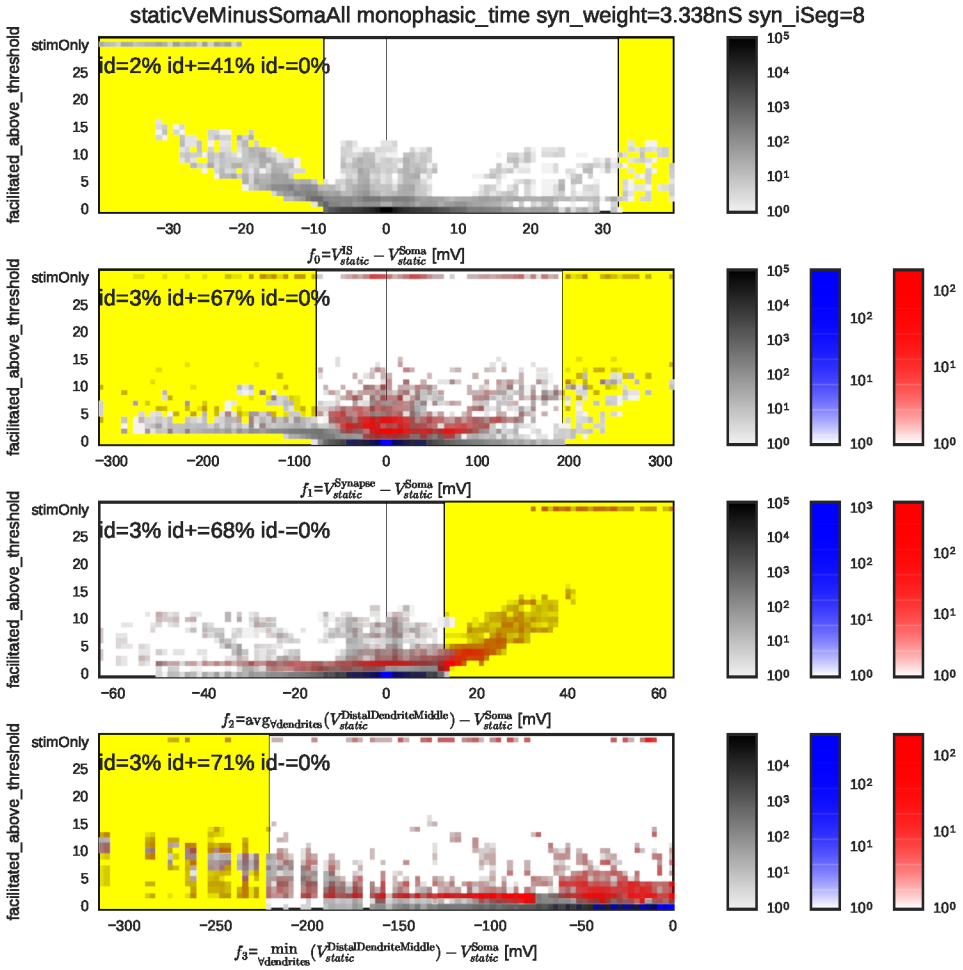


Figure 5.60: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.338 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 16246 are facilitated, and 410789 are non-active.

IF (f_0 < −8.645 mV) THEN (T=1) /* 6745 samples */
ELIF (−0.000 150 6 mV < f_0 < 0.000 150 6 mV) THEN (T=0) /* 1760 samples */
ELIF (32.04 mV < f_0) THEN (T=1) /* 200 samples */
ELIF (f_1 < −76.77 mV) THEN (T=1) /* 4177 samples */
ELIF (−0.001 207 mV < f_1 < 0.001 207 mV) THEN (T=0) /* 1582 samples */
ELIF (192.5 mV < f_1) THEN (T=1) /* 317 samples */
ELIF (−0.000 236 4 mV < f_2 < 0.000 236 4 mV) THEN (T=0) /* 258 samples */
ELIF (12.69 mV < f_2) THEN (T=1) /* 141 samples */
ELIF (f_3 < −220.9 mV) THEN (T=1) /* 474 samples */
ELIF (−0.001 754 mV < f_3 < 0.001 632 mV) THEN (T=0) /* 288 samples */
ELSE (T=Unknown) /* 411738 samples */

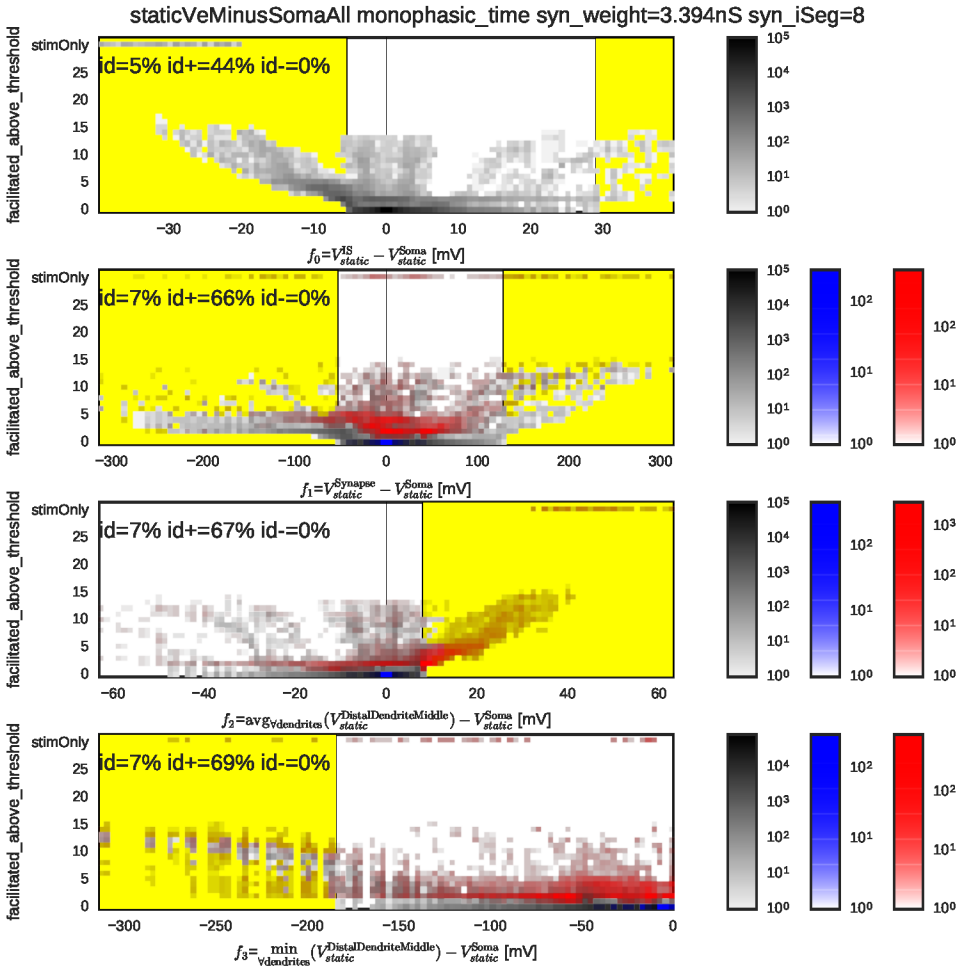


Figure 5.61: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.394 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 46322 are facilitated, and 380713 are non-active.

IF ($f_0 < -5.424$ mV) THEN (T=1) /* 20355 samples */
ELIF (-4.263×10^{-5} mV $< f_0 < 4.263 \times 10^{-5}$ mV) THEN (T=0) /* 780 samples */
ELIF (28.91 mV $< f_0$) THEN (T=1) /* 325 samples */
ELIF ($f_1 < -52.6$ mV) THEN (T=1) /* 9370 samples */
ELIF ($-0.000\,113\,1$ mV $< f_1 < 0.000\,113\,1$ mV) THEN (T=0) /* 266 samples */
ELIF (127.6 mV $< f_1$) THEN (T=1) /* 972 samples */
ELIF ($-0.000\,116\,6$ mV $< f_2 < 0.000\,116\,6$ mV) THEN (T=0) /* 172 samples */
ELIF (7.952 mV $< f_2$) THEN (T=1) /* 457 samples */
ELIF ($f_3 < -184.1$ mV) THEN (T=1) /* 953 samples */
ELIF ($-0.000\,265\,3$ mV $< f_3 < 0.000\,347\,5$ mV) THEN (T=0) /* 147 samples */
ELSE (T=Unknown) /* 393883 samples */

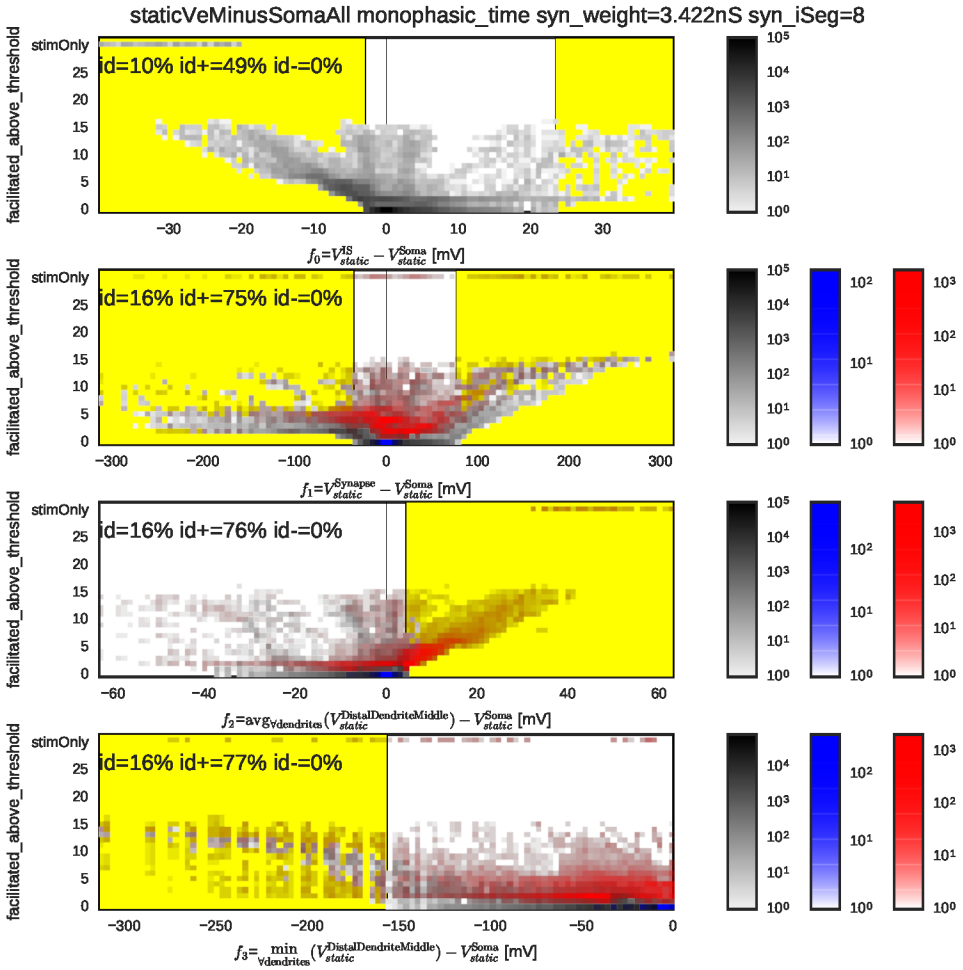


Figure 5.62: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.422 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 87686 are facilitated, and 339349 are non-active.

IF ($f_0 < -2.88$ mV) THEN (T=1) /* 43085 samples */
ELIF (-1.937×10^{-5} mV $< f_0 < 1.937 \times 10^{-5}$ mV) THEN (T=0) /* 370 samples */
ELIF (23.34 mV $< f_0$) THEN (T=1) /* 755 samples */
ELIF ($f_1 < -35.16$ mV) THEN (T=1) /* 20543 samples */
ELIF ($-0.000\,584\,4$ mV $< f_1 < 0.000\,584\,4$ mV) THEN (T=0) /* 1100 samples */
ELIF (76.18 mV $< f_1$) THEN (T=1) /* 2626 samples */
ELIF (-5.332×10^{-5} mV $< f_2 < 5.332 \times 10^{-5}$ mV) THEN (T=0) /* 70 samples */
ELIF (4.31 mV $< f_2$) THEN (T=1) /* 565 samples */
ELIF ($f_3 < -156.4$ mV) THEN (T=1) /* 900 samples */
ELIF ($-0.000\,552\,6$ mV $< f_3$) THEN (T=0) /* 227 samples */
ELSE (T=Unknown) /* 357439 samples */

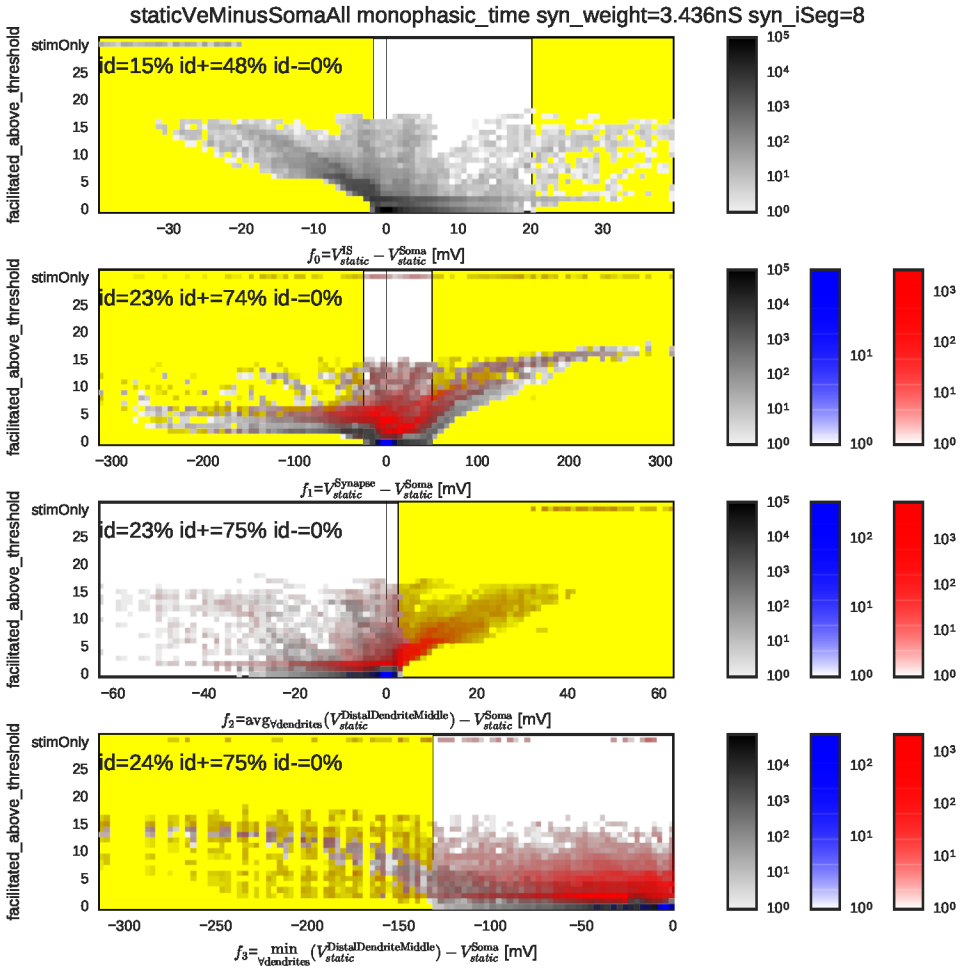


Figure 5.63: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.436 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 133965 are facilitated, and 293070 are non-active.

