Spike Initiation in a Hippocampal Interneuron Model ⋆

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Abstract

Interneurons are heterogeneous in their morphologies, biophysical properties and pharmacological sensitivities. Recently, the dendrites of the oriens/alveus interneuron have been shown to contain a high density of sodium and potassium channels. These active dendrites contribute to the various signals produced by this cell. The initiation of spikes and their back-propagation into the dendritic tree has not yet been explored in interneurons. We use a computational model of an oriens/alveus interneuron with appropriate passive properties, channels, and distributions to explore where spikes initiate. We show that spike initiation depends on both the location and amount of input in our model.

Keywords: signal propagation, compartmental models, ion channel kinetics, interneurons.

1 Introduction

GABAergic inhibitory interneurons consist of only ∼10 % of the neuronal hippocampal population but critically regulate principal cell output. Unlike the more homogeneous population of principal pyramidal neurons, interneurons are diverse in many ways including their electrophysiological responses and their ion channel content. These differences imply that interneurons should not be viewed as simple inhibitors but have functionally distinct roles depending on the interneuron type [8].

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Given this diversity in interneurons we focus on the oriens/alveus interneuron for which there is experimental data describing the channel kinetics and distributions particular to this cell [7,6]. By looking at a specific interneuron type we can begin to understand its distinctive role in the network situation.

We specifically explore the site of action potential initiation and its dependence on the strength and location of tonic input. We find that a larger input into the soma can result in a shift of the initiation site from the soma to the dendrite.

2 Model

We use the multi compartment model developed in [10,11]. Briefly, the 84-compartment neuron model is based on the morphology and characteristics of an oriens/alveus hippocampal interneuron (Fig. 1 A). This model was created using the software package NEURON [4] and has a surface area of $9.884 \times 10^{-5} cm^2$. Passive properties were chosen so as to match experimental values of input resistance and membrane time constant for this interneuron type: membrane capacitance (1.3 $\mu F/cm^2$), axial resistivity (150 Ωcm), leak conductance (50 $\mu S/cm^2$), input resistance (215 $M\Omega$), and membrane time constant (23.3 ms). Passive properties were distributed uniformly to all compartments of the model interneuron.

The ion channels included in the model are the Hodgkin-Huxley (HH) sodium, I_{Na}, and potassium, I_K, current, a transient potassium channel, I_A, and a hyperpolarization-activated channel, I_h. The equations governing these currents are described in [10]. All four channel types were included in the soma. The dendrites contained both the HH channels but with modified kinetics and conductances as in [7] ($g_{Na,soma/dendrites} = 107/117\ pS/\mu m^2$, $g_{K,soma/dendrites} = 319/230\ pS/\mu m^2$, $g_A = 165\ pS/\mu m^2$, $g_h = 13.85\ pS/\mu m^2$). The density of the dendritic channels was kept constant along the dendritic tree.

3 Results

The location of spike initiation depends on both the amount and the location of the injected tonic current. Figure 1 A shows the input site as the soma (arrow), with voltage recordings taken from the soma (black trace), and two different sites on a dendrite (dotted and grey traces) in Figures B, C, and D. A small amount of tonic current (Figure 1 B; 0.01 nA) results in the soma spiking ahead of the dendrites. Increasing the amount of current injected into

Fig. 1. Location of spike initiation depends on amount of tonic current injected into the soma. A: Circles on compartmental model indicate the location from which voltage recordings were taken. Dotted circle corresponds to dotted line traces, grey circle to grey lines, and soma to black lines in B, C, and D. Arrow indicates location of tonic current injection; B: $I_{ext} = 0.01$ nA, soma (black trace) spikes first; C: $I_{ext} = 0.1$ nA, soma and dendrites spike simultaneously; D: $I_{ext} = 0.3$ nA, distal dendrite (dotted trace) spikes first. Insets show order of spikes.

