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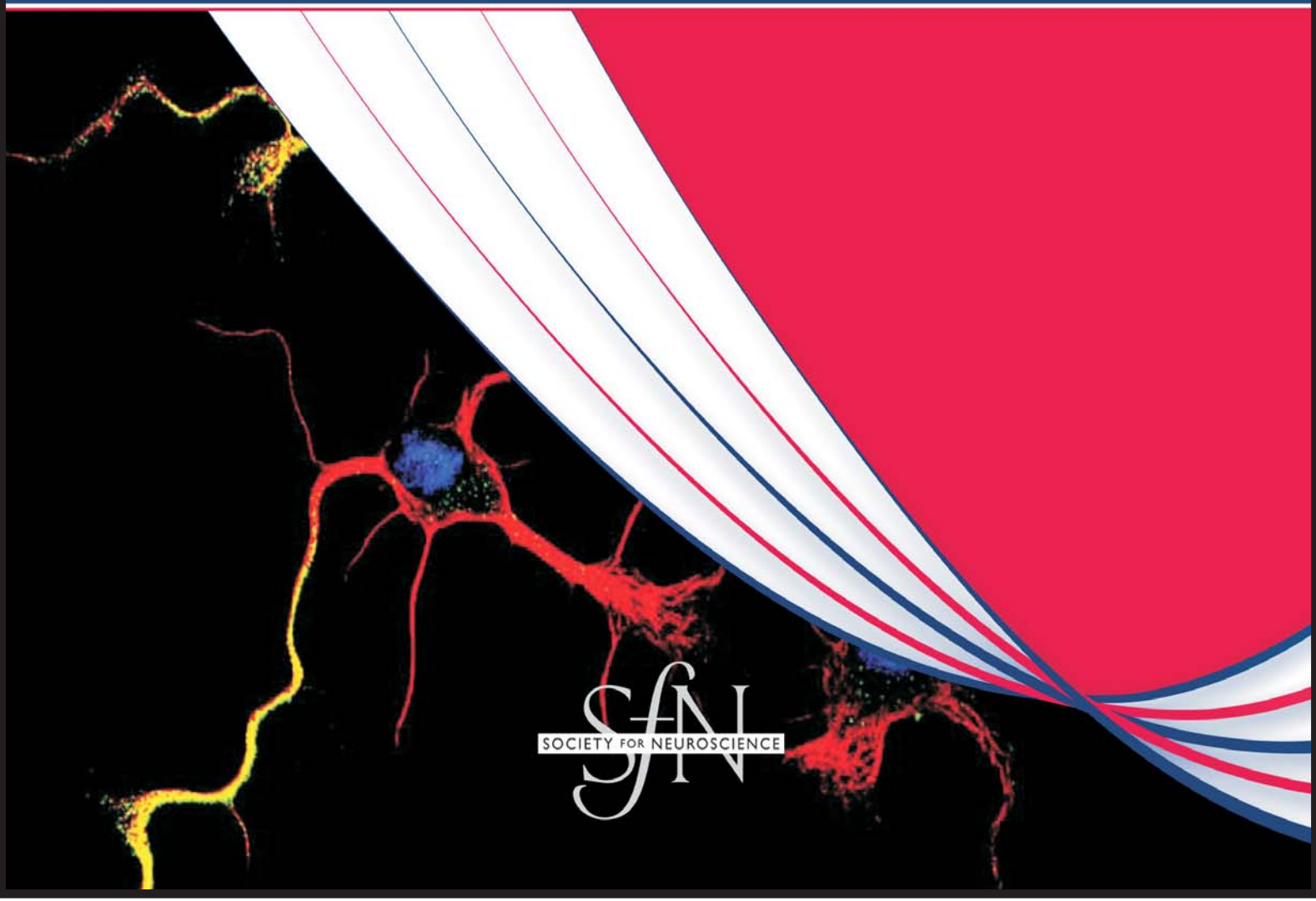