IF ($f_0 < -1.776$ mV) THEN (T=1) /* 64145 samples */
ELIF (-1.268×10^{-5} mV $< f_0 < 1.268 \times 10^{-5}$ mV) THEN (T=0) /* 230 samples */
ELIF (20.14 mV $< f_0$) THEN (T=1) /* 1095 samples */
ELIF ($f_1 < -24.89$ mV) THEN (T=1) /* 28472 samples */
ELIF ($-0.000\,239$ mV $< f_1 < 0.000\,239$ mV) THEN (T=0) /* 578 samples */
ELIF (49.9 mV $< f_1$) THEN (T=1) /* 6178 samples */
ELIF (-4.675×10^{-5} mV $< f_2 < 4.675 \times 10^{-5}$ mV) THEN (T=0) /* 66 samples */
ELIF (2.565 mV $< f_2$) THEN (T=1) /* 1146 samples */
ELIF ($f_3 < -131.3$ mV) THEN (T=1) /* 993 samples */
ELIF ($-0.000\,926$ mV $< f_3 < 0.001\,075$ mV) THEN (T=0) /* 157 samples */
ELSE (T=Unknown) /* 324620 samples */

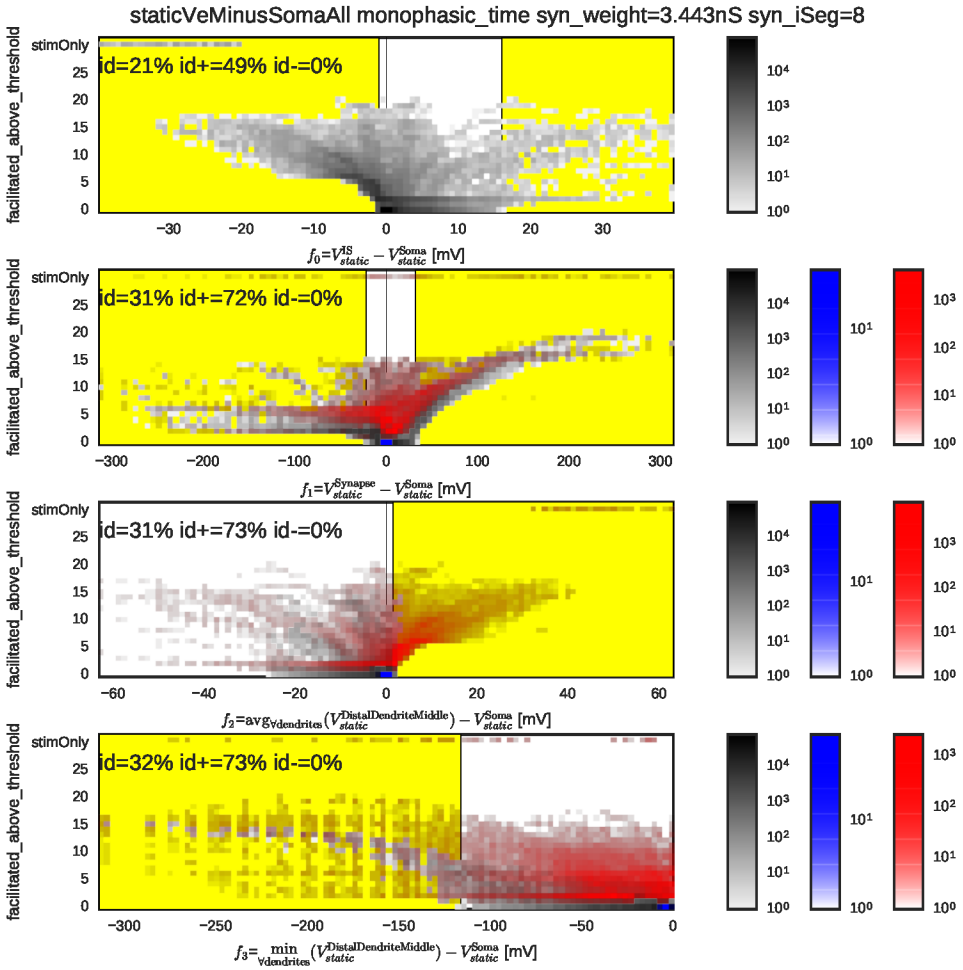


Figure 5.64: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.443 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 185287 are facilitated, and 241748 are non-active.

IF ($f_0 < -1.028$ mV) THEN (T=1) /* 90650 samples */
ELIF (-6.339×10^{-6} mV $< f_0 < 6.339 \times 10^{-6}$ mV) THEN (T=0) /* 70 samples */
ELIF (15.96 mV $< f_0$) THEN (T=1) /* 1830 samples */
ELIF ($f_1 < -22.01$ mV) THEN (T=1) /* 28829 samples */
ELIF (-1.885×10^{-5} mV $< f_1 < 1.885 \times 10^{-5}$ mV) THEN (T=0) /* 88 samples */
ELIF (31.85 mV $< f_1$) THEN (T=1) /* 14065 samples */
ELIF (-2.666×10^{-5} mV $< f_2 < 2.666 \times 10^{-5}$ mV) THEN (T=0) /* 40 samples */
ELIF (1.484 mV $< f_2$) THEN (T=1) /* 1101 samples */
ELIF ($f_3 < -116.2$ mV) THEN (T=1) /* 1079 samples */
ELIF (-3.4×10^{-5} mV $< f_3 < 5.135 \times 10^{-5}$ mV) THEN (T=0) /* 17 samples */
ELSE (T=Unknown) /* 289911 samples */

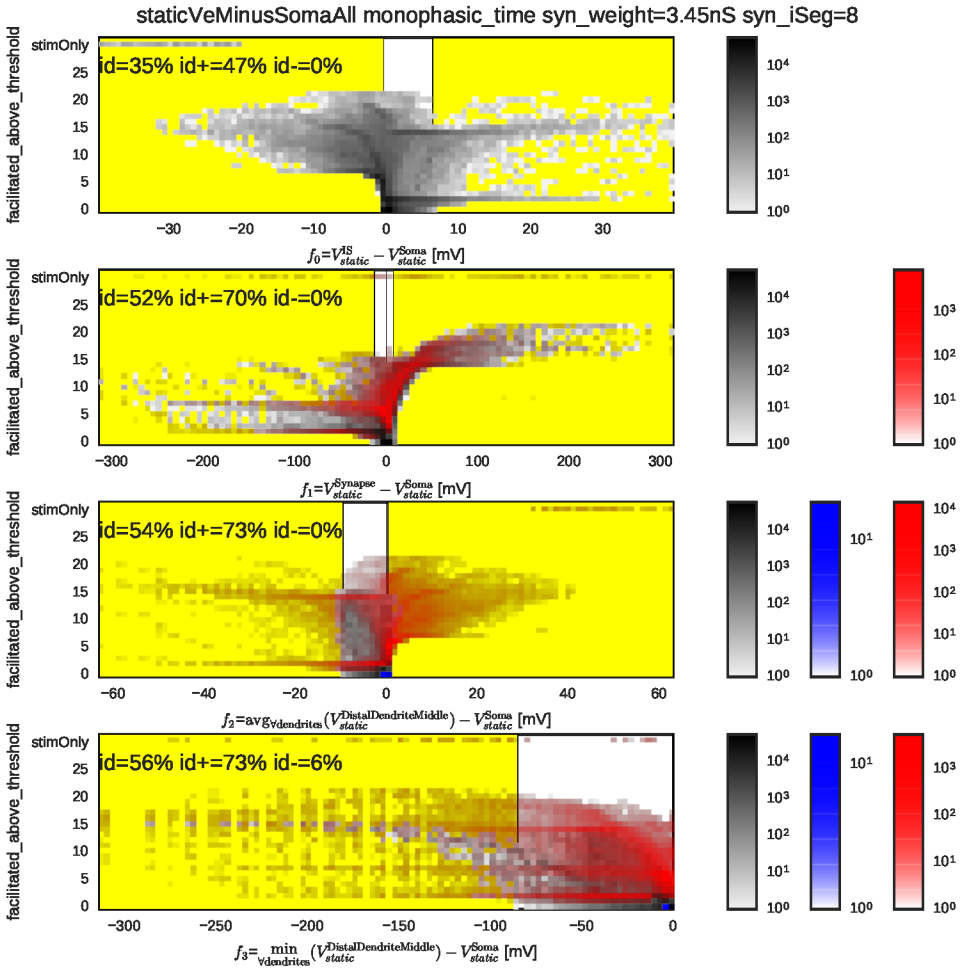


Figure 5.65: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.45 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 319226 are facilitated, and 107809 are non-active.

IF (f_0 < −0.355 mV) THEN (T=1) /* 139035 samples */
ELIF (6.437 mV < f_0) THEN (T=1) /* 13775 samples */
ELIF (f_1 < −12.83 mV) THEN (T=1) /* 35623 samples */
ELIF (-7.299×10^{-6} mV < f_1 < 7.299×10^{-6} mV) THEN (T=0) /* 40 samples */
ELIF (7.584 mV < f_1) THEN (T=1) /* 37256 samples */
ELIF (f_2 < −9.452 mV) THEN (T=1) /* 87 samples */
ELIF (-1.293×10^{-5} mV < f_2 < 1.293×10^{-5} mV) THEN (T=0) /* 10 samples */
ELIF (0.3935 mV < f_2) THEN (T=1) /* 8296 samples */
ELIF (f_3 < −84.92 mV) THEN (T=1) /* 962 samples */
ELIF (−0.238 mV < f_3) THEN (T=0) /* 7175 samples */
ELSE (T=Unknown) /* 185421 samples */

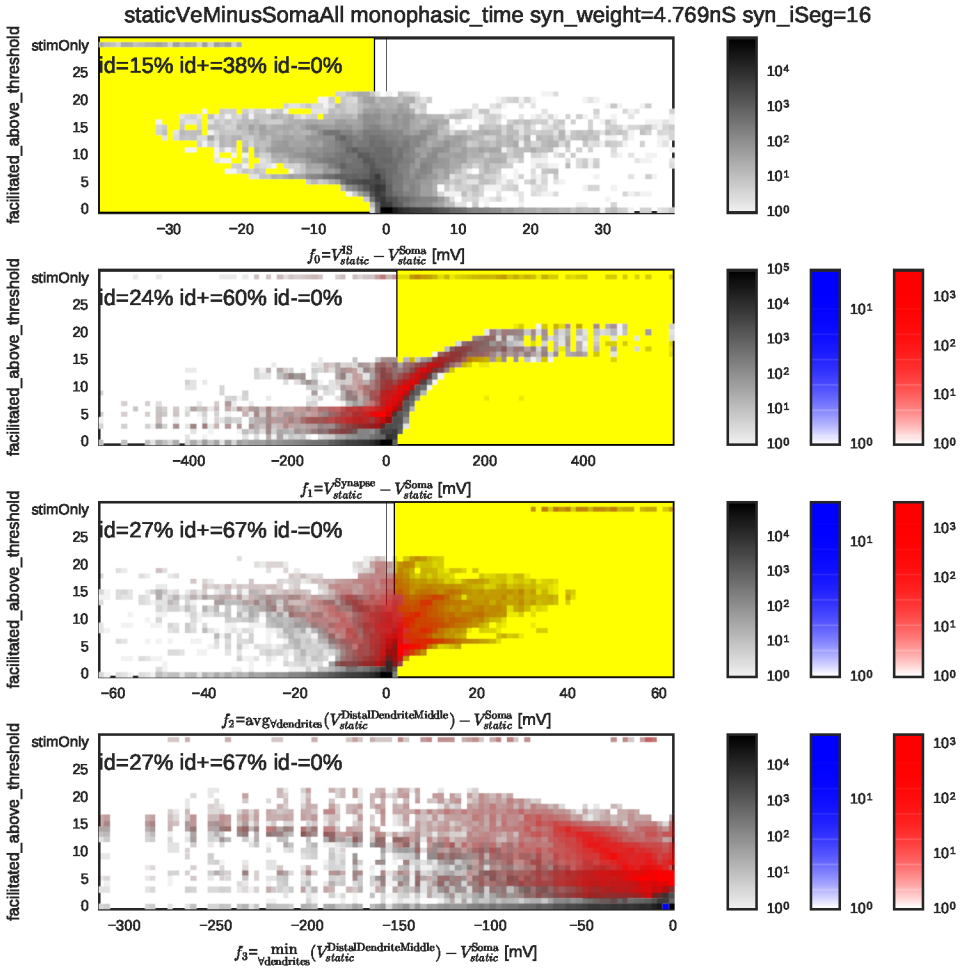


Figure 5.66: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.769 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 176092 are facilitated, and 250943 are non-active.

