Action potential backpropagation in a model thalamocortical relay cell.

Nada A.B. Yousif and Mike J. Denham
Plymouth Institute of Neuroscience
University of Plymouth, UK

Introduction

Thalamocortical (TC) cells are the basic components that relay all sensory information, bar olfactory, to the neocortex. Therefore the details of thalamocortical signalling are of great importance. There is a clear segregation of sensory and cortical afferents to TC cells, with cortical inputs located mainly in distal dendrites and sensory inputs in proximal dendrites [1]. Knowledge of way that TC cells integrate their various inputs (primarily cortical and sensory inputs) is crucial for accurate modelling of thalamocortical circuits and hence to understanding the role of TC cells in these circuits. For example, the shunting of EPSPs by backpropagating action potentials (APs) has recently been shown [2] to variably reset the membrane potential, depending on the type of cell and the kinetics, location and timing of synaptic input. These results indicate that, in the cells studied, a layer 5 pyramidal cell and a cerebellar Purkinje cell, distal synapses may contribute to synaptic integration to a far greater extent than proximal synapses.

This paper investigates action potential backpropagation in a multi-compartment model of a TC cell described by Destexhe et al [3], and compares the results from simulations of this model with experimental results on the backpropagation characteristics of TC cells by Williams and Stuart [4]. In [4], simultaneous whole-cell current-clamp recordings were made from the dendrites and soma of TC neurons, in slices of the rat dorsal lateral geniculate nucleus, which preserve the dendritic morphology. These show that APs are initiated near the soma and backpropagate into the dendritic tree, for both proximal (optic tract) and distal (cortical) stimulation (Figure 1). These experiments also demonstrated a significant attenuation of amplitude, and an increased duration, of the backpropagating APs, generated by somatic current stimulation, dependent on the dendritic recording location (Figure 2). This indicated a strong influence of the dendritic morphology on the AP propagation, and suggests that APs may fail to propagate into the most distal parts of the dendritic tree. Further results in [4] indicate that AP backpropagation is an active process, dependent on the voltage-activation of dendritic sodium channels, and that there is a non-uniform distribution of these channels. The results also indicated an on-average uniform density of potassium channels across the somatodendritic area studied.

Simulation Results

The model [2] used in these simulations was obtained from a TC cell from the rat ventrobasal nucleus, which was stained, reconstructed and incorporated into NEURON [5]. The model has a total of 206 compartments, which includes 11 dendrites with varying numbers of sections. The model contains Hodgkin Huxley (HH) type sodium and potassium currents, located solely in the soma, a leak current, a calcium pump, and I_T, the low-threshold Ca^{2+} current, to which burst activity is attributed. The I_T model is based on a model by Huguenard and McCormick [6], which involves fitting current traces when I_T is evoked.

Initially the cell was stimulated proximally (corresponding to sensory input) or distally (corresponding to cortical input), as described by Destexhe [7], by a single presynaptic AP. The resulting APs were observed at various membrane potentials, and the results are shown in Figure 3. Similar results to the experimental results of Williams and Stuart [4] were obtained. Action potentials are always measured earlier at the soma, and the backpropagated APs in the dendrites are attenuated. This result is expected, as the model does not contain sodium channels in the dendrites, just the low-threshold calcium channels. However, the results do not show the same pattern of response with respect to varying membrane potential.

Next, the backpropagating AP was measured before and after successive branch points of a dendrite. As expected, and as shown in [4], the attenuation increases after each branch point, and the APs become of progressively longer duration (Figure 4a). The relationship between AP attenuation and dendritic location in the model cell is shown in Figure 4b and compared to the experimental results from [4] (see Figure 2) in table 1. The attenuation in the model cell is much less than in the real cell, although the percentages are of the same order of magnitude. As the lengths of the dendritic trees are comparable, it appears that this discrepancy must arise from the passive membrane properties of the model cell dendrites.

	AP attenuation (% per μm)	
	Experimental results	Model results
Proximal dendrites	3.8	2.5
Distal dendrites	9.0	4.2

Table 1

Discussion

The model TC cell does not reproduce the experimental results of [4] in respect of either the voltage dependence of the firing properties of the cell or the attenuation rate of the amplitude of APs with respect to dendritic location. We are currently investigating a number of changes to the model cell in order to better replicate the experimental results of [4]. These include:

- Inserting active dendritic sodium and potassium channels into the model.
- Changing the properties of the dendritic low-threshold calcium channels. A non-uniform distribution of I_T already exists in the model, as also observed in [4]. However, it is reported in [4] that measuring from soma to proximal dendrites to distal dendrites, there is a shift in the activation and inactivation curves for I_T.
- Modifying the passive transmission characteristics of the dendritic processes. The transmission of an action potential across a branch point depends on the ratio of resistances [8].
- Modifying the synaptic conductances. In order to replicate the pattern of responses accurately, it is important to know synaptic conductances accurately. Here, the synaptic conductance used was the threshold conductance reported by Destexhe and Sejnowski previously [9].

