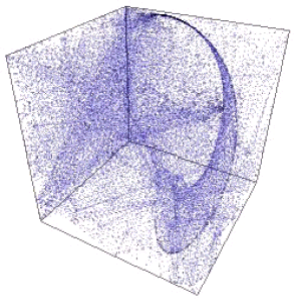
PRINCIPLES OF AUTONOMOUS NEURODYNAMICS 2006
Marine Biology Station, Eilat, Israel
July 3-4, 2006



3rd Annual Meeting of the Society for Autonomous Neurodynamics (SAND)

Sponsoring Institutes and Programs:

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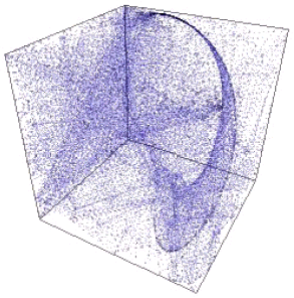

July 3 - Program Schedule

Registration		08:30 - 9:00	

EPILEPSY AND PHYSIOLOGICAL HOMEODYNAMICS
Chair: P.L. Carlen

Marija Cotic	Opening Remarks	09:00 - 09:10	
Kirk Nylen	Using Diet to Treat Seizure Disorders: Implications for Autonomy	09:10 - 09:30	p.1
Kathryn Hum	The Effects of Seizures on Hormonal Feedback Systems: Implications for Patient Autonomy	09:30 - 09:50	p.1
Sofia Megna	The Long-Term Effects of Seizures on Reproductive Cycles	09:50 - 10:10	p.2
Peter A. Abdelmalik	Neuronal Depolarization Accompanies Seizure Activity Induced by Transient Hypoglycemia	10:10 - 10:30	p.2
Group Discussion		10:30 - 10:50	
Kristi Nylen-Burns	Finding a Space for Sam	10:50 - 11:10	p.3
Coffee Break		11:10 - 11:30	

EPILEPSY: IN VITRO AND TRANSITIONS
Chair: P. Wang

Liang Zhang	Cobalt Induced Epileptiform Discharges in Mouse Hippocampus In Vitro	11:30 - 11:50	p.4
Peter L. Carlen	The Dynamics of Seizure Transition: The Role of Interneurons and Pyramidal Neurons in Epileptogenesis	11:50 - 12:10	p.5
Piotr Suffczynski	Epileptic Transitions - Insight from a Hippocampal Model	12:10 - 12:30	p.5
Group Discussion		12:30 - 12:50	
Lunch		12:50 - 14:00	

NEURODYNAMICS
Chair: K. Hum

Elan Liss Ohayon	Architectures of Autonomy: Spatiotemporal Patterns in Heterogeneous Laminar Networks	14:00 - 14:20	p.6
Stiliyan N. Kalitzin	Unidirectional Associations Between Neuronal Activities	14:20 - 14:50	p.7
Uzi Awret & Hava Siegelman	Self Reference in Brain Dynamics	14:50 - 15:20	p.8

FEATURED SPEAKER: Katarzyna J. Blinowska, Department of Biomedical Physics, Warsaw University

Piotr Suffczynski	Introduction	15:20 - 15:30	
K. J. Blinowska	Neurodynamic Studies by Directed Transfer Function	15:30 - 16:20	p.9
Dinner		19:00	

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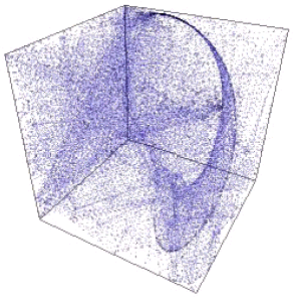