Detailed cable models of fast-spiking basket cells in the dentate gyrus

Anja Nörenberg, M. Bartos, I. Vida, H. Hu, P. Jonas

Fast-spiking, parvalbumin-expressing basket cells (BCs) act as fast signaling devices in cortical neuronal networks. They receive fast excitatory synaptic inputs, generate high-frequency trains of action potentials, and provide a fast inhibitory output onto their postsynaptic target cells. BCs are activated by excitatory synapses on apical and basal dendrites emerging from a variety of different sources. How synaptic events are integrated in the apical and basal dendrites to generate a unified action potential output, however, has remained unknown. To assess dendritic integration in BCs quantitatively, we developed detailed passive cable models of these neurons. Passive voltage responses to short current pulses (0.5 or 2 ms, 100-500 pA) were recorded from BCs in hippocampal slices from 17- or 18-day-old rats at 32-34°C in the presence of tetrodotoxin, blockers of excitatory and inhibitory synaptic currents, and (in a subset of experiments) the Ih channel blocker ZD7288. To minimize series resistance artifacts, a dual somatic recording configuration was used. BCs were filled with biocytin during recording, visualized by 3,3'-diaminobenzidine after fixation, and identified based on the axonal arborization in the granule cell layer. Soma, dendrites, and the entire axonal arborization were reconstructed with a Neurolucida system. In four fully reconstructed BCs, the mean surface area of apical dendrites, basal dendrites, and axon was 7600, 2200, and 31200 µm2, respectively. Uniform cable parameters Rm, Cm, and Ri were obtained by direct fitting of the experimental voltage transients with the model, using the simulation platform NEURON 6.1. On average, we obtained Rm = 18.4 kΩ cm2 (6.3 kΩ cm2, n = 2 without ZD7288, 30.5 kΩ cm2, n = 2 with ZD7288), Cm = 1.1 ± 0.1 µF cm-2, and Ri = 121 ± 21 Ω cm. Thus, in comparison to hippocampal principal neurons, BCs show a substantially lower Rm. Simulation of synaptic events in BC cable models shows that (1) temporal summation of EPSPs is restricted to a narrow time window (~10 ms), (2) the extensive axonal arbor of BCs has little influence on dendritic integration, suggesting functional separation of somatodendritic and axonal domains of BCs, and (3) shunting inhibition on the proximal apical dendrite reduces EPSPs generated at the distal apical dendrite, suggesting that perforant path inputs may be under the powerful control of shunting inhibition.

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Consistency of in vitro and in vivo connectivity estimates: statistical assessment and application to cortical network modeling

Tobias C. Potjans, M. Diesmann

The precise relationship between the specific structure of the local cortical network and its function as a basic information-processing unit is under intense investigation but nevertheless elusive. Modeling efforts join in the task to tackle this decisive issue, requiring, however, comprehensive data in a suitable format. In order to consolidate models and the increasing specificity in published connectivity data, we statistically assess prominent results on laminar cortical connectivity from in vitro physiology and in vivo based anatomy. This analysis enables us to formulate an integrated data set based on [1, 2] and complemented by suitable additional data using the following constraints: the conservation of invariant measures, scaling according to a lateral connectivity model and consolidation in compliance with target-type specificity.

Considerable differences in methodology are reflected in apparent inconsistencies of the layer-specific connection matrices. We introduce and statistically analyze measures that capture invariants of anatomical [1] and physiological [2] data sets. A gaussian model of lateral connectivity accounts for the spatial confinement of in vitro data and predicts, based on [1, 2], a lateral spread of connections consistent with other studies such as [3, 4]. The remaining inconsistencies express the fact that functional connections are target-type specific. We utilize the connectivity based on anatomical reconstructions to generate surrogate structures. This demonstrates that, in general, functional inter-layer projections [2] significantly violate the homogeneity assumptions on which Peters' rule [1] is based. Consequently, we find target-type specificity to be indispensable for the description of the layer-specific connectivity structure. Finally, the resulting data set allows us to investigate the dynamical properties induced by layer- and type-specific connectivity by means of numerical simulations of a local cortical network consisting of 80,000 neurons, linking the structure of the cortex to its activity.

