An Introduction to Computational Neuroscience: from Brain simulation to NeuroAI - Lab 2

Aiyu Wang * Yueying Luo † Jiarui Sun ‡

October 23, 2024

Dendritic Computation

In the spatial-extended neurons, action potentials initiated in the axon can backpropagate into dendritic trees. Experiments show that backpropagating action potentials (bAPs) have significant physiological functions in neural signal processing and inter-neuron communications.

Below are our simulation results, respectively with somatic current injection only, synaptic input only, and the combination of the two.

Parameter set (if not specially stated):

stim-soma.dur = 5, stim-soma.amp = 1.9, apic-start = 200

Notifications:

Distance to soma(0.5):

- apic[0]: 0.0, 46.13561036852839
- apic[1]: 46.13561036852839, 111.23530625006572
- apic[42]: 1202.2902401840129, 1247.0596848173532
- apic[50]: 626.7875537775292, 688.7145529843525

*School of Physics, Student Number 2200011451

†Yuanpei College, Student Number 2300017819

‡School of Life Science, Student Number 2200012191

- apic[80]: 140.106850137604, 161.57193911533125

L5 pyramidal cell Morphology:

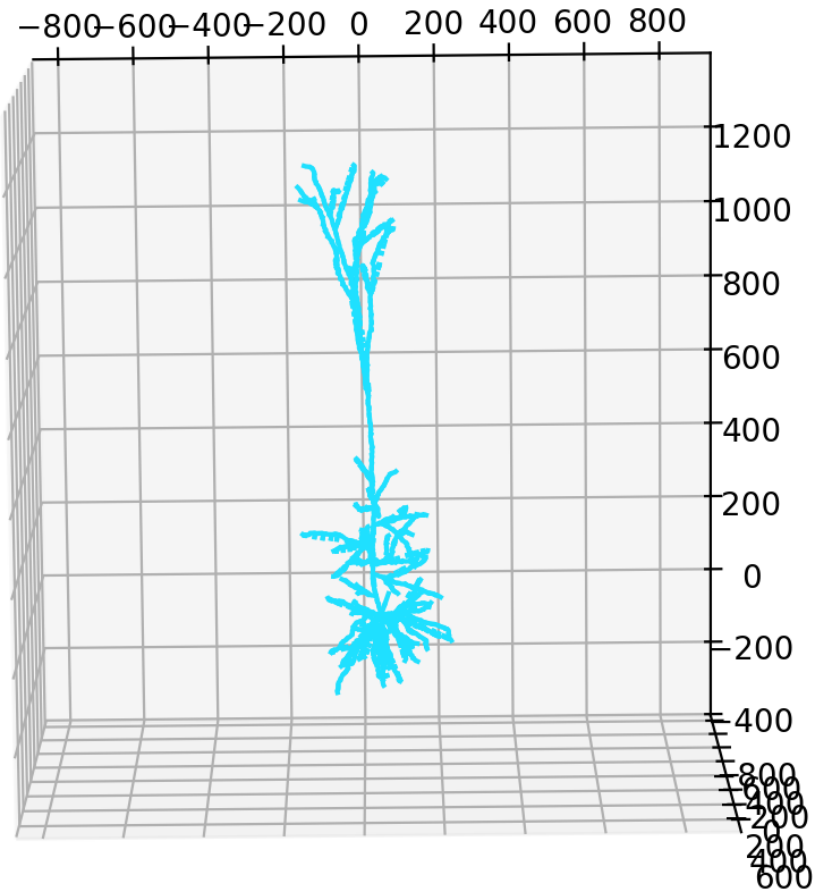


Figure 1: L5 pyramidal cell Morphology:

1 bAPs only

Show the L5 pyramidal cell (Hay, 2011) can generate bAPs on apical dendrites with somatic current injection. Remove all sodium channels in proximal dendrites and give the same current injection, what happen to the bAPs on apical dendrites? What is the principal mechanism of bAPs?

1.1 bAPs on Apical Dendrites with Somatic Current Injection

A 5ms,1.9nA suprathreshold current is injected in the model soma.

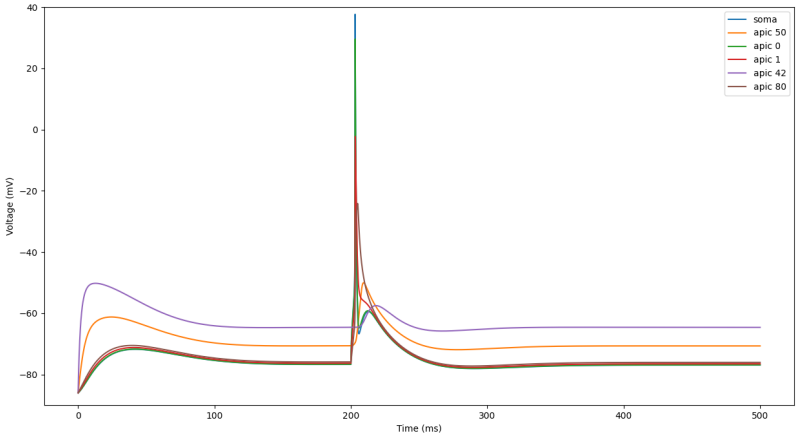


Figure 2: voltage response to 5ms,1.9nA suprathreshold current injection

We can see that when the current is injected in the soma, the membrane potential of the soma increases rapidly and then falls down to the resting value. The membrane potential of apical dendrite increases shortly after the increase of the membrane potential of the soma, and then falls down to the resting value.

1.2 bAPs' Performance when Remove All Sodium Channel

The sodium channels in proximal apical dendrites are removed, and a 5ms,1.9nA suprathreshold current is injected in the model soma.

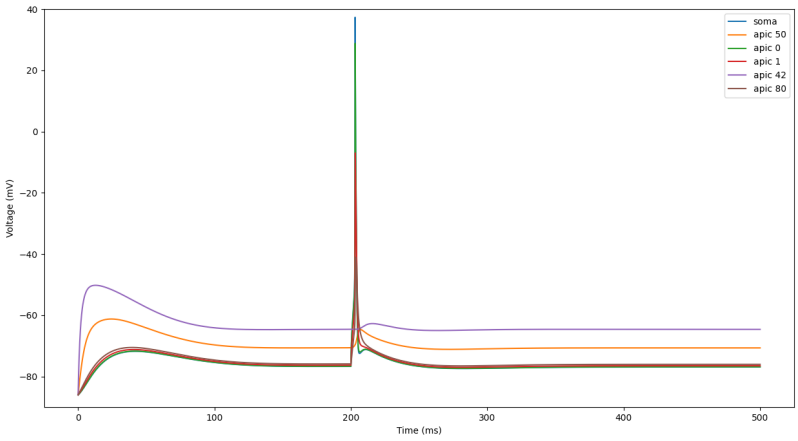


Figure 3: voltage response to 5ms,1.9nA suprathreshold current injection, when sodium channels are removed

We can observe that when the sodium channels in proximal apical dendrites are removed, the membrane potential of the soma and apical dendrites repolarizes in a shorter time, and the maximum value of the membrane potential of apical dendrites becomes smaller.

