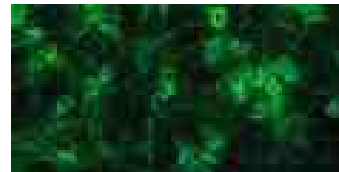
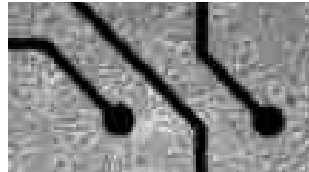
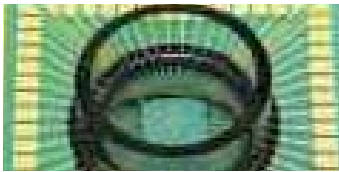


# Advances in Microelectrode and Multielectrode Recording Techniques

2<sup>nd</sup> e.IP workshop at the  
Annual Meeting of the Society of Neuroscience  
November 15, 2005, 5:30PM to 8:00PM, Room 209A  
Convention Center, Washington DC



## Topics

- Pharmacology of two nicotinic acetylcholine receptor subtypes on insect CNS neurons studied with the Single-Electrode Voltage Clamp Technique  
Vincent L. Salgado, BASF Corporation
- Neuronal avalanches and information storage: A few strong connections  
John Beggs, Indiana University
- Leading and dominance asymmetry In coupled neural networks  
Itay Baruchi, Tel Aviv University
- The synapse is not everything: Modulation of excitability and electrical coupling and their contribution to learning  
Brian D. Burrell, University of South Dakota
- Perforated microelectrode arrays optimize oxygen availability and signal-to-noise ratio in brain slice recordings  
Uli Eger, University Freiburg

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## **Pharmacology of two Nicotinic Acetylcholine Receptor Subtypes on Insect CNS Neurons Studied with the Single-Electrode Voltage Clamp Technique.**

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Neuronal somata isolated from the insect CNS typically contain a rich assortment of voltage- and ligand-gated ion channels that can be studied quantitatively under voltage-clamp conditions. The single-electrode voltage-clamp (SEVC) method with intracellular microelectrodes offers several advantages over the more commonly used patch clamp method for these studies. Because the smaller tip opening of the intracellular microelectrode minimizes exchange of electrode and intracellular contents, the cell can be held for a longer time and there is less rundown of ionic currents, allowing precise measurement of dose-response relations of compounds with very slow receptor interactions, typical of lipophilic or high-affinity compounds.

Using this technique, two  $\alpha$ -bungarotoxin-sensitive nicotinic acetylcholine receptor (nAChR) subtypes were characterized in cockroach neurons. A desensitizing subtype (nAChD) was selectively inhibited by the neonicotinoid insecticide imidacloprid at 100 nM, and a non-desensitizing subtype (nAChN) was selectively inhibited by 100 pM methyllycaconitine, and is the subtype measured in binding studies with radiolabeled  $\alpha$ -bungarotoxin. The pharmacology of both nAChR subtypes measured with SEVC corresponded closely with binding data.

### **Reference:**

Vincent L. Salgado, Raimund Saar Desensitizing and non-desensitizing subtypes of  $\alpha$ -bungarotoxin-insensitive nicotinic acetylcholine receptors in cockroach neurons. *Journal of Insect Physiology* 50 (2004) 867–879, [www.elsevier.com/locate/jinsphys](http://www.elsevier.com/locate/jinsphys)

## **Neuronal avalanches and information storage: A few strong connections**

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A central task in cortical physiology is to determine how local cortical networks store memories. The synaptic hypothesis states that information can be retained in the connection strengths, or weights, between neurons, yet details of this scheme are incompletely understood. Some investigators argue that individual synaptic connections in cortex are weak, suggesting a nearly homogeneous weight distribution. Others, however, argue that a few strong connections dominate, indicating a more biased weight distribution. These two views lead to substantially different pictures of cortical network operation and storage capacity. To address this issue, we recorded spontaneous local field potentials from cortical slice networks using a 60 channel microelectrode array. We also used a parsimonious model that captures central features of the data (Haldeman and Beggs, 2005). Previous work showed that cortical slice networks produce neuronal activity patterns that are statistically similar to avalanches seen in critical sand pile models (Beggs and Plenz, 2003). These neuronal avalanches may serve as a substrate for information storage since they occur in patterns that are temporally precise and repeatable for over 10 hrs (Beggs and Plenz, 2004). By varying connection weights in the model, we found that the biased distribution not only best fit the data, but also produced the largest number of repeatable avalanche patterns. Interestingly, this result is also consistent with recent triple patch clamp data from cortical slices (Song et al, 2005). These findings suggest that a few strong connections dominate in local cortical networks and that this connection scheme yields the largest memory capacity.

### **References:**

Haldeman, C. and Beggs, J.M. Critical branching captures activity in living neural networks and maximizes the number of metastable states. Physical Review Letters, 94: 058101, 2005.

Beggs, J.M., and Plenz D. Neuronal avalanches in neocortical circuits. The Journal of Neuroscience, 23(35): 11167-77, 2003.

Beggs, J.M., and Plenz D. Neuronal avalanches are diverse and precise activity patterns that are stable for many hours in cortical slice cultures. The Journal of Neuroscience, 24(22): 5216-29, 2004.

