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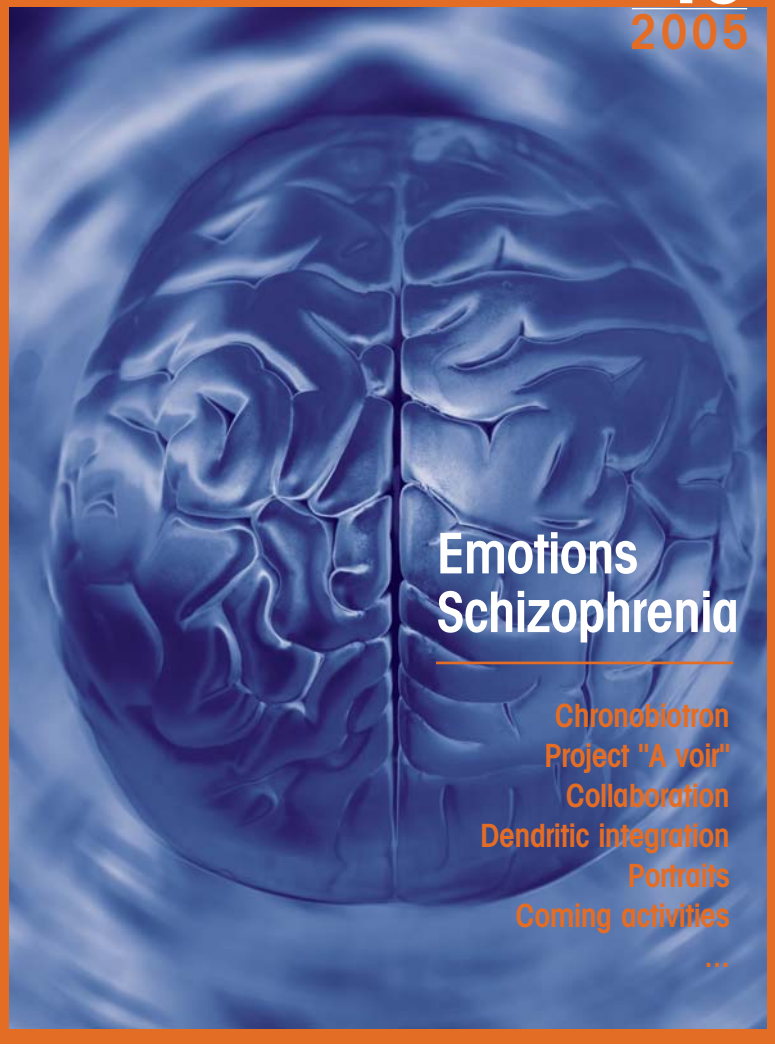

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Reliability of dendritic integration in neocortical neurons

Studying the dynamics of neuronal networks is essential for the understanding of the working principles of the brain. A promising route towards an increasingly realistic picture of the neocortex is the interplay of experimental and theoretical investigation of neural computation at the level of individual cells as well as on the level of groups of cells embedded in an active neocortical network. In the recently founded Bernstein Center for Computational Neuroscience (BCCN) at the University of Freiburg, the group of Dr. Clemens Boucsein studies signal propagation in the neocortex and the influence of network activity on neuronal physiology, combining in vivo-recordings of intra- and extracellular signals with new, innovative experimental in vitro-designs.

Recent advances in the characterization of neuronal physiology, especially of pyramidal cells, have revealed a wealth of mechanisms which can turn a single cell into a highly complicated and non-linear signal integrator. Prominent examples are dendritic Calcium- or NMDA spikes and back-propagating action potentials, but also plasticity phenomena. Most of these mechanisms depend strongly on the membrane potential and on the history of synaptic activity in the different dendritic branches of the cell. In principle, they can lead to a highly variable spike output pattern as a reaction to the same or similar synaptic input patterns, depending on the actual activity state of the surrounding cortical network, as well as the activity history of the individual neuron. In an active network, which provides single cells with vivid synaptic input, these mechanisms could lead to a profound influence on the dynamics of signal propagation and information processing. It is, thus, essential to study the effectiveness and impact of these mechanisms in the context of an active neuronal network.

