Journal Club

Editor's Note: These short, critical reviews of recent papers in the *Journal*, written exclusively by graduate students or postdoctoral fellows, are intended to summarize the important findings of the paper and provide additional insight and commentary. For more information on the format and purpose of the Journal Club, please see http://www.jneurosci.org/misc/ifa_features.shtml.

Parsing and Predicting Increased Noise in Visual Cortex

Tucker G. Fisher
University of California at Davis, Center for Neuroscience, Davis, California 95618
Review of Schölvinck et al.

The variability of spike trains recorded from cortical neurons in response to identical stimuli is striking. Although cortical response variability has been extensively studied, particularly in primary visual cortex (V1), the origin of this variability is largely unknown. It is unlikely that cortical response variability originates at the cellular level, given that experiments attempting to attribute variance to either noisy integration of synaptic input or noisy spike production find that these processes do not account for a sufficient amount of response variability (Softky and Koch, 1993; Mainen and Sejnowski, 1995). Thus, the origin of response variability likely involves network interactions. Although some evidence points toward a thalamic contribution to response variability (Sadagopan and Ferster, 2012), it is generally accepted that the spike count response of V1 neurons is more variable than that of neurons in the lateral geniculate nucleus (LGN) of the thalamus (Goris et al., 2014). Consequently, it seems likely that a large amount of cortical response variability originates from circuits within the cortex (Tsodyks et al., 1999; Kenet et al., 2003). Understanding response variability is an important step toward deciphering and distinguishing signal from noise in the cortex as well as understanding the communication of information between cortical neurons (Ecker and Tolias, 2014).

In a recent publication appearing in *The Journal of Neuroscience*, Schölvinck et al. (2015) describe results from experiments aimed at identifying the origin of response variability in cat visual cortex. The authors describe three primary reasons as to why the field has had difficulty reaching a consensus about the origins of cortical variability. First, although the LGN is consistently reported to be less variable than V1, the amount of variability reported in V1 is not consistent in the literature (Kara et al., 2000; Carandini, 2004; Goris et al., 2014; Schölvinck et al., 2015). Second, the level of variability across neurons in V1 has rarely been analyzed among large populations of neurons (Goard and Dan, 2009); instead, the majority of studies have focused on single-unit variability or shared variability between pairs of V1 cells (Carandini, 2004; Cohen and Kohn, 2011). Examining patterns of variability, for example, by comparing variability between locations with similar orientation preference, should help to place constraints on the nature of the circuit interactions. Third, and particularly important, the effect of cortical state on shared variability is uncertain. For instance, when the cortical network is in a synchronized state, as occurs with sleep, periods of low arousal, and anesthesia, cortical neurons are more highly correlated than when the cortical network is in a desynchronized state, which is typical during alert sensory processing (Steriade, 2003; Goard and Dan, 2009). Although it is generally accepted that neuronal correlations change as the cortex transitions between synchronized and desynchronized states (Steriade, 2006), the extent to which cortical-state-dependent correlations contribute to cortical response variability is unclear. To this end, Schölvinck and colleagues (2015) developed a global noise model to investigate the relationship between shared variability and cortical state.

To provide a foundation for their later experiments, Schölvinck et al. (2015) began by comparing LGN spike count variability to V1 spike count variability using the same stimuli recorded with single electrodes. This was necessary to overcome obstacles associated with making quantitative comparisons between results previously reported in studies that used different stimuli to drive activity. For the remainder of Schölvinck et al.'s (2015) study, multiple repeats of sequences of flashed stationary gratings that varied in stimulus orientation and spatial phase were presented to anesthetized cats while recording neuronal responses with multielectrode arrays. Importantly, the stimulus sequences presented while recording from the LGN and V1 were identical with the exception that frame duration was adjusted for the lower preferred temporal frequencies of V1 neurons (Movshon et al., 1978; Alitto and Usrey, 2004).

To quantify the difference in response variability between the LGN and V1, the variability index (VIn) was computed for each neuron: the ratio of variance to mean spike count, or Fano factor. Consistent with previous results (Carandini, 2004; Sadagopan and Ferster, 2012; Goris et al., 2014), Schölvinck et al. (2015) deter-

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Correspondence should be addressed to Tucker Goodroe Fisher, 1544 Newton Court, Davis, CA 95618. E-mail: tgfisher@ucdavis.edu.
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mined that spike count variability in V1 was on average greater than in the LGN (V1 = 2.7 ± 0.3, LGN = 1.0 ± 0.1).

Next, Schölvinck et al. (2015) quantified the variability shared across V1 neurons using a model supplied with cortical responses recorded with a multielectrode array. With this model, called the global noise model (GNM), the authors predicted the responses of each V1 neuron by combining the noise of the surrounding cortex with the average response for that neuron. Noise was calculated for each location and trial by subtracting the actual response from the average trial response at that location. The average of noise terms across all surrounding locations was considered the noise of the surrounding cortex for that particular location. Results of this effort revealed that knowledge of the trial-to-trial response variability of large numbers of neighboring cortical neurons significantly improved the ability to predict cortical responses. In particular, the GNM accounted for a statistically greater amount of the response variability compared with predictions made using the average response alone for both single-unit activity (~50–70%) and multiunit activity (~80–95%).

