Chapter 4

ACTIVATING NEURONS USING EPIDURAL STIMULATION IN THE ABSENCE OF EXCITATORY POSTSYNAPTIC POTENTIALS (EPSPS)

This chapter looks at the effect of epidural stimulation on spinal neurons when there is no synaptic input. Specifically, this chapter looks for the stimulation conditions in which epidural stimulation causes neuronal activation (release of neurotransmitters). The next chapter will build upon these results in order to look how epidural stimulation facilitates neuron activation when a single EPSP occurs at a synaptic input. This computational study uses the volume conductor model presented in Chapter 2 and the neuron models from Chapter 3. Although epidural stimulation is often used with a sequence of stimulation pulses, this thesis focuses on understanding the response to a single stimulation pulse. If the stimulation pulses are sufficiently far apart in time, the single pulse analysis is a useful simplification, otherwise complex interactions between pulse responses may occur.

As described in Chapter 2, volume conductor simulations for both biphasic and monophasic stimulation (1 V peak voltage amplitude) were computed for the 18 electrode pair combinations listed in Section 2.2.1. Section 4.1 discusses the location of simulated neurons in these simulations, and Section 4.2 discusses the extraction of the extracellular voltage time series from the volume conductor studies for application to simulated neurons. Section 4.3 discusses and plots the total number of active neurons broken down by stimulation type, neuron dorsal-ventral location, and axon orientation. Section 4.4 compares the effect of monophasic and biphasic stimulation on the membrane voltage at a number of probe locations as a function of stimulation voltage. Section 4.5 looks at the simulations using ≤ 5 V which re-

sult in the axon tip having a membrane voltage of $> -10\,\text{mV}$ which, based on the discussion in Section 3.3.2, is believed to release neurotransmitters and is referred to as an *active* neuron. The stimulation voltage required to activate a neuron will be important in the next chapter because facilitation of neuron activation with an EPSP should ideally occur using stimulation less than that required to activate a neuron without EPSPs. Section 4.5.1 examines active neurons with monophasic stimulation. Section 4.5.2 examines active neurons under biphasic stimulation. Section 4.6 looks at ways of predicting neuron activation from static volume conductor simulations. Section 4.A shows the locations and orientations of activated neurons in the spinal cord for all 18 characteristic bipolar combinations.

These studies yield some interesting results, such as the fact that monophasic stimulation is much more likely to lead to a non-linear membrane voltage response between the stimulation voltage and the membrane voltage at the axon tip. Biphasic stimulation is more likely to maintain a linear relationship between stimulation voltage and membrane voltage at the axon tip (without synaptic input). This means that researchers using monophasic stimulation should expect a non-linear activation profile when increasing stimulation voltage. Section 4.6 may also be of particular interest because it shows that neuron activation can be predicted from the difference in the static simulated voltage between the axon tip and the soma.

4.1 Locations of simulated neurons

First, recall from Section 2.2.1 that:

- $+\hat{z}$ points in the caudal direction and increasing electrode array row number.
- $-\hat{z}$ points in the rostral direction and decreasing array row number.
- $+\hat{y}$ points in the dorsal direction.
- $-\hat{y}$ points in the ventral direction.

- $+\hat{x}$ points to the animals right side and towards the C column.
- $-\hat{x}$ points to the animals left side and towards the A column.

In order to simulate a representative set of neurons in the spinal cord, 3 soma positions labeled GM1 (most dorsal), GM2 (most ventral), and GM3 (between GM1 and GM2), were chosen in the (x, y) transverse plane, such that the entire neuron remained inside the gray matter and the neurites spanned most of the gray matter. These 3 soma positions were mirrored across the (y, z) sagittal plane (see Fig. 4.1). z positions were then selected to place neurons directly under and halfway between each row of electrodes, as seen in Fig. 4.2. As seen in Fig. 4.2, the rows of electrodes are numbered 1 through 7. Neurons located directly under a row of electrodes are labeled with "r[row number]". Neurons located between 2 rows are labeled with "r[smaller row number]and[larger row number]".

This distribution of neuron models allows simulation of the influence of stimulation on neurons at varying depth and rostral-caudal position in the spinal cord. All six neuron models (with the axon along the $-\hat{x}$, $+\hat{x}$, $-\hat{y}$, $+\hat{y}$, $-\hat{z}$, and $+\hat{z}$ directions) were placed at each of the soma positions and the position of each neuron segment (center of each modeled compartment) recorded to allow voltage time series extraction from the volume conductor models.

In this thesis, a specific neuron can be referenced by "GM[1, 2, or 3]" (the neuron's dorsal-ventral position and part of the left-right position), [L or R] (whether it's on the left or right of the spinal cord), row specification ("r[row number]" or between electrode rows "r[smaller row number]and[larger row number]"), and an orientation ($-\hat{x}$, $+\hat{x}$, $-\hat{y}$, $+\hat{y}$, $-\hat{z}$, and $+\hat{z}$). Sometimes the orientation will be referred to as (Xn, Xp, Yn, Yp, Zn, and Zp). For example, GM1_L_r2and3_Xp would indicate a neuron location in the left dorsal horn of the gray matter between electrode rows 2 and 3 with an axon pointing in the $+\hat{x}$ direction. GM2_R_r5_Zn would indicate a

neuron location in the right ventral horn of the gray matter under electrode rows 5 with an axon pointing in the $-\hat{z}$ direction.

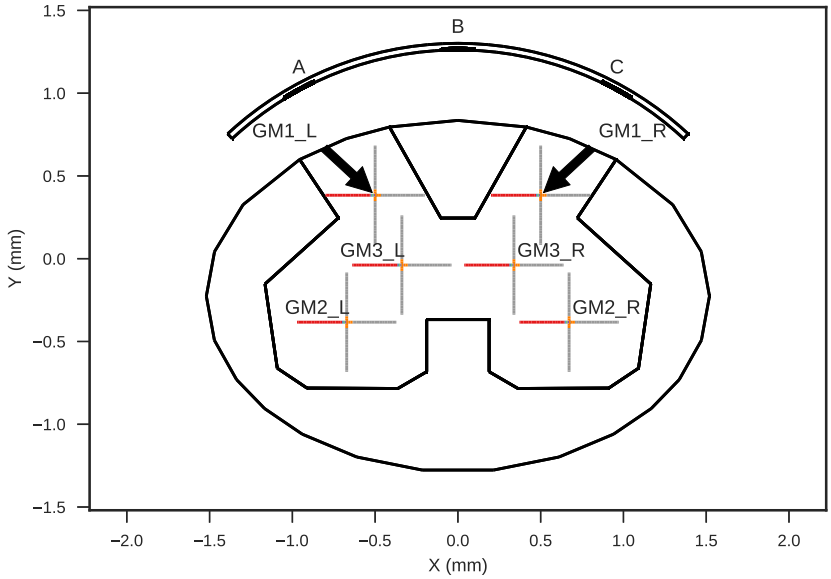


Figure 4.1: soma-positions

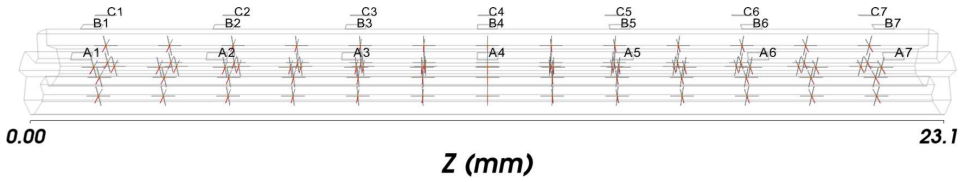


Figure 4.2: Locations of neurons in the simulated spine (with the axon (red) along the $-\hat{x}$ direction). Axis units are in mm.

4.2 Extracellular voltage and neuron simulations

The volume conductor model was discussed in Chapter 2. The monophasic and biphasic stimulation waveforms were discussed in Section 2.1.3. Specifically, the monophasic Gaussian pulse was defined in Eq. (2.13) and the biphasic Gaussian derivative pulse was defined in Eq. (2.17). The 18 stimulation patterns were discussed in Section 2.2.1. For reference, the stimulation parameters for monophasic and biphasic Gaussian stimulation are summarized in Table 4.1.

Table 4.1: Volume conductor simulation parameters. ς is the width parameter used in the monophasic (Eq. (2.13)) and biphasic (Eq. (2.17)) stimulation waveforms. $f^{\max}$ is the dominate frequency of a single stimulation pulse. This frequency was used to determine the material properties in Tables 2.4 and 2.5. The volume conductor simulation was run from $-t_{mag}$ to t_{mag} in steps with stepsize Δt.

	Biphasic	Monophasic
ς	166.04 µ sec	112.84 µ sec
$f^{\max}$	958.5 Hz	0 Hz
t_{mag}	1.66 ms	1.12 ms
Δt	0.01 ms	0.01 ms

For each of the six neuron models and each of the 18 electrode combinations, the extracellular voltage was extracted from the volume conductor simulations for each segment in each neuron and saved to an HDF5 file. As described in Section 2.2.1, the COMSOL volume conductor simulations are linear in the applied voltage, so that scalar multiples of the 6*18 datasets can then be used to derive the extracellular voltages that are applied to the neuron models.

For each type of stimulation (monophasic and biphasic) and electrode pair combination, there are (6 neuron locations for each constant z plane) * (6 geometry types) * (5 z planes under electrode rows +6 z planes between electrode rows (ignoring neurons under rows 1 and 7)) * (2 positive and negative voltage amplitude) = 792 simulation configurations. This means that there are a total of 792 * (18 combinations) * (2 stimulation types) = 28512 total simulation configurations. NEURON simulations were run with stimulation voltages from 0 V to 10 V in steps of 250 mV (yielding 40 unique simulations). The work in this chapter therefore required a

minimum of 792 * 18 * 2 * 40 = 1,140,480 NEURON simulations. Each NEURON simulation simulated 151.0 ms of time using a timestep of 0.01 ms. The stimulation pulse was started 1 ms of simulation time after the saved steady state was loaded. During the NEURON simulations, maximum and minimum membrane voltages were recorded at several locations (axon proper distal tip (seg=16), axon proper middle (seg=8), initial segment ("IS", seg=0), axon hillock ("AH",seg=0), soma (seg=0), distal tip of distal dendrite (seg=16), and the middle of distal dendrite (seg=8). (See Fig. 3.3 for probe locations.)

4.3 Active neurons for monophasic and biphasic stimulation

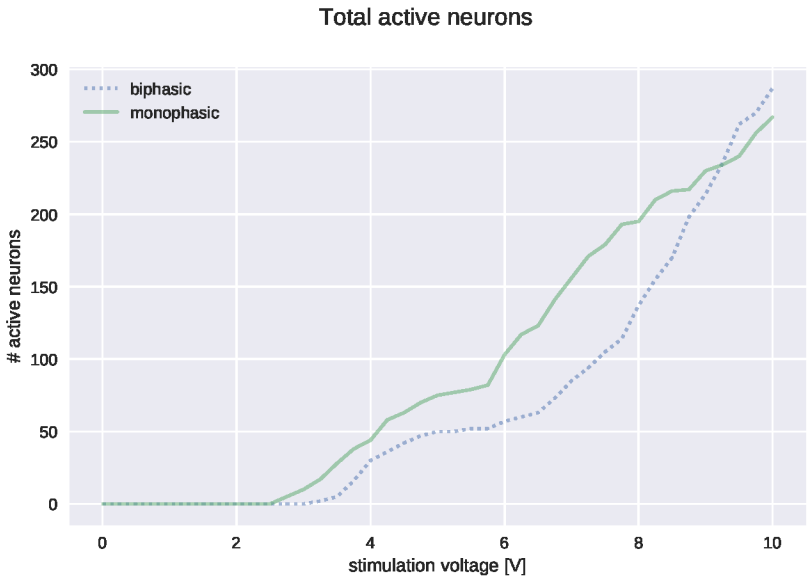


Figure 4.3: The total number of active neurons (neurons with axon tip membrane voltage > -10 mV) for all 18 bipolar stimulation combinations (listed in Section 2.2.1), all neuron locations, and all 6 axon orientations. For each type of stimulation and stimulation voltage magnitude, 14,256 neurons were tested.

As discussed in Section 3.3.2, a neuron is considered *active* (and to have released neurotransmitters) if the membrane voltage on the distal tip of the axon goes above -10 mV. The number of active neurons as a function of stimulation voltage for both biphasic and monophasic stimulation is plotted in Fig. 4.3. From this plot, it appears that monophasic stimulation activates more neurons at lower stimulation

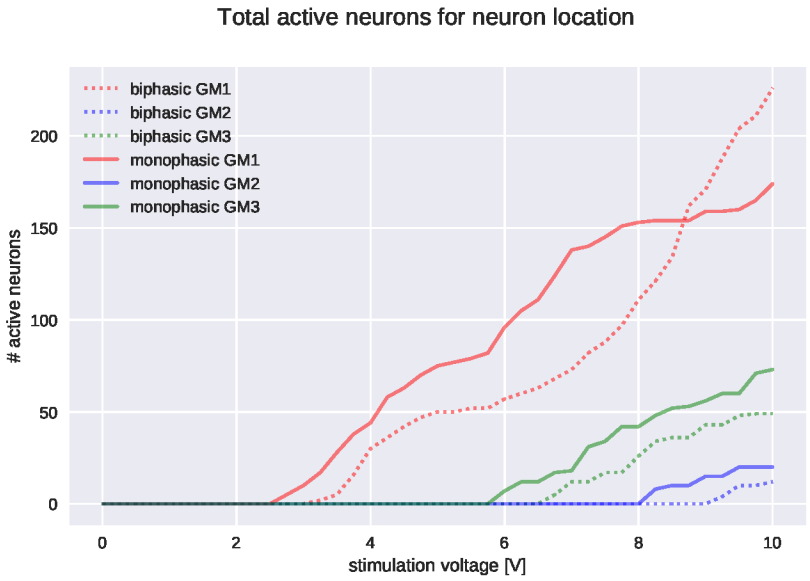


Figure 4.4: The total number of active neurons (neurons with axon tip membrane voltage $> -10\,\text{mV}$ in response to stimulation, as plotted in Fig. 4.3) separated by location in the transverse plane, for all 18 bipolar stimulation combinations (listed in Section 2.2.1), all neuron locations, and all 6 axon orientations. Note that GM1 is most dorsal, GM2 is most ventral, and GM3 is in between. For each type of stimulation, stimulation voltage magnitude, and position in the transverse plane, 4,752 neurons were tested.

magnitudes, but this reverses at higher stimulation magnitudes. Figure 4.4 shows that neurons closer to the electrodes are most easily activated. Figure 4.5 shows the total number of active neurons for each axon orientation. Over-all, more axons pointing in the $+\hat{y}$ direction are activated (likely because the axon tip is closer to the electrodes). Total active neurons by electrode combination can be seen in Fig. 4.6. The neurons activated by each electrode combination can also be seen in the spinal cord in figures in Section 4.A.

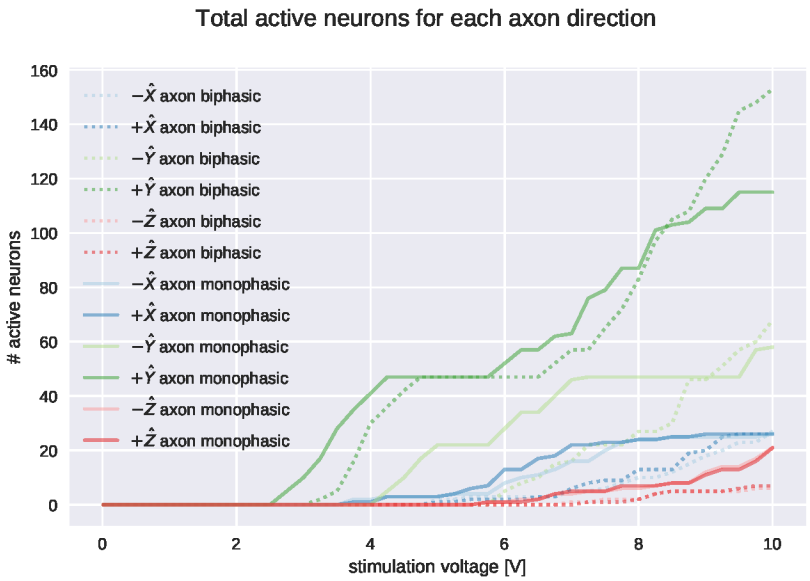


Figure 4.5: The total number of active neurons (neurons with axon tip membrane voltage $> -10\,\text{mV}$ in response to stimulation, as plotted in Fig. 4.3) separated by axon orientation, for all 18 bipolar stimulation combinations (listed in Section 2.2.1) and all neuron locations. Axons are labeled by the direction of the distal tip from the soma. Note that axons pointing in the $+\hat{y}$ direction are the easiest to activate, followed by $-\hat{y}$ with monophasic stimulation. For each type of stimulation, stimulation voltage magnitude, and axon orientation, 2,376 neurons were tested.

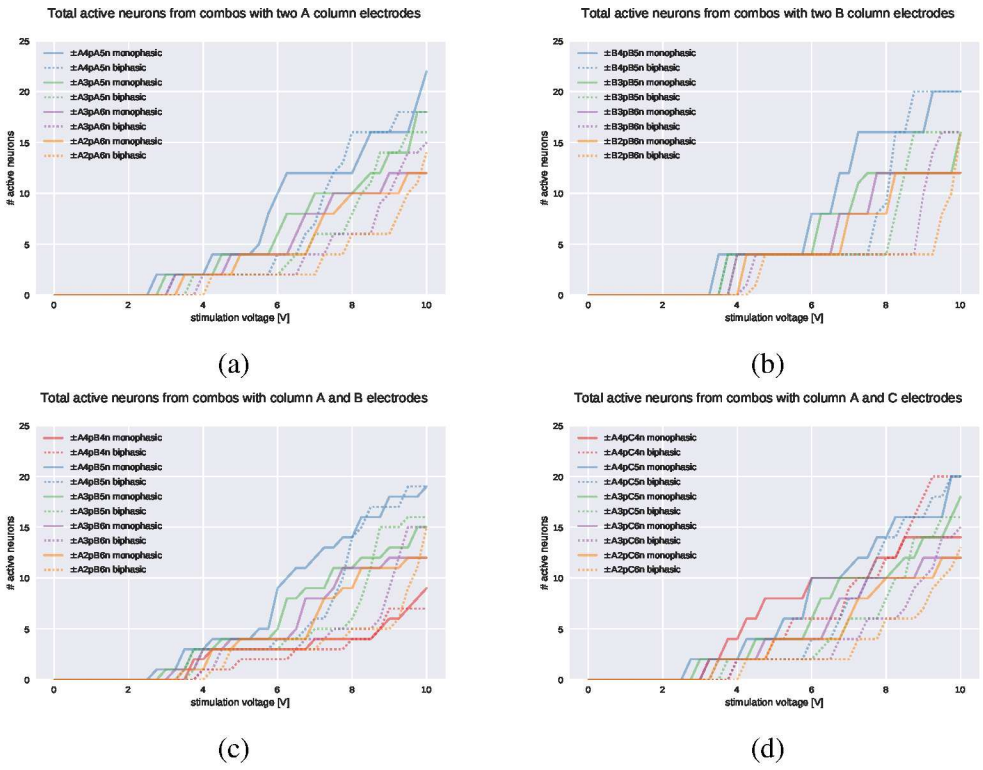


Figure 4.6: The total number of active neurons (neurons with axon tip membrane voltage $> -10\,\text{mV}$ in response to stimulation, as plotted in Fig. 4.3) separated by electrode combination for all neuron locations and all 6 axon orientations. Each sub-figure plots a subset of the combinations: (a) all combinations that have both active electrodes in the A column, (b) all combinations with both active electrodes in the B column, (c) combinations with one A electrode and one B electrode, and (d) combinations with one A electrode and one C electrode. 792 neurons were tested at each stimulation magnitude (x-axis) for each combination.

4.4 Comparison of membrane voltage distribution for monophasic and biphasic stimulation

The previous section looked at counts of active neurons as a function of stimulation voltage. For understanding the process of *facilitation* in the next chapter, it is important to understand how other parts of the neurons respond to stimulation. Figures 4.7 to 4.13 show 2d histograms of the number of neurons with a maximum membrane voltage in mV (y-axis) at probe locations (one for each figure) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 bipolar stimulation combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The colored dots in each figure represent neuron parameters whose axon tip has a maximum membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation required to activate that neuron (see right colorbar). The color of these dots is consistent across stimulation voltages and plots with the same stimulation type. Comparing the location of dots in each plot allows one to determine the maximum membrane voltage at each probe location for neurons that are activated using less than 5 V magnitude of stimulation.

Starting with the distal tip of the axon (seg=16) in Fig. 4.7, there are visibly different responses from biphasic and monophasic stimulation. The monophasic response is clearly non-linear with respect to stimulation magnitude and yields a non-continuous response in some neurons starting around 2750 mV of stimulation. This non-linearity means that for most of the active neurons, the maximum membrane voltage at the axon tip jumps from -30 mV to above -10 mV with a small change in stimulation input. The biphasic response is almost completely linear except for a small region above 8000 mV of stimulation and around 20 mV of membrane voltage. Also note that the maximum membrane voltage resulting from biphasic

stimulation (for a given stimulation amplitude) is larger than that of the equivalent monophasic stimulation, except for the beginning of the nonlinear response curve (between 2750 mV of stimulation and 4000 mV of stimulation).

In the middle of the axon (seg=8), as seen in Fig. 4.8, the maximum membrane voltage's response to monophasic stimulation continues to show the non-continuous jump behavior seen at the axon tip. The biphasic stimulation response continues to be mostly linear, but the non-continuous response above 8 V of stimulation is clearly visible in the Fig. 4.8b.

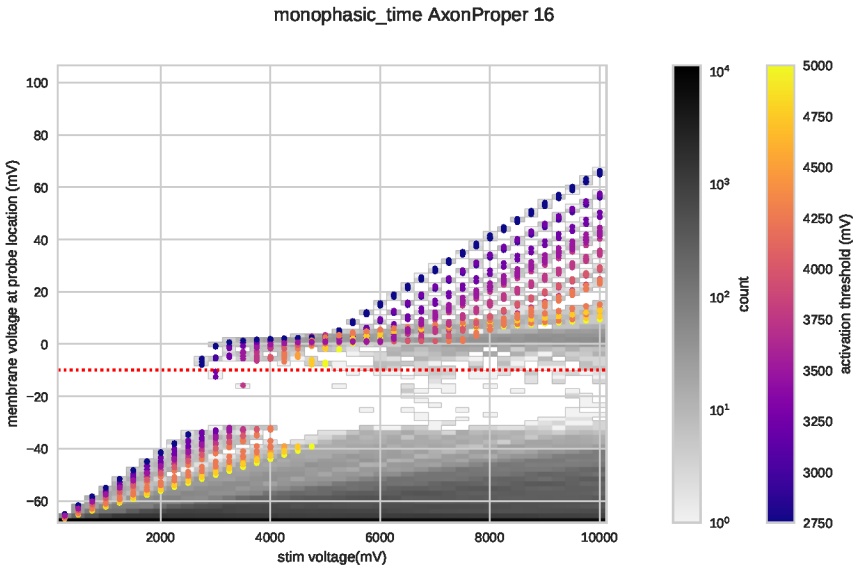
The maximum membrane voltages (or "probes") in the initial segment (IS) of the axon show a similar response (seen in Fig. 4.9) to that of the middle of the axon. However, in the monophasic response (top), some of the active neurons show a reduction in max membrane voltage starting at 9250 mV of stimulation. The axon hillock (Fig. 4.10) and soma (Fig. 4.11) show a similar response to that of the IS, except that most of the soma response is reduced to a membrane voltage below -60 mV, likely because the soma has a much larger membrane surface area.

Figure 4.12 shows the maximum membrane voltage response in the middle of the distal dendrites (seg=8). The response to monophasic stimulation shows at least two types of responses: the maximum membrane voltages of the active neurons jump to around -31 mV and increase continuously from there (with a few exceptions). The maximum membrane voltages of other neurons seem to increase continuously with increasing stimulus, but not linearly. The maximum membrane response to biphasic stimuli in the middle of the distal dendrite is lower than the monophasic response and is mostly continuous and linear (with the exception starting at 8 V of stimulation) with respect to increasing stimulation voltage.

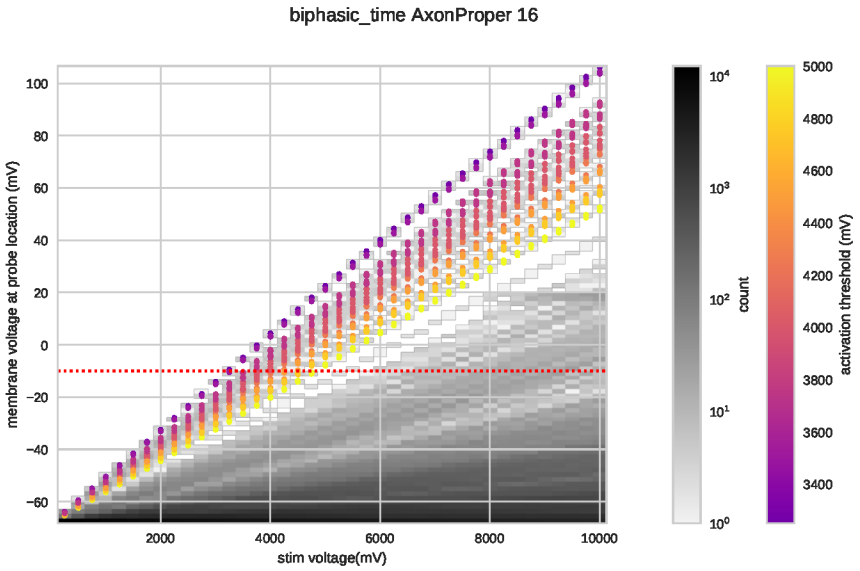
The maximum membrane voltage response of the distal tips of the dendrites (seg=16) to monophasic and biphasic stimulation can be seen in Fig. 4.13. For

biphasic stimulation, the 2D-histogram of maximum membrane voltages appears to be almost identical to the histogram of biphasic responses at the axon tip Fig. 4.7 (bottom). The maximum monophasic response is less than that of the biphasic response and shows some discontinuous behavior (jump to around -27 mV for active neurons). The discontinuous behavior is likely due to orthodromic propagation of an action potential into the dendrites.

The membrane voltage in the dendrites will be discussed more in the next chapter in regards to facilitation.

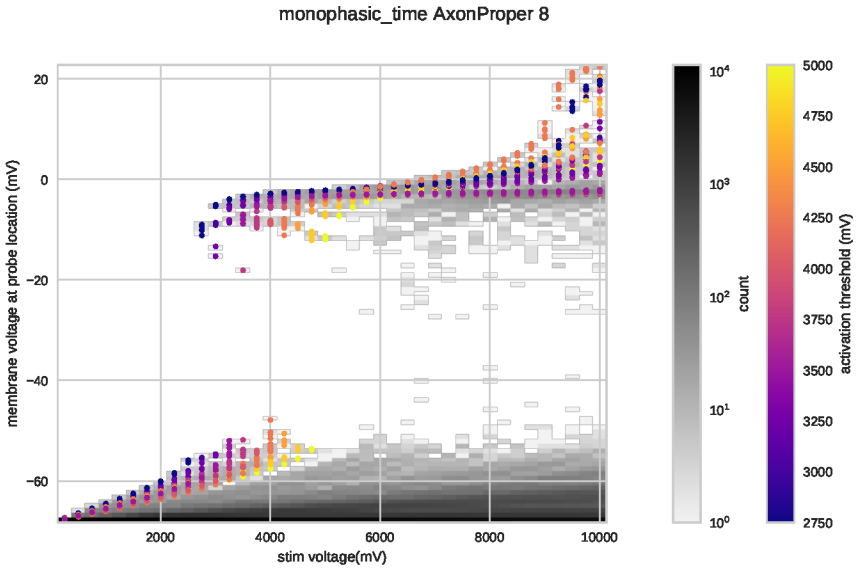


(a) monophasic

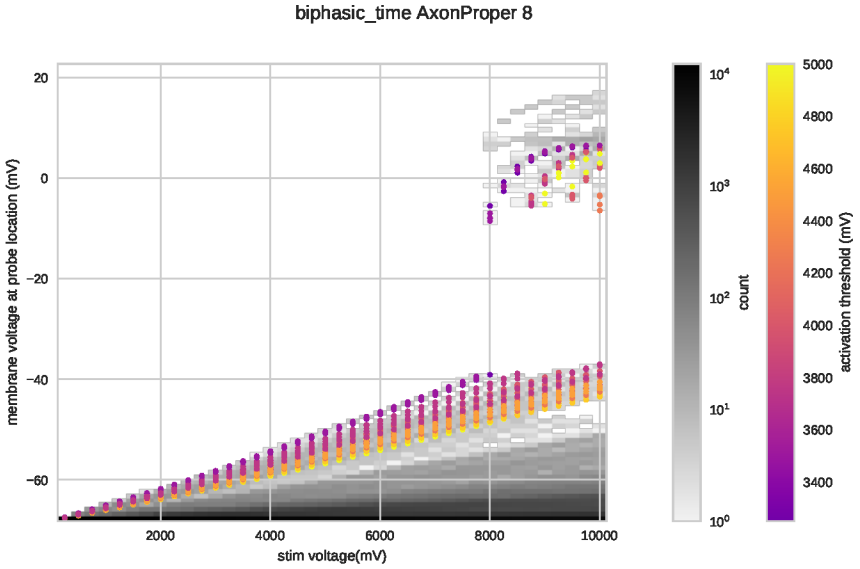


(b) biphasic

Figure 4.7: Maximum membrane voltage in mV at the axon distal tip (segment 16) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar). The red dotted horizontal line indicates the activation threshold (dots and gray rectangles above this line indicate activated neurons).

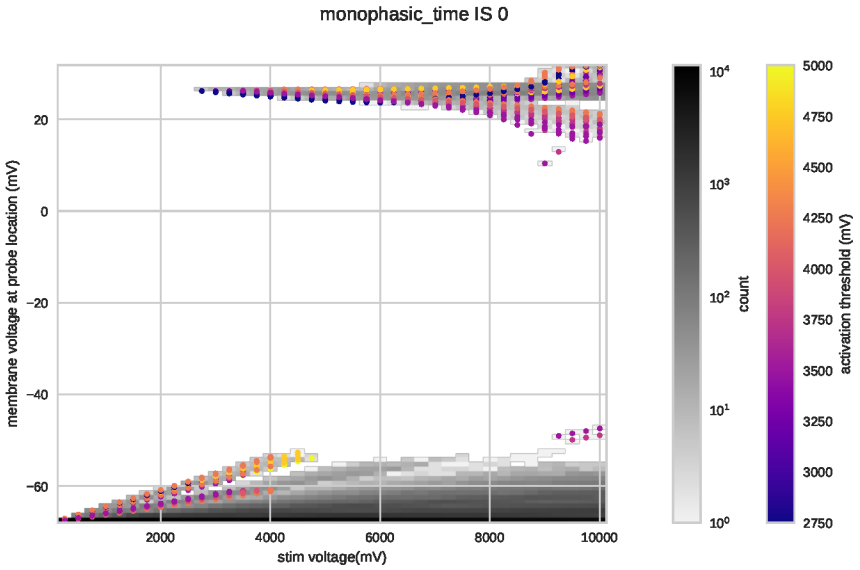


(a) monophasic

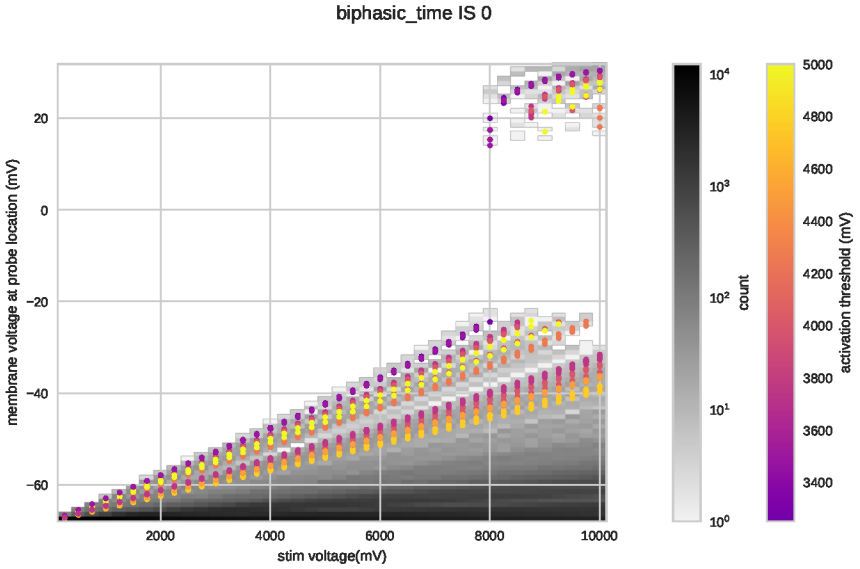


(b) biphasic

Figure 4.8: Maximum membrane voltage in mV at the axon proper middle (segment 8) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).

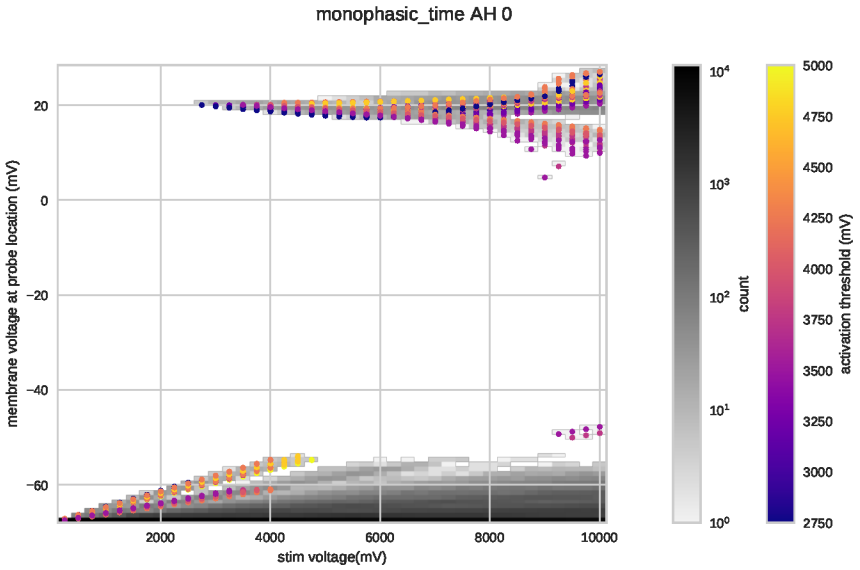


(a) monophasic

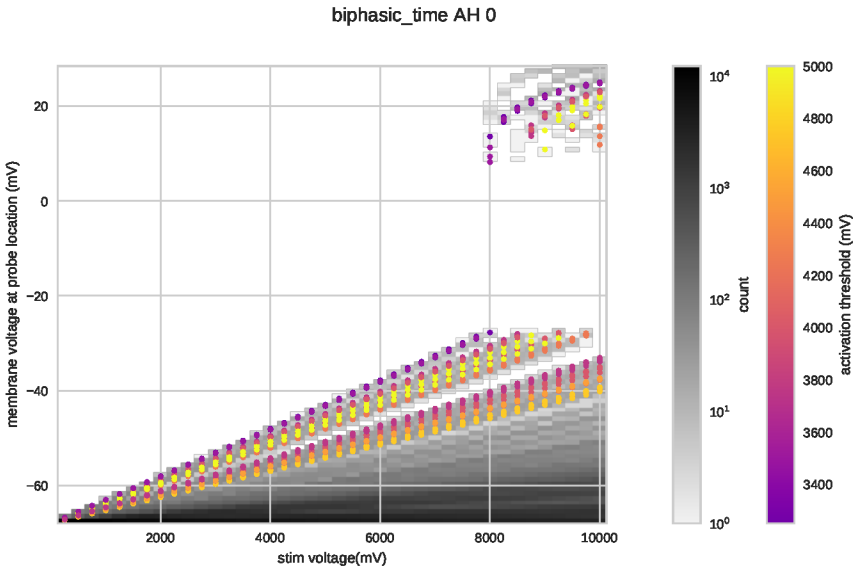


(b) biphasic

Figure 4.9: Maximum membrane voltage in mV at the initial segment (segment 0) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than −10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).

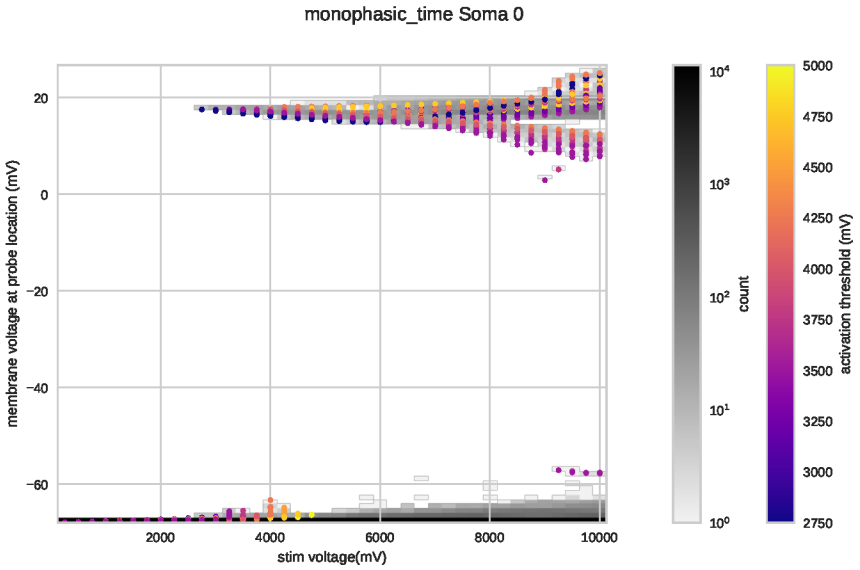


(a) monophasic

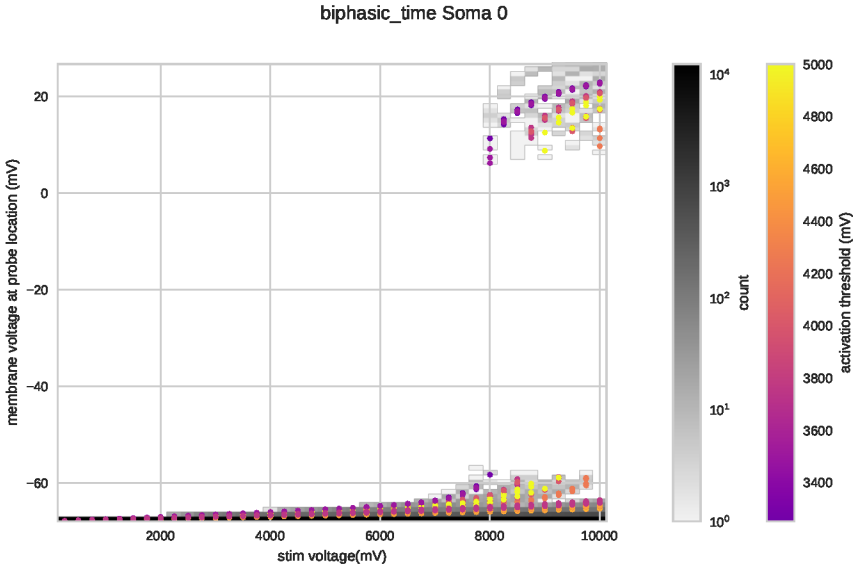


(b) biphasic

Figure 4.10: Maximum membrane voltage in mV at the axon hillock (segment 0) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).

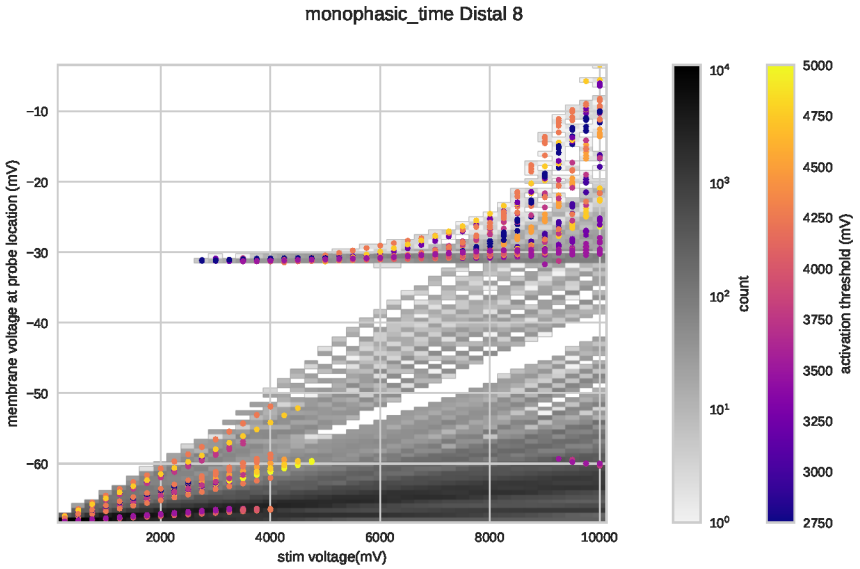


(a) monophasic

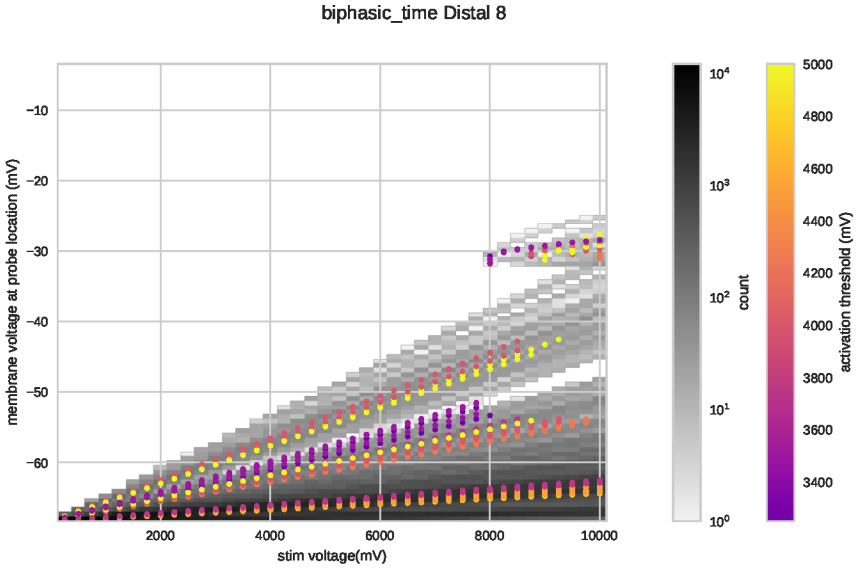


(b) biphasic

Figure 4.11: Maximum membrane voltage in mV at the soma (segment 0) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).

