Evidence for slow (2-10 Hz) and gamma frequency coherence between spike trains and local field potentials in the cerebellum

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Abstract

A method for detecting relationships between single-unit spike trains and local field potentials (LFPs) was developed and applied to recordings from rat cerebellum. LFPs were repeatedly filtered with a shifting frequency window. The resulting traces were transformed into peak-time point processes for comparison with spike trains using 'relative-phase' analysis (Chen and Nitz, in press). Discharge of some Purkinje cells was phase-related to LFP oscillations in the 2-10 Hz and 30-50 Hz frequency ranges. This analysis method revealed hidden coherency between spike-trains and LFPs. The findings suggest that cerebellar activity is, to some extent, temporally organized according to both slow and fast rhythms.

Keywords: Cerebellum; Spike trains; Local Field Potential (LFP); Coherence

1 Introduction

The correlation of single-unit neuronal recordings to their associated LFPs can be difficult to study because spike trains are discrete point processes and LFPs are continuous. Direct cross-correlation (spike-triggered averaging) of these mixed time series is not always appropriate because it requires averaging of multiple trials or time windows and can be dominated by the frequency having greatest power in the LFP. Thus, this method cannot determine the time-series of interactions between spike-trains and LFPs and is incapable of measuring transient periods of coherence. Furthermore, fluctuations of LFP frequencies exhibiting relatively high spectral power can mask significant correlations at other higher frequencies.

For these reasons, we developed a novel method by which to study correlations between mixed time series more effectively. The method, 'relative-phase' analysis, was then used to address an outstanding question concerning cerebellar function. That is, is simple-spike discharge of Purkinje cells coherent, and at what frequencies, with population activity within the cerebellum as measured by the LFP?

2 Materials and Method

Cerebellar, single-unit spike trains of putative Purkinje cells and their associated LFPs were recorded using stereotrodes. Recordings were made as rats performed a simple shuttling task for food reward [4]. LFPs were filtered with a shifting (0.5Hz-step), narrow-range (2 Hz) frequency window. The filtered traces were then converted to point processes by determining peak times. The temporal relationship between these LFP "events" and single-unit action potentials were studied for each narrow frequency range. Relative phase analysis was used to determine the instantaneous phase relationship between the converted LFPs and single unit spike trains. Relative phase here is defined as the relative timing difference between two point processes normalized by the associated interval of one process. The time of each single unit action potential was assigned a normalized phase (from 0 to 1) based on its temporal position between two peak times of the LFP for each frequency range tested (1-50 Hz). Thus, for all frequencies between 0 and 50 Hz, an averaged plot of phase versus spike discharge can be generated. The phase associated with each spike can also be analyzed as a time series in which transient periods of phase-locking to one or more LFP frequencies may be found. Note that this method also bypasses potential artifactual cross-correlations that occur between two point processes when one or both exhibit a high level of rhythmicity [5].

Figure 1 demonstrates the idea of the method. A trace of LFP was filtered at a specified frequency window while preserving the phase information using Matlab (Mathworks, MA). The peak (or valley) timing of the filtered LFP was identified across the whole recording. The relative phase of a spike discharge in relation to the LFP was calculated based upon the timing differences between the spike and the peak (or valley) of the LFP normalized by the adjacent inter-peak distance. The correlation between the spike and the associated LFP can be revealed by the probability distribution of the relative phase between the two. If there is no correlation, the relative phase should distribute evenly between 0 and 1. Otherwise, peaks or valleys in the phase distribution imply correlation and preferred phase relations between the discharge of the spike and the LFP at a certain frequency range.

3 Results

Strong phase relationships between spike discharge and particular LFP frequencies were found for some cells. In cells exhibiting activity coherent with the LFP, there was a strong tendency for phase relationships to be confined to the 2-10 Hz and/or 30-50 Hz frequency ranges. Overall, of 32 cells examined (15 recordings from 6 rats), 9 cells exhibited phase relation to the LFP in the 2 to 10Hz range, 4 cells exhibited phase relation to the LFP in the 20 to 50Hz range. Notably, phase relationships were found for frequencies that did not stand out in power spectral analysis of the LFP or in autocorrelations of the spike train.