IF ($f_0 < -1.649$ mV) THEN (T=1) /* 67650 samples */
ELIF (-5.329×10^{-6} mV $< f_0 < 5.329 \times 10^{-6}$ mV) THEN (T=0) /* 40 samples */
ELIF (21.64 mV $< f_1$) THEN (T=1) /* 38439 samples */
ELIF (-1.293×10^{-5} mV $< f_2 < 1.293 \times 10^{-5}$ mV) THEN (T=0) /* 10 samples */
ELIF (1.729 mV $< f_2$) THEN (T=1) /* 13201 samples */
ELSE (T=Unknown) /* 308340 samples */

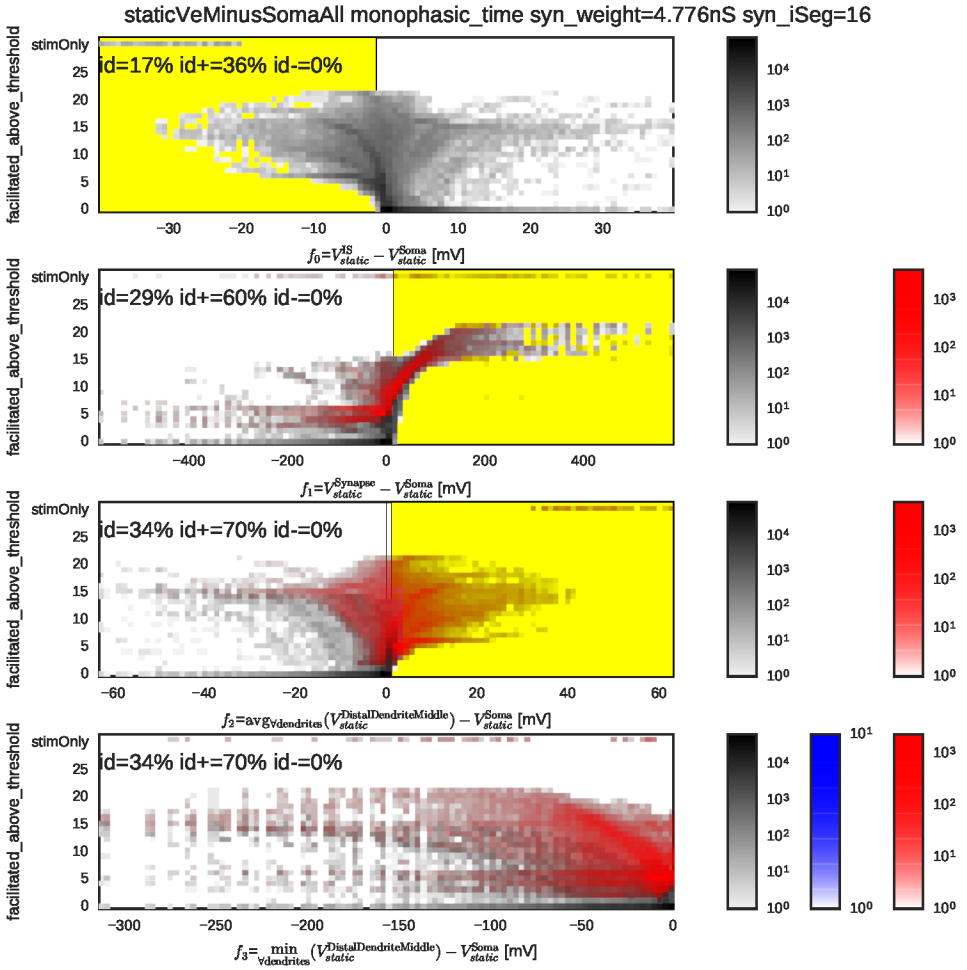


Figure 5.67: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.776 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall \text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 209901 are facilitated, and 217134 are non-active.

IF ($f_0 < -1.378$ mV) THEN (T=1) /* 76010 samples */
ELIF (14.14 mV $< f_1$) THEN (T=1) /* 51673 samples */
ELIF (-1.293×10^{-5} mV $< f_2 < 1.293 \times 10^{-5}$ mV) THEN (T=0) /* 10 samples */
ELIF (1.121 mV $< f_2$) THEN (T=1) /* 20700 samples */
ELSE (T=Unknown) /* 279287 samples */

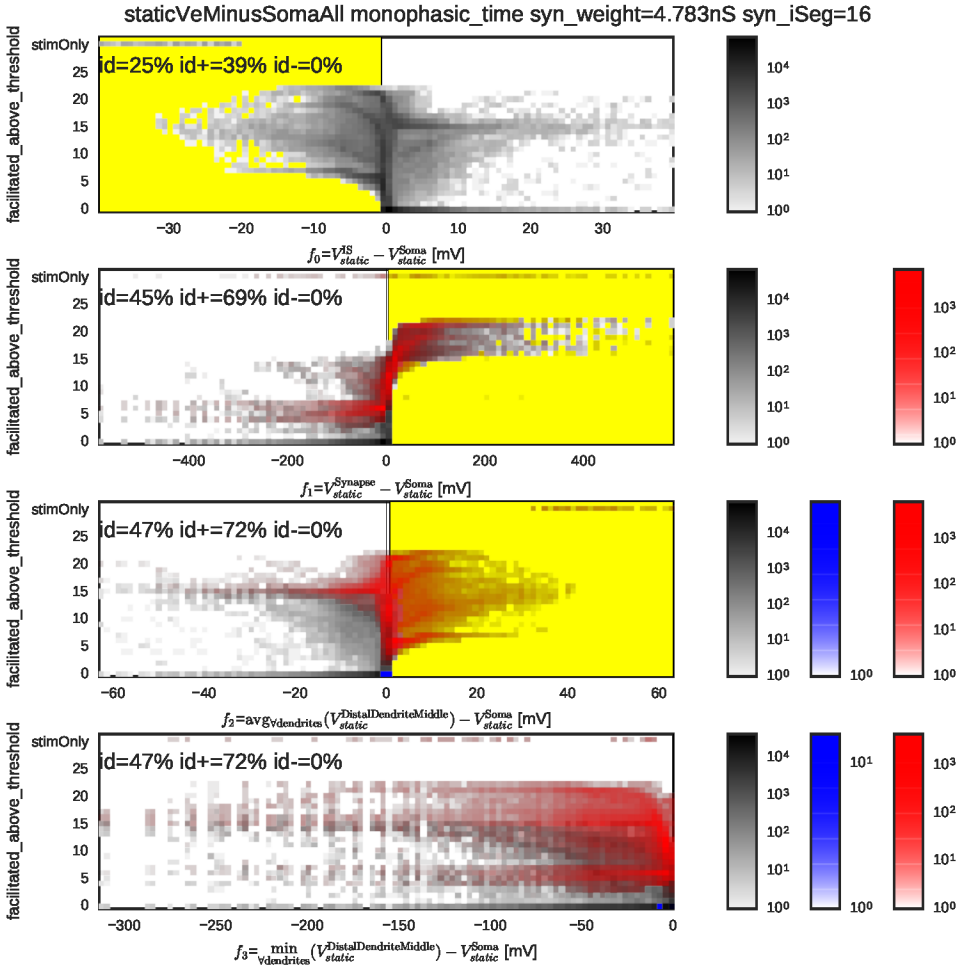


Figure 5.68: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.783 nS using features $f_0 = V^{\text{IS}}_{static} - V^{\text{Soma}}_{static}$, $f_1 = V^{\text{Synapse}}_{static} - V^{\text{Soma}}_{static}$, $f_2 = \text{avg}_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$, and $f_3 = \min_{\forall\text{dendrites}}(V^{\text{DistalDendriteMiddle}}_{static}) - V^{\text{Soma}}_{static}$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 278554 are facilitated, and 148481 are non-active.

IF ($f_0 < -0.6751$ mV) THEN (T=1) /* 110560 samples */
ELIF (-3.574×10^{-5} mV $< f_1 < 3.574 \times 10^{-5}$ mV) THEN (T=0) /* 16 samples */
ELIF (4.074 mV $< f_1$) THEN (T=1) /* 83187 samples */
ELIF (-1.854×10^{-5} mV $< f_2 < 1.854 \times 10^{-5}$ mV) THEN (T=0) /* 18 samples */
ELIF (0.7406 mV $< f_2$) THEN (T=1) /* 8076 samples */
ELIF ($-0.062\,25$ mV $< f_3$) THEN (T=0) /* 710 samples */
ELSE (T=Unknown) /* 225113 samples */

5.D Appendix: Supplementary figures for separating facilitated and non-activated neurons using stimulation-only membrane voltages

This appendix contains supplementary figures for Section 5.4.2.

Figures 5.69-5.79 show the result of the greedy search using membrane voltage features for biphasic stimulation and Figs. 5.80-5.90 show the result for monophasic stimulation. A summary of the results is available in Table 5.3.

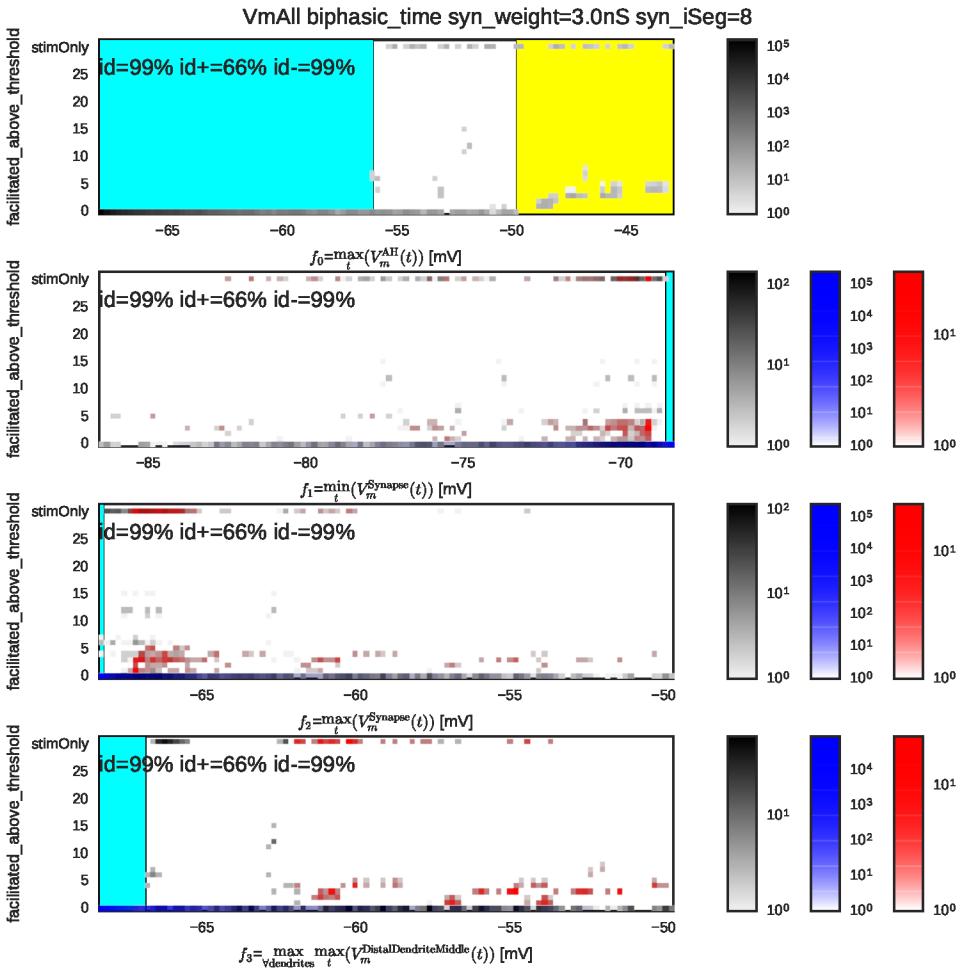


Figure 5.69: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.0 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 537 are facilitated, and 426743 are non-active.

IF (f_0 < −56.03 mV) THEN (T=0) /* 425230 samples */
ELIF (−49.81 mV < f_0) THEN (T=1) /* 625 samples */
ELIF (−68.58 mV < f_1) THEN (T=0) /* 111 samples */
ELIF (f_2 < −68.18 mV) THEN (T=0) /* 2 samples */
ELIF (f_3 < −66.82 mV) THEN (T=0) /* 6 samples */
ELSE (T=Unknown) /* 1706 samples */

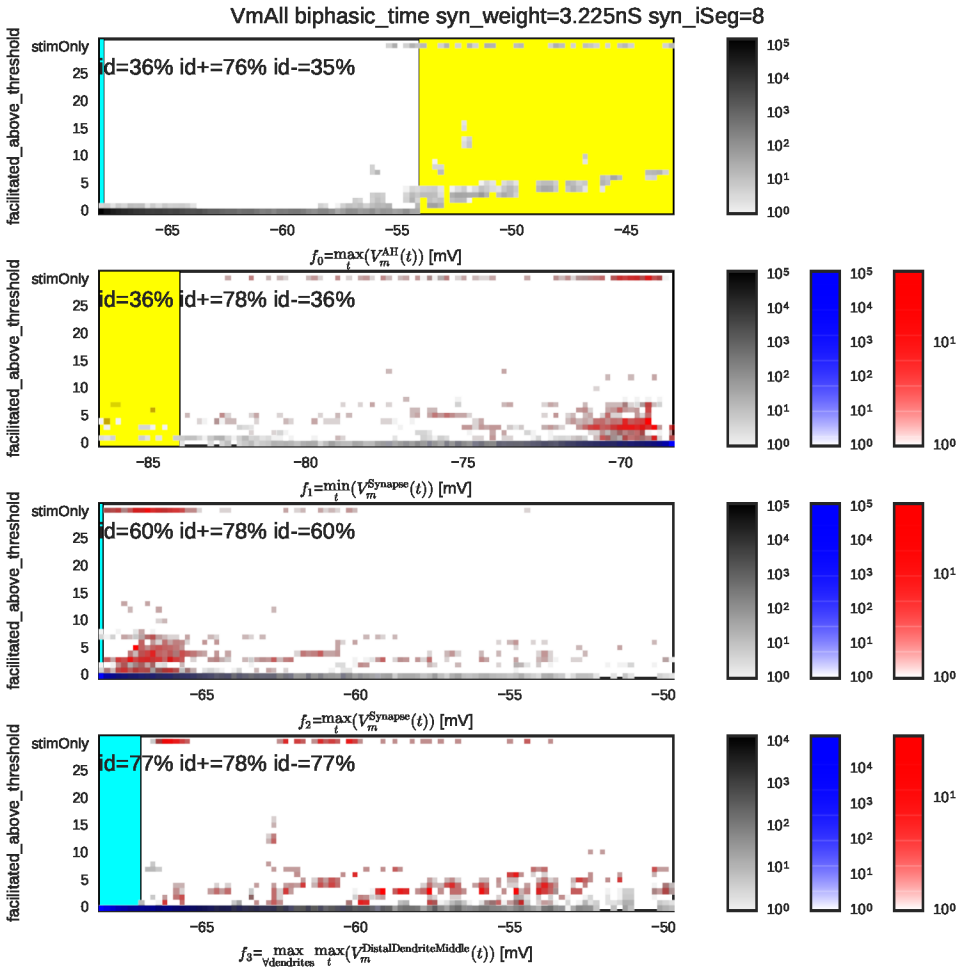


Figure 5.70: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.225 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 1647 are facilitated, and 425633 are non-active.

