



Identifying neural contributions to the local field potential through modeling: a review of Barbieri et al. (2014)

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ABSTRACT

This is a journal-club style review of the paper “Stimulus dependence of local field potential spectra: experiment versus theory” by Barbieri et al. (2014).

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Measuring which neurons spike at what times in relation to an organism’s perceptions and actions is crucial for establishing how computations are implemented in the brain. Recording spikes from more than a few neurons at a time, though, is difficult, and even modern recording technologies that allow spikes from hundreds of neurons to be recorded simultaneously (Stevenson and Kording, 2011) massively under-sample the spikes fired in a local neural population. This limitation has led to an interest in methods for inferring spiking activity from gross measures of population dynamics such as the local field potential (LFP). The LFP, which is the low frequency part (≤ 500 Hz) of the signal measured by an extracellular electrode, primarily reflects synaptic currents near the electrode (Einevoll et al. 2013). Though synaptic activity is directly related to spiking, inferring local spiking from the LFP is non-trivial: each neuron receives thousands of synapses, from both local and distant sources, with temporally overlapping currents. The LFP is also affected by other slow, non-synaptic neuronal membrane currents, further complicating its interpretation (Einevoll et al., 2013).

In a recent study published in the *Journal of Neuroscience*, Barbieri et al. (2014) attempt to disambiguate the neuronal contributions to the LFP by using mathematical modeling, extending previous work by Mazzoni et al. (2008). Mazzoni et al. proposed that stimulus-induced gamma frequency (30-100 Hz) LFP fluctuations in primary visual cortex are generated within the cortical network and are caused by high thalamic firing rates, while low-frequency LFP fluctuations reflect slow variations in the thalamic input. To investigate their hypothesis, they simulated a cortical network made up of recurrently connected excitatory and inhibitory model neurons. They stimulated the network with time-varying inputs, based on multi-unit activity (MUA) recordings from the lateral geniculate nucleus (LGN) of anaesthetized monkeys being shown movies (Belitski et al. 2008), thus representing an estimate of the spiking input to the cortical network from the thalamus. They then calculated how much information each frequency in the simulated LFP signal conveyed about the input stimulus, confirming that low LFP frequencies reflected slow input fluctuations, while gamma frequency power independently increased with increasing input firing rate.

This model provides a mechanistic explanation for how stimulus features modulate network activity, and in turn how that activity affects the LFP. However, while conceptually simple, the model is too computationally demanding to fit its parameters to experimental data; instead, they were set using

literature-derived values and hand-tuned so the simulated and experimental LFPs matched (Mazzoni et al. 2008). Barbieri et al. (2014) address this issue by deriving a simplified model that retains the key dynamical properties of Mazzoni et al.'s network while allowing model output to be calculated analytically rather than requiring long simulation runs. Their model builds on recent work analyzing spiking neural network model responses to fluctuating inputs (Ledoux and Brunel 2011) by deriving an analytical expression to calculate the LFP power spectrum from such a model. This crucial step allows the model to be fit to experimental LFP data.

After checking that their analytical expressions produced similar LFP profiles to the network model they were reduced from, Barbieri et al. (2014) tested their model fitting procedure by using it to recover model parameters from analytically calculated LFP spectra. This represents the lowest hurdle the fitting method should overcome: finding the correct parameters when fit to data generated by the same model. Though seemingly trivial, success was not guaranteed because the model can produce very similar LFP spectra with very different sets of parameters. In fact, the fitting procedure produced many well-fitting parameter sets that were far away in parameter space from the true parameters. However, the median values from the parameter distributions producing good fits were found to provide reliable estimates of the true parameter values.