Figure 2 shows an example of a LFP recording and two simultaneously recorded cerebellar spike trains. Figure 3 shows the relative phase distributions (histograms) of these same two cells in relation to the LFP at

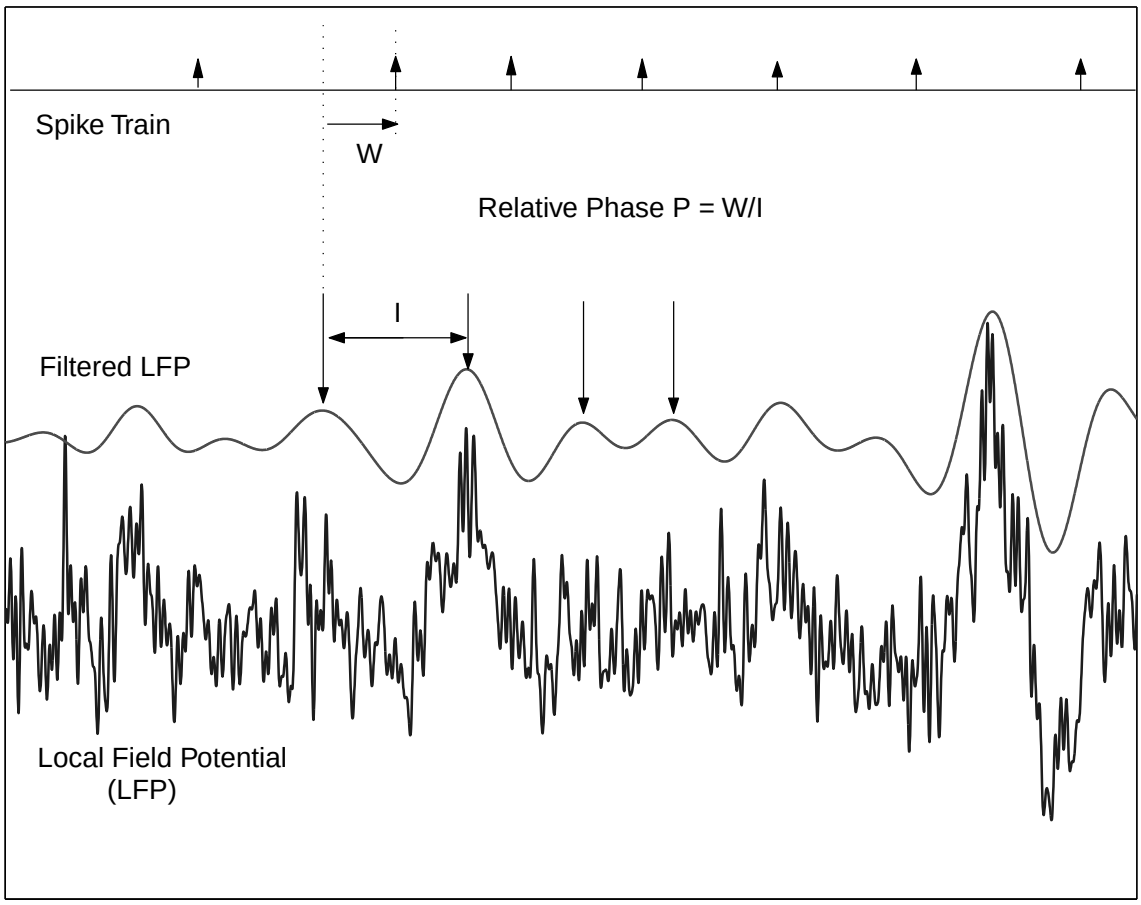

Figure 1: An illustration of the method used in this paper to study the relation between a neuronal spike train and its associated Local Field Potential (LFP). The original LFP is filtered at a specified frequency window (e.g., 1 to 3Hz in this example). The timing of the peak (or valley) of the filtered LFP is identified. The relative phase measure (P) is defined as the timing difference between a spike and the nearest peak of the filtered LFP normalized by the timing interval between two adjacent peaks. The correlation between a spike train and a LFP recording can be studied by analyzing the distribution of their relative phases calculated cross the whole spike train. Detailed discussions about the property of relative phase can be found in [2].