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Control of the temporal interplay between excitation and inhibition by the statistics of visual input: a V1 network modelling study

Jens J. Kremkow, L. Perrinet, P. Baudot, M. Levy, O. Marre, C. Monier, Y. Frégnac, G.S. Masson, A. Aertsen

In the primary visual cortex (V1), single cell responses to simple visual stimuli (gratings) are usually dense but with a high trial-by-trial variability. In contrast, when exposed to full field natural scenes, the firing patterns of these neurons are sparse but highly reproducible over trials (Marre et al., 2005; Frégnac et al., 2006). It is still not understood how these two classes of stimuli can elicit these two distinct firing behaviours.

A common model for simple-cell computation in layer 4 is the "push-pull" circuitry (Troyer et al. 1998). It accounts for the observed anti-phase behaviour between excitatory and inhibitory conductances in response to a drifting grating (Anderson et al., 2000; Monier et al., 2008), creating a wide temporal integration window during which excitation is integrated without the shunting or opponent effect of inhibition and allowed to elicit multiple spikes.

This is in contrast to recent results from intracellular recordings in vivo during presentation of natural scenes (Baudot et al., submitted). Here the excitatory and inhibitory conductances were highly correlated, with inhibition lagging excitation only by few milliseconds (~6 ms). This small lag creates a narrow temporal integration window such that only synchronized excitatory inputs can elicit a spike, similar to parallel observations in other cortical sensory areas (Wehr and Zador, 2003; Okun and Lampl, 2008).

To investigate the cellular and network mechanisms underlying these two different correlation structures, we constructed a realistic model of the V1 network using spiking neurons with conductance based synapses. We calibrated our model to fit the irregular ongoing activity pattern as well as in vivo conductance measurements during drifting grating stimulation and then extracted predicted responses to natural scenes seen through eye-movements.

Our simulations reproduced the above described experimental observation, together with anti-phase behaviour between excitation and inhibition during gratings and phase lagged activation during natural scenes.

In conclusion, the same cortical network that shows dense and variable responses to gratings exhibits sparse and precise spiking to natural scenes. Work is under way to show to which extent this feature is specific for the feedforward vs recurrent nature of the modelled circuit.

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A biologically realistic model of correlation based structural plasticity

Moritz Helias, S. Rotter, M.-O. Gewaltig,

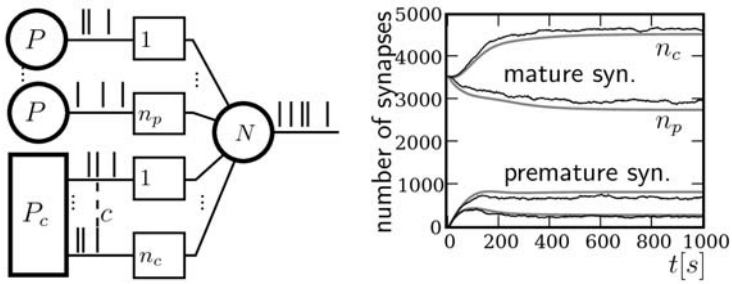
To understand the fine scale connectivity and its plastic changes in cortical networks, the neuronal mechanisms controlling synapse formation and death must be elucidated. In particular the correlation of pre- and postsynaptic spiking activity plays a key role in the theories of Hebbian learning and correlation based sorting during development [1]. Recent experiments [2] provide support for activity dependent synapse formation.

Here we present a synaptic learning rule based on the calcium influx into spines through NMDA receptors. Our model shows that the calcium signal is suitable for correlation detection: it is confined to the spine volume, it depends on the relative timing of pre- and postsynaptic action potentials, and it is independent of the distance of the synapse from the soma [3,4]. We further base our model on the calcium/calmodulin dependent protein kinase II (CaMKII), an ubiquitous downstream effector protein.