1.3 Principal Mechanism of bAPs

When the suprathreshold current is injected in the soma, the sodium channels in the soma get activated, allowing Na^+ ions to flow into the cell, initiates Na^+ action potentials(APs). APs propogates back along apical dendrites, leads to the activation of sodium channels in apical dendrites, facilitates the Na^+ influx, which facilitates the depolarization of apical dendrites' membrane potential, and increases the maximum value of the membrane potential of apical dendrites.

2 Synaptic inputs only

Place a single synapse on the L5 pyramidal cell model, how the synaptic input location (e.g. soma, basal/apical dendrite shafts, spines) influence the voltage responses at the input site and the soma? How about the case when the synaptic inputs are clustered (n synapses at one location, n=5,10,20)?

2.1 Voltage Response(Single Case)

There's a synaptic input in the 200th ns.

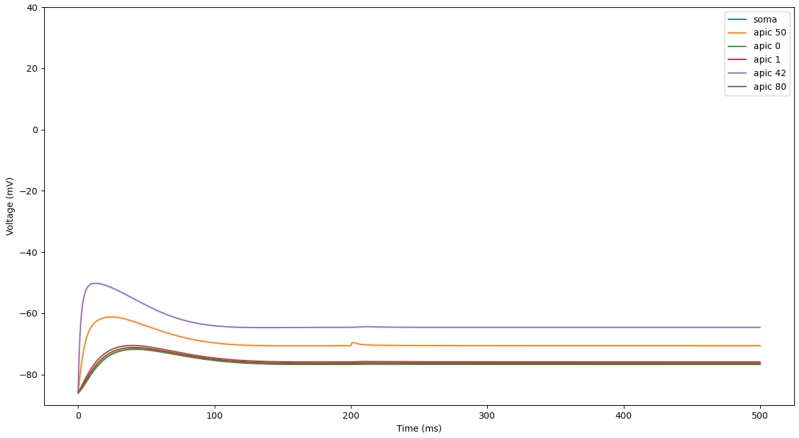
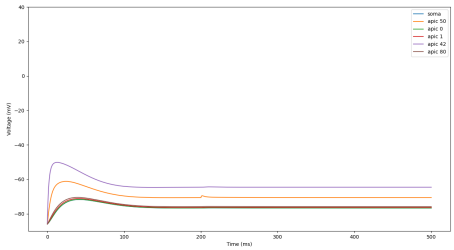


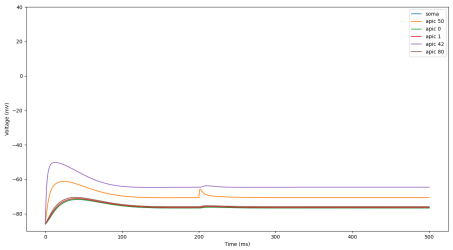
Figure 4: voltage response to synaptic input, when single synapse is placed on apic[50]

We notice that when synaptic input occurs, there's a little spike on the apical dendritic membrane potential, but we can hardly notice any change in the membrane potential of the soma.

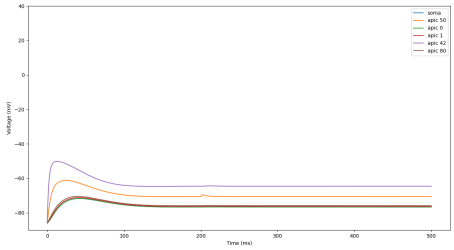
2.2 Influence of Synaptic Input Location (Single Case)



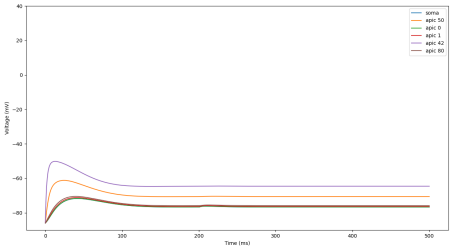
(a) dend[50]



(b) soma



(c) apic shaft[50]

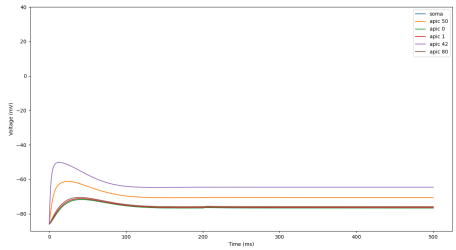


(d) dend shaft[50]

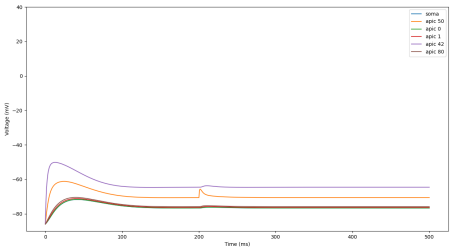
Figure 5: voltage response to different synaptic input locations

We can find that when the synapse is placed on the basal dendrite spine, the basal dendrite shaft or the soma, there won't be a spike at 200th ns, but when the synapse is placed on the apical dendrite shaft, there will be a spike similar to the case when the synapse is placed on the apical dendrite spine. When the synapse is placed on the soma, we can find a very small increase in the membrane potential of the soma, while in the other cases, the membrane potential of the soma remain unchanged.