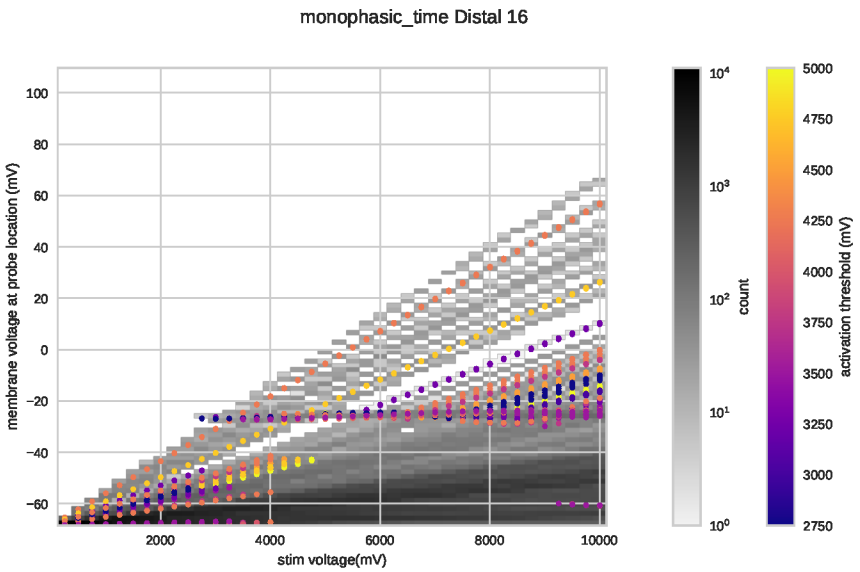


(a) monophasic

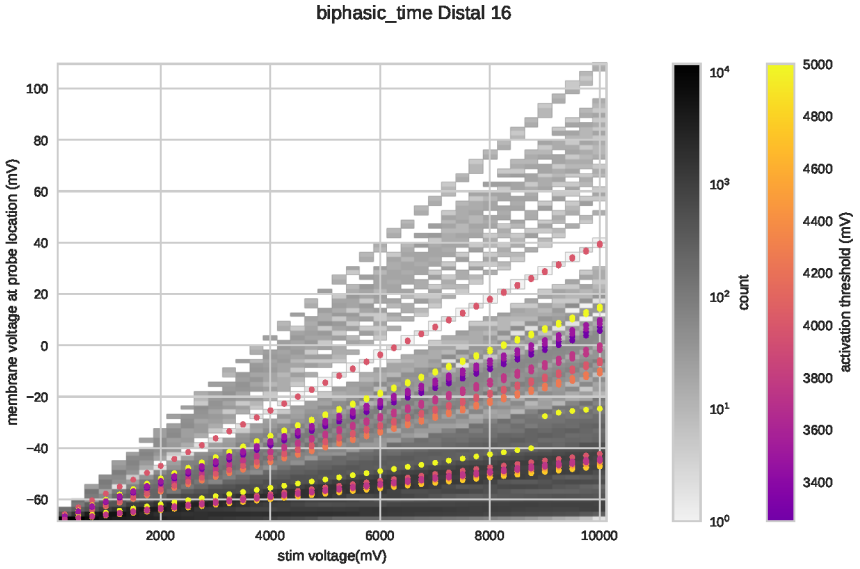


(b) biphasic

Figure 4.12: Maximum membrane voltage in mV at the distal dendrite middle (segment 8) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than −10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).



(a) monophasic



(b) biphasic

Figure 4.13: Maximum membrane voltage in mV at the distal dendrite tip (segment 16) (y-axis) plotted against stimulation voltage in mV (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of simulated neurons exhibiting given the voltage level (see gray colorbar). The colored dots represent neurons selected because their axon tip has a membrane voltage greater than -10 mV (referred to in this thesis as activation) using less than or equal to 5 V of stimulation. The color of each dot indicates the lowest magnitude of stimulation voltage required to activate that neuron (see right colorbar).

4.5 Neurotransmitter release with $\leq 5\,\mathrm{V}$ of stimulation

This section will analyze those combinations of stimuli and neuron configurations that lead to the release of neurotransmitters when using stimulation amplitudes of less than or equal to 5 V. This range of stimulation voltage has a limited amount of neuron activation without synaptic input and will also be used to look for facilitation in the next chapter. These neurons/simulations were plotted as colored dots on Figs. 4.7 to 4.13. As discussed in Section 3.3.2, a model neuron is considered to be *active* and to have released neurotransmitters if the membrane voltage (V_m) at the distal end of the axon tip goes above $-10\,\mathrm{mV}$ in response to the external stimulation.

4.5.1 Monophasic stimulation

The active neurons for all stimulus combinations using no more than 5 V of monophasic stimulation are listed in Table 4.2. Recall from Section 2.2.1 that electrode pair combinations are denoted by the notation [column letter][row number][p for +1V or n for -1V] repeated for each active electrode. In this thesis, nonactive electrodes have a floating voltage. The simulation shows that under these conditions, all of the active neurons are in the GM1 level (closest to the dorsal side of the spinal cord). All of the active axons point towards the negative electrode or away from the positive electrode (see also figures of Section 4.A.1). This implies that it is easier to activate the neuron if the axon tip has a lower extracellular voltage than the soma and other parts of the neuron. This fact is supported by the rest of the monophasic stimulation data (see Fig. 4.22) and is discussed in more detail in Section 4.6. Of the 75 active neurons, 44 had axons pointing in the $+\hat{y}$ direction near negative electrodes, 21 had axons pointing in the $-\hat{y}$ direction near positive electrodes, and 10 were inside a single row combination (3 with axons pointing in the $-\hat{x}$ direction, 3 with axons pointing in the $+\hat{x}$ direction, 1 with an axon pointing in the $-\hat{y}$ direction, and 3 with axons pointing in the $+\hat{y}$ direction) that also follows

the "axon points to the negative electrode or away from the positive electrode" rule. Also note that the stimulation voltage necessary to raise the membrane voltage of the IS probe above $-20\,\text{mV}$ is close to the stimulation voltage needed to activate the axon tip. This indicates that a significant portion of the cell is involved in the generation of the action potential, not just the tip of the axon.

Table 4.2: Monophasic simulations which result in the membrane voltage of the axon tip being above $-10\,\text{mV}$ ($V_m > -10\,\text{mV}$) while the stimulation voltage is below an amplitude of $5\,\text{V}$ ($|V_{stim}| < 5\,\text{V}$). The combo column indicates which electrodes are active. (Recall from Section 2.2.1 that electrode combinations use the notation [column letter][row number][p for +1V or n for -1V] repeated for each active electrode.) Nonactive electrodes are floating. A value of -1 in the sign column reverses the sign of the electrodes in the combination. The side, row, and dorsal-ventral columns indicate the location of the neuron. The axon column indicates the direction of the distal tip of the axon from the soma. In this table, column A16 captures the magnitude of the stimulation voltage necessary to cause the membrane voltage at the axon tip (segment 16) to exceed $-10\,\text{mV}$. Column S-A16 tabulates the additional amount of stimulation necessary to cause the soma membrane voltage to exceed $-10\,\text{mV}$. Columns D8-A16 and D16-A16 are the additional amount of stimulation (beyond that in column A16) necessary to cause the membrane voltage of the middle (seg=8) and distal tip (seg=16) of the distal dendrite respectively to exceed $-40\,\text{mV}$.

combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
A2pA6n	-1	L	r2	GM1	Yp	3500	0	0	0
			r6		Yn	5000	0	0	0
	1		r2			5000	0	0	0
			r6		Yp	3500	0	0	0
A2pB6n	-1		r2			3500	0	0	0
	1				Yn	5000	0	0	0
			r6		Yp	4250	0	0	0
		R				4250	0	0	0
A2pC6n	-1	L	r2			3500	0	0	0
		R	r6		Yn	5000	0	0	0
	1	L	r2			5000	0	0	0
		R	r6		Yp	3500	0	0	0
A3pA5n	-1	L	r3			3000	0	0	0
			r5		Yn	4500	0	0	0

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combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
	1		r3			4500	0	0	0
			r5		Yp	3000	0	0	0
A3pA6n	-1		r3			3250	0	0	0
			r6		Yn	4750	0	0	0
	1		r3			4750	0	0	0
			r6		Yp	3250	0	0	0
A3pB5n	-1		r3			3000	0	0	0
	1				Yn	4500	0	0	0
			r5		Yp	3750	0	0	0
		R				3750	0	0	0
A3pB6n	-1	L	r3			3250	0	0	0
	1				Yn	4750	0	0	0
			r6		Yp	4000	0	0	0
		R				4000	0	0	0
A3pC5n	-1	L	r3			3000	0	0	0
		R	r5		Yn	4500	0	0	0
	1	L	r3			4500	0	0	0
		R	r5		Yp	3000	0	0	0
A3pC6n	-1	L	r3			3250	0	0	0
		R	r6		Yn	4750	0	0	0
	1	L	r3			4750	0	0	0
		R	r6		Yp	3250	0	0	0
A4pA5n	-1	L	r4			2750	0	0	0
			r5		Yn	4250	0	0	0
	1		r4			4250	0	0	0
			r5		Yp	2750	0	0	0
A4pB4n	-1		r4		Xn	3750	0	0	0
	1				Xp	4250	0	0	0
		R			Yp	3750	-250	-250	-250
A4pB5n	-1	L				2750	0	0	0
	1				Yn	4250	0	0	0
			r5		Yp	3500	0	0	0
		R				3500	0	0	0
A4pC4n	-1	L	r4		Xn	4250	0	0	-1750
					Yp	3250	-250	-250	-250
		R			Xn	3750	0	0	0

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combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
					Yn	4750	0	0	-1500
	1	L			Xp	3750	0	0	0
					Yn	4750	0	0	-1500
		R			Xp	4250	0	0	-1750
					Yp	3250	-250	-250	-250
A4pC5n	-1	L				2750	0	0	0
		R	r5		Yn	4250	0	0	0
	1	L	r4			4250	0	0	0
		R	r5		Yp	2750	0	0	0
B2pB6n	-1	L	r2			4250	0	0	0
		R				4250	0	0	0
	1	L	r6			4250	0	0	0
		R				4250	0	0	0
B3pB5n	-1	L	r3			3750	0	0	0
		R				3750	0	0	0
	1	L	r5			3750	0	0	0
		R				3750	0	0	0
B3pB6n	-1	L	r3			4000	0	0	0
		R				4000	0	0	0
	1	L	r6			4000	0	0	0
		R				4000	0	0	0
B4pB5n	-1	L	r4			3500	0	0	0
		R				3500	0	0	0
	1	L	r5			3500	0	0	0
		R				3500	0	0	0

The minimum amount of monophasic stimulation to activate a neuron was 2750 mV. A total of five neurons were activated at that stimulation level using combinations ±A4pA5n, -A4pB5n, and ±A4pC5n. All of the active neurons were directly under the negative electrode.

The membrane voltage as a function of time for all segments of the neuron located at GM1_L_r5 with an axon pointing in the $+\hat{y}$ direction exposed to 2750 mV of monophasic stimulation using combination A4pA5n is plotted in Fig. 4.14. Note that the action potential starts at the axon tip and travels in the antidromic direction until it reaches the initial segment (IS). Then an orthodromic conduction occurs (back towards the axon tip) but is diminished in strength by the time it reaches the axon tip. All of the neurons activated using less than or equal to 10 V of monophasic stimulation show similar behavior (in some cases the second conduction merges with the first). Figure 4.15 shows the membrane voltage for the probe locations as a function of stimulation voltage. In this case, the axon tip has the highest membrane voltage when the stimulation voltage is below the level required to "activate" (i.e. membrane voltage at the axon tip goes above -10 mV) the neuron. This is not always the case. In some of the simulated neurons, a dendrite tip is most stimulated. The bottom plot of Fig. 4.15 also confirms that the axon tip reaches maximum membrane voltage first, followed by the axon middle, then the AH, IS, and soma at the same time.

4.5.2 Biphasic stimulation

The active neurons (with axon tip membrane voltage > -10 mV) for all combinations using no more than 5 V of biphasic stimulation are listed in Table 4.3. Similar to the monophasic simulation seen in Table 4.2, all of the active neurons are in the GM1 layer. Of the 50 active neurons (25 fewer than monophasic), 44 had axons pointing in the $+\hat{y}$ direction and were located near electrodes whose biphasic stim-

ulation has a leading edge which is negative. The other 6 active neurons (2 with axons pointing in the $-\hat{x}$ direction, 1 with an axon pointing in the $+\hat{x}$ direction, and 3 with axons pointing in the $+\hat{y}$ direction) are stimulated by electrodes in a single row and have axons that point towards the electrode whose biphasic stimulation has a leading edge which is negative.

All of the active neurons were positioned directly under the electrode with the negative leading edge. Note that it takes a substantially larger stimulation voltage for the Initial Segment (IS) to be involved (at least 4V). This suggests that biphasic stimulation of neurons in the spinal cord (without additional synapse involvement) does not usually involve the whole cell. This can also be seen in the biphasic plots in Figs. 4.7 to 4.13.

Table 4.3: Biphasic simulations which result in the membrane voltage of the axon tip being above $-10\,\text{mV}$ ($V_m > -10\,\text{mV}$) while the stimulation voltage is below an amplitude of $5\,\text{V}$ ($|V_{stim}| < 5\,\text{V}$). The combo column indicates which electrodes are active. (Recall from Section 2.2.1 that electrode combinations use the notation [column letter][row number][p for +1V or n for -1V] repeated for each active electrode.) Nonactive electrodes are floating. A value of -1 in the sign column reverses the sign of the electrodes in the combination. The side, row, and dorsal-ventral columns indicate the location of the neuron. The axon column indicates the direction of the distal tip of the axon from the soma. In this table, column A16 captures the magnitude of the stimulation voltage necessary to cause the membrane voltage at the axon tip (segment 16) to exceed $-10\,\text{mV}$. Column S-A16 tabulates the additional amount of stimulation necessary to cause the soma membrane voltage to exceed $-10\,\text{mV}$. Columns D8-A16 and D16-A16 are the additional amount of stimulation (beyond that in column A16) necessary to cause the membrane voltage in the middle (seg=8) or distal tip (seg=16) of one of the distal dendrites respectively to exceed $-40\,\text{mV}$. A value of OSR means Outside Search Range (i.e. more than $\pm 10\,\text{V}$ of stimulation is necessary).

combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
A2pA6n	-1	L	r2	GM1	Yp	4250	5750	5750	750
	1		r6			4250	5750	5750	750
A2pB6n	-1		r2			4250	5750	5750	750

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combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
	1		r6			4750	OSR	OSR	OSR
		R				4750	OSR	OSR	OSR
A2pC6n	-1	L	r2			4250	5750	5750	750
	1	R	r6			4250	5750	5750	750
A3pA5n	-1	L	r3			3750	5000	5000	750
	1		r5			3750	5000	5000	500
A3pA6n	-1		r3			4000	5500	5500	750
	1		r6			4000	5500	5500	750
A3pB5n	-1		r3			3750	5000	5000	750
	1		r5			4000	OSR	OSR	OSR
		R				4000	OSR	OSR	OSR
A3pB6n	-1	L	r3			4000	5500	5500	750
	1		r6			4500	OSR	OSR	OSR
		R				4500	OSR	OSR	OSR
A3pC5n	-1	L	r3			3750	5000	5000	750
	1	R	r5			3750	5000	5000	500
A3pC6n	-1	L	r3			4000	5500	5500	750
	1	R	r6			4000	5500	5500	750
A4pA5n	-1	L	r4			3250	4750	4750	750
	1		r5			3250	5000	5000	750
A4pB4n	-1		r4		Xn	5000	4000	4000	4000
	1	R			Yp	4000	OSR	OSR	OSR
A4pB5n	-1	L				3500	4500	4500	250
	1		r5			3750	OSR	OSR	OSR
		R				3750	OSR	OSR	OSR
A4pC4n	-1	L	r4			4000	4750	4750	-1250
		R			Xn	5000	4500	4500	-1500
	1	L			Xp	5000	4000	4000	-1500
		R			Yp	4000	4750	4750	-1250
A4pC5n	-1	L				3500	4500	4500	250
	1	R	r5			3500	4500	4500	250
B2pB6n	-1	L	r2			4500	OSR	OSR	OSR
		R				4750	OSR	OSR	OSR
	1	L	r6			4750	OSR	OSR	OSR
		R				4750	OSR	OSR	OSR
B3pB5n	-1	L	r3			4000	OSR	OSR	OSR

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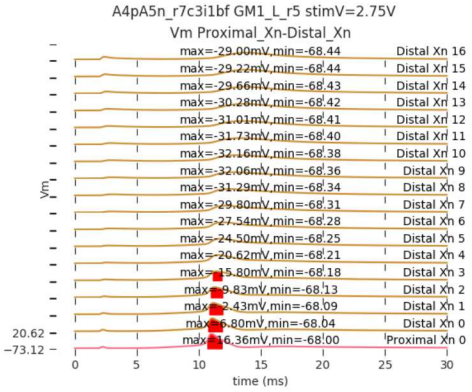
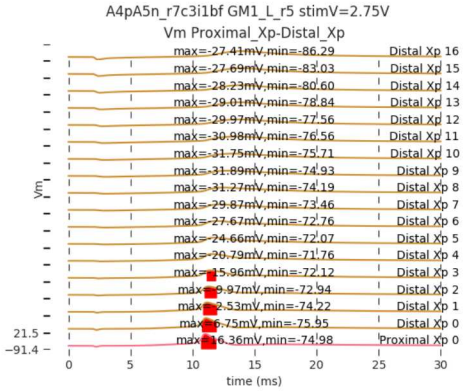
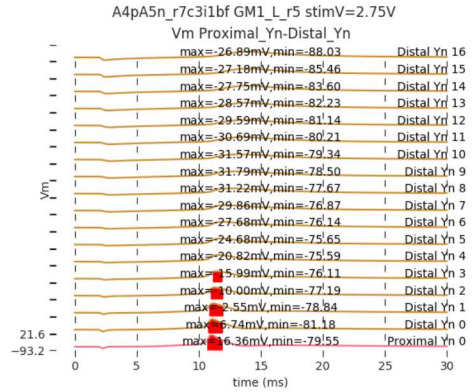
combo	sign	side	row	dorsal-ventral	axon	A16	S-A16	D8-A16	D16-A16
		R				4000	OSR	OSR	OSR
	1	L	r5			4000	OSR	OSR	OSR
		R				4000	OSR	OSR	OSR
B3pB6n	-1	L	r3			4250	OSR	OSR	OSR
		R				4500	OSR	OSR	OSR
	1	L	r6			4500	OSR	OSR	OSR
		R				4500	OSR	OSR	OSR
B4pB5n	-1	L	r4			3750	OSR	OSR	OSR
		R				3750	OSR	OSR	OSR
	1	L	r5			3750	OSR	OSR	OSR
		R				3750	OSR	OSR	OSR



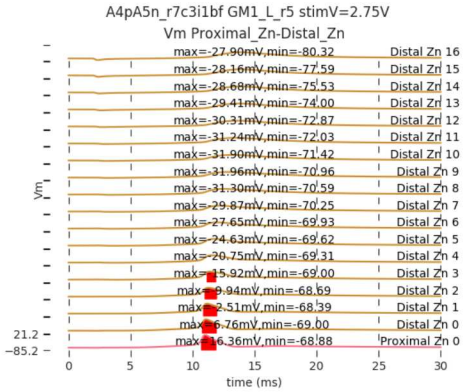
(a) Proximal_Xn-Distal_Xn



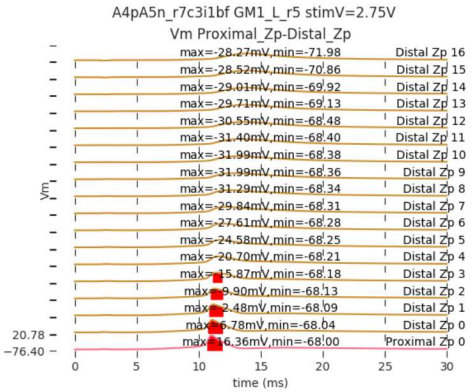
(b) Proximal_Xp-Distal_Xp



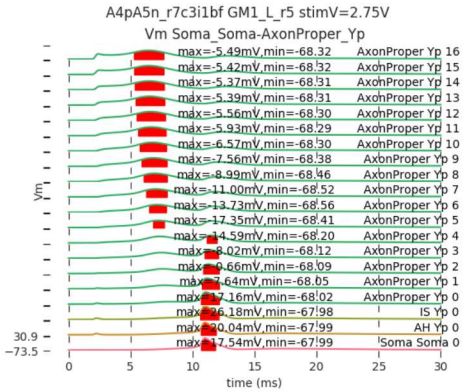
(c) Proximal_Yn-Distal_Yn



(d) Proximal_Zn-Distal_Zn



(e) Proximal_Zp-Distal_Zp



(f) Soma_Soma-AxonProper_Yp

Figure 4.14: Membrane voltage (V_m) vs time, for a neuron with axon pointing towards Yp located at GM1_L_r5 exposed to 2.75 V of monophasic stimulation using combination A4pA5n. Each subfigure (a-f) plots V_m on a each segment of a different neurite: (a) $-\hat{x}$ dendrite, (b) $+\hat{x}$ dendrite, (c) $-\hat{y}$ dendrite, (d) $-\hat{z}$ dendrite, (e) $+\hat{z}$ dendrite, and (f) $+\hat{y}$ axon + soma. For each subfigure (a-f): The horizontal axis is the simulation time in ms. Each segment plot is labeled on the right side with (section type, orientation, segment number). The range of the vertical axis for the segment plots is indicated in the lower left corner. The minimum and maximum V_m for each segment is in the middle of each segment plot. Red areas under each segment plot indicate time periods in which V_m at that segment exceeds -10 mV.
Subfigure (f) shows an antidromic action potential starting at the axon tip followed by an orthodromic action potential starting at the IS. The second action potential fails to cause neurotransmitter release most likely because of the refractory period of the axon.

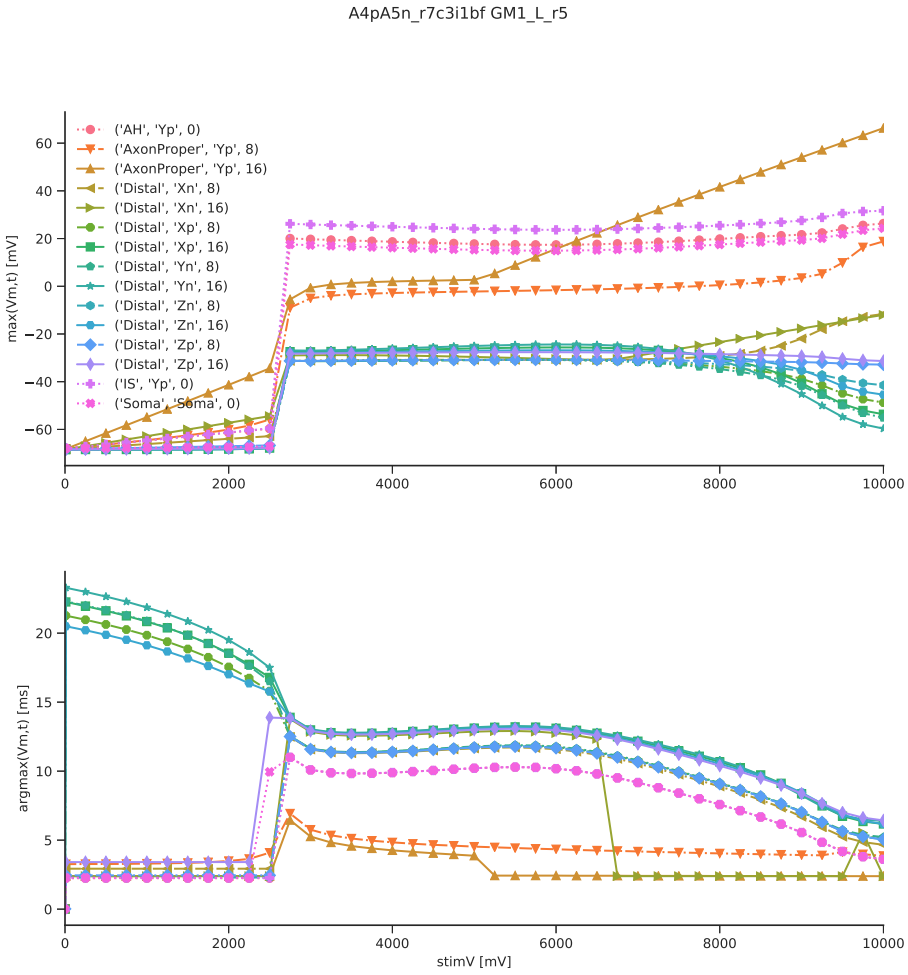


Figure 4.15: (top): Membrane voltage (in mV) at different locations on a simulated neuron as a function of stimulation voltage (in mV, axis shared with bottom plot) for monophasic stimulation with combination A4pA5n, location GM1_L_r5, and axon in the $+\hat{y}$ direction. This is one of the configurations that results in neuron activation with the minimum amount of monophasic stimulation (in this case 2.75 V). The legend labels in the top plot are in the format (section type, orientation, segment number). See Fig. 3.3 for segment number locations by section type. Note that the axon tip (AxonProper, Yp, 16) is most stimulated compared to other probe locations if the stimulation voltage amplitude is less than 2.75 V. (bottom): The time of the maximum membrane voltage (in ms) for each probe vs stimulation voltage (in mV). The time of the maximum membrane voltage helps explain which parts of the neuron reach maximum first. Note that the stimulation pulse starts at 1 ms and peaks at 2.12 ms.

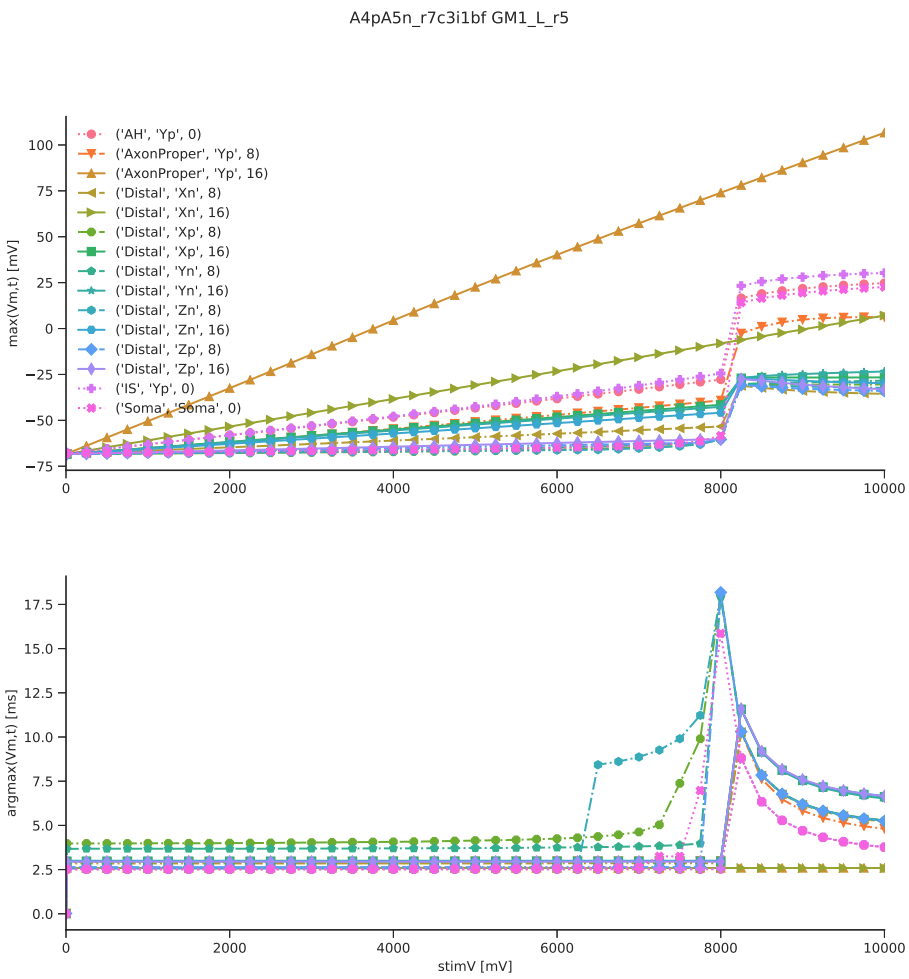


Figure 4.16: (top): Membrane voltage (in mV) at different locations on a simulated neuron as a function of stimulation voltage (in mV, axis shared with bottom plot) for biphasic stimulation with combination A4pA5n, location GM1_L_r5, and axon in the $+\hat{y}$ direction. This is the same configuration as in Fig. 4.15, except biphasic instead of monophasic stimulation. This is one of the configurations that results in neuron activation with the minimum amount of biphasic stimulation (in this case 3.25 V). The legend labels in the top plot are in the format (section type, orientation, segment number). See Fig. 3.3 for segment number locations by section type. Note that the axon tip (AxonProper, 'Yp' ,16) is most stimulated compared to other probe locations and linear as expected from Fig. 4.7b. (bottom): The time of the maximum membrane voltage (in ms) for each probe vs stimulation voltage (in mV). The time of the maximum membrane voltage helps explain which parts of the neuron reach maximum first. Note that the stimulation pulse starts at 1 ms the middle of the pulse is at 2.66 ms and the maximum amplitudes of the pulse occur at 2.66 ms ± 0.16 ms. The first maximum amplitude occurs at 2.5 ms and the maximum in the axon proper tip, and the $-\hat{x}$ distal dendrite tip occurs very shortly after.

Table 4.4: Biphasic simulations which result in an orthodromic action potential using less than 10V of biphasic stimulation. The simulation voltage necessary (V_{stim}) is listed in volts.

combo	sign	side	row	dorsal-ventral	axon	V_{stim}
A2pA6n	1	L	r6	GM1	Yn	10.0
A2pA6n	-1	L	r2	GM1	Yn	9.75
A2pB6n	-1	L	r2	GM1	Yn	9.75
A2pC6n	1	R	r6	GM1	Yn	10.0
A2pC6n	-1	L	r2	GM1	Yn	9.75
A3pA5n	1	L	r5	GM1	Yn	8.75
A3pA5n	-1	L	r3	GM1	Yn	8.75
A3pA6n	1	L	r6	GM1	Yn	9.25
A3pA6n	-1	L	r3	GM1	Yn	9.5
A3pB5n	-1	L	r3	GM1	Yn	8.75
A3pB6n	-1	L	r3	GM1	Yn	9.5
A3pC5n	1	R	r5	GM1	Yn	8.75
A3pC5n	-1	L	r3	GM1	Yn	8.75
A3pC6n	1	R	r6	GM1	Yn	9.25
A3pC6n	-1	L	r3	GM1	Yn	9.5
A4pA5n	1	L	r5	GM1	Yn	8.0
A4pA5n	-1	L	r4	GM1	Yn	8.0
A4pB4n	1	L	r4	GM1	Xn	9.0
A4pB4n	-1	L	r4	GM1	Xp	8.75
A4pB5n	-1	L	r4	GM1	Yn	8.0

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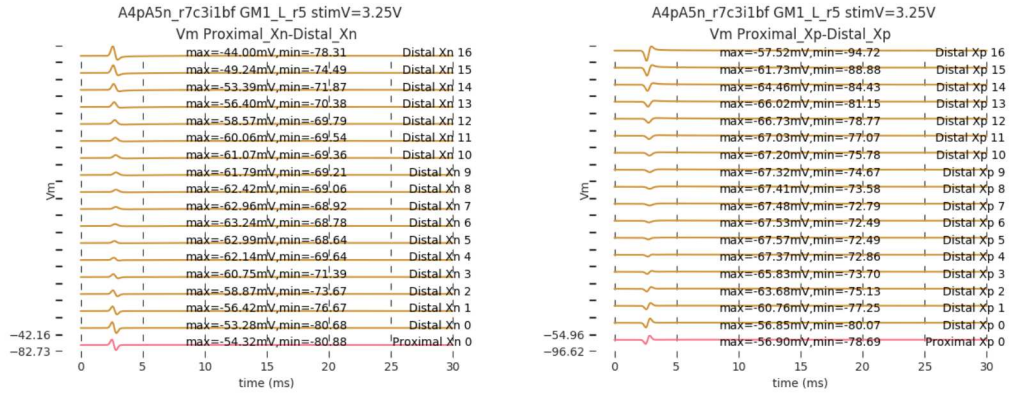
combo	sign	side	row	dorsal-ventral	axon	V_{stim}
A4pC4n	1	L	r4	GM1	Xn	9.0
A4pC4n	1	L	r4	GM1	Yp	8.5
A4pC4n	1	R	r4	GM1	Xn	9.25
A4pC4n	1	R	r4	GM1	Yn	8.75
A4pC4n	-1	L	r4	GM1	Xp	9.0
A4pC4n	-1	L	r4	GM1	Yn	8.5
A4pC4n	-1	R	r4	GM1	Xp	9.25
A4pC4n	-1	R	r4	GM1	Yp	8.75
A4pC5n	1	R	r5	GM1	Yn	8.0
A4pC5n	-1	L	r4	GM1	Yn	8.0

The minimum amount of biphasic stimulation magnitude to activate a neuron was 3250 mV (500 mV more than monophasic). Two neurons were activated at that stimulation level using combinations ±A4pA5n (A4pA5n means electrode A4 has a positive leading edge of the biphasic stimulation and A5 has a negative leading edge. -A4pA5n means electrode A4 has the negative leading edge and A5 the positive leading edge). One of these neurons happens to be the same neuron examined with monophasic stimulation in Figs. 4.14 and 4.15. The membrane voltage as a function of time for all segments with 3.25 V of biphasic stimulation (just enough to activate the neuron), combination A4pA5n, axon along the $+\hat{y}$ direction, location GM1_L_r5 (most dorsal, left side, row 5) is plotted in Fig. 4.17. In this case, the axon tip is activated, but when the voltage is reversed, the cell returns to resting potential and no action potential is formed. The linear nature of this response to stimulation voltage below 8 V of stimulation can be seen in Fig. 4.16. It is impor-

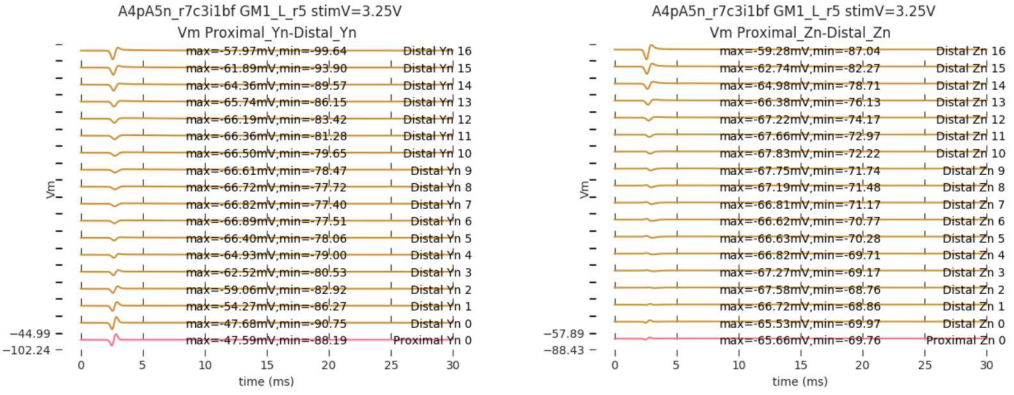
tant to remember that although the membrane voltage returns to resting potential in a short time frame, the state of the ion channels and ion concentrations inside the cell may take longer to return to steady state and could help or hinder facilitation, as will be studied in the next chapter.

As seen in Figs. 4.7 to 4.13, the response of other neurons to stimulation is also mostly linear below 8 V. Those neurons with a non-linear action-potential-like response in the axon tip are listed in Table 4.4. One or more of the dendrites in these neurons are strongly stimulated, and this effect seems to generate an orthodromic action potential starting at the IS. One example of an orthodromic action potential occurs using 8 V biphasic stimulation, combination A4pA5n, location GM1_L_r5 (most dorsal, left side, row 5)), but with the axon along the $-\hat{y}$ direction instead of the $+\hat{y}$ direction in the previous examples. The membrane voltage as a function of time can be seen in Fig. 4.18. Although many parts of the cell are hyperpolarized (have a lower membrane voltage) and depolarized (higher membrane voltage) compared to resting potential at different times in the simulation, the $+\hat{y}$ direction is notably strongly depolarized and the $-\hat{x}$ dendrite moderately depolarized compared to the other dendrites. This can also be seen in as a function of stimulation voltage in Fig. 4.19 where the $+\hat{y}$ and $-\hat{x}$ dendrites are most depolarized at stimulation voltages less than 8 V.



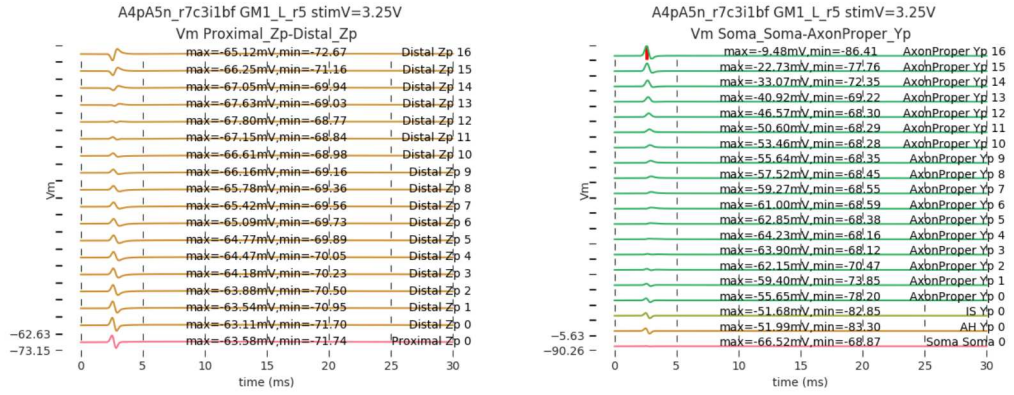
(a) Proximal_Xn-Distal_Xn

(b) Proximal_Xp-Distal_Xp



(c) Proximal_Yn-Distal_Yn

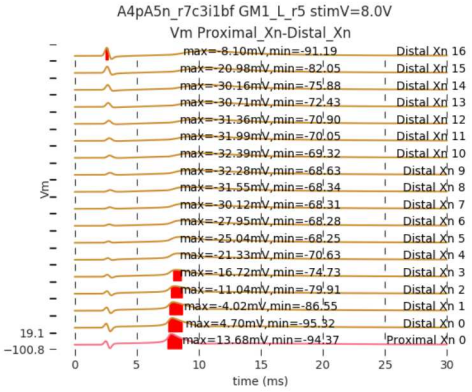
(d) Proximal_Zn-Distal_Zn



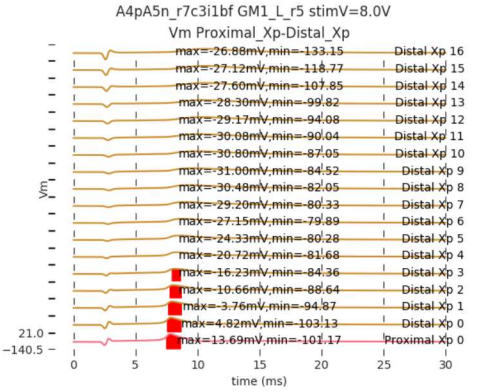
(e) Proximal_Zp-Distal_Zp

(f) Soma_Soma-AxonProper_Yp

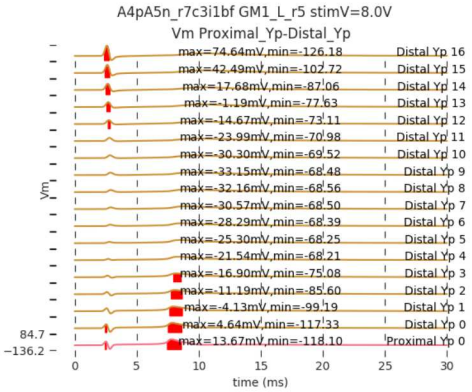
Figure 4.17: Membrane voltage (V_m) vs time, for a neuron with axon pointing towards Yp located at GM1_L_r5 exposed to 3.25 V of biphasic stimulation using combination A4pA5n. Each subfigure (a-f) plots V_m on each segment of a different neurite: (a) $-\hat{x}$ dendrite, (b) $+\hat{x}$ dendrite, (c) $-\hat{y}$ dendrite, (d) $-\hat{z}$ dendrite, (e) $+\hat{z}$ dendrite, and (f) $+\hat{y}$ axon + soma. For each subfigure (a-f): The horizontal axis is the simulation time in ms. Each segment plot is labeled on the right side with (section type, orientation, segment number). The range of the vertical axis for the segment plots is indicated in the lower left corner. The minimum and maximum V_m for each segment are in the middle of each segment plot. Red areas under each segment plot indicate time periods in which V_m at that segment exceeds -10 mV.
Subfigure (f) shows that no action potential occurs, and instead the stimulation pulse causes V_m at the axon tip to exceed -10 mV (and release neurotransmitters) directly.



