8.1 pA pF^{-1} (n = 8) after 24 hours induction with 1.5 μg/ml tetracycline and, which remained stable up to 72 hours. The mean current density in sham-tetracycline induced cells was -0.39 ± 1.2 $pApF^{-1}$ (n = 24) in 72 hours, demonstrating the tight control of expression in the inducible system. Analysis of the biophysical and pharmacological properties of the exogenous $Ca_v2.2$ channels revealed that the properties were comparable to native N-type currents. The IC_{50} for the $Ca_v2.2$ blocker, -conotoxin GVIA was 18.9 ± 2.8 nM and a fit of the mean data with a Boltzmann function revealed parameters for steady-state activation of $V_{1/2} = -2.6 \pm 0.1$ mV (n = 6), $Vh_{1/2}= -43.3 \pm 1.4$ mV (n = 7) for steady-state inactivation.. The utilization of this cell line on an automated patch-clamp system will also be discussed. *J. Mezeyova and X. Jiang contributed equally to the project

Neuronal Systems & Modeling

3148-Pos Strong Adhesion Identifies Potential Neurite Extension And Polarization Sites In PC12 Cells

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Board B451

The dynamic process of neuronal polarization involves the development of neurites into an axon and dendrites. Important intracellular mechanisms have been identified during this process, including actin assembly and disassembly in the growth cone, microtubule dynamics, and cellular tension. It has been suggested that these mechanisms may play a role in axonal specification; however, little attention has been placed on cell spreading and adhesion occurring prior to neurite extension. Here we begin to describe the role of strong adhesion and spreading during the initial polarization stages for PC12 cells, which in the presence of neurotrophic factors, are capable of differentiating into sympathetic-like neurons. We evaluated initial attachment, cell-substrate adhesion, and spreading dynamics of PC12 cells on collagen coated substrates using Interference Reflection Microscopy, and developed an image process algorithm to measure cell spreading area and strong adhesion zones during initial neurite outgrowth. A correlation between zones of adhesion and neurite development was identified to occur in three different stages during the first 90 minutes of spreading. The first stage occurs during initial spreading before neurites have developed, and when zones of adhesion are localized within the cell body. Spreading boundaries reveal anisotropic growth, with a rate of growth of 0.26 (micron2/min) during this early stage. Total spreading area continues to increase during stage two, with a similar speed. Neurites begin to develop and a competition effect is observed, where strong adhesion occurs at multiple neurite anchoring sites. The level of adhesion appears to specify which neurite develops versus those which retract. In stage three, maximum spreading area is achieved, and polarization appears to begin, with strong adhesion localized at the site of polarization. This data suggests an importance in adhesion dynamics during both neuronal spreading and polarization.

3149-Pos Live Imaging of Neural Differentiation in the Developing Brain Using 2-Photon Laser Scanning Microscopy

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Board B452

During cortical development, neural migration and differentiation are precisely regulated by complex signaling cascades. To further our understanding of these essential mechanisms for embryonic cortical development we have to monitor these signaling events in the living brain. We performed live-imaging studies of neural progenitor migration/differentiation and calcium (Ca^{2+}) signaling in the embryonic neocortical environment. Using high-end customized 2-photon laser scanning microscopy, we examined these deep-tissue cellular events in brain slices from transgenic mouse strains expressing GFP under the promoter of the differentiation stage-specific markers GFAP (Glial Acidic Fibrillary Protein) and tau.

Our results show that GFAP-expressing neural progenitors are dividing in the subventricular zone and migrate radially towards the pia whereas tau-expressing cells migrate mostly tangentially. GFAP-expressing cells are mainly located in the ventricular and subventricular zones whereas the tau-expressing cells are more diversely spread. Moreover, intracellular Ca^{2+} recordings point towards a Ca^{2+} signaling-dependency of these critical differentiation and migration processes. In summary, here we show distinct neural migration patterns of neural progenitors and neurons in the embryonic neocortical environment of the living brain which are crucial for the establishment of the cortical architecture during embryonic development.

3150-Pos A Computational Approach Describing The Distinct Effects Of Topographical Versus Chemical Cues On Axogenesis

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Board B453

Understanding how external cellular cues affect axogenesis, the formation of an axon in neurons, is a necessity for the development of novel scaffolds for nerve repair. Of particular interest is the distinct behavior Hippocampal neurons exhibit when comparing topographical cues to immobilized chemical cues (i.e. Neural Growth Factor). In order to further understand this behavior a two fold approach involving computation modeling and experiments was employed. Assuming that the decisive factor between these cues is an effective surface concentration of cues, our model successfully described previous neuronal behavior seen by Gomez et al as well as made predictions that were then tested experimentally. The model considers the following factors: excluded volume of the growing neurites as well as the cell soma, number of initial

neurite processes, spacing between cues (i.e. feature size for topography and surface concentration for chemical cues), and an experimentally testable persistence length, l*, of each neurite process. The results for several neurite persistence lengths as a function of different topographical feature size keeping chemical cues constant at 0.11 ng/mm2 is shown in Figure 1.

