Multiple resonance peaks generated by active ionic currents in neurons

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Introduction: Ionic channels are responsible for the different voltage responses that neurons can exhibit when submitted to external currents. Depending on a combination of ionic channel and input frequency, voltage response can exhibit sub-threshold resonance properties which are usually measured by the impedance magnitude [1]. An example of current that provokes resonance in neurons is the hyperpolarization-activated current (I_h) [2,3]. Nevertheless, standard ionic currents that are responsible for the generation of action potentials, such as sodium (I_{Na}) and potassium (I_{Kd}), have their roles on the sub-threshold resonance properties neglected. This usually happens because supra-threshold effects tend to hide sub-threshold oscillations, specially during spontaneous activity. In this study we investigated how the sub-threshold resonance properties of neurons can be determined and shaped with the inclusion of different ionic channels.

Materials and Methods: Our approach involves a neuron model based on the Hodgkin-Huxley equations containing different ionic currents. We investigate the resonance properties of the neuron by including I_{Na}, I_{Kd} and I_h.The problem is investigated with computational simulations of the neuron when submitted to the so-called "ZAP" current. Our results are concentrated at the impedance magnitude of the neuron. Although the impedance is usually defined as the ratio of the Fourier transforms between the output voltage and input current [1], here we used a simpler expression to capture the neuronal response without considering its spikes: we take as output a voltage series discretized in time whereby only local minima conveyed by the oscillatory output are considered.

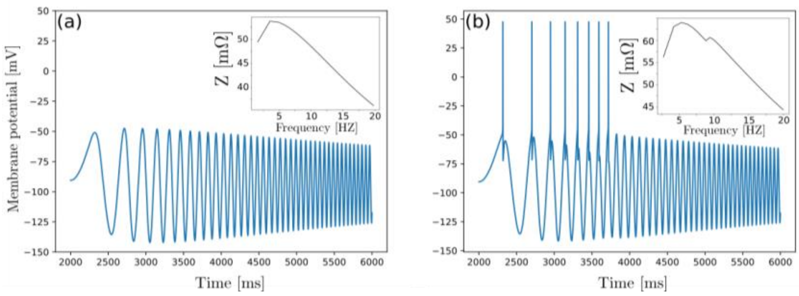

Fig.1: Neuron model submitted to the "ZAP" current. (a) Neuron model containing only I_h. (b) Neuron model containing I_{Na}, I_{Kd} and I_h. Insets in the figure are the impedance magnitude of these neurons using our procedure as described in the methods section

Results: Our results show that the resonance properties can be easily shaped by the inclusion of the different currents considered here. Surprisingly, a combination of different time constants of the ionic currents can shape the impedance creating: (i) a low-pass filtered response, (ii) band-pass filtered response, and more importantly (iii) multiple resonance peaks.

Discussion: The results show for the first time that a combination of ionic currents can create multiple resonance peaks. Such property emerges from the combination of the different time constants and is observed here due to the definition of the impedance magnitude. By neglecting the spiking activity and considering only the minima as responses to measure the impedance, we were able to capture the impedance that is created only by properties of the sub-threshold response of the neuron, even though action potentials were present.

Conclusion: Different combinations and alterations in ionic channels can elicit pathologies [4]. We believe that our results have important implications in explaining response properties of neurons and can be used to predict and explain altered resonance properties.

References: [1] doi: 10.1016/S0166-2236(00)01547-2; [2] Pena RF et al., arXiv preprint arXiv:1712.00306, 2017; [3] doi: 10.1113/jphysiol.2009.185975. [4] doi: 10.1016/j.pneurobio.2008.09.007