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Correlation between visual stimulus eccentricity and multiscale neuronal activity in the lateral geniculate nucleus

Ágnes Farkas, Nikolaos Tsarouchas, Péter Gombkötő, Attila Nagy, György Benedek, Anastasios Bezerianos, Antal Berényi

Abstract— **Single unit activity (SUA) was extensively studied in the lateral geniculate nucleus (LGN) but less attention was paid to the analysis of the local field potentials (LFP). In the present study, we investigate how and to what extent LFP and SUA correlate with visual stimulus eccentricity. SUAs and LFPs recorded extracellularly from 52 electrode positions were analyzed. Both LFP and SUA recordings contained well defined time-segments, which correlated with stimulus eccentricity. The spectral analysis of the LFPs indicated that in addition to the phasic, short latency activity of the 20 Hz frequency band, a tonic, 2-10 Hz, elongated component was also present. The time-domain analysis of the phasic and tonic LFP segments revealed a non-linear decrease of the mean LFP amplitude. The frequency-domain investigation made it obvious that the low and high frequency components exhibit a spatially localized increase of the response, in contrast to the time-domain curve. Our results confirm that the local field potentials as a measure of the mesoscopic level neuronal activity provide additional information concerning the activity of neuronal populations, thus enhancing our present knowledge about the functional circuitry as the foundation of various neuronal processes.**

I. Introduction

ENSEMBLE activity of groups of neurons (mesoscopic scale dynamics) and the way ensemble activity relates to single-unit activity (SUA) are likely to be important clues to understanding the functional organization of neuronal circuitry [1]. The raw field potentials recorded with high impedance intracortical electrodes consist of high-frequency (300Hz up to 3KHz) SUA and low-frequency (<50 Hz) local field potential (LFP) components. The low-frequency fluctuations are thought to be dominated by current flow generated by synaptic activity, whereas the high-frequency components (>300 Hz) are probably dominated by the currents associated with neuronal action potentials [2].

The lateral geniculate nucleus (LGN) of the cat is a first-order thalamic relay to the primary visual cortex with fairly regular organization and spatial architecture. It has been extensively studied via SUA recordings for the last fifty years [3], [4]. The feline LGN neurons possess receptive fields, which are concentrically organized (excitatory center-inhibitory surround, or *vice versa*), and have diameters of the same order as retinal ganglion cells, although the receptive field sizes increase with retinal eccentricity [4], [5]. The surround exerts an inhibitory influence on the center, thus enhancing the contrast sensitivity of the LGN [6]. On the basis of receptive field properties, three types of neurons (X, Y, and W) have been identified in the LGN of the cat. X cells have a sustained, Y cells have a transient response, while W cells form a heterogeneous group that exhibits some properties of both X and Y neurons [7], [8].

Unlike SUA, less attention was paid to the analysis of LFPs in the LGN. To investigate into this aspect, we focused on the mesoscopic scale dynamics underlying the spatial and functional organization of the neuronal receptive fields. Due to the 3D spreading of the generated potential changes in the extracellular space with homogeneous conductance, it is attenuated according to a hyperbolic function. To test this hypothesis we investigated how and to what extent LFP and SUA correlate with visual stimulus eccentricity as well as with each other (time-lags), thus examining the mesoscopic-level dynamics (time and frequency domain) of the spatial - functional organization of LGN from a novel aspect.

II. Materials and Methods

The experiments were carried out on 5 adult cats. All procedures followed the European Communities Council Directive of 24 November 1986 (86/609 ECC) and the National Institutes of Health Guidelines for the Care and Use of Animals for Experimental Procedures. The experimental protocol had been accepted by the Ethical Committee for Animal Research of the University of Szeged. For a detailed description of surgical methods and anesthesia, see our previous publication [9].

Electrophysiological SUA and LFP recordings were performed extracellularly with parylene-insulated tungsten microelectrodes (AM System Inc., 2 MΩ). The LGN was approached through vertical penetrations. Individual action potentials were selected with the help of a spike sorting system (SciWorks Datawave system) after band-pass filtering the recorded signal between 300-3000 Hz. The local field-potentials were recorded after applying a low-pass filter (0-45 Hz). For investigation of the influence of eccentric stimulation over the SUAs and LFPs a light spot of

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A. Farkas, P. Gombkötő, A. Nagy, G. Benedek and A. Berényi are with the Department of Physiology, University of Szeged, 10 Dóm sqr., Szeged, H-6720 Hungary (A. Berényi is the corresponding author to provide phone: +36-62-545373; e-mail: tony@phys.szote.u-szeged.hu)