July 4 - Program Schedule

MEASURING AND MODULATING NEURONAL NETWORKS
Chair: P. Abdelmalik

Steven Claus	Pharmacologically Induced Neuromodulation	09:00 - 09:20	*p.10*
Ante L. Padjen	Axons: The Missing Link in Networks	09:20 - 09:40	*p.11*
Berj L. Bardakjian	Coupled Oscillators as Adaptive High Pass Filters for Epileptiform Activity	09:40 - 10:00	*p.12*
Marija Cotic	Spatiotemporal Frequency Profiles of Hippocampal Electrical Activity: A Homology Function Approach	10:00 - 10:20	*p.13*
Ping Wang	Static in the Brain: Implications of Stochastic Neural Activity for Brain Function and Neural Coding	10:20 - 10:40	*p.13*
Group Discussion		10:40 - 11:00	
Coffee Break		11:10 - 11:20	

ROUND TABLE DEBATE
Chairs: S.N. Kalitzin and E.L. Ohayon

Round Table	Will Identifying and Modulating Brain States Effect Autonomy?	11:20 - 12:20
Marija Cotic & Peter L. Carlen	Closing Remarks	12:20 - 12:30

Post Conference Events

July 5 - Desert Expeditions / Diving

July 6 - 9 - Hebrew University in Jerusalem, Seminars and Lab Visits

USING DIET TO TREAT SEIZURE DISORDERS: IMPLICATIONS FOR AUTONOMY

Kirk Nylen
University of Toronto Epilepsy Research Program & Department of Pharmacology, University of Toronto

It has been known for centuries that fasting is anticonvulsant. Fasting is limited in the treatment of chronic seizure disorders, so in the 1920s Wilder devised a “ketogenic diet” (KD) to mimic the physiological effects of fasting. The KD is a high fat, low carbohydrate and adequate protein diet that is highly efficacious in the treatment of drug-resistant seizures. The KD, however, is extremely rigorous. In terms of autonomy, the KD improves autonomy through its broad spectrum anticonvulsant actions. The KD is also associated with significant improvements in both the patient’s mood and cognition. The KD, however, can have deleterious effects on the more protracted aspects of autonomy. Parents must oftentimes lock up foods. Preparation of the KD requires more time and energy as both a KD and a normal meal must be prepared at each mealtime. Preparation of the KD can also be very tedious as food must be weighed to a 100th of a gram. Recently, there has been a discovery that the more popular, less stringent Atkins and low-glycemic index diets share the KD’s anticonvulsant efficacy. These diets are much less rigorous and thus have fewer negative effects on autonomy. The purpose of this talk is to introduce the various “anticonvulsant” diets, review their potential mechanisms of action, and discuss their impact on the autonomy of individuals with seizures and their family.

THE EFFECTS OF SEIZURES ON HORMONAL FEEDBACK SYSTEMS: IMPLICATIONS FOR PATIENT AUTONOMY

Kathryn M. Hum
University of Toronto Epilepsy Research Program & Department of Pharmacology, University of Toronto

Kathryn M. Hum & W. McIntyre Burnham

Introduction: Epileptic patients often suffer from menstrual dysfunction and/or obesity. In addition to seizures, these co-morbidities adversely impact the quality of life for an individual with epilepsy. A better understanding of the effects of seizure activity on hormonal reproductive and feeding feedback systems may lead to the development of novel treatment solutions for these co-morbidities, thereby improving the autonomy of patients living with epilepsy.
Methods: Thirty-four female Wistar rats were implanted with electrodes aimed at the amygdala. Two weeks post-surgery, vaginal smears were obtained daily from all subjects to monitor the phases of the estrous cycle. They were also weighed weekly for the duration of the study. Kindled subjects were given seizure-inducing electrical stimulation via the implanted electrode, while sham-kindled subjects were handled similarly but not stimulated. Twenty-four hours after the 40th generalized seizure, kindled subjects together with yoked controls were sacrificed and blood was collected for hormone analysis.
Results: After four weeks of stimulation, kindled subjects were significantly heavier than controls, a difference that increased for the remainder of the study. Examination of the estrous cycle revealed significantly more abnormal estrous cycle days in kindled subjects. Serum analysis revealed a significant elevation in leptin levels of kindled subjects. Leptin levels were significantly correlated with abnormal estrous cyclicity.
Conclusions: Seizures originating from the limbic system are sufficient to disrupt multiple hormone feedback systems. These data suggest that seizure induced weight gain and elevations in leptin levels may lead to abnormal estrous cyclicity to enhance reproductive abnormalities. Potential physiological mechanisms are discussed.

