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Precise timing of neuronal discharges within and across cortical areas: Implications for synaptic transmission

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Summary — Multielectrode recordings were performed in a variety of structures of structures of the mammalian brain in order to examine temporal relations among simultaneously measured neuronal responses. Data indicate close correlations between perceptual phenomena and zero-time lag synchronization of distributed neuronal discharges.

synchrony / oscillation / cortico-cortical connections / correlation / interocular rivalry / synaptic input selection / visual cortex

Introduction

Evidence indicates that visual stimuli do not only modulate the discharge rate of neurons in subcortical and cortical structures but induce in addition a characteristic temporal patterning of the responses (for reviews see Singer, 1993; Singer and Gray, 1995). Whenever such patterning becomes detectable it consists of a rather precise synchronization of discharges of spatially distributed but functionally related neuron populations. Frequently, this synchronization phenomenon is associated with an oscillatory patterning of the population responses, whereby preferred frequencies depend on the respective neuronal structures and on variations of the brain's central state.

In the retina, individual ganglion cells with similar center characteristics synchronize their responses with a precision in the ms range over large distances provided that they are activated by a continuous stimulus. This synchronization is not phase-locked to the stimulus-onset and is tightly associated with an oscillatory patterning of the responses in the frequency range from 60 to 100 Hz. Both the synchronization and the oscillatory patterning of the responses have to be attributed to intraretinal interactions. Relay cells in the lateral geniculate reliably transmit these synchronized responses, and hence discharge in synchrony when receiving input from the same eye, irrespective of whether they are distributed across laminae within the same hemisphere or across the geniculates of the two hemispheres (Neuenschwander and Singer, 1996). Under certain stimulation conditions the responses of neurons in area 18 but not in area 17 of the cat's visual cortex may become phase-locked to this synchronous subcortical input.

Independent synchronization mechanisms exist at the cortical level that are capable of synchronizing discharges of neurons both within and across areas. This cortically mediated synchronization is often associated with an oscillatory patterning of population responses in the beta- and gamma-frequency range. Synchronization at the cortical level also occurs with high temporal precision and zero phase-lag. Stimulus-dependent cortical synchronization becomes particularly pronounced during states characterized by desynchronized EEG (Munk *et al*, 1996) and in awake preparations during phases where the animals have to attend to the stimuli (Roelfsema *et al*, 1995). This facilitation of synchronization is not associated with a reduction of the feature selectivity of the synchronization phenomenon (Munk *et al*, 1996).

Synchronized cortical activity during attentive behaviour

Experiments in cats trained to perform a visual discrimination and a precisely timed motor response indicate that neurons distributed across several cortical areas including visual, association and sensory motor cortex, synchronize their activities in a task-dependent way. Transcortically recorded local field potentials exhibit an oscillatory patterning in the high beta- and low gamma-range while the animal attends to the stimulus, detects its change, and executes the motor response, and this activity exhibits a strong synchronization with zero phase-lag across cortical areas. Similar correlations are found when single units in one area are correlated with field potentials in other areas. Correlations are particularly strong among areas 17 and 18 both within and across hemispheres, between these primary visual areas and area 21, between area 21 and area 7, between area 7 and lateral area 5, between lateral area 5 and medial area 5, and between medial area 5 and area 4 in the hemisphere contralateral to the paw used to execute the motor response. However, as soon as the reward becomes available, this pattern of coherent activity breaks down and is replaced by oscillatory activity in the alpha-range that fails to exhibit systematic phase relations, and also shows no preferential coupling between functionally related areas. These results suggest that populations of neurons distributed in cortical areas that are supposed to be engaged in the execution of the required behaviour transiently synchronize their responses in a non-transitive way during execution of the task (Roelfsema *et al*, 1995).

Two experiments in awake behaving animals suggest that there may be instances where the occurrence of synchronized discharges shows better correlation with changes in stimulus configuration and perception than modulation of discharge rates. One set of data comes from multielectrode recordings performed in area MT of the monkey. As in the visual cortex of cats (Engel *et al*, 1991; Freiwald *et al*, 1995) cells synchronize their responses with a precision in the ms range if activated with a single stimulus but they no longer do so if driven by two simultaneously presented stimuli that have different orientations and move in different directions. These changes in correlation patterns occur without significant changes in discharge frequency. Hence, it is possible to infer from the correlation pattern whether pairs of neurons are activated by a single moving contour or by two different contours with differing motion trajectories while no such inferences can be made from changes in discharge rate. If neurons at subsequent processing stages can evaluate the synchronicity of discharges in area MT this would permit extraction of information about stimulus configurations that is not available from analysis of discharge rates alone.

The other example for a close relation between synchronization patterns and visual functions comes from multielectrode recordings in area 17 and 18 of awake, strabismic cats that were exposed to dichoptic stimulation conditions leading to interocular rivalry and suppression. Cross-correlation functions were computed for the responses of monocular neurons driven either by the right or the left eye. Under conditions of interocular rivalry, response synchronization increased for neurons driven by the dominating eye and decreased for neurons driven by the suppressed eye. In contrast, there was no systematic relation between modifications of discharge rate and eye dominance (Fries *et al*, 1996)

Synchronization and synaptic input selection

These data suggest that synchronization of responses might be used as a mechanism complementary to the modulation of discharge rates in order to select responses by enhancing their saliency. Because synchronization defines relations with high temporal precision it is proposed that it is particularly suited to select and group responses for further joint processing. The advantage of such a complementary selection mechanism is that it reduces substantially transmission times because coincident EPSPs summate very effectively and reach threshold with minimal delays. Moreover, response selection can operate with great specificity because no temporal integration is required, thus allowing for selection at the level of individual spikes. However, in order to support such a mechanism, neurons have to meet several constraints concerning their temporal integration properties. In order to examine whether neurons meet these requirements we have performed experiments in slices of the visual cortex, studying the influence of an oscillatory modulation of the membrane potential on synaptic transmission (Volgushev *et al*, in preparation). Together with theoretical considerations the data gathered so far seem compatible with the possibility that neurons can act as very selective temporal filters. This is particularly true when the network in which they are embedded engages in oscillatory activity.

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