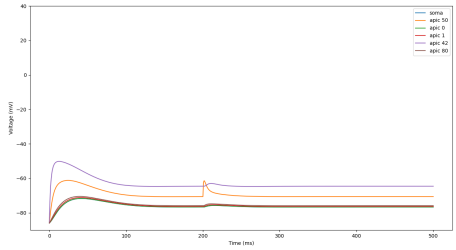
2.3 Voltage Response(Cluster Case)



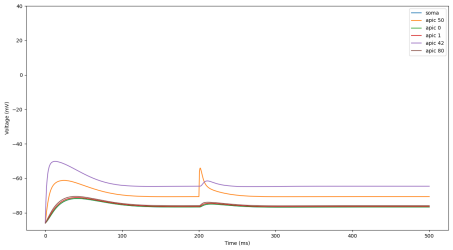
(a) single synapse



(b) cluster size=5



(c) cluster size = 10

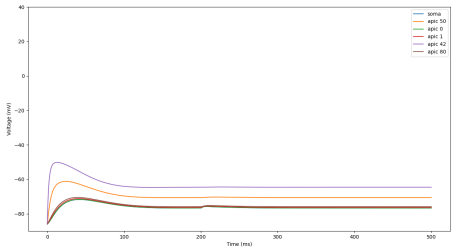


(d) cluster size =20

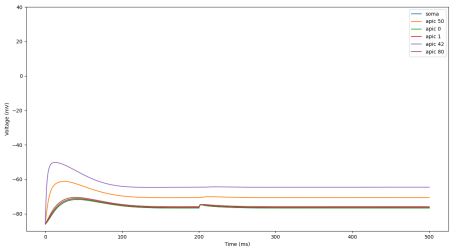
Figure 6: voltage response when synaptic inputs are clustered, clusterd synapses are placed on apic[50]

We can find that when synaptic inputs occurs, the more synapses being placed at one location, the bigger the maximum value of the apical dendritic membrane potential will be, and a greater increase will occur to the membrane potential of the soma, though the increase itself remains relatively little.

2.4 Influence of Synaptic Input Location (Cluster Case)

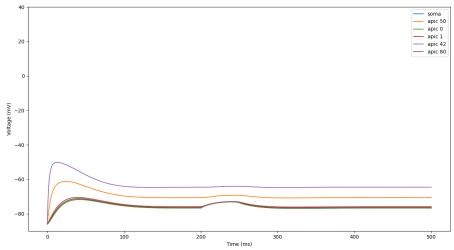


(a) dend[50]

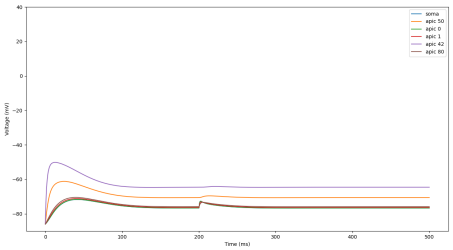


(b) soma

Figure 7: voltage response to different clustered synaptic inputs locations, cluster size=5

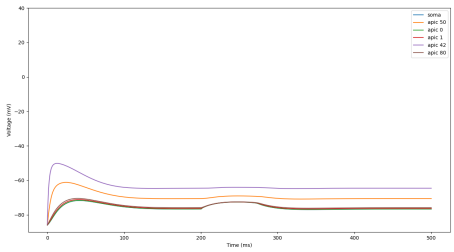


(a) dend[50]

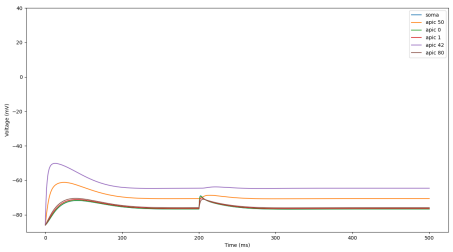


(b) soma

Figure 8: voltage response to different clustered synaptic inputs locations, cluster size=10



(a) dend[50]



(b) soma

Figure 9: voltage response to different clustered synaptic inputs locations, cluster size=20

As cluster size increases, the voltage response to different synaptic input location gets more clear. We can see a long-span, complanate curve in dend[50] case, while a steep rise in soma case.

3 Difference as bAPs and clustered synaptic inputs

Apply both the somatic current injection and clustered synaptic inputs to the L5 pyramidal cell, how does the somatic/input site' s voltage response differ from previous results when only bAPs / synaptic inputs exist? Interpret your result from the aspect of the (in)activation of ion channels.

3.1 Voltage Response(Applying both the somatic current injection and clustered synaptic inputs)

A 5ms, 1.9nA suprathreshold current is injected in the model soma and clustered synapses are added with the size of 20. We changed synaptic input location(apic[50], dend[50], soma[0]) and checked the voltage response.

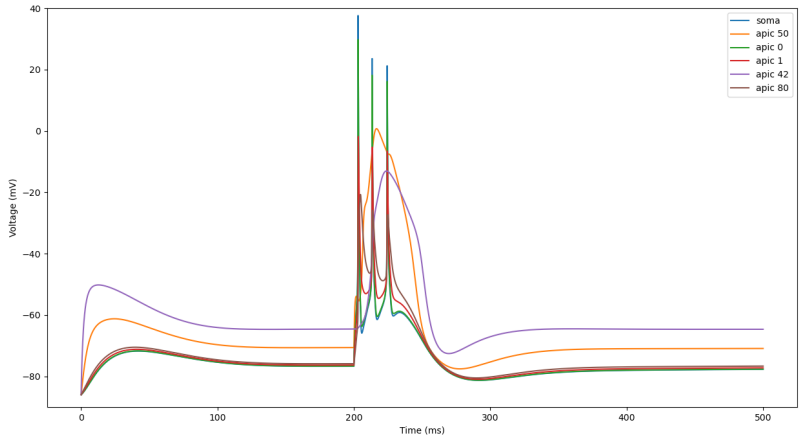


Figure 10: voltage response to somatic current injection and clustered synaptic inputs, apic[50] as input location

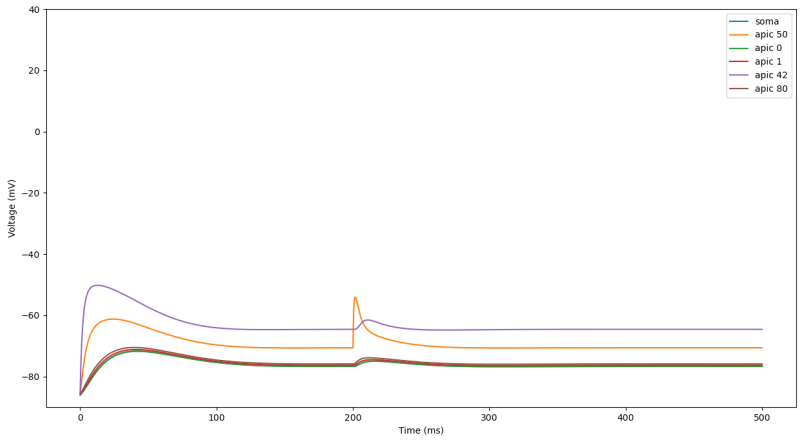


Figure 11: voltage response to only clustered synaptic inputs, apic[50] as input location