IF (f_0 < −67.78 mV) THEN (T=0) /* 152735 samples */
ELIF (−54.06 mV < f_0) THEN (T=1) /* 1575 samples */
ELIF (f_1 < −83.99 mV) THEN (T=1) /* 39 samples */
ELIF (−68.34 mV < f_1) THEN (T=0) /* 1536 samples */
ELIF (f_2 < −68.21 mV) THEN (T=0) /* 103534 samples */
ELIF (f_3 < −66.98 mV) THEN (T=0) /* 70643 samples */
ELSE (T=Unknown) /* 97618 samples */

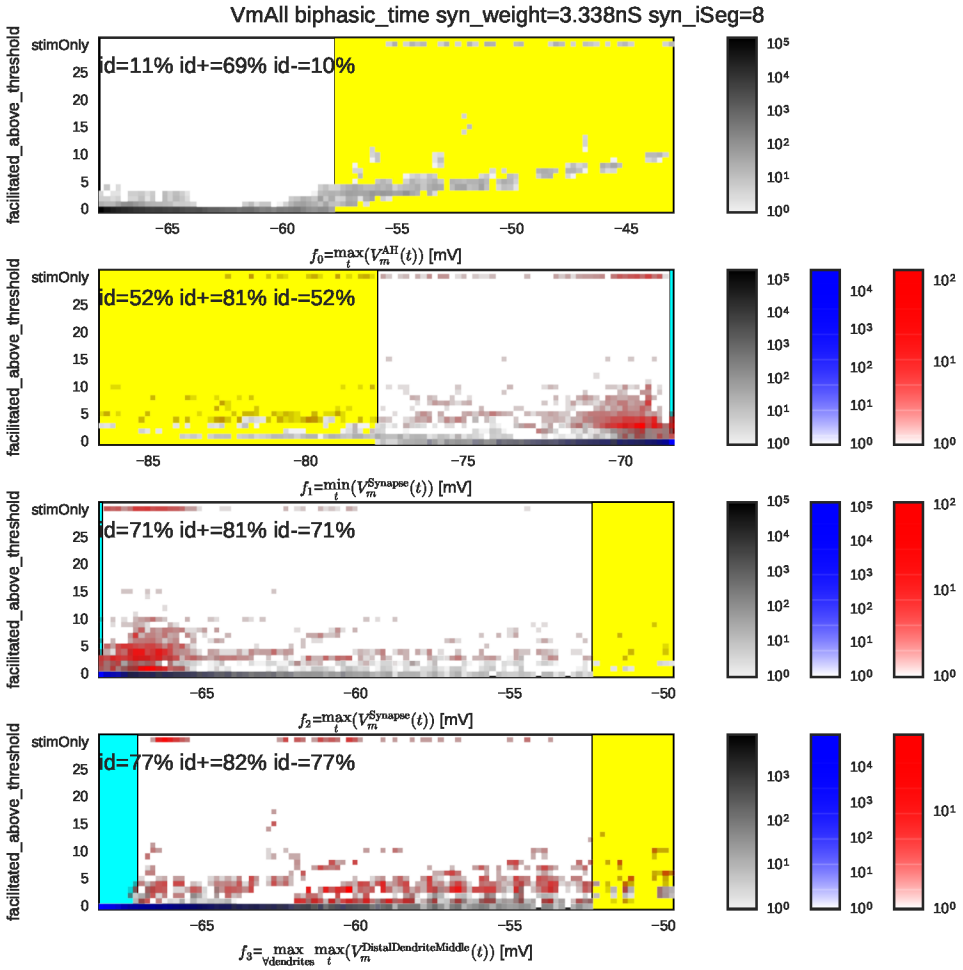


Figure 5.71: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.338 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 4248 are facilitated, and 423032 are non-active.

IF (f_0 < −67.97 mV) THEN (T=0) /* 44845 samples */
ELIF (−57.74 mV < f_0) THEN (T=1) /* 3235 samples */
ELIF (f_1 < −77.72 mV) THEN (T=1) /* 537 samples */
ELIF (−68.45 mV < f_1) THEN (T=0) /* 176734 samples */
ELIF (f_2 < −68.23 mV) THEN (T=0) /* 80163 samples */
ELIF (−52.33 mV < f_2) THEN (T=1) /* 22 samples */
ELIF (f_3 < −67.08 mV) THEN (T=0) /* 25044 samples */
ELIF (−52.33 mV < f_3) THEN (T=1) /* 63 samples */
ELSE (T=Unknown) /* 97037 samples */

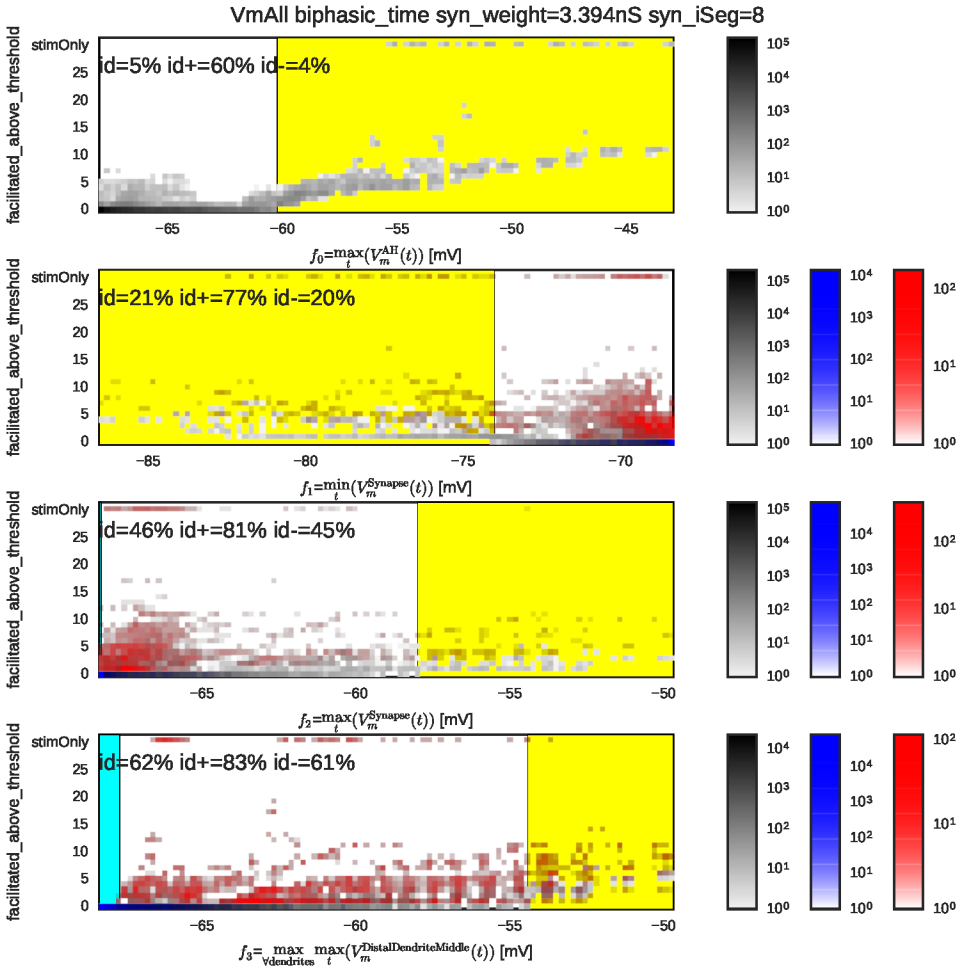


Figure 5.72: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.394 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 9670 are facilitated, and 417610 are non-active.

IF (f_0 < −67.98 mV) THEN (T=0) /* 17160 samples */
ELIF (−60.24 mV < f_0) THEN (T=1) /* 6100 samples */
ELIF (f_1 < −74.01 mV) THEN (T=1) /* 1695 samples */
ELIF (−68.35 mV < f_1) THEN (T=0) /* 68263 samples */
ELIF (f_2 < −68.27 mV) THEN (T=0) /* 105836 samples */
ELIF (−58 mV < f_2) THEN (T=1) /* 363 samples */
ELIF (f_3 < −67.68 mV) THEN (T=0) /* 65502 samples */
ELIF (−54.42 mV < f_3) THEN (T=1) /* 259 samples */
ELSE (T=Unknown) /* 162502 samples */

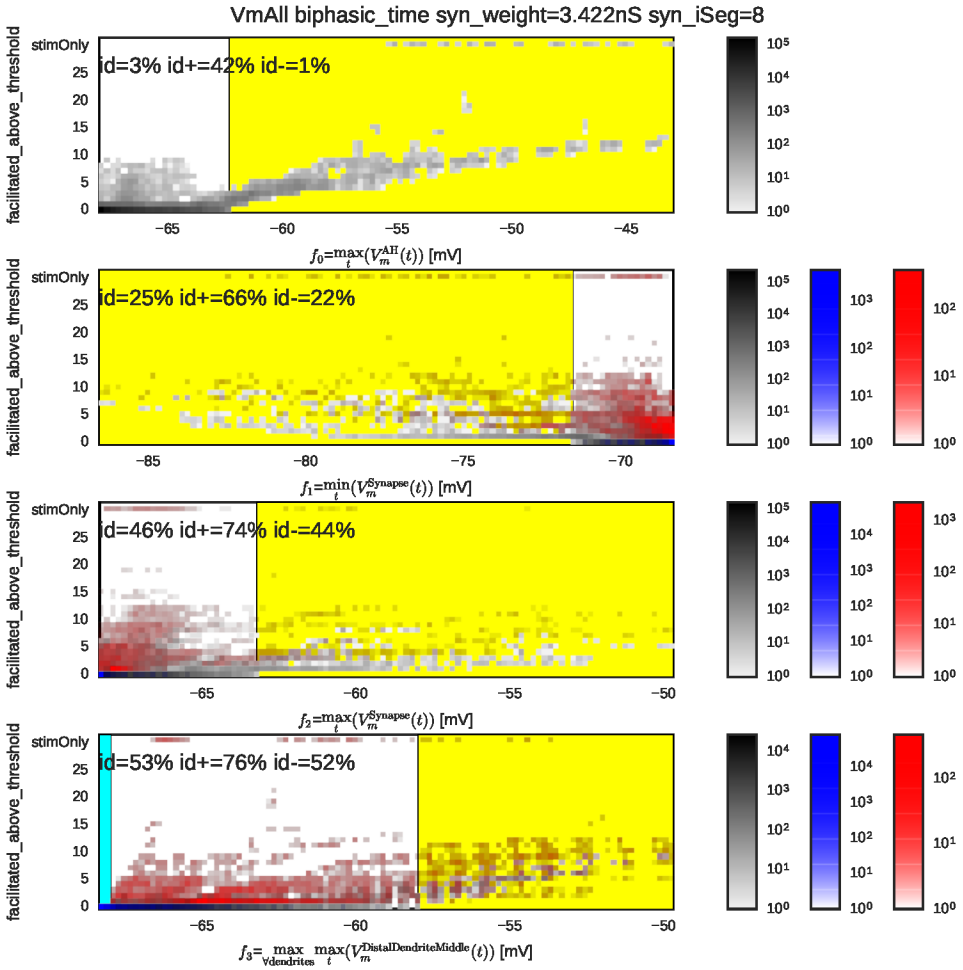


Figure 5.73: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.422 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 24532 are facilitated, and 402748 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 5740 samples */
ELIF (−62.33 mV < f_0) THEN (T=1) /* 10690 samples */
ELIF (f_1 < −71.52 mV) THEN (T=1) /* 5843 samples */
ELIF (−68.36 mV < f_1) THEN (T=0) /* 85974 samples */
ELIF (f_2 < −68.29 mV) THEN (T=0) /* 86844 samples */
ELIF (−63.22 mV < f_2) THEN (T=1) /* 2019 samples */
ELIF (f_3 < −67.95 mV) THEN (T=0) /* 31397 samples */
ELIF (−57.99 mV < f_3) THEN (T=1) /* 639 samples */
ELSE (T=Unknown) /* 198534 samples */

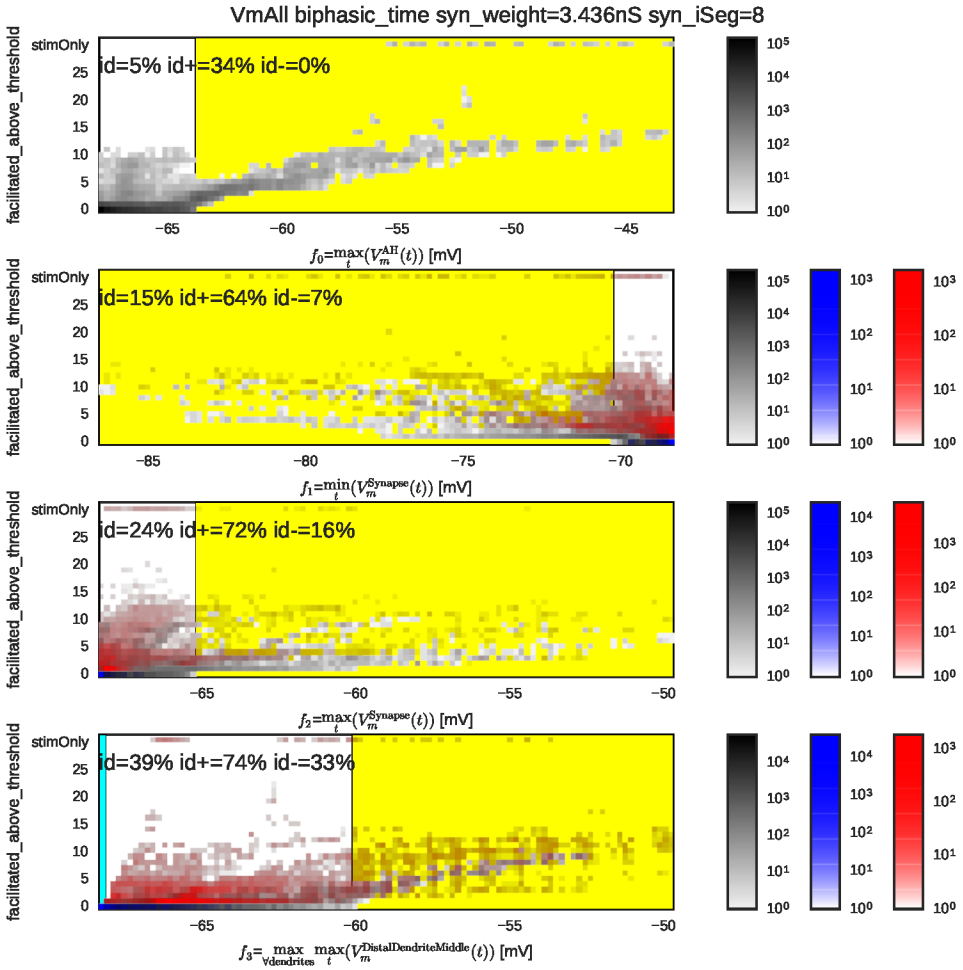


Figure 5.74: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.436 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 62471 are facilitated, and 364809 are non-active.