The first two of these changes have been implemented in the model, and the results are shown in table 2. The effects are not significant, however we feel that the major influence will come from the resistance change across a branch point. These results will be reported in the full paper.

Conditions	**% Attenuation per 10um**	
	Proximal dendrites	**Distal dendrites**
Control	2.5	4.2
K channels in dendrites	2.7	4.7
Na channels in dendrites	2.1	4.1
Shift of IT activation curve	2.4	4.1
All three changes	2.3	4.7

Table 2

References

[1] Liu XB, Honda CN and Jones EG. J Comp Neurol. 352(1): 69-91 (1995).

[2] Häusser M, Major G and Stuart GJ. Science. 291(5501): 138-141, (2001)

[3] Destexhe A, Neubig M, Ulrich D, and Huguenard JR. Journal of Neuroscience. 18 (10): 3574-3588, (1998).

[4] Williams SR and Stuart GJ. J Neurosci. 20(4):1307-1317, (2000).

[5] Hines ML and Carnevale NT. Neural Computation. 9:1179-1209, (1997).

[6] Huguenard JR and McCormick DA. Journal of Neurophysiology. 68(4):1384-1400, (1992).

[7] Destexhe A. Journal of Physiology (Paris). 94: 391-410, (2000)

[8] Vetter P, Roth A and Häusser M. J Neurophysiol. 85: 926-937 (2001).

[9] Destexhe A and Sejnowski TJ. Phil. Trans. Roy. Soc. Lond. Series B. 357: 1649-1657 (2002).

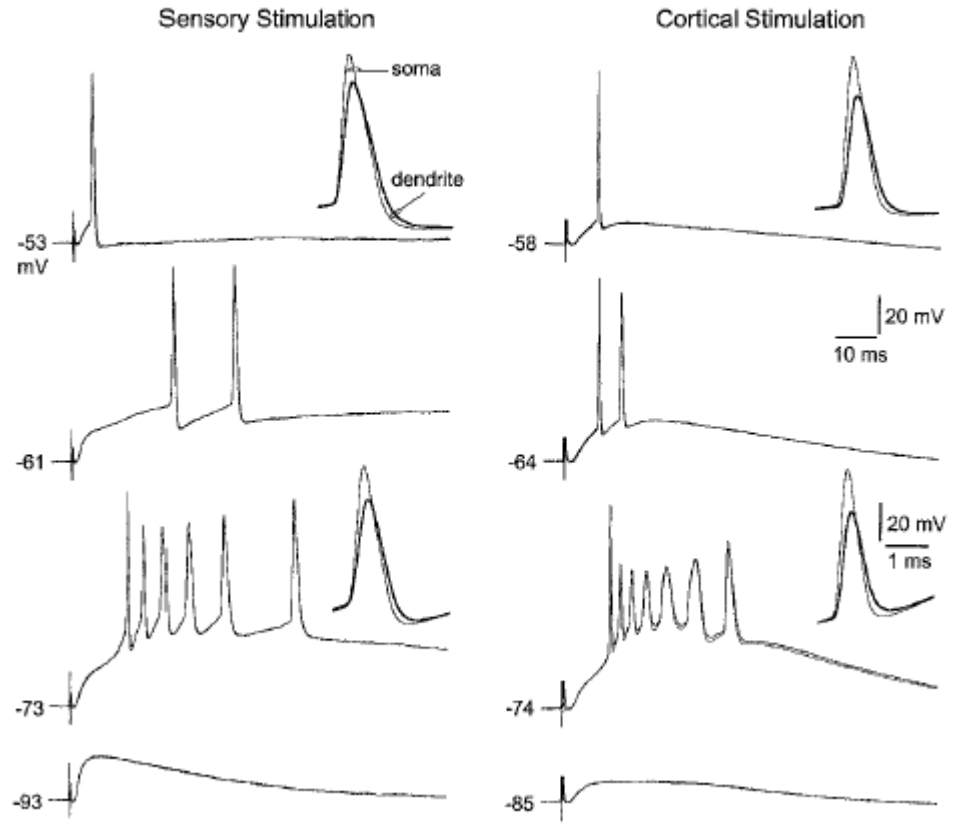

Figure 1: From Williams and Stuart [3]