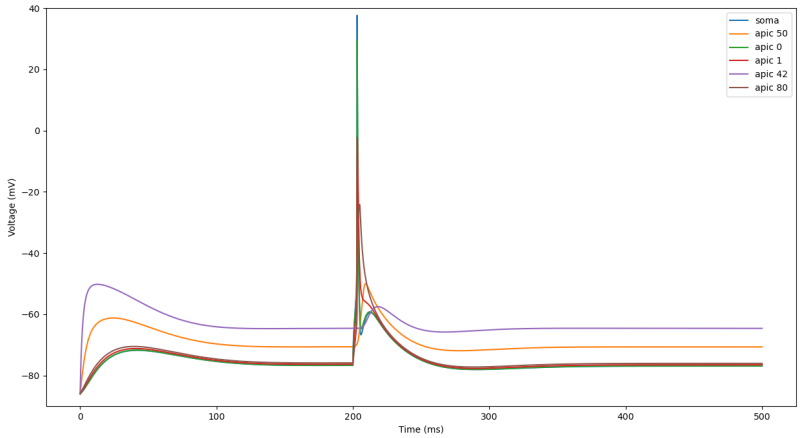


Figure 12: voltage response to only somatic current injection

As is shown in the figures, the voltage response to somatic current injection and clustered synaptic inputs show three continous spikes in a row in soma, and gradually the spikes become less high as the site becomes further to soma, ultimately shows a relatively flat curve in apic 50 and 80.

On the contrary, the voltage response to only somatic current injection or clustered synaptic input does not show continuous spikes or platform (one much lower spike in the case of clustered synaptic input, and a steep spike(or two) in the case of only somatic current injection)

For the forming reason of plateau potential on the dendrite, see Further Analysis.

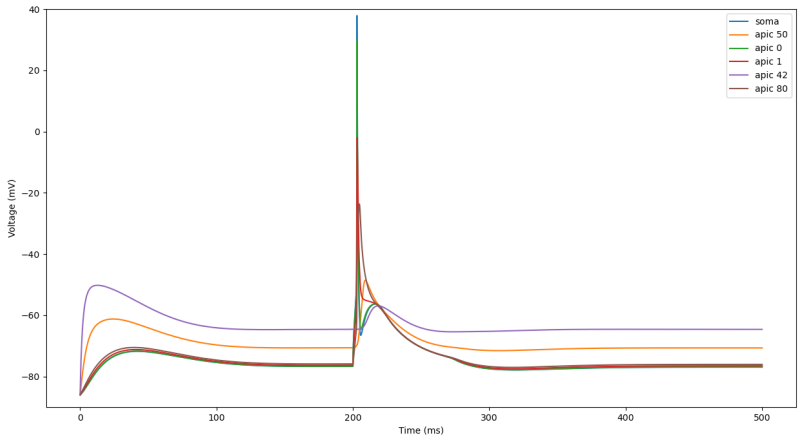


Figure 13: voltage response to somatic current injection and clustered synaptic inputs, dend[50] as input location

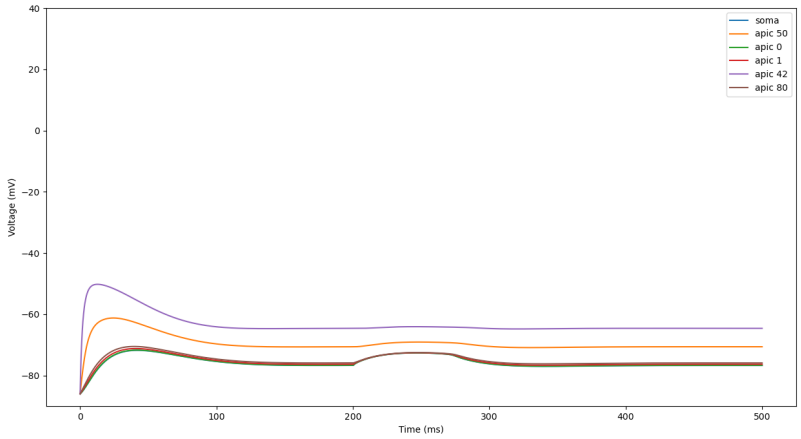


Figure 14: voltage response to only clustered synaptic inputs, dend[50] as input location

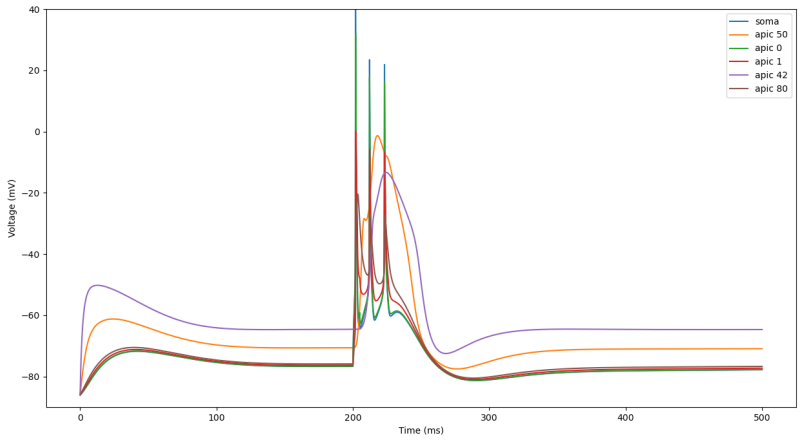


Figure 15: voltage response to somatic current injection and clustered synaptic inputs, soma[0] as input location

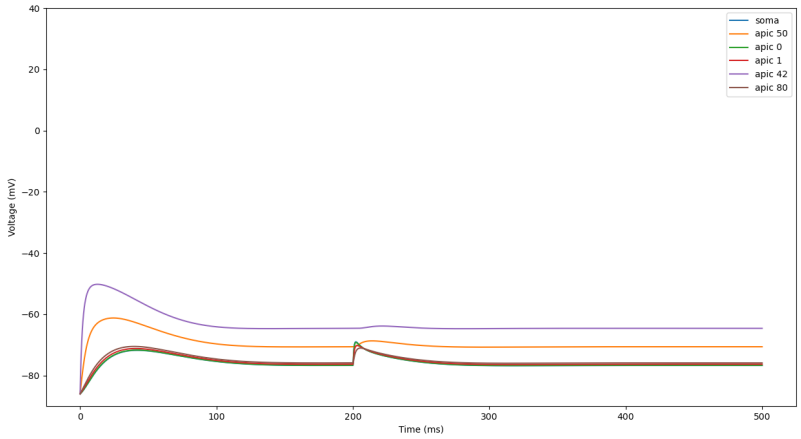


Figure 16: voltage response to only clustered synaptic inputs, soma[0] as input location

The case when we choose soma[0] as the injection location is quite the same as apic[50], only the spike become even smaller, while in dend[50] we find that voltage response to only clustered synaptic inputs is similar to that with only somatic current injection, and voltage response to only clustered synaptic inputs is super flat. Since the distance from dend[50] to soma[0] is about 90 while that from apic[50] to soma[0] is about 650, the interpretation is clustered synaptic inputs on dend do not noticeably differ from somatic current injection itself.

