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Calcium-dependent subthreshold fluctuations in membrane voltage; a modeling study

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Membrane potential noise plays multiple functional roles in the nervous system, as described in the review by Faisal *et al* [1]. Calcium-dependent potassium (K_{Ca}) channels are ion channels whose conductance depends on intracellular calcium concentration. Previous work by Diba *et al* suggests that such channels play a central role in subthreshold voltage noise [2]. While most channels generate noise through their inherent thermal fluctuations, we hypothesize that K_{Ca} channels also generate low-frequency subthreshold oscillations by transmitting stochastic fluctuations in intracellular calcium.

Methods

We have produced a stochastic computer model that incorporates K_{Ca} channels and calcium dynamics into a CA3 pyramidal neuron, which is based on the biophysically realistic Traub model [3]. To introduce channel noise, we replaced all Hodgkin-Huxley (HH) channels with equivalent Markov models [4]. There is also an intracellular calcium pool, with Ca^{2+} levels that vary stochastically due to influx through Markovian calcium channels.

Results

Preliminary simulation results show that, for the default parameters used by Traub, there is anti-correlation between intracellular calcium and membrane voltage (Figure 1); this suggests intracellular calcium fluctuations may partially drive low-frequency voltage noise.

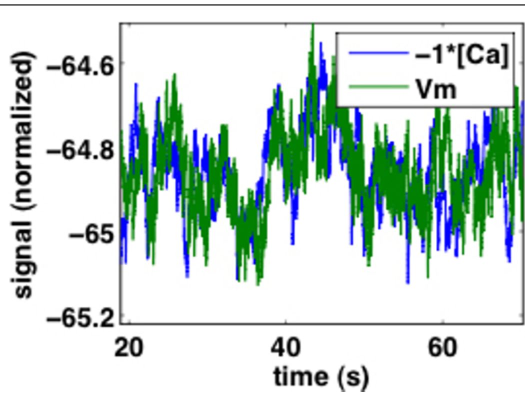

Figure 1 Relationship between intracellular calcium and membrane voltage. Intracellular calcium (blue, arb units) is inverted and scaled to show anti-correlation with membrane voltage (green). (Correlation coefficient -56.4%, Vm phase lag ~600ms, Traub model default parameters.)

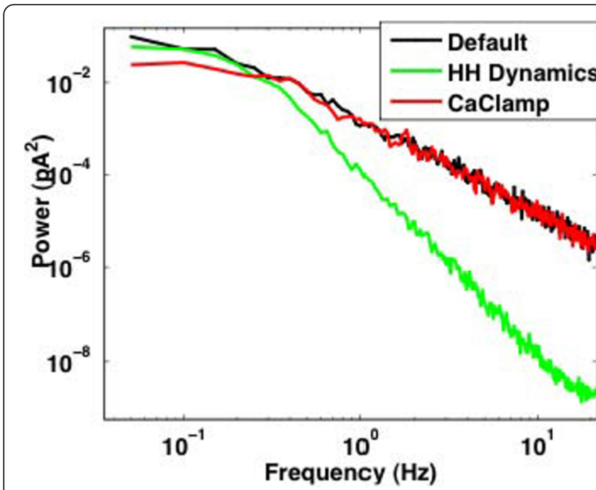

Figure 2 Power spectral density for stochastic I_{AHP} current Black trace is simulation under default settings. Red trace shows the effects of clamping intracellular calcium, which reduces low-frequency power. Green trace shows the I_{AHP} current when inherent thermal fluctuations are removed by switching channel dynamics from Markov to HH. The crossover of these two signals suggests that intracellular calcium fluctuations can contribute to low-frequency voltage noise.

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Additional modeling has implicated the Ca^{2+}-dependent afterhyperpolarization current (I_{AHP}) as the primary linkage between these two signals. Power spectrum analysis suggests that the contribution of intracellular calcium fluctuations is dominant at low frequencies, below the natural cutoff for I_{AHP} noise (Figure 2). We believe that this linkage between membrane potential noise and intracellular calcium could regulate many of the well-documented roles of noise in the nervous system [1].

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