the soma (Figure 1 D; 0.3 nA) allows the distal dendrite to spike first. The signal then propagates towards the soma. At a current injection value of 0.1 nA (Figure 1 C), all three voltage recording locations are seen to spike at the same time. This ordering of the spikes can be explained by considering the surface areas of the compartments and the relative current that each compartment experiences. The distal dendrite has a smaller diameter and therefore a smaller surface area than the soma, or even the more proximal dendritic segment. The amount of absolute or total current needed to allow the dendritic membrane to spike is much less than that needed for the larger somatic surface area. When a large amount of current is injected into the soma ($> 0.1\ nA$), the depolarization felt by the dendrite allows it to spike before the soma. A smaller amount of current ($< 0.1\ nA$) does not have the strength to excite the dendrite

Fig. 2. Soma spike precedes dendritic spike when injection site is placed at a distal dendrite. Time delay between somatic and dendritic spikes increases and then decreases with increasing current injection value. A: Circles on compartmental model indicate the location from which voltage recordings were taken. Dotted circle corresponds to dotted line traces, grey circle to grey lines, and soma to black lines in B, C, and D. Arrow indicates location of tonic current injection; B: $I_{ext} = 0.01$ nA, time delay between somatic spike (black trace) and dendritic spike (dotted trace) is 23 ms; C: $I_{ext} = 0.1$ nA, time delay is 63 ms; D: $I_{ext} = 0.3$ nA, time delay is 0.53 ms. Insets show order of spikes.

and therefore the soma spikes first.

When current is injected into a distal dendrite (shown by arrow in Figure 2 A), the initiation of the spike is *always* in the soma. The signal then back-propagates into the dendrites (Figures B, C, and D). Although the absolute amount of current injected into the dendrite is the same as that in Figure 1, the relative amount of current felt by the small dendrite is much larger than that felt by the soma previously. The dendrite therefore saturates to a depolarized value and this depolarization is propagated along the dendrite towards the soma. The spike is initiated in the soma and then traverses back

along the dendrite but cannot produce the same amplitude of spike in the smaller compartments due to their persistent level of depolarization. This is most clearly seen in Figure 2 D where the distal dendritic recording (dotted trace) is depolarized relative to the somatic recording (black trace).

The time delay between somatic and dendritic spikes changes with the amount of injected current. Injected currents into the dendrite of 0.01 nA, 0.1 nA, and 0.3 nA produce time delays of 0.23 ms, 0.63 ms, and 0.53 ms respectively in the distal dendrite (dotted traces in Figures 2 B, C, and D). This model neuron can spontaneously fire without any current injection [10], therefore small current injections into the dendrite will not have a large effect on this firing. The entire membrane is oscillating almost at the same time without a significant delay between the somatic and dendritic spikes (Figure 2 B). As the level of current injected into the dendrite is increased, the depolarization felt by the soma is passed on to the soma where a spike is initiated and then actively back-propagates into the dendrites. This is seen in the increased time delay between the somatic and dendritic spikes (Figure 2 C). With larger current injection, this time delay shortens (Figure 2 D).

4 Discussion

Recent experiments have shown that dendrites are rich in voltage-gated ion channels. The types and distributions of ion channels in hippocampal pyramidal cells has been extensively examined. The dendrites of interneurons are just beginning to be examined, but already experiments [7] have found that the density of sodium and potassium channels in the dendrites of oriens/alveus interneurons are comparable to those found in the soma with some slight differences in kinetics. This density is much larger than that found in the dendrites of cortical principal neurons implying a possible difference in action potential initiation and propagation in interneurons. [7] showed that the action potential initiation site could shift along the cell body depending on the injected current properties. Our model shows similar findings (Figure 1).

The role of back-propagating signals in neurons has been examined both experimentally and in simulations [5,9,2]. These signals are highly dependent on dendritic voltage-gated ion channels. Recently, a dichotomy of the amplitude of back-propagated action potentials was seen in CA1 pyramidal neurons [2]. This dichotomy could be explained by exploring small changes in the distribution of dendritic ion channels in compartmental neuronal models. Back-propagating signals could provide a link between neuronal output and the synapse by acting as a retrograde signal to the synapse that the soma has fired. This could provide a means for the synapse to 'self-regulate' its strength

in response to the back-propagated signal [3].