THE LONG-TERM EFFECTS OF SEIZURES ON REPRODUCTIVE CYCLES

Sofia Megna
University of Toronto Epilepsy Research Program & Department of Pharmacology, University of Toronto

People with epilepsy are more likely to suffer from reproductive dysfunction than the general population. Attributing the cause of this trend to seizure activity alone is difficult due to the use of antiepileptic medications in epileptics. Using an animal model of epilepsy, such as the amygdala-kindling model in rats, allows for the study of the effects of seizures on the reproductive system without the interference of antiepileptic medications. The amygdala-kindled female rat is a model for complex partial seizures of temporal lobe origin in women. Many of the seizure-related disorders in women, such as disruptions in reproductive cyclicity, have also been demonstrated in the amygdala-kindled female rat. The relationship between seizure occurrence and disruptions in estrous cyclicity were examined in the amygdala-kindled female rat during kindling and the cessation of kindling. The question of whether seizure-induced disruptions in reproductive cyclicity are permanent will be addressed.

NEURONAL DEPOLARIZATION ACCOMPANIES SEIZURE ACTIVITY INDUCED BY TRANSIENT HYPOGLYCEMIA

Peter A. Abdelmalik
University of Toronto Epilepsy Research Program & Department of Pharmacology, University of Toronto

Peter A. Abdelmalik[1,2,3], W. MacIntyre Burnham[1,2] and Peter L. Carlen[2,3]
[1]Department of Pharmacology, University of Toronto, Toronto, Canada
[2]University of Toronto Epilepsy Research Program, Toronto, Canada
[3]Toronto Western Research Institute, University Health Network, Toronto, Canada

For more than 80 years, type 1 insulin dependant diabetes mellitus has been treated by the exogenous application of synthetic insulin, which has considerable difficulty mimicking normal physiological fluctuations. When the actions of insulin in the peripheral nervous system are severe; hypoglycemia ensues, which has dire consequences in the central nervous system. End stage hypoglycemia results in seizures, coma and death. Repeated severe episodes are detrimental to cognition, especially in the developing brain. Previous intracellular recordings from hippocampal slices under hypoglycemic conditions in the absence of seizure activity suggest neuronal hyperpolarization mediated by K+. However, using in vitro seizure models of epilepsy, it has been demonstrated that neurons depolarize during seizure activity. We have recently characterized a model of hypoglycemic seizures in the isolated intact hippocampus of the mouse, in vitro. Using this model, we have demonstrated that neurons, both pyramidal cells and interneurons, depolarize during seizure activity induced by transient hypoglycemia. Remarkably, when the seizure activity is inhibited by the GABAA agonist midazolam (50 nM), pyramidal cells and interneurons still depolarize during hypoglycemia. Regular spiking cells of the neocortex also depolarize during hypoglycemia in the absence of seizure activity. Hypoglycemic neuronal depolarization in the hippocampus was also observed in the presence of CNQX/APV/gabazine, suggesting that the depolarization is not synaptically mediated. Together, our data suggest that neurons depolarize during hypoglycemia, both in the presence and absence of seizure activity, which may be a cause of the excitotoxic cell death associated with hypoglycemia. Surprisingly there was no clear relationship between the neuronal spiking activity and the epileptiform fields.

