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WHY DO CORTICAL NEURONS SPIKE IRREGULARLY? M. Tsodyks, A. Bell, Z.F. Mainen and T.J. Sejnowski,* Howard Hughes Medical Institute, Salk Institute, La Jolla, CA 92037

The spike trains of many cortical neurons in vivo are highly irregular during both spontaneous and driven activity. Although this variability may simply reflect large correlated fluctations in synaptic input, an additional consideration is the balance between synaptic drive and the intrinsic conductances generating action potentials.

Using a single-compartment Hodgkin-Huxley model, we show that when excitation and inhibition are balanced to maintain the neuron in the region of optimal sensitivity, near firing threshold, then variable spike trains result even in the absence of large input fluctuations. Increased levels of balanced synaptic input increase the rate of input fluctuations, producing higher firing rates with maintained irregularity. Decreased spike repolarization (weaker K^+ rectification) increased the steepness of the input-firing curve, giving greater sensitivity to input fluctuations.

Very similar results were obtained with a simpler integrate-and-fire model, which was used to explore networks of interacting excitatory and inhibitory neurons. Despite positive feedback between the excitatory neurons, proper balance was achieved robustly through inhibitory feedback. With weak repolarization, the network was sensitive to small inputs and could be switched rapidly between stable states dominated by fluctuations. This regime is not consistent with the mean-field approximations commonly made in network models. We propose that neuromodulatory control of K^+ conductances (weakening or strengthening spike repolarization) may dynamically regulate the time-scale of information to which cortical networks are sensitive. (We are grateful to M. Shadlen for useful discussion. Supported by ONR. ZFM is an HHMI Predoctoral Fellow.)