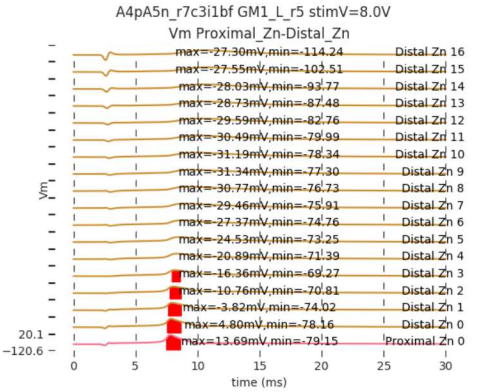
(a) Proximal_Xn-Distal_Xn



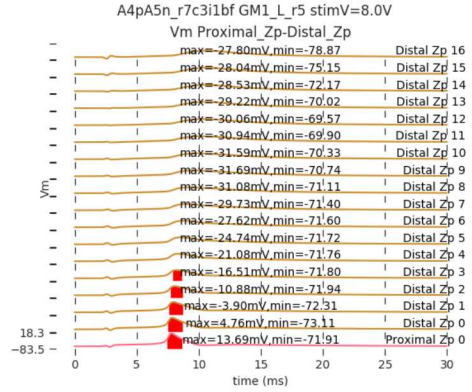
(b) Proximal_Xp-Distal_Xp



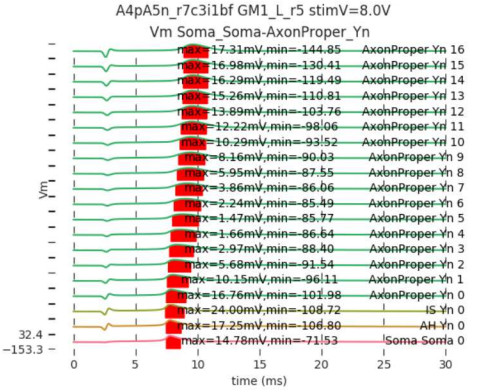
(c) Proximal_Yp-Distal_Yp



(d) Proximal_Zn-Distal_Zn



(e) Proximal_Zp-Distal_Zp



(f) Soma_Soma-AxonProper_Yn

Figure 4.18: Membrane voltage (V_m) vs time, for a neuron with axon pointing towards Yn located at GM1_L_r5 exposed to 8.0 V of biphasic stimulation using combination A4pA5n.
Each subfigure (a-f) plots V_m on each segment of a different neurite: (a) $-\hat{x}$ dendrite, (b) $+\hat{x}$ dendrite, (c) $+\hat{y}$ dendrite, (d) $-\hat{z}$ dendrite, (e) $+\hat{z}$ dendrite, and (f) $-\hat{y}$ axon + soma. For each subfigure (a-f): The horizontal axis is the simulation time in ms. Each segment plot is labeled on the right side with (section type, orientation, segment number). The range of the vertical axis for the segment plots is indicated in the lower left corner. The minimum and maximum V_m for each segment are in the middle of each segment plot. Red areas under each segment plot indicate time periods in which V_m at that segment exceeds -10 mV.
Subfigure (f) shows an orthodromic action potential starting at the IS traveling to the axon tip and causing neurotransmitter release.

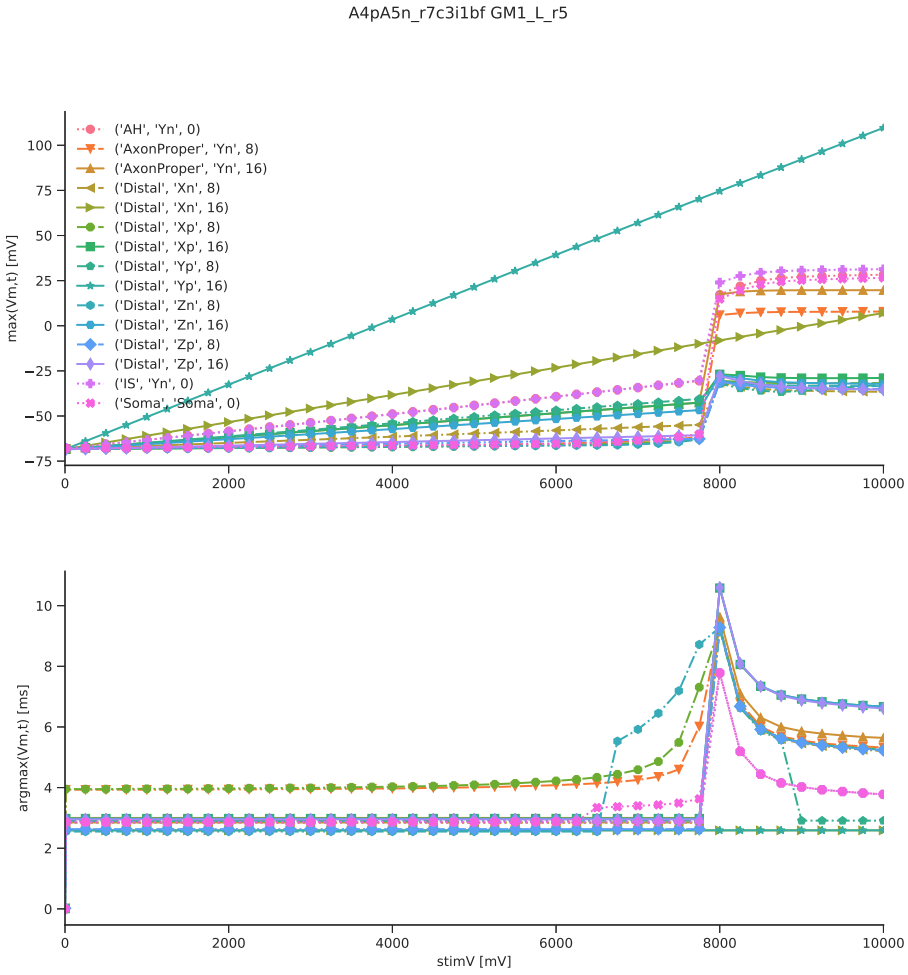


Figure 4.19: (top): Membrane voltage (in mV) as a function of stimulation voltage (in mV, axis shared with bottom plot) for biphasic stimulation with combination A4pA5n, location GM1_L_r5, and axon in the $-\hat{y}$ direction. This is the same configuration as in Fig. 4.16 except the axon is in the $-\hat{y}$ direction. This configuration results in an orthodromic action potential starting at the initial segment (IS) with 8 V of stimulation. This is one of the few neurons in Fig. 4.7b with a nonlinear response in the axon tip above 8 V. The legend labels in the top plot are in the format (section type, orientation, segment number). See Fig. 3.3 for segment number locations by section type. (bottom): The time of the maximum membrane voltage (in ms) for each probe vs stimulation voltage (in mV). The time of the maximum membrane voltage helps explain which parts of the neuron reach maximum first. Note that the stimulation pulse starts at 1 ms the middle of the pulse is at 2.66 ms and the maximum amplitudes of the pulse occur at 2.66 ms ± 0.16 ms. The first maximum amplitude occurs at 2.5 ms and the maximum in the $+\hat{y}$ distal dendrite tip occurs very shortly after.

4.6 Predicting neuron activation

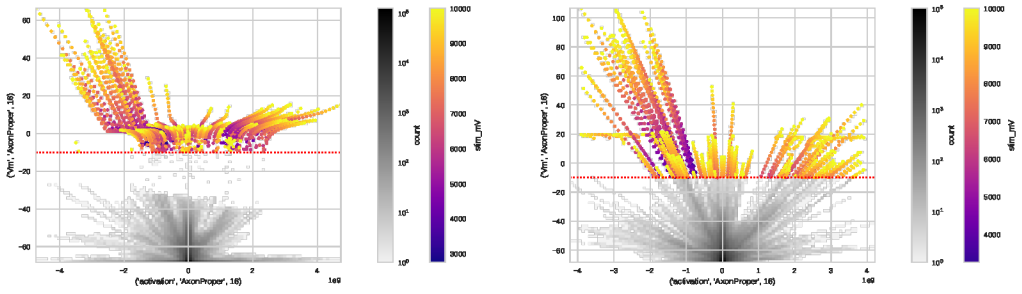
The computational cost of running time-domain finite element simulations and NEURON simulations limits the number of simulations possible. A less computationally intensive method for predicting whether a particular configuration of electrodes would activate a particular neuron would make it easier to tailor electrode arrays and stimulation for particular applications and subjects. In this section, I explore a few possibilities for predicting activation based on static volume conductor simulations.

The second spatial derivative of the static voltage [a] is often used as a proxy for activation. Figure 4.20 shows that the second spatial derivative of the static voltage (V_{static}) along a vector pointing towards the soma cannot be used to separate active neurons from non-active neurons. Figure 4.21 shows that a wide range of extracellular voltages result in the axon tip membrane voltage going above $-10\,\text{mV}$, so that cannot be used either. However, the results in Section 4.5.1 hinted that perhaps the difference in the extracellular voltage between the axon tip and the soma could be used to predict neuron activation. Figure 4.22 shows the static voltage at the axon tip ($V_{static}^{\text{AxonTip}}$) minus the static voltage at the soma (V_{static}^{Soma}) plotted against the membrane voltage at the axon tip (V_m^{AxonTip}). This estimate of the first spatial derivative is useful to separate activated neurons from non-activated neurons. For this dataset and monophasic stimulation, the neuron is guaranteed to be active if $V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}} < -373\,\text{mV}$ and guaranteed not active if $-279\,\text{mV} < V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}}$. These equations match the "axon points to the negative electrode or away from the positive electrode" rule mentioned in Section 4.5.1 for monophasic stimulation. For biphasic stimulation, the neuron is guaranteed to be active if $V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}} < -492\,\text{mV}$ or $V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}} > 872\,\text{mV}$. The neuron is guaranteed not active if $-290\,\text{mV} < V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}} < 580\,\text{mV}$. Using biphasic

[a] referred to in some of the literature as the activating function (Rattay, 1999)

stimulation, it takes less magnitude of stimulation voltage to activate a neuron if the electrode with the negative leading edge is closer to the axon tip and further away from the soma. This generally results in the axon tip exceeding −10 mV but no cell wide action potential. If instead there is an electrode with a positive leading edge closer to the axon tip and further from the soma, then it takes a larger magnitude of stimulation voltage, but the stimulation first affects the membrane voltage in one or more of the dendrites before an orthodromic action potential occurs.

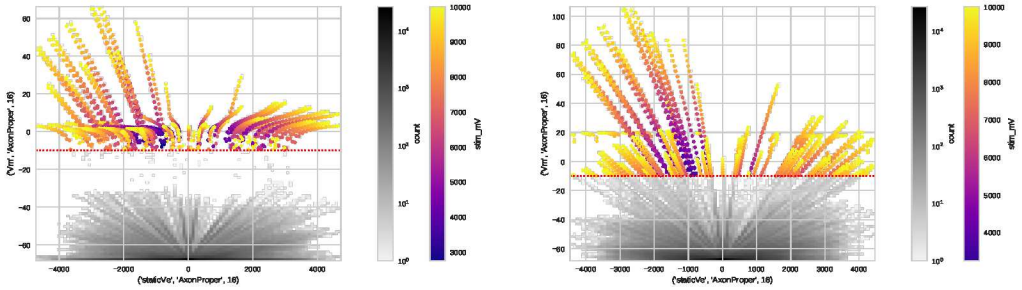
While the numerical values in the above rules are likely to change for different neurons (geometry, ion channel density, etc.), this study shows that features similar to $V_{static}^{\text{AxonTip}} - V_{static}^{\text{Soma}}$ could be useful for estimating when electrically stimulated neurons would be activated without running large numbers of NEURON simulations. The success of these simple rules based on static features for separating active neurons from inactive neurons also shows that the geometry of the stimulation field plays a critical role.



(a) monophasic activation

(b) biphasic activation

Figure 4.20: Maximum membrane voltage in mV at the axon distal tip (segment 16) (y-axis) plotted against the second spatial derivative of the static extracellular voltage V_e along a vector pointing towards the soma at the axon distal tip (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (left plot) and biphasic stimulation (right plot). The gray rectangles are a 2d histogram of the number of neurons (see gray colorbar). The colored dots are active neurons (axon tip has a membrane voltage greater than −10 mV) and are colored based on the stimulation voltage (see right colorbar). The red dotted horizontal line indicates the activation threshold (dots and gray rectangles above this line indicate activated neurons).

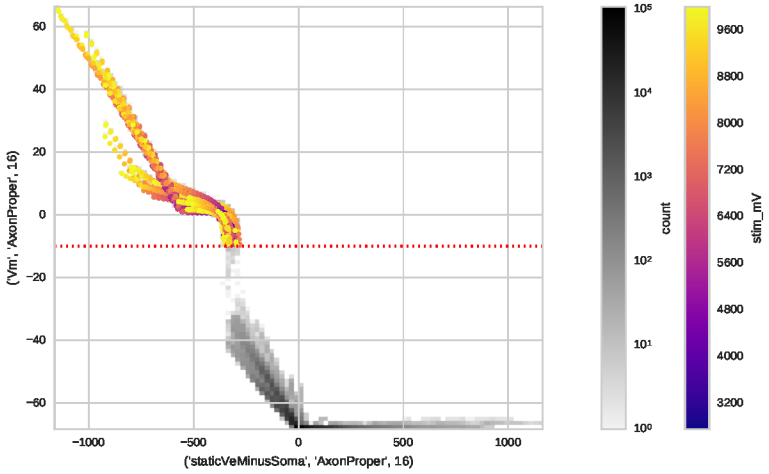


(a) monophasic static V_e (b) biphasic static V_e

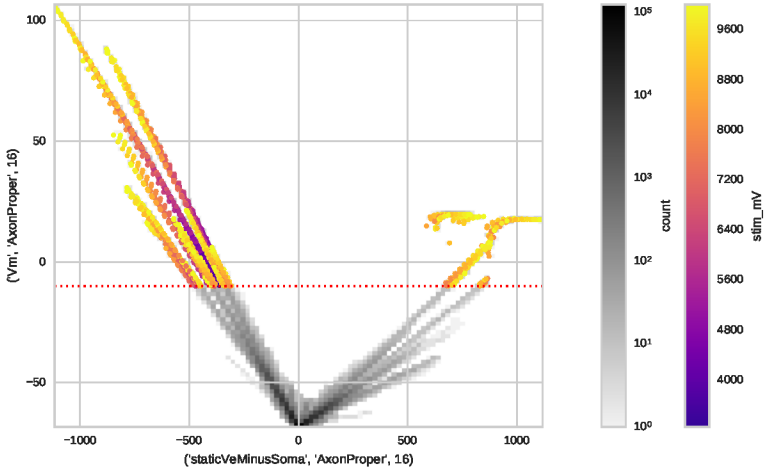
Figure 4.21: Maximum membrane voltage in mV at the axon distal tip (segment 16) (y-axis) plotted against the static extracellular voltage at the axon distal tip (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (left plot) and biphasic stimulation (right plot). The gray rectangles are a 2d histogram of the number of neurons (see gray colorbar). The colored dots are active neurons (axon tip has a membrane voltage greater than -10 mV) and are colored based on the stimulation voltage (see right colorbar). The red dotted horizontal line indicates the activation threshold (dots and gray rectangles above this line indicate activated neurons).

4.7 Discussion

Based on simulations, both biphasic and monophasic stimulation (without additional synaptic input) can cause the membrane voltage in the axon tip of interneurons in the spinal cord to go above -10 mV, and therefore release neurotransmitters, using less than 5 V of stimulation (minimum of 2.75 V for monophasic and 3.25 V for biphasic). This is in the same range of voltages that are used in actual epidural stimulation experiments with rats (3 V (P. Gad et al., 2012), 5 V to 7 V (Desautels et al., 2015), 4 V (Parag Gad, Roy, Choe, Creagmile, et al., 2015), and 1 V to 8 V (Parag Gad, Roy, Choe, Zhong, et al., 2015)). Monophasic stimulation resulted in antidromic action potentials and biphasic stimulation resulted in no action potentials inside the cell at stimulation voltages of < 8 V (even if the tip of the axon went above -10 mV, which is considered to be enough to release neurotransmitters into the presynaptic cleft), but a few neurons generated orthodromic action potentials at stimulation voltages ≥ 8 V. Simple rules using the difference in static voltage at



(a) monophasic



(b) biphasic

Figure 4.22: Maximum membrane voltage in mV at the axon distal tip (segment 16) (y-axis) plotted against the static extracellular voltage at the axon distal tip minus the static extracellular voltage at the soma (x-axis) for all neuron locations and all 18 electrode pair combinations using monophasic stimulation (top plot) and biphasic stimulation (bottom plot). The gray rectangles are a 2d histogram of the number of neurons (see gray colorbar). The colored dots are active neurons (axon tip has a membrane voltage greater than -10 mV) and are colored based on the stimulation voltage (see right colorbar). The red dotted horizontal line indicates the activation threshold (dots and gray rectangles above this line indicate activated neurons).

the axon and the soma were found that could be useful for predicting neuron activation without costly time-domain simulations. This would allow faster design of

stimulation protocols for particular applications and/or subjects.

Additional simulations of the neurons that are activated using a magnitude of stimulation of 5 V or less (listed in Tables 4.2 and 4.3) using passive dendrites instead of active dendrites found little change in the amount of stimulation necessary to activate the neurons. This implies that these neurons are mostly activated by stimulation of the axon.

Most existing studies would stop here and completely ignore the possibility of the interaction of synaptic input in the spinal cord with the stimulation pulses. The next chapter will examine how epidural stimulation can facilitate synaptic input to generate neurotransmitter release.

4.A Appendix: Stimulation Thresholds

This appendix contains figures showing which axons are activated (axon tip membrane voltage $\geq -10\,\text{mV}$) using $\leq 10\,\text{V}$ of stimulation voltage magnitude. Each figure shows the results for one of the 18 bipolar combinations listed in Section 2.2.1 with either a positive or a negative voltage and either monophasic or biphasic stimulation (36 plots for monophasic and 36 plots for biphasic). Please note that in each of the plots, the spinal cord is oriented such that the head of the rat would be outside the lower left corner and the tail of the rat would be beyond the upper right corner. In each plot, the active electrodes are labeled by name and a "+" symbol if they have a positive initial phase or a "-" symbol if they have a negative initial phase. The electrode labels are also colored blue for negative and red for positive. The soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Since 6 neurons are plotted at the same location, dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. A list of the active neurons is included in each caption as a location, orientation (Yp=$+\hat{y}$, Yn=$-\hat{y}$, etc), and the threshold to cause that neuron to activate in Volts.

4.A.1 Monophasic

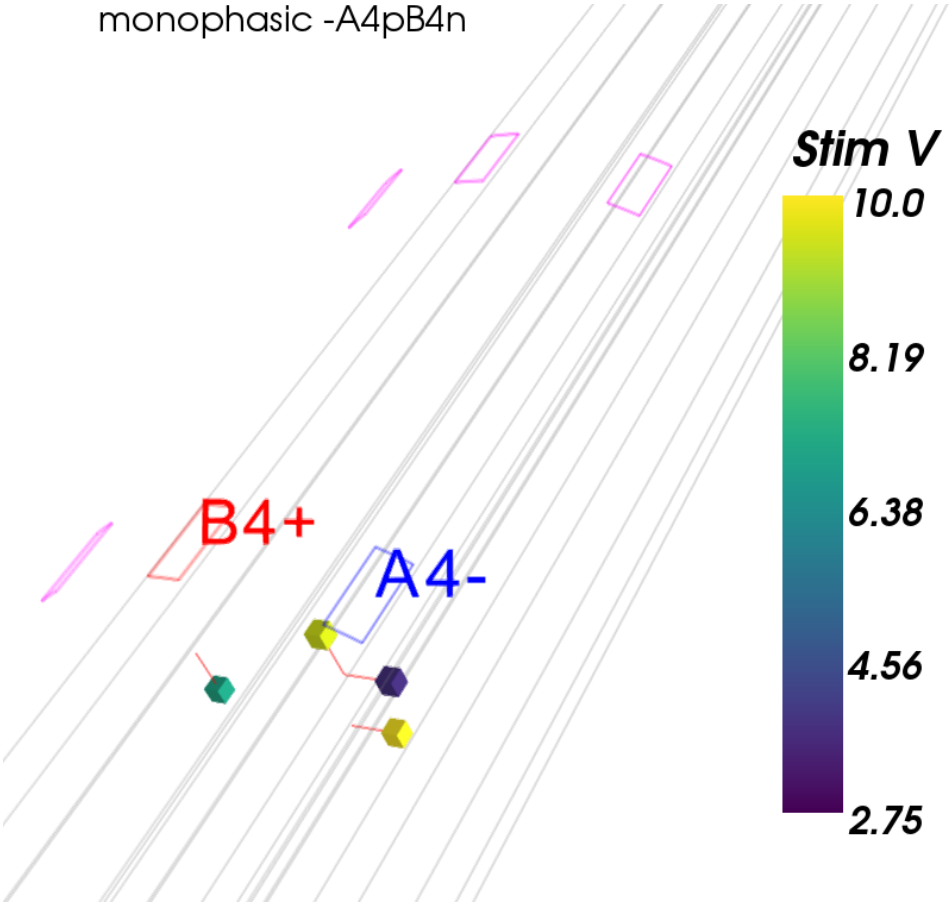


Figure 4.23: Monophasic stimulation using combination -A4pB4n. Electrode B4 has a positive phase and is labeled red. Electrode A4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 9.5 V), (GM1_L_r4, Xn, 3.75 V), (GM3_L_r4, Xn, 10.0 V), and (GM1_R_r4, Yn, 7.0 V).

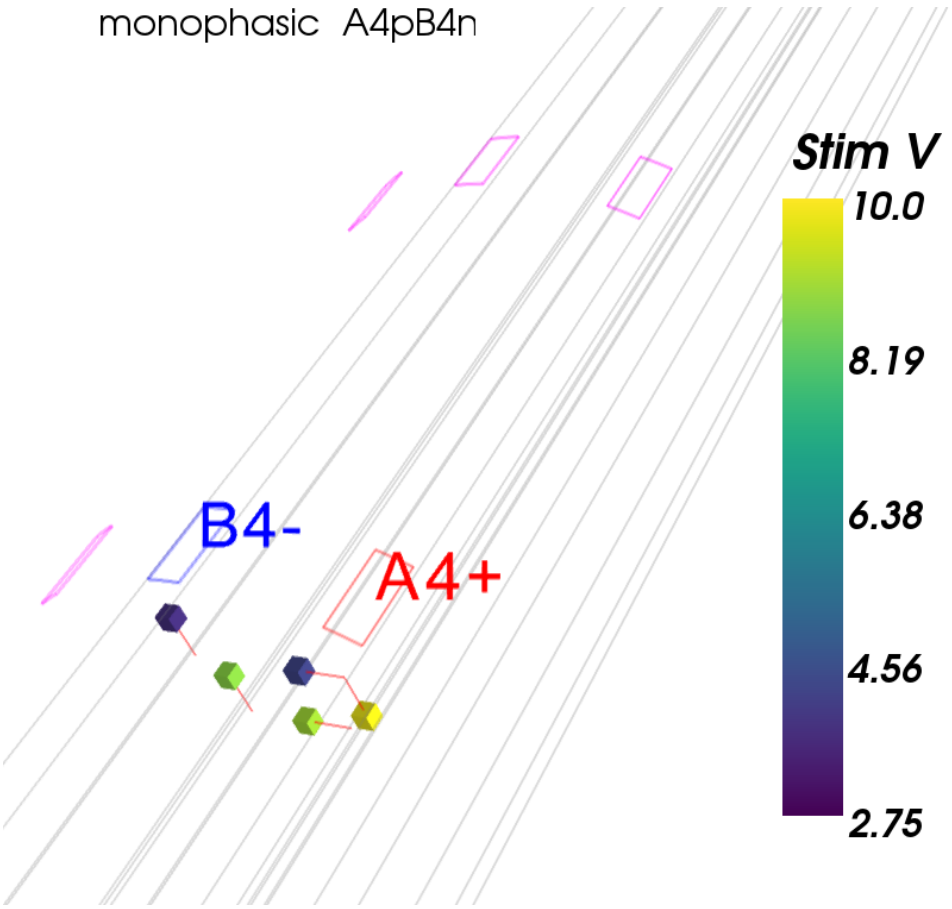


Figure 4.24: Monophasic stimulation using combination A4pB4n. Electrode A4 has a positive phase and is labeled red. Electrode B4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r4, Yp, 3.75 V), (GM3_R_r4, Yp, 8.75 V), (GM1_L_r4, Xp, 4.25 V), (GM3_L_r4, Xp, 9.0 V), and (GM1_L_r4, Yn, 9.75 V).

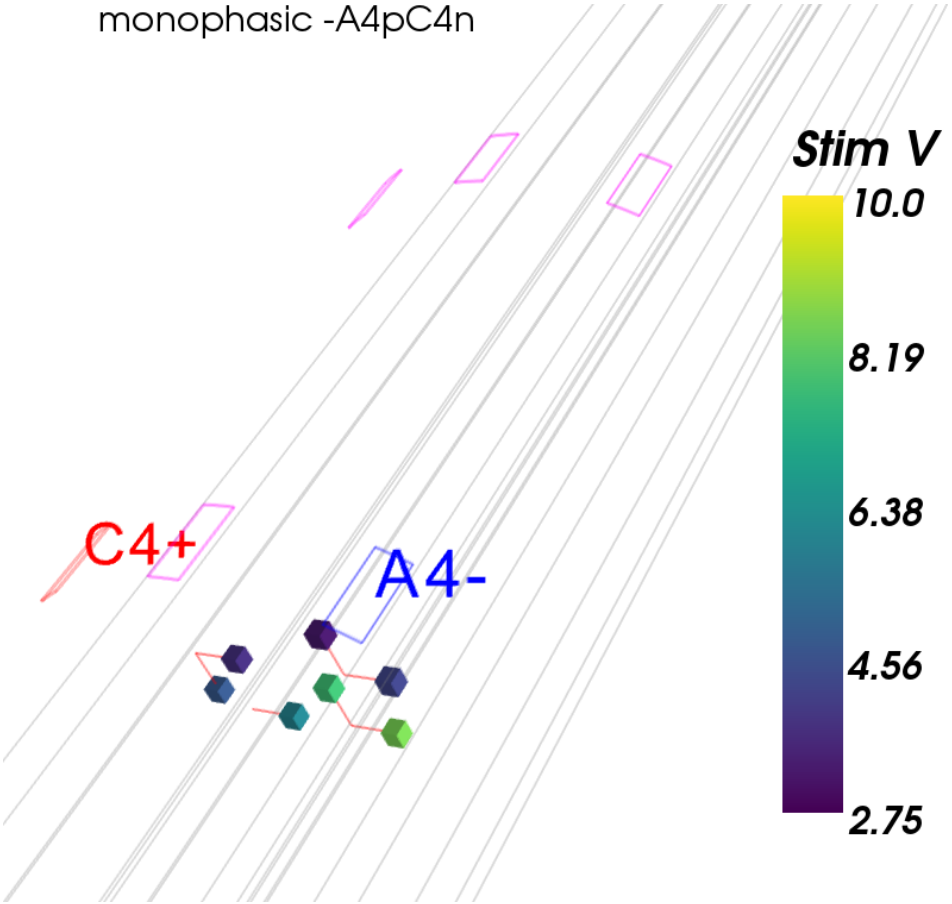


Figure 4.25: Monophasic stimulation using combination -A4pC4n. Electrode C4 has a positive phase and is labeled red. Electrode A4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 3.25 V), (GM3_L_r4, Yp, 7.75 V), (GM1_L_r4, Xn, 4.25 V), (GM1_R_r4, Xn, 3.75 V), (GM3_L_r4, Xn, 8.5 V), (GM3_R_r4, Xn, 6.0 V), and (GM1_R_r4, Yn, 4.75 V).

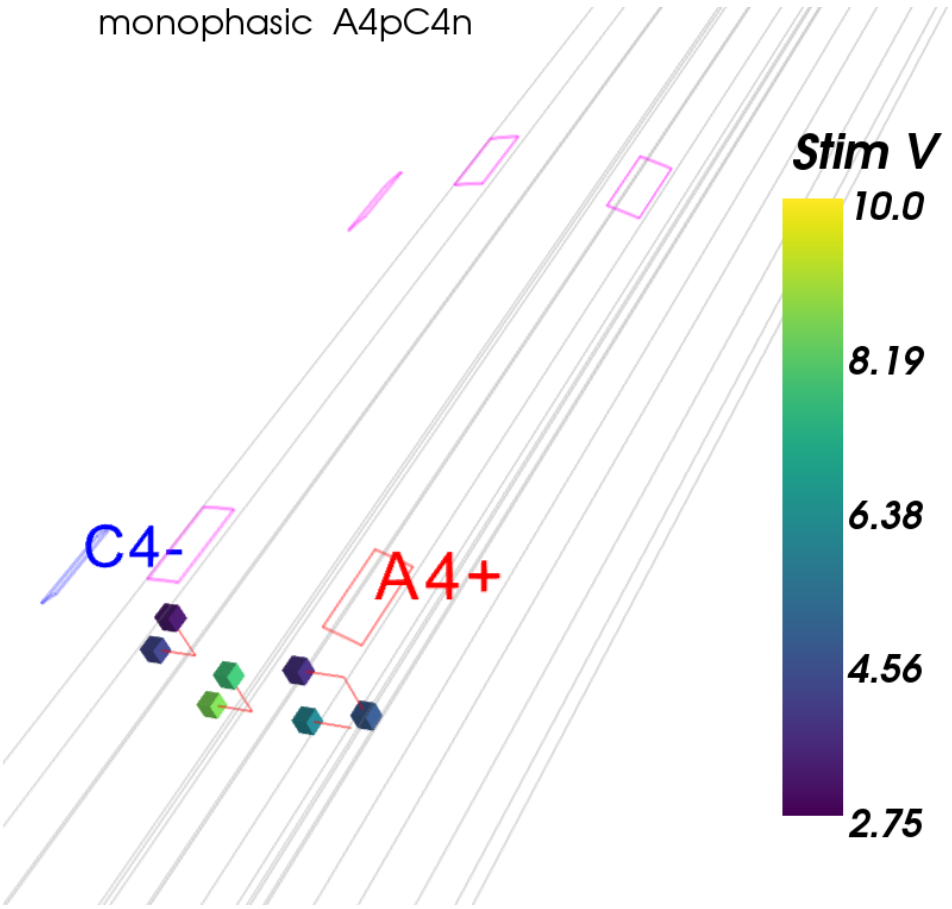


Figure 4.26: Monophasic stimulation using combination A4pC4n. Electrode A4 has a positive phase and is labeled red. Electrode C4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r4, Yp, 3.25 V), (GM3_R_r4, Yp, 7.75 V), (GM1_L_r4, Xp, 3.75 V), (GM1_R_r4, Xp, 4.25 V), (GM3_L_r4, Xp, 6.0 V), (GM3_R_r4, Xp, 8.5 V), and (GM1_L_r4, Yn, 4.75 V).

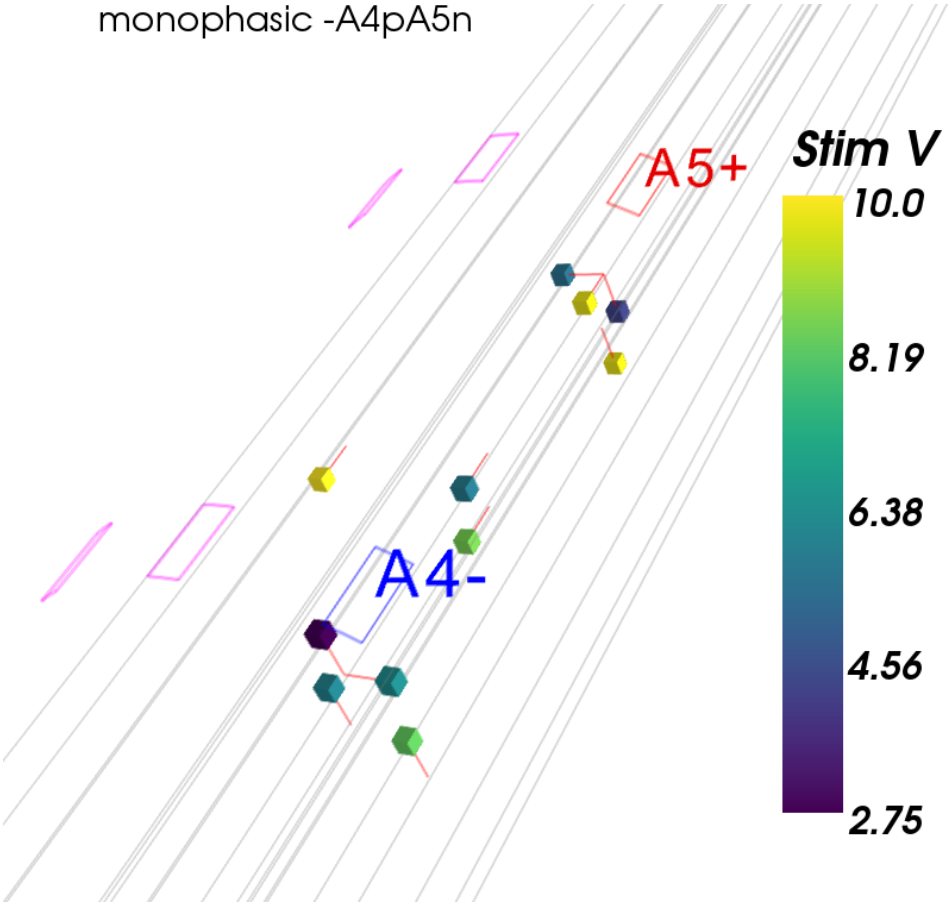


Figure 4.27: Monophasic stimulation using combination -A4pA5n. Electrode A5 has a positive phase and is labeled red. Electrode A4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r5, Zn, 9.75 V), (GM1_L_r4and5, Zn, 5.75 V), (GM3_L_r4and5, Zn, 8.5 V), (GM1_R_r4and5, Zn, 10.0 V), (GM1_L_r4, Yp, 2.75 V), (GM3_L_r4, Yp, 6.0 V), (GM2_L_r4, Yp, 8.25 V), (GM1_L_r5, Xp, 5.5 V), (GM1_L_r4, Xn, 6.25 V), (GM1_L_r5, Yn, 4.25 V), and (GM3_L_r5, Yn, 9.75 V).

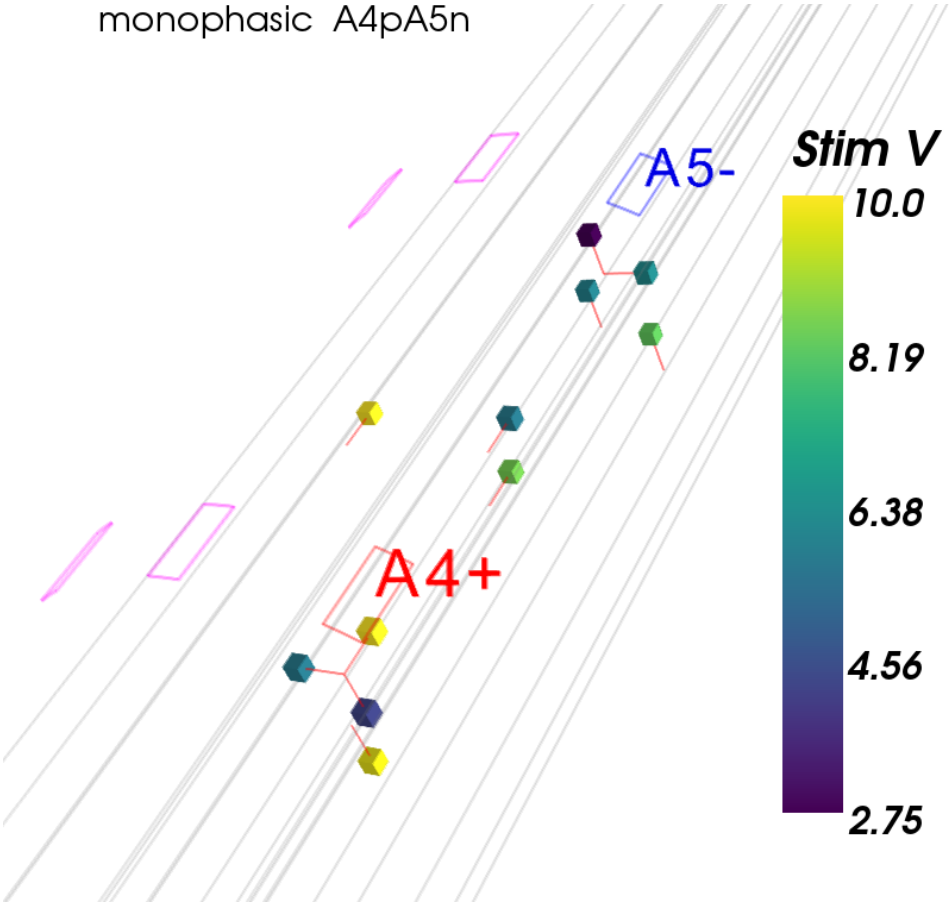


Figure 4.28: Monophasic stimulation using combination A4pA5n. Electrode A4 has a positive phase and is labeled red. Electrode A5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r5, Yp, 2.75 V), (GM3_L_r5, Yp, 6.0 V), (GM2_L_r5, Yp, 8.25 V), (GM1_L_r4, Xp, 5.75 V), (GM1_L_r5, Xn, 6.25 V), (GM1_L_r4, Yn, 4.25 V), (GM3_L_r4, Yn, 9.75 V), (GM1_L_r4, Zp, 10.0 V), (GM1_L_r4and5, Zp, 5.75 V), (GM3_L_r4and5, Zp, 8.5 V), and (GM1_R_r4and5, Zp, 10.0 V).

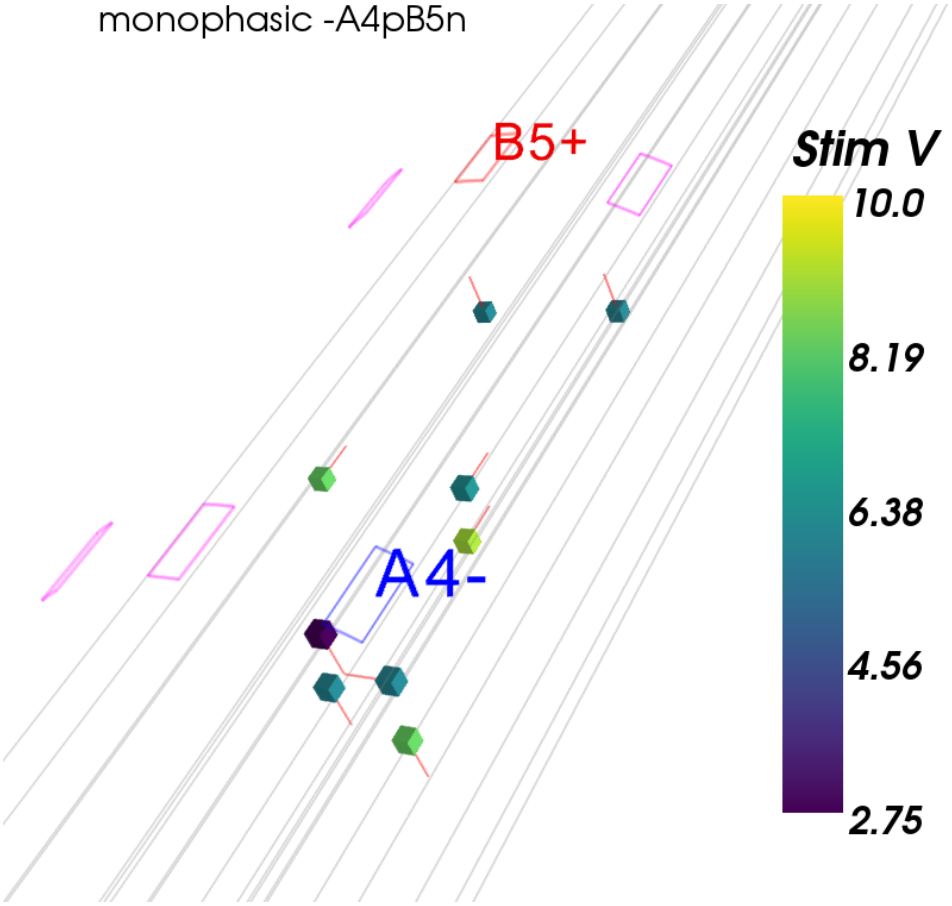


Figure 4.29: Monophasic stimulation using combination -A4pB5n. Electrode B5 has a positive phase and is labeled red. Electrode A4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4and5, Zn, 6.25 V), (GM1_R_r4and5, Zn, 8.25 V), (GM3_L_r4and5, Zn, 9.0 V), (GM1_L_r4, Yp, 2.75 V), (GM3_L_r4, Yp, 6.0 V), (GM2_L_r4, Yp, 8.25 V), (GM1_L_r4, Xn, 6.0 V), (GM1_R_r5, Yn, 6.0 V), and (GM1_L_r5, Yn, 6.0 V).