Schölvinck et al. (2015) suggest the increased predictability of multiunit activity is a natural consequence of single-unit activity summation. That is, when summing the activity of multiple units, the shared noise will sum together constructively whereas private noise (i.e., that which is not shared among neurons) will likely sum destructively to zero. The nature of the GNM is to make a prediction of the noise at a single neuron (or electrode, in the case of multiunit activity) based on the noise of the neurons (or electrodes) surrounding it. Augmented shared noise present in multiunit activity enables the GNM to make a more effective inference as to the noise that is present at the electrode in question.

Schölvinck et al. (2015) also found that response variability tended to be higher in sessions where recent ongoing activity was characterized by large fluctuations. The existence of global fluctuations was quantified as the standard deviation divided by the mean of the ongoing activity collected during presentations of a gray screen between stimulus sequences [global fluctuation index (GFIn)]. The stimulus-driven VIn was positively correlated with GFIn ($r = 0.71$), indicating that variability during ongoing activity and variability during stimulus-driven activity may have a common source.

In a separate study, Ecker et al. (2014) described global fluctuations in V1 variability in the anesthetized macaque monkey across similar timescales as those in Schölvinck et al. (2015). Ecker and colleagues (2014) parameterized spike count variability in their study with the Gaussian process factor analysis (GFPA) model (Yu et al., 2009). Unlike the GNM, where a new prediction is made for each time point independent of past predictions, the predictions in the GPFA model are tethered to past predictions. The GPFA requires the variable representing the network state covariance to change smoothly through time, constrained by a Gaussian, the standard deviation of which is a free parameter fit to the data, centered at $\Delta t = 0$. Schölvinck et al. (2015) found the timescale of global fluctuations present in single-trial data to approximately match the timescale of the median time constant for network state dynamics in anesthetized V1 (mean = 207 ms) from Ecker et al. (2014). Ecker et al. (2014) reported that the GFPA model was not as effective in awake, fixating macaque, where network state fluctuations are relatively small and rapid. However, the unconstrained GNM would likely do very well with data from alert animals because global noise is calculated for each time point independently from another, allowing for accurate predictions during rapid changes in cortical state.

The GNM suggests that a large amount of cortical variability can be accounted for by non-stimulus-driven fluctuations in cortical activity that are shared across large populations of cortical neurons. Previous work has established a relationship between neuronal variability and cortical network state (for review, see Schölvinck et al., 2015). Schölvinck et al., 2015 provide evidence that the higher pairwise correlations in V1 arise from global fluctuations present in synchronized cortex. Pairwise correlations were consistently higher in synchronized cortex (defined as GFI > 0.6) compared with desynchronized cortex (GFI < 0.6) across the spontaneous correlations, stimulus-driven correlations, and noise correlations. Importantly, single-trial spontaneous activity, stimulus-driven activity, and noise isolated from synchronized cortex were all characterized by global fluctuations, whereas global fluctuations were absent in desynchronized cortex.

Interestingly, Schölvinck et al., 2015 did not find a pattern of increased pairwise correlations among cells with shared orientation preference during fluctuations in global activity. Data from Tsodyks et al. (1999) suggested that correlations may be higher among neurons of similar orientation preference in both ongoing and stimulus-driven activity. Additionally, an equation proposed by Harris and Thiele (2011) predicts some positive correlations between neurons but does not specify correlation amplitudes between individual neurons or determine whether correlation amplitude depends on orientation preference. Schölvinck et al., 2015, however, identified cortical state, not orientation preference, as the major determinate of cross-correlation strength. In short, increased pairwise correlations in more synchronized states are largely due to global activity fluctuations.

To strengthen this notion, Schölvinck et al. (2015) investigated the contribution of local noise to variability. The GNM suggests that local noise, defined as the difference between the real response and the GNM prediction, makes a much smaller contribution to cortical variability than shared global noise. Because pairwise correlations in local noise are equivalent between synchronized and desynchronized states, the differences seen in spontaneous, stimulus-driven, and noise pairwise correlations as the network state shifts toward a synchronized state are likely due to global activity. In other words, global noise is found to increase as the cortex shifts toward a synchronized state, whereas local noise remains constant.

In summary, Schölvinck et al., 2015 connected three fairly discrete aspects of the shared cortical variability and noise-correlation literature. Namely, they provided a concise comparative examination of spike-count variability between the LGN and V1 and attribute depth of anesthesia as a potential muddling factor in the literature. They then created a predictive model that used shared noise among large populations of cortical neurons to explain the majority of variance observed in single-unit and multiunit activity. In so doing, they tied global fluctuations to stimulus-driven as well as spontaneous activity. And finally, they showed that correlation strength in anesthetized animals is influenced by relative cortical state.

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