3.2 Result Interpretation: From the aspect of the (in)activation of ion channels

We examine conductance, current, and state variables to see what makes the difference. And here we take apic[50] as the injection location example.

3.2.1 conductance

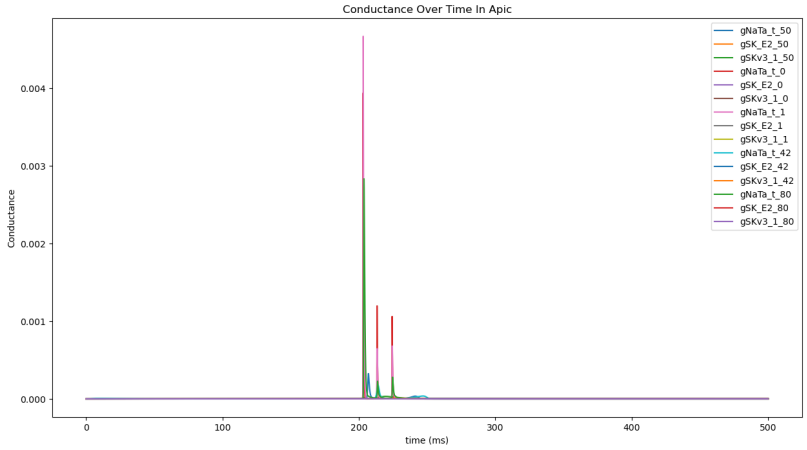


Figure 17: conductance of apic to somatic current injection and clustered synaptic inputs, apic[50] as input location

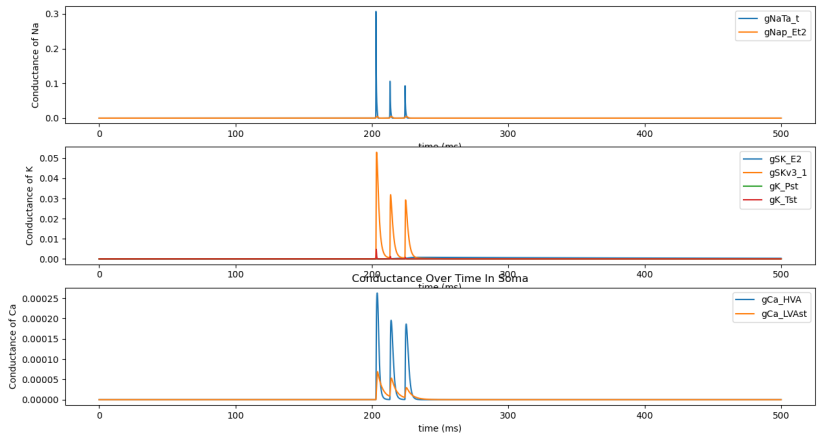


Figure 18: conductance of soma to somatic current injection and clustered synaptic inputs, apic[50] as input location

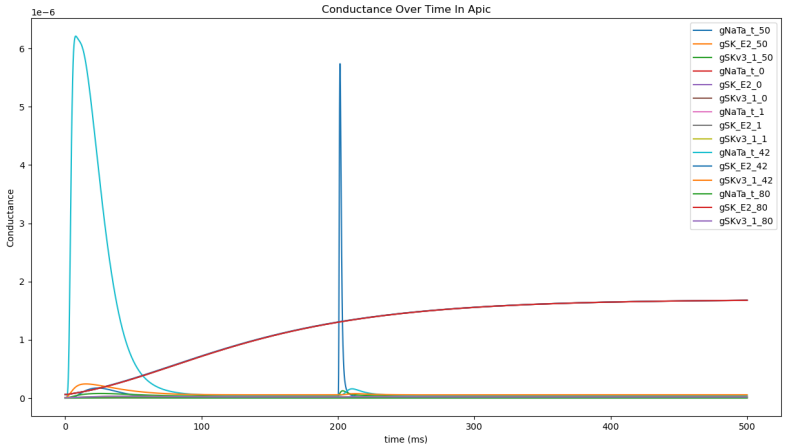


Figure 19: conductance of apic to clustered synaptic inputs, apic[50] as input location

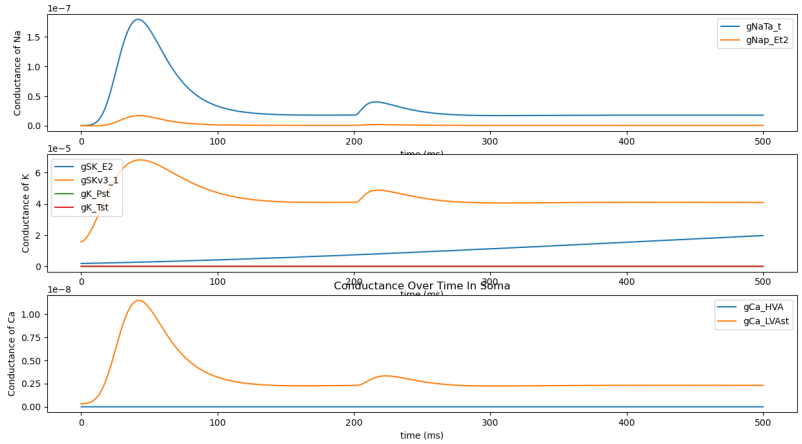


Figure 20: conductance of soma to clustered synaptic inputs, apic[50] as input location