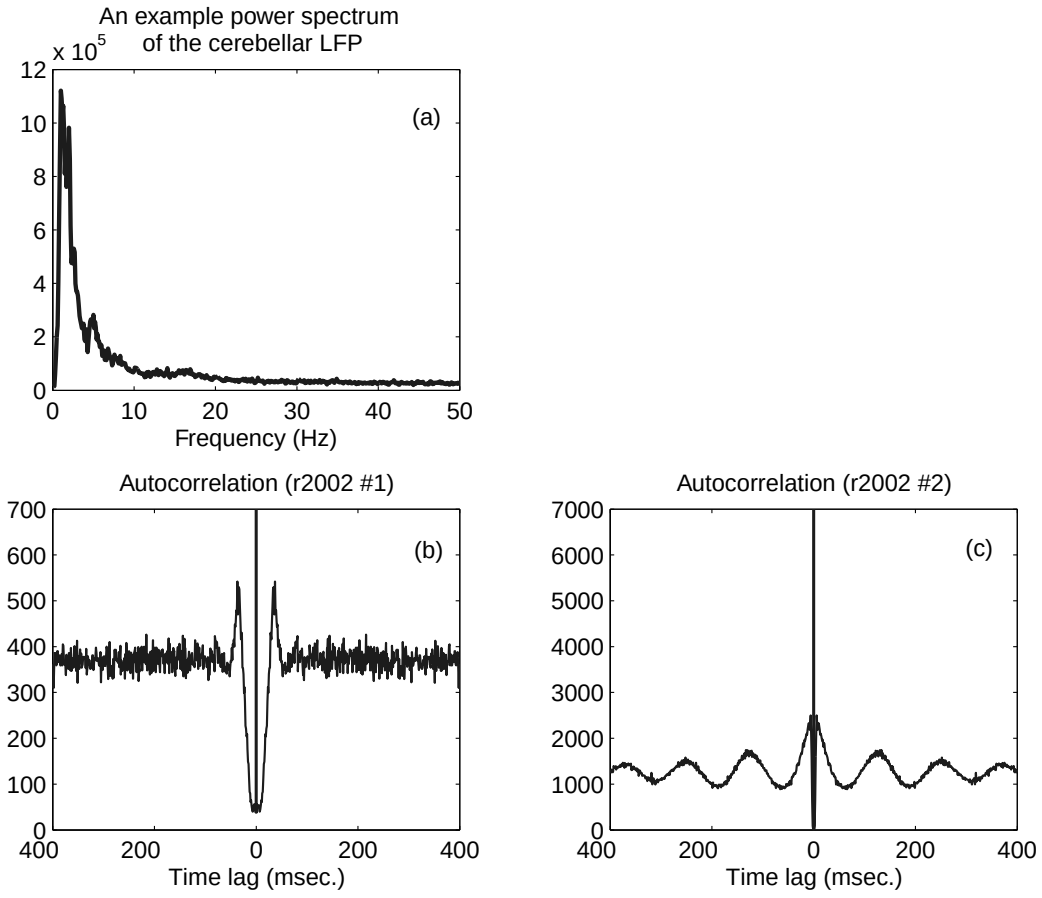

Figure 2: Power spectrum of an example LFP and autocorrelations of two cerebellar spike trains recorded from the same wire.

