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Synchronization between patches of local excitation in a cerebellar granular layer model

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Abstract

In a model of the cerebellar granular layer, pairs of neurons aligned along the parallel fiber axis fired synchronized over long distances provided the afferent mossy fibers were spatially uniformly excited. Here, we applied a nonuniform mossy fiber input pattern and found that local patches of increased granule cell activity were sharpened by the feedback inhibition which granule cells received from Golgi cells. These local patches maintained their own rhythm, or synchronized with each other, depending on the distance between them and on their absolute and relative levels of activity. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Cerebellum; Parallel fibers; Synchronization

1. Introduction

The synaptic organization of the granular layer of the cerebellum has been described in considerable detail, but the firing patterns of the major input fibers (mossy fibers, MFs, the terminal axons of spinocerebellar and cerebro-ponto-cerebellar pathways) and output fibers (parallel fibers, PFs, the transverse trajectories of the granule cell axons) are poorly understood (see [2,3] for references).

In a recent computer model [3], Golgi and granule cells aligned along the PF axis fired synchronized and at regular intervals (base frequency 10–40 Hz) when all MFs fired randomly at the same, constant average rate. The prediction that pairs of Golgi cells would fire synchronized if they were aligned along the PF axis, whereas

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orthogonally oriented pairs of Golgi cells not linked by common PF input would not, was confirmed afterwards in multi-electrode recordings of the spontaneous activity of Golgi cells in anesthetized rats [6].

In these same experiments, punctate and brush stimulation of the rat facial skin revealed that Golgi cells had large but spatiotemporally distinctly organized receptive fields [7]. More particularly, a central receptive field patch of high Golgi cell responsiveness, probably caused by monosynaptic MF excitation, was surrounded by a much larger area from which Golgi cells received weaker, presumably PF excitation. A patchy excitation of the granular layer by peripheral stimulation has been described earlier (see [8]).

In the present paper, we study the effect on granular layer synchrony produced by such a spatially inhomogeneous MF input.

2. Simulation methods

We simulated the one-dimensional standard model of the granular layer [3]. The model contained 60 Golgi cells (separated 300 μm), 4305 granule cells and 1080 MFs, all aligned along the same PF axis. Granule cells received MF excitation and Golgi cell inhibition. Golgi cells received only granule cell (i.e. PF) excitation. PFs had a length of 5 mm and a conduction speed of 0.5 m/s. In this version of the model, Golgi cells neither received synapses from MFs or ascending granule cell axons, nor did they receive stellate cell inhibition. Because Golgi cells received only PF and no MF input, this allowed us to test the capacity of PFs for synchronizing over large distances their target Golgi cells [4]. Strong monosynaptic MF excitation tends to desynchronize Golgi cells [3].

The spatial profile of MF activity was varied between simulations by superimposing upon the background firing rate level of 10 spikes/s two patches of increased MF activity. The patches had a fixed width of 60 MFs (about 1 mm), and the distance between them was varied. In a first series of simulations, MFs had the same firing rate in both patches. In a second series, MFs in different patches had different firing rates (see example in Fig. 1). All profiles were static, i.e. a constant average firing rate was maintained in each MF throughout a 10 s simulation. Simulations were performed with GENESIS [1].

The degree of synchrony and rhythmicity was assessed qualitatively by inspection of the spike rasterograms of Golgi and granule cells (an example of which is shown in Fig. 1) and quantitatively by means of a synchronization index (SI [3]). The SI scales between 0 (incoherent population firing) and 1 (all neurons fire synchronized and with the same interspike interval or integer multiples of this).

To quantify synchrony *within* a patch, the SI was calculated on the population autocorrelogram, as explained in [3]. To quantify synchrony *between* patches, the SI was calculated on the cumulative cross-correlogram over all pairs of granule cells taken from different patches. The SI expresses the relative power of the first harmonic frequency of the analyzed time series.

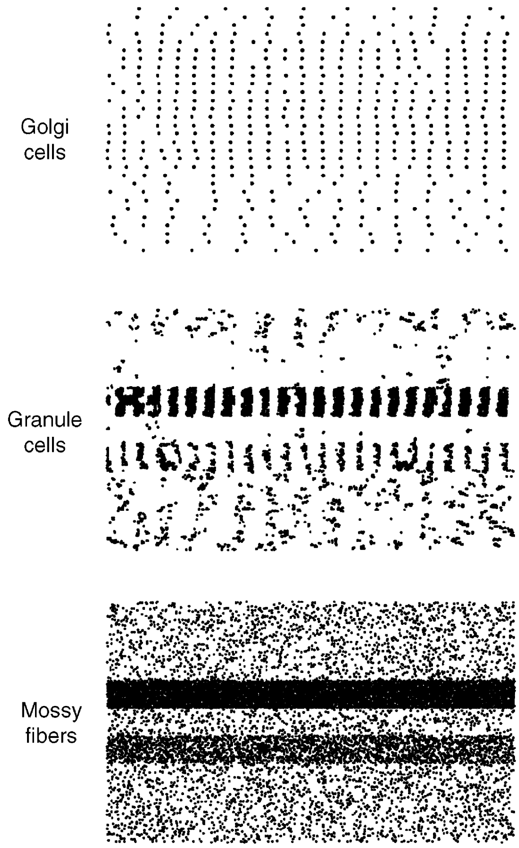

Fig. 1. Spike rasterogram of a 9 mm slice comprising the central 30 Golgi cells, 2100 granule cells and 525 mossy fibers (vertical axes) during one second network time (horizontal axis). The MFs fired randomly at 10 spikes/s, except for two patches of increased activity. MFs fired at 40 spikes/s in the lower patch (MF 451–510) and at 100 spikes/s in the upper patch (MF 571–630).

