Modeling optogenetic manipulation of neural circuits in macaque visual cortex

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In recent years, a host of optogenetic tools have been developed, enabling experimentalists to manipulate neuronal activity with high temporal precision and cell-type specificity. This positions us to causally perturb the cortical circuit in ways that, when linked with computational modeling techniques, make it possible to test specific hypotheses about cortical circuits.

Using optogenetics in the awake macaque, recent research in our lab has shown that activation of pyramidal neurons results in both facilitation and suppression of visually-evoked neuronal responses. These effects can be additive, multiplicative, or reflect competitive interactions between visual and laser-evoked responses (Figure 1A). We find that many of these changes can be accounted for by a simple normalization model (Figure 1B), in which laser activation of excitation results in indirect activation of inhibition, modulating the gain of neurons. This model, however, is abstract, and does not adequately account for the dynamics of the neuronal response. We have therefore developed a Hodgkin-Huxley model in which we explicitly model light-activated opsin conductances (Figure 1C).

The model makes testable predictions about changes in spiking response dynamics across different temporal patterns of laser stimulation. For example, the model predicts that phase-randomized, slow oscillating inputs leads to increases in Fano Factor and coefficient of variation (Figure 1D). These findings provide insight into how temporally-patterned optogenetic stimulation leads to changes in neuronal dynamics. More importantly, this illustrates how computational neural modeling can be combined with optogenetics to gain insight into cortical information processing.

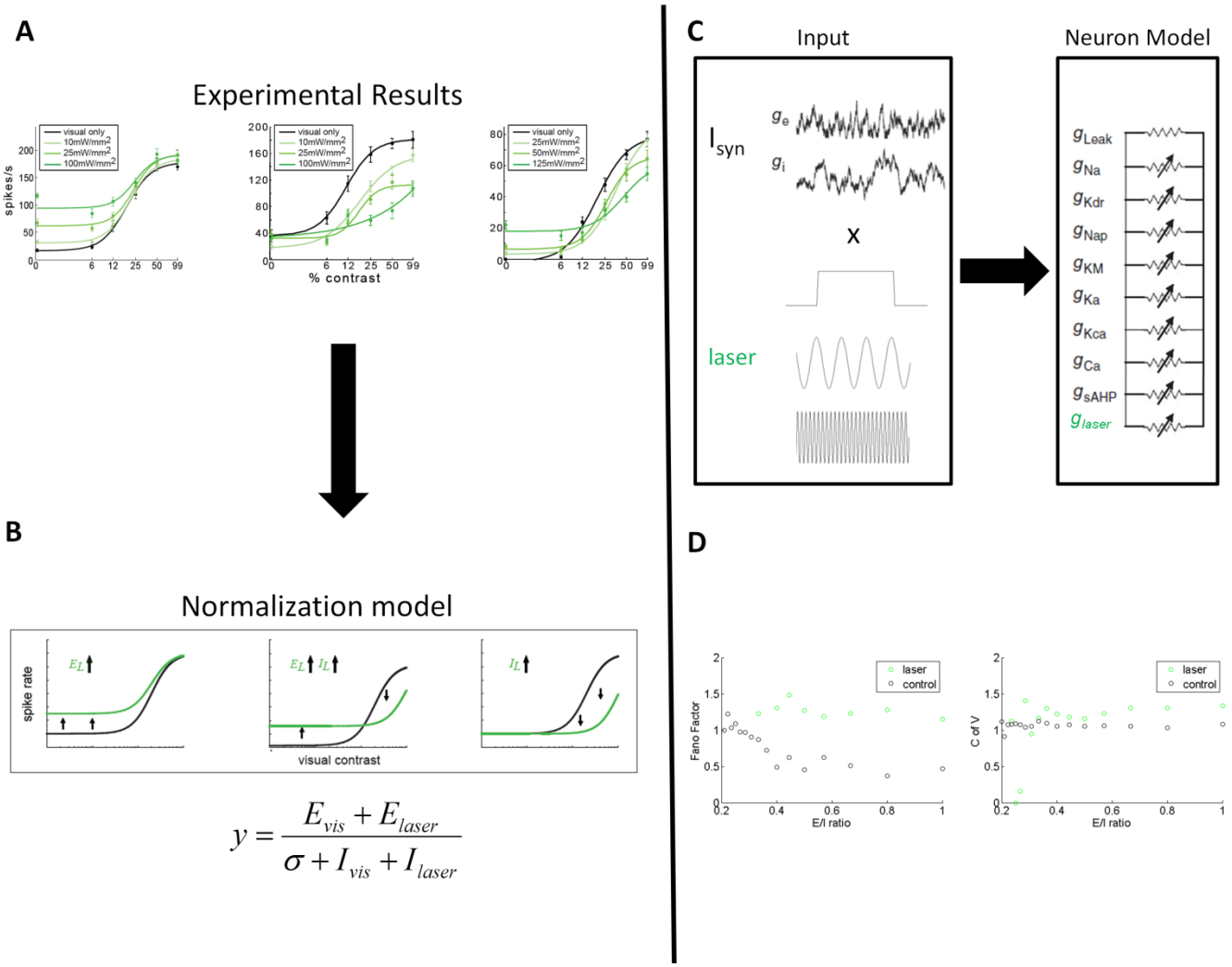

Figure 1: (A) Laser stimulation of excitatory pools of neurons leads to many changes in neuron responses including facilitative (left), suppressive (center) and mixed (right) responses. (B) These changes can be accounted for by the normalization model, where laser activation of pyramidal neurons increases excitation and inhibition at different levels. This model, however, is abstract and does not take into account the dynamics of the neurons. (C) A more realistic Hodgkin Huxley model was developed to make testable predictions about how these neurons responses will change under laser stimulation conditions, including sustained laser activation and laser activation across a range of biologically relevant temporal frequencies. The simulated laser is incorporated into the model by modulating the excitatory and inhibitory synaptic inputs to the cell as well as adding a opsin conductance to the neuron model. (D) Plots showing the change in Fano Factor and coefficient of variation as a function of excitation-inhibition ratio. Phase-randomized, slow oscillating (5Hz) current introduced to the synaptic current leads to increases in Fano Factor (left) and the coefficient of variation (right) in the laser condition relative to the control.