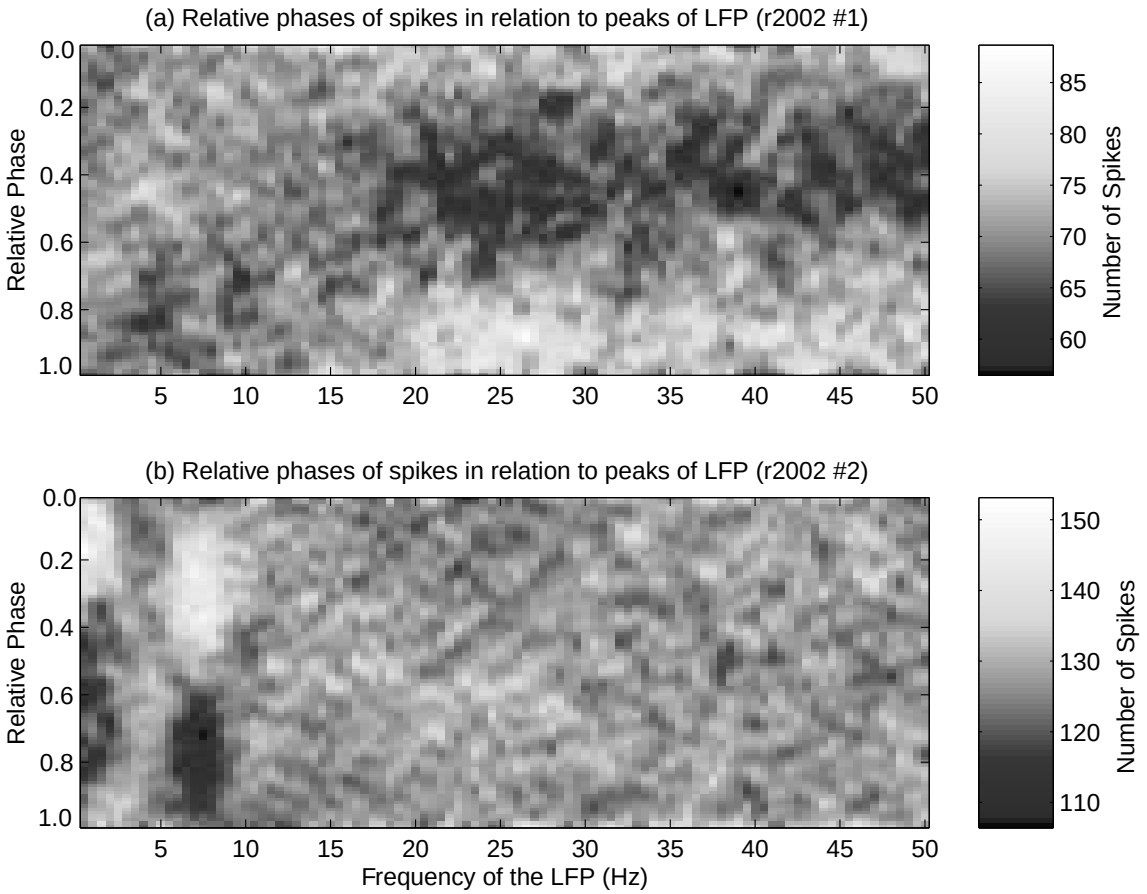

Figure 3: Relative phase distributions of two cerebellar spike trains in relation to their associated LFP. Power spectrum of the LFP and autocorrelations of the two spike trains are shown in Figure 1. In each plot, the horizontal axis is the frequency (0 to 50Hz) of the filtered LFP, and the vertical axis is the relative phase (0 to 1). Gray level coded colorbars represent the number of spikes distributed between phase 0 and 1 at each frequency window of the filtered LFP.

frequency ranges from 1 to 50Hz. Plotted are number of spikes occurring between phase 0 and 1 (equivalent to the interval between two peaks of LFP filtered at the corresponding frequency windows) from 0 to 50Hz. The top plot shows that cell 1 has a slightly higher probability to fire close to the peaks of LFP in the 20 to 50Hz frequency range. The second cell, however, did not show any phase relationship with LFP at 20 to 50Hz range, but did exhibit two different preferred phase relationships, one below 3 Hz, the other between 5 and 10Hz. A second example in Figure 4 shows the relative phase distributions of two different cerebellar cells in relation to their associated LFP. It can be seen that they have two different phase relationships with the LFP around 5Hz, and one cell has a tendency to fire between two peaks of LFP in the 20 to 50Hz range. In both examples (Figures 3 an 4), neither LFPs, nor the single neuron spike trains exhibited strong activity in the gamma (20 to 50Hz) range. Nevertheless, the relative phase method was able to reveal clear relationships between spikes and LFPs at particular frequency ranges.

