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.

Neural Correlates of High-Frequency Intracortical and Epicortical Field Potentials

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Review of Ray et al. (<http://www.jneurosci.org/cgi/content/full/28/45/11526>)

Electrocorticography (ECoG), the use of nonpenetrating electrodes to record brain potentials directly from the surface of the cerebral cortex, has emerged as a promising tool for obtaining recordings of high spatial and temporal resolution. Numerous studies have described the patterns of ECoG activity associated with various sensory, motor, and cognitive tasks in different cortical areas (see references in Ray et al., 2008). It has been suggested that high (>60 Hz) frequency components of these signals represent activation of neuronal populations in the underlying cortex (Crone et al., 2006), but experimental evidence is, at best, scarce. More data exist on the relationship between intracortical local field potentials (LFPs) and neuronal activity (Logothetis et al., 2007), but the picture is far from complete. Despite the fact that ECoG and LFP are thought to be generated by similar mechanisms operating at different spatial scales, their relationship is still unclear. The study by Ray et al. (2008) addresses the issue of what the neuronal correlates of these high frequency LFP and ECoG modulations

might be, from both an experimental and a theoretical perspective.

The study comprises two parts. In the first, the authors recorded single units and LFPs, through the same electrodes, from the secondary somatosensory cortex (S-II) of the monkey, while delivering vibratory tactile stimuli on the contralateral hand. When aligned at the onset of the stimulus, average firing rate of those neurons that were excited by the stimulus (the “excited” population) showed a characteristic biphasic pattern, with an early peak followed by a more sustained, relatively slowly decaying, phase [Ray et al. (2008), their Fig. 1A (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F1>)]. An almost identical time course was seen in the average, normalized power of the high-gamma (60–150 Hz) component of the LFP (hgLFP) recorded in the same sessions [Ray et al. (2008), their Fig. 1B, top (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F1>)]. Although correlation coefficients between the average time courses of firing rate and hgLFP power across all excited neurons were very high (up to 0.92 at the highest stimulus intensity), in the case of individual neurons they were much lower; only in a small subset of these neurons correlation reached statistical significance (fewer than 6 of 72 neurons, at any stimulus intensity). It seems as if neuronal firing and hgLFP power exhibit similar evoked changes on average, but their covariance is weak [Ray et al. (2008), their

supplemental Fig. 2 (<http://www.jneurosci.org/cgi/content/full/28/45/11526/DC1>)].

It is unclear what the physiological cause of this discrepancy could be, but it could provide some insight into what the sources of hgLFP might be. Had action potentials of the recorded cell been the sole source of power in the high-gamma range, one would have expected a tight relationship, on a cell-by-cell, even on a trial-by-trial basis. In a recent study, it was found that after removing the spike waveform-associated component from high-frequency LFP, there was still enough information in the latter that allowed the prediction of the exact timing of a significant proportion of the removed spikes (Zanos et al., 2008). Contamination from spike waveforms from nearby cells, too small or too variable to be detected as single unit spikes, sometimes called multiunit activity (MUA), could be another potential source for hgLFP. In that sense, it would be interesting to assess the correlation between MUA rates (extracted by high-pass filtering of the raw signal and applying a threshold) and hgLFP power on a trial-by-trial basis (Bereins et al., 2008). A stronger covariance of MUA and hgLFP than that of single unit activity (SUA) and hgLFP would in addition imply a certain amount of correlation in the firing of nearby neurons, something of particular relevance to the modeling section of this study. A third possibility is that evoked hgLFP captures part of the afferent, thalamocortical, synaptic input to

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S-II. That would explain why the time courses of evoked spiking activity and hgLFP power match so closely on average, reflecting the relatively consistent time course of their common source. It would also explain why they differ so greatly in amplitude from trial to trial, each bearing a different, and stochastic, relationship to the thalamocortical input that drives them.

An indirect way to test that would be to compare the direction and/or orientation selectivity of evoked neural responses in S-II, similar to what has been done in visual cortex (Berens et al., 2008). Finding different spatial distributions of feature selectivity for SUA versus MUA versus hgLFP would point to different sources and generating mechanisms for these three signals. There are neural models of how afferent and intracortical processes possess or generate feature selectivity in primate somatosensory cortex which could help explain the anatomic basis of such spatial distributions and, in effect, of unit-LFP activity relationships (DiCarlo and Johnson, 2000; Temereanca and Simons, 2003).