IF ($f_0 < -67.99$ mV) THEN (T=0) /* 2035 samples */
ELIF (-63.8 mV $< f_0$) THEN (T=1) /* 21630 samples */
ELIF ($f_1 < -70.22$ mV) THEN (T=1) /* 18660 samples */
ELIF (-68.34 mV $< f_1$) THEN (T=0) /* 24218 samples */
ELIF ($f_2 < -68.33$ mV) THEN (T=0) /* 34178 samples */
ELIF (-65.21 mV $< f_2$) THEN (T=1) /* 5375 samples */
ELIF ($f_3 < -68.12$ mV) THEN (T=0) /* 60313 samples */
ELIF (-60.12 mV $< f_3$) THEN (T=1) /* 918 samples */
ELSE (T=Unknown) /* 260353 samples */

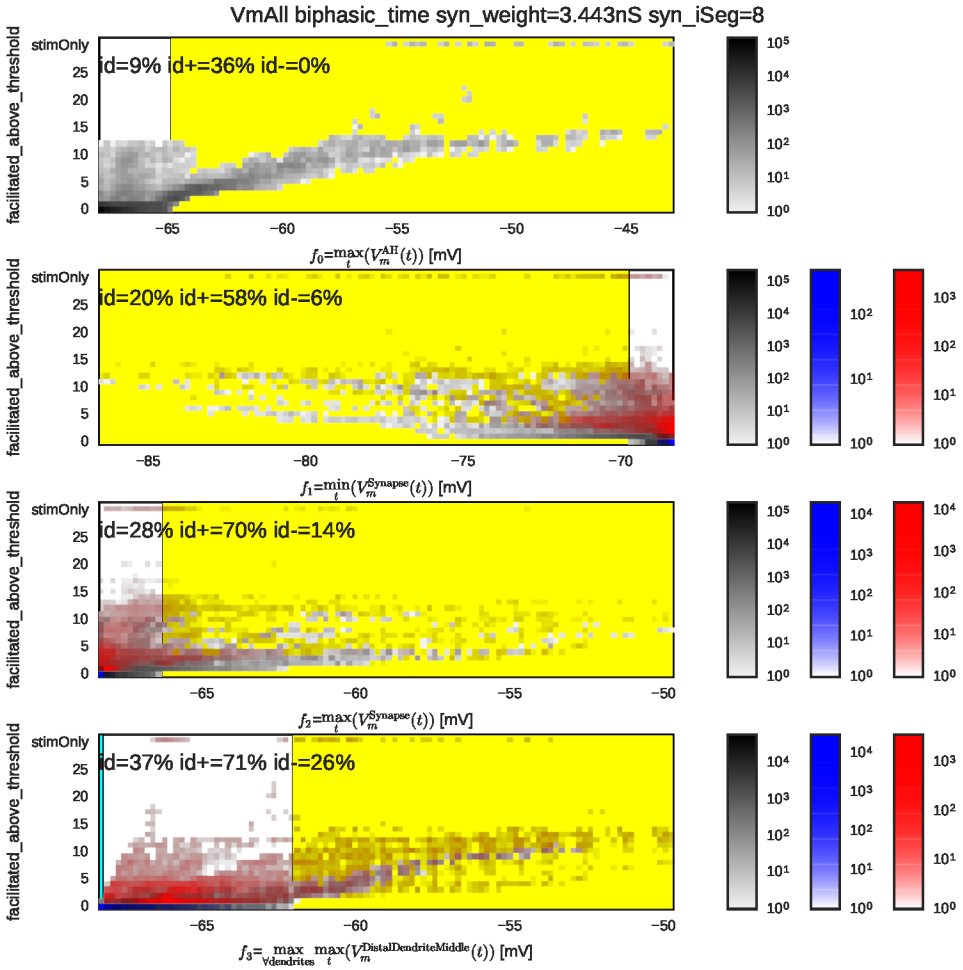


Figure 5.75: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.443 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 110804 are facilitated, and 316476 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 640 samples */
ELIF (−64.87 mV < f_0) THEN (T=1) /* 40050 samples */
ELIF (f_1 < −69.74 mV) THEN (T=1) /* 25504 samples */
ELIF (−68.34 mV < f_1) THEN (T=0) /* 20618 samples */
ELIF (f_2 < −68.33 mV) THEN (T=0) /* 23330 samples */
ELIF (−66.29 mV < f_2) THEN (T=1) /* 13057 samples */
ELIF (f_3 < −68.21 mV) THEN (T=0) /* 37738 samples */
ELIF (−62.07 mV < f_3) THEN (T=1) /* 1309 samples */
ELSE (T=Unknown) /* 265434 samples */

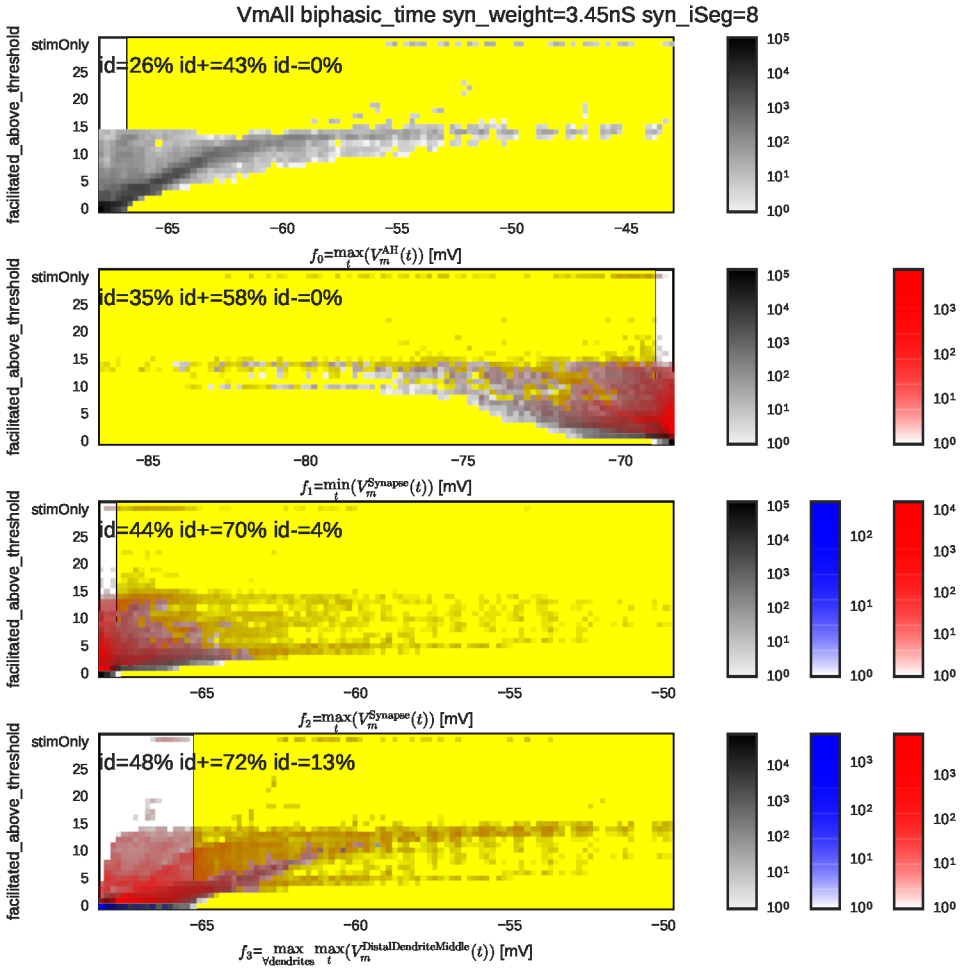


Figure 5.76: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.45 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 257472 are facilitated, and 169808 are non-active.

IF (−66.78 mV < f_0) THEN (T=1) /* 113350 samples */
ELIF (f_1 < −68.89 mV) THEN (T=1) /* 36955 samples */
ELIF (−68.34 mV < f_1) THEN (T=0) /* 323 samples */
ELIF (f_2 < −68.34 mV) THEN (T=0) /* 7123 samples */
ELIF (−67.77 mV < f_2) THEN (T=1) /* 32725 samples */
ELIF (f_3 < −68.31 mV) THEN (T=0) /* 15857 samples */
ELIF (−65.27 mV < f_3) THEN (T=1) /* 2643 samples */
ELSE (T=Unknown) /* 218704 samples */

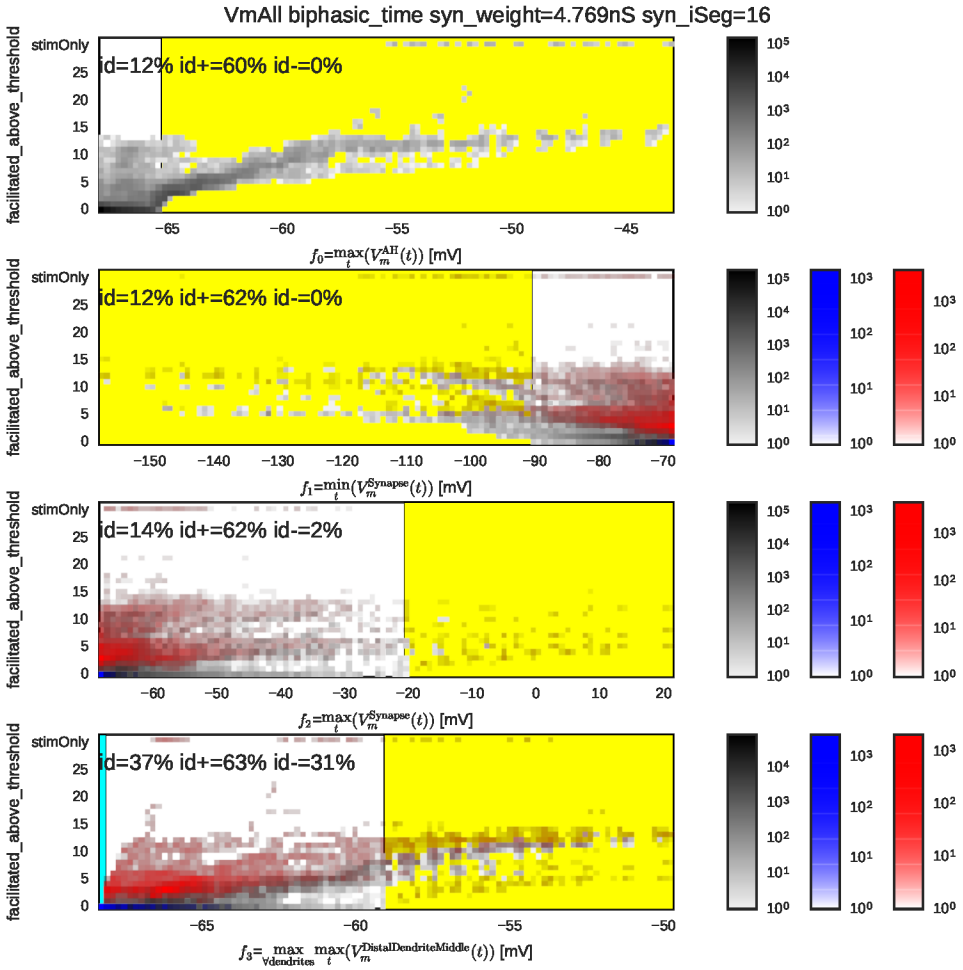


Figure 5.77: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.769 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 82986 are facilitated, and 344294 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 2035 samples */
ELIF (−65.28 mV < f_0) THEN (T=1) /* 50105 samples */
ELIF (f_1 < −90.43 mV) THEN (T=1) /* 2032 samples */
ELIF (−68.44 mV < f_1) THEN (T=0) /* 7 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 6938 samples */
ELIF (−20.68 mV < f_2) THEN (T=1) /* 29 samples */
ELIF (f_3 < −68.12 mV) THEN (T=0) /* 99306 samples */
ELIF (−59.09 mV < f_3) THEN (T=1) /* 1189 samples */
ELSE (T=Unknown) /* 266039 samples */

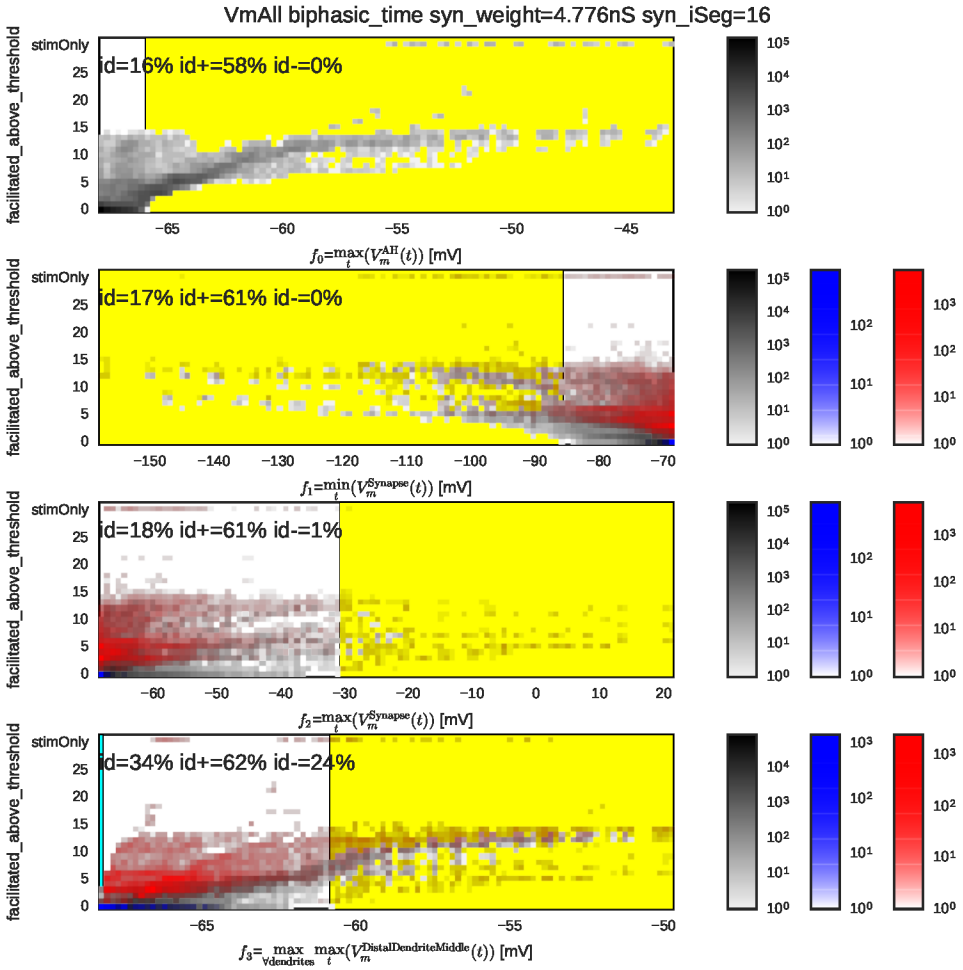


Figure 5.78: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.776 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 120616 are facilitated, and 306664 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 1200 samples */
ELIF (−65.98 mV < f_0) THEN (T=1) /* 70970 samples */
ELIF (f_1 < −85.59 mV) THEN (T=1) /* 3104 samples */
ELIF (−68.44 mV < f_1) THEN (T=0) /* 33 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 4818 samples */
ELIF (−30.8 mV < f_2) THEN (T=1) /* 51 samples */
ELIF (f_3 < −68.21 mV) THEN (T=0) /* 67587 samples */
ELIF (−60.85 mV < f_3) THEN (T=1) /* 1795 samples */
ELSE (T=Unknown) /* 278122 samples */