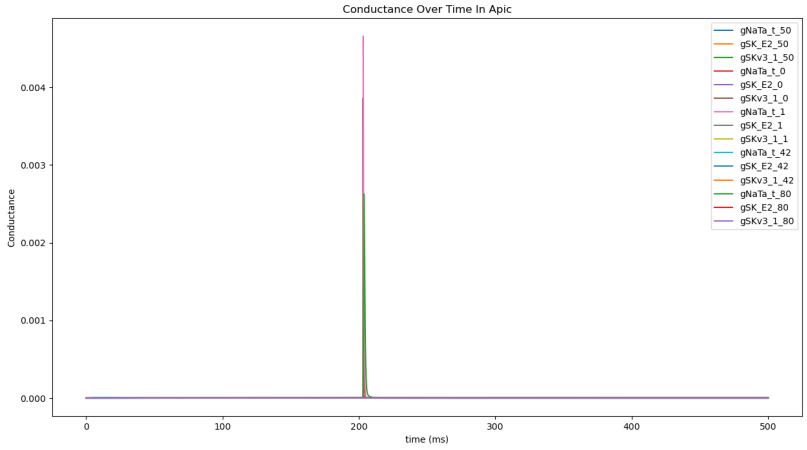


Figure 21: conductance of apic to somatic current injection

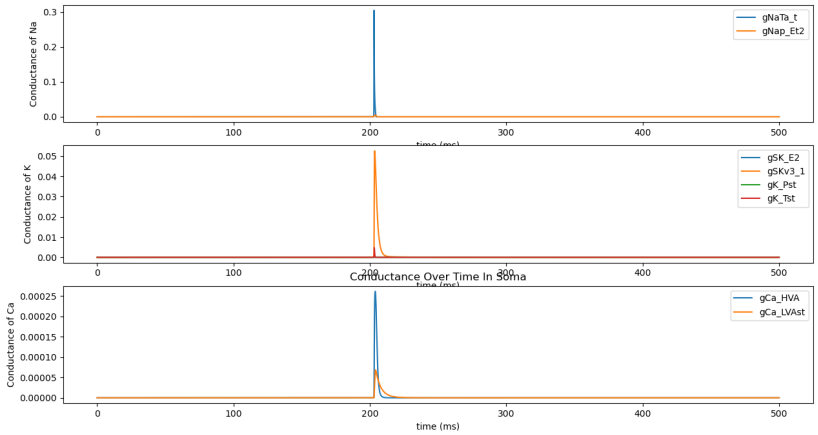


Figure 22: conductance of soma to somatic current injection

The voltage response is in accordance with ion channel conductance, spiking at the same time, frequecy and amplitude. (pay attention to the unit of measurement)

3.2.2 current

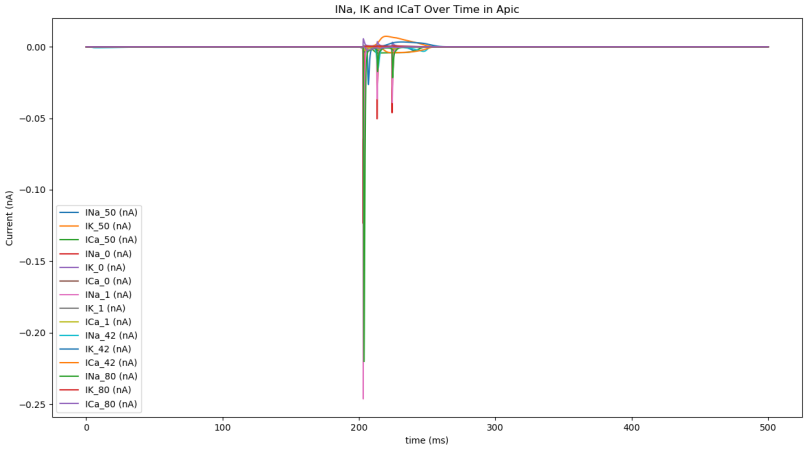


Figure 23: current of apic to somatic current injection and clustered synaptic inputs, apic[50] as input location

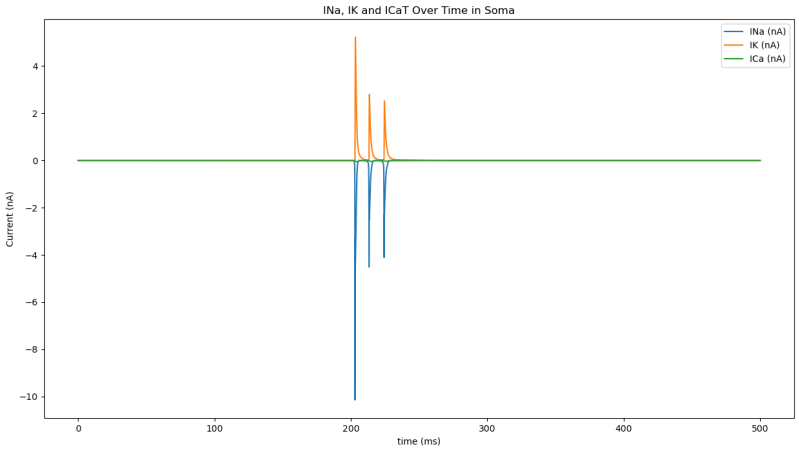


Figure 24: current of soma to somatic current injection and clustered synaptic inputs, apic[50] as input location

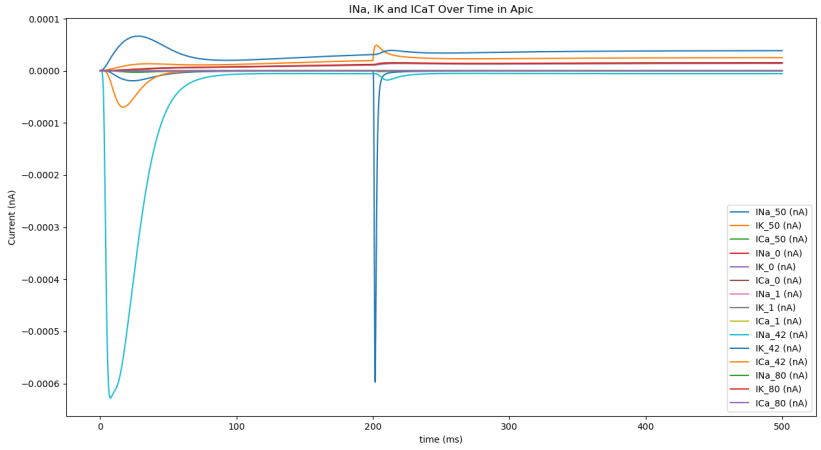


Figure 25: current of apic to clustered synaptic inputs, apic[50] as input location

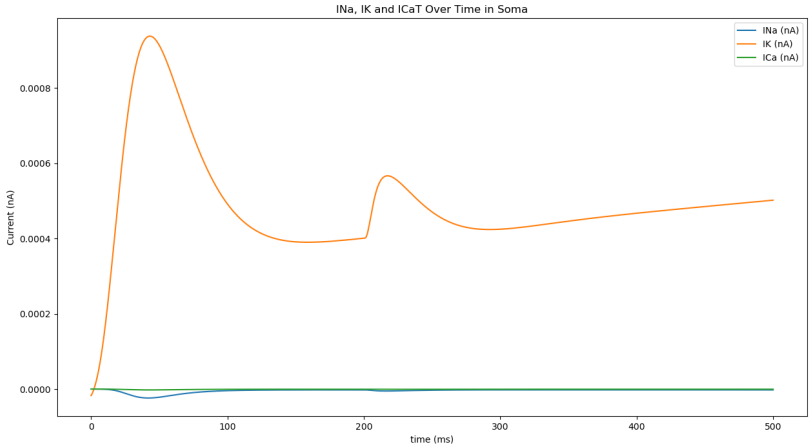


Figure 26: current of soma to clustered synaptic inputs, apic[50] as input location

