e.IP Symposium

Neuroscience Meeting 2004
Monday, October 25, 6:30PM to 9:00PM
San Diego Convention Center, Room 6DE

Speakers present results illustrating advances in neuroscience due to advances in instrumentation. The first half will focus on microelectrode and chemical/thermal stimulation techniques. The second half will be devoted to multielectrode techniques.

<u>About e.IP (Electrophysiology Innovation Partnership)</u>: e.IP has the legal status of a friendly and incorporated society with the objective to further science and technology in the field of electrophysiology and to communicate and promote innovative developments, solutions, and products enabling high-end electrophysiology in the field of basic research, drug discovery, and neurotechnology.

Synaptic Integration in the Cortex Shaped by Network Activity

<u>Detlef Heck</u>, University of Tennessee Health Science Center, Department of Anatomy and Neurobiology, Memphis, TN

Neocortical neurons *in vivo* receive massive synaptic input from the permanently active surrounding network. How this ongoing network activity affects the neurons' integrative properties and what function this may imply at the network level remains largely unknown. Most of our knowledge regarding synaptic communication and integration is based on recordings *in vitro*, where network activity is strongly diminished or even absent. Here, we present results from two complementary series of experiments based on intracellular *in vivo* recordings in anaesthetized rat prefrontal cortex. Specifically, we measured (i) the relationship between the excursions of a neuron's membrane potential and the spiking activity in the surrounding network; (ii) how summation of several inputs to a single neuron is affected during the different levels of its membrane potential excursions and phases of network activity. The combination of these measurements allows to assess how different levels of network activity influence synaptic integration. We present direct evidence that integration of synaptic inputs is linear, independent of the level of network activity. However, during periods of high network activity, the neurons' response to synaptic input is markedly reduced in both amplitude and duration. This results in a drastic shortening of its window for temporal integration, requiring more precise coordination of presynaptic spike discharges to drive the neuron to spike under conditions of high network activity. We conclude that ongoing activity, as present in the active brain, emphasizes the need for neuronal cooperation at the network level, and cannot be ignored in the exploration of cortical function.

Reference: Leger JF, Stern EA, Aertsen A, Heck D. Synaptic Integration in Rat Frontal Cortex Shaped by Network Activity. J Neurophysiol. 2004 Aug 11 [Epub ahead of print] PMID: 15306631

Investigating endocannabinoid signalling in the amygdala - extracellular and intracellular recordings with the SEC-10L

<u>Gerhard Rammes</u>, Clinical Neuropharmacology, Max Planck Institute for Psychiatry, Munich, Germany

Cannabinoids and the endogenous cannabinoid system have been shown to modulate amygdala-associated processes including pain perception and extinction of aversive memories. However, little is known about the endocannabinoid signaling in the amygdala on the cellular level. To detail the effects of the activation of cannabinoid receptors (CB1), patch-clamp and field potential recordings of synaptic responses in the basolateral amygdala were performed by the stimulation of afferents in the lateral amygdala using an *in vitro* slice preparation. Application of the CB1 receptor agonist WIN 55,212-2 (WIN-2) reduces excitatory and inhibitory synaptic transmission and blocked long-term depression induced by low frequency stimulation (LFS) with 900 pulses/1 Hz.

The application of LFS with 100 pulses/1Hz (LFSi) induces a long-term depression of inhibitory GABAergic synaptic transmission. Stimulation by LFSi releases endocannabinoids postsynaptically and, thereby, via a presynaptic mechanism reduces the inhibitory synaptic transmission of GABAergic interneurons.

Lowering inhibitory synaptic transmission significantly increases the amplitude of excitatory synaptic currents in principal neurons of the central nucleus, which is the main output site of the amygdala. Since endocannabinoid levels are increased in the amygdala during the extinction of conditioned fear, endocannabinoids might selectively modulate local inhibitory networks in the amygdala and thus facilitate extinction of aversive memories.

