DIMACS Workshop on

Data Mining, Systems Analysis, and Optimization in Neuroscience

February 15 – 17, 2006
J. Wayne Reitz Union
University of Florida

Conference Organizers:

W. Art Chaovalitwongse, Rutgers University
Panos M. Pardalos, University of Florida
Leonidas D. Iasemidis, Arizona State University

Program and Abstracts

Local Organizers:

Onur Seref (Chair)
Wichai Sudharitdamrong
Stanislav Busygin
Chang-Chia (Jeff) Liu
Alla Kammerdiner

Advisory Committee:

Sergiy Butenko, Texas A&M University
Paul R. Carney, University of Florida
Mingzhou Ding, University of Florida
Ding-Zhu Du, University of Texas at Dallas
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J. Chris Sackellares, University of Florida
Justin C. Sanchez, University of Florida
Deng S. Shiau, University of Florida
Onur Seref, University of Florida
Weili Wu, University of Texas at Dallas

WEDNESDAY, FEBRUARY 15

8:00 – 1:00	**Registration** Conference Registration Desk
8:45	Opening Remarks from the Conference Organizers
Session W1	Chairman: Panos M. Pardalos
9:00	**KEYNOTE SPEAKER: Walter J. Freeman** *Sourcing Organizing Concepts for Neocortical Dynamic Data from Many-Body Physics*
10:00	**Kostas Tsakalis** *A Feedback Control Systems View of Epileptic Seizures*
10:30 – 10:50	**Coffee Break**
Session W2	Chairman: W. Art Chaovalitwongse
10:50	**Justin C. Sanchez** *Choosing the Appropriate Level of Abstraction for Brain Machine Interfaces: Data Collection and Analysis Insights*
11:15	**Kay A. Robbins** *Visual Analysis for Comparing Structure, Timing and Synchronization Properties of Neural Populations*
11:40	**Paul R. Carney** *Dynamical EEG Properties in the Limbic Epilepsy Rat Model*
12:05	**Sandeep P. Nair** *Dynamical State Dependent Electrical Stimulation for Seizure Control in a Chronic Limbic Epilepsy Model*
12:30 – 2:00	**Lunch**
Session W3	Chairman: Leonidas D. Iasemidis
2:00	**Aparna Gupta** *Online Analysis of Device-Tissue Interactions - Modeling Tissue Impedance Spectra*
2:25	**David Rosenbluth** *Group Sensing with Electroencephalograms (EEG)*
2:50	**Michael Bewernitz** *A Novel In-Vivo Model of Basal Frontal Forebrain Origin Seizures in Anolis Lizards*
3:15	**Jeff Knisley** *Neural Networks, Monte Carlo Methods, and Real-world Neurons*

3:40 – 4:00 **Coffee Break**

Session W4 Chairman: Onur Seref

4:00 **Maya Maimon**
A Simulation Tool Using Discrete Integrate and Fire Neurons: Modeling the Influence of Anatomy on Information Flow in Very Large Simulated Networks

4:25 **Monica K. Hurdal**
Shape Analysis for Automated Sulcal Classification and Parcellation of MRI Data

4:50 **Nadia Mammone**
A New Brain Mapping Based on the Visualization and Modeling of the Short Term Maximum Lyapunov Exponent

THURSDAY, FEBRUARY 16

8:00 – 1:00 **Registration**
Conference Registration Desk

Session T1 Chairman: Panos M. Pardalos

8:30 **KEYNOTE SPEAKER: Andreas Ioannides**
Probing Brain Function Across Different Spatial and Temporal Scales with Tomographic Analysis of Magnetoencephalographic Signals

9:30 **Mingzhou Ding**
Statistical Modeling of Neurobiological Data

10:00 – 10:20 **Coffee Break**

Session T2 Chairman: Leonidas D. Iasemidis

10:20 **Linda Hermer-Vazquez**
Adaptations of Stationary Analytics Techniques to Understand the Nonstationary Neural Activity Underlying Performance of a Complex Cognitive Task

10:45 **Kevin K.W. Wang**
Differential Proteomic Analysis of Traumatic Brain Injury Biomarker Study

11:10 **Anant Hegde**
Tracking Spatio-Temporal Changes in ECOG

11:35 **Su-Shing Chen**
Probability Distribution Function and Optimal Strategy for Natural Selection

12:00 – 1:30 **Lunch**

Session T3 Chairman: W. Art Chaovalitwongse

1:30 **Fred Glover**
Discrimination and Classification by Mixed Integer Programming

1:55 **Fang Liang**
Computational Evaluation of Mixed Integer Programming Models for Discrimination and Classification