Supported by the JDRF

FINDING A SPACE FOR SAM

Kristi Nylen-Burns
Wynyard, Saskatchewan

The life my family changed drastically on September 29th 2005, when our then two year old son Sam had his first seizure. This started the long task of uncovering the cause, prognosis and treatment of his myoclonic epilepsy. This has greatly affected the autonomy of Sam, our family and our greater family. Sam loses his autonomy when he is seizing as he has no contact with the world around him. We hold him, protect him and talk to him as though he can hear us, it makes us feel better. My husband and I have lost autonomy as we wouldn't leave Sam alone for 6 months after his first seizure- not that being there changes the seizure-but we were unsure of how others would handle it. We followed him around like he was going to fall apart, which really cramps the style of a three year old boy. Our extended family has also lost autonomy. Our family has moved time and space to help with our other 3 kids so that my husband and I can be with Sam for various tests. Sam gets unexplained hugs and some extra presents, all because he is "sick." We sometimes worry about Sam's quality of life as he grows and wants to become more independent. We worry about his development. We worry about how he will be accepted when he goes to school and how the teachers will handle it if he does have a seizure at school. Mostly we worry.

COBALT INDUCED EPILEPTIFORM DISCHARGES IN MOUSE HIPPOCAMPUS IN VITRO

Liang Zhang
Toronto Western Research Institute, University Health Network

Jiwei He1, Hwa-Lin Hsiang, Chiping Wu and Liang Zhang

Animal models of cobalt-induced epileptic seizures have been frequently used since 1960s, but the underlying cellular mechanisms are largely unknown. We developed an in vitro model to explore this issue. Hippocampal slices were prepared from adult mice and treated with CoCl2 (2 mM for 10 minutes or 0.1 mM for 1 hour). Spontaneous epileptiform discharges were consistently observed in these slices after washing cobalt, manifesting with oscillatory spike waveform lasting several seconds. These epileptiform discharges were originated from the CA3/hilar areas and correlated with high-frequency firings of in individual CA3 pyramidal neurons. The cobalt-induced epileptiform discharges were dependent upon the activities of glutamate AMPA receptors but not NMDA receptors, but their generation could not be mimicked in naïve slices by pharmacological antagonism of GABA-A/GABA-B receptors or by increasing synaptic and neuronal activities with high external K+ or 4-aminopyrid ine. The cobalt-induced epileptiform discharges were readily suppressed by phenytoin (50 mM), TTX (50 nM) or high extracellular Ca2+ (4 mM), and their incidence was reduced by pre-treatment of slices with ascorbic acid (0.5 mM). We suggest that free radical-dependent modulation of persistent Na+ currents and resulting excessive neuronal firings play a major role in cobalt-induced epileptiform activities in mouse hippocampal slices. The role of intrinsic CA3 network activities in initiation of cobalt-induced epileptiform discharges was discussed.

THE DYNAMICS OF SEIZURE TRANSITION: THE ROLE OF INTERNEURONS AND PYRAMIDAL NEURONS IN EPILEPTOGENESIS

Peter Carlen
Toronto Western Research Institute, University Health Network

Derchansky M., Mamani M., Carlen PL

Seizures occur when populations of neurons discharge synchronously. Our current understanding of the neuronal dynamics that produce such hyper-synchronicity is lacking. Utilizing the intact isolated mouse hippocampus exposed to low-magnesium artificial cerebral spinal fluid, recurrent spontaneous seizures were produced with a distinct pre-seizure transition phase. Intra- and extracellular electrophysiological recordings were obtained from fast spiking (FS) and non-fast spiking (nonFS) interneurons in the stratum oriens, and pyramidal cells in the CA1 region of this structure. This study utilized perforated patch, normal whole cell and high-chloride whole cell recording techniques to monitor spontaneous synaptic and other epileptiform activity during the transition and seizure phases. In pyramidal cells, and FS and nonFS interneurons, the reversal potentials during the transition period (-60mV) were significantly more hyperpolarized than the reversal potentials observed during the seizure (+30mV in interneurons, -30mV in pyramidal cells). Increasing the chloride concentration in the patch pipette (30mM, ECl = -40mV) depolarized the reversal potential during seizure transition to -38mV in all neuronal subtypes, as well as depolarizing the seizure reversal potential in pyramidal cells (-7mV), but not in interneurons. The GABAA receptor antagonist, BMI, completely abolished the seizure transition phase in all three neuronal subtypes, and produced fragmented, shorter seizure-like activity. The reversal potentials of these seizures did not change in FS and nonFS interneurons as compared to low-magnesium induced seizures, but were significantly more positive in pyramidal cells exposed to BMI (23mV). These data suggest that stratum oriens interneurons and CA1 pyramidal cells are exclusively GABAergically driven during the seizure transition and that during a seizure, interneurons are driven by glutamatergic pyramidal cells vis-à-vis a feedback loop, while pyramidal cells are functionally controlled by a mixture of GABAergic and glutamatergic inputs during seizures.