Recently, Dr. Boucsein together with Dr. Nawrot established the new in vitro method of Dynamic Photo Stimulation [1], which allows to study activity-dependent phenomena in identified neurons in the acute slice preparation. It utilizes pulses of locally confined neurotransmitter release from a caged precursor to activate cells at predefined target locations within the slice. A fast sequence of several tens or hundreds of stimulation pulses per second can generate intense synaptic input in an identified post-synaptic neuron using intact functional synaptic projections. At the same time, the post-synaptic cell is accessible to conventional electrophysiological methods that have been used to reveal the above mentioned mechanisms.

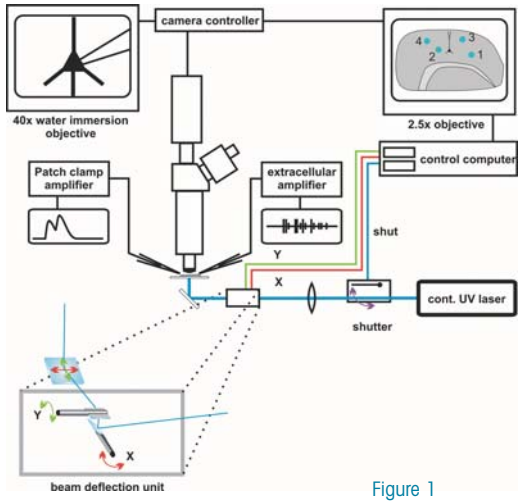

Figure 1

The particular strength of the new method is that it allows to activate neurons hundreds of microns away from the post-synaptic cell. Thus, pre-synaptic cells can be activated without directly stimulating the post-synaptic cell, so that the natural characteristics of the synaptic input can be preserved, in particular the specific strength, input location on the dendrite and spatial distribution of individual synapses.

In a first attempt to address the reliability of activity propagation using Dynamic Photo Stimulation, it was shown that synaptic transmission and dendritic integration of synaptic inputs can be highly reliable [1,2]. This was revealed by somatic measurement of the integrated memebane potential in response to identical repeated stimulation sequences that activated presynaptic neurons in rapid succession (cf. Figure 2).

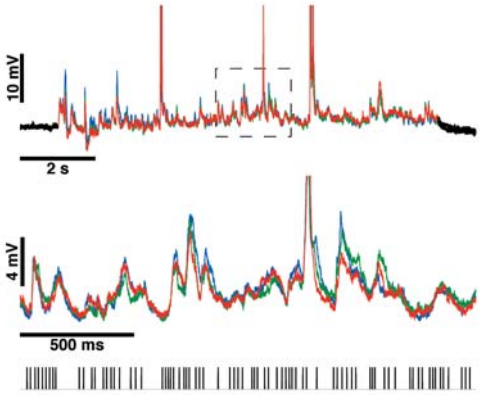

Figure 2

In how far this reliability is preserved under varying activity conditions is one of the questions that will be addressed in the group of Dr. Boucsein. ■ C.B. & MP. N.

Figure 1 legend:
For Dynamic Photo Stimulation, a conventional upright microscope is equipped with an illumination unit consisting of a continous UV-laser, a variable shutter and a beam deflection unit. When illuminating the slice tissue from below (through the bottom of the recording chamber), the spatial range is independent from the objective and the space above the slice is available for conventional recording or stimulation electrodes. Time resolution in this setup is appr. 1 millisecond for beam positioning and shutter opening, allowing for stimulation frequencies of up to 300 Hz.

Figure 2 legend:
Somatic voltage recordings from a layer V pryamidal neuron during 3 identical repetitions (colored traces) of a dynamic photostimulation sequence, 400 stimulations at 34 presynaptic sites during 10s (spikes clipped). The blow-up demonstrates the highly reproducible responses (avg. linear correlation is c=0.88). Tick marks indicate the temporal sequence of individual photostimulations.

[1]

C. Boucsein, M. Nawrot, S. Rotter, A. Aertsen, and D. Heck (2005) Controlling Synaptic Input Patterns In Vitro by Dynamic Photo Stimulation. J Neurophysiol 94: 2948

[2]

C. Boucsein, A. Aertsen, and M. Nawrot (2005) Precision and Reliability of Activity Propagation in the Neocortex. Soc Neurosci Abstr 35: 276.16