N. Tsarouchas and A. Bezerianos are with the Department of Medical Physics, School of Medicine, University of Patras, 26500 Patras, Greece. (e-mail: bezer@upatras.gr)

A. Farkas and N. Tsarouchas contributed equally to this work.

1° diameter was projected repetitively in the visual field, at different positions relative to the receptive field of the recorded neuron. The stimulus was initially applied in central positions, to cover the small center part of the receptive fields, and the effect caused by switching the stimulus on and off was recorded in intervals of 1500 ms. Later on, the stimulation was repeated at increasingly eccentric positions by shifting the light spot by 1° stepwise. Altogether the effect of 10 stimulus positions was analyzed (marked as Left – Centered – Right1 - … - Right8). Each stimulus was presented at least 100 times.

Correlation analysis (Pearson's *r*) was applied for every time-point along individual and grand-average LFPs and SUAs vs. spatial windows of incremental eccentricity (time-dependent spatial correlograms). The correlation of individual LFPs and SUAs were also evaluated to reveal their significant temporal correlation and time-lags (time-dependent temporal correlograms). The significance level of correlation was taken for zero for non significant places and rescaled for significant ones:

$$f(p) = \begin{cases} 0, & p > 0.05 \\ 1 - 20p, & p \leq 0.05 \end{cases} \quad (1)$$

and smoothened with a moving average filter of 20 ms width. To quantify the nature of relationship between stimulus position and LFPs on the time-domain, we separately calculated the mean, minimum, and maximum amplitudes of the overall-mean LFP of all recordings, in two separate time frames, that is, to the early phasic component (50-200 ms after stimulation) and to the late tonic component of the LFP (200-950 ms after stimulation). To reveal the power of different frequency bands in the background of the amplitude changes in the LFPs, the signal was decomposed into frequency domains, using a discrete Fourier transformation with 128 ms window width at 8 ms steps. The peri-event energy changes of the LFP responses were calculated at three characteristic frequency bands (2, 10, and 20 Hz) for each eccentricity.

III. RESULTS

SUAs and LFPs recorded from 52 electrode positions were analyzed. Fig. 1 shows examples of 'on' and 'off' type sustained (a, b), and transient (c) neuronal activities.