EPILEPTIC TRANSITIONS - INSIGHT FROM A HIPPOCAMPAL MODEL

Piotr Suffczynski
Department of Biomedical Physics, Warsaw University

It has been shown that an enhancement of relative Phase Clustering Index (rPCI) measured from evoked EEG signals anticipates the spontaneous transition to an epileptic seizure (Kalitzin et al., 2005). Using a computational model of a hippocampal CA1 region we investigated a possible explanation for the dependence between rPCI measure and the probability of ictal transition. We identified a number of network parameters that bring the network closer to the seizure threshold and increase rPCI at the same time. The increase of rPCI ‘en route’ to a seizure always came through the decrease of phase coherency at the lowest (i.e., stimulation) frequency. Model predictions are compared with the experimental data and prospective development of seizure prediction method is suggested.

References: Kalitzin SN, Velis DN, Suffczynski P, Parra J, Lopes da Silva FH. Intermittent electrical brain-stimulation paradigm for estimating the seizure onset site and the time to ictal transition in temporal lobe epilepsy. Clin Neurophysiol 2005;116(3):718-28.

ARCHITECTURES OF AUTONOMY: SPATIOTEMPORAL PATTERNS IN HETEROGENEOUS LAMINAR NETWORKS

Elan Liss Ohayon
University of Toronto Epilepsy Research Program & Collaborative Program in Neuroscience, University of Toronto

Candidate principles for achieving autonomous neurodynamics include: (i) the capacity to maintain persistent activity (ii) an ability to avoid falling prey to pathological synchrony and limit cycles (iii) a substantial degree of independence from the environment such that transition between activity states or phases can occur in the absence of external input (iv) that patterns and transitions can also be maintained *despite* a sustained external drive (v) all this while simultaneously remaining responsive to the environment and interacting in the world. This presentation continues an ongoing investigation into the characteristics of network architectures that might support such dynamics. Specifically, I will examine spatiotemporal pattern formation in laminar networks with varying levels of connectivity, ranging from networks with homogeneous unit placement to highly diffuse networks. In these locally connected computational models, the degree of heterogeneity in connectivity is shown to correlate with a propensity to enter sustained activity as a response to both localized and spatially-distributed random input. For a broad range of diffuse networks, the activity triggered by external input displayed sustained patterns of propagating waves. The response, however, was not monotonic and networks showed varying forms of activity ranging from spiral waves to increasingly localized limit-cycle patterns. Changes to threshold and complex pattern formation in these models did not require modification to excitatory-inhibitory balance nor did they require alterations to intrinsic cell properties. These findings highlight the importance of structure to activity pattern formation as well as threshold shifts. Relating network structure to neural dynamics may thus elucidate the architecture principles by which networks support the forms of spatiotemporal patterns most essential for autonomous activity.

UNIDIRECTIONAL ASSOCIATIONS BETWEEN NEURONAL ACTIVITIES

Stiliyan Kalitzin
Dutch Epilepsy Clinics Foundation, Heemstede, The Netherlands

S.Kalitzin[1], J.Parra[1], F.S.S. Leijten[2], D. Velis[1], F. Lopes da Silva[3]
[1]Dutch Epilepsy Clinics Foundation, Heemstede, The Netherlands
[2]Department of Clinical Neurophysiology, University Medical Centre Utrecht, The Netherlands
[3]Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, The Netherlands