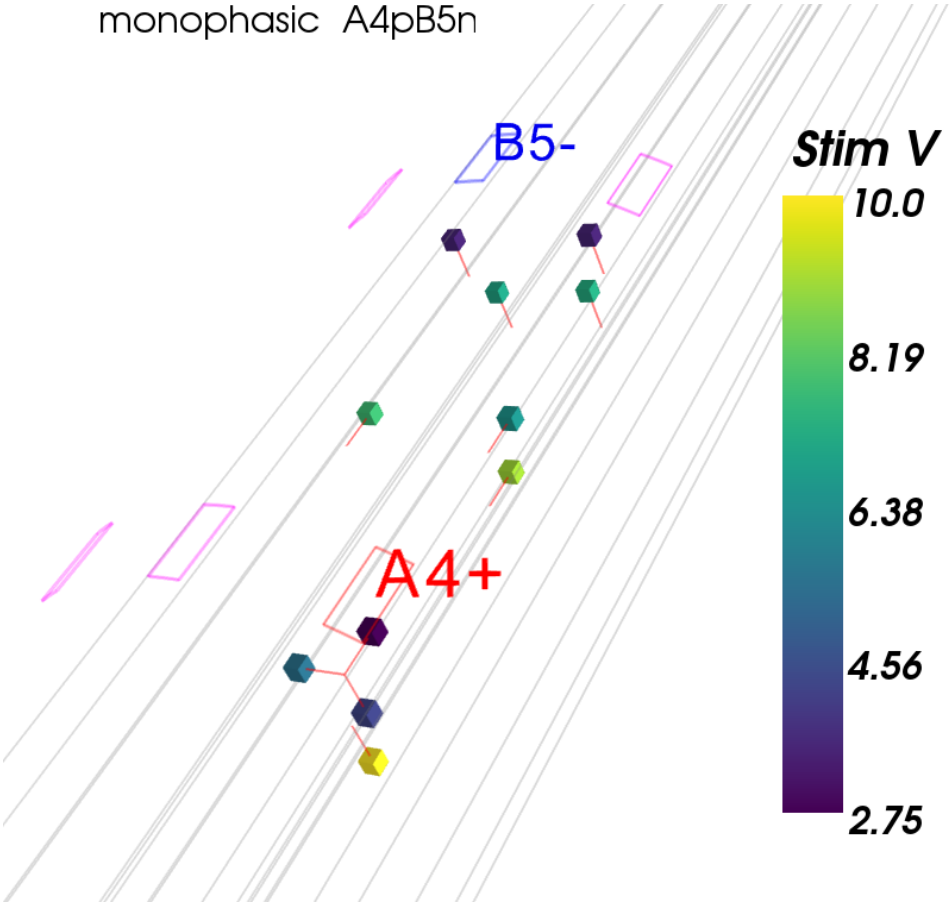


Figure 4.30: Monophasic stimulation using combination A4pB5n. Electrode A4 has a positive phase and is labeled red. Electrode B5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r5, Yp, 3.5 V), (GM1_L_r5, Yp, 3.5 V), (GM3_R_r5, Yp, 7.0 V), (GM3_L_r5, Yp, 7.25 V), (GM1_L_r4, Xp, 5.5 V), (GM1_L_r4, Yn, 4.25 V), (GM3_L_r4, Yn, 10.0 V), (GM1_L_r4, Zp, −1.0 V), (GM1_L_r4and5, Zp, 6.5 V), (GM1_R_r4and5, Zp, 7.75 V), and (GM3_L_r4and5, Zp, 9.0 V).

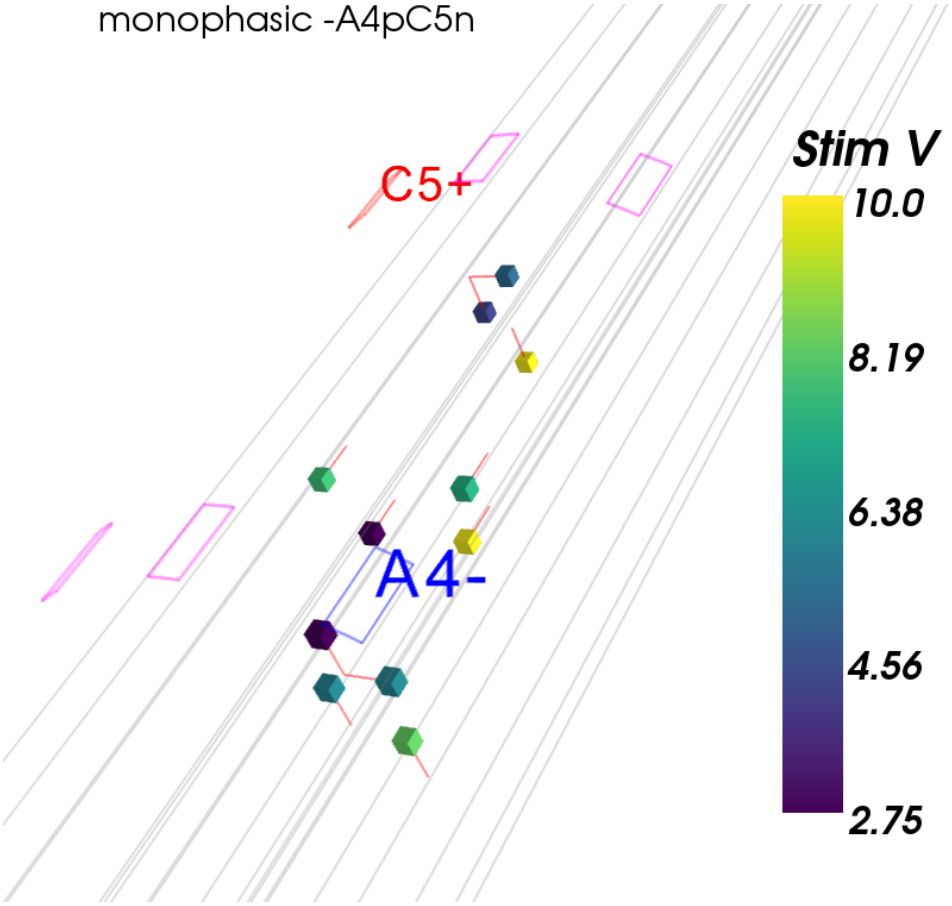


Figure 4.31: Monophasic stimulation using combination -A4pC5n. Electrode C5 has a positive phase and is labeled red. Electrode A4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4and5, Zn, 7.25 V), (GM3_L_r4and5, Zn, 9.75 V), (GM1_R_r4and5, Zn, 7.75 V), (GM3_R_r4and5, Zn, −1.0 V), (GM1_L_r4, Yp, 2.75 V), (GM3_L_r4, Yp, 6.0 V), (GM2_L_r4, Yp, 8.25 V), (GM1_L_r4, Xn, 6.0 V), (GM1_R_r5, Xn, 5.25 V), (GM1_R_r5, Yn, 4.25 V), and (GM3_R_r5, Yn, 9.75 V).

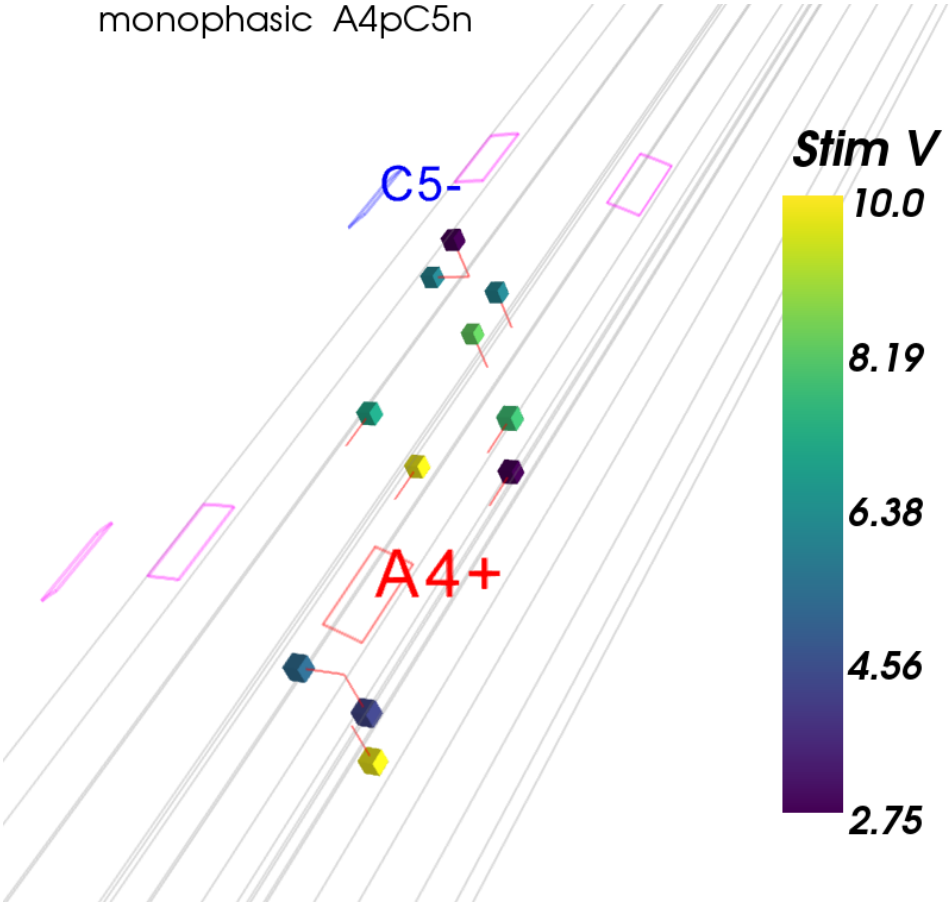


Figure 4.32: Monophasic stimulation using combination A4pC5n. Electrode A4 has a positive phase and is labeled red. Electrode C5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r5, Yp, 2.75 V), (GM3_R_r5, Yp, 6.0 V), (GM2_R_r5, Yp, 8.25 V), (GM1_L_r4, Xp, 5.25 V), (GM1_R_r5, Xp, 6.0 V), (GM1_L_r4, Yn, 4.25 V), (GM3_L_r4, Yn, 9.75 V), (GM1_L_r4and5, Zp, 7.75 V), (GM3_L_r4and5, Zp, −1.0 V), (GM1_R_r4and5, Zp, 7.0 V), and (GM3_R_r4and5, Zp, 9.75 V).

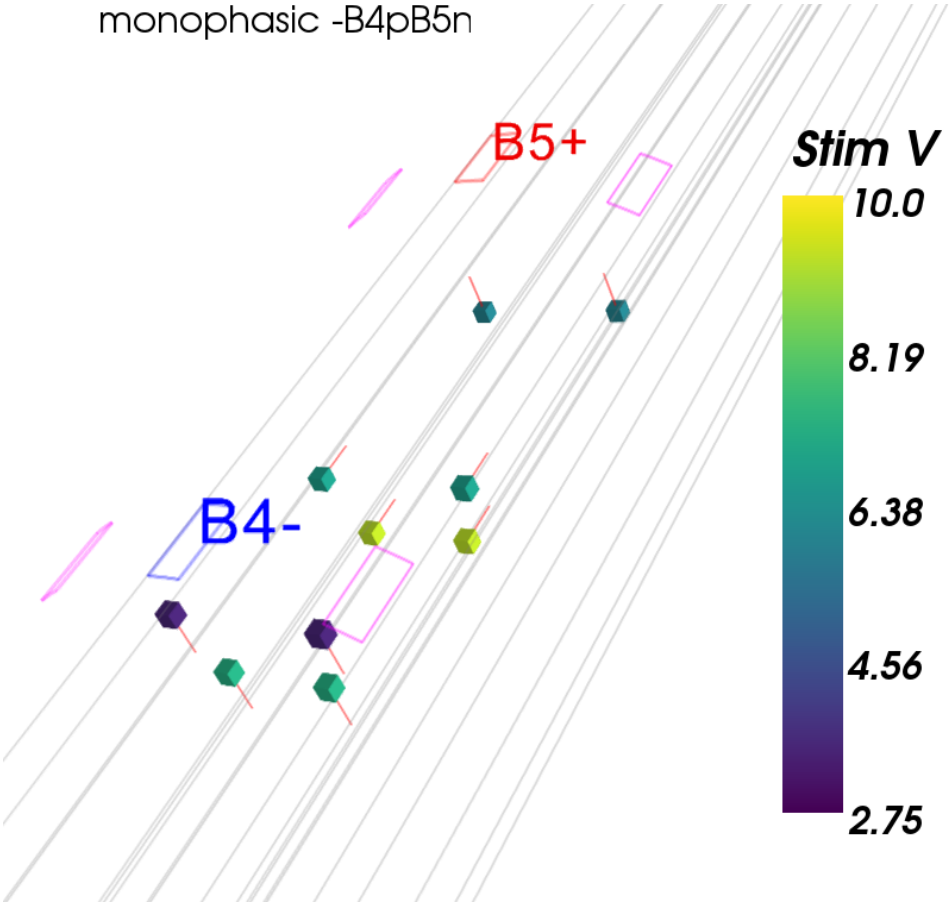


Figure 4.33: Monophasic stimulation using combination -B4pB5n. Electrode B5 has a positive phase and is labeled red. Electrode B4 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\mathrm{mV}$ with no more than $10\,\mathrm{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\mathrm{mV}$. List of location, axon direction, and threshold: (GM1_R_r4and5, Zn, 6.75 V), (GM1_L_r4and5, Zn, 6.75 V), (GM3_L_r4and5, Zn, 9.25 V), (GM3_R_r4and5, Zn, 9.25 V), (GM1_L_r4, Yp, 3.5 V), (GM1_R_r4, Yp, 3.5 V), (GM3_R_r4, Yp, 7.25 V), (GM3_L_r4, Yp, 7.25 V), (GM1_L_r5, Yn, 6.0 V), and (GM1_R_r5, Yn, 6.0 V).

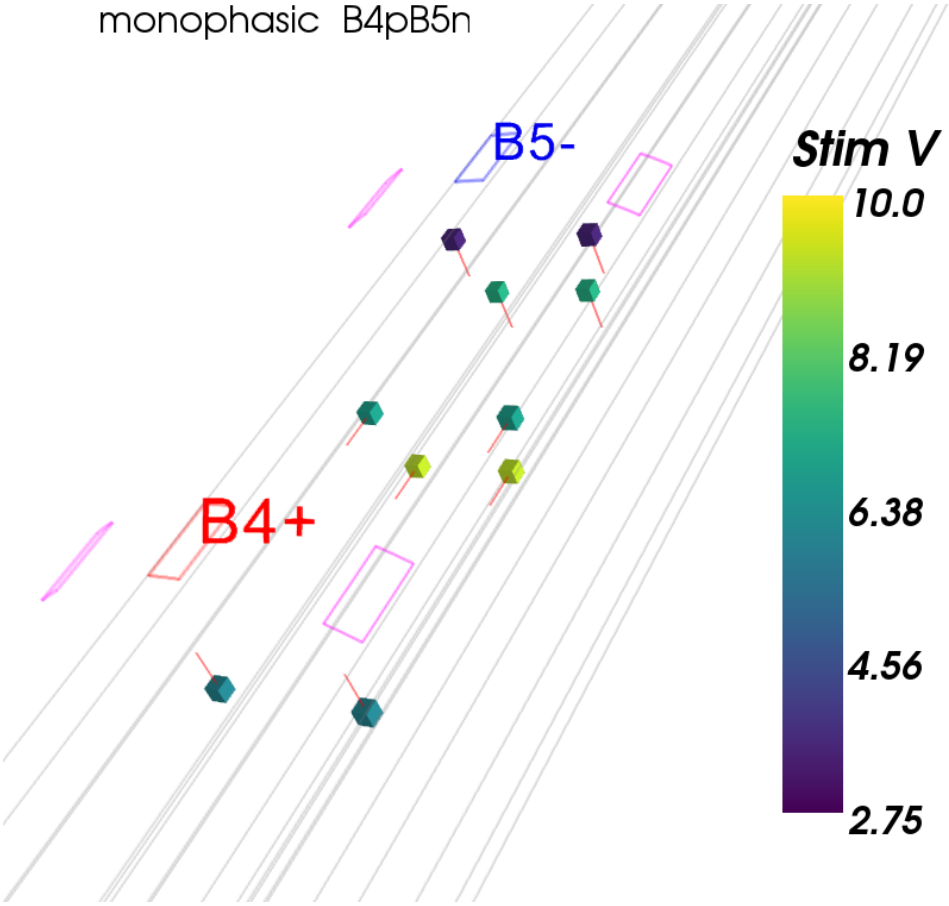


Figure 4.34: Monophasic stimulation using combination B4pB5n. Electrode B4 has a positive phase and is labeled red. Electrode B5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r5, Yp, 3.5 V), (GM1_R_r5, Yp, 3.5 V), (GM3_L_r5, Yp, 7.25 V), (GM3_R_r5, Yp, 7.25 V), (GM1_L_r4, Yn, 6.0 V), (GM1_R_r4, Yn, 6.0 V), (GM1_R_r4and5, Zp, 6.75 V), (GM1_L_r4and5, Zp, 6.75 V), (GM3_L_r4and5, Zp, 9.25 V), and (GM3_R_r4and5, Zp, 9.25 V).

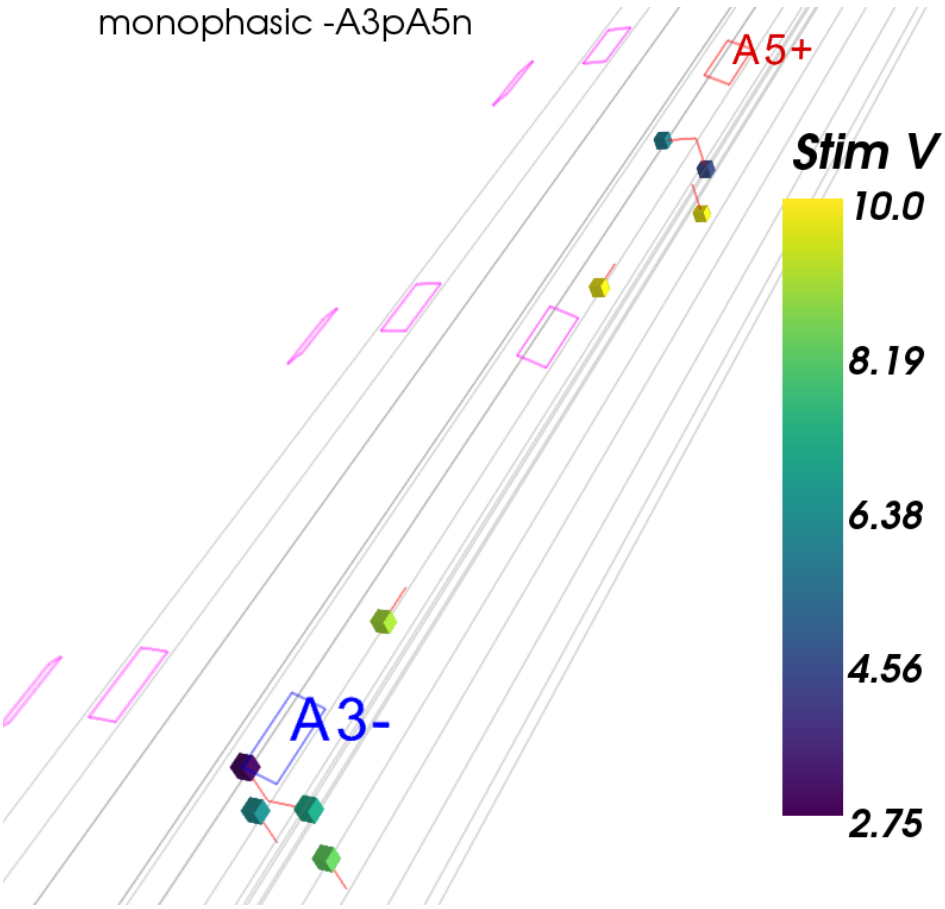


Figure 4.35: Monophasic stimulation using combination -A3pA5n. Electrode A5 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3and4, Zn, 9.0 V), (GM1_L_r4and5, Zn, 9.75 V), (GM1_L_r3, Yp, 3.0 V), (GM3_L_r3, Yp, 6.25 V), (GM2_L_r3, Yp, 8.25 V), (GM1_L_r5, Xp, 6.0 V), (GM1_L_r3, Xn, 7.0 V), (GM1_L_r5, Yn, 4.5 V), and (GM3_L_r5, Yn, 9.75 V).

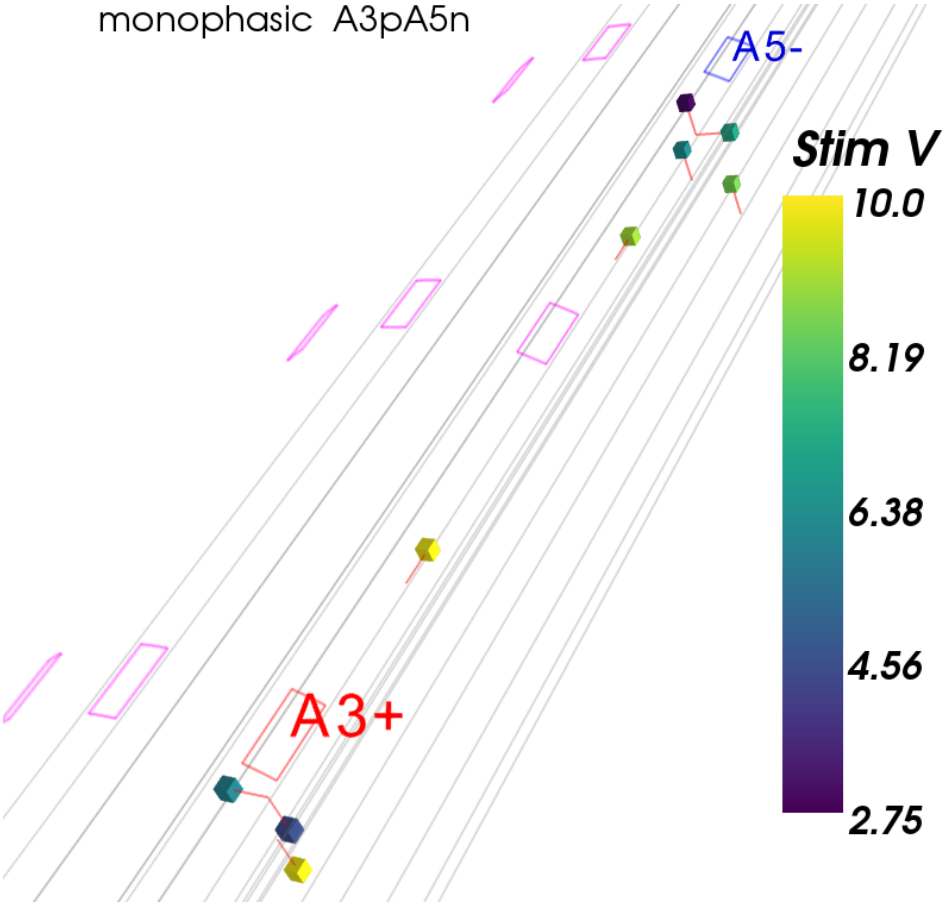


Figure 4.36: Monophasic stimulation using combination A3pA5n. Electrode A3 has a positive phase and is labeled red. Electrode A5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r5, Yp, 3.0 V), (GM3_L_r5, Yp, 6.25 V), (GM2_L_r5, Yp, 8.5 V), (GM1_L_r3, Xp, 6.0 V), (GM1_L_r5, Xn, 7.0 V), (GM1_L_r3, Yn, 4.5 V), (GM3_L_r3, Yn, 9.75 V), (GM1_L_r3and4, Zp, 9.75 V), and (GM1_L_r4and5, Zp, 9.0 V).

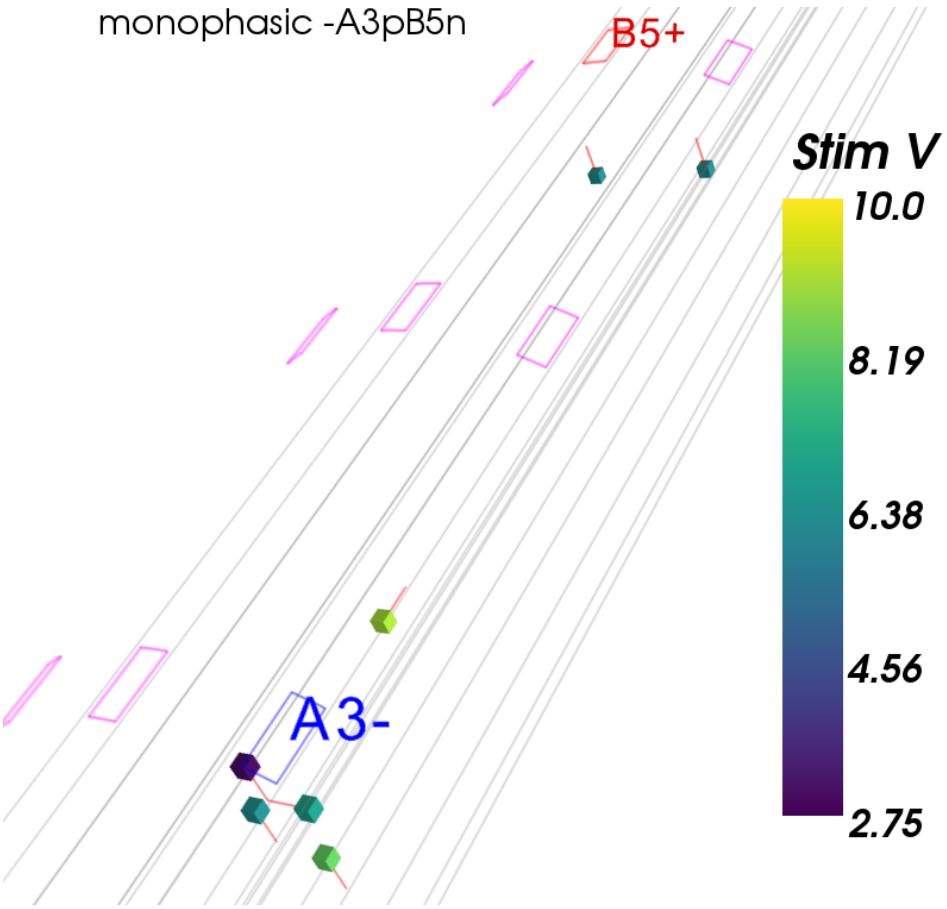


Figure 4.37: Monophasic stimulation using combination -A3pB5n. Electrode B5 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3and4, Zn, 9.0 V), (GM1_L_r3, Yp, 3.0 V), (GM3_L_r3, Yp, 6.25 V), (GM2_L_r3, Yp, 8.25 V), (GM1_L_r3, Xn, 6.75 V), (GM1_R_r5, Yn, 6.25 V), and (GM1_L_r5, Yn, 6.25 V).

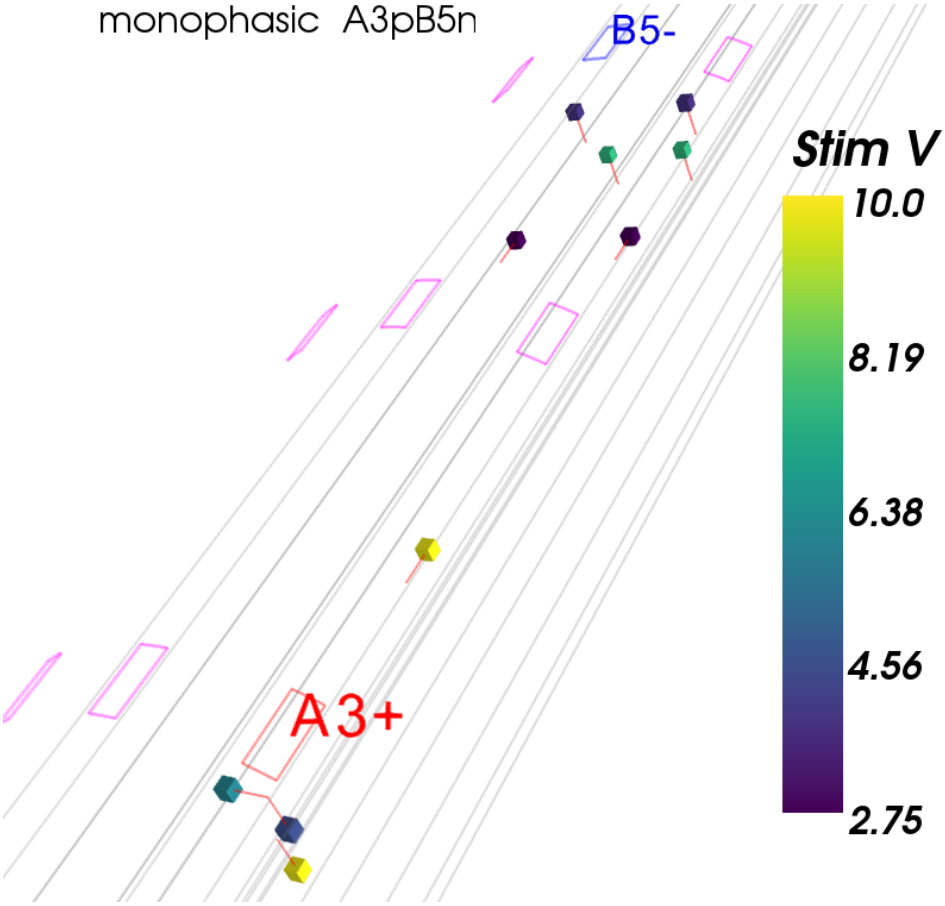


Figure 4.38: Monophasic stimulation using combination A3pB5n. Electrode A3 has a positive phase and is labeled red. Electrode B5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r5, Yp, 3.75 V), (GM1_L_r5, Yp, 3.75 V), (GM3_R_r5, Yp, 7.5 V), (GM3_L_r5, Yp, 7.5 V), (GM1_L_r3, Xp, 6.0 V), (GM1_L_r3, Yn, 4.5 V), (GM3_L_r3, Yn, 9.75 V), (GM1_L_r3and4, Zp, 9.75 V), (GM1_R_r4and5, Zp, −1.0 V), and (GM1_L_r4and5, Zp, −1.0 V).

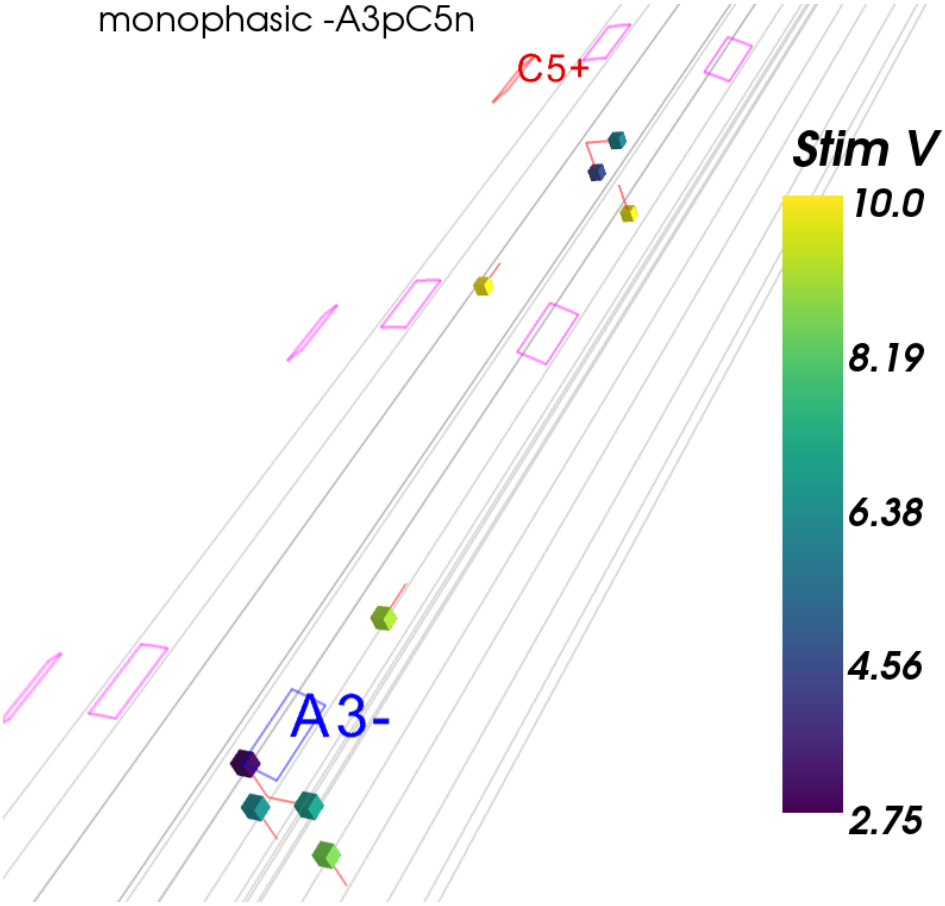


Figure 4.39: Monophasic stimulation using combination -A3pC5n. Electrode C5 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3and4, Zn, 9.0 V), (GM1_R_r4and5, Zn, 10.0 V), (GM1_L_r3, Yp, 3.0 V), (GM3_L_r3, Yp, 6.25 V), (GM2_L_r3, Yp, 8.5 V), (GM1_L_r3, Xn, 6.75 V), (GM1_R_r5, Xn, 6.0 V), (GM1_R_r5, Yn, 4.5 V), and (GM3_R_r5, Yn, 9.75 V).

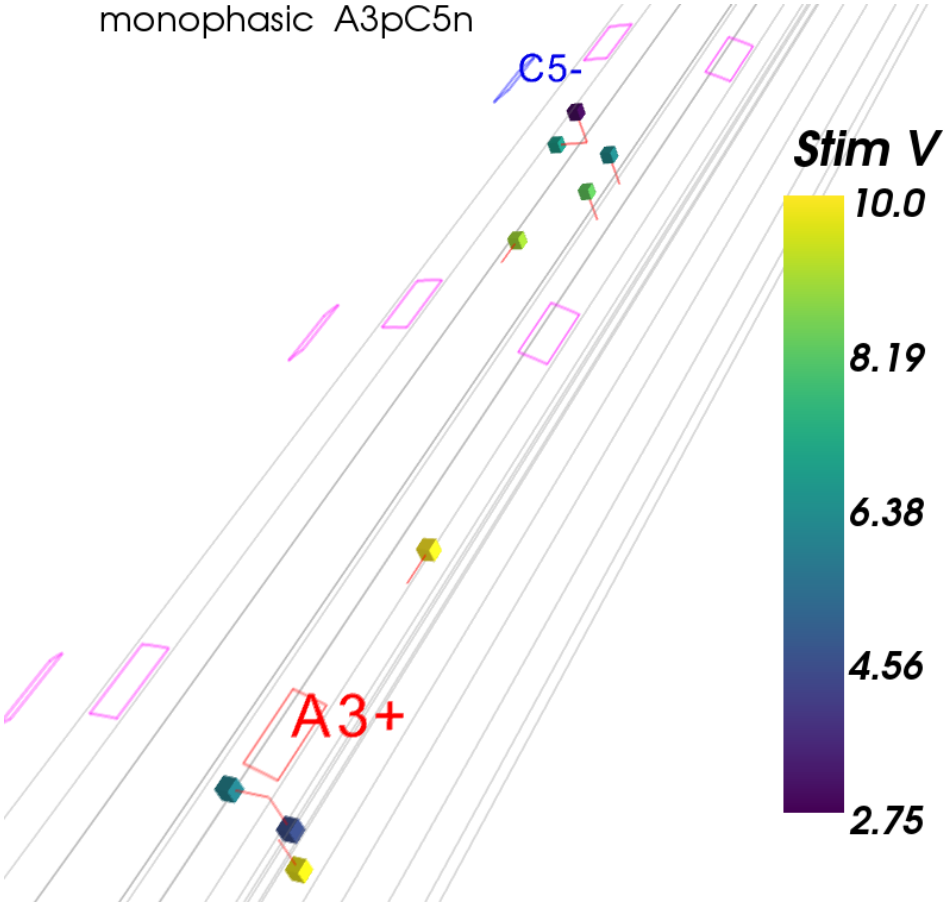


Figure 4.40: Monophasic stimulation using combination A3pC5n. Electrode A3 has a positive phase and is labeled red. Electrode C5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_R_r5, Yp, 3.0 V), (GM3_R_r5, Yp, 6.25 V), (GM2_R_r5, Yp, 8.25 V), (GM1_L_r3, Xp, 6.0 V), (GM1_R_r5, Xp, 6.75 V), (GM1_L_r3, Yn, 4.5 V), (GM3_L_r3, Yn, 9.75 V), (GM1_L_r3and4, Zp, 10.0 V), and (GM1_R_r4and5, Zp, 9.0 V).

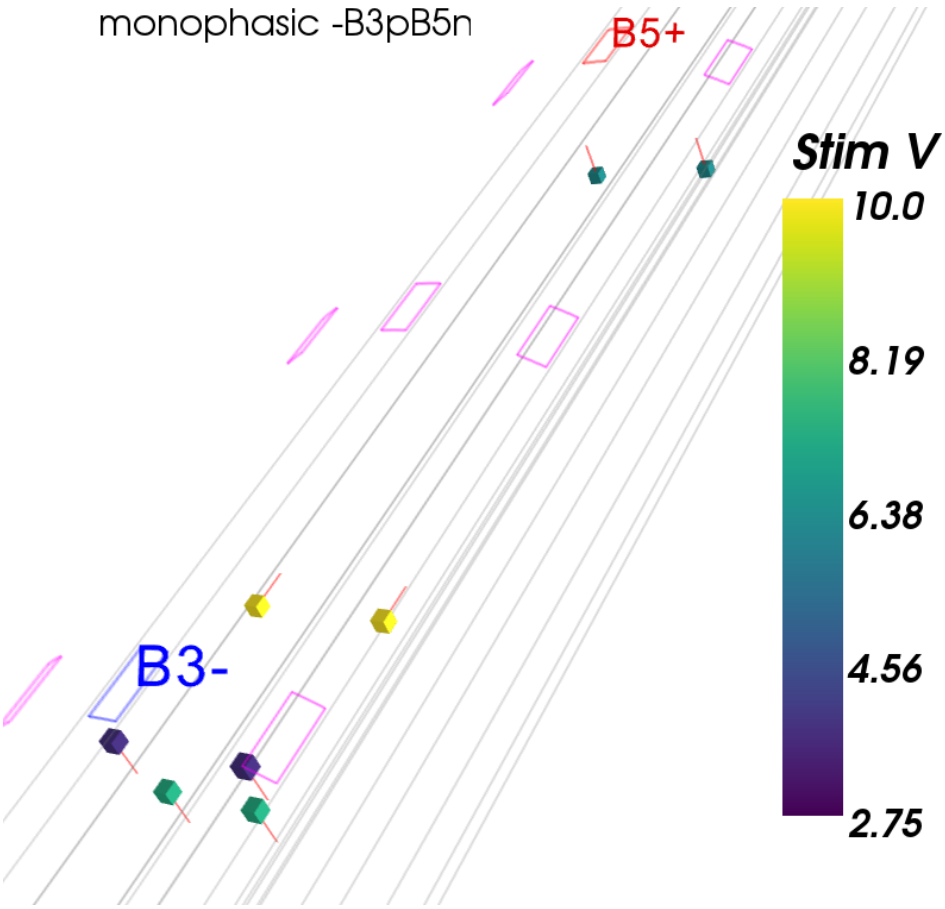


Figure 4.41: Monophasic stimulation using combination -B3pB5n. Electrode B5 has a positive phase and is labeled red. Electrode B3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r3and4, Zn, 10.0 V), (GM1_R_r3and4, Zn, 10.0 V), (GM1_L_r3, Yp, 3.75 V), (GM1_R_r3, Yp, 3.75 V), (GM3_L_r3, Yp, 7.25 V), (GM3_R_r3, Yp, 7.25 V), (GM1_L_r5, Yn, 6.25 V), and (GM1_R_r5, Yn, 6.25 V).

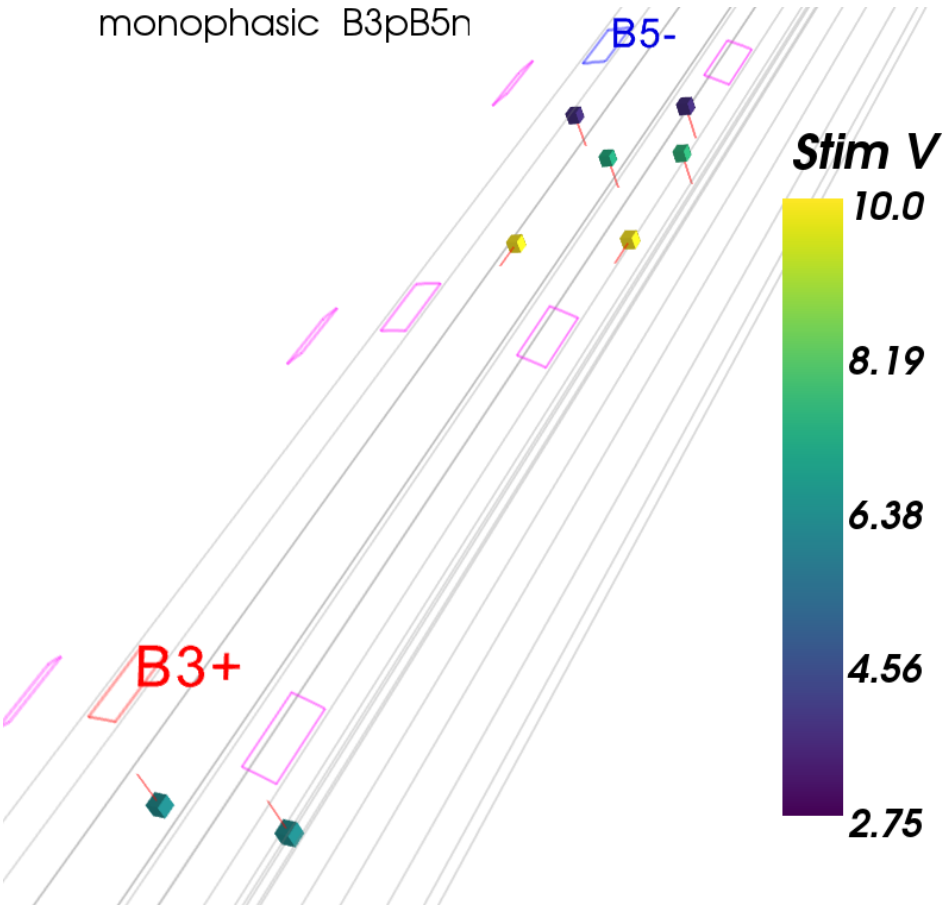


Figure 4.42: Monophasic stimulation using combination B3pB5n. Electrode B3 has a positive phase and is labeled red. Electrode B5 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r5, Yp, 3.75 V), (GM1_R_r5, Yp, 3.75 V), (GM3_L_r5, Yp, 7.5 V), (GM3_R_r5, Yp, 7.25 V), (GM1_L_r3, Yn, 6.25 V), (GM1_R_r3, Yn, 6.25 V), (GM1_L_r4and5, Zp, 10.0 V), and (GM1_R_r4and5, Zp, 10.0 V).