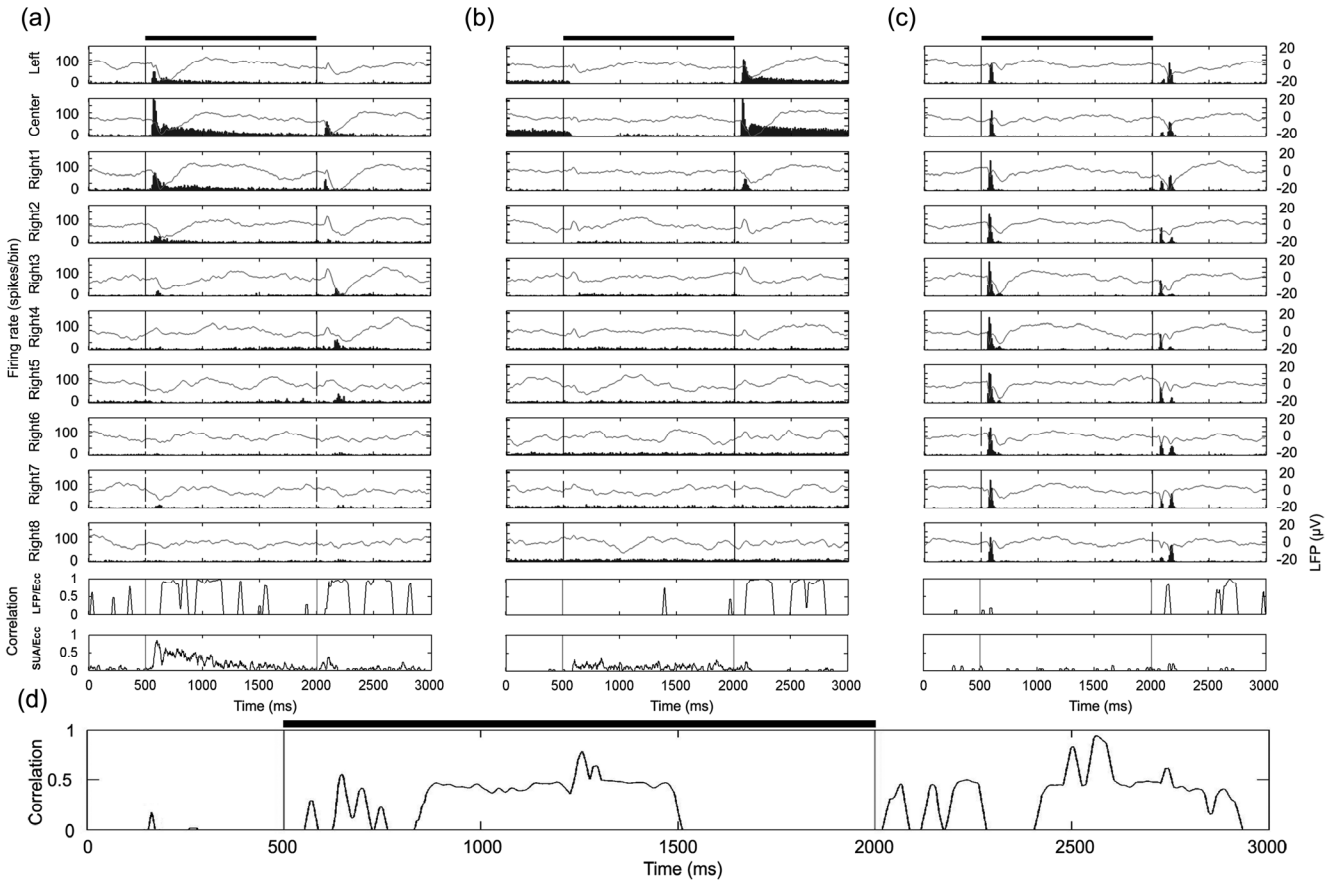

Fig. 1. SUA and LFP responses of characteristic neuron types in the LGN. Panels (a), (b), and (c), are demonstrating the responses of a sustained 'on', a sustained 'off' and a transient type neuron (respectively), in the form of peristimulus time histograms and LFP curves recorded during stimulation at different eccentricities. The abscissa denotes the time elapsed in ms. The duration of the stimulus (light on) is marked with a thick black line above the PSTHs. The left ordinate refers to the firing rate of the recorded SUA (spikes/bin), while the right ordinate shows the amplitude of the LFP in mV. The correlation graphs of each example denotes the LFP-eccentricity and SUA-eccentricity correlation (upper and lower correlogram, respectively). Panel (d) refers to the correlation of overall-mean LFPs with eccentricity. For the meaning of the correlation value, see METHODS.

The transient-type neurons possess large homogeneous receptive fields, in contrast to the sustained-type neurons. All tonic, sustained responses were initiated with a pronounced phasic component. Both the LFP (d) and the SUA (a, b, c) contained well defined time-segments, which showed correlation with the stimulus eccentricity. The last eccentricity-correlated component of the LFP occurred approx. 1000 ms after the luminance change. The non-correlating LFP segments were present only during the early phase of the LFP. A detailed spectral analysis of the LFPs (Fig 2.) indicated a complex frequency composition of the time-domain signal. In addition to the phasic, short latency activity of the 20 Hz frequency band, a tonic, elongated component was found at lower frequency ranges (2 and 10 Hz) for a group of particular eccentricities.

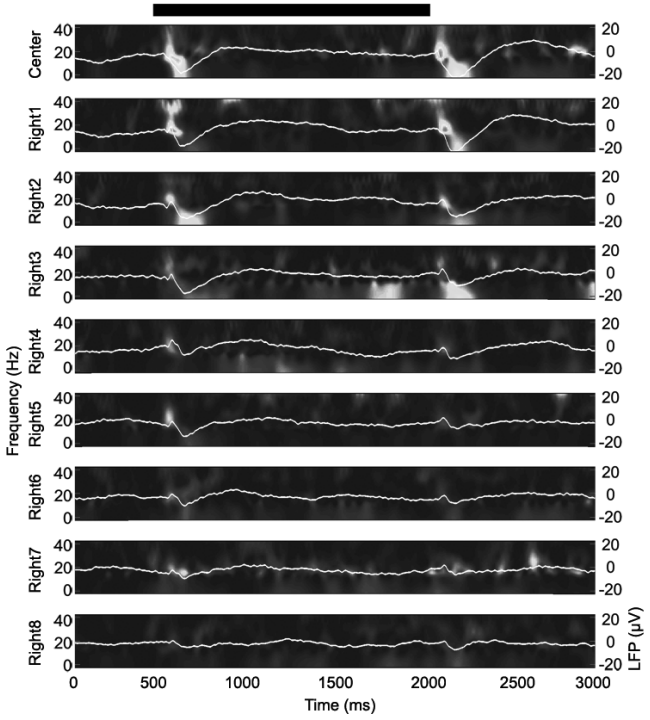

Fig. 2. Time-frequency spectrogram of the overall-mean LFP. The left ordinate refers to the frequencies of the spectrogram, while the brightness of the map is proportional to the energy density of the given frequency at a given time. The other conventions are the same as on Fig. 1.