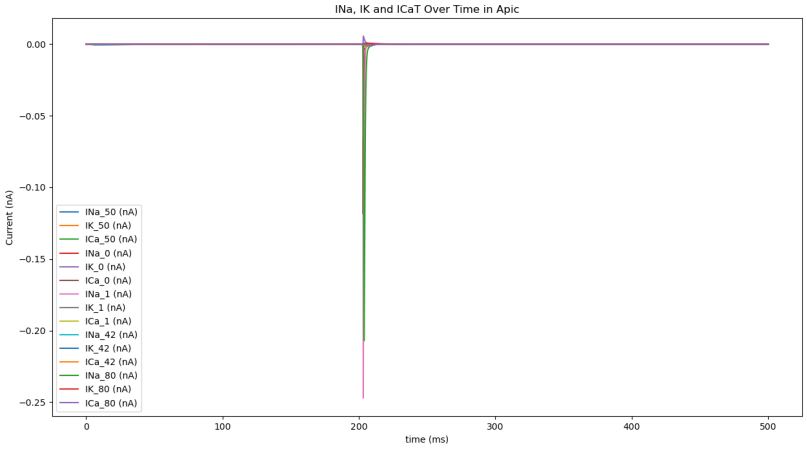


Figure 27: current of apic to somatic current injection

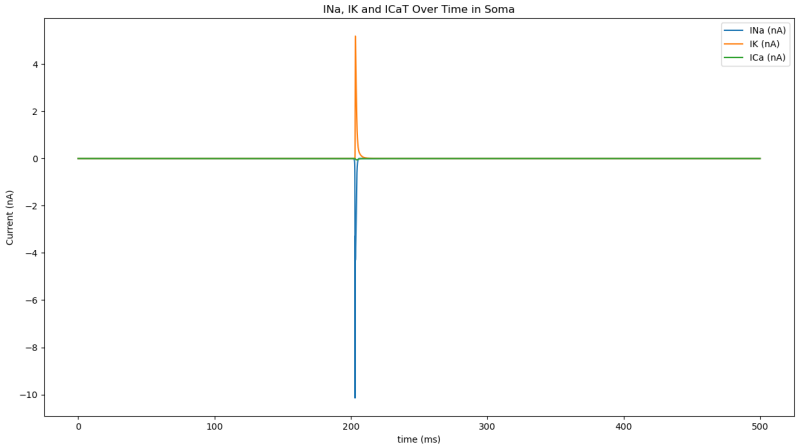


Figure 28: current of soma to somatic current injection

Action potentials are initiated in the axon, leading to the opening of voltage-gated sodium channels. This influx of Na ions causes rapid depolarization, hence the rising phase of the action potential. Backpropagation can also activate Calcium Channels, leading to an influx of Ca^2 ions

3.2.3 state variables

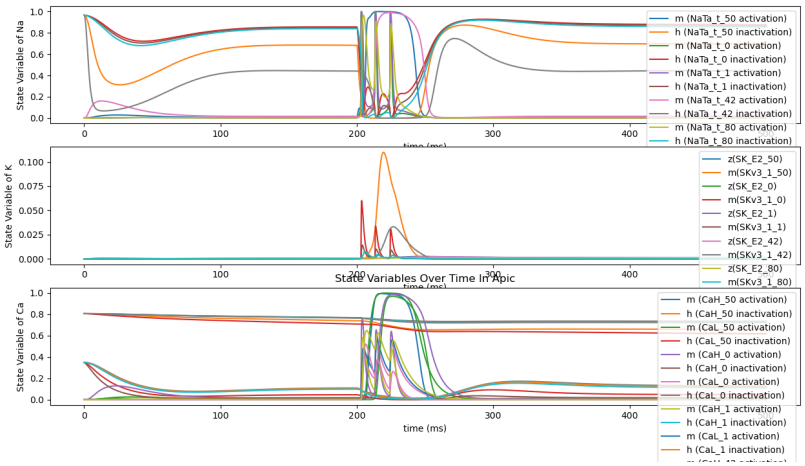


Figure 29: state variables of apic to somatic current injection and clustered synaptic inputs, apic[50] as input location

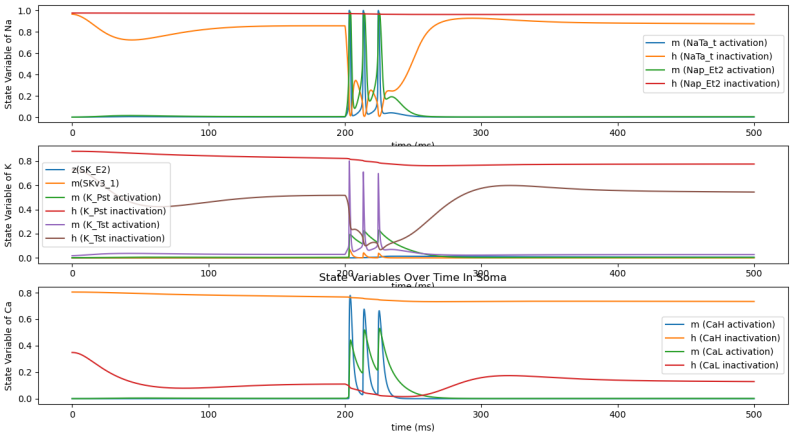


Figure 30: state variables of soma to somatic current injection and clustered synaptic inputs, apic[50] as input location