Major components of the model are analytically tractable and can be implemented in a computationally efficient way suitable for large-scale simulations [5].

Under realistic conditions of irregular spike trains, we show that our model is a viable mechanism to sense the correlation between pre- and postsynaptic activity. Controlling synaptic pruning, it can implement a firing rate homeostasis in recurrent networks. Furthermore, we demonstrate that cooperation and competition between synapses emerges naturally from the microscopic model, enabling a neuron to learn the correlations between neighboring inputs (see figure).

Continuous generation of premature synapses and correlation dependent maturation and pruning lead to stable populations of mature and premature synapses. Correlated inputs recruit more functional synapses (nc) then uncorrelated inputs (np).



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Altered layering of the dentate gyrus in reeler mice results in a reduced efficiency and precision of synaptic activation of hilar mossy cells

Janina Kowalski, M. Geuting, A. Drakew, C. Haas, S. Zhao, M. Frotscher, I. Vida

The dentate gyrus, similarly to other cortical areas, has a strictly layered anatomical structure. Although disrupted layering has been found to be associated with pathological conditions such as epilepsy, the primary functional relevance of cortical layering is unknown. In the mouse mutant reeler, migration defects lead to a severely altered lamination of the dentate gyrus. In the present series of experiments, we have investigated how the input-output relation of the dentate network is changed in reeler mice by stimulating its main input, the perforant path, and recording its synaptic output in hilar mossy cells. In wild-type mossy cells, synaptic responses elicited by perforant path stimulation were uniform and were dominated by a short-latency, long-lasting inhibition and a longer-latency, brief excitatory component corresponding to a disynaptic EPSC. In reeler, the synaptic responses were heterogeneous. In most neurons inhibition was markedly enhanced and the disynaptic EPSC reduced. Additionally, in many mossy cells, a short-latency monosynaptic EPSC was observed. As a consequence, action potentials were generated with reduced probability over a broader temporal window. Consistent with the electrophysiological findings, visualization of the intracellular labeled mossy cells revealed dramatic changes and a large degree of heterogeneity in their localization and the distribution of their dendrites and axons. While in the wild-type hippocampus mossy cells and their dendrites were confined to the hilus, in reeler the cells and their dendrites were often found in the molecular layer where they are likely to form synapses with perforant path fibers. In summary, changes in the morphology of reeler mossy cells enable them to receive direct synaptic input from the perforant path; however, the excitatory synaptic input via dentate granule cells is strongly reduced and feed-forward inhibition is increased. Thus, changes in the connectivity associated to the altered lamination in reeler mice result in a reduced efficiency and lower temporal precision of synaptic activation in the dentate-hilar network.

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NEST, a parallel and distributed simulator for large networks of spiking neurons

Marc-Oliver Gewaltig, M. Diesmann, H.E. Plesser, A. Morrison

NEST is a simulation environment for large heterogeneous networks of point-neuron models or neuron models with a small number of compartments [1]. It supports spike based as well as continuous (e.g.rate, currents) interaction between the nodes of the network. We present NEST2 with its new Python-based user interface (www.python.org) PyNEST. PyNEST makes NEST easy to learn and use. Python provides a large number of libraries for scientific computing (www.scipy.org), making it a powerful alternative to Matlab. Users can simulate, analyze, and visualize networks and simulation data in a single interactive Python session. Other features of NEST 2 include support for synaptic plasticity, a wide range of model neurons, and parallel simulation on multi-processor (core) computers as well as computer clusters [2]. To customize NEST to their own purposes, users can add new neuron and synapse models, as well as new connection and analysis functions, by writing their own NEST modules in C++. Pre-releases of NEST 2 have already been used with great success and appreciation at European Advanced Course in Computational Neuroscience 2007 and the FIAS Summer School 2007. NEST is released under an open source license for non-commercial use. For details visit the NEST Initiative at http://www.nest-initiative.org.

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