3. Results

Application of a very fine-coarse MF pattern in which each MF was assigned a different average firing rate, drawn from a uniform distribution, did not affect global network synchrony at all [3]. Indeed, the massive convergence of PFs on Golgi cells ensured that the Golgi cells were sensitive to the *average* level of activity in the granule cell population. This average level of granule cell activity was similar for the two applied spatial profiles of MF activity (homogeneous versus fine-coarsed).

Local patches in the MF firing profile, if broad enough, caused islands of synchrony in the granular layer. A local patch of increased MF activity generated more readily local synchrony than did a patch of decreased MF activity (critical width when using the standard parameter setting: 0.5–1 mm versus 4 mm, or 10–20% versus 80% of the

PF length). In general, owing to the fact that the granular layer network synchronized more precisely at high firing rates [3], the critical width was lowest for patches with the highest firing rate.

Pairs of granular layer patches receiving increased MF excitation could fuse when they were separated by a distance smaller than half the PF length (2.5 mm). The effect was different for Golgi and granule cells. The firing rates of Golgi cells lying in between the patches were enhanced to almost the same level as those of Golgi cells lying within the patches (Fig. 1, Golgi cells). For granule cells, in contrast, there was a drop in firing rate in between the two patches, even below the background level, because the enhanced inhibition which these granule cells received from Golgi cells was not balanced here by an increased MF input (Fig. 1, granule cells). Nevertheless, the Golgi and granule cells did not only synchronize within each patch, but also between the patches.

The degree of synchronization between two patches depended primarily on the distance between them. Fig. 2 shows the effect of interpatch distance on interpatch synchronization for five levels of patch excitation (MF firing rates within each patch from 50 to 150 Hz). The curves labeled 'absolute' show the raw SIs for the granule cell population calculated *between* patches. The SIs measured *within* patches are not shown but are very similar. Because a patch presented alone reached SIs of at most 0.1, this means that the presence of a second patch within its neighborhood actually increased the synchronization within that patch. The curves labeled 'relative' are the absolute SIs between the granule cell populations of each patch but normalized over the mean SI within each patch. Synchrony clearly breaks down when the patches are separated by half a PF length, i.e. when the granule cells of one patch are not able to excite the Golgi cells overlying the other patch.

The synchronization between two patches was robust against imbalances in their degree of excitation, as can be seen in the example of Fig. 1. The granule cells overlying

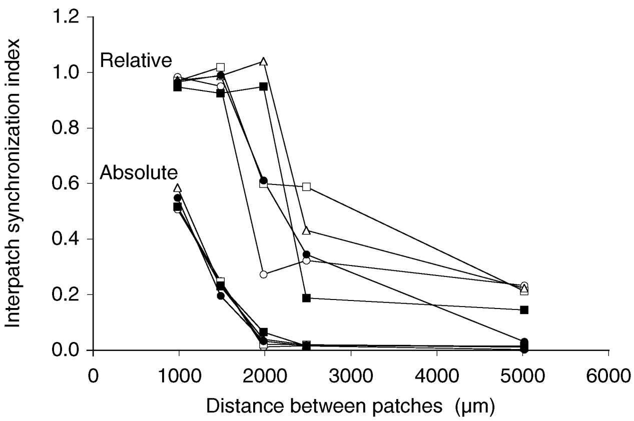

Fig. 2. The effect of interpatch distance and intrapatch mossy fiber firing rate on synchronization between granule cells in different patches. The mean MF firing rate in *both* patches was 50 (open circles), 70 (open boxes), 90 (open triangles), 120 (closed circles) or 150 spikes/s (closed boxes). See text for details.

the lower patch fired at the same basic rhythm as the granule cells in the upper patch, although they received less MF excitation and hence fired at a much lower rate (10 versus 40 spikes/s). Granule cells firing at different rates were able to become locked in a single rhythm by failing to fire, to different degrees, at each cycle of the oscillation.

4. Conclusion

A patchy MF excitation of the model granular layer generated robust synchronous bursts of activity in the granule cell population, provided the interpatch distance was smaller than half a PF length. This was a constant observation, although other simulation results might have depended to some extent on the choice of parameter values. For example, the critical patch *width* for synchronization probably decreases with increasing numbers of MFs and granule cells, and the frequency of the synchronous oscillations depends on the kinetics and strength of the synapses in the Golgi-granule cell feedback loop as well as on the PF conduction speed [3].

The resulting volleys of PF spikes might be functionally important at the target Purkinje cells, either for the induction of synaptic plasticity, or for the selective detection of particular combinatorial patterns of active PFs in a pattern recognition paradigm (see Steuber and De Schutter, this volume). Finally, with respect to the synchrony experimentally observed between Golgi cells [6], these PF bursts might account for the fraction of synchrony that could not be explained by a model in which Golgi cells received only input from *randomly* firing PFs [5].

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