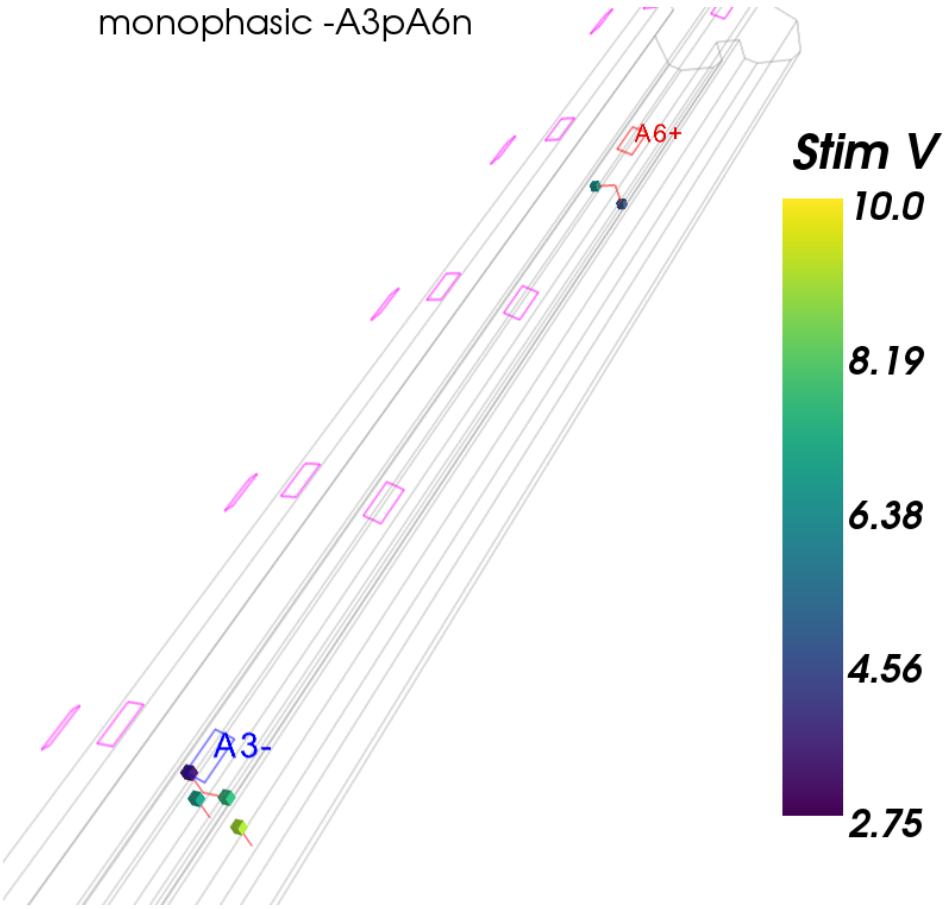


Figure 4.43: Monophasic stimulation using combination -A3pA6n. Electrode A6 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.25 V), (GM3_L_r3, Yp, 6.75 V), (GM2_L_r3, Yp, 9.0 V), (GM1_L_r6, Xp, 6.5 V), (GM1_L_r3, Xn, 7.5 V), and (GM1_L_r6, Yn, 4.75 V).

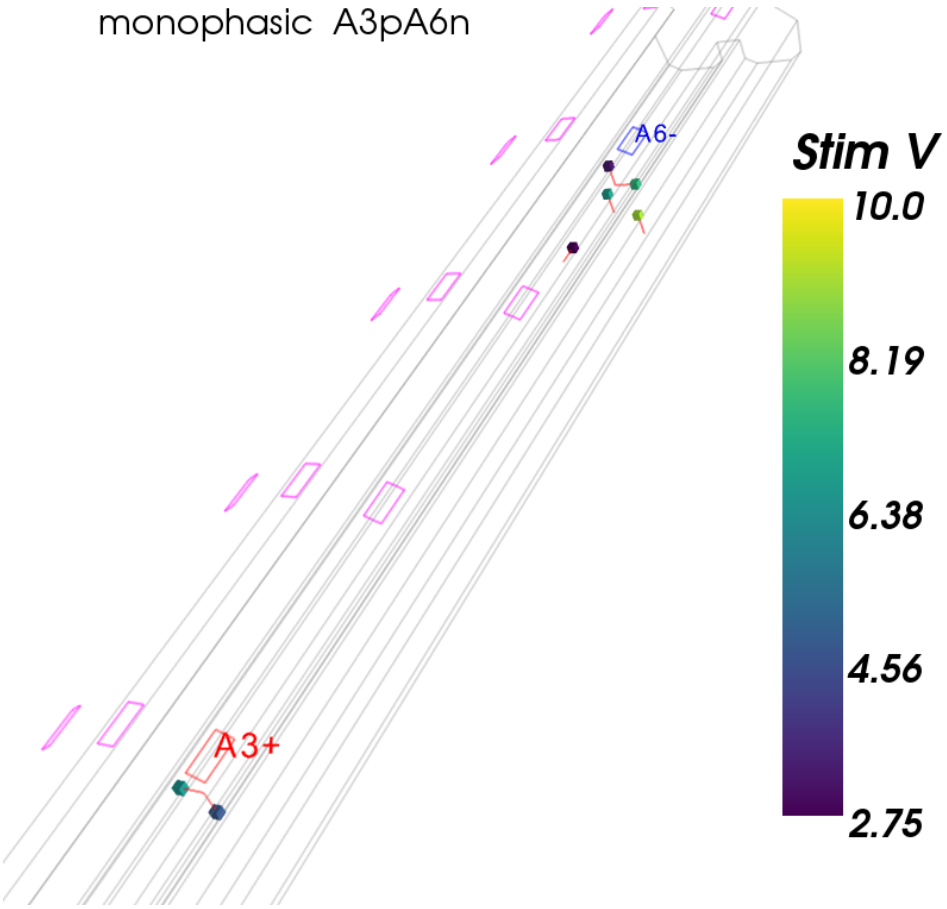


Figure 4.44: Monophasic stimulation using combination A3pA6n. Electrode A3 has a positive phase and is labeled red. Electrode A6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r6, Yp, 3.25 V), (GM3_L_r6, Yp, 6.75 V), (GM2_L_r6, Yp, 9.0 V), (GM1_L_r3, Xp, 6.5 V), (GM1_L_r6, Xn, 7.5 V), (GM1_L_r3, Yn, 4.75 V), and (GM1_L_r5and6, Zp, −1.0 V).

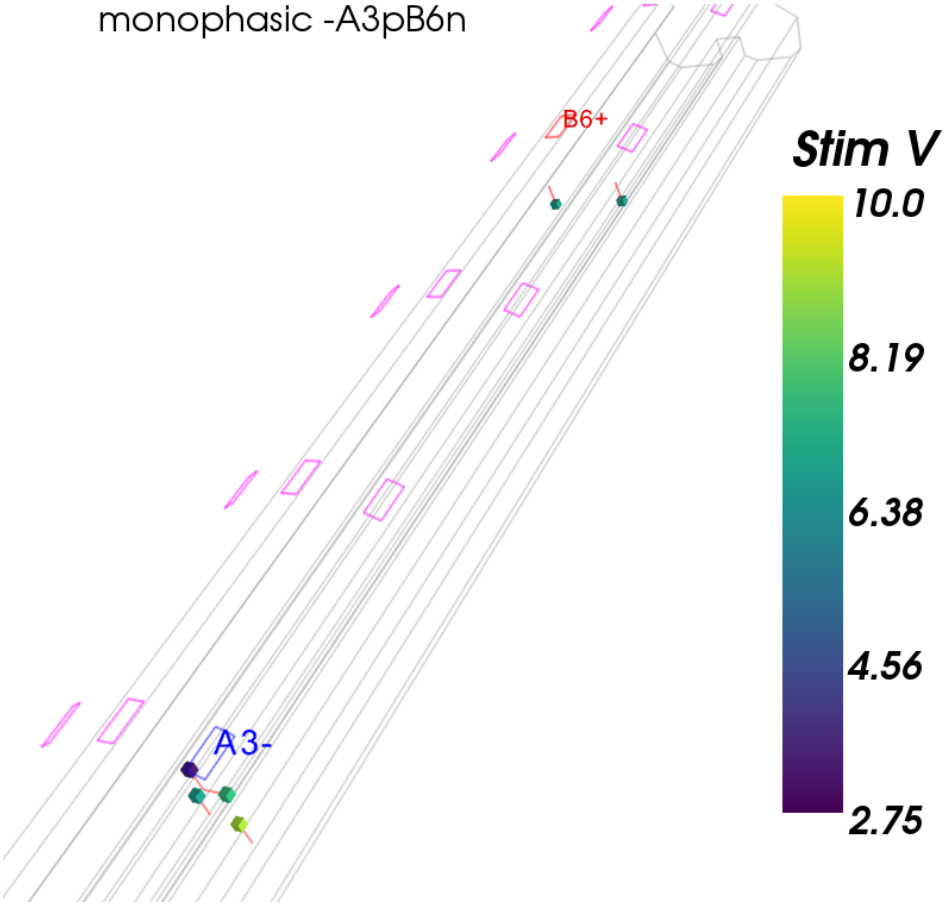


Figure 4.45: Monophasic stimulation using combination -A3pB6n. Electrode B6 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.25 V), (GM3_L_r3, Yp, 6.75 V), (GM2_L_r3, Yp, 9.0 V), (GM1_L_r3, Xn, 7.5 V), (GM1_R_r6, Yn, 6.75 V), and (GM1_L_r6, Yn, 6.75 V).

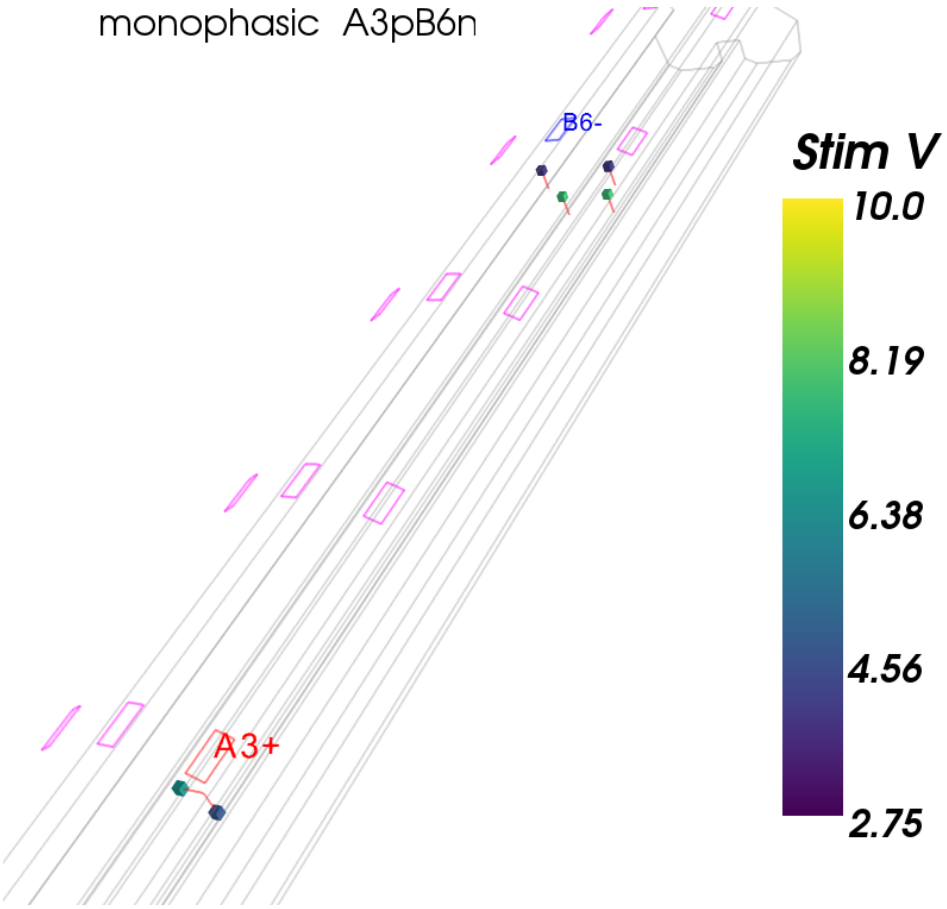


Figure 4.46: Monophasic stimulation using combination A3pB6n. Electrode A3 has a positive phase and is labeled red. Electrode B6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r6, Yp, 4.0 V), (GM1_L_r6, Yp, 4.0 V), (GM3_L_r6, Yp, 7.75 V), (GM3_R_r6, Yp, 7.75 V), (GM1_L_r3, Xp, 6.5 V), and (GM1_L_r3, Yn, 4.75 V).

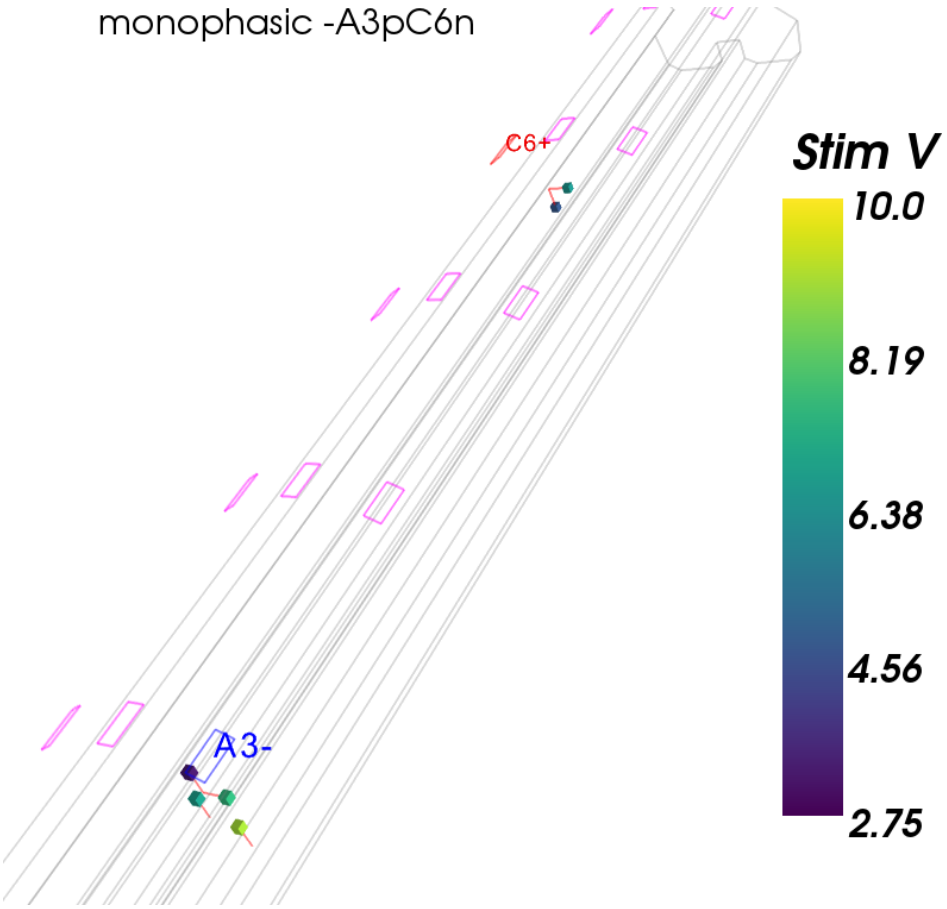


Figure 4.47: Monophasic stimulation using combination -A3pC6n. Electrode C6 has a positive phase and is labeled red. Electrode A3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.25 V), (GM3_L_r3, Yp, 6.75 V), (GM2_L_r3, Yp, 9.0 V), (GM1_L_r3, Xn, 7.5 V), (GM1_R_r6, Xn, 6.5 V), and (GM1_R_r6, Yn, 4.75 V).

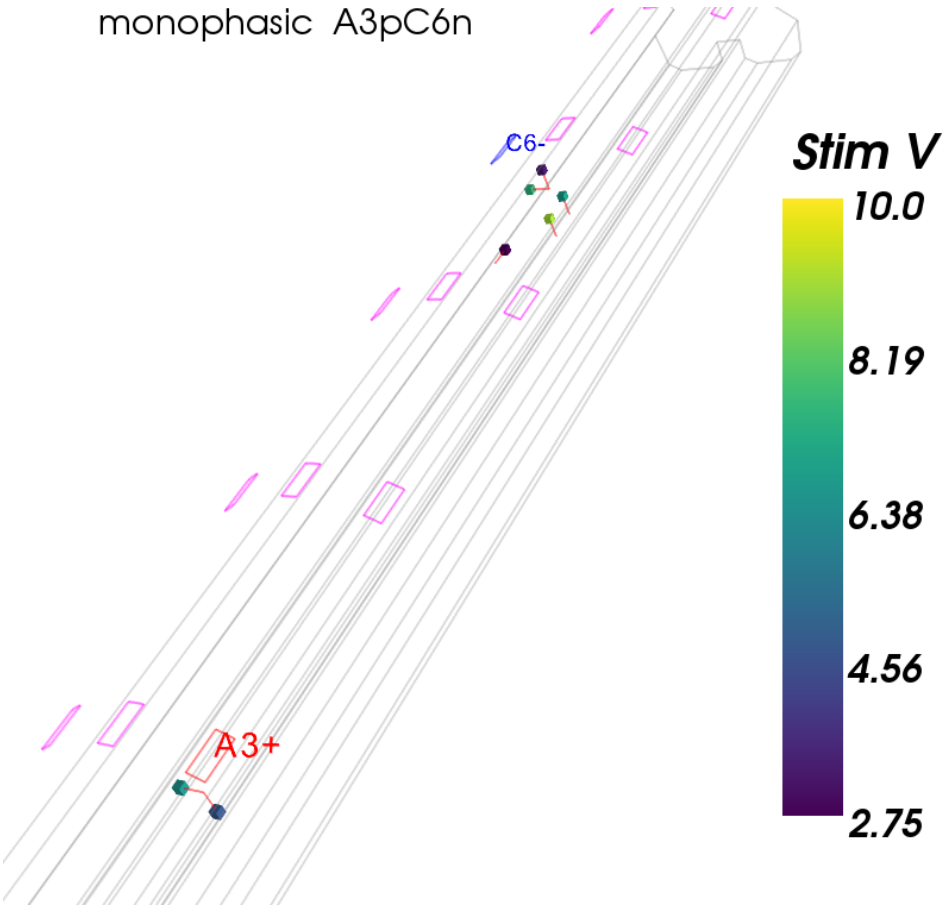


Figure 4.48: Monophasic stimulation using combination A3pC6n. Electrode A3 has a positive phase and is labeled red. Electrode C6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r6, Yp, 3.25 V), (GM3_R_r6, Yp, 6.75 V), (GM2_R_r6, Yp, 9.0 V), (GM1_L_r3, Xp, 6.5 V), (GM1_R_r6, Xp, 7.5 V), (GM1_L_r3, Yn, 4.75 V), and (GM1_R_r5and6, Zp, −1.0 V).

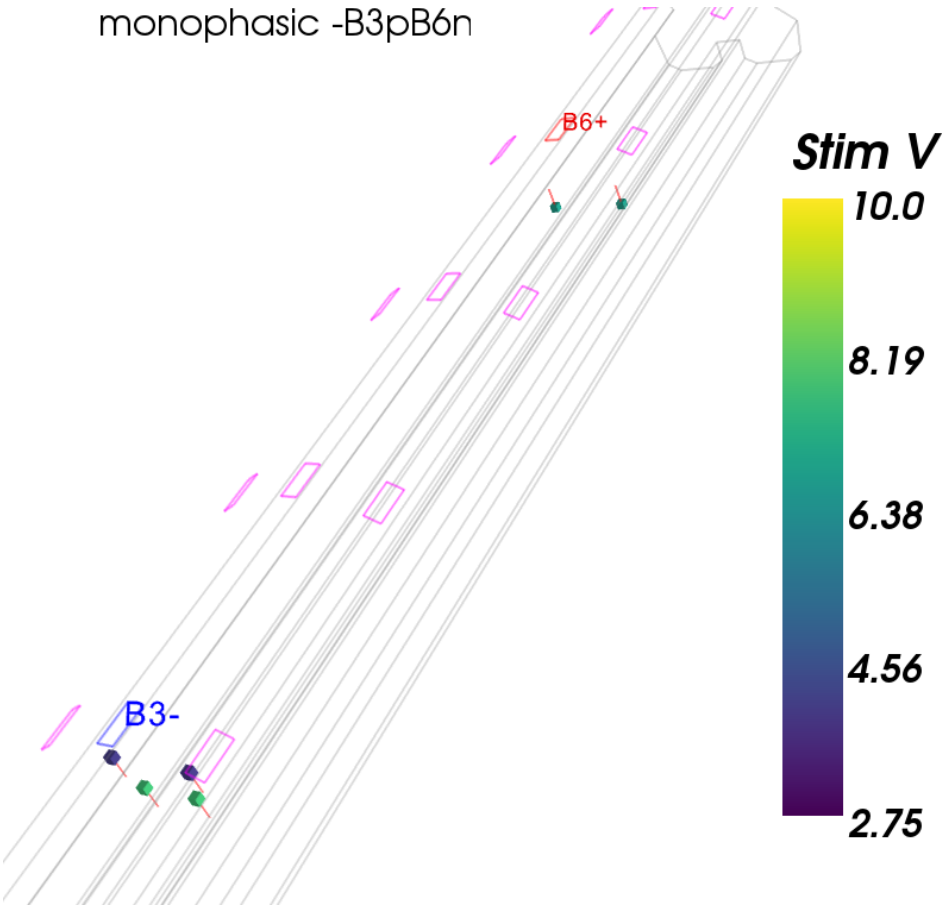


Figure 4.49: Monophasic stimulation using combination -B3pB6n. Electrode B6 has a positive phase and is labeled red. Electrode B3 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.0 V), (GM1_R_r3, Yp, 4.0 V), (GM3_L_r3, Yp, 7.75 V), (GM3_R_r3, Yp, 7.75 V), (GM1_L_r6, Yn, 6.75 V), and (GM1_R_r6, Yn, 6.75 V).

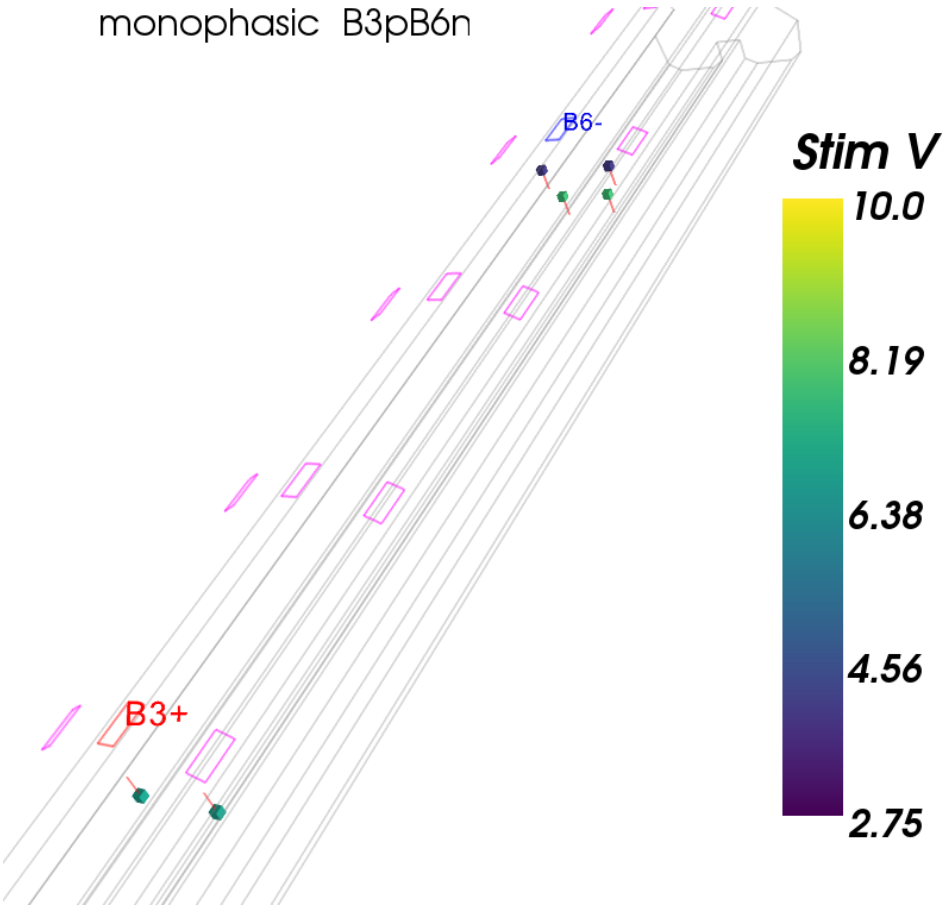


Figure 4.50: Monophasic stimulation using combination B3pB6n. Electrode B3 has a positive phase and is labeled red. Electrode B6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r6, Yp, 4.0 V), (GM1_R_r6, Yp, 4.0 V), (GM3_L_r6, Yp, 7.75 V), (GM3_R_r6, Yp, 7.75 V), (GM1_L_r3, Yn, 6.75 V), and (GM1_R_r3, Yn, 6.75 V).

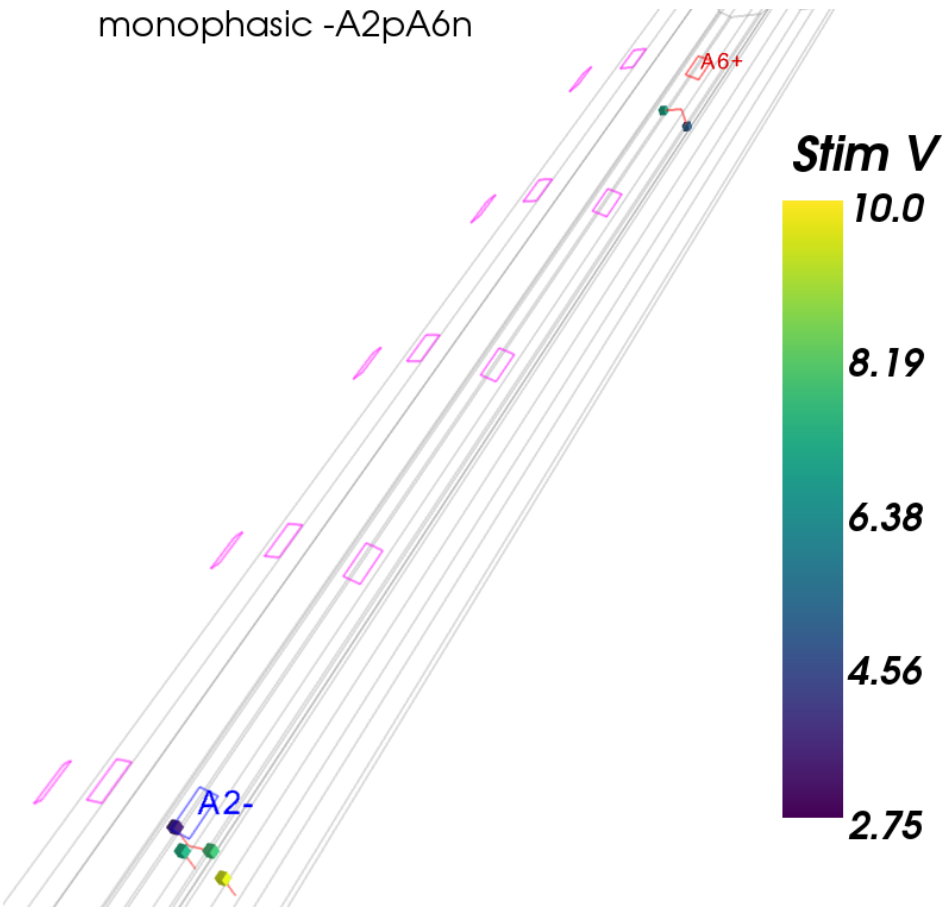


Figure 4.51: Monophasic stimulation using combination -A2pA6n. Electrode A6 has a positive phase and is labeled red. Electrode A2 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 3.5 V), (GM3_L_r2, Yp, 7.25 V), (GM2_L_r2, Yp, 9.5 V), (GM1_L_r6, Xp, 7.0 V), (GM1_L_r2, Xn, 7.75 V), and (GM1_L_r6, Yn, 5.0 V).

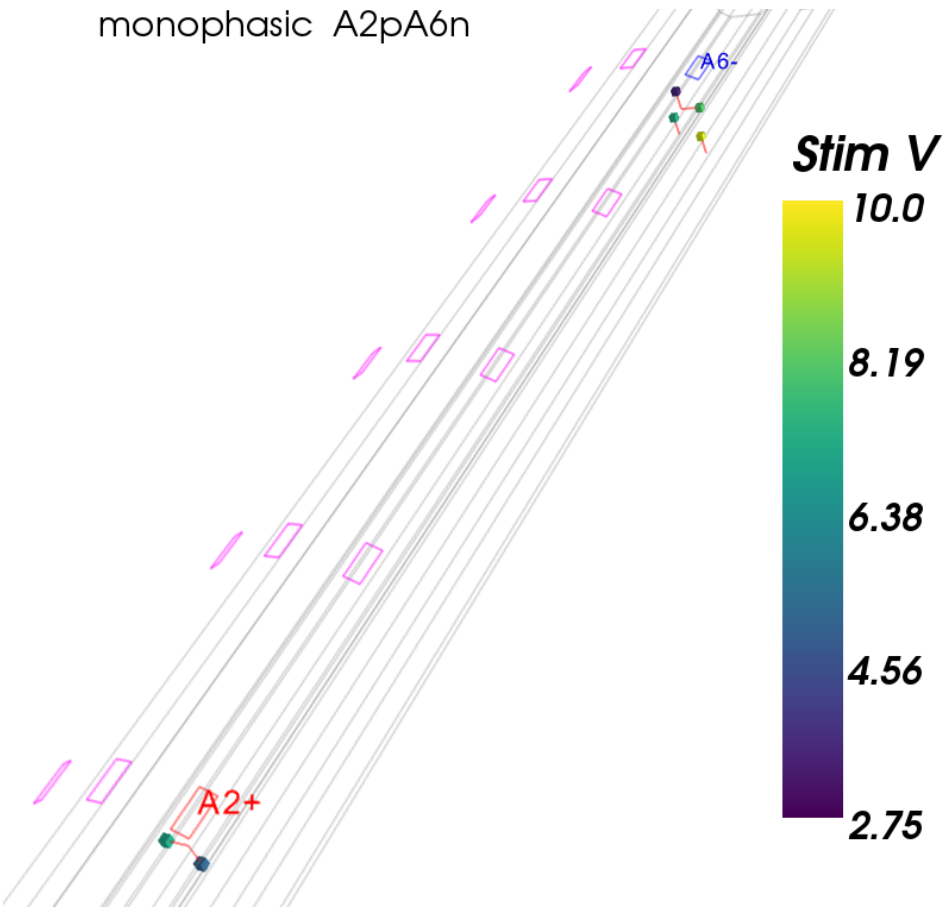


Figure 4.52: Monophasic stimulation using combination A2pA6n. Electrode A2 has a positive phase and is labeled red. Electrode A6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r6, Yp, 3.5 V), (GM3_L_r6, Yp, 7.25 V), (GM2_L_r6, Yp, 9.5 V), (GM1_L_r2, Xp, 7.0 V), (GM1_L_r6, Xn, 8.0 V), and (GM1_L_r2, Yn, 5.0 V).

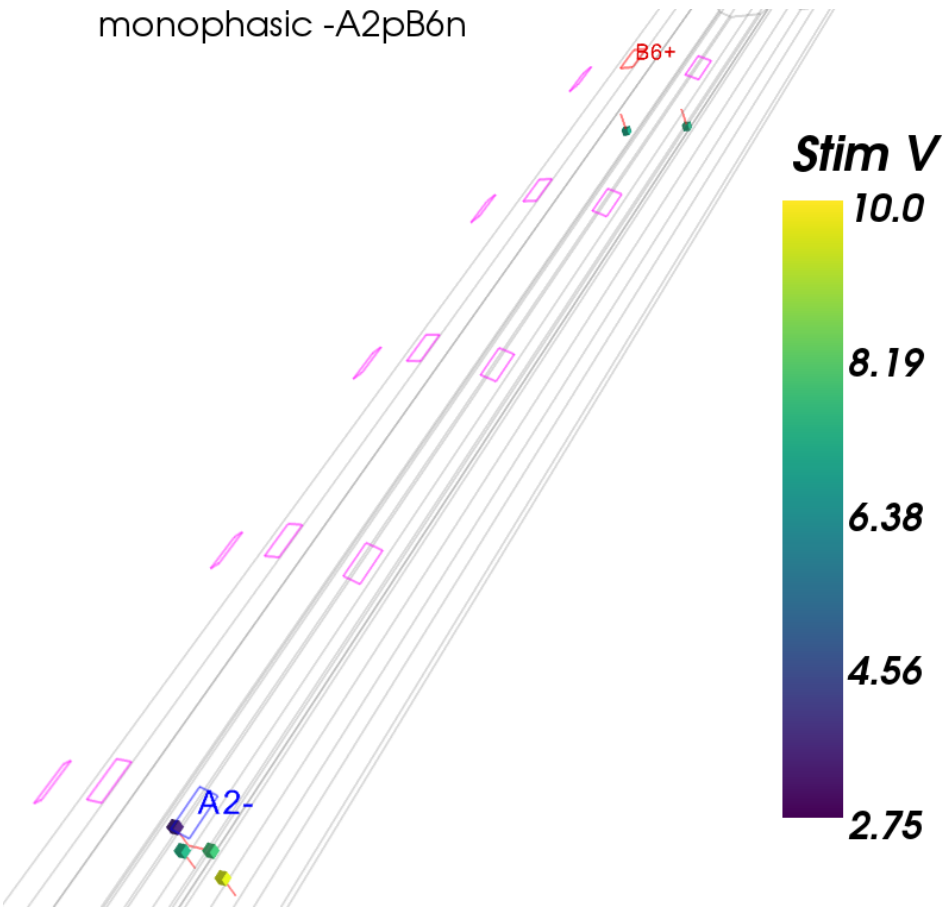


Figure 4.53: Monophasic stimulation using combination -A2pB6n. Electrode B6 has a positive phase and is labeled red. Electrode A2 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 3.5 V), (GM3_L_r2, Yp, 7.25 V), (GM2_L_r2, Yp, 9.5 V), (GM1_L_r2, Xn, 7.75 V), (GM1_L_r6, Yn, 7.25 V), and (GM1_R_r6, Yn, 7.0 V).

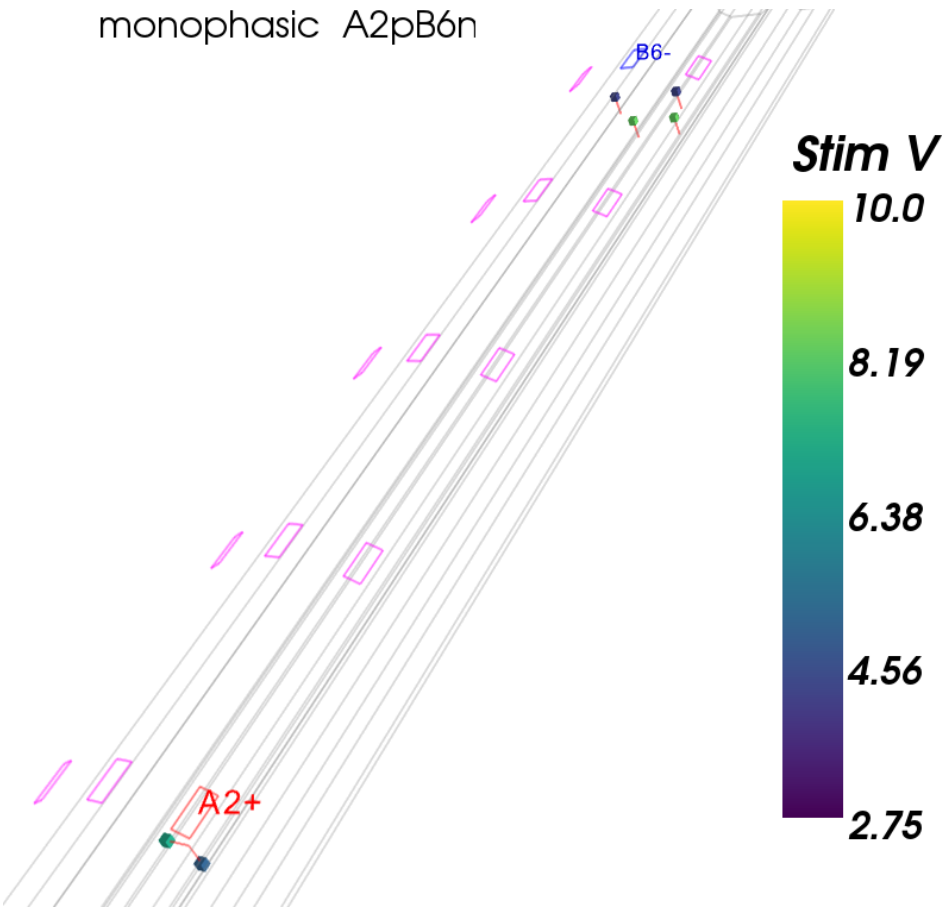


Figure 4.54: Monophasic stimulation using combination A2pB6n. Electrode A2 has a positive phase and is labeled red. Electrode B6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r6, Yp, 4.25 V), (GM1_R_r6, Yp, 4.25 V), (GM3_L_r6, Yp, 8.25 V), (GM3_R_r6, Yp, 8.25 V), (GM1_L_r2, Xp, 7.0 V), and (GM1_L_r2, Yn, 5.0 V).

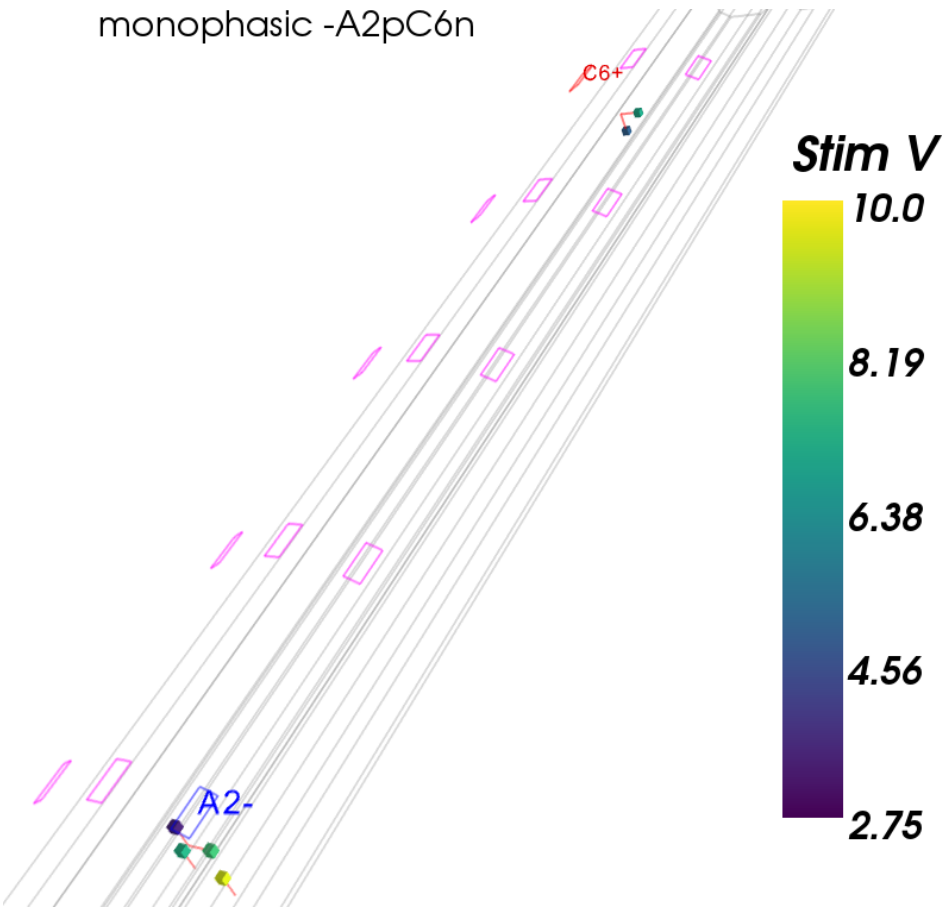


Figure 4.55: Monophasic stimulation using combination -A2pC6n. Electrode C6 has a positive phase and is labeled red. Electrode A2 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 3.5 V), (GM3_L_r2, Yp, 7.25 V), (GM2_L_r2, Yp, 9.5 V), (GM1_L_r2, Xn, 7.75 V), (GM1_R_r6, Xn, 7.0 V), and (GM1_R_r6, Yn, 5.0 V).