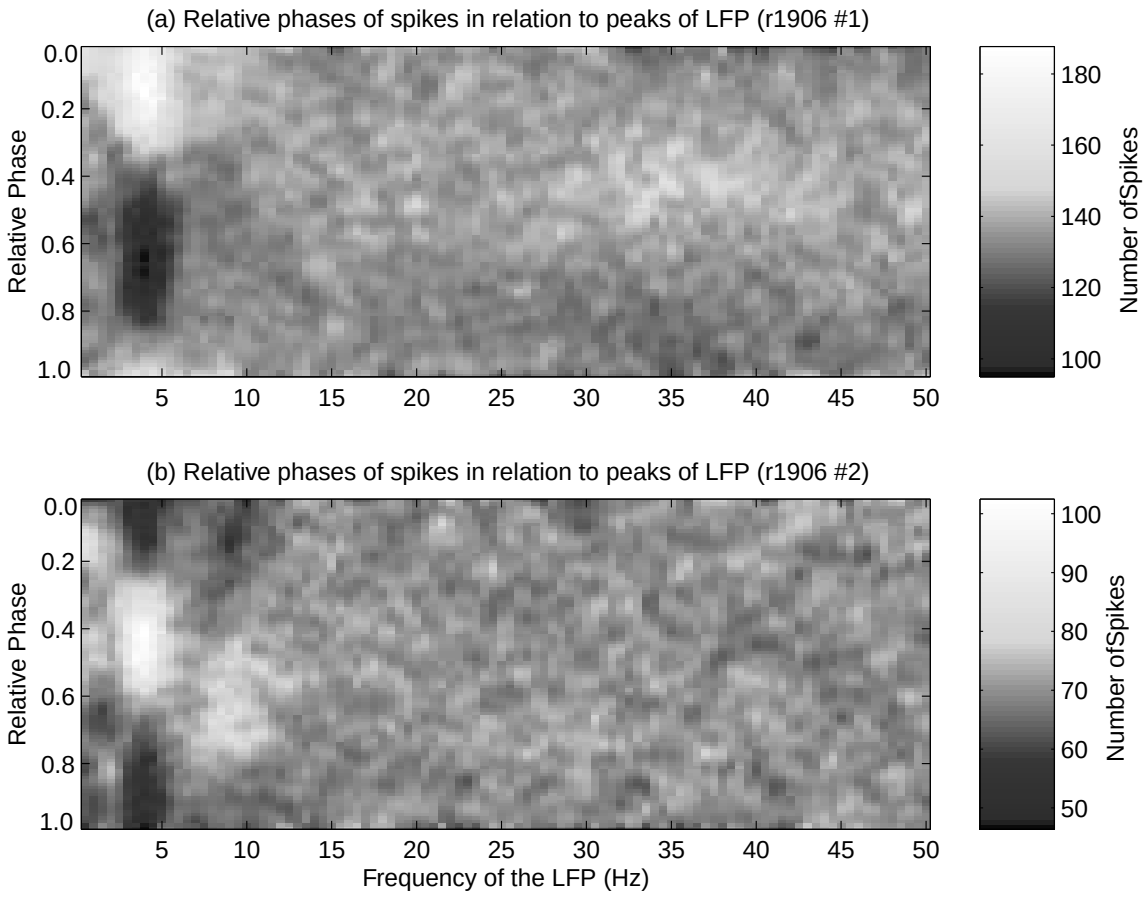

Figure 4: Phase relations between two cerebellar spike trains recorded simultaneously and their associated LFP.

4 Summary and Conclusions

The findings indicate that relative-phase analysis as applied to combined spike train/LFP recordings is a useful tool to uncover hidden temporal relationships between single unit activity and activity of the larger cerebellar network of which they are a small part. Similar to what has previously been shown for neocortical [3] and hippocampal [1] spike-train/LFP recordings, we have found that the simple-spike discharge of putative Purkinje cells is organized, to some extent, relative to the timing of cerebellar population activity as measured by the local field potential. Notably, this finding is consistent with recent work demonstrating: 1. the existence of cerebellar neurons in lobule II which exhibit tonically rhythmic discharge patterns at either slow (approximately 4-6 Hz) or high (approximately 20-50 Hz) frequencies [4]; 2. the presence of transient periods (5-8 consecutive spike intervals) during which seemingly arrhythmic cerebellar neurons discharge spikes at regular intervals [6]. The functional role of such coherence and the extent to which it pervades the entire cerebellar network remains to be determined.

Acknowledgments

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