Neuronal subsystems have the remarkable properties of showing coherent, functionally coordinated behavior, while at the same time retaining their independent degrees of freedom. Such duality of simultaneous cooperation and autonomy can be explained by state-dependant, asymmetric relations between the various subsystems. We speculate that asymmetric or ultimately unidirectional interactions play essential role in allowing the exchange of information between the neuronal subsystems and at the same time in preserving the relative autonomy of the various components. The purpose of this contribution is to introduce a suitable measure that can detect asymmetric state relations between activities measured from electrophysiological signals. We use the established non-linear association index, known as h^2, and its extension to the unidirectional phase clustering index (PCI). The last provides a unidirectional measure of the phase synchronization between two signals. Non-stationary frequency representation based on a sequence of Gabor filters can be used for a spectral decomposition of the signals that generates a phase synchronization spectrum. We have studied the behavior of the unidirectional state associations in cases of partial motor seizures and have quantified the associations between ECoG and EMG activities. Using our techniques we can distinguish between causal and deterministic cortical involvement in the seizure generation process. Such analysis can be relevant for a successful epilepsy surgery. Cortical areas that are for example necessary to trigger motor seizures might be better candidates for resection that areas that are just sufficient.

SELF REFERENCE IN BRAIN DYNAMICS

Hava Siegelmann and Uzi Awret
Department of Computer Science, University of Massachusettes

Self Reference in group behavior can be described by the riddle: “If eight birds sit on a branch and you scare one of them, how many will stay on the branch?” The answer is “none” since a bird in the group looks at its comrades in addition to its own input to tune its behavior. The same type of self reference, we notice, is an important principle in many biological systems: a component of a system does not behave by mere considering external input, but only after taking into account the behavior of other components of the system it belongs to. On the system level, self referencing will be that the system acts on input after comparing and referencing it to its own internal condition and representation. We propose that self-reference is crucial in brain dynamics and will demonstrate it in various levels from synapse of behavior.

FEATURED SPEAKER
Katarzyna J. Blinowska
Department of Biomedical Physics, Warsaw University
Introduction by Piotr Suffczynski

NEURODYNAMICS STUDIES BY DIRECTED TRANSFER FUNCTION

K. J. Blinowska
Department of Biomedical Physics, Warsaw University

K. J. Blinowska, M. Kaminski, R.Kus

The study of neurodynamic phenomena involves determination of the direction of the information transfer between brain structures or pools of neurons. These quantities can be estimated by means of Directed Transfer Function (DTF). DTF is based on multivariate autoregressive model (MVAR) and can be regarded as an extension of the Granger causality measure to the arbitrary number of channels. In case of brain studies simultaneous fitting of all interconnected channels to the model is crucial, since in case of mutually dependent signals, bivariate measures lead to erroneous results. In case when multiple repetitions of the experiment are available short-time DTF (SDTF) allows for the determination of propagation not only in function of frequency, but also in time. In this way dynamical pattern of the information transfer may be obtained.

DTF is very robust in respect of noise, it can detect phase differences in the signals where contribution of noise is several times higher than the signal itself. Since DTF is sensitive to the phase differences it discriminates effectively against disturbances of a constant phase e.g. volume conduction, which involves zero phase propagation. The properties of DTF will be demonstrated by means of simulations and applications to different experimental data involving: sleep studies, comparison of information processing during real and imaginary task and detection of causal relations between spike discharges and local field potentials. The method can be used for analysis of spike trains as well as for the slow brain activity.

PHARMACOLOGICALLY INDUCED NEUROMODULATION

Steven Claus
Dutch Epilepsy Foundation Netherlands (SEIN)

Steven Claus[1], Frans Leijten[2], Demetrios Velis[1], Stiliyan Kalitzin1
[1]Dutch Epilepsy Foundation Netherlands (SEIN),
[2]Department of Clinical Neurophysiology, University Medical Centre Utrecht, The Netherlands

Provocation of brain rhythms to study the system: when I kick the tree and the leaves rustle differently what does it tell me about the system?