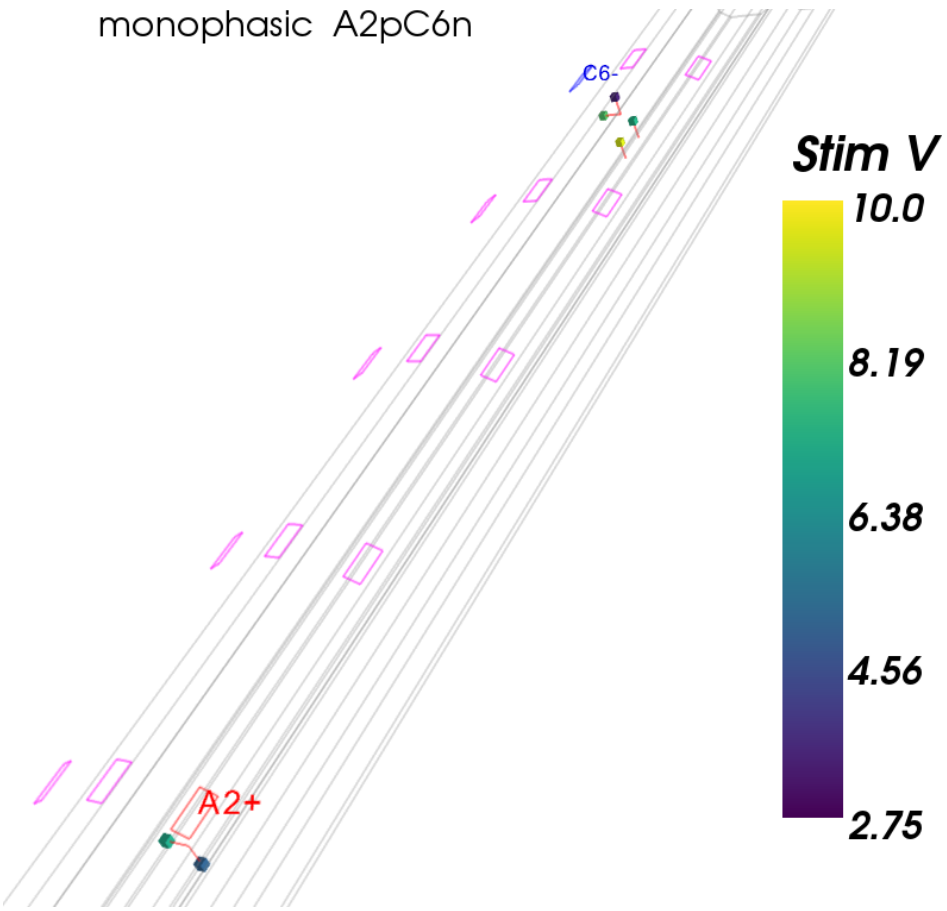


Figure 4.56: Monophasic stimulation using combination A2pC6n. Electrode A2 has a positive phase and is labeled red. Electrode C6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r6, Yp, 3.5 V), (GM3_R_r6, Yp, 7.25 V), (GM2_R_r6, Yp, 9.5 V), (GM1_L_r2, Xp, 7.0 V), (GM1_R_r6, Xp, 8.0 V), and (GM1_L_r2, Yn, 5.0 V).

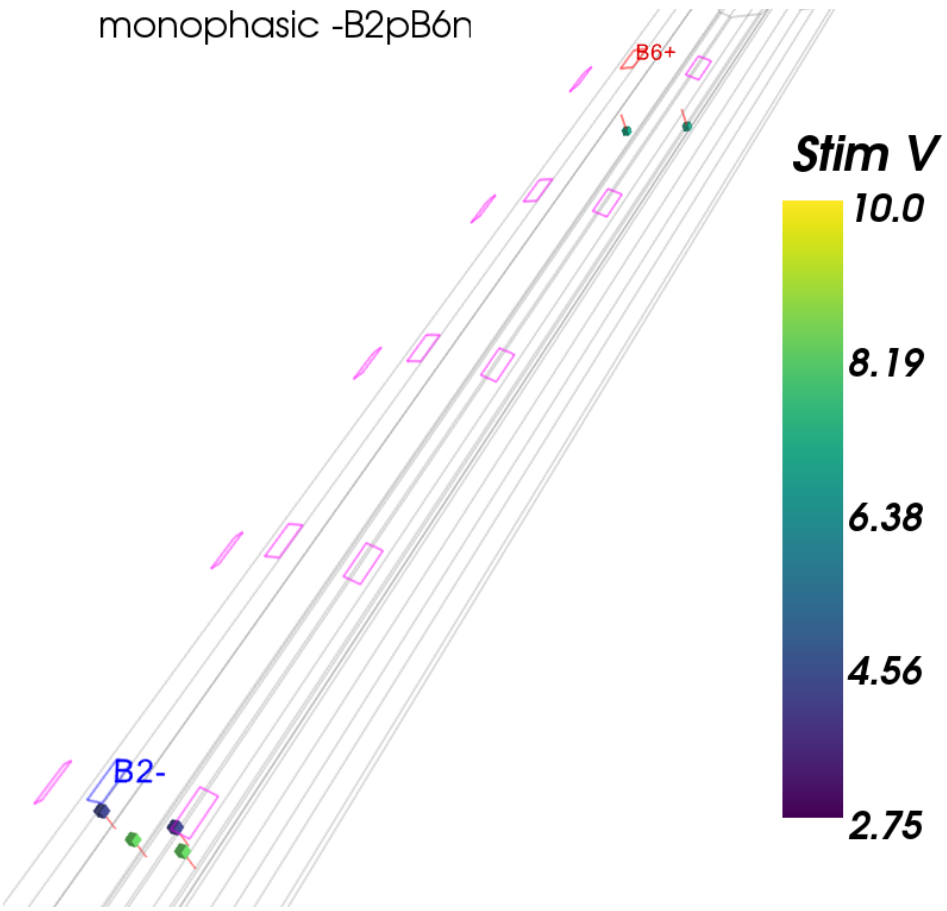


Figure 4.57: Monophasic stimulation using combination -B2pB6n. Electrode B6 has a positive phase and is labeled red. Electrode B2 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 4.25 V), (GM1_R_r2, Yp, 4.25 V), (GM3_L_r2, Yp, 8.25 V), (GM3_R_r2, Yp, 8.25 V), (GM1_L_r6, Yn, 7.0 V), and (GM1_R_r6, Yn, 7.0 V).

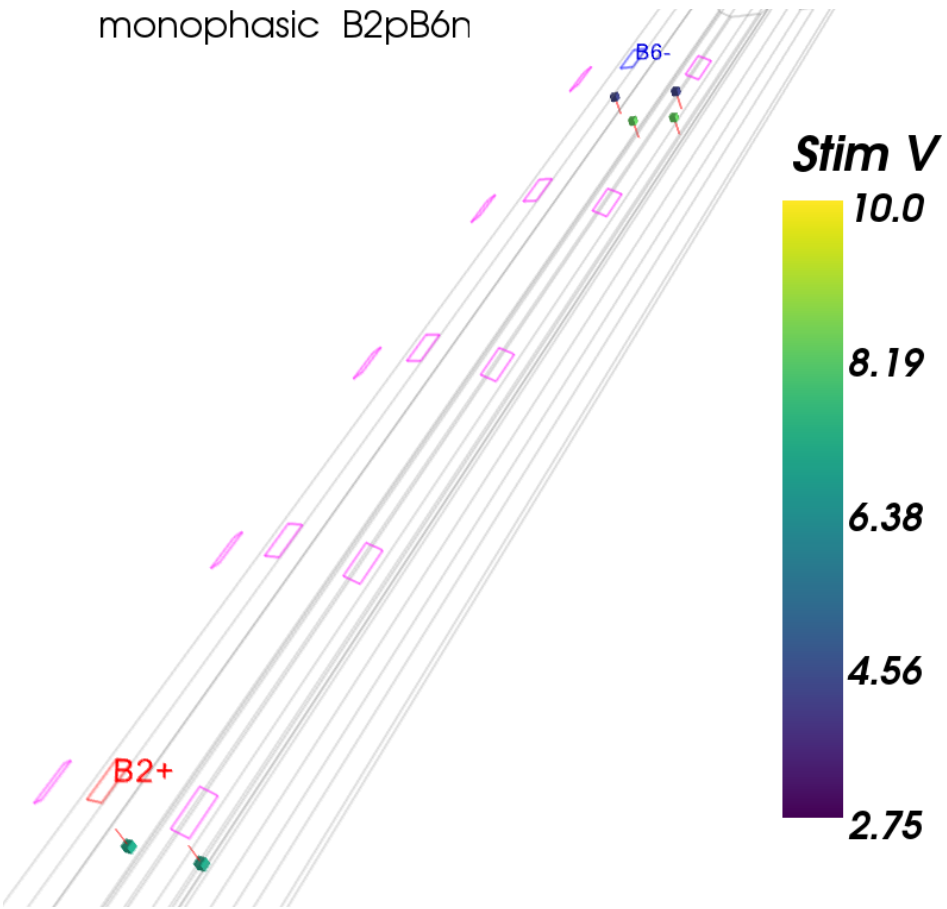


Figure 4.58: Monophasic stimulation using combination B2pB6n. Electrode B2 has a positive phase and is labeled red. Electrode B6 has a negative phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r6, Yp, 4.25 V), (GM1_R_r6, Yp, 4.25 V), (GM3_L_r6, Yp, 8.25 V), (GM3_R_r6, Yp, 8.25 V), (GM1_L_r2, Yn, 7.0 V), and (GM1_R_r2, Yn, 7.0 V).

4.A.2 Biphasic

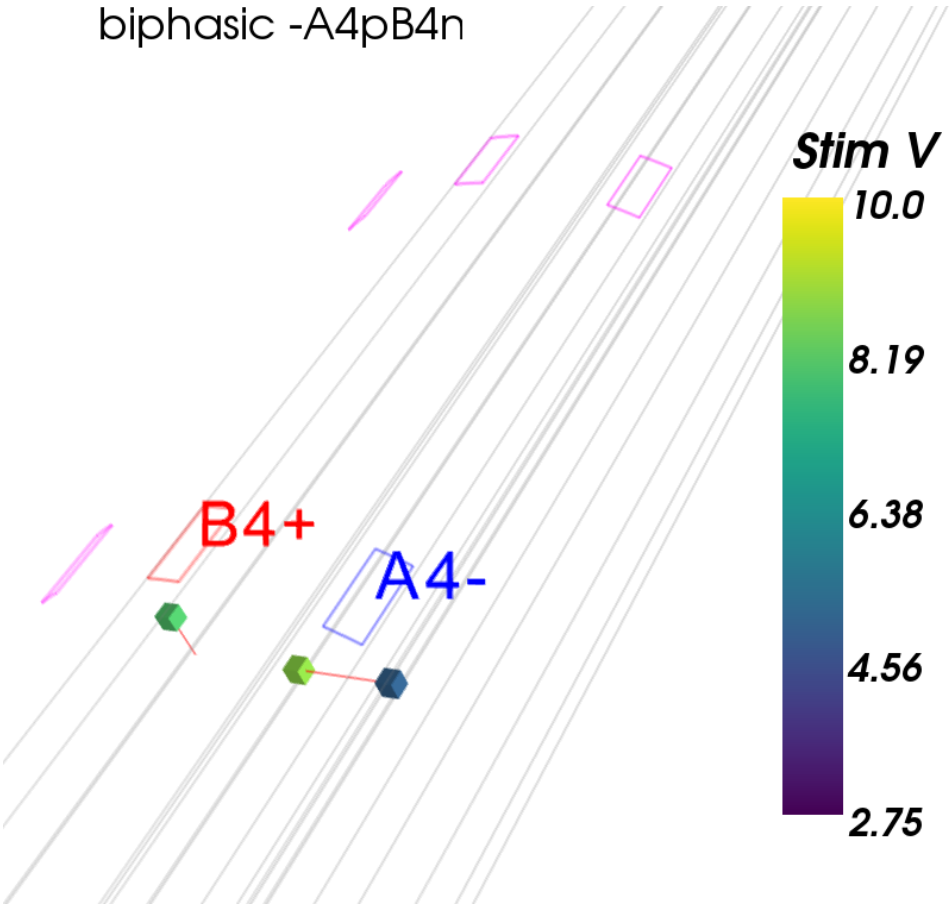


Figure 4.59: Biphasic stimulation using combination -A4pB4n. Electrode B4 has a positive phase first followed by a negative phase and is labeled red. Electrode A4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r4, Yp, 8.0 V), (GM1_L_r4, Xp, 8.75 V), and (GM1_L_r4, Xn, 5.0 V).

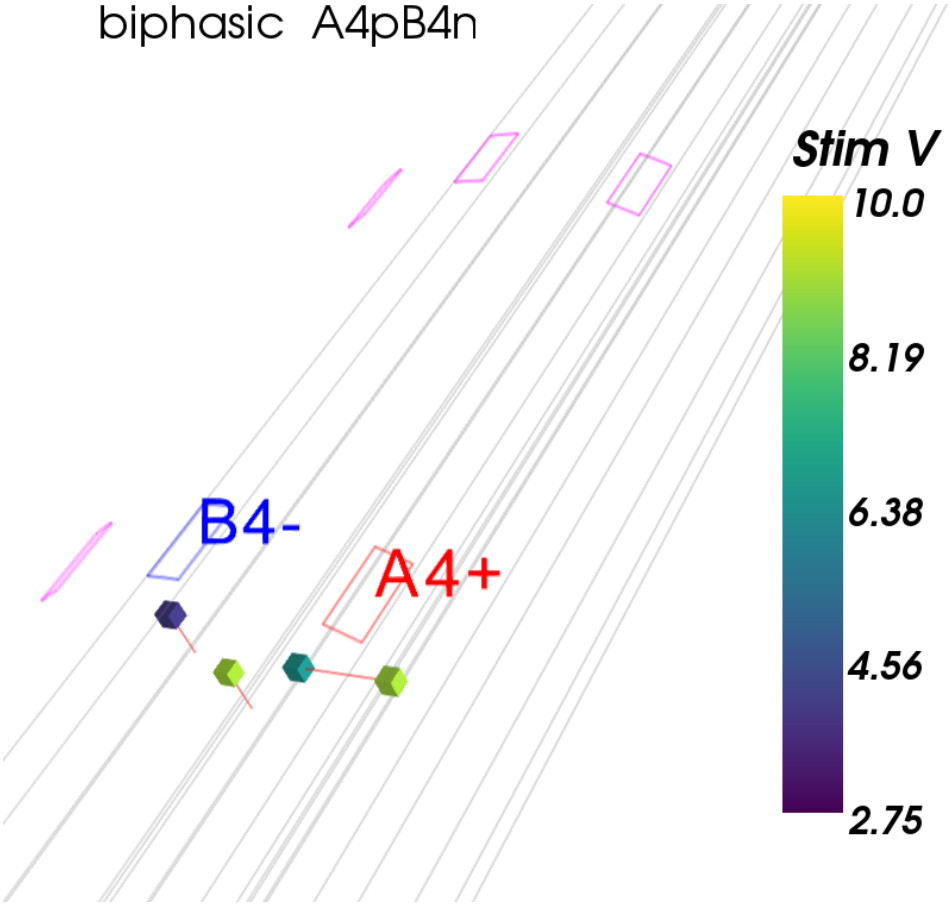


Figure 4.60: Biphasic stimulation using combination A4pB4n. Electrode A4 has a positive phase first followed by a negative phase and is labeled red. Electrode B4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r4, Yp, 4.0 V), (GM3_R_r4, Yp, 9.0 V), (GM1_L_r4, Xp, 6.5 V), and (GM1_L_r4, Xn, 9.0 V).

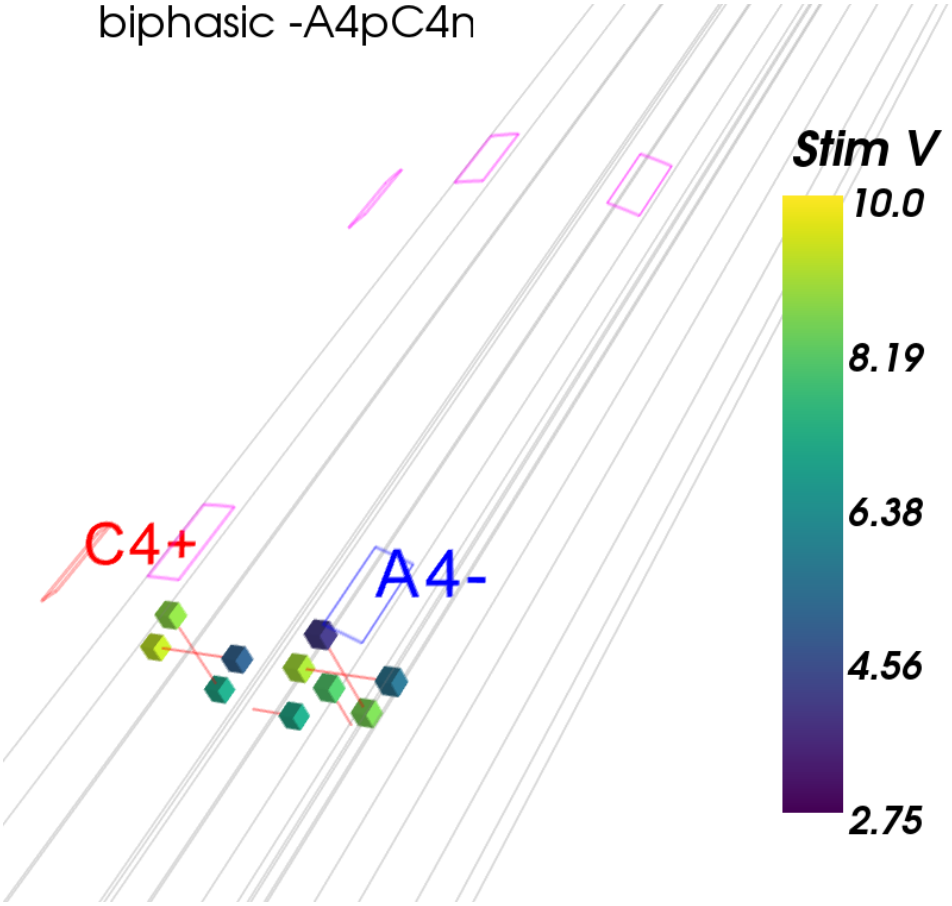


Figure 4.61: Biphasic stimulation using combination -A4pC4n. Electrode C4 has a positive phase first followed by a negative phase and is labeled red. Electrode A4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 4.0 V), (GM1_R_r4, Yp, 8.75 V), (GM3_L_r4, Yp, 8.0 V), (GM1_L_r4, Xp, 9.0 V), (GM1_R_r4, Xp, 9.25 V), (GM1_L_r4, Xn, 5.5 V), (GM1_R_r4, Xn, 5.0 V), (GM3_R_r4, Xn, 7.0 V), (GM1_L_r4, Yn, 8.5 V), and (GM1_R_r4, Yn, 7.0 V).

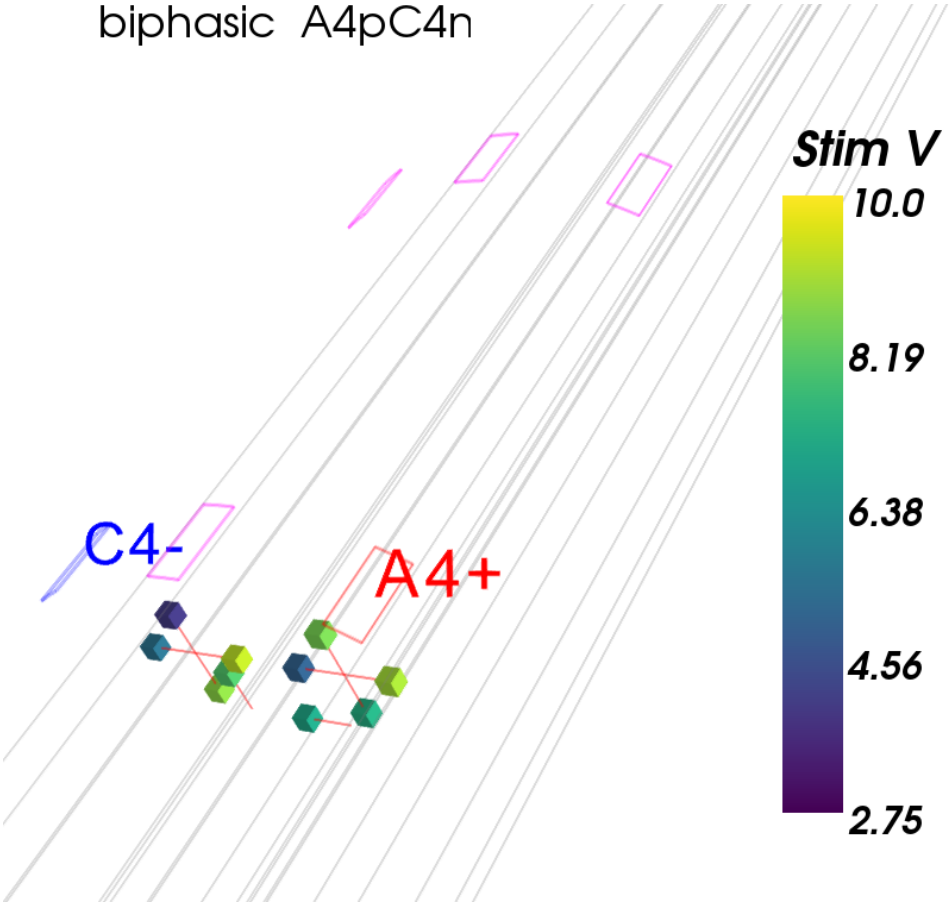


Figure 4.62: Biphasic stimulation using combination A4pC4n. Electrode A4 has a positive phase first followed by a negative phase and is labeled red. Electrode C4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 8.5 V), (GM1_R_r4, Yp, 4.0 V), (GM3_R_r4, Yp, 8.0 V), (GM1_L_r4, Xp, 5.0 V), (GM1_R_r4, Xp, 5.5 V), (GM3_L_r4, Xp, 7.0 V), (GM1_L_r4, Xn, 9.0 V), (GM1_R_r4, Xn, 9.25 V), (GM1_L_r4, Yn, 7.25 V), and (GM1_R_r4, Yn, 8.75 V).

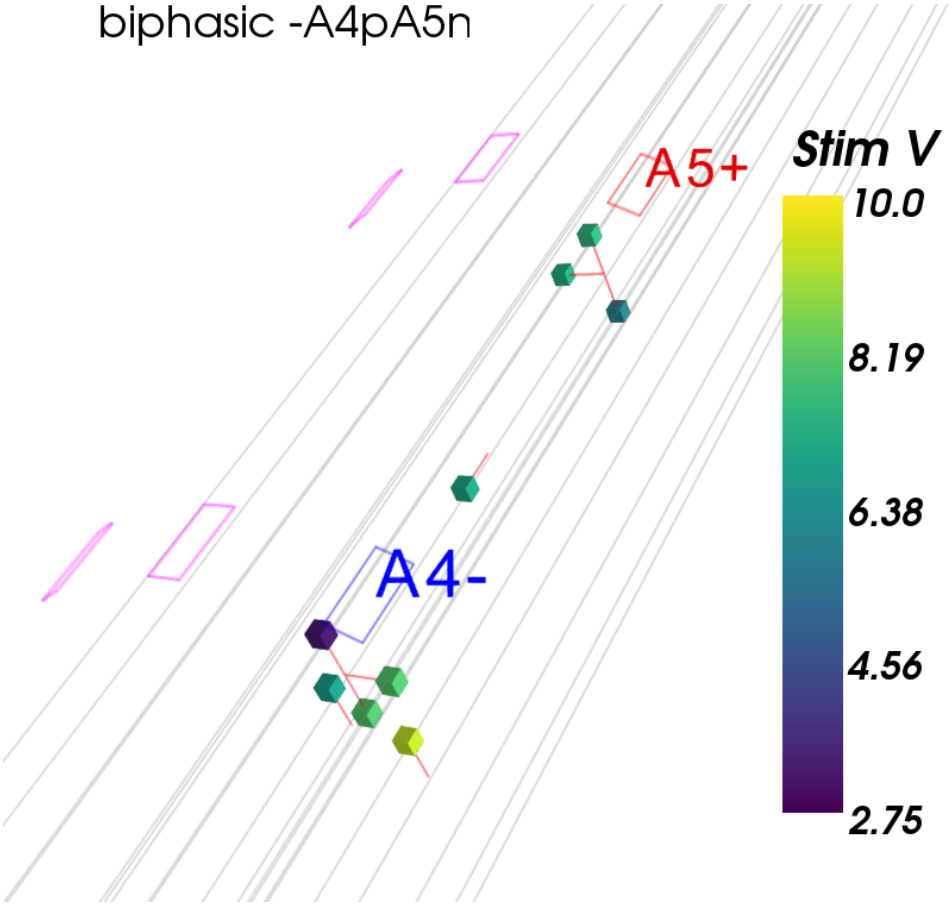


Figure 4.63: Biphasic stimulation using combination -A4pA5n. Electrode A5 has a positive phase first followed by a negative phase and is labeled red. Electrode A4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4and5, Zn, 7.0 V), (GM1_L_r4, Yp, 3.25 V), (GM1_L_r5, Yp, 7.5 V), (GM3_L_r4, Yp, 6.75 V), (GM2_L_r4, Yp, 9.25 V), (GM1_L_r5, Xp, 7.25 V), (GM1_L_r4, Xn, 8.0 V), (GM1_L_r4, Yn, 8.0 V), and (GM1_L_r5, Yn, 6.0 V).

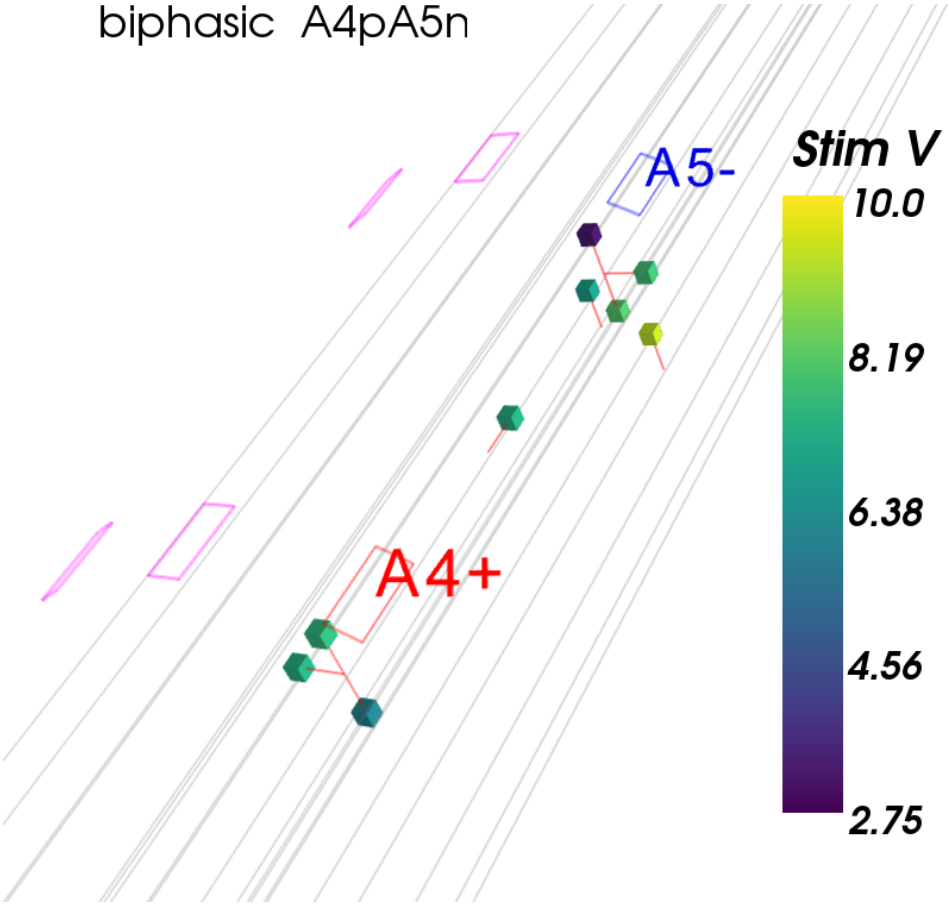


Figure 4.64: Biphasic stimulation using combination A4pA5n. Electrode A4 has a positive phase first followed by a negative phase and is labeled red. Electrode A5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 7.5 V), (GM1_L_r5, Yp, 3.25 V), (GM3_L_r5, Yp, 6.75 V), (GM2_L_r5, Yp, 9.25 V), (GM1_L_r4, Xp, 7.25 V), (GM1_L_r5, Xn, 7.75 V), (GM1_L_r4, Yn, 6.0 V), (GM1_L_r5, Yn, 8.0 V), and (GM1_L_r4and5, Zp, 7.25 V).

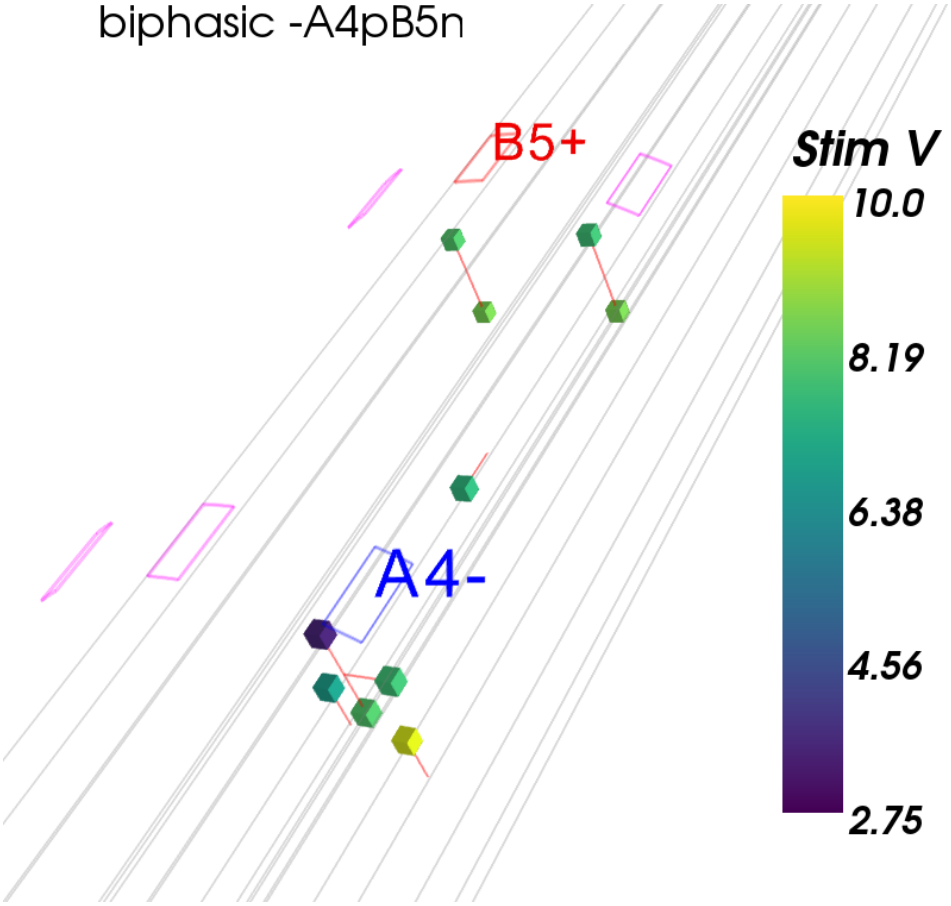


Figure 4.65: Biphasic stimulation using combination -A4pB5n. Electrode B5 has a positive phase first followed by a negative phase and is labeled red. Electrode A4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4and5, Zn, 7.5 V), (GM1_L_r4, Yp, 3.5 V), (GM1_R_r5, Yp, 8.0 V), (GM1_L_r5, Yp, 7.75 V), (GM3_L_r4, Yp, 6.75 V), (GM2_L_r4, Yp, 9.5 V), (GM1_L_r4, Xn, 7.75 V), (GM1_L_r4, Yn, 8.0 V), (GM1_R_r5, Yn, 8.5 V), and (GM1_L_r5, Yn, 8.5 V).

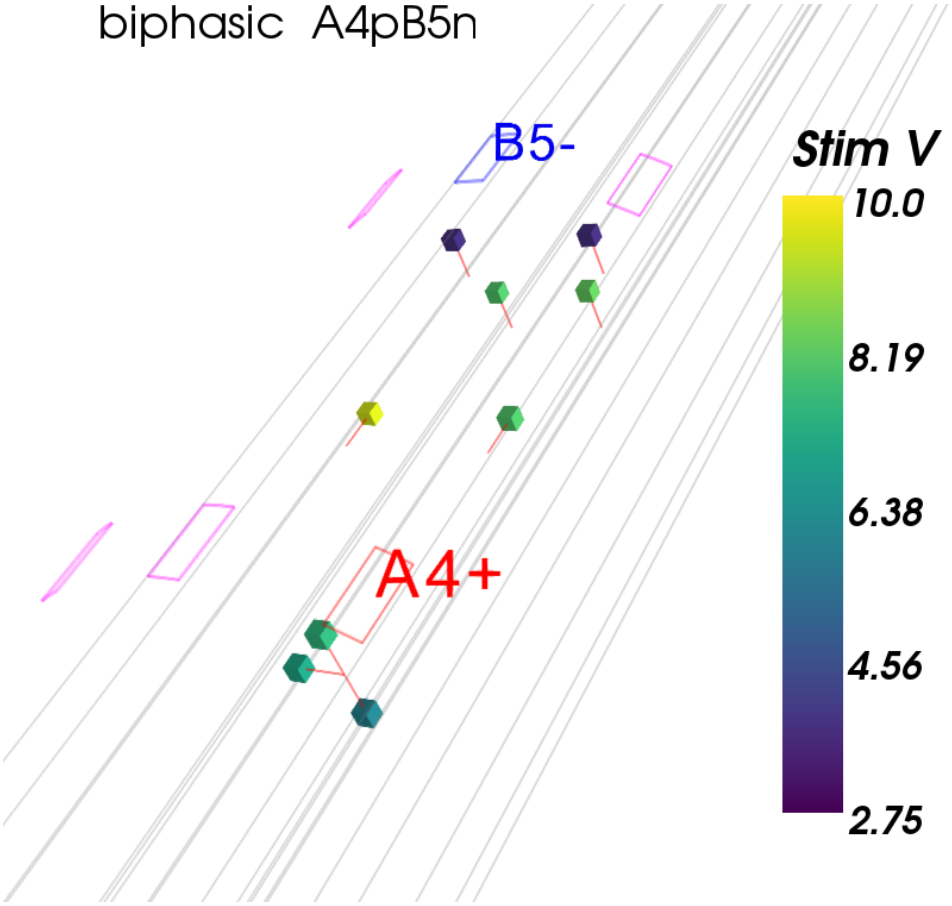


Figure 4.66: Biphasic stimulation using combination A4pB5n. Electrode A4 has a positive phase first followed by a negative phase and is labeled red. Electrode B5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 7.5 V), (GM1_R_r5, Yp, 3.75 V), (GM1_L_r5, Yp, 3.75 V), (GM3_R_r5, Yp, 8.0 V), (GM3_L_r5, Yp, 8.25 V), (GM1_L_r4, Xp, 7.0 V), (GM1_L_r4, Yn, 6.0 V), (GM1_L_r4and5, Zp, 8.0 V), and (GM1_R_r4and5, Zp, 9.5 V).

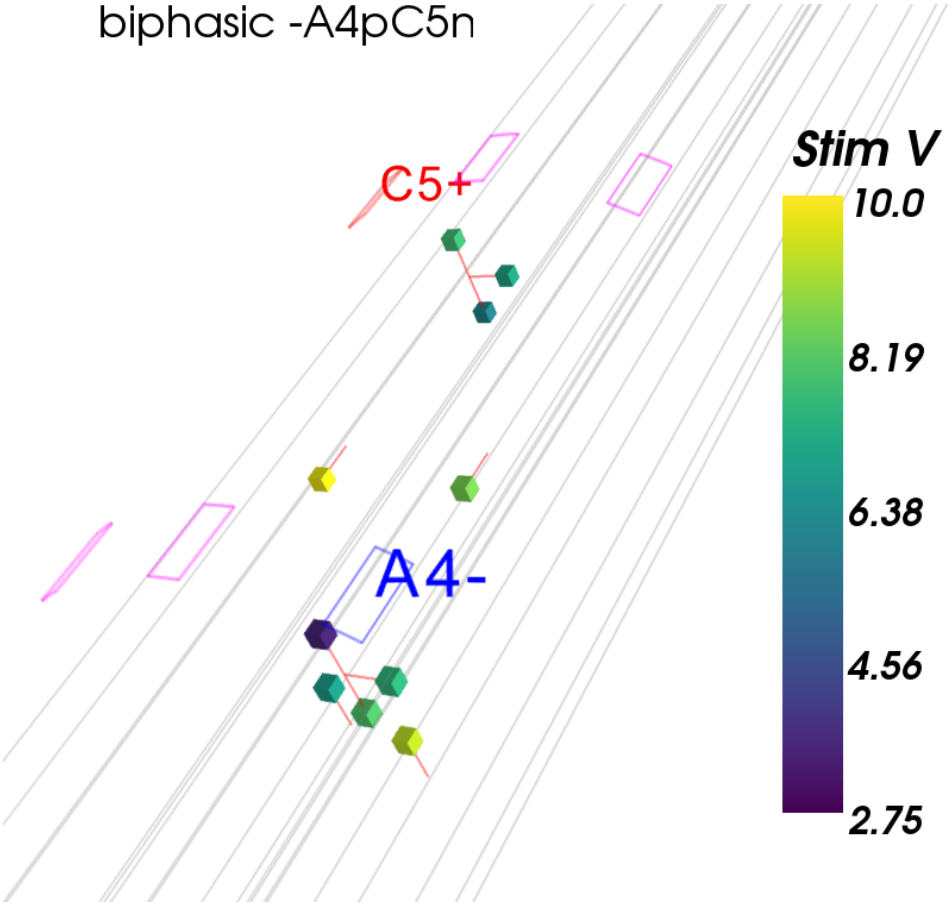


Figure 4.67: Biphasic stimulation using combination -A4pC5n. Electrode C5 has a positive phase first followed by a negative phase and is labeled red. Electrode A4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r4and5, Zn, 8.5 V), (GM1_R_r4and5, Zn, 9.75 V), (GM1_L_r4, Yp, 3.5 V), (GM1_R_r5, Yp, 7.75 V), (GM3_L_r4, Yp, 6.75 V), (GM2_L_r4, Yp, 9.25 V), (GM1_L_r4, Xn, 7.5 V), (GM1_R_r5, Xn, 7.0 V), (GM1_L_r4, Yn, 8.0 V), and (GM1_R_r5, Yn, 6.0 V).

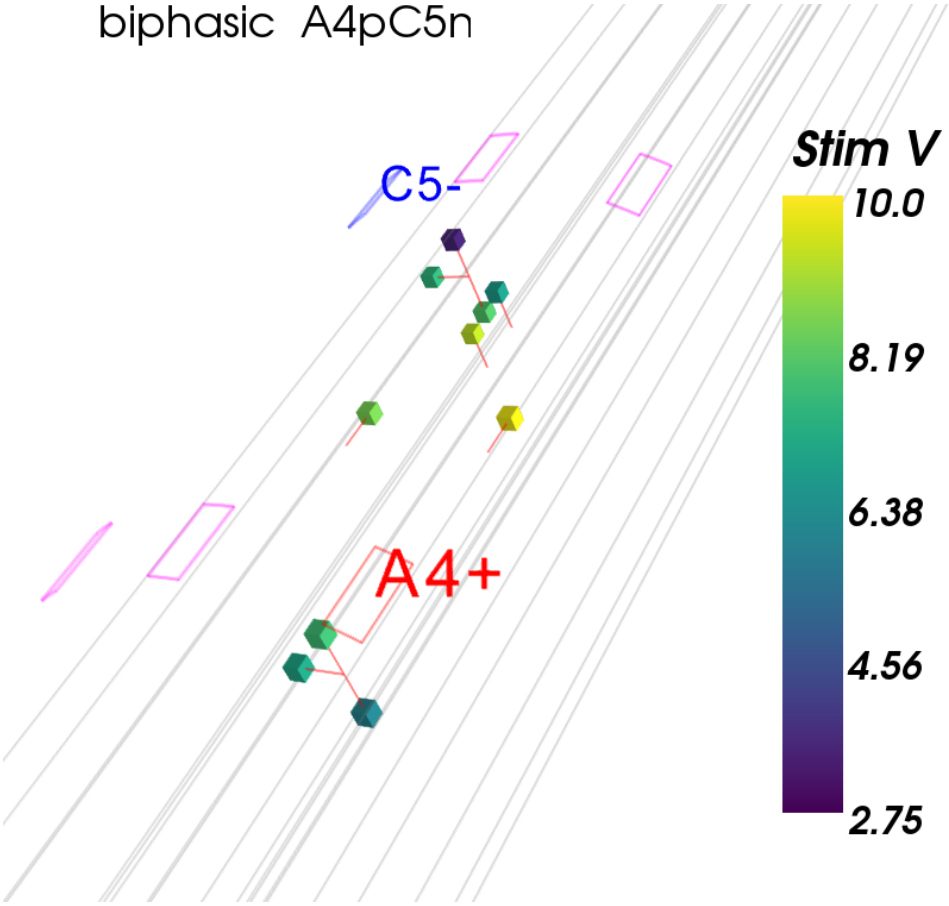


Figure 4.68: Biphasic stimulation using combination A4pC5n. Electrode A4 has a positive phase first followed by a negative phase and is labeled red. Electrode C5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 7.75 V), (GM1_R_r5, Yp, 3.5 V), (GM3_R_r5, Yp, 6.75 V), (GM2_R_r5, Yp, 9.25 V), (GM1_L_r4, Xp, 7.0 V), (GM1_R_r5, Xp, 7.5 V), (GM1_L_r4, Yn, 6.0 V), (GM1_R_r5, Yn, 8.0 V), (GM1_L_r4and5, Zp, 9.75 V), and (GM1_R_r4and5, Zp, 8.5 V).