FIG. 1. Probability of Polarization as a function of Neurite Persistence Length and Topographical Feature Size. Features size was allowed to vary from 0.02 to 1000 um while keeping the chemical concentration constant at 0.11 ng/mm*2. At equal spacing, the probability of observing a polarized neuron in a topographical environment will be equal to that of observing a polarized neuron in a chemical environment. As the feature size increases so does the probability that more neurons will be polarized in a topographical environment rather than a chemical one. However, as the feature size approaches its upper limit polarization due to chemical cues becomes more probable as the neuritis no longer "sense" the topography. This sensing ability is shown to be a function of a persistence length, l*. This bimodal distribution and dependence on persistence length was then lesied via experiments.

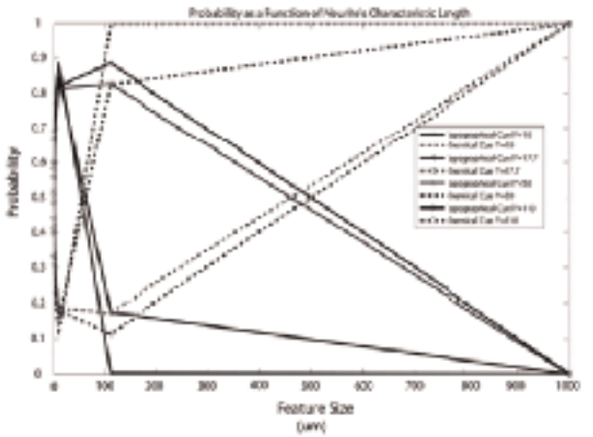

FIG. 1. Probability of Polarization as a function of Neurite Persistence Length and Topographical Feature Size. Feature size was allowed to vary from 0.02 to 1000 um while keeping the chemical concentration constant at 0.11 ng/mm*2. At equal spacing, the probability of observing a polarized neuron in a topographical environment will be equal to that of observing a polarized neuron in a chemical environment. As the feature size increases so does the probability that more neurons will be polarized in a topographical environment rather than a chemical one. However, as the feature size approaches its upper limit, polarization due to chemical cues becomes more probable as the neuritis no longer "sense" the topography. This sensing ability is shown to be a function of a persistence length, l*. This bimodal distribution and dependence on persistence length was then tested via experiments.

3151-Pos An Essence Of "Bursting"; Reliable Information Transfer Between A Spinal Neural Network And Myofibrils

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Board B454

The mechanism of muscle activation from axon to endplate potential which results in Ca2+ twitch contraction is well understood. Recordings of rhythmic patterns that are responsible for scratching, walking, running and flying are usually done on in vivo extra cellular neurons does not directly address how bursting activates a muscle fibre. The amount of bursting activity generated by a motor neuron pool in vivo for muscle activation should produce higher frequency Ca2+ twitch potentials. Also, an axon's electrical properties prevent it from being able to conduct "bursts" as it can only conduct lower frequency action potential.

We utilise a micro electrode array the surface of which is micro engineered to support the different cell types used (motoneurons, myofibrils and DRG sensory neurons). The chip is selectively functionalized with collagen and laminin. The collagen's elasticity is characterized by scanning with an AFM in liquid. This system proves to be amenable to chemical and electrical manipulation without evoking unwanted effects as might occur in vivo. Myofibrils are used in this experiment but muscle fibres in vivo possess an intricate network of tubules which sequester Ca2+ and endplate potential propagates on the surface of the sarcolemma. We address this in vivo - in vitro dichotomy by staining for neuromusclar junctions using bungarotoxin, showing that this co-localization of AChR and neurite extensions is functional using Tubocurarine an AChR antagonist. The bursting in the network is shown not to translate to neurite bursting, while network bursting is maintained concurrently. Furthermore, the Ca2+ regime is manipulated with AcH to investigate nature of Ca2+ sequestering in vitro. Finally, we show that bursting activity results in fast Ca2+ transients but not all twitch transients are accompanied by a burst.