The time-domain analysis of the early and late segment of the peri-event LFP response revealed a non-linear decrease of the mean LFP amplitude both in the 'on' and 'off' conditions (Fig. 3). The early phase (50-200 ms) was consistently a strict negative potential change (the maximum amplitude of this segment was always around the isoelectric line), in contrast to the multiphasic late component. The monotonic decrease of potential change is interrupted by local enhancements at different eccentricities, although the localizations of the increases were not consequent. The frequency-domain investigation of the LFP curves (Fig. 4) made it obvious that the low and high frequency components exhibit a spatially fixated increase of response, in contrast to the time-domain curve.

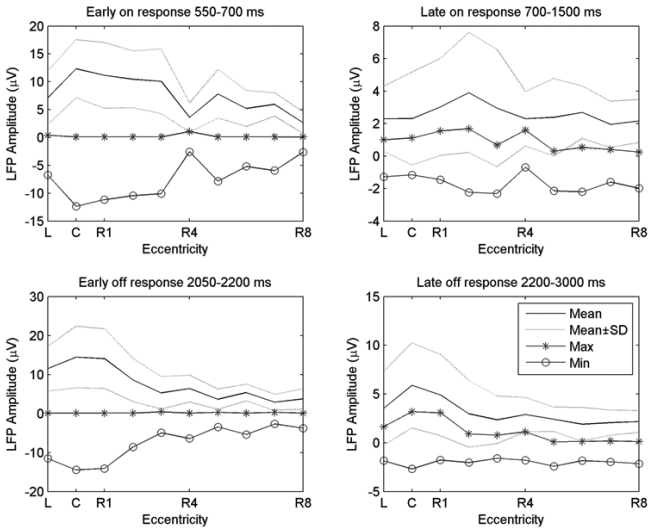

Fig. 3. Time-domain analysis of early and late LFP segments. Graphs of the upper row represent the overall 'on' responses, while the bottom ones show the 'off' responses. LFP amplitudes (ordinate) are marked for different stimulation sites (abscissa). Abbreviations L, C, R1, …, R8 refer to Left, Center, Right1, ..., Right8 stimulus positions. For further details, see METHODS.

While the increase of the energy content of the 2 and 10 Hz bands are most expressed at positions R2-R3 (2°-3° away from the center of the receptive field), the 20 Hz component was reactivated from a consistently more eccentric site (R7). This peripheral 20 Hz response occurs with slightly longer latency then more central ones (see Fig. 2).

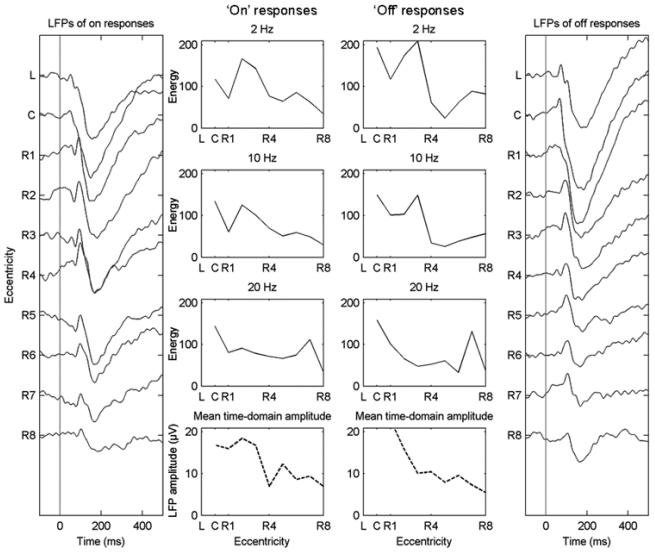

Fig. 4. Frequency-domain analysis of specific frequency bands of the overall-mean LFP. The left and right vertical panels show the early LFPs of 'on' and 'off' responses. The abscissa denotes the time, while the ordinate marks the relative amplitudes and eccentricities. The thin vertical line at 0 ms signifies the change of the stimulus luminance (on-off). The two middle columns represent the dependency of LFP power in 3 different frequency bands on the stimulus eccentricity (from top- to down 2, 10 and 20 Hz) and the related time-domain LFP amplitudes. The other conventions are the same as on Fig. 2 and 3.