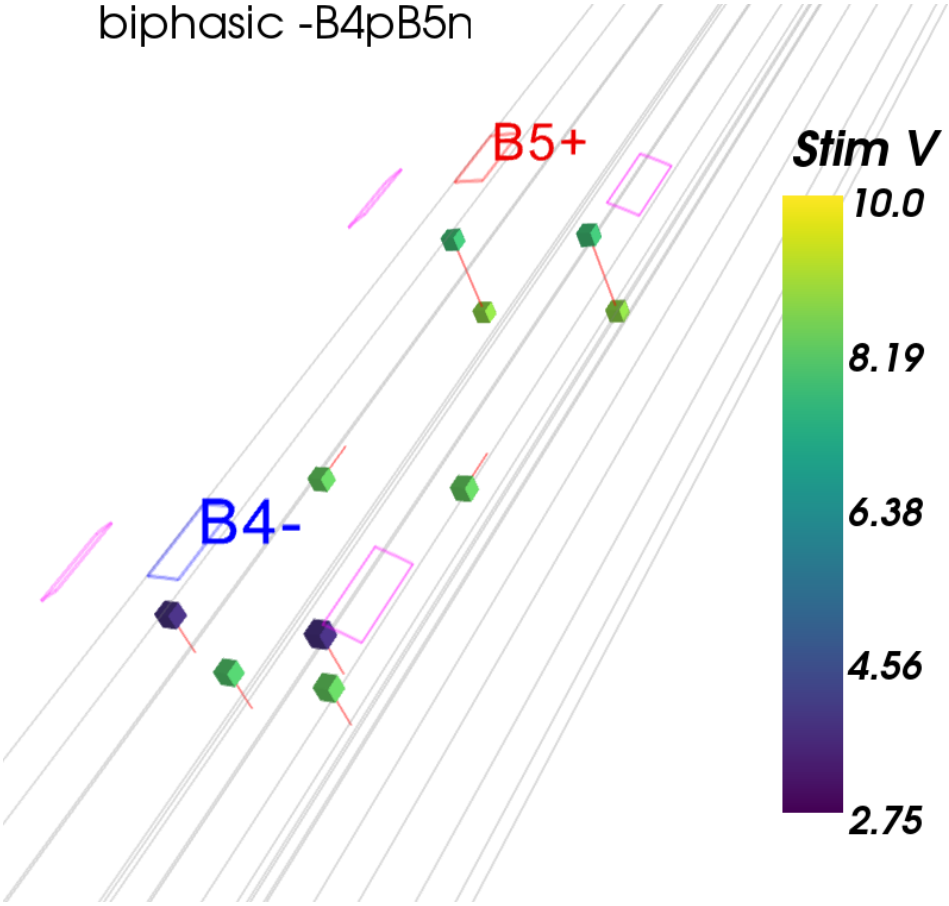


Figure 4.69: Biphasic stimulation using combination -B4pB5n. Electrode B5 has a positive phase first followed by a negative phase and is labeled red. Electrode B4 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_R_r4and5, Zn, 8.25 V), (GM1_L_r4and5, Zn, 8.25 V), (GM1_L_r4, Yp, 3.75 V), (GM1_R_r4, Yp, 3.75 V), (GM1_L_r5, Yp, 7.75 V), (GM1_R_r5, Yp, 7.75 V), (GM3_R_r4, Yp, 8.0 V), (GM3_L_r4, Yp, 8.25 V), (GM1_L_r5, Yn, 8.75 V), and (GM1_R_r5, Yn, 8.75 V).

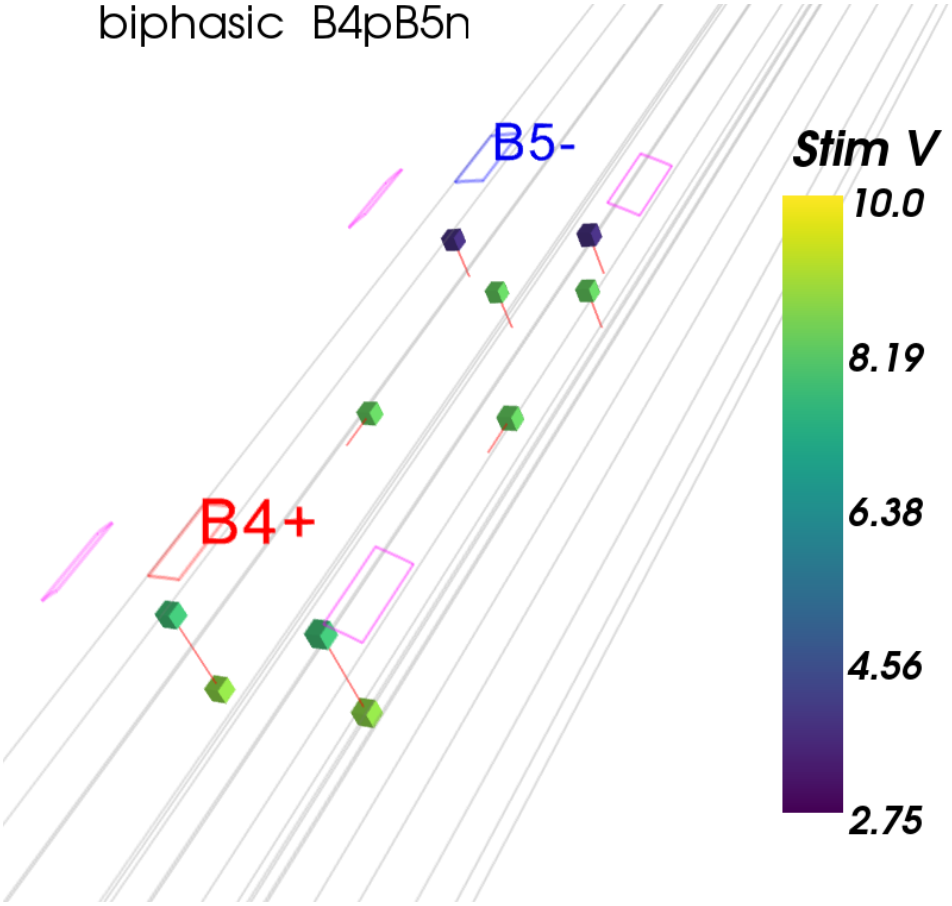


Figure 4.70: Biphasic stimulation using combination B4pB5n. Electrode B4 has a positive phase first followed by a negative phase and is labeled red. Electrode B5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r4, Yp, 7.75 V), (GM1_R_r4, Yp, 7.75 V), (GM1_L_r5, Yp, 3.75 V), (GM1_R_r5, Yp, 3.75 V), (GM3_L_r5, Yp, 8.25 V), (GM3_R_r5, Yp, 8.25 V), (GM1_L_r4, Yn, 8.75 V), (GM1_R_r4, Yn, 8.75 V), (GM1_R_r4and5, Zp, 8.25 V), and (GM1_L_r4and5, Zp, 8.25 V).

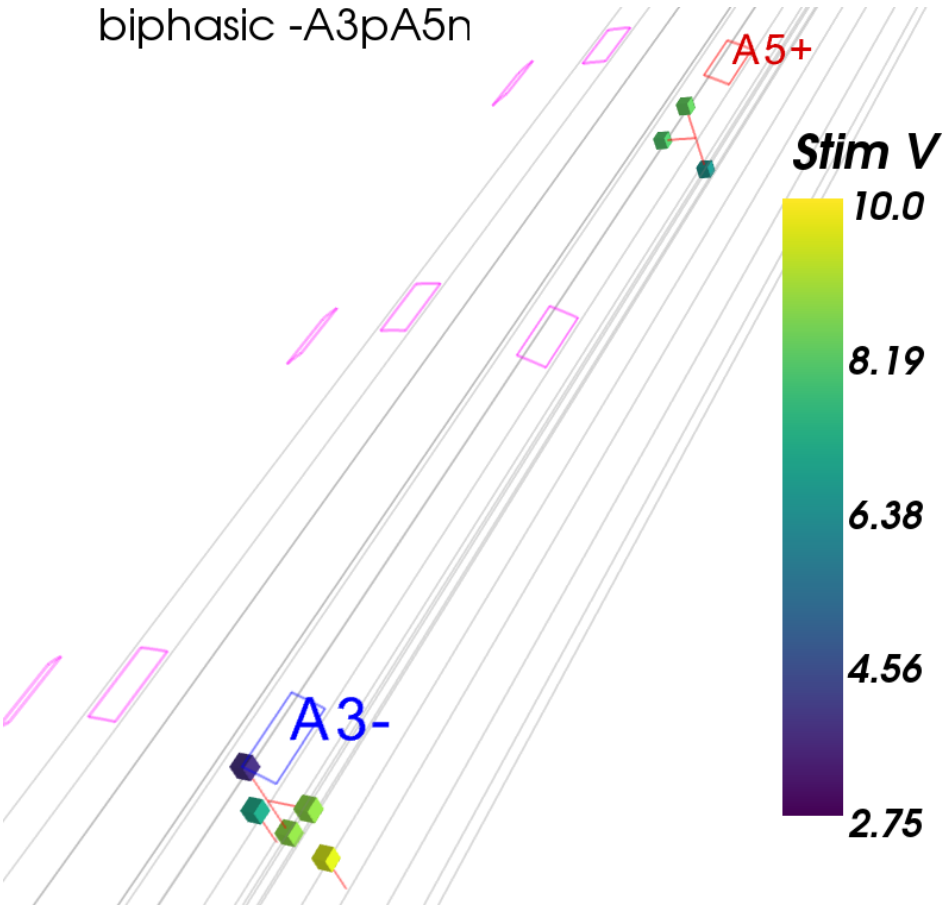


Figure 4.71: Biphasic stimulation using combination -A3pA5n. Electrode A5 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.75 V), (GM1_L_r5, Yp, 8.25 V), (GM3_L_r3, Yp, 7.0 V), (GM2_L_r3, Yp, 9.5 V), (GM1_L_r5, Xp, 8.0 V), (GM1_L_r3, Xn, 8.75 V), (GM1_L_r3, Yn, 8.75 V), and (GM1_L_r5, Yn, 6.5 V).

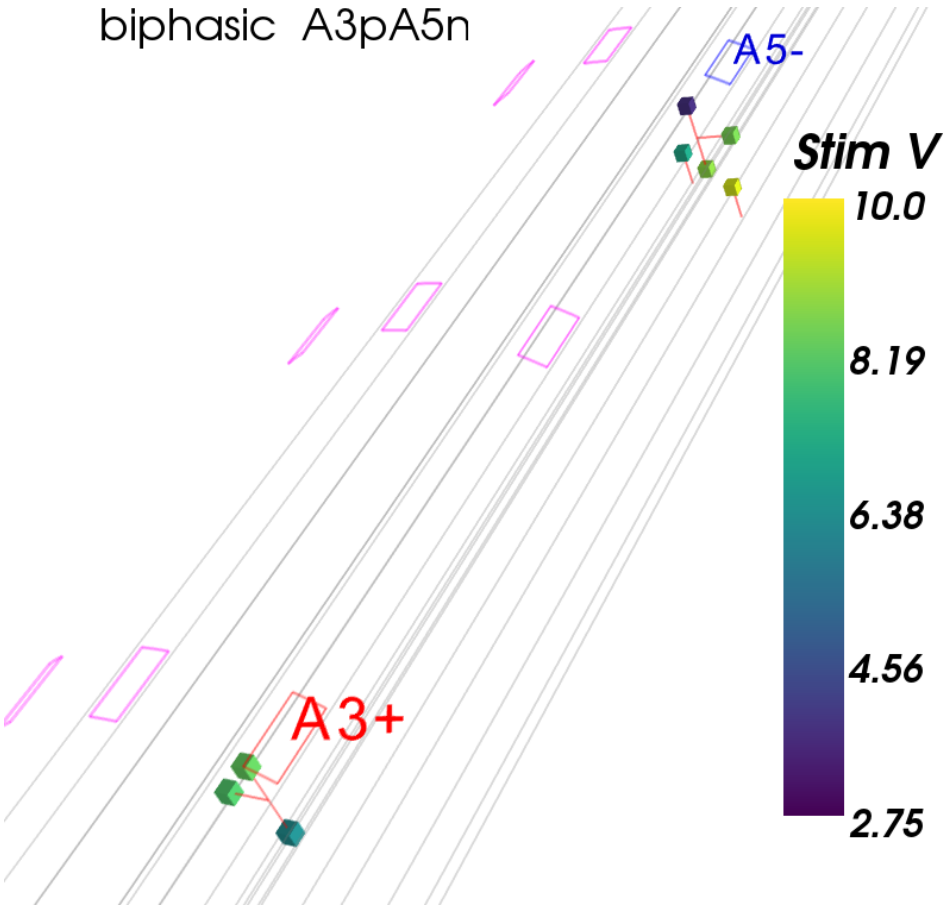


Figure 4.72: Biphasic stimulation using combination A3pA5n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode A5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 8.25 V), (GM1_L_r5, Yp, 3.75 V), (GM3_L_r5, Yp, 7.0 V), (GM2_L_r5, Yp, 9.5 V), (GM1_L_r3, Xp, 8.0 V), (GM1_L_r5, Xn, 8.5 V), (GM1_L_r3, Yn, 6.25 V), and (GM1_L_r5, Yn, 8.75 V).

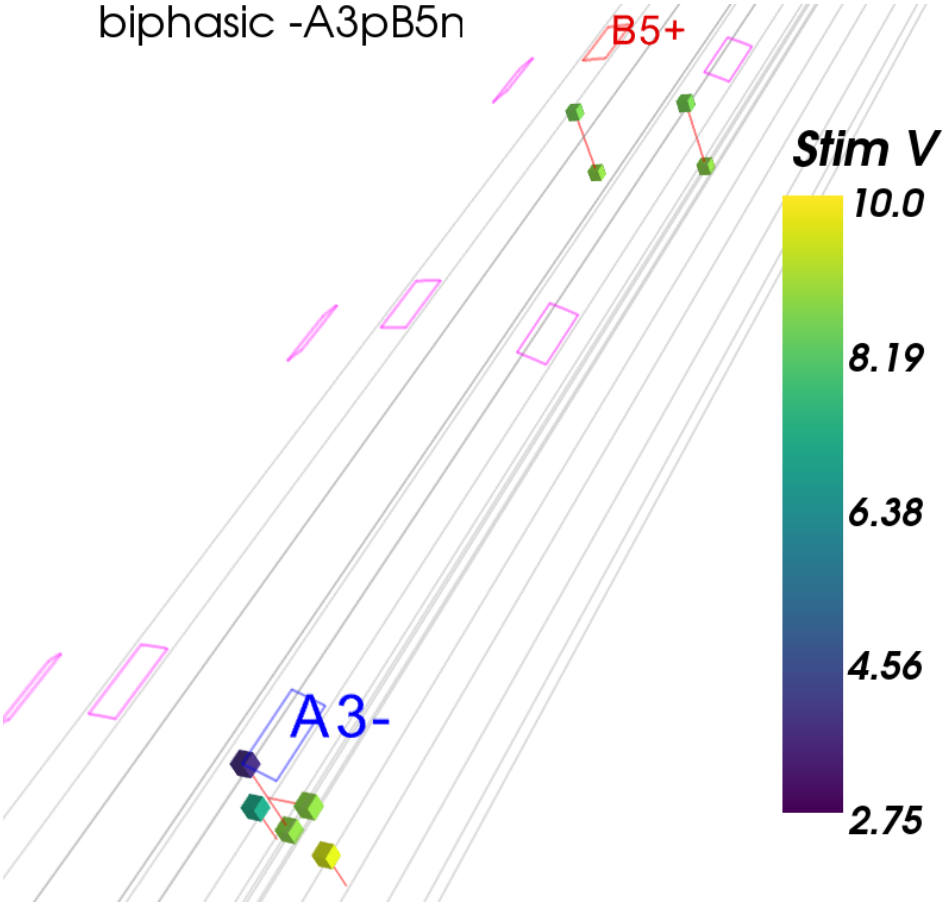


Figure 4.73: Biphasic stimulation using combination -A3pB5n. Electrode B5 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.75 V), (GM1_R_r5, Yp, 8.5 V), (GM1_L_r5, Yp, 8.5 V), (GM3_L_r3, Yp, 7.0 V), (GM2_L_r3, Yp, 9.5 V), (GM1_L_r3, Xn, 8.75 V), (GM1_L_r3, Yn, 8.75 V), (GM1_R_r5, Yn, 8.75 V), and (GM1_L_r5, Yn, 8.75 V).

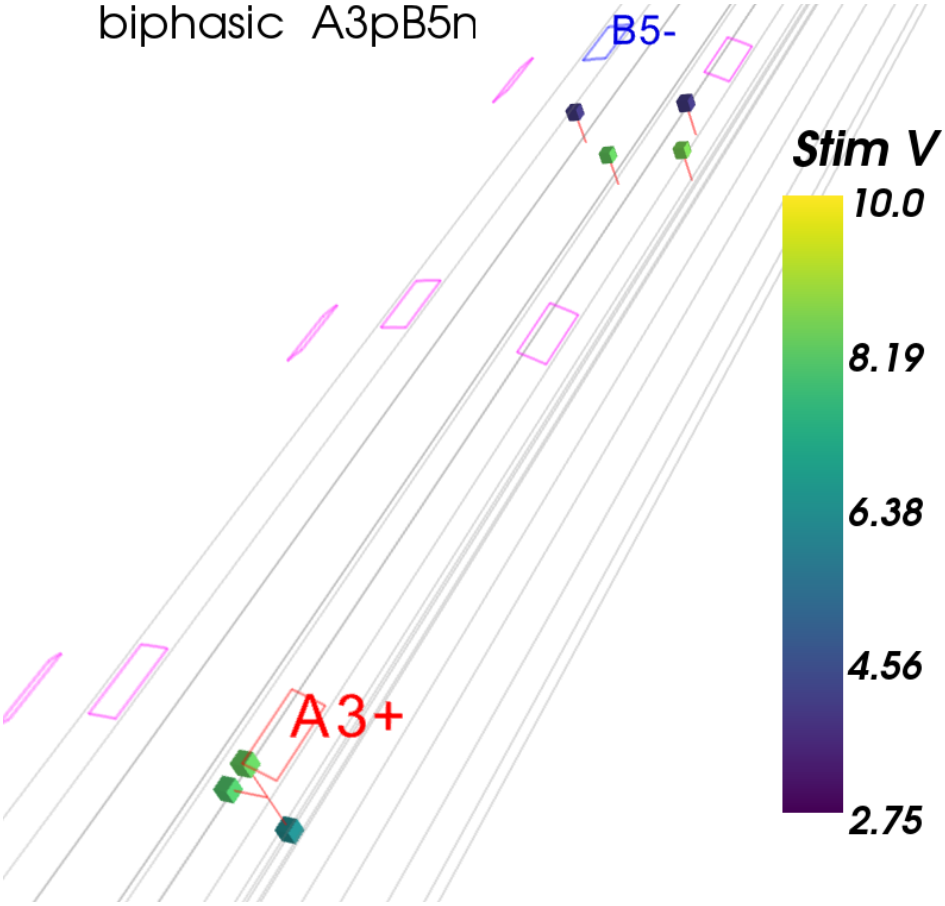


Figure 4.74: Biphasic stimulation using combination A3pB5n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode B5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 8.25 V), (GM1_R_r5, Yp, 4.0 V), (GM1_L_r5, Yp, 4.0 V), (GM3_R_r5, Yp, 8.25 V), (GM3_L_r5, Yp, 8.5 V), (GM1_L_r3, Xp, 8.0 V), and (GM1_L_r3, Yn, 6.25 V).

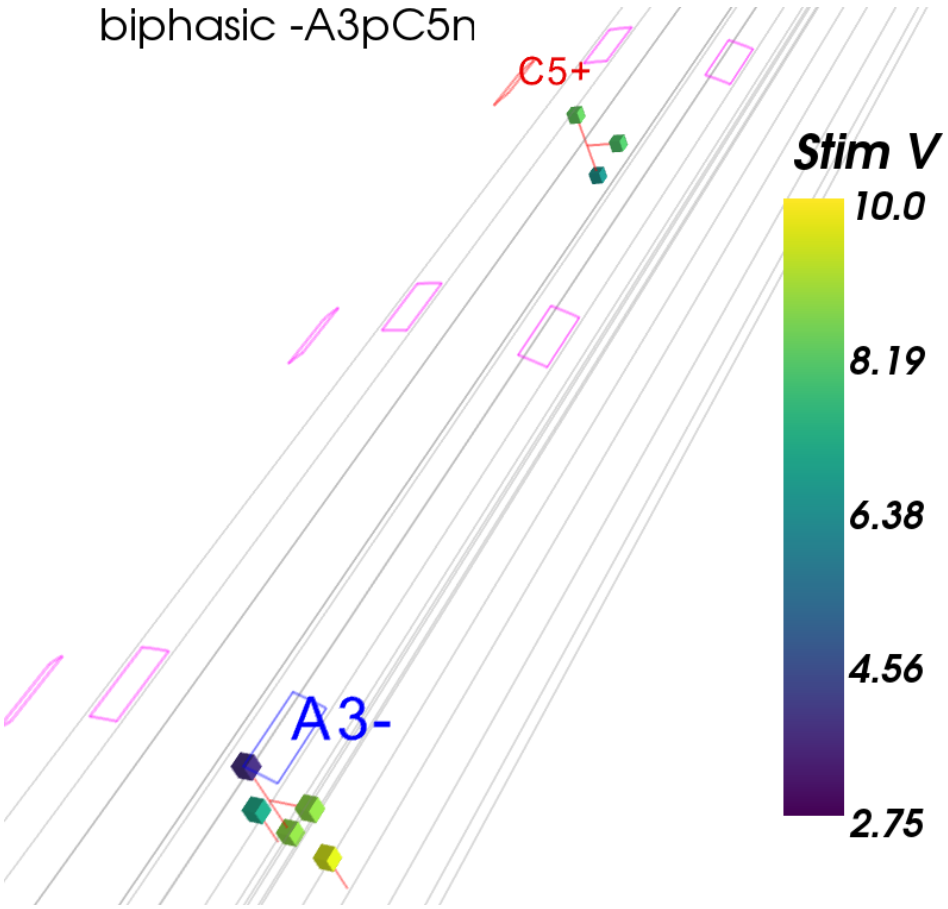


Figure 4.75: Biphasic stimulation using combination -A3pC5n. Electrode C5 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 3.75 V), (GM1_R_r5, Yp, 8.25 V), (GM3_L_r3, Yp, 7.0 V), (GM2_L_r3, Yp, 9.5 V), (GM1_L_r3, Xn, 8.75 V), (GM1_R_r5, Xn, 8.0 V), (GM1_L_r3, Yn, 8.75 V), and (GM1_R_r5, Yn, 6.5 V).

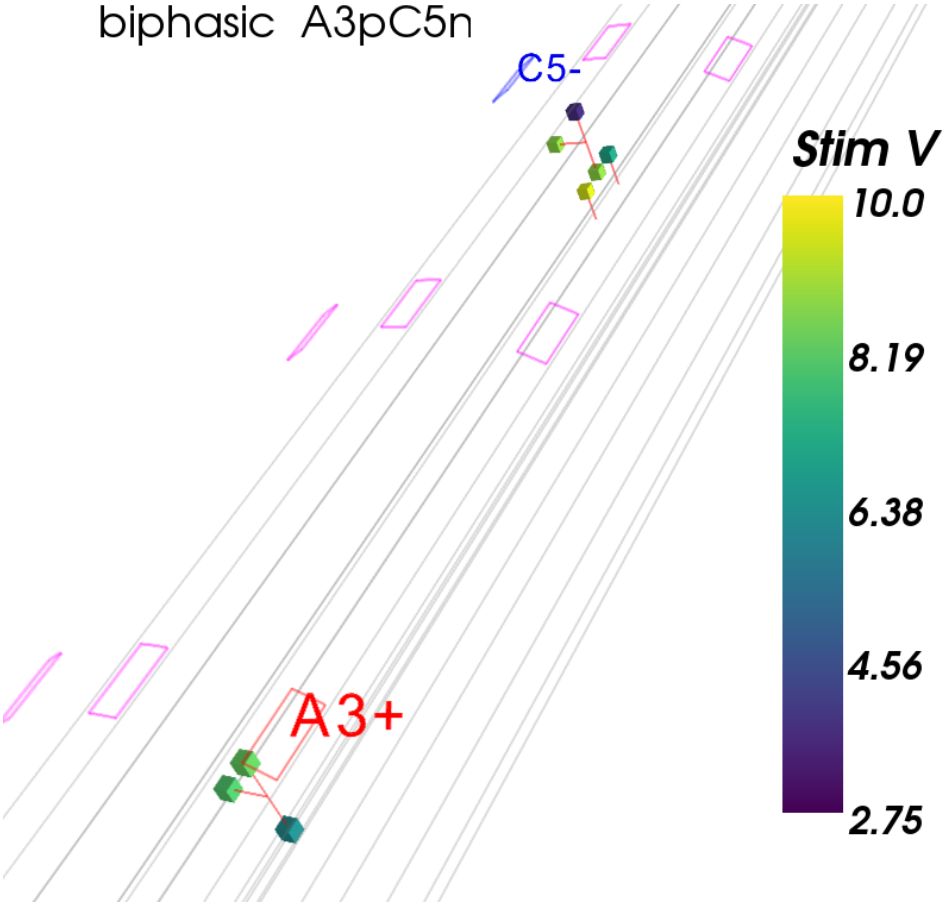


Figure 4.76: Biphasic stimulation using combination A3pC5n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode C5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 8.25 V), (GM1_R_r5, Yp, 3.75 V), (GM3_R_r5, Yp, 7.0 V), (GM2_R_r5, Yp, 9.5 V), (GM1_L_r3, Xp, 8.0 V), (GM1_R_r5, Xp, 8.75 V), (GM1_L_r3, Yn, 6.25 V), and (GM1_R_r5, Yn, 8.75 V).

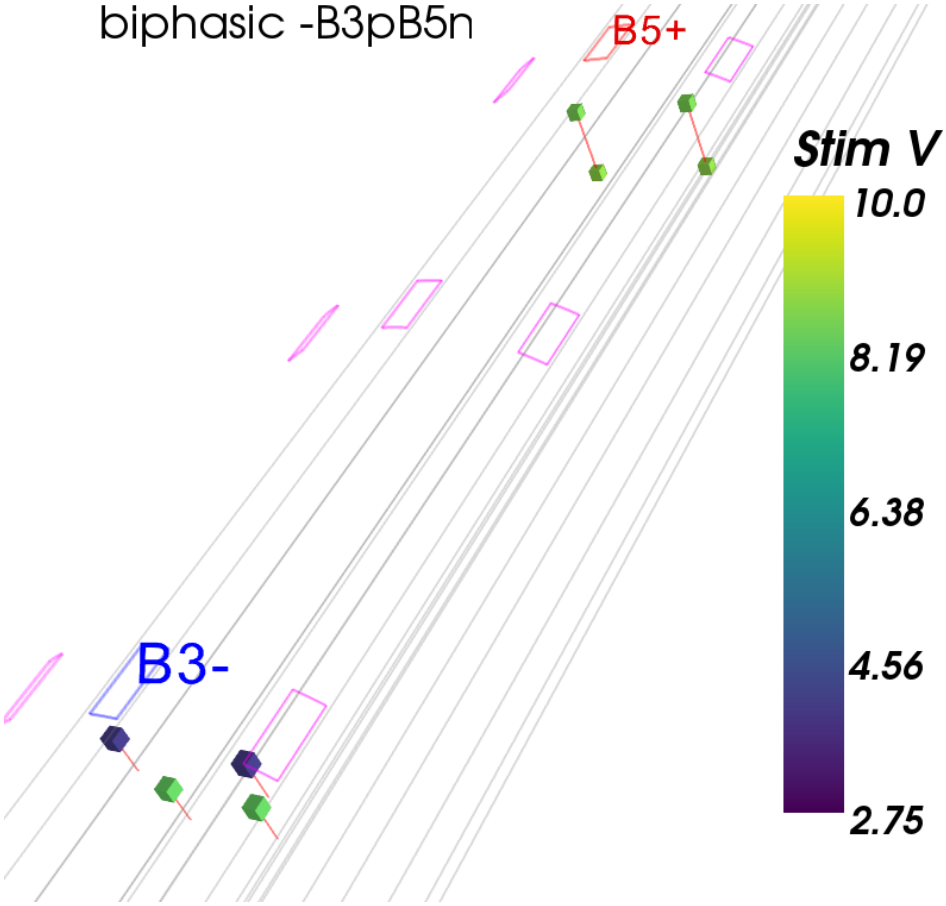


Figure 4.77: Biphasic stimulation using combination -B3pB5n. Electrode B5 has a positive phase first followed by a negative phase and is labeled red. Electrode B3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.0 V), (GM1_R_r3, Yp, 4.0 V), (GM1_L_r5, Yp, 8.5 V), (GM1_R_r5, Yp, 8.5 V), (GM3_L_r3, Yp, 8.25 V), (GM3_R_r3, Yp, 8.25 V), (GM1_L_r5, Yn, 8.75 V), and (GM1_R_r5, Yn, 8.75 V).

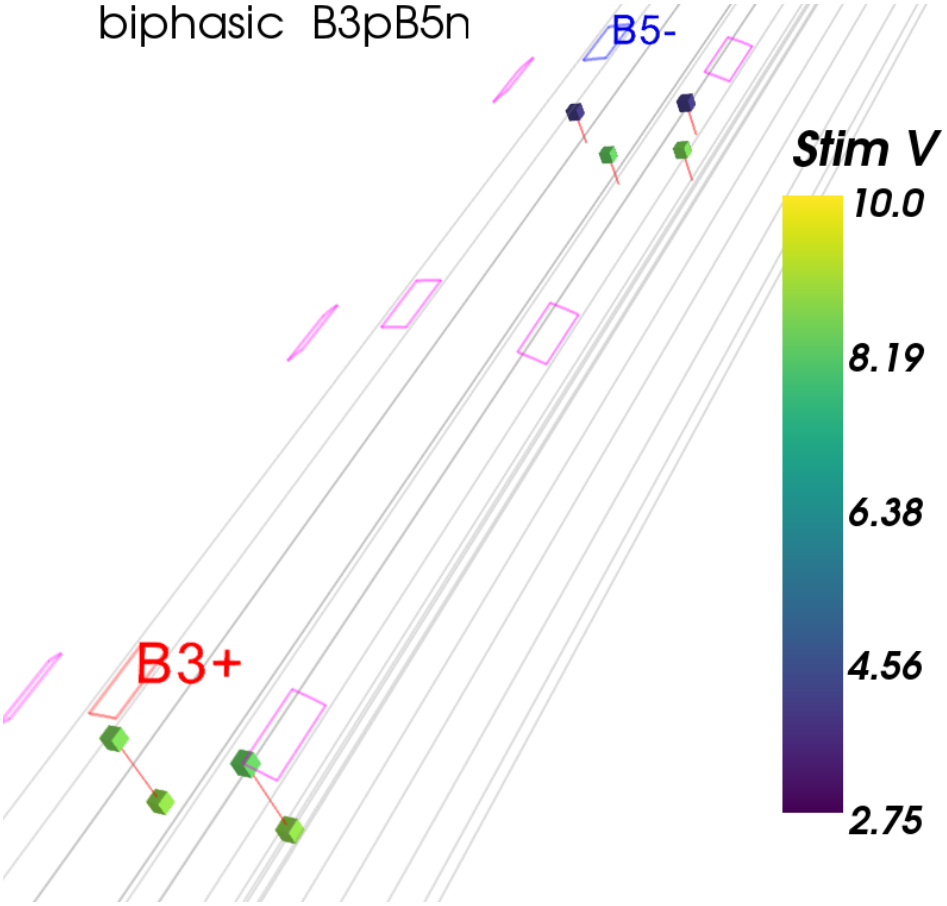


Figure 4.78: Biphasic stimulation using combination B3pB5n. Electrode B3 has a positive phase first followed by a negative phase and is labeled red. Electrode B5 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds $-10\,\text{mV}$ with no more than $10\,\text{V}$ of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10\,\text{mV}$. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 8.25 V), (GM1_R_r3, Yp, 8.5 V), (GM1_L_r5, Yp, 4.0 V), (GM1_R_r5, Yp, 4.0 V), (GM3_L_r5, Yp, 8.5 V), (GM3_R_r5, Yp, 8.25 V), (GM1_L_r3, Yn, 8.75 V), and (GM1_R_r3, Yn, 8.75 V).

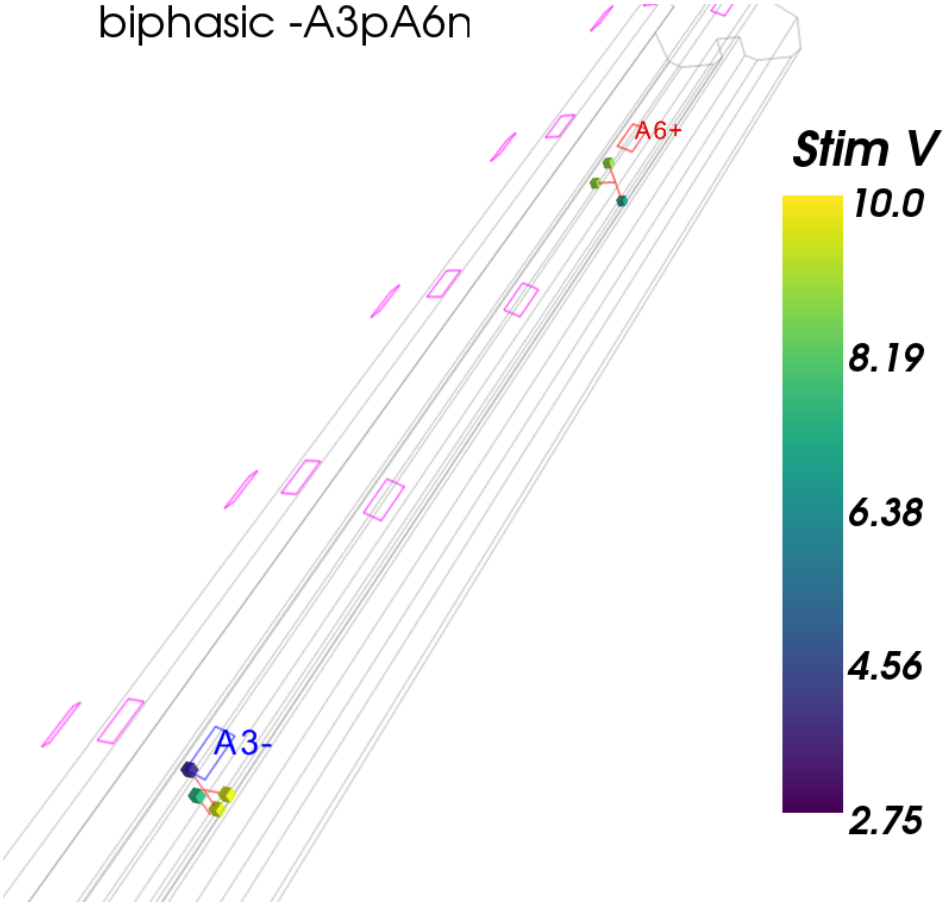


Figure 4.79: Biphasic stimulation using combination -A3pA6n. Electrode A6 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.0 V), (GM1_L_r6, Yp, 8.75 V), (GM3_L_r3, Yp, 7.5 V), (GM1_L_r6, Xp, 8.75 V), (GM1_L_r3, Xn, 9.5 V), (GM1_L_r3, Yn, 9.5 V), and (GM1_L_r6, Yn, 6.75 V).

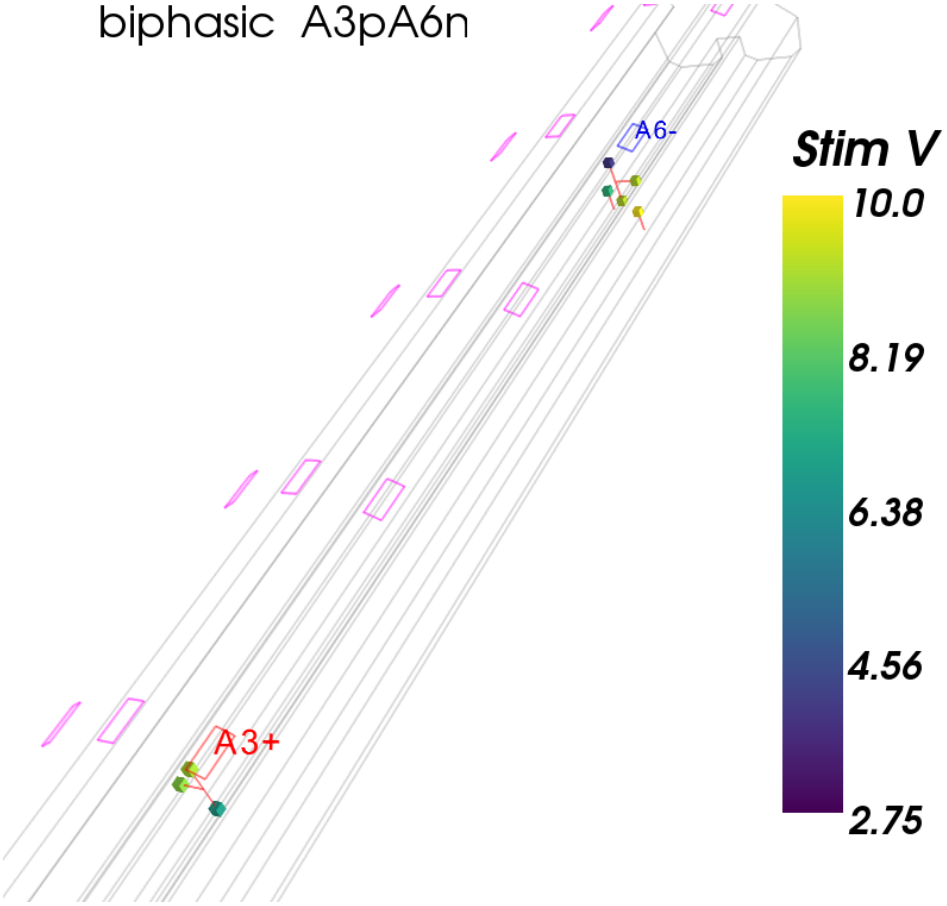


Figure 4.80: Biphasic stimulation using combination A3pA6n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode A6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 9.0 V), (GM1_L_r6, Yp, 4.0 V), (GM3_L_r6, Yp, 7.5 V), (GM2_L_r6, Yp, 10.0 V), (GM1_L_r3, Xp, 8.75 V), (GM1_L_r6, Xn, 9.25 V), (GM1_L_r3, Yn, 6.75 V), and (GM1_L_r6, Yn, 9.25 V).

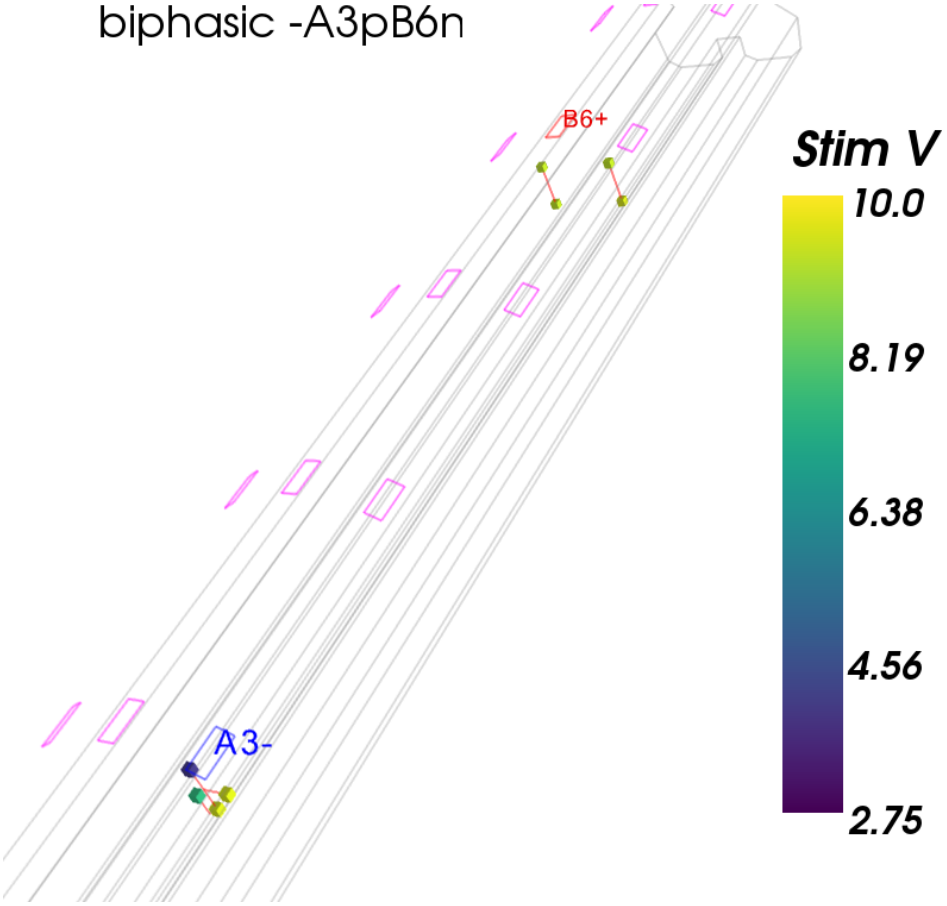


Figure 4.81: Biphasic stimulation using combination -A3pB6n. Electrode B6 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.0 V), (GM1_R_r6, Yp, 9.25 V), (GM1_L_r6, Yp, 9.25 V), (GM3_L_r3, Yp, 7.5 V), (GM1_L_r3, Xn, 9.5 V), (GM1_L_r3, Yn, 9.5 V), (GM1_R_r6, Yn, 9.25 V), and (GM1_L_r6, Yn, 9.5 V).