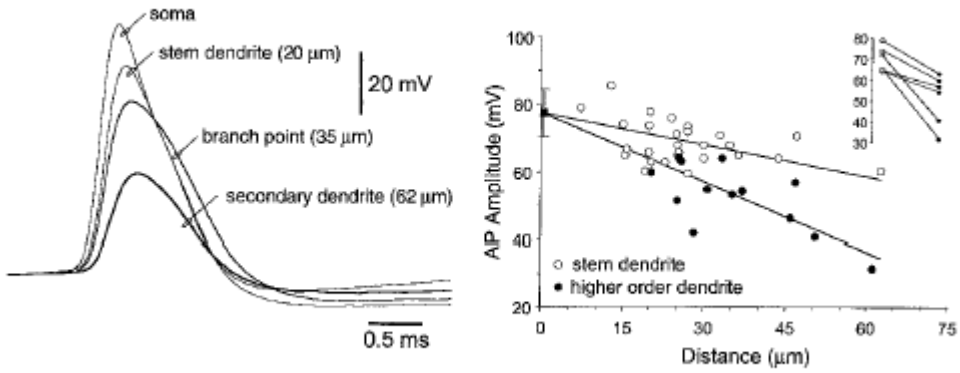

Figure 2: From Williams and Stuart [3]

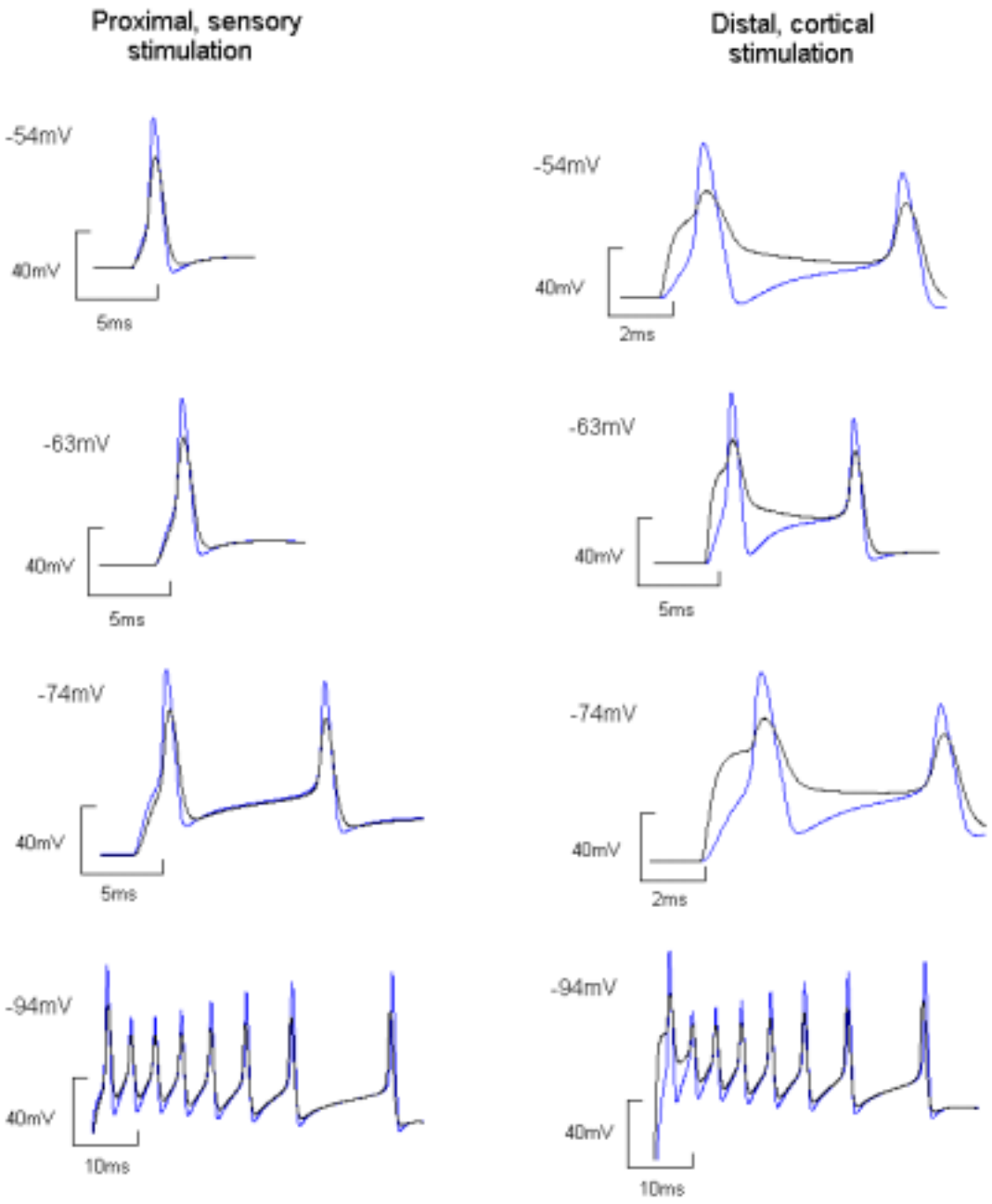

Figure 3: Response of TC cell to a single AP applied proximally (left hand results) or distally (right hand results) at various membrane potentials. Shows the difference between the somatic response (in blue) and the response at a distal dendritic site (in black).

