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Effects of ih-current modulation in a Corticospinal cell model

The Hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channel is a non-selective monovalent cation channel, permissive to K+ and Na+ at a 4:1 ratio, and whose conductance increases as membrane voltage decreases. Its activity is quantified in terms of its ih-current, which is a hyperpolarization-induced cationic current. The ih-current is active during rest, inducing a depolarizing effect in the cell and a decrease in neuronal input resistance. HCN channels can be blocked by administration of the drug ZD7288.
The ih-current appears to play a key role in the switching from motor planning to execution. HCN channels are present in pyramidal tract projecting (PT) neurons, part of the corticospinal tract, which forwards motor commands to lower motor neurons. PT cells are strategically located in layer 5B, a known output route from the cortical circuit. The HCN channels are a distinguishing feature between the PT cells and its other neighbouring pyramidal cell type, the Intratelencephalic projecting neurons (IT), which project mainly to Basal Ganglia.
In this project we implemented a PT cell model with a variation in the kinetics of the HCN channel proposed by Migliore et al. (2012) and compared with the results shown by Sheets et. al. (2011) in recordings of PT neurons with and without administration of ZD7288.
Our results show that the model reproduces the relevant features observed in the electrophysiological recordings applying ZD7288 (Sheets et al., 2012), such as: inversion of peak response to subthreshold stimulation, temporal summation response, and increase in firing rate. Blocking of HCN channels in the model also removes the membrane sag response and changed the profile of membrane response to spatially distributed stimuli, in line with the results reported by Sheets et al (2011). We plan to integrate this model in a large scale model of motor cortex circuits (Dura-Bernal et al., 2019), to explore the effects of HCN at the network level.

Additional contributors to this project:
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