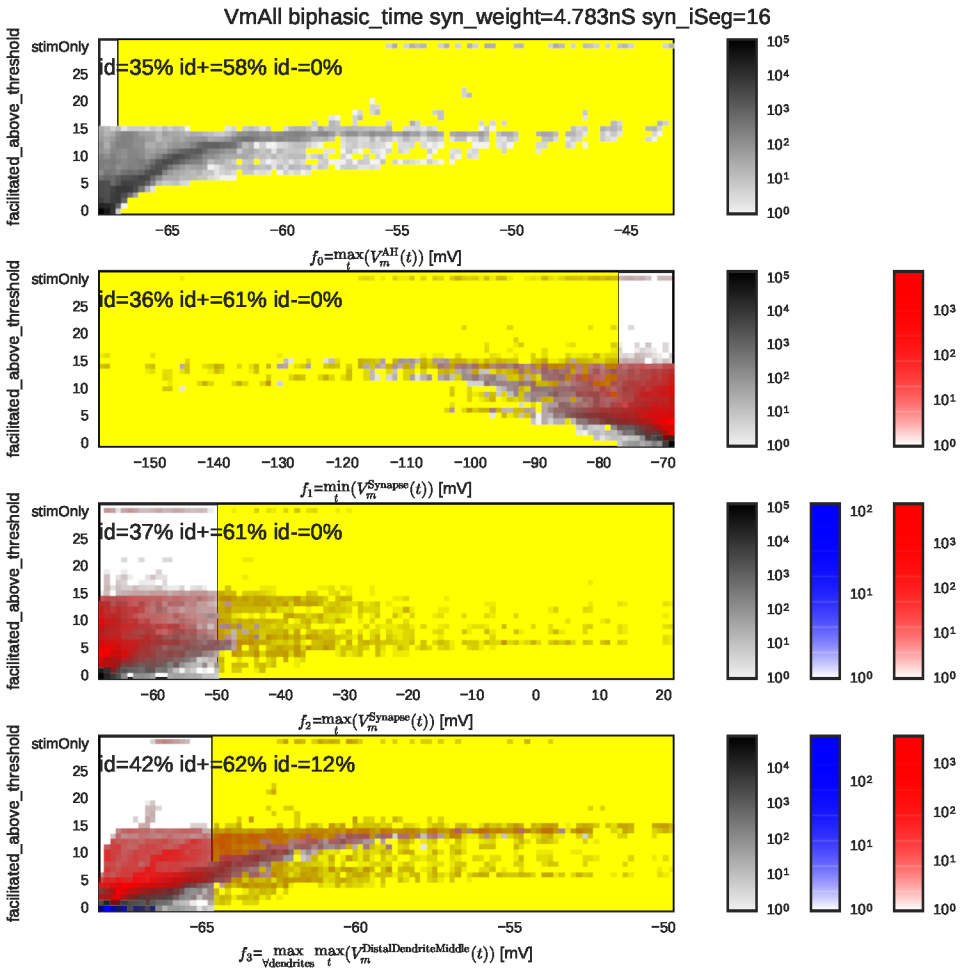


Figure 5.79: Predicting facilitation for all combinations using biphasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.783 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 400 are active without the EPSP, 256925 are facilitated, and 170355 are non-active.

IF (−67.18 mV < f_0) THEN (T=1) /* 150740 samples */
ELIF (f_1 < −76.98 mV) THEN (T=1) /* 7124 samples */
ELIF (−68.44 mV < f_1) THEN (T=0) /* 126 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 1314 samples */
ELIF (−49.93 mV < f_2) THEN (T=1) /* 222 samples */
ELIF (f_3 < −68.31 mV) THEN (T=0) /* 19128 samples */
ELIF (−64.67 mV < f_3) THEN (T=1) /* 3171 samples */
ELSE (T=Unknown) /* 245855 samples */

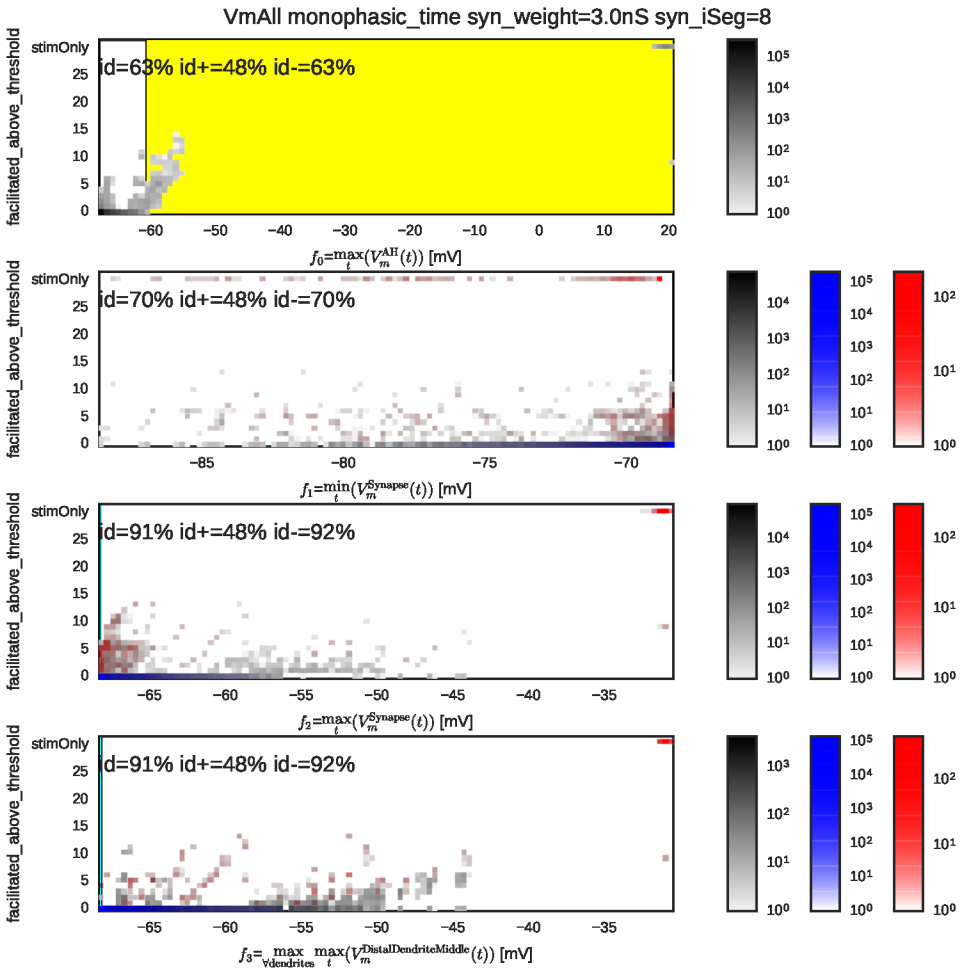


Figure 5.80: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.0 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 2562 are facilitated, and 424473 are non-active.

IF (f_0 < −67.92 mV) THEN (T=0) /* 271235 samples */
ELIF (−60.77 mV < f_0) THEN (T=1) /* 1565 samples */
ELIF (−68.34 mV < f_1) THEN (T=0) /* 29915 samples */
ELIF (f_2 < −68.24 mV) THEN (T=0) /* 90119 samples */
ELIF (f_3 < −68.16 mV) THEN (T=0) /* 494 samples */
ELSE (T=Unknown) /* 34352 samples */

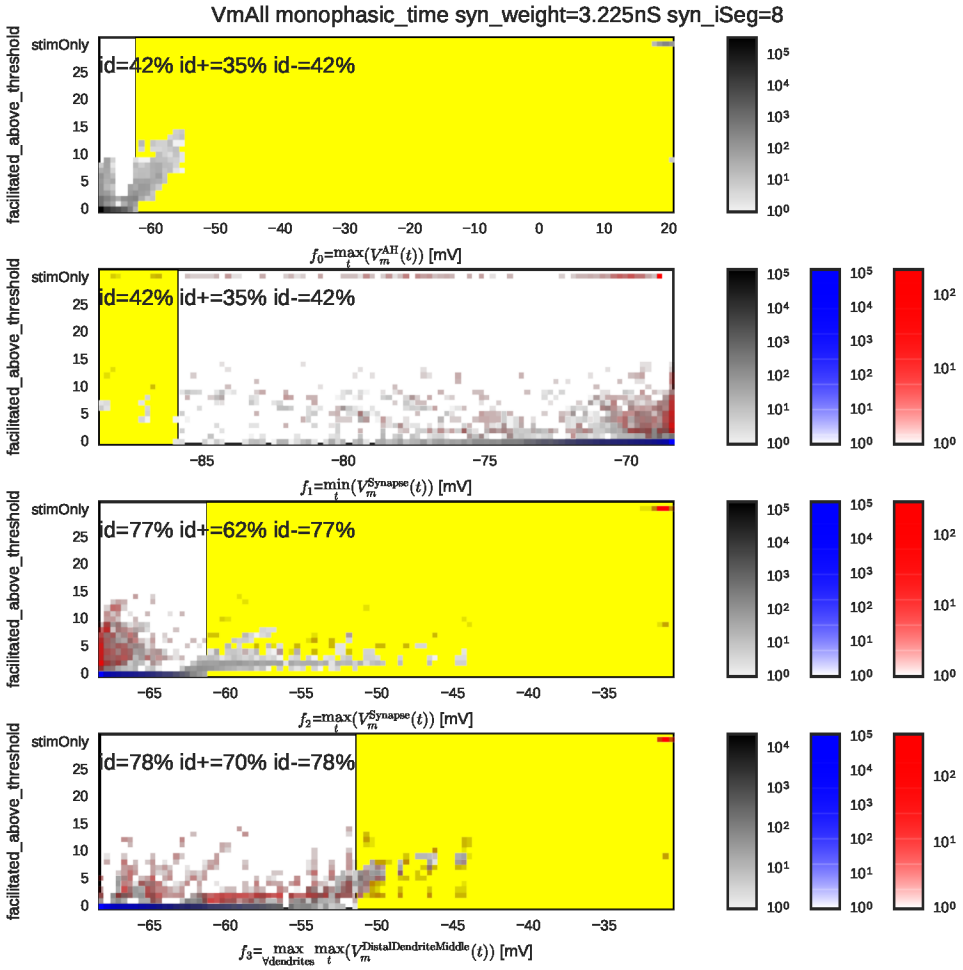


Figure 5.81: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.225 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 6522 are facilitated, and 420513 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 179395 samples */
ELIF (−62.41 mV < f_0) THEN (T=1) /* 2530 samples */
ELIF (f_1 < −85.86 mV) THEN (T=1) /* 37 samples */
ELIF (f_2 < −68.29 mV) THEN (T=0) /* 146246 samples */
ELIF (−61.26 mV < f_2) THEN (T=1) /* 1936 samples */
ELIF (f_3 < −68.24 mV) THEN (T=0) /* 3440 samples */
ELIF (−51.41 mV < f_3) THEN (T=1) /* 527 samples */
ELSE (T=Unknown) /* 93569 samples */

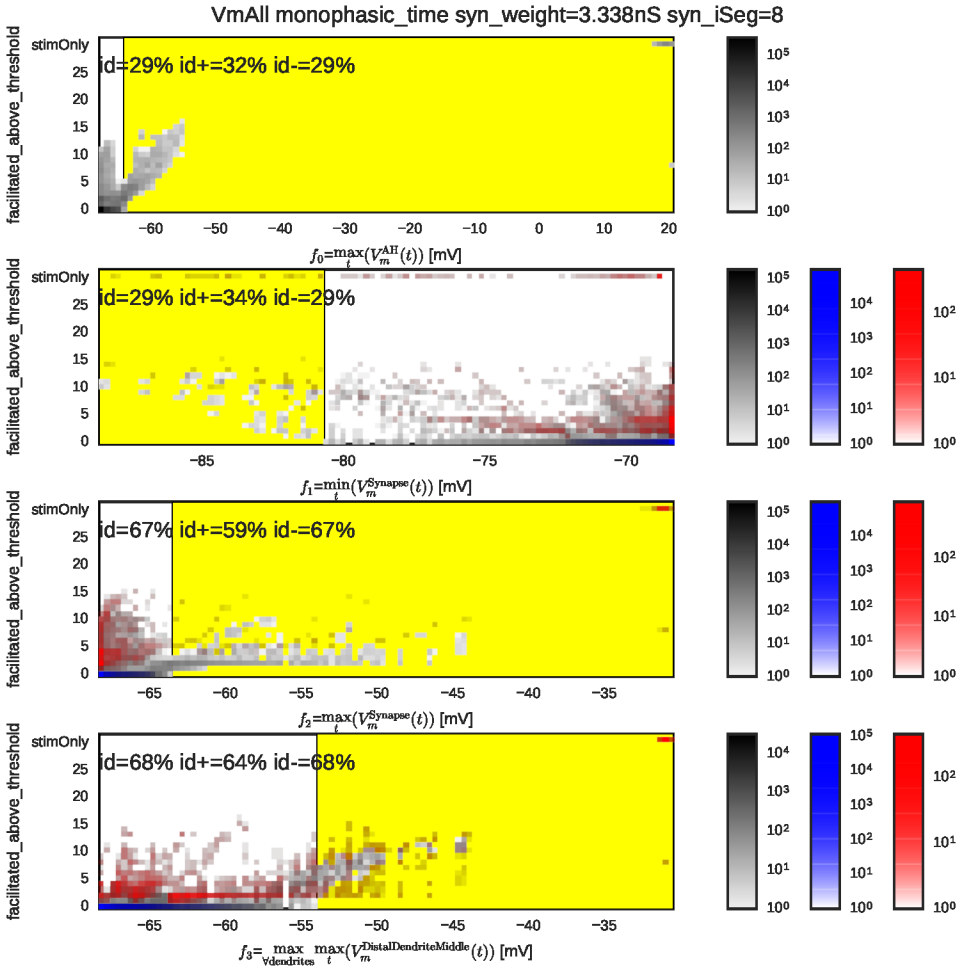


Figure 5.82: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.338 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 16246 are facilitated, and 410789 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 120685 samples */
ELIF (−64.26 mV < f_0) THEN (T=1) /* 5520 samples */
ELIF (f_1 < −80.68 mV) THEN (T=1) /* 346 samples */
ELIF (f_2 < −68.32 mV) THEN (T=0) /* 156974 samples */
ELIF (−63.52 mV < f_2) THEN (T=1) /* 4137 samples */
ELIF (f_3 < −68.28 mV) THEN (T=0) /* 3682 samples */
ELIF (−53.98 mV < f_3) THEN (T=1) /* 881 samples */
ELSE (T=Unknown) /* 135455 samples */

