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Model of hyperpolarization dependent LTD in MVN neurons

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Introduction

Whole cell patch clamp recordings from rat MVN neurons have revealed a hyperpolarization dependent LTD at vestibular afferent synapses [1]. The induction protocol consisted of a brief 20 ms membrane hyperpolarization (to mimic the time-course of IPSPs from Purkinje cells converging on the MVN neuron), paired with a single vestibular afferent stimulus which was applied at various times relative to the membrane hyperpolarization (Fig. 1). The LTD of afferent synapses was observed when vestibular stimuli arrived from 20 to 40 ms after the onset of the hyperpolarization. Simulations of a compartmental model of a MVN type B neuron [2] were used to study the ionic currents and calcium transients at synaptic locations on dendrites during the same stimulation protocols that resulted in LTD in the tissue slice preparations.

Methods

The cell model contained 61 electrical compartments, comprising the cell body and four dendrites. A variety of ionic conductances, including low- and high-voltage-activated calcium conductances, were distributed non-uniformly across the cell membrane. Calcium influx, buffering and extrusion were modeled in every cell compartment. Full details of the model can be found in [2]. For the simulations described here, the model was modified and extended from [2] as follows. The density of LVA calcium channels and persistent sodium channels were reduced to match the excitability of the cells recorded in slice preparations. An AMPA/NMDA receptor-mediated excitatory synapse was added to the dendrites. The conductance time course, and voltage dependence in the case of the NMDA component, were set to average values determined for deep cerebellar nucleus cells [3]. Hyperpolarization was achieved either by current injection to the soma, or by an IPSP collocated in the dendrite with the afferent EPSP.

Results

The computer simulations clearly demonstrate that rebound from hyperpolarization results in a transiently enhanced LVA calcium current. During this rebound, calcium influx via NMDA and LVA channels may summate to provide a larger change in calcium than seen either during the hyperpolarization or during stimulation without an accompanying hyperpolarization. For single afferent stimuli, the relative timing of the stimulus with respect to the offset of the hyperpolarization determines the magnitude of the calcium influx. The timings that produced LTD in the tissue slice experiments correspond to mid-range peak calcium, which corresponds to a maximal change in calcium from its level immediately prior to the synaptic stimulation. An intermediate calcium level has been hypothesized to produce LTD by a number of proposed synaptic learning rules [4].

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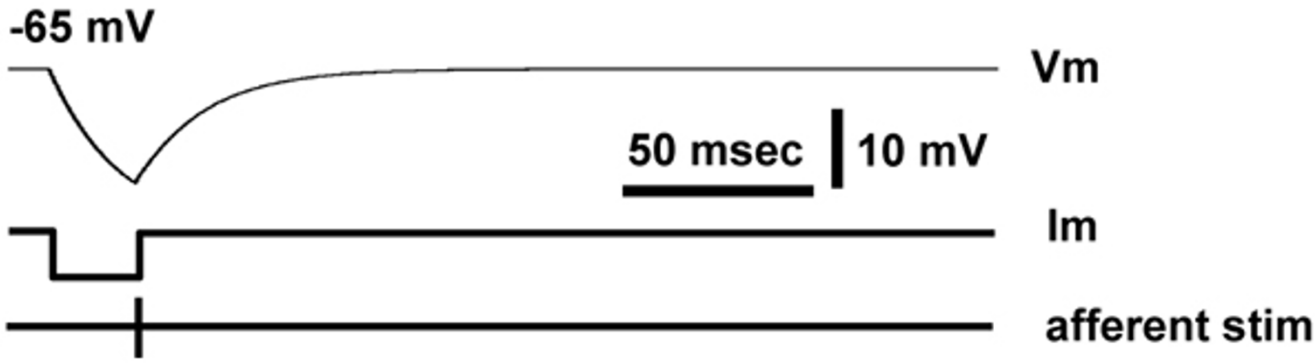

Figure 1
Simulation protocol with vestibular stimulus 20 ms after onset of hyperpolarization.

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