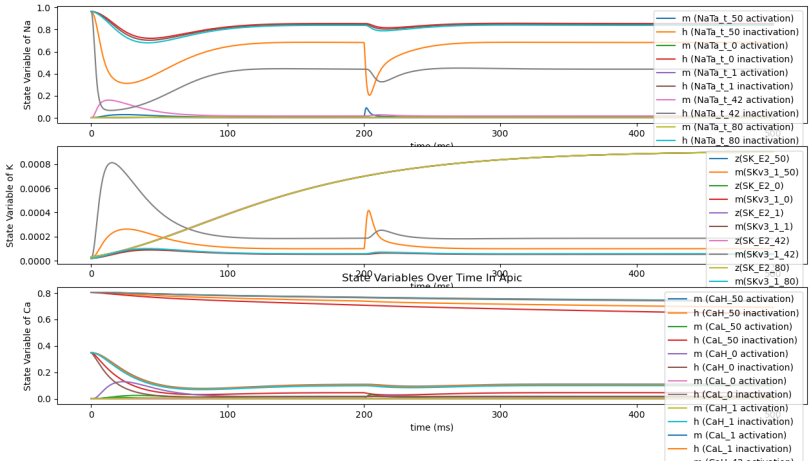


Figure 31: state variables of apic to clustered synaptic inputs, apic[50] as input location

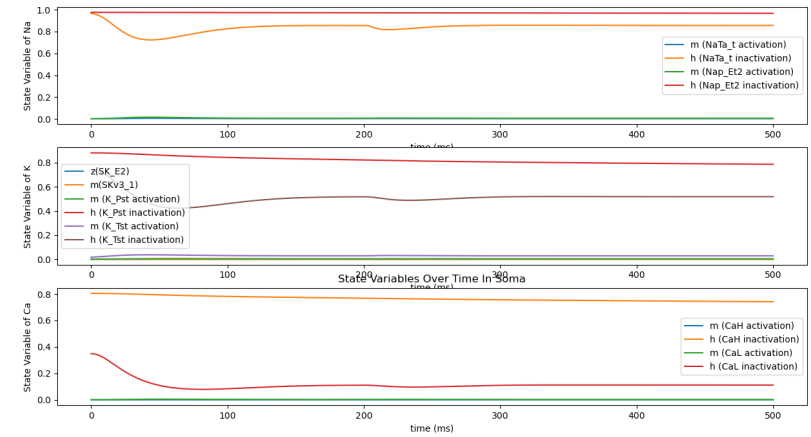


Figure 32: state variables of soma to clustered synaptic inputs, apic[50] as input location

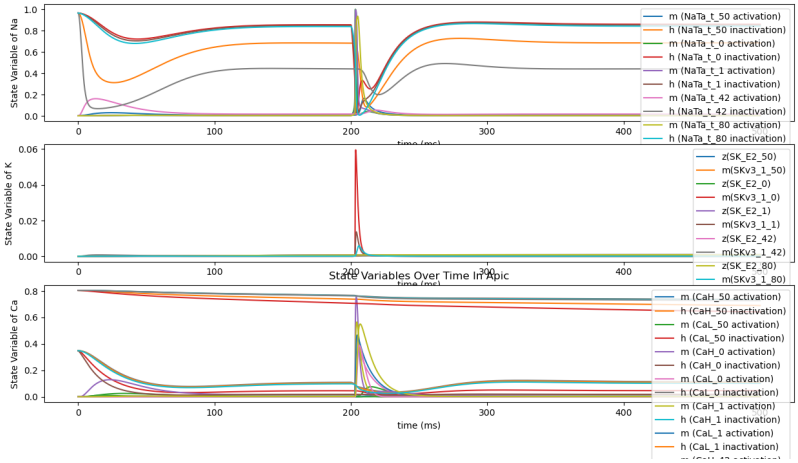


Figure 33: state variables of apic to somatic current injection

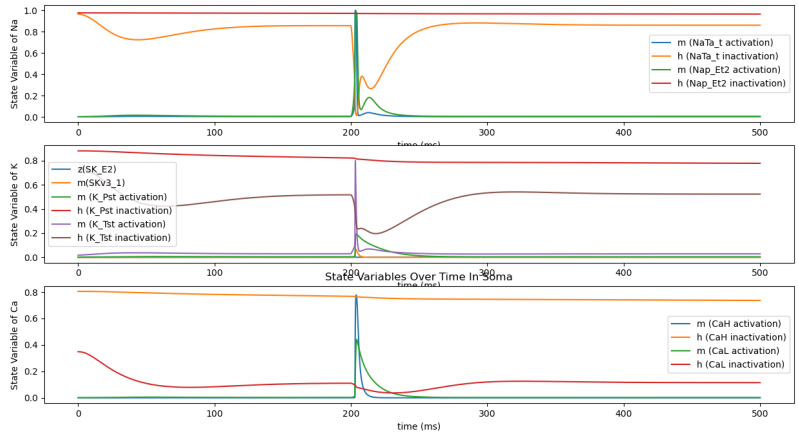


Figure 34: state variables of soma to somatic current injection

When both somatic current injection and cluster synaptic inputs are added, in apic[50] we can see rapid increase in the m variable of Na, slow decrease in the h variable, and they remain the level for about 40ms. Following the peak of the bAP, K channels begin to activate, which is characterized by the m variable. Backpropagation also activate Calcium Channels. While with either somatic current injection or cluster synaptic inputs is moved, no continuous spike or platform can be seen.

3.3 Further Analysis

As shown in the figure, the ion channels NaTa_t, SKc3_1 and Ca_HVA play the main rples upon current injection and synaptic input. The NaTa_t channel is a type of voltage-gated sodium channel. It plays a crucial role in the initiation and propagation of action potentials, particularly in the axon initial segment and dendrites of neurons. This type of channel is essential for the generation and back-propagation of action potentials in dendrites.

The SKv3_1 channel is a type of small-conductance calcium-activated potassium channel. It is activated by increases in intracellular calcium levels and helps to regulate the membrane potential by promoting potassium efflux. While SKv3_1 channels do not directly contribute to the back-propagation of action potentials, they can influence the refractory period and the after-potentials following an action potential. This can indirectly affect the likelihood of a bAP reaching the dendritic tree and the overall excitability of the neuron. By activating upon increases in intracellular calcium, these potassium channels can help to terminate or modulate the duration of plateau potentials.

The Ca_HVA channel is a high-voltage activated calcium channel that opens in response to strong membrane depolarization. It allows calcium ions to flow into the cell, which can trigger various cellular processes, including the release of neurotransmitters and the modulation of gene expression. If a bAP reaches the dendrites and activates these calcium channels, the influx of calcium can further depolarize the membrane, thus contributing to the plateau potential.

Conclusion

In summary, backpropagating action potentials (bAPs) are driven by the activation and inactivation of ion channels in response to voltage changes as the action potential travels back into the dendrites. By utilizing state variables that describe the dynamics of ion channel behavior, we can understand how bAPs contribute to neural signal processing and inter-neuron communication. This mechanism is fundamental for the computational capabilities of neurons, allowing them to integrate signals over different timescales and modulate synaptic connections effectively.