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A new measure to evaluate subthreshold resonance in neurons

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Background, Motivation and Objective. The subthreshold resonance properties of neurons are usually measured by submitting a neuron to the so-called ZAP function and constructing the impedance amplitude profile as the ratio of Fourier transforms of output and input: $Z(f)=FFT_{out}/FFT_{in}$ (10.1016/S0166-2236(00)01547-2; 10.1007/s10827-013-0483-3). The resonance frequency corresponds to a peak in $Z(f)$. In general, for low amplitude (~10 pA) ZAP functions the voltage response oscillations are symmetric about a reference voltage line. However, there is evidence of asymmetric responses to ZAP functions, with non-coincident depolarizing and hyperpolarizing membrane resonance frequencies (10.3389/fncel.2018.00008). Here we study this effect for high amplitude ZAP functions (>10 pA). We propose two different measures than the usual $Z(f)$.

Methods. We take the holding membrane potential (V_{hold}) as reference voltage line (voltages above/below it are positive/negative) and, for each frequency, measure the magnitudes of the maximum and minimum voltages normalized by the ZAP amplitude. These will be called $Z^+(f)$ and $Z^-(f)$. We studied $Z^+(f)$ and $Z^-(f)$ for a neuron model (arXiv:1712.00306; 10.1007/s00422-008-0263-8) submitted to a ZAP function.

Results. For low ZAP amplitudes, $Z^+(f)$ and $Z^-(f)$ are identical but for high ZAP amplitudes, $Z^+(f)$ and $Z^-(f)$ have different resonance frequencies. We characterized the differences between magnitudes $\Delta Z = Z^+(f^+) - Z^-(f^-)$ and resonance frequencies $\Delta f = f^+ - f^-$ in the two-dimensional diagram spanned by V_{hold} and the time constant of the hyperpolarization-activated current I_h. There are regions in the diagram where the neuron can discriminate the frequency change of the input current based on its voltage response profile.

Discussion and Conclusions. This suggests that a neuron can be sensitive to changes in the frequency of its synaptic inputs, and this sensitivity depends on intrinsic parameters of its ionic currents. Our theoretical results reproduce a phenomenon which has been observed experimentally (10.3389/fncel.2018.00008) suggesting that the quantities $Z^+(f)$ and $Z^-(f)$ as defined here can be useful in further studies of resonance phenomena in neurons.

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