The diagnostic process in epilepsy can be quite tedious. Documenting the epileptiform abnormalities on scalp EEG that are needed to support a diagnosis of epilepsy can be quite time-consuming. Considerable effort has been invested in finding ways to perturb the brain into revealing some of its secrets. Although perturbation might intuitively compromise the idea of autonomy of a system, it could also be considered as any type of input that elicits reaction from this innate interactive system, that also reveals part of its mechanisms. Examples of perturbation as applied in a clinical setting of EEG recordings are sleep deprivation, and pharmacological sleep induction.

In our institute we administer benzodiazepines to the brain to look at changes in the generation of activity in the beta band. Benzodiazepines have a GABA-ergic effect that is associated with an increase in beta-activity in the scalp EEG. Lesions show less flumazenil (benzodiazepine antagonist acting through competitive binding to the GABA-receptor site) binding in PET scans, which led to the hypothesis that alterations in number or structure of GABA-receptors could be associated with changes in evoked beta-band activity. Questions have been raised as to the real origin of the evoked beta-band activity: could such be due to an amplification of original activity, or perhaps due to a slowing down of faster (gamma) activity that is reflected in the beta-band. How does this reflect on the system's autonomy? So far the relative phase clustering index (rPCI) in the beta-band shows an increase. What does this tell us? Hopefully, our findings shall lead to a discussion on the true meaning of our observations with regard to the brain as a dynamical system.

AXONS: THE MISSING LINK IN NETWORKS

Ante L. Padjen
Dept of Pharmacology & Therapeutics, McGill University, Montreal, QC, Canada.

Even though the myelinated and unmyelinated axons are standard elements of neuronal circuits it is generally assumed that the interesting dynamics and plasticity of circuits resides in the synaptic events. Substantial number of studies of peripheral and central myelinated axons identified multitude of ion channel with specific distribution in different regions: high concentration of Na channels in the nodal region while a variety of K channels are distributed internodally (fast K channels) and nodally (slow K) with a variety of structural proteins securing their precise distribution.

The purpose of this presentation is to provide evidence about the complexities of functional and molecular organization of (myelinated) axons and to discuss axonal contribution in the plasticity of neuronal circuits with a bias towards the conductions of impulses in normal and pathologic states.

The results of our computational modeling of myelinated axons (containing experimentally obtained parameters of conductances and realistic morphology, implemented in NEURON) revealed that in order to simulate long charging and discharging processes of the electrotonic potentials (ETPs) obtained by intracellular recordings from spinal roots ETPs, the myelin leakage conductance and the ionic conductance of internodal membrane are the crucial factors. In contrast to the classical estimate of 1.5 $\mu S/cm^2$ a much larger value of 80 $\mu S/cm^2$ is required as specific myelin conductance ("leaky myelin model").

The model is in agreement with the idea that the internodal axolemma contributes to the conductance mechanism in myelinated axons, with possibility of local modulation of conduction.
The studies of axons in animal models of neurodegenerative diseases reveal the appearance of a slow Na conductance with characteristic pharmacological sensitivities to local anaestetics.

These results imply that the axons contribute in more than one way to the plasticity of neuronal circuits.

(Supported in part by ALS, CDA and CIHR)

COUPLED OSCILLATORS AS ADAPTIVE HIGH PASS FILTERS FOR EPILEPTIFORM ACTIVITY

Berj. L. Bardakjian
Institute of Biomaterials and Biomedical Engineering, University of Toronto

Berj L. Bardakjian and Osbert Zalay
Institute of Biomaterials and Biomedical Engineering, University of Toronto

Learning and memory rely on the regulation of communication between neurons in the hippocampus. The mossy fiber (MF) pathway connects the dentate gyrus (DG) to the auto-associative CA3 network, and the information it carries is controlled by a feed forward circuit having (i) excitatory synapses between granule cells and both pyramidal cells and interneurons, and (ii) inhibitory synapses between interneurons and pyramidal cells.

