Symposium at the 39th Annual SFN Meeting in Chicago, Il.

Microelectrode and Multielectrode Recording Techniques

Monday, October 19th 2009, 6.30 p.m.- 9 p.m.
McCormick Place campus Rm # S405-AB

Intended for scientists interested in electrophysiology, this symposium will include methodological talks by international scientists within the field. Speakers from diverse areas will present results illustrating advances in neuroscience made possible by advances in instrumentation.
The first half of the symposium will be devoted to multielectrode techniques and the second half will be devoted to microelectrode techniques. The multielectrode techniques will illustrate the growing field of multielectrode array technology on different preparations *in vitro*. The microelectrode techniques section will illustrate a variety of new applications such as electroporation, single cell stimulation, and high resolution recording addressable with improved devices.

Topics:

Simultaneous micro-electrode array recording and two-photon calcium imaging in rat cortex slices

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Obtaining high temporal resolution measurements of activity among large groups of neurons in local cortical circuits is crucial for understanding network-level brain function. Two-photon calcium imaging (2PI) and micro-electrode array (MEA) recordings are both important tools for such investigation, but each has disadvantages. For example 2PI has relatively poor temporal resolution, while MEAs cannot access information about inactive neurons or the relative spatial locations and morphologies of active neurons. Here we describe a method for combined, simultaneous 2PI and MEA measurements. Here we demonstrate this technique in acute slices of 3 week old rat somatosensory cortex. We show that spontaneous local field potential (LFP) fluctuations measured from cortical networks with suppressed inhibition are generated by network-wide synchronous spiking neurons. In contrast, spontaneous activity in a cortical network with inhibition intact shows diverse activity patterns that sample a wide range of spatial scales from single cells up to millimeter-sized networks.

Modulating GABAergic network activity in an *in vitro* slice epilepsy model using a perforated multielectrode array

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Dynamic interplay between glutamatergic pyramidal cells and GABAergic interneurons is responsible for neural circuit activity ranging from distinct cognitive states to epileptic seizures. While the variation of pyramidal cell types is small, heterogeneity flourishes within the interneuron family. What roles do these interneurons play in network activity? We will probe these interactions by varying the tonic GABA current in an *in vitro* epilepsy model. Tonic GABA current is important in the modulation of network electrical activity. To identify one class of GABAergic interneuron subtypes, we will use coronal cortico-hippocampal brain slices from GFP-tagged NPY-positive mice ranging from postnatal day 14 to 18. In addition, we will identify fast-spiking basket cells by their firing patterns. Slices will be exposed to an *a*CSF solution containing the potassium channel blocker, 4-aminopyridine (4AP, 100µM) and a reduced concentration of MgCl2 (0.6 mM) which is a model of *in vitro* seizures as described by Netoff et. al. (J. Neurosci **22** (16), 7297-307, (2002)). Extracellular recordings with patch electrodes will first assess the presence of coordinated network activity in individual locations in CA1, CA3 and dentate gyrus in cortico-hippocampal slices. Next, using a 60 channel perforated multi-electrode array (pMEA), we will simultaneously record field potentials and multi unit activity from several distinct anatomical regions. We will use a GABAA receptor agonist 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridine-3-ol (THIP, 10µM) in which preliminary results suggests a decrease in the durations of interictal-like discharges and increase in their intervals. Next, we will apply the GABAA receptor antagonist to Gabazine (GBZ, 200nM) to elucidate its effect on the network. The parallel studies of distinct brain areas using the perforated multielectrode array, taking advantage of the increased excitability induced by 4AP and reduced $MgCl_2$, has great potential in providing important information for neuronal interactions resulting in brain activity and behavior with relevance to epilepsy and several neurological disorders.

Two Distinct Mechanisms That Regulate Stimulus Detection in a Model Organism.

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Regulating incoming information is one of the central tasks of the nervous system. To understand the cellular mechanisms utilized, we study sensory regulation in an easy-to-study invertebrate model system - the sea slug *Aplysia californica*. This system allows us to take advantage of a variety of classical and modern techniques. We monitor changes in membrane potential using extra- and intracellular recording techniques, and perform voltage clamp experiments using SEVC and TEVC. In some experiments electrophysiological techniques are combined with functional imaging, e.g., to detect changes in the intracellular calcium concentration. Using these techniques, we have characterized two mechanisms that regulate afferent transmission between an identified sensory neuron, *B21*, and its postsynaptic follower neurons. In current and voltage clamp experiments in which B21 was impaled with multiple sharp electrodes, we demonstrated that motor program induced changes in membrane potential regulate spike propagation in B21 thereby determining whether peripherally induced action potentials are transmitted to output regions of the cell. In imaging/electrophysiology experiments, we demonstrated that once spikes propagate, the baseline membrane potential further determines the efficacy of synaptic transmission. The latter mechanism is graded and involves the induction of nifedipine sensitive calcium current. In conclusion, the experimentally advantageous features of our preparation have enabled us to gain important insights into mechanisms that regulate afferent transmission and thereby determine whether a peripherally evoked stimulus is detected.

Measuring efferent connections of single neurons in the hippocampal slice

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Within the first three weeks after a prolonged seizure (status epilepticus) the adult rat hippocampus begins to produce spontaneous epileptiform burst discharges that can be recorded *in vitro* extracellularly and intracellularly under normal recording conditions. Anatomical evidence suggests that increased axon collateralization of dentate granule cells[1] and CA3 pyramidal cells[2] coincide with the emergence of this spontaneous epileptiform activity. The purpose of the current investigation is to test whether the functional output of individual dentate gyrus and CA3 principal cells is increased during this period of epileptogenesis. To this end, we combine loose cell attached[3] stimulation of neurons of interest with multielectrode array recording of efferent target areas to determine the number of monosynaptic connections cells of interest make under control and experimental conditions. Microstimulation of a single neuron with supra and subthreshold stimuli combined with online spike detection within a field of target neurons provides a useful tool to determine the number of synaptic targets of a neuron.

1. Cronin, J., and Dudek, F. E. (1988) Chronic seizures and collateral sprouting of dentate mossy fibers after kainic acid treatment in rats. *Brain Res.* 474: 181-184.
2. Siddiqui, A.H., and Joseph, S.A.,(2005). CA3 axonal sprouting in kainate-induced chronic epilepsy. *Brain Res.* 1066: 129–14.
3. Barbour, B. and Isope, P. (2000) Combining loose cell-attached stimulation and recording, *J. Neurosci. Methods* 103: 199–208.