The ability of O/A interneurons to initiate dendritic spikes and to back-propagate somatic spikes allows them a more diverse control of the CA1 pyramidal neurons that they synapse onto. This control could result in changes in the efficacy and plasticity of entorhinal inputs onto the pyramidal cells [1] thereby having a large effect on hippocampal output.

5 References

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Biosketches

Fernanda Saraga is currently working on her Ph.D. at the University of Toronto. She graduated from the University of Toronto (B.Sc. (physics) and M.Sc. (physiology)). She is interested in creating computational models of inhibitory interneurons to understand their complex role in signal generation.

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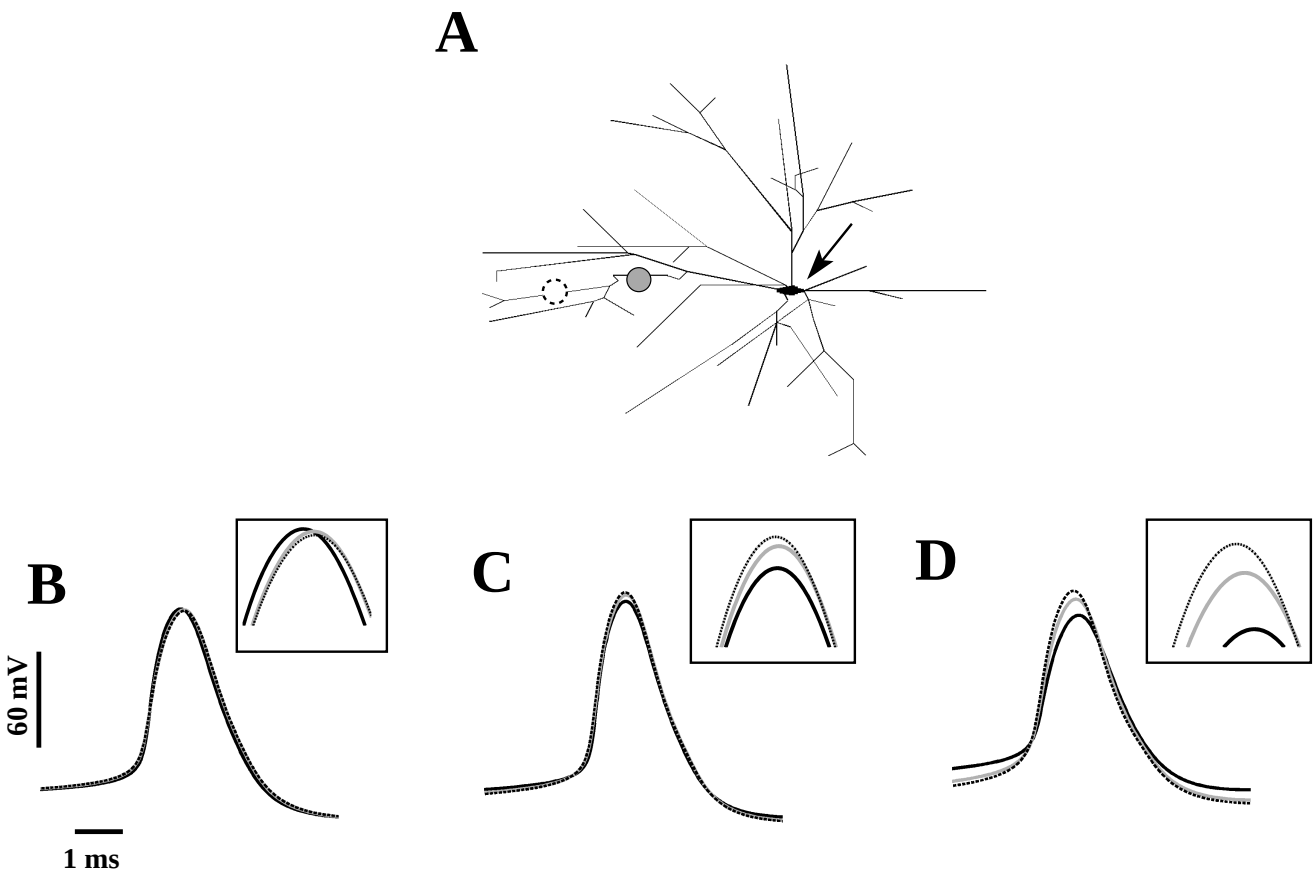