This neural circuit was modeled by coupled mapped clock oscillators (MCOs) which demonstrated that the MF associated feed forward network acts as a high pass filter for inputs to the CA3 originating from the DG. But the circuit is not a simple filter composed of passive components. It is a dynamic filter with active components arranged in a feed forward control loop that mediates the opposing forces of inhibition and excitation. Moreover, it is an adaptive filter with flexible connections. The MF associated synapses exhibit plasticity and are subject to associative strengthening or weakening in relation to long-term potentiation or depression. For MCO simulations involving the same circuit configuration but using different coupling factors, filter characteristics such as the slope (order) and switching-frequency (cutoff) differed accordingly. These aspects suggest the MF associated feed forward circuit may adapt to favor certain network oscillatory modes or frequencies under the right conditions, with implications toward seizure development and the appearance of super-gamma hippocampal rhythms. The MCO model was able to verify many of the experimental observations, including the biphasic nature of the pyramidal postsynaptic potentials (PSPs) and the frequency-dependent switching from inhibition to excitation for GC frequencies greater than 10 Hz.

Evidence from the model and experiments indicate that the MF associated feed forward circuit plays an important regulatory role in auto-associative learning and information processing in the hippocampus, reserving access to the sensitive recurrent collaterals of the CA3 for those DG inputs that carry the appropriate temporal code.

SPATIOTEMPORAL FREQUENCY PROFILES OF HIPPOCAMPAL ELECTRICAL ACTIVITY: A HOMOLOGY FUNCTION APPROACH

Marija Cotic
[1]Department of Electrical and Computer Engineering and the Institute of Biomaterials and Biomedical Engineering, University of Toronto, [2]Toronto Western Research Institute, University Health Network

Marija Cotic[1], Miron Derchansky[2], Peter L. Carlen[2], Berj L. Bardakjian[1]

Several signal processing tools analyze the level of synchronous neuronal activity or correlation within and between different regions of the brain, as synchronous oscillations are believed to play a large role in neuronal function. Coherence tools have provided effective analysis options, but are constrained by stationarity conditions, time-frequency resolution and the ability to identify non-concurrent commonalities arising from shifts or delays in signal conduction. METHODS: We are proposing a homology function to study concurrent and non-concurrent commonalities in non-stationary neuronal electrical activities. We utilize a modified Multichannel Blind System Identification (MBSI) algorithm with a feature tracking strategy. Here we have implemented the homology function to characterize the commonalities of four extracellular field recordings in the CA1 region of the intact mouse hippocampus under low-Mg2+ conditions. The modified MBSI algorithm identified a generic signal from the four observed signals, which contained their common time-frequency information. The tracking strategy matched these commonalities, via energy peak tracking, to the time-frequency domains of the observed signals to identify concurrent and non-concurrent events. DISCUSSION: Our tracking strategy identified and matched concurrent and non-concurrent features (i.e. frequency bands) amongst the recordings, mapping out their spatiotemporal spread. These common features were observed to propagate in different ways. Future work will involve the implementation of additional tracking strategies.

STATIC IN THE BRAIN: IMPLICATIONS OF STOCHASTIC NEURAL ACTIVITY FOR BRAIN FUNCTION AND NEURAL CODING

Ping Wang
Computational Neurobiology Laboratory, The Salk Institute for Biological Studies

A perplexing phenomenon is the often stochastic nature of neural spiking, often considered “noise” that obfuscates neural signal transmission. This stochasticity results from probabilistic synaptic release, background synaptic activity, and intrinsic properties of the neuron, such as ion channel noise and sub-threshold oscillations among various other factors. Using NEURON models to simulate the mammalian thalamocortical visual pathway, our study focuses on three aspects. First, we explore many of the potential sources of noise, and devise methods of modeling them. Second, we try to understand how neurons are able to retain their precise and reliable transmission of information despite noise. And finally, we look at possible useful functions of stochasticity, ultimately trying to answer: Is it a bug or a feature? We also discuss implications that this phenomenon has for the nature of neural coding, connectivity, autonomous neural dynamics, and overall brain function.