Having performed this check, Barbieri et al. then fit the model to Belitski et al.'s experimental LFP recordings (Belitski et al. 2008) using a two-step procedure – the first step to fix the synaptic strength parameters, and the second to find the base firing rates and external input parameters for each movie scene. This procedure reflects that the visual input, and therefore input to the cortical network from the LGN, could vary substantially between movie scenes, while the synaptic weights will not fluctuate dramatically. As before, the distribution of well-fitting synaptic parameters was broad, and median values were chosen and fixed before the second fitting stage.

As the relevant parameters could not be measured experimentally to verify the model fits, Barbieri et al. assessed whether the model predicted other experimental measurements that had not been used to constrain the parameters. The most direct of these was the MUA, measured with the same electrodes as the LFPs. The MUA is a proxy measure for the local network firing rate, so the model firing rate should correlate with the MUA if it captures the network dynamics accurately. Indeed, model firing rates correlated significantly with the MUA in over half the movie scenes, with a mean correlation coefficient of ~ 0.5 . They also correlated with the movie scene spatial contrast in $\sim 30\%$ of scenes, and movie temporal contrast in $\sim 15\%$ of scenes (both with mean correlation coefficient ~ 0.4). This lower level of correlation than for the MUA suggests a complex relationship between stimulus features and primary visual cortex firing rate. This relationship is influenced by the nonlinear amplification of correlations in natural images by the LGN (Lesica et al. 2004). Indeed, the relatively low number of scenes with significant correlations between the parameter controlling model input fluctuations and movie spatial/temporal contrast ($\sim 20\%/\sim 40\%$, both with correlation coefficient ~ 0.4) suggests that the model's simplified input representation may not be a generally suitable representation of the LGN response. Finally, Barbieri et al. calculated the information content of the LFP power in both model and experimental recordings. In both cases, most information about the stimulus was represented in the gamma frequency band and at low frequencies, as explained previously by Mazzoni et al. (2008).

This set of results is encouraging, indicating that a simple yet biologically relevant model can be fit to experimental measures of population activity, and provide insights into the underlying neuronal dynamics. This raises some intriguing possibilities for using such models when interpreting LFP signals for controlling neuroprosthetics. Ideally, spiking output would be used to control such devices, but the technical challenges required to record single neurons reliably for extended periods are prohibitive, leading to interest in the LFP as a control signal (Andersen et al. 2004). Recently, Hall et al. (2014) showed that single neuron firing rates in monkey motorcortex could be estimated using multiple low frequency (< 5 Hz) LFP recordings. It would be interesting to see if their estimates, which relied on particular low-frequency features identified in the spike-triggered-average LFP, could be improved by

using firing rate estimates from a model similar to Barbieri et al.'s. The model's formulation, allowing the firing rate to be calculated analytically, offers the potential to do this in real time, making it practical for neuroprosthetic control. The network model could also prove useful in establishing the mechanisms underlying the low-frequency LFP features identified by Hall et al., which remain unknown.

However, further analysis is required prior to such practical applications. Firstly, the model should be fit to LFPs generated by more detailed cortical models so that its reliability can be assessed with "ground truth" data (Einevoll et al. 2013), and to establish the crucial elements affecting parameter estimation. For example, Barbieri et al.'s best-fitting parameter sets suggest electrode position plays an important role, as the parameter distributions across several electrodes were much broader than for single electrodes. Several detailed cortical models designed for investigating LFP variation across space were recently developed (Lindén et al. 2011, Tomsett et al. 2014), so this kind of analysis is already possible. Secondly, while input parameters and synaptic weights were fit to data, some parameter values – such as membrane and synaptic time constants – were built into the model. The sensitivity of the parameter fits on these built-in values should be thoroughly assessed. Finally, good fits were not achieved for a proportion of the experimental data, and firing rate predictions from well-fitting models did not always correlate with the MUA. In particular, the chosen input representation may not be suited to modeling LGN responses to naturalistic stimuli. Identifying the origins of each discrepancy between model output and experimental data will inform us of the conditions under which the model provides a valid description of the neural activity, and could give insights into the mechanisms behind dynamics not captured by the model.

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