

Dendritic Calcium Channels Amplify the Variability of Postsynaptic Responses

CONCURRENT SUPERCOMPUTING CONSORTIUM
1994-1995 Report

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Abstract

Over the last years it has become increasingly clear that many neurons possess dendritic calcium channels. The cerebellar Purkinje cell is the classic example (Llinás and Sugimori 1980), but pyramidal cells in the cortex (Amitai *et al.* 1993) and in the hippocampus (Jaffe *et al.* 1994) also have high densities of calcium channels in their dendrite. The role of such channels in dendritic processing is not entirely clear. Spencer and Kandel (1961) first proposed that voltage-dependent dendritic channels could amplify large synaptic inputs, presumably resulting in a larger somatic response. Recently, Markram and Sakmann (1994) demonstrated in cortical pyramidal cells that single (subthreshold) EPSPs can cause activation of dendritic calcium channels. Similar results were reported for Purkinje cells (Eilers *et al.* 1995).

We have previously used a detailed compartmental model of the cerebellar Purkinje cell (De Schutter and Bower 1994a) to study synaptic integration in an active dendrite. In this model, dendritic calcium channels amplify small, synchronous synaptic inputs (De Schutter and Bower 1994c). Distal inputs get amplified more than proximal ones, resulting in a similar amplitude of the somatic response. We showed that the presence of continuous background synaptic inputs, i.e. small subthreshold excitatory inputs and inhibitory inputs, is essential to get amplification. These background inputs depolarize the Purkinje cell dendrite, bringing it closer to the activation threshold of its main calcium channel.

Further study demonstrated that the background inputs themselves interact also with the dendritic calcium channels. We used the *in vivo* state of the Purkinje cell model, where background asynchronous excitatory and inhibitory inputs would cause the model to fire at a normal rhythm of about 65 Hz (De Schutter and Bower 1994b), but removed the firing mechanism by making the soma passive (De Schutter and Bower 1994c). This allowed us to study the background input induced fluctuations of the somatic membrane potential in a model with active dendrite compared to a totally passive model. To examine effects on somatic EPSP amplitude we sometimes synchronously activated 200 excitatory synapses, equally distributed over the dendrite.

The membrane potential was more depolarized in the active dendrite model

compared to the passive dendrite model. This reflected the activation of dendritic calcium channels by the background inputs (De Schutter and Bower 1994c). However, the SD for the active membrane model (1.14 mV) was twice as large as for the passive model (0.57 mV). Consequently, the membrane potential fluctuated more with an active dendrite under identical conditions of subthreshold synaptic inputs. These fluctuations did not have an intrinsic frequency.

When a synchronous input, large enough to be suprathreshold, was added to the background inputs, the amplitude of the somatic response was larger in the active dendrite model (4.6 +/- 0.9 mV) compared to the passive dendrite (3.4 +/- 0.3 mV). This reflected the amplification of the synaptic response by dendritic calcium channels. Again, the variability of the active membrane EPSP was much larger than for the passive membrane EPSP. In both models, the EPSP variability was completely determined by the pattern of firing of the background inputs. Statistical analysis showed that for the passive membrane EPSP, the variability in amplitude was equal to the variability of the baseline membrane potential. In the active membrane model, however, the variability of EPSP amplitude was larger than that of the baseline potential. The coefficient of variance remained constant with increasing sizes of the synchronous input applied. Finally, the time to peak was delayed and much more variable in the active dendrite model (8.2 +/- 2.7 ms) than in the passive model (4.0 +/- 0.7 ms).

We conclude that dendritic calcium channels amplify both the size and variability of the EPSP. The extra variability of the amplification is due to background input induced changes in the state of activation of dendritic calcium and calcium-activated channels, which also cause the larger membrane potential fluctuations. This results in varying levels of dendritic excitability at the time of the synchronous synaptic input.

These effects are robust for different combinations of background excitatory and inhibitory input rates, provided the total drive is sufficient to slightly depolarize the dendrite so that the calcium channels can be activated (De Schutter and Bower 1994c).

While these results were obtained with a model of the Purkinje cell, we think that our conclusions also apply to other neurons with dendritic calcium channels. As was mentioned in the introduction, both in cortical pyramidal cells (Markram and Sakmann 1994) and in Purkinje cells (Eilers *et al.* 1995) subthreshold synaptic inputs can activate dendritic calcium channels, which is the basis of the effects reported here.

Several groups have shown that background synaptic inputs can have significant effects on the properties of passive membrane dendrites (Bernander *et al.* 1991; Rapp *et al.* 1992). Our results demonstrate that in an active membrane dendrite the effects are even more profound. Moreover, these results suggest that the interactions between subthreshold synaptic inputs and dendritic calcium channels add increased information processing capacity to the dendrite. In effect, the dendritic excitability will determine whether the somatic response to an incoming synchronous input is suprathreshold or not.

Acknowledgements

Supported by NFWO (Belgium) and NIMH MH52903. I thank J.M. Bower for access to the Intel Touchstone Delta System operated by Caltech on behalf of the Concurrent Supercomputing Consortium.

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