3152-Pos Dynamical Modeling of Decision Making Based on Hierarchically Optimized Memory

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Board B455

Prediction of results based on experience is a critical step in decision making. Recent discovery of network-level memory coding units in the hippocampus indicates that daily experiences are converted into generalized knowledge and concepts in brain and organized in a categorical and hierarchical manner. This kind of system enables to encode nearly infinite amount of episodic events for quick reference, however, detailed mechanism is not revealed yet. We develop a dynamical model to verify the information processing systems which can access hierarchical memory and make an effective decision according to individual experiences. We focus on the intrinsic function of working memory which is considered to be related to unified information processing and discuss the fundamental process of retention and selection of memory for decision making from the viewpoint of energetics by analyzing both equilibrium states and dynamical properties in writing, reading, and deleting processes using this model. The simulation results show that the optimization of trade-off between processing speed and flexibility of strategy drives the evolution of the brain systems. This study will provide the extended theoretical model to reveal the mechanism of

remarkable information processing which make it possible to deal with the enormous data using the limited memory in the brain and how to encode them in neural activity. We expect that findings of our study will be applied to design the effective learning systems and reasonable decision making systems in future.

3153-Pos Dynamic Space-time Representation in the Neural System: A Novel Formulation using Tensor Image Analysis

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Board B456

Objective: A fundamental problem in neurophysics is to understand the plasticity of spatiotemporal representation in neural systems, regarding moving objects. For this, our aim is to use tensor analysis that has been successfully used in (i) investigation of spacetime representation in cortical networks (ii) imaging of transport processes in neural parenchyma, as electrical conductivity or information connectivity.

Method: We consider propagation of signal in neuronal system at limiting neural conduction velocity c*, and analyze the neural impulse transmission equation from a neurochemical perspective, using Maxwellian cross-coupling in the electrochemical field. Using Zeeman group theory approach, we formulate the causality principle for neural interaction whereby information causality provides Lorentzian group structure to neural spatiotemporal representation.

Results: We show that causal group structure indicates that a Lorentz-Fitzgerald type relativistic equation applies to neural spacetime representation. Since c*-value is modest (in metres/sec), we predict that normally a subject should report length-contraction and time-dilatation of the perceptual image of an externally moving pulsating object. We illustrate collateral experimental data of the perceptual metric tensor, confirming our model of the principle of relativity in neurocognitive spatiotemporal representation. We elucidate how neuronal systems act as Lorentz generators by adapting well-known empirical findings of Hoffman whereby neuronal systems can operate as differential Lie group generators.

Conclusion: Utilizing functional neuroimaging and tensorial connectivity data of cortical activation when the subject observes moving external objects, we infer that the geometric Lorentzian generators correspond to inferior parietal neurons (supramarginal gyrus) which impart spatiotemporal coupling, being responsible for paradoxical perceptual relativistic effects. Practical bioengineering applications include

(i) compensation of perceptual distortion hazards experienced by pilots, or by epileptic patients having cortical spreading depression,
(ii) unification of tensor calculus basis of neural space-time and that of functional neuroimaging.

3154-Pos Increased Intraneuronal Resting [Ca^{2+}] In Adult Alzheimer's Disease Mice

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Board B457

Neurodegeneration in Alzheimer's disease (AD) has been linked to intracellular accumulation of misfolded proteins and dysregulation of intracellular Ca^{2+}. In the current work, we determined the contribution of specific Ca^{2+} pathways to an alteration in Ca^{2+} homeostasis in primary cortical neurons from an adult triple transgenic (3xTg-AD) mouse model of AD that exhibits intraneuronal accumulation of β-amyloid proteins. Resting $[Ca^{2+}]_i$, as measured with Ca^{2+}-selective microelectrodes, was greatly elevated in neurons from 3xTg-AD and APP_{SWE} mice strains as compared to their respective non-transgenic neurons, while there was no alteration in the resting membrane potential. In the absence of the extracellular Ca^{2+}, the $[Ca^{2+}]_i$ returned to near normal levels in 3xTg-AD neurons, demonstrating that extracellular Ca^{2+} contributed to elevated $[Ca^{2+}]_i$. Application of nifedipine, or a non-L-type channel blocker, SKF-96365, partially reduced $[Ca^{2+}]_i$. Blocking the RyRs, with ryanodine or FLA-365 had no effect, suggesting that these channels do not contribute to the elevated $[Ca^{2+}]_i$. Conversely, inhibition of IP_3Rs with xestospongin C produced a partial reduction in $[Ca^{2+}]_i$. These results demonstrate that an elevation in resting $[Ca^{2+}]_i$, contributed by aberrant Ca^{2+} entry and release pathways, should be considered a major component of the abnormal Ca^{2+} homeostasis associated with Alzheimer's disease.

Cell Mechanics & Motility - I

3155-Pos Effects of Mechanical Stretch on Syndecan-4, Focal Adhesion Complexes, and Site-Specific FAK Phosphorylation in Fibroblasts

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Board B458

Cellular mechanics involves the ability of cells to sense and respond to external forces. The type of mechanical stimulation that cells experience, which includes stretching, compression or shearing, depends on a variety of factors such as how muscle deforms. In this present study, we have fabricated a custom-made device that constrains a soft membrane to modulate mechanical stimulation of cells via their ECM connections while incorporating scaffolding and