References: Azad SC, Eder M, Marsicano G, Lutz B, Zieglgansberger W, Rammes G. Activation of the cannabinoid receptor type 1 decreases glutamatergic and GABAergic synaptic transmission in the lateral amygdala of the mouse. *Learn Mem. 2003 Mar-Apr;10(2):116-28.*

Shahnaz C. Azad, Krisztina Monory, Giovanni Marsicano, Benjamin F. Cravatt, Beat Lutz, Walter Zieglgänsberger, Gerhard Rammes Circuitry for associative plasticity in the amygdala involves endocannabinoid signaling *J Neurosci in press*

Exploring temperature-sensitive currents with rapid, focal thermal stimulation.

Todd C. Pappas[1], *Alan Kriegstein*[3], *Malcolm Brodwick*[2], *Massoud Motamedi*[1,2].
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The recent characterization and isolation of a number of vertebrate temperature-sensitive conductances and ion channels has necessitated development of more sophisticated tools to study the biophysics of temperature sensation. We have collaborated with ALA Scientific Instruments to develop a pressure-driven, rapid, hydronic focal temperature stimulator similar to a "temperature clamp" for study of temperature-sensitive conductances. In this device, buffer solutions are rapidly perfused across four independent Peltier elements mounted on a "front end" that can be positioned very close to the sample. Complex heating and cooling profiles were created from the four temperature channels using a computer interface and software (HEKA Pulse+PulseFit v. 8.54) that also controlled a single electrode clamp amplifier (SEC 05-LX, npi electronic). We were able to attain rapid, repeatable and symmetrical heating and cooling profiles in a standard 35 mm diameter tissue culture dish (3 mL buffer volume). Heating ramps were as rapid as 1 °C / 38 ms (≈ 26 °C/s) at perfusion rates that did not affect patch integrity. The duration of the steady-state temperature plateau was best at lower perfusion rates as it was limited by the volume of the heated reservoir. Using this system we have replicated temperature- and voltage-dependent characteristics of temperature-sensitive currents in snake trigeminal ganglion cells and HEK293 cells transfected with TREK1. Additionally, we report novel characteristics of these conductances that are revealed through rapid focal thermal stimulation. (Funded by AFOSR F49620-01-1-0552 [TCP] and 1R41NSO46182-01 [AK]).

Neuronal avalanches in neocortical circuits

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Networks of living neurons exhibit diverse patterns of activity including oscillations, synchrony and waves. Recent work in physics has shown yet another mode of activity in systems composed of many non-linear units interacting locally. For example, avalanches, earthquakes, and forest fires all propagate in systems organized into a critical state where event sizes show no characteristic scale and are described by power laws. We hypothesized that a similar mode of activity with complex emergent properties could exist in networks of cortical neurons. We investigated this issue in mature organotypic cultures and acute slices of rat cortex by recording spontaneous local field potentials (LFP) continuously using a 60 channel multi-electrode array. Here we show that propagation of spontaneous activity in cortical networks is described by equations that govern avalanches. As predicted by theory for a critical branching process, the propagation obeys a power law with an exponent of -3/2 for event sizes, with a branching parameter close to the critical value of 1. Simulations show that a branching parameter at this value optimizes information transmission in feed-forward networks, while preventing runaway network excitation. Our findings suggest that "neuronal avalanches" may be a generic property of cortical networks, and represent a mode of activity that differs profoundly from oscillatory, synchronized, or wave-like network states. In the critical state, the network may satisfy the competing demands of information transmission and network stability.

Spontaneous calcium waves in the ventricular zone of the developing mammalian retina.

Z. Jimmy Zhou, *Dept of Physiology and Biophysics, University of Arkansas for Medical Science, Little Rock, AR*

Propagating waves of spontaneous activity were previously thought to appear only in the inner layers of the developing mammalian retina, where the cells (amacrine and ganglion) are already differentiated. Here, we show that undifferentiated cells in the outer retinal layer (ventricular zone) also display spontaneous activity that propagates laterally as Ca waves. Using multielectrode array (MEA) recording in the inner rabbit retina and Ca imaging in the ventricular zone of the same retina simultaneously, we demonstrate that the waves in the inner and outer retinal layers were correlated in both spatial and temporal domains. Pharmacological characterizations further demonstrate that the waves were initiated in the inner retina and then back spread to the ventricular zone. The results suggest that differentiated cells in the inner retina may send a retrograde developmental signal to undifferentiated/differentiating cells in the ventricular zone via propagating Ca waves.