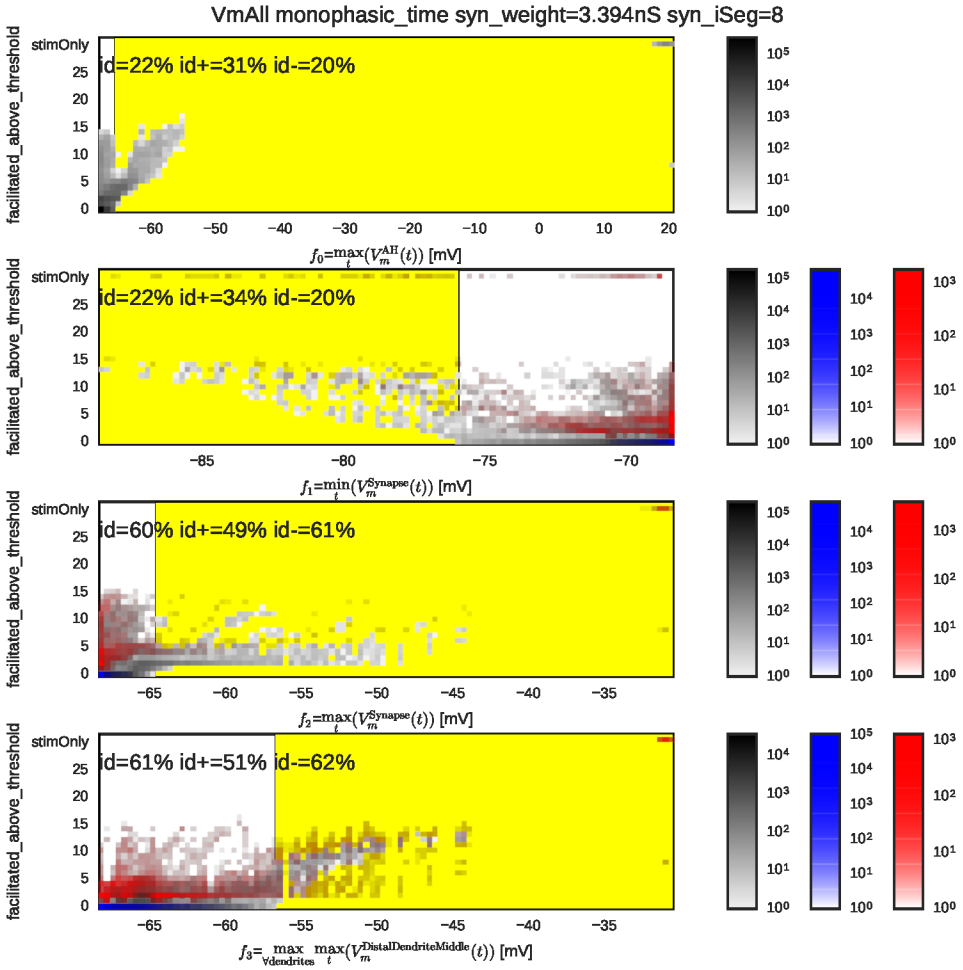


Figure 5.83: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.394 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 46322 are facilitated, and 380713 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 79800 samples */
ELIF (−65.65 mV < f_0) THEN (T=1) /* 14995 samples */
ELIF (f_1 < −75.91 mV) THEN (T=1) /* 1243 samples */
ELIF (f_2 < −68.33 mV) THEN (T=0) /* 154338 samples */
ELIF (−64.64 mV < f_2) THEN (T=1) /* 6889 samples */
ELIF (f_3 < −68.3 mV) THEN (T=0) /* 3433 samples */
ELIF (−56.74 mV < f_3) THEN (T=1) /* 1294 samples */
ELSE (T=Unknown) /* 165688 samples */

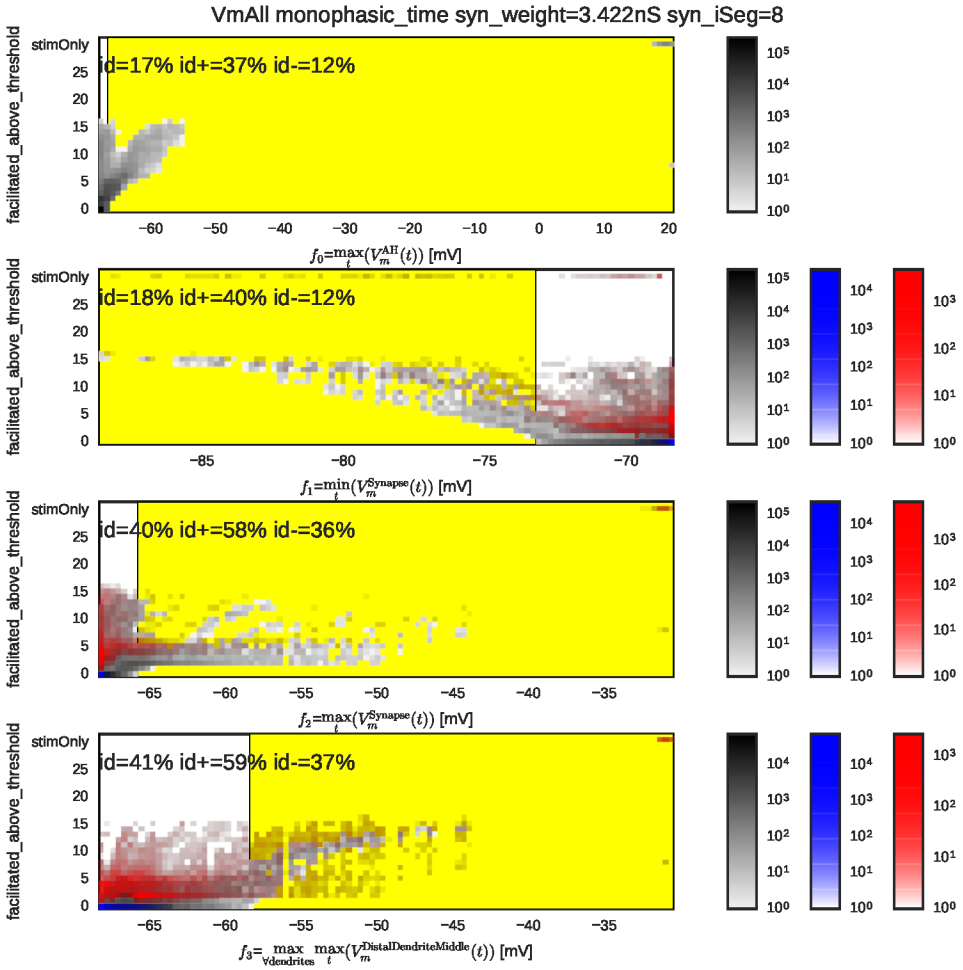


Figure 5.84: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.422 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 87686 are facilitated, and 339349 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 41635 samples */
ELIF (−66.7 mV < f_0) THEN (T=1) /* 33365 samples */
ELIF (f_1 < −73.2 mV) THEN (T=1) /* 2591 samples */
ELIF (f_2 < −68.34 mV) THEN (T=0) /* 81426 samples */
ELIF (−65.8 mV < f_2) THEN (T=1) /* 15461 samples */
ELIF (f_3 < −68.32 mV) THEN (T=0) /* 3562 samples */
ELIF (−58.41 mV < f_3) THEN (T=1) /* 1389 samples */
ELSE (T=Unknown) /* 248251 samples */

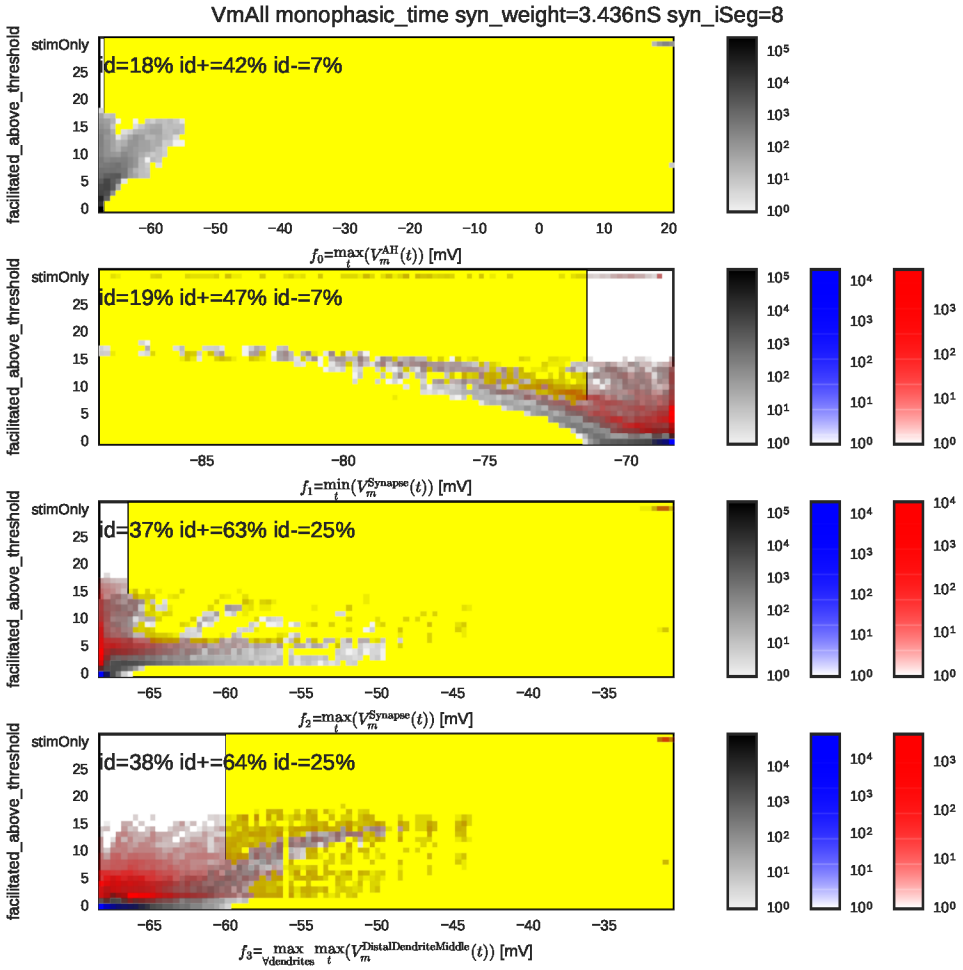


Figure 5.85: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.436 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 133965 are facilitated, and 293070 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 21180 samples */
ELIF (−67.26 mV < f_0) THEN (T=1) /* 57530 samples */
ELIF (f_1 < −71.4 mV) THEN (T=1) /* 6249 samples */
ELIF (f_2 < −68.34 mV) THEN (T=0) /* 52115 samples */
ELIF (−66.43 mV < f_2) THEN (T=1) /* 22165 samples */
ELIF (f_3 < −68.33 mV) THEN (T=0) /* 1924 samples */
ELIF (−60 mV < f_3) THEN (T=1) /* 1400 samples */
ELSE (T=Unknown) /* 265117 samples */

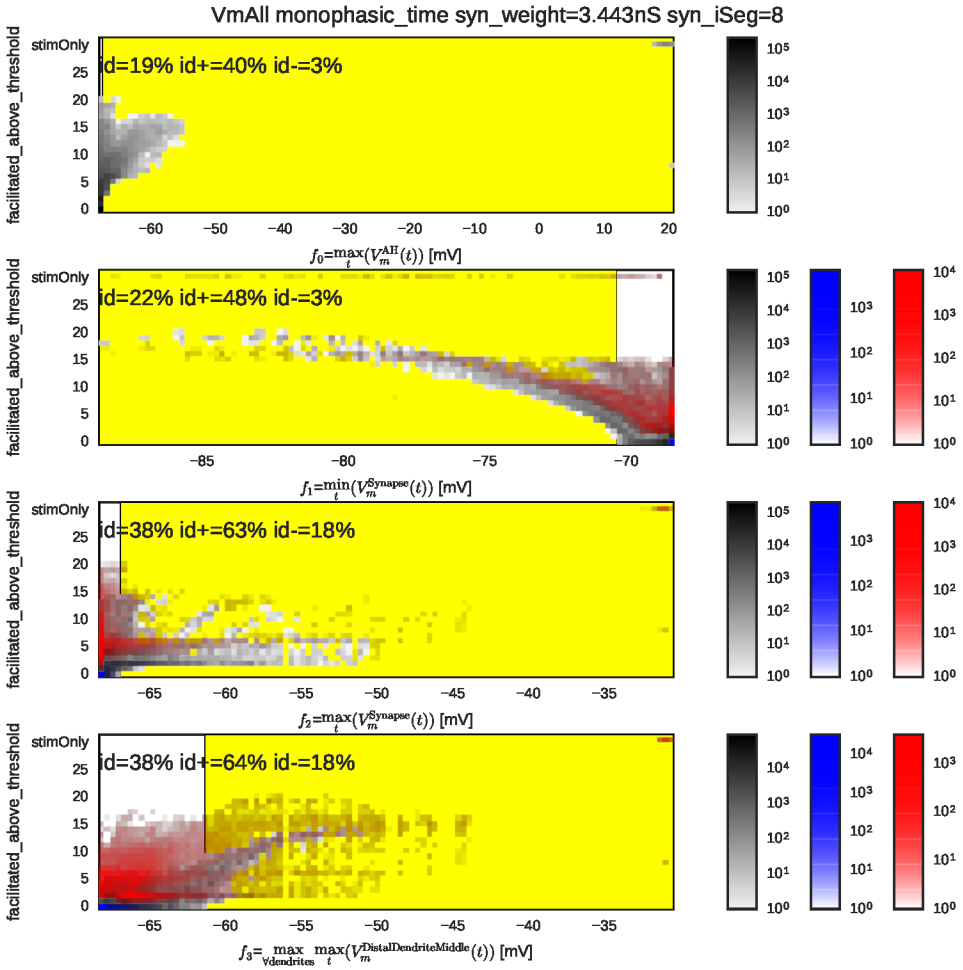


Figure 5.86: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.443 nS using features $f_0 = \max_t(V_m^{AH}(t))$, $f_1 = \min_t(V_m^{Synapse}(t))$, $f_2 = \max_t(V_m^{Synapse}(t))$, and $f_3 = \max_{\forall dendrites} \max_t(V_m^{DistalDendriteMiddle}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 185287 are facilitated, and 241748 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 7255 samples */
ELIF (−67.51 mV < f_0) THEN (T=1) /* 75585 samples */
ELIF (f_1 < −70.34 mV) THEN (T=1) /* 13998 samples */
ELIF (−68.34 mV < f_1 < −68.34 mV) THEN (T=0) /* 9 samples */
ELIF (f_2 < −68.34 mV) THEN (T=0) /* 35775 samples */
ELIF (−66.95 mV < f_2) THEN (T=1) /* 29475 samples */
ELIF (f_3 < −68.33 mV) THEN (T=0) /* 936 samples */
ELIF (−61.36 mV < f_3) THEN (T=1) /* 1368 samples */
ELSE (T=Unknown) /* 263279 samples */