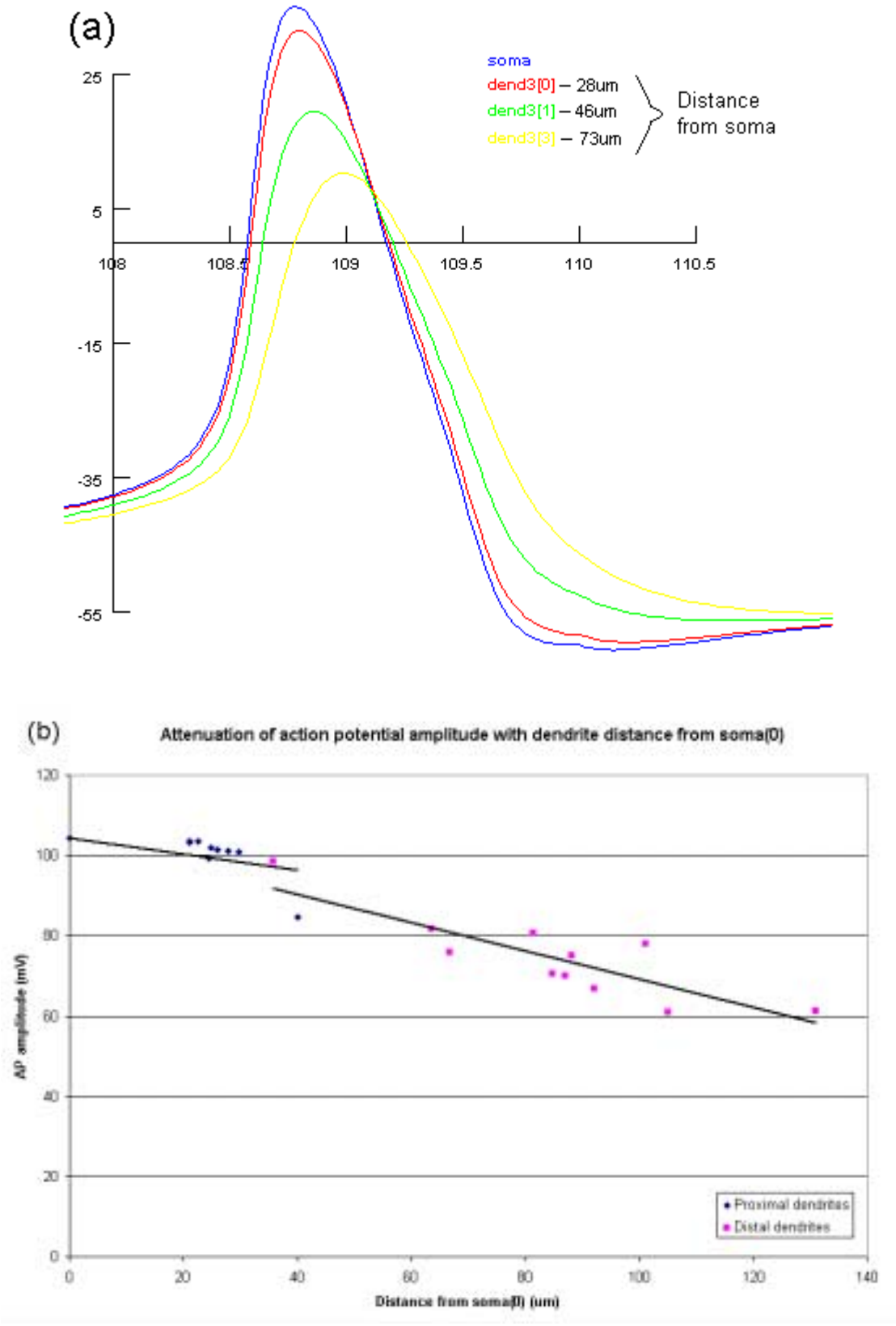

Figure 4: (a) Recording of the AP at various points throughout the dendritic tree. Dend3[0] is a section of dendrite 3 connected directly to the soma, dend3[1] is a section following the first branch point and dend3[3] is a section after a second branching of the dendrite. (b) AP attenuation with increasing distance from soma.