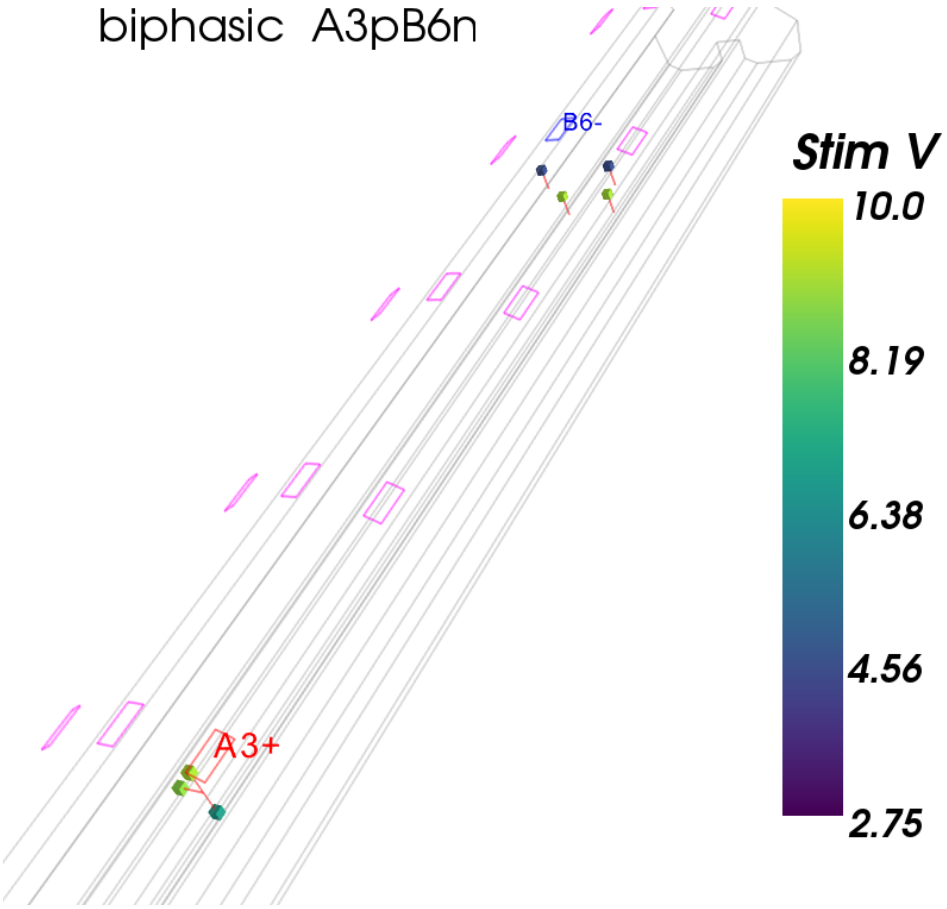


Figure 4.82: Biphasic stimulation using combination A3pB6n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode B6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds -10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 9.0 V), (GM1_R_r6, Yp, 4.5 V), (GM1_L_r6, Yp, 4.5 V), (GM3_L_r6, Yp, 9.0 V), (GM3_R_r6, Yp, 9.0 V), (GM1_L_r3, Xp, 8.75 V), and (GM1_L_r3, Yn, 6.75 V).

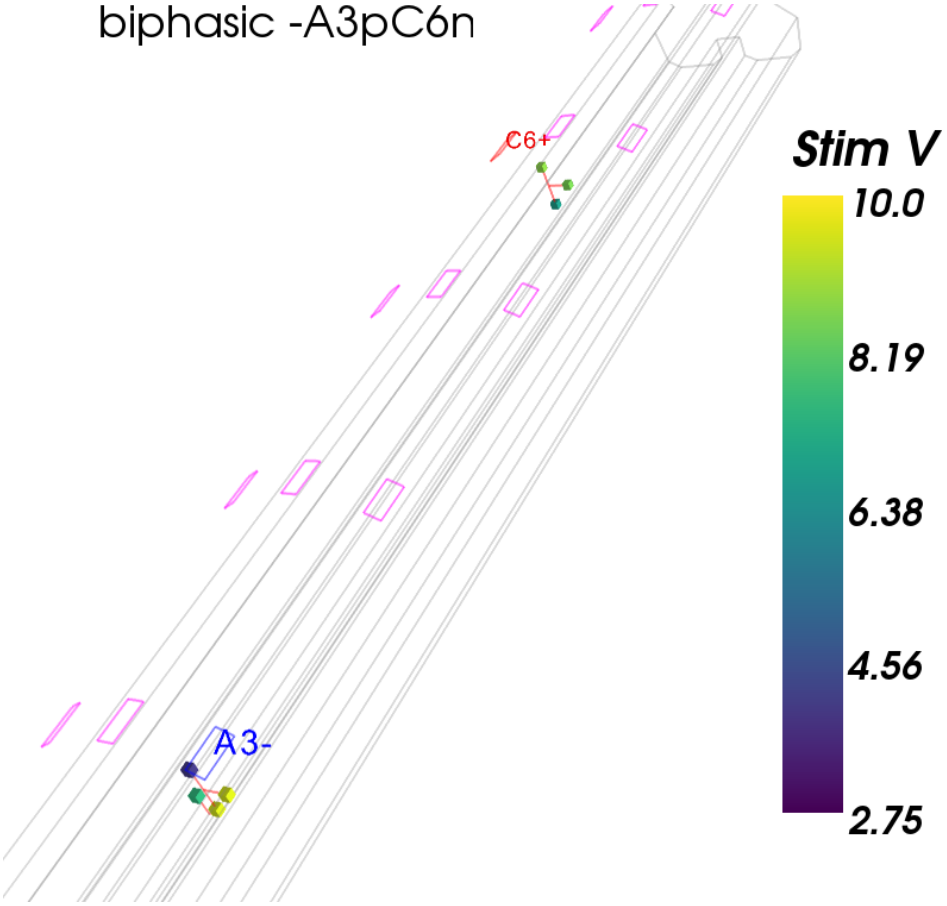


Figure 4.83: Biphasic stimulation using combination -A3pC6n. Electrode C6 has a positive phase first followed by a negative phase and is labeled red. Electrode A3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.0 V), (GM1_R_r6, Yp, 8.75 V), (GM3_L_r3, Yp, 7.5 V), (GM1_L_r3, Xn, 9.5 V), (GM1_R_r6, Xn, 8.5 V), (GM1_L_r3, Yn, 9.5 V), and (GM1_R_r6, Yn, 6.75 V).

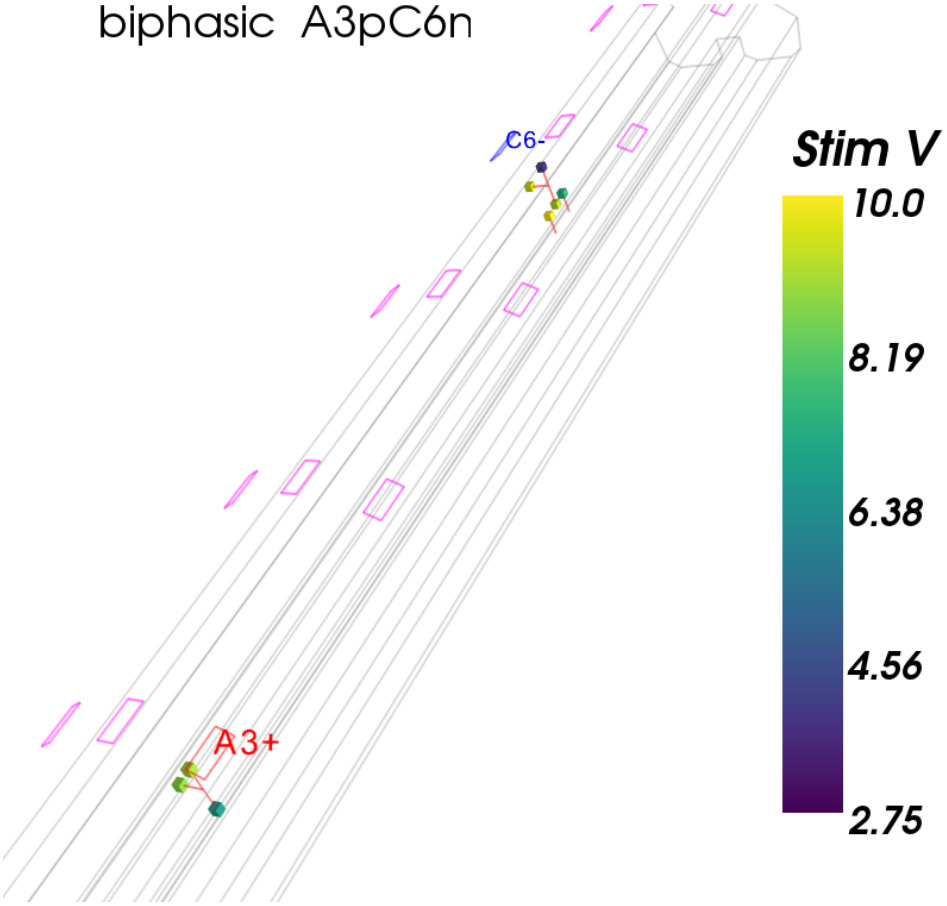


Figure 4.84: Biphasic stimulation using combination A3pC6n. Electrode A3 has a positive phase first followed by a negative phase and is labeled red. Electrode C6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 9.0 V), (GM1_R_r6, Yp, 4.0 V), (GM3_R_r6, Yp, 7.5 V), (GM2_R_r6, Yp, 10.0 V), (GM1_L_r3, Xp, 8.75 V), (GM1_R_r6, Xp, 9.5 V), (GM1_L_r3, Yn, 6.75 V), and (GM1_R_r6, Yn, 9.25 V).

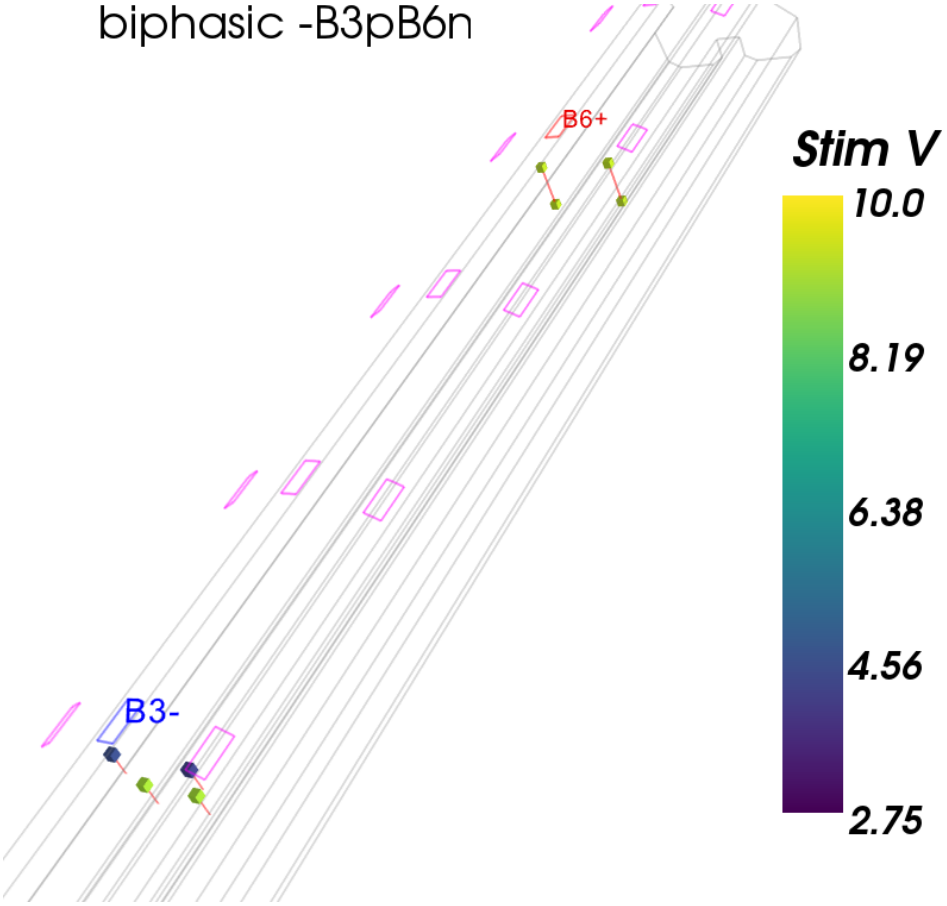


Figure 4.85: Biphasic stimulation using combination -B3pB6n. Electrode B6 has a positive phase first followed by a negative phase and is labeled red. Electrode B3 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 4.25 V), (GM1_R_r3, Yp, 4.5 V), (GM1_L_r6, Yp, 9.25 V), (GM1_R_r6, Yp, 9.25 V), (GM3_L_r3, Yp, 9.0 V), (GM3_R_r3, Yp, 9.0 V), (GM1_L_r6, Yn, 9.25 V), and (GM1_R_r6, Yn, 9.25 V).

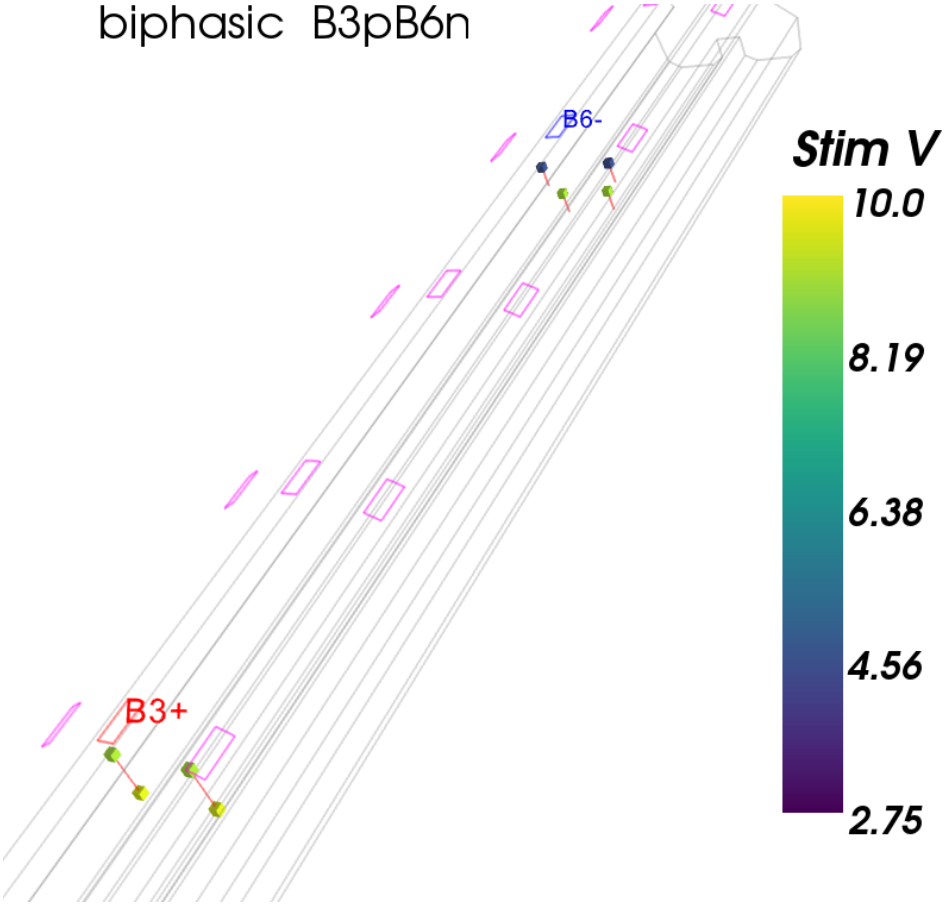


Figure 4.86: Biphasic stimulation using combination B3pB6n. Electrode B3 has a positive phase first followed by a negative phase and is labeled red. Electrode B6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r3, Yp, 9.0 V), (GM1_R_r3, Yp, 9.0 V), (GM1_L_r6, Yp, 4.5 V), (GM1_R_r6, Yp, 4.5 V), (GM3_L_r6, Yp, 9.0 V), (GM3_R_r6, Yp, 9.0 V), (GM1_L_r3, Yn, 9.5 V), and (GM1_R_r3, Yn, 9.5 V).

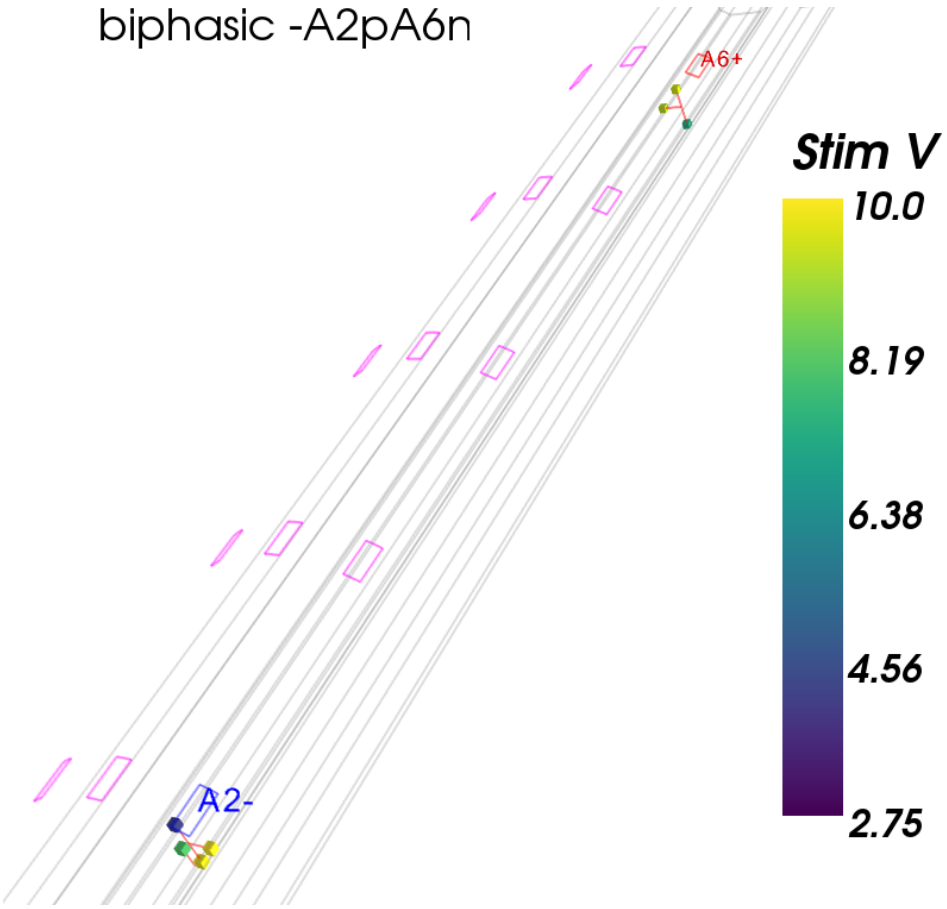


Figure 4.87: Biphasic stimulation using combination -A2pA6n. Electrode A6 has a positive phase first followed by a negative phase and is labeled red. Electrode A2 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 4.25 V), (GM1_L_r6, Yp, 9.5 V), (GM3_L_r2, Yp, 8.0 V), (GM1_L_r6, Xp, 9.25 V), (GM1_L_r2, Xn, 10.0 V), (GM1_L_r2, Yn, 9.75 V), and (GM1_L_r6, Yn, 7.25 V).

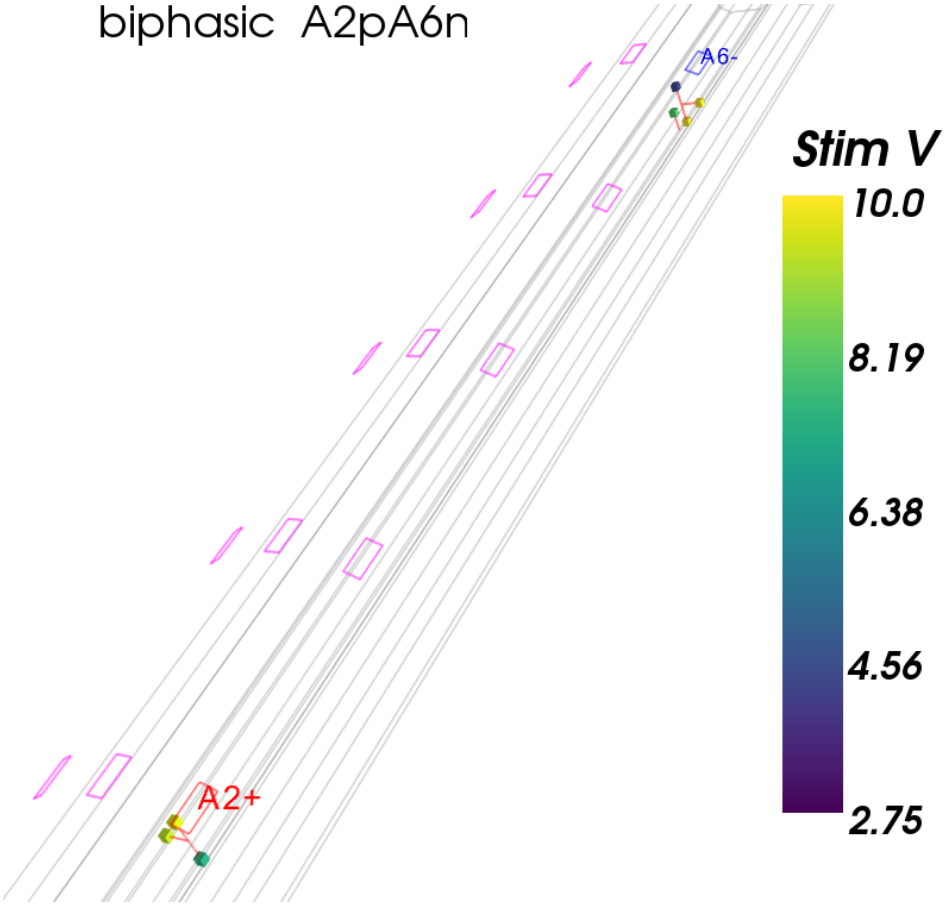


Figure 4.88: Biphasic stimulation using combination A2pA6n. Electrode A2 has a positive phase first followed by a negative phase and is labeled red. Electrode A6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 9.5 V), (GM1_L_r6, Yp, 4.25 V), (GM3_L_r6, Yp, 8.0 V), (GM1_L_r2, Xp, 9.25 V), (GM1_L_r6, Xn, 10.0 V), (GM1_L_r2, Yn, 7.25 V), and (GM1_L_r6, Yn, 10.0 V).

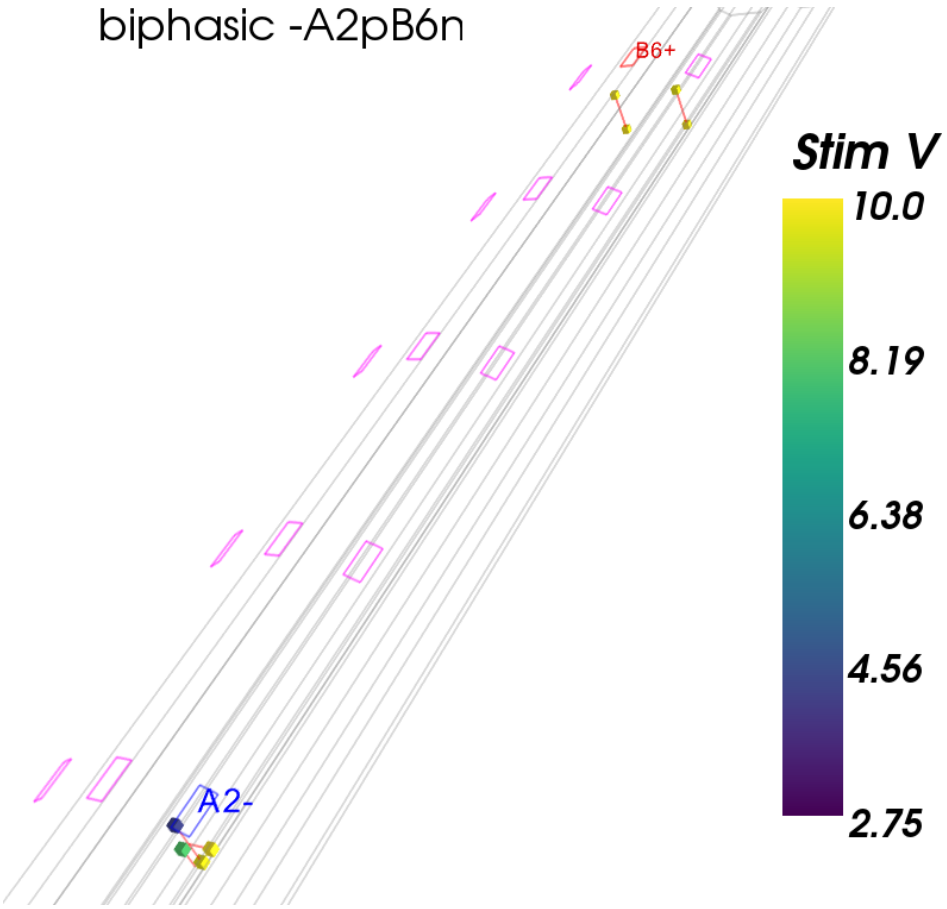


Figure 4.89: Biphasic stimulation using combination -A2pB6n. Electrode B6 has a positive phase first followed by a negative phase and is labeled red. Electrode A2 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 4.25 V), (GM1_L_r6, Yp, 9.75 V), (GM1_R_r6, Yp, 10.0 V), (GM3_L_r2, Yp, 8.0 V), (GM1_L_r2, Xn, 10.0 V), (GM1_L_r2, Yn, 9.75 V), (GM1_L_r6, Yn, 10.0 V), and (GM1_R_r6, Yn, 10.0 V).

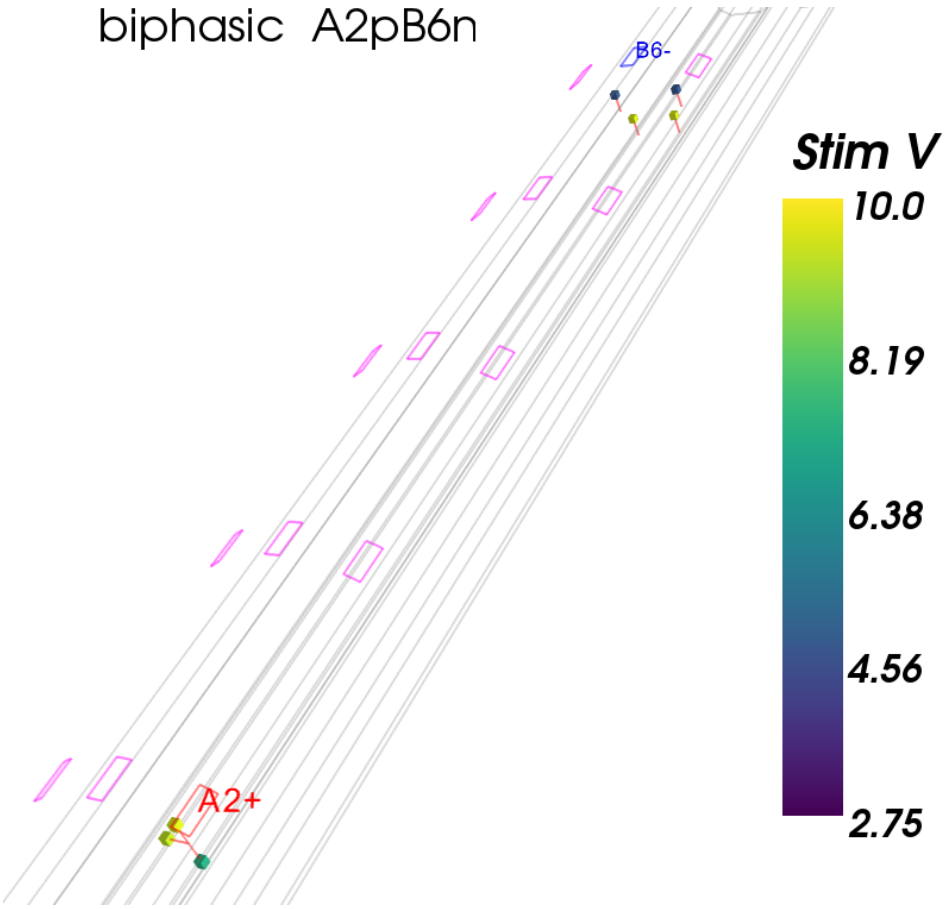


Figure 4.90: Biphasic stimulation using combination A2pB6n. Electrode A2 has a positive phase first followed by a negative phase and is labeled red. Electrode B6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 9.5 V), (GM1_L_r6, Yp, 4.75 V), (GM1_R_r6, Yp, 4.75 V), (GM3_L_r6, Yp, 9.5 V), (GM3_R_r6, Yp, 9.5 V), (GM1_L_r2, Xp, 9.25 V), and (GM1_L_r2, Yn, 7.25 V).

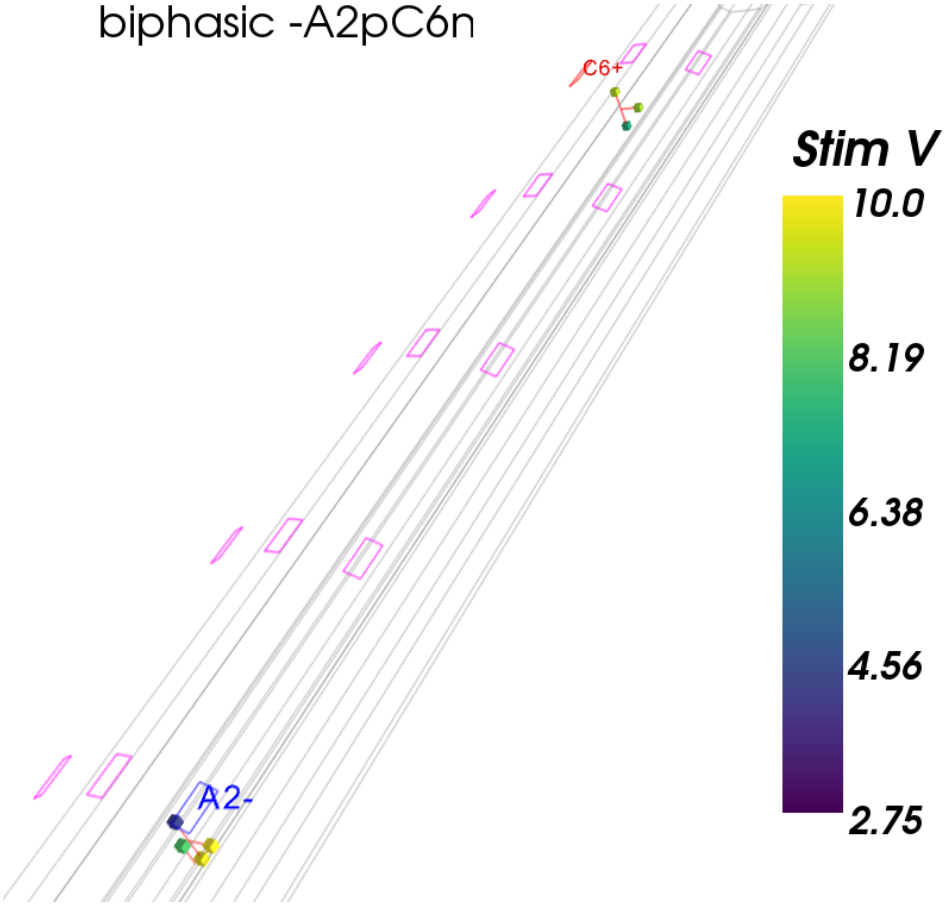


Figure 4.91: Biphasic stimulation using combination -A2pC6n. Electrode C6 has a positive phase first followed by a negative phase and is labeled red. Electrode A2 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 4.25 V), (GM1_R_r6, Yp, 9.25 V), (GM3_L_r2, Yp, 8.0 V), (GM1_L_r2, Xn, 10.0 V), (GM1_R_r6, Xn, 9.0 V), (GM1_L_r2, Yn, 9.75 V), and (GM1_R_r6, Yn, 7.25 V).

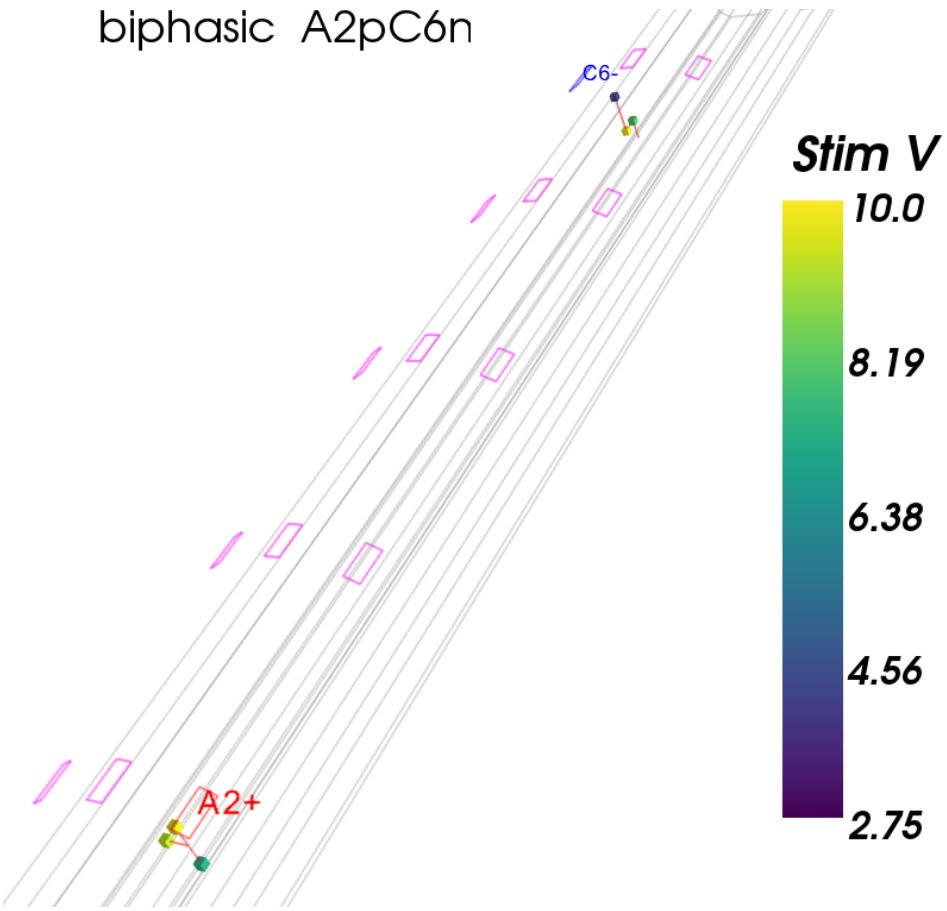


Figure 4.92: Biphasic stimulation using combination A2pC6n. Electrode A2 has a positive phase first followed by a negative phase and is labeled red. Electrode C6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 9.5 V), (GM1_R_r6, Yp, 4.25 V), (GM3_R_r6, Yp, 8.0 V), (GM1_L_r2, Xp, 9.25 V), (GM1_L_r2, Yn, 7.25 V), and (GM1_R_r6, Yn, 10.0 V).

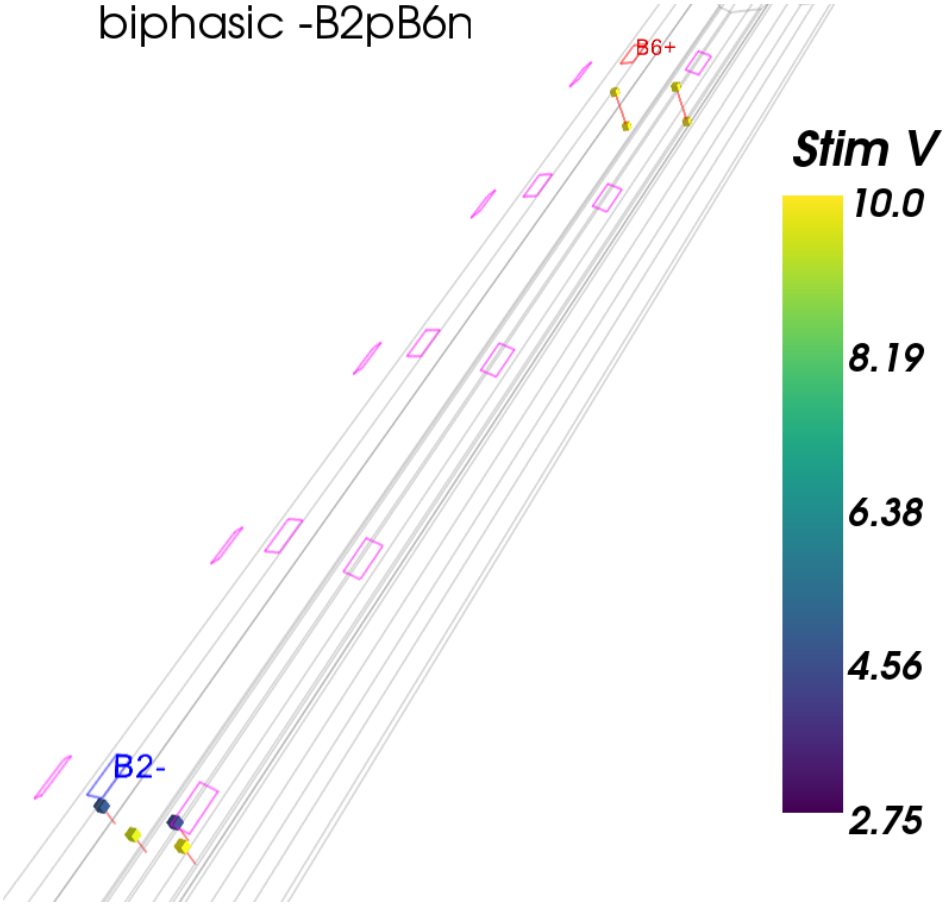


Figure 4.93: Biphasic stimulation using combination -B2pB6n. Electrode B6 has a positive phase first followed by a negative phase and is labeled red. Electrode B2 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 4.5 V), (GM1_R_r2, Yp, 4.75 V), (GM1_L_r6, Yp, 9.75 V), (GM1_R_r6, Yp, 10.0 V), (GM3_L_r2, Yp, 9.75 V), (GM3_R_r2, Yp, 9.5 V), (GM1_L_r6, Yn, 10.0 V), and (GM1_R_r6, Yn, 10.0 V).

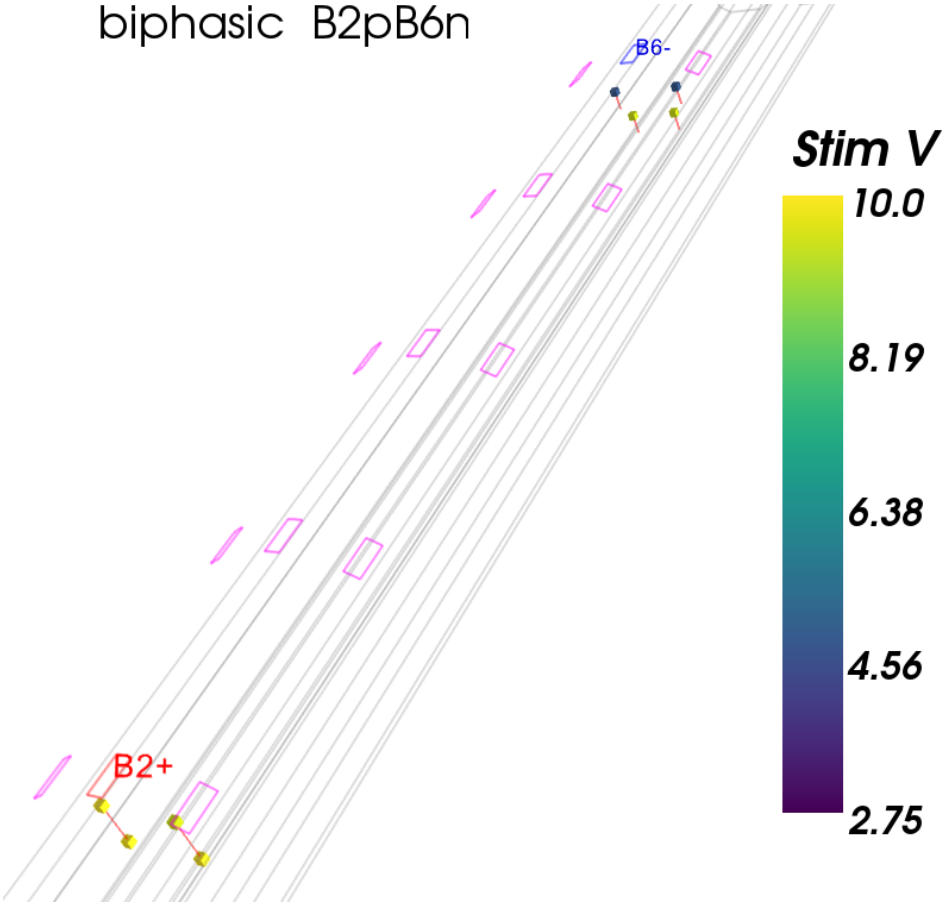


Figure 4.94: Biphasic stimulation using combination B2pB6n. Electrode B2 has a positive phase first followed by a negative phase and is labeled red. Electrode B6 has a negative phase first followed by a positive phase and is labeled blue. All other electrodes are floating and labeled purple. Soma, AH, IS, and AP are displayed as red lines for those neurons whose axon tip membrane voltage exceeds −10 mV with no more than 10 V of stimulation. Dendrites are not displayed. The color of the cube at each axon tip indicates stimulation voltages required for axon tip to reach $V_m > -10$ mV. List of location, axon direction, and threshold: (GM1_L_r2, Yp, 9.5 V), (GM1_R_r2, Yp, 10.0 V), (GM1_L_r6, Yp, 4.75 V), (GM1_R_r6, Yp, 4.75 V), (GM3_L_r6, Yp, 9.5 V), (GM3_R_r6, Yp, 9.5 V), (GM1_L_r2, Yn, 10.0 V), and (GM1_R_r2, Yn, 10.0 V).