In the second part of the study, Ray et al. (2008) used a computational model to explore one of the alternatives for what might be mediating high-gamma changes, namely neuronal synchrony. In their model, the ECoG signal is produced by the temporal summation of voltage dipoles generated from individual action potentials of cells at different vertical distances from the surface recording electrode [Ray et al. (2008), their supplemental Fig. 1 (<http://www.jneurosci.org/cgi/content/full/28/45/11526/DC1>)]. The generated ECoG signal comprises a range of different frequencies, including high-gamma. The authors separately assessed the effect on high-gamma ECoG (hgECoG) power of changes of the average firing rate of cells [Ray et al. (2008), their Fig. 4A (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F4>)] and of the amount of synchrony between them [Ray et al. (2008), their Fig. 4B (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F4>)]. They found that increases in either firing rate or synchrony lead to increases in high-gamma power, but at different rates, at least for the range of values reported. To use their example, the same increase in hgECoG power was obtained by either a 10-fold increase in firing rate (from 10 spikes/s to 100 spikes/s) or an increase in synchrony by two percentage points (from 0% to 2% of all cells firing synchronously) [Ray et al. (2008),

their Fig. 4C (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F4>)]. The proportion of synchronous cells needed to obtain the same high-gamma power increase as a 10-fold increase in firing rate, for the case where action potentials were modeled as dipoles (model exponent of 2), ranged roughly between 0.5% and 2.7%, depending on the size of the modeled neuronal population [Ray et al. (2008), their Fig. 4D (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F4>)]. Similar results were produced by increasing the correlation between the spike trains generated by all model neurons; a correlation coefficient between $0.1-0.8 \times 10^{-3}$ was needed to obtain the same high-gamma power increase as a 10-fold increase in firing rate, under the same model conditions as before [Ray et al. (2008), their Fig. 5 (<http://www.jneurosci.org/cgi/content/full/28/45/11526/F5>)].

One of the central assumptions of the model is that ECoG reflects only contributions from action potentials, arising at different cortical depths. That assumption predictably accentuates the effect of spike synchrony. However, whereas, as the authors point out, spike waveforms dominate the high-gamma component of the LFP recorded immediately next to each cell, it is not clear whether that is the case for more distant recording sites. In fact, there are a number of reasons why one would not expect that in the case of ECoG. The larger and more numerous pyramidal cells have their somata residing mainly in cortical layer V and their dendritic arbors in more superficial layers, i.e., closer to the ECoG electrode. Rates of excitatory and inhibitory PSPs generated on the dendrites of any pyramidal cell outnumber that cell's firing rate by several orders of magnitude. A typical action potential is no more than a couple orders of magnitude larger than a typical EPSP. Finally, a typical PSP is ~ 10 ms long, and its frequency components are well inside the high-gamma range. It would be interesting to examine what the effects of rate and synchrony, or correlation, of synaptic inputs to a neuronal population would be on a modeled ECoG signal. It might turn out, for example, that because PSPs are much more numerous and longer in duration than spikes, there would be substantial temporal summation during increases in PSP rates. Such temporal summation could potentially generate the increases in hgECoG power typically seen in experiments, without changes in synchrony. However, synchrony on the synaptic in-

put side has been proposed as an important mechanism for dendritic integration in pyramidal cells (Spruston, 2008), and it might well turn out to be a very effective means for driving hgECoG.

The ranges of synchrony and correlation values used in this model seem plausible, but ultimately they require experimental confirmation. As the authors point out, the few studies that have provided quantitative measures of neuronal correlations and synchrony in sensory cortices suggest that the selected ranges in the model possibly overestimate the amount of correlated firing (Gray and Viana Di Prisco, 1997; Steinmetz et al., 2000; Maldonado et al., 2008). However, those studies included relatively small numbers of pairs of simultaneously recorded neurons. The widespread availability of various chronic, multielectrode recording techniques may eventually provide a more accurate estimate of cortical synchrony.

The development of a biology-driven model in this study represents a first significant attempt to bridge scales: the microscopic neural signals recorded intracortically next to single cells, with the macroscopic potentials recorded on the surface of the cerebral cortex. In most of the previous computational models of evoked cortical responses, only intracortical neuronal and LFP activations were considered (Pettersen et al., 2008). In those studies, however, as well as in numerous experimental ones (Temereanca and Simons, 2003), it has been shown that different cortical layers possess different response properties, in terms of both LFP and neuronal activity. It would be interesting to examine what the effects of this laminar organization of the neural response would be on the simulated ECoG signal.

Both experimental and theoretical studies, including this one, suggest that local neuronal activation is a likely source of high frequency LFP and ECoG modulations in the cortex. In addition to modeling work, it will be essential to perform simultaneous intracortical and epicortical recordings in behaving animals, under various behaviors, to directly address what exact aspects of neural activity generate the ECoG signal.

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