Fig. 1

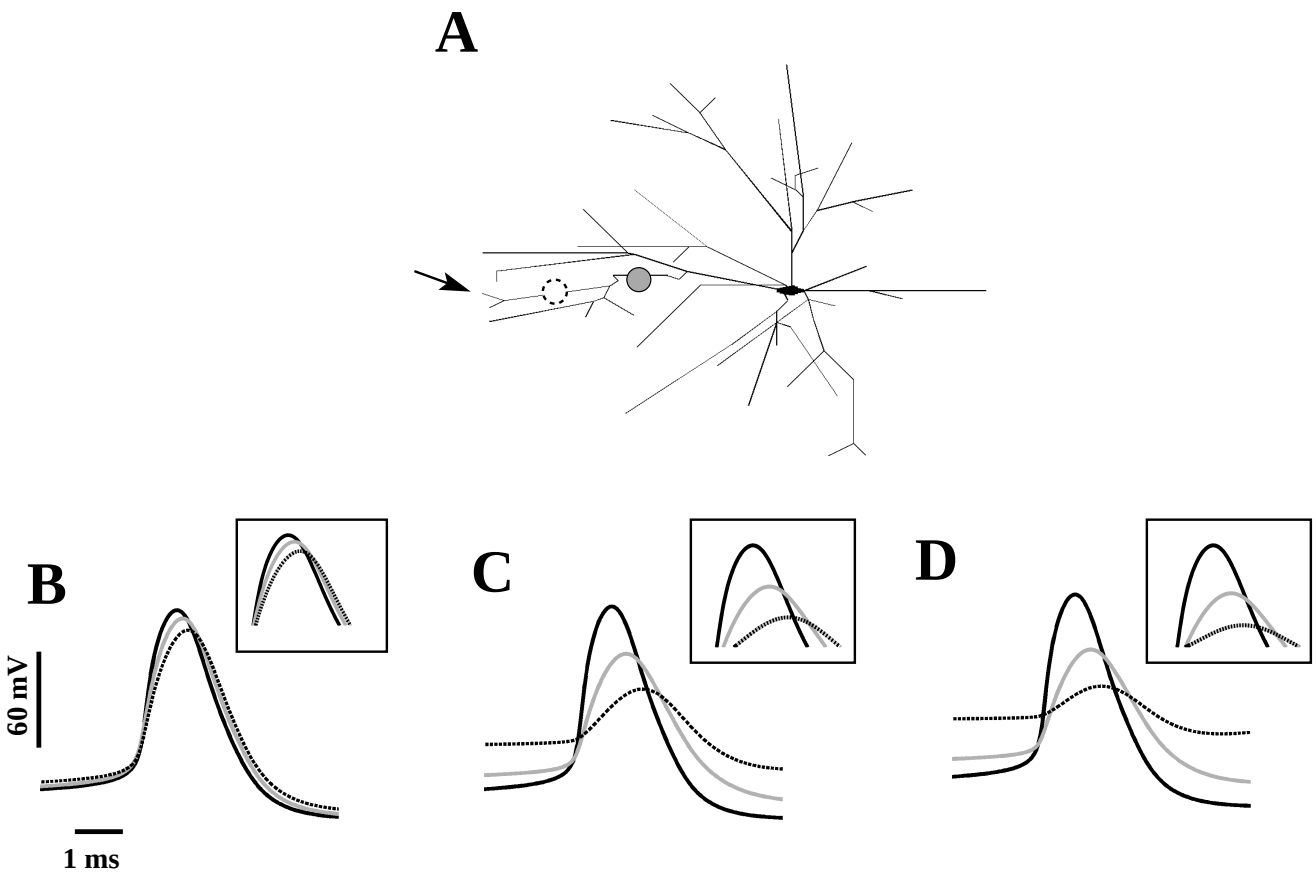

Fig. 2