Interaction of segregated resonant mechanisms along the dendritic axis in CA1 pyramidal cells: Interplay of cellular biophysics and spatial structure | Horacio G. Rotstein

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Neuronal frequency filters play a crucial role in cognition, motor behavior, and the dynamics of information processing in neural networks in both health and disease. The filtering properties of neurons are shaped by several factors, including the intrinsic properties of neurons, their dendritic geometry, and the heterogeneous distribution of ionic currents [1]. Experimental results show the existence of two distinct theta ($\sim 4 - 10$ Hz) resonant mechanisms in CA1 pyramidal neurons: (i) a perisomatic resonance mediated by an M-type potassium current (IM) and amplified by a persistent sodium current (INap), and (ii) a dendritic resonance mediated by a hyperpolarization-activated current (Ih) [2].

While the propagation of (amplitude) resonances along dendritic trees has been investigated before [3], a number of biologically and mathematically relevant questions remain open. It is unclear how the two experimentally observed biophysically different and spatially segregated types of resonance interact in the presence of a heterogeneous distribution of ionic currents and membrane potential variations. It is also unknown what are the interaction and propagation properties of the associated phasonances (phase-resonances). In this study, we address these issues using CA1 pyramidal neurons as a case study.

We use a multicompartmental model based on the Hodgkin-Huxley formalism. The model includes IM , INap and Ih, spatially and heterogeneously distributed along the dendrites. We also use a linearized version of this model that allows for mathematical tractability. The model is minimal in the sense that it includes enough compartments to capture the filtering properties of CA1 pyramidal cells, but this number is small enough to allow for the conceptual understanding of the underlying mechanisms. In practice we use 20 compartments, which we found to be appropriate to preserve the experimentally observed segregation of the two resonant mechanisms, while allowing for their interaction without creating unrealistic interferences. We apply sinusoidal inputs at proximal, distal, and intermediate dendritic locations, we compute the amplitude and phase profiles across all compartments, and describe them for a number of realistic scenarios.

Our results reveal that voltage variations along the dendritic cable differentially activate ionic channels, creating a diverse range of resonant and phasonant responses. The spatial structure of the dendrites provides the neuron with remarkable flexibility to process these inputs and support a variety of scenarios of resonance interaction. Our findings highlight the complex relationship between dendritic structure, ionic mechanisms, and neuronal filtering properties. These flexible filtering capabilities not only enable individual neurons to adapt to spatially and frequency-specific inputs, but also significantly contribute to the generation of network rhythms and the regulation of neural activity at the network level.

References

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