Voltage-triggered methods for intracellular neural characterization in visual cortex

Evan Archer, Nicholas J. Priebe & Jonathan W. Pillow, University of Texas at Austin

Summary: Sensory neurons respond to a limited number of stimulus features, ignoring most axes in the high-dimensional space of natural signals. Neural characterization methods therefore seek to identify the low-dimensional “feature space” to which neurons are sensitive. Previous work has focused on “spike-triggered” methods for identifying features that drive binary spiking responses, but has not examined the subthreshold membrane potential that underlies these responses. Here we compare and contrast the stimulus features drove both analog membrane potential and binary spike responses using intracellular recordings of single neurons in primary visual cortex. We begin by introducing several moment-based estimators for dimensionality reduction of analog data that were (independently) developed in statistics, a group of methods known as *inverse regression.* We applied four of these methods, and one novel method (“voltage triggered covariance”), to recordings of simple and complex cells in V1, which were stimulated with a 1D white noise (“flickering bars”) stimulus. Compared to spike-triggered analysis, voltage-triggered analyses recovered more dimensions (“filters”) for the same neuron. Moreover, predictions of membrane potential based on a quadratic model of filter responses yielded more accurate predictions of voltage than did a corresponding model of spike trains. While these methods are especially successful in predicting the responses of simple cells (mean R^2=.65), they yield more–and more functionally significant–filters for complex cells (mean R^2=.23) [Fig. 1]. Taken together, these methods hold great promise for illuminating the transformations from stimulus to membrane potential in visual cortex, and the mechanisms by which a neuron filters and transforms these signals in order to emit spikes.

Additional detail: We analyze the performance and theoretical properties of four moment-based estimators from the statistics literature: Sliced Inverse Regression (SIR), Sliced Average Variance Estimation (SAVE), Directional Regression (DR), and Likelihood Acquired Dimensionality Reduction (LAD). In addition, we introduce voltage-triggered average and covariance analysis (VTA / VTC), which is a direct analogue of STA and STC. Each of these techniques, including STA and STC, may be understood as methods of inverse regression where, in contrast to the “forward” approach of modeling the conditional distribution of the response given the predictors, $Y|X$, we instead model $X|Y$. In inverse regression, we use changes in the conditional mean and variance, $E[X|Y]$ and $E[XX^T|Y]$, to select relevant features from the high-dimensional stimulus X. From the reduced feature spaces estimated using the above methods, we are free to model $Y|X$. We review several models in addition to the above-mentioned quadratic nonlinearity; in particular, LAD models $P(X|Y)$ as Gaussian (a model that is closely related to "iSTAC", Pillow & Simoncelli 2006), which may then be inverted using Bayes rule to obtain $P(Y|X) = P(X|Y)P(Y)/P(X)$, and thus a model for the expected response for a given stimulus. We compare the number of features relevant to prediction of both simple and complex cells, and quantify the ability of these models to capture the spatial and temporal frequency tuning in response to drifting gratings.

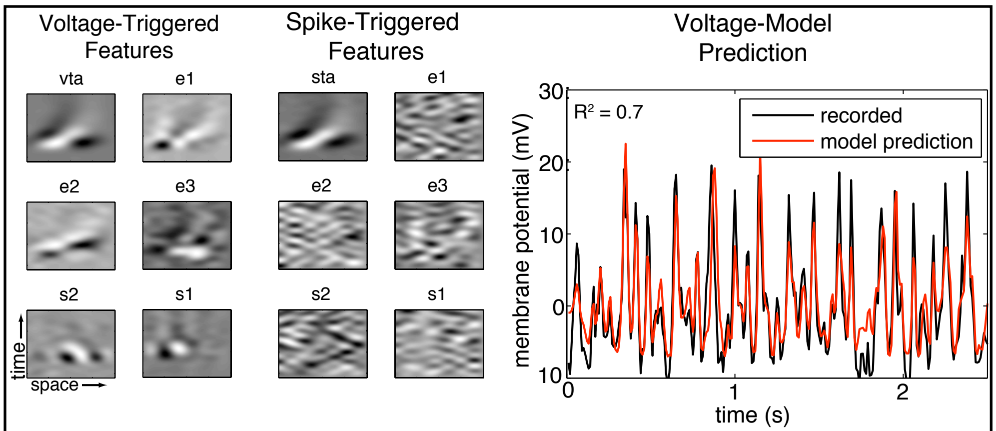

Fig 1. Simple cell responses analyzed with spike-triggered and voltage-triggered analyses. Left: excitatory (e) and suppressive (s) stimulus features affecting the voltage and spiking responses for a single cell. Right: predicted vs. recorded voltage response to a test stimulus.