1 Introduction

- Denervation of connections from the entorhinal cortex induce loss of synapses and subsequently dendritic retraction in the postsynaptic target area containing granule cells of the dentate gyrus [1].
- Previous models showed dendritic retraction is capable of increasing the excitability of neurons, thus compensating for the denervation-evoked loss of synapses. However, this was shown only for stochastically stimulated AMPA synapses [2, see figures below].

Therefore, here we investigate the consequences of dendritic retraction for 1. firing rate homeostasis and 2. NMDA-dependent synaptic plasticity in compartmental dentate granule cells driven by AMPA/NMDA synapses.

2 Methods

- Compartmental modeling in the NEURON environment and newly established T2N software [3,4].
- Reconstructed mouse granule cells (GCCs, 15 cells) were used as well as compared to artificial cells [5,6]. We used an established biophysical model of a detailed granule cell [4] and Mainen-Sejnowski spiking model (ModelDB online database #2488) [7]. Excitatory AMPA and NMDA synapses were homogeneously distributed in the dendritic tree and simulated as biexponential conductance changes (AMPA: rise time = 0.2ms, decay time = 2.5ms; NMDA: rise time = 0.3ms, decay time = 50ms) with lognormal weights – (p,o). Simulations were performed in “active” as well as “passive” cells.
- Stimulation protocol: a) A Poisson generated spike train between 0.1 and 1 Hz for stochastically activated synapses and b) a 100Hz high-frequency input to the synapses.
- Inhibitory synapses with positive \( E_{\text{GABA}} \) shift due to change in KCC2 pump in denervated cells [8].

As output we computed the somatic voltage and the firing rate. Backpropagating action potential was analyzed. Synaptic NMDA current was a measure of capability for synaptic plasticity induction.

3 Distributed synaptic stimulation leads to similar somatic voltage responses in passive & similar firing rates in active GC models

4 The enhanced backpropagating action potential (bAP) reduces the inward NMDA current in granule cell models slightly

5 Similar synaptic NMDA currents are present in denervated GC models with retracted dendrites despite their loss of synapses

6 Denervation-induced positive shift in \( E_{\text{GABA}} \) enhances the boost of NMDAR activation & can lead to full NMDA current compensation

7 Generalisation to other dendritic morphologies: Firing rate homeostasis and compensation of NMDAR activation is present in artificial dendritic morphologies

Conclusion

- For passive models, driven by distributed AMPA/NMDA synapse stimulation, somatic output voltage homeostasis was present both in granule cells and artificial cell morphologies.
- Propagation of action potentials was enhanced in the denervated regions of the granule cells as well as artificial cells. This enhancement impaired the NMDAR activation boost slightly when close to \( E_{\text{GABA}} \).
- Dendritic retraction leads to a compensatory boost of NMDAR activation which might support homeostasis for the induction of NMDAR-dependent plasticity.
- Positive shift in \( E_{\text{GABA}} \) (inhibitory ionic plasticity) can contribute to homeostasis of NMDA-dependent synaptic plasticity.

References