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Poster presentation

Modeling the excitability of the cerebellar Purkinje cell with detailed calcium dynamics

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Previous studies have suggested that the activity pattern of a cerebellar Purkinje cells (PC) is significantly controlled by voltage activated Ca^{2+} channels and Ca^{2+} activated K^{+} channels, present mainly on its elaborate dendritic tree [1]. Although the main somatic excitatory drive propagates very weakly into the dendritic tree [2], somehow a significant interaction between somatic and dendritic spiking occurs. Ca^{2+} entering through P-type channel is thought to be the main source of this excitability modulation, and this Ca^{2+} influx also activates large conductance (BK) and small conductance (SK) Ca^{2+} dependent K^{+} channels [1,3]. This interaction often results in the counter-intuitive computational somatic and dendritic spiking behavior of PCs [4], but nevertheless this important aspect has not been thoroughly investigated in previous computational modeling studies.

In this work, we try to integrate known aspects of Ca^{2+} dynamics in PC dendrites by building a new model, which would help us understand the consequent computational properties of a PC. Recently, it has been shown that BK channels are in close vicinity of Ca^{2+} sources as compared to SK channels [5], suggesting that BK channels require a brief large amount (~10–100 μM) of Ca^{2+} whereas SK channels require a long yet small quantity (~0.1–2 μM) of Ca^{2+} for the activation. Therefore it might be interesting to see how this spatiotemporal interaction of Ca^{2+} sources with Ca^{2+} activated K^{+} channels takes place in simulation. Due to lack of sufficient experimental data about the interaction between Ca^{2+} sources and Ca^{2+} activated channels in PCs, we could only capture temporal interaction by including Ca^{2+} dynamics with several buffers and pumps [6] in our model. We expect that this will be sufficient to activate the BK and SK channel correctly. In addition to introducing complex Ca^{2+} dynamics to our model, we also built new kinetic models of the P-type Ca^{2+} channel and BK channel based on the recent experimental data [7] and gating kinetics with both voltage and Ca^{2+} dependence [8].

Not only the composition of active ionic mechanisms, the dendritic morphology can also significantly modify the spiking pattern [9]. However, simulation on the detailed reconstructed morphology of a PC dendritic tree is not suitably efficient for parameter tuning to obtain a desired behavior. Therefore, to investigate the morphological significance in firing behaviors, we have built and used an electrotonically accurate reduced morphology of a PC as well as an even simpler three-compartment model comprising of soma, smooth dendrite and spiny dendrite.

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