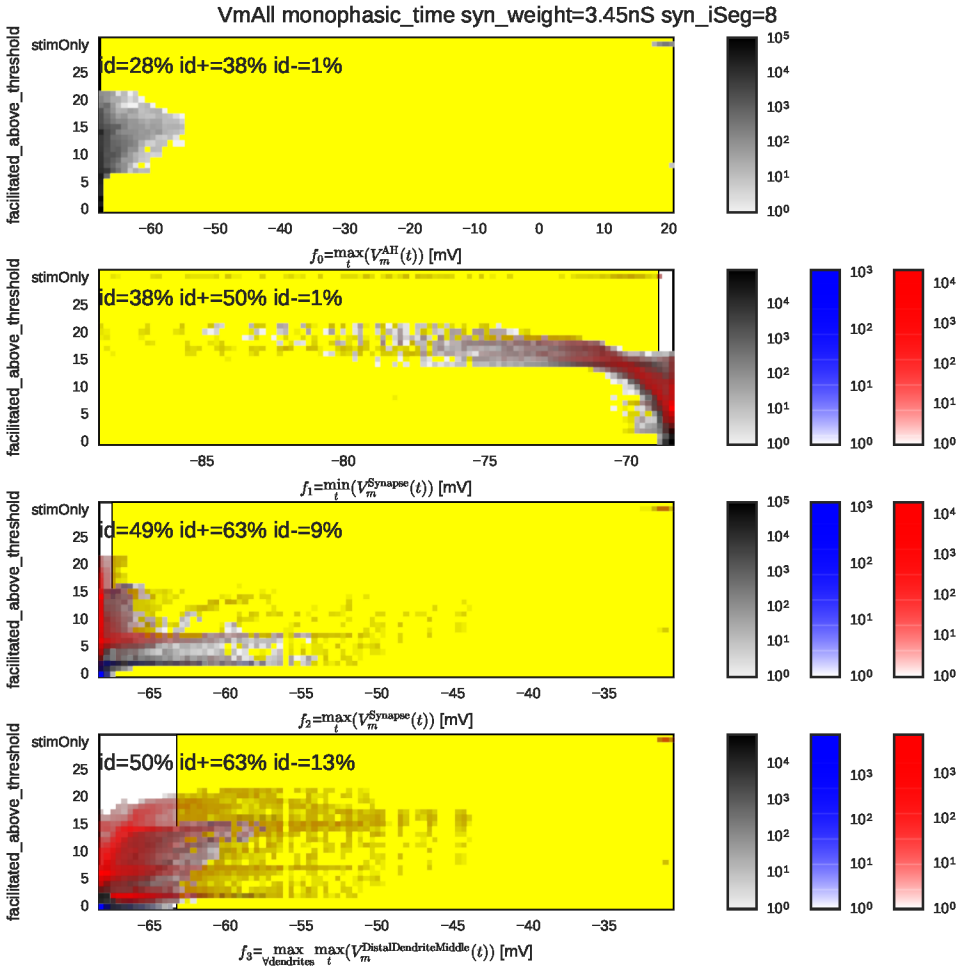


Figure 5.87: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 8 with weight 3.45 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall\text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 319226 are facilitated, and 107809 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 1125 samples */
ELIF (−67.81 mV < f_0) THEN (T=1) /* 121900 samples */
ELIF (f_1 < −68.86 mV) THEN (T=1) /* 40879 samples */
ELIF (−68.34 mV < f_1 < −68.34 mV) THEN (T=0) /* 2 samples */
ELIF (f_2 < −68.34 mV) THEN (T=0) /* 7846 samples */
ELIF (−67.49 mV < f_2) THEN (T=1) /* 39693 samples */
ELIF (f_3 < −68.32 mV) THEN (T=0) /* 4468 samples */
ELIF (−63.24 mV < f_3) THEN (T=1) /* 1145 samples */
ELSE (T=Unknown) /* 210622 samples */

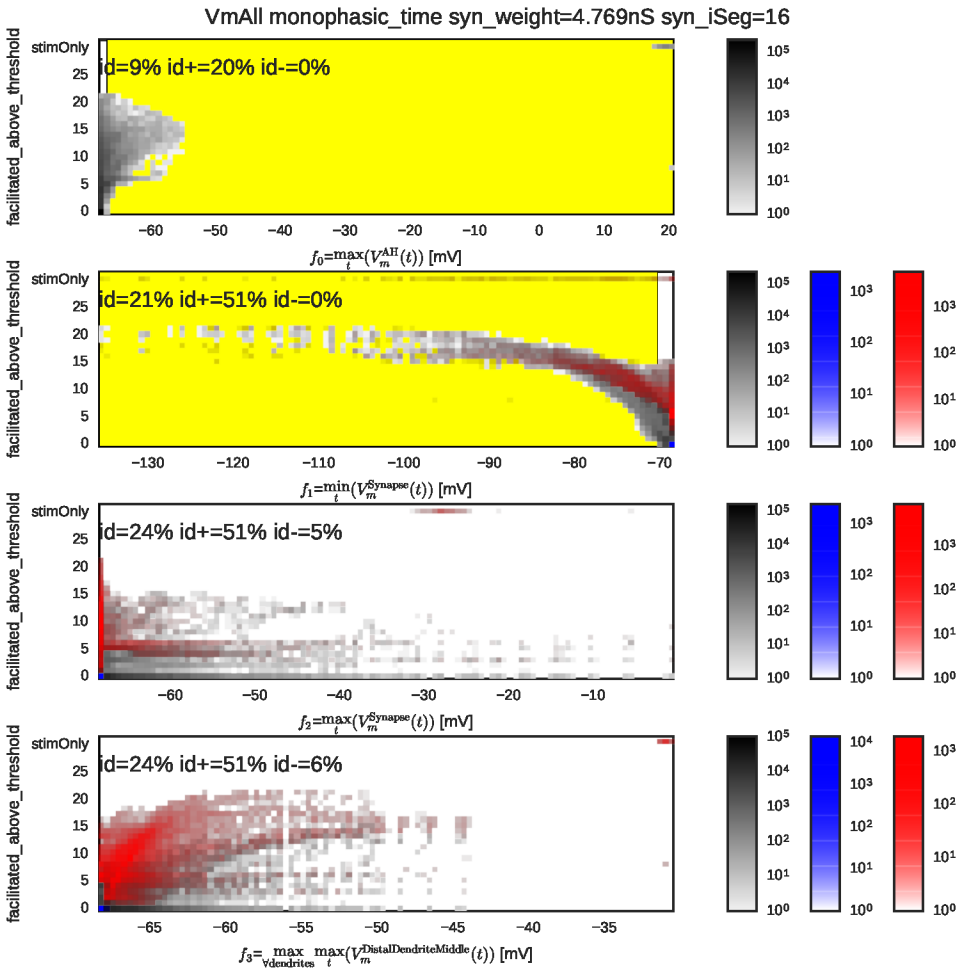


Figure 5.88: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.769 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 176092 are facilitated, and 250943 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 2495 samples */
ELIF (−66.81 mV < f_0) THEN (T=1) /* 37100 samples */
ELIF (f_1 < −70.29 mV) THEN (T=1) /* 53545 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 12443 samples */
ELIF (f_3 < −68.33 mV) THEN (T=0) /* 561 samples */
ELSE (T=Unknown) /* 321536 samples */

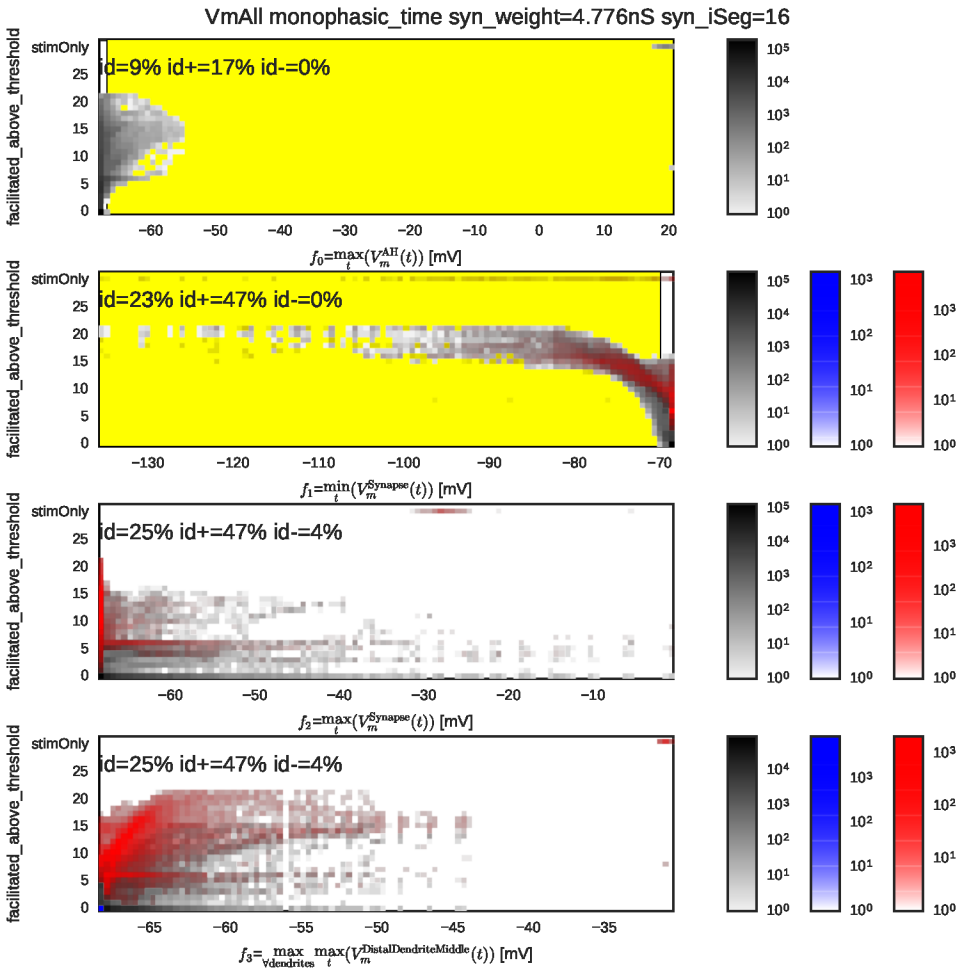


Figure 5.89: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.776 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 209901 are facilitated, and 217134 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 1460 samples */
ELIF (−66.81 mV < f_0) THEN (T=1) /* 37100 samples */
ELIF (f_1 < −69.96 mV) THEN (T=1) /* 62159 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 7970 samples */
ELIF (f_3 < −68.33 mV) THEN (T=0) /* 645 samples */
ELSE (T=Unknown) /* 318346 samples */

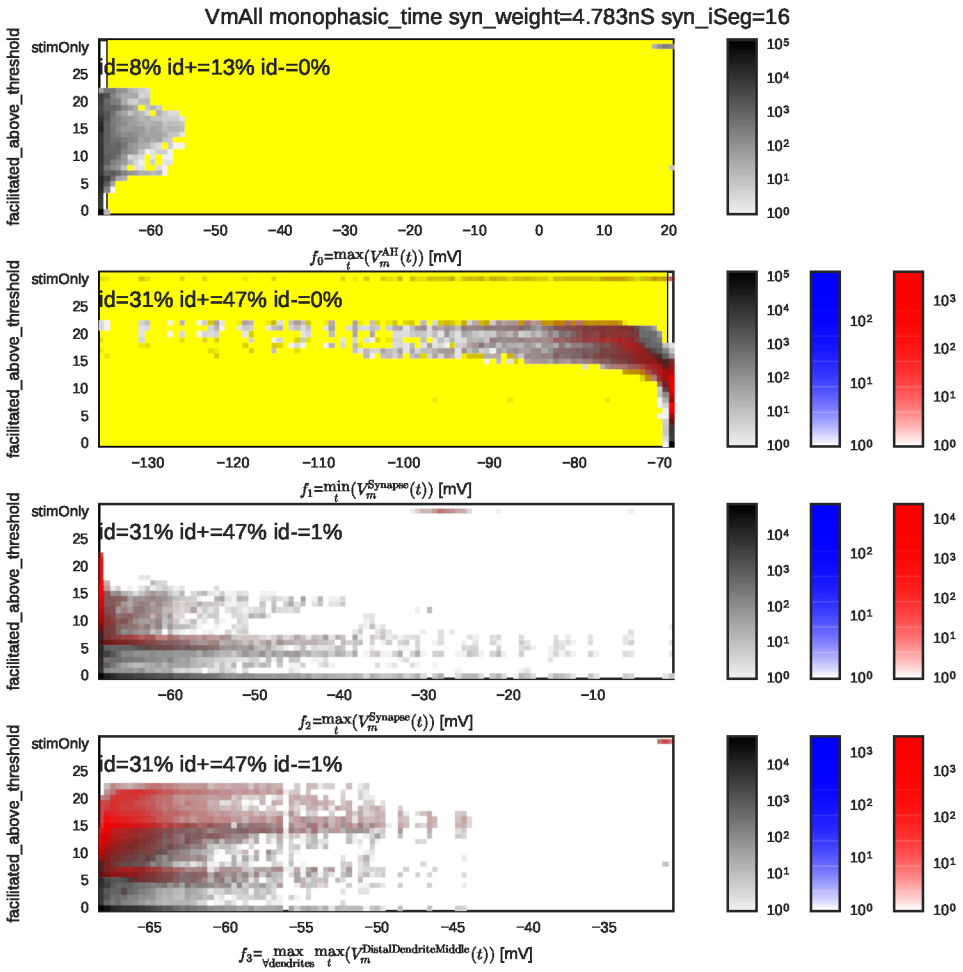


Figure 5.90: Predicting facilitation for all combinations using monophasic epidural stimulation with a synapse triggered on a distal dendrite at segment 16 with weight 4.783 nS using features $f_0 = \max_t(V_m^{\text{AH}}(t))$, $f_1 = \min_t(V_m^{\text{Synapse}}(t))$, $f_2 = \max_t(V_m^{\text{Synapse}}(t))$, and $f_3 = \max_{\forall \text{dendrites}} \max_t(V_m^{\text{DistalDendriteMiddle}}(t))$. Each feature is on the x-axis in a separate subplot above with the number of trigger points facilitated above threshold (−10 mV) as the y-axis. Each subplot consists of three 2D histograms (showing the number of neuron simulations in each square), shades of grey (unclassified), shades of red (classified as active), and shades of blue (classified as non-active). For each feature active and non-active classification regions of unclassified samples are drawn with a yellow and cyan background respectively. These classification regions are also written as rules below, where T=1 and T=0 indicates that the neuron is active and non-active respectively. The number of samples of neurons caught by each rule is specified in the comment after each rule. Using the decision regions in that subplot and those above, the percent of all samples classified (id), active samples classified (id+), and non-active samples classified (id-) are labeled in each subplot. There are a total of 427680 samples of which 645 are active without the EPSP, 278554 are facilitated, and 148481 are non-active.

IF (f_0 < −67.99 mV) THEN (T=0) /* 645 samples */
ELIF (−66.81 mV < f_0) THEN (T=1) /* 37100 samples */
ELIF (f_1 < −69.13 mV) THEN (T=1) /* 96685 samples */
ELIF (f_2 < −68.44 mV) THEN (T=0) /* 1492 samples */
ELIF (f_3 < −68.33 mV) THEN (T=0) /* 787 samples */
ELSE (T=Unknown) /* 290971 samples */