2:20 **Michele Samorani**
Hyperplane-Based Decision Trees and Their Optimization

2:45 **Larry Manevitz**
Reading the Mind: fMRI Analysis Via One-Class Machine Learning Techniques

3:10 – 3:30 **Coffee Break**

Session T4 Chairman: Wichai Suharitdamrong

3:30 **Xue Bai**
Tabu Search Enhanced Graphical Models for Classification of High Dimensional Data

3:55 **Kevin Kelly**
Development of a Rodent Seizure Control System Using Intracerebroventricular Injections of Midazolam

4:20 **Chang-Chia Liu**
Distinguishing Independent Bi-Temporal from Unilateral Onset in Epileptic Patients by the Analysis of Nonlinear Characteristics of EEG Signals

Conference Dinner

6:30 University Hotel and Conference Center (Hilton Hotel)

FRIDAY, FEBRUARY 17

Session F1 Chairman: Panos M. Pardalos

8:30 **KEYNOTE SPEAKER: Dmitri Chklovskii**
Evolution as the Blind Engineer: Wiring Minimization in the Brain

9:30 **Leonidas D. Iasemidis**
Resetting of Brain Dynamics by Epileptic Seizures

10:00 – 10:20 **Coffee Break**

Session F2 Chairman: Onur Seref

10:20 **Andrew K. Ottens**
Biomarker Discovery in Ischemic Stroke - A Neuroproteomic Study

10:45	**Mukesh Dhamala** *Current Source Density Analysis of Ongoing Neural Activity: Theory and Applications*
11:10	**Alexander Hartemink** *Neural Information Flow Networks in Songbirds*
11:35	**Pando Georgiev** *Fuzzy Hyperplane Clustering Algorithm and Applications to Sparse Representations*
12:00 – 1:30	**Lunch**
Session F3	Chairman: W. Art Chaovalitwongse
1:30	**W. Art Chaovalitwongse** *Quadratic Programming Approach for Clustering Epileptic Brain*
1:55	**Moongu Jeon** *Parallel Image Clustering using Level Set Methods*
2:20	**Richard E. Frye** *Dyslexia: An Example of Natural Variation in Large-Scale Neural Network organization*
2:45	**Onur Seref** *Kernel Based Methods Applied to Single Trial Neural Signals*
3:10 – 3:30	**Coffee Break**
Session F4	Chairman: Chang-Chia Liu
3:30	**Yan Zhang** *MEG in Dyslexia: A Power and Coherence Study*
3:55	**Wichai Suharitdamrong** *Graph Theory-Based Data Mining Techniques to Study Brain Similarity Network of Epileptic Brain*
4:20 – 4:45	**Closing Remarks**

Plenary Talks:

1. **Evolution as the Blind Engineer: Wiring Minimization in the Brain**
   Dmitri Chklovskii (Cold Spring Harbor Laboratory)

2. **Sourcing organizing concepts for neocortical dynamic data from many-body physics**
   Walter J. Freeman (University of California, Berkeley)

3. **Probing Brain Function Across Different Spatial and Temporal Scales with Tomographic Analysis of Magnetoencephalographic Signals**
   Andreas Ioannides (Brain Science Institute, RIKEN, Japan)

Invited and Contributed Talks:

4. **Tabu Search Enhanced Graphical Models for Classification of High Dimensional**
   Xue Bai (Carnegie Mellon University)

5. **A Novel In-Vivo Model of Basal Frontal Forebrain Origin Seizures in Anolis Lizards** [1]
   Michael Bewernitz (University of Florida)

6. **Dynamical EEG Properties in the Limbic Epilepsy Rat Model**
   Paul R. Carney (University of Florida)

7. **Cluster Analysis of Epileptic Brains**
   W. Art Chaovalitwongse (Rutgers University)

8. **Probability Distribution Function and Optimal Strategy for Natural Selection**
   Su-Shing Chen (University of Florida)

9. **Current Source Density Analysis of Ongoing Neural Activity: Theory and Applications**
   Mukesh Dhamala (University of Florida)

10. **Statistical Modeling of Neurobiological Data**
    Mingzhou Ding (University of Florida)

11. **Dyslexia: An Example of Natural Variation in Large-Scale Neural Network Organization**
    Richard E. Frye (University of Florida)

12. **Fuzzy Hyperplane Clustering Algorithm and Applications to Sparse Representations**
    Pando Georgiev (University of Cincinnati)

13. **Discrimination and Classification by Mixed Integer Programming**
    Fred Glover (University of Colorado)

14. **Online Analysis of Device-Tissue Interactions - Modeling Tissue Impedance Spectra**
    Aparna Gupta (Resselaer Polytechnic Institute)

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[1] See page 37

15. **Reading the Mind: fMRI Analysis Via One-Class Machine Learning Techniques**
Larry Manevitz (University of