Song S, Sjöström PJ, Reigl M, Nelson S, Chklovskii DB. Highly nonrandom features of synaptic connectivity in local cortical circuits. Public Library of Science Biology. 2005 Mar; 3(3):e68. Epub 2005 Mar 1.

## **Leading and Dominance Asymmetry In Coupled Neural Networks**

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Motivated by the quest to understand synchronization, lateralization and dominance in human brain activity, we studied the dynamics of coupled cultured networks grown on top of Multi-Electrode-Arrays (MEA). Using a special lithographic method we grow coupled *in vitro* networks (from cortical cultures of neurons and glia cells drawn from one day old Charles River Rats) with engineered coupling properties. Like for single (unitary) cultured networks, the activity of each of the sub-networks is marked by the formation of synchronized bursting events (SBEs) – short time windows (~200ms) during which most of the neurons exhibit rapid firing, separated by loge (~seconds) time intervals of sporadic neuronal firing. Additional phenomenon characteristic to the coupled networks' activity is that of mutual synchronization of SBEs between the coupled networks. According to the properties of the coupling regime (width, length, density of neurons etc) the mutual synchronization can vary from about 25% to about 80%. Using clustering algorithm we reveal existence of two types of mutual SBE patterns, each is characterized by a directional propagation of the activity - in the first type the activity begins in one of the sub-network and propagates to the other, while in the second type the activity propagates the other way around. Consequently, we define as the leading network to be the one in which a larger fraction of mutual SBEs are initiated.

Interestingly, we found that the leading sub-network is not necessarily the also the dominate one. The latter refers to the sub-network for which the level of inter-neurons correlations is higher. We propose that this result is connected to the fact that the activity propagation is regulated largely by the coupling régime while the dominance is related to the relative inter-neuron connectivity in each sub-network.

### **Reference:**

Volman V, Baruchi I, Ben-Jacob E. Manifestation of function-follow-form in cultured neuronal networks. Phys Biol. 2005 Jun;2(1-2):98-110.

## **The synapse is not everything: Modulation of excitability and electrical coupling and their contribution to learning**

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Although changes in synaptic efficacy are thought to play a critical role in learning and memory, they are not the only forms of neuroplasticity that contribute learning-related changes in behavior. Specifically, modulation of neuronal excitability has received increased attention as an important cellular mechanism that contributes to learning. Using the medicinal leech as a model system, my colleagues and I have been examining the role of serotonin-dependent changes in excitability in an interneuron (the S-cell) thought to be critical for sensitization-type learning of the leech shortening reflex. During sensitization, excitability of the S-cell increases through the activation of a metabotropic 5HT receptor coupled to a cAMP/PKA pathway. This increase in excitability is mediated, at least in part, by a decrease in S-cell afterhyperpolarization. Increased excitability contributes to an increase in the frequency of S-cell activation in the sensitized animal and this increase in activity alters S-cell synaptic signaling to follower neurons in the shortening neural circuit. In addition, serotonin also modulates axo-axonal electrical synapses that link the S interneurons to one another, increasing the instantaneous frequency of action potentials as they propagate through this electrically-coupled network.

### **References:**

Brian D. Burrell and Christie L. Sahley Multiple Forms of Long-Term Potentiation and Long-Term Depression Converge on a Single Interneuron in the Leech CNS. *Journal of Neuroscience*, 24(16):4011–19

B. L. Moss, A. D. Fuller, Ch. L. Sahley, and B. D. Burrell Serotonin modulates axo-axonal coupling between neurons critical for learning in the leech. *J Neurophysiol.* 2005 Oct;94(4):2575-89.

## **Perforated Microelectrode Arrays Optimize Oxygen Availability and Signal-to-Noise Ratio in Brain Slice Recordings.**

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Complementing single electrode recordings, passive, substrate-integrated thin-film microelectrode arrays (MEAs) have become established tools to investigate spatio-temporal patterns of electrical activity and neuronal interaction in-vitro. In the neurosciences, acute brain slices with accessible and well-preserved neuronal microcircuitry have become the most widespread preparation, that can also be recorded with MEAs for spike activity and local field potentials. Oxygen and nutrients are, however, supplied to the slice tissue by diffusion only (usually from one side) and can become limiting for tissue stability viability, and slice thickness. Since MEAs record on the face of the slice not directly exposed to the continuous stream of buffer, this might become critical. We therefore developed and compared solid and perforated MEAs for extracellular recording and stimulation, the latter to provide a second exchange surface. For each array we determined the depth profile of the local O<sub>2</sub>-partial pressure (pO<sub>2</sub>) in cerebellar brain slices. On impermeable MEAs, pO<sub>2</sub> decreased linearly with depth in the tissue. Added diffusion through the perforated MEA surface decreased the slope of the pO<sub>2</sub> gradient and the minimum level reached within the tissue. In addition, signal-to-noise ratios (SNR) in the recordings increased. Improved supply also allows thicker slices and thus the preservation of larger networks, i.e. more complex and in-vivo-like networks. Furthermore, drug accessibility to the recorded cells is improved, accelerating dose-response studies.