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*The Origins of Irregular Spiking in the Neocortex*

I am interested in mechanisms underlying response properties of neurons in primary sensory cortex using both electrophysiology and imaging. I became interested in neuroscience as an undergraduate studying computer science and cognitive science at the University of California, San Diego. Upon graduation I worked in Dr. Terry Sejnowski's Computational Neuroscience Lab, where I enjoyed lively conversations and daily afternoon tea. I then entered graduate school at the University of California, San Francisco, where I worked initially with Dr Kenneth Miller using computational techniques and then completed my thesis with Dr Stephen Lisberger, in whose lab I studied the mechanisms of cortical adaptation and the neural representation of speed in the dorsal visual pathway. I then moved to Northwestern University to examine the mechanisms for selectivity in visual cortex using intracellular recordings with Dr David Ferster. We embarked on a series of studies testing whether a feedforward model could account for cortical motion and orientation selectivity. Following my work with Dr Ferster I established my lab at the University of Texas, Austin, where I study visual processing using a combination of 2 photon microscopy and electrophysiology in rodents and primates.

**Abstract:** The spiking responses of neocortical neurons are remarkably variable. Distinct patterns are observed when the same stimulus is presented in the sensory areas or when the same action is executed in motor areas. This is quantified across trials by measuring the Fano factor of the neuronal spike counts, which is generally near 1, consistent with spiking times following a noisy Poisson process. The two candidate sources for noise are the synaptic drive that converges on individual neurons or intrinsic transducing processes within neurons. To parse the relative contributions of these noise sources, we made whole-cell intracellular recordings from cortical slices and used in the whole cell dynamic clamp configuration while using dynamic clamp to injecting excitatory and inhibitory conductances previously recorded in vivo from visual cortical neurons (Tan et al. 2011). By controlling the conductance directly, we can test whether intrinsic processes contribute to poisson firing. We found that repeated injections of the same excitatory and inhibitory conductance evoked stereotypical spike trains, resulting in fano factors near 0.2. Varying the amplitude of both excitatory and inhibitory conductances changed the firing rate of recorded neurons but not the Fano factor. These records indicate that intrinsic processes do not contribute substantially to the Poisson spiking of cortical cells. Next, to test whether

differences in network input are responsible for Poisson spike patterns, we examined spike trains evoked by injecting excitatory and inhibitory conductances recorded from different presentations of the same visual stimulus. These records exhibited different behaviors depending on whether the injected conductances were from visually-driven or spontaneous epochs: during visually-driven epochs, spiking responses were Poisson (Fano factor near 1); during spontaneous epochs spiking responses were super-Poisson (fano factors above 1). Both of these observations are consistent with the quenching of variability by sensory stimulation or motor behavior (Churchland et al. 2010). We also found that excitatory conductances, in the absence of inhibition, are sufficient to generate spike trains with Poisson statistics. In summary, our results indicate that the Poisson spiking emerges not from intrinsic sources but from differences in the synaptic drive across trials, the nature of this synaptic drive can alter the nature of variability, and that that excitatory input alone is sufficient to generate Poisson spiking.