IV. DISCUSSION

As it was predictable, changes in the LFPs more or less coincide with the SUA. In contrast to the SUA of the sustained type neurons in the LGN, which did not adapt to the stimulus during the stimulation period (1500 ms), the LFPs revealed a more differentiator-like behavior. The peristimulus LFP did not differ significantly from the prestimulus potential after 1000 ms of stimulation. This temporal pattern of responsiveness consistently appeared in both 'on' and 'off' responses. The decrease of LFP amplitude due to the increasingly eccentric stimulation could be a result of the physical rules of volume conduction. The generated potential drops following a smooth hyperbolic function with the increasing distance, and accordingly, highly correlates with the stimulus eccentricity. Our results demonstrate that the peristimulus LFP contains narrow time-segments, which are not correlating with the eccentricity; moreover, the predicted theoretically hyperbolic, monotonically decreasing amplitude-eccentricity curve is regularly distorted with local augmentations at well defined stimulus positions. The spectral analysis of the LFPs supports the notion that the different frequency bands are influenced by different stimulus positions, which do not precisely overlap with the time-domain enhancement. Presumably the blurred time-domain increases of LFP at R4-R6 stimulus positions are a geometric sum of the low (R2-R3) and high frequency (R7) components.

The synchronized activity of neurons in a certain volume of tissue causes oscillations in the extracellular space with a frequency equaling their firing pattern. This phenomenon is confirmed by the 20 Hz components of the LFPs, which show high correlation with the transient components of the single unit responses. However, the consequent increase of the activity in this particular frequency band during R7 eccentric stimulation may raise doubts about the homogenous origin of the local-field oscillations. Neurons with a receptive field centered at the stimulating site R7 are lying approximately 500-1500 μm away from the recording site, depending on the distance from the central fovea. According to the results of Katzner et al. [10], most of the energy of the local-field potentials is originating from the 250 μm surroundings of the recording site, thus the volume conduction of distant neuronal activation as a source can be excluded. The local field potentials may also be influenced by transient-type neurons in the close vicinity of the electrode tip, given their differentiator-like behavior and large receptive fields, enabling them to perceive distant stimuli. However, these transient-type LGN neurons (presented on Fig. 1c) show a steadily eccentricity dependent response profile, which should result in the persistent presence of this 20 Hz component. Based on the observations above and the slightly longer latency of the fast response component during peripheral stimulation, we hypothesize that this distant spatial reactivation may be due to an intra or extrageniculate feedback circuitry, realized by interneurons. We suggest that these interneurons transmit inhibitory signals, since their activation is presented in the LFPs, but the SUAs are not increased at all. This local network may be an essential component of the lateral inhibition phenomenon.

Our results confirm that the local field potentials as a measure of the mesoscopic level neuronal activity provide additional information concerning the activity of neuronal populations, thus enhancing our present knowledge about the functional circuitry as the foundation of various neuronal processes.

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REFERENCES

[1] G. Buzsáki, "Large-scale recording of neuronal ensembles," *Nat. Neurosci.,* vol. 7, pp. 446-451, 2004.

[2] W. J. Freeman, "Mesoscopic neurodynamics: from neuron to brain," *J. Physiol.,* vol. 94, pp. 303-322, 2000.

[3] D. H. Hubel, "Single unit activity in lateral geniculate body and optic tract of unrestrained cats," *J. Physiol.,* vol. 150, pp. 91-104, 1960.

[4] D. H. Hubel, and T. N. Wiesel, "Integrative action in the cat's lateral geniculate body," *J. Physiol.,* vol. 155, pp. 385-398, 1961.

[5] K. P. Hoffmann, J. Stone, and S. M. Sherman, "Relay of receptive-field properties in dorsal lateral geniculate nucleus of the cat," *J. Neurophysiol.*, vol. 35, pp. 518-531, 1972.

[6] O.D. Creutzfeldt, S. Kastner, X. Pei, and A.Valberg, "The neurophysiological correlates of colour and brightness contrast in lateral geniculate neurons. II. Adaptation and surround effects," *Exp. Brain Res.* vol. 87, pp. 22-45, 1991.

[7] H. Ikeda and M. J. Wright, "Receptive field organization of 'sustained' and 'transient' retinal ganglion cells which subserve different function roles," *J. Physiol.,* vol. 227, pp. 769-800, 1972.

[8] P.D. Wilson, M. H. Rowe and J. Stone, "Properties of relay cells in cat's lateral geniculate nucleus: a comparison of W-cells with X- and Y-cells," *J. Neurophysiol.,* vol. 39, pp. 1193-1209, 1976.

[9] A. Nagy et al., "Drifting grating stimulation reveals particular activation properties of visual neurons in the caudate nucleus," *Eur. J. Neurosci.*, vol. 27, pp. 1801-1808, 2008.

[10] S. Katzner et al., "Local origin of field potentials in visual cortex," *Neuron*, vol. 61, pp. 35-41, 2009.