Scientific Instruments

multichannel systems

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Symposium at the 38th Annual SFN Meeting in Washington, DC.

Microelectrode and Multielectrode Recording Techniques

Monday, November 17, 6:30 pm –8:30 pm
Walter E. Washington Convention Center Room 159AB

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 microelectrode techniques and the second half will be devoted to multielectrode techniques. 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. The multielectrode techniques will illustrate the growing field of MEA technology on different preparations *in vivo*.

Methodological approaches to exploring epileptic disorders in the human brain *in vitro*

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Brain surgery in general, but especially epilepsy surgery, offers the intriguing opportunity to study viable human central nervous tissue in vitro. Epilepsy in this context can be considered not only to be a disease, but to also act as a model. Investigations on surgical tissue not only allow us to address basic mechanisms underlying human disease, such as epilepsy, but it opens the opportunity to investigating neurophysiological functions as such. In the talk, the most commonly used methods in the electrophysiological (and also, albeit less extensively, histochemical and molecular) analyses of human tissue in vitro. Particular attention will be paid to pitfalls and limitations of such studies, and the important issue of tissue sampling procedures and control experiments will be discussed.

Gradients of synaptic strengths in a neural circuit that coordinates limb movements

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Coordinated movements of different limbs are fundamental features of effective locomotion, but the organization and dynamics of the neural circuits that accomplish this coordination are still essentially unknown. We studied the neuronal components and synaptic organization of a circuit in the crayfish nervous system that coordinates limbs used for forward swimming. Using the npi SEC 05 amplifier, we succeeded in mapping the patterns of synaptic connections and the relative strengths of different synapses in this circuit. In this talk we will illustrate results of discontinuous current-clamp and discontinuous single-electrode voltage clamp experiments obtained with these npi amplifiers using sharp microelectrodes. The quality and bandwidth of these results contrast with those from earlier experiments using the same microelectrodes but an amplifier of older design. We will discuss features of microelectrodes, perfusion techniques, and switching amplifiers that have influenced our experiments. This map of synaptic connections and synaptic strengths has changed our understanding of this coordinating circuit, and led to a novel hypothesis about the mechanism producing the characteristic pattern of limb movements.

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Please visit our exhibits (Sun.–Wed., Nov. 16-19, 9:30 am-5:00 pm)

Booth no. 2416, 2415, 2414

Perforated Multielectrode Array in Drug Discovery

Jonathan M. Levenson[1], *Arnold J. Heynen*[2] *and Margaret E. Levin*[1]
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The field of CNS drug discovery is faced with two major obstacles in translating novel bench-side discoveries into viable clinical development candidates: a lack of good animal models and a lack of *in vitro* tools that accurately model *in vivo* effects. While progress has been made in addressing the lack of animal models, there remains a critical need for *in vitro* tools. One of the more predictive *in vitro* tools available for use in CNS drug discovery is the acute brain slice. However, a number of challenges are encountered with its use, including ensuring optimal slice health, delivering compounds appropriately into the slice, and potential variability in results. Galenea has taken a unique approach to developing improved predictive *in vitro* assays by combining standard *in vitro* brain slice techniques with the newly developed, perforated multielectrode array (MEA) technology from Multichannel Systems (Reutlingen, Germany). MEA technology has existed for over two decades; however, in the past, use of this system to analyze brain slices resulted in compromised slice health and poor signal-to-noise ratios. With the advent of the new perforated MEA system, slice health and signal-to-noise parameters that rival those obtained using traditional interface chambers can be achieved, while the convenience of a submerged chamber is retained. Moreover, the MEA can be used to monitor synaptic transmission in multiple brain regions, simultaneously. Using this new technology, we have developed a number of broadly applicable methods including measures of excitability, synaptic transmission and synaptic plasticity that we now routinely employ to test compounds generated through in-house medicinal chemistry efforts. These methods assist us in developing secondary assays to examine on- and off-target effects and provide critical information required for structure-activity relationship studies. In addition, we apply these methods when creating filtering assays that are used to determine which compounds progress to *in vivo* animal testing. Adoption of perforated MEA technology has facilitated detection of compounds that exhibit physiologically relevant efficacy in targeted brain regions, which has greatly enhanced our CNS drug discovery process.

This work was generously supported through a research and development agreement with Otsuka Pharmaceutical Co., Ltd.

Determination of relative potencies for chemical inhibition of spontaneous neuronal activity using a four amplifier MEA system.

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Patch clamp recordings to determine the relative potency of compounds are often utilized drug discovery and safety assessment, and to much less extent for characterizing effects of environmental toxicants. While useful, this approach is either low throughput, or if using HTP screening devices, often limited to non-neuronal, transfected cells expressing only one channel type. In addition, spatial and temporal information regarding network responses cannot be assessed using this approach. The effects of two voltage-sensitive sodium channel activator compounds were compared using patch and multiple electrode array (MEA) recordings in hippocampal neurons. Both compounds similarly affected the rate of spontaneous EPSCs (patch) and network spiking rates (MEA). Analysis of burst activity indicated that both compounds also increased the interspike interval within bursts of action potentials. The relative potencies of 11 compounds from the same class of chemicals were then determined using a 4 amplifier MEA approach. Relative potencies ranged from 0.11 to 2 times as potent as a selected, prototypical, index chemical, and were similar, though not identical to relative potency measurements in vivo. These results demonstrate the utility of multi-amplifier MEA systems to determine relative potencies of drugs and chemicals. (This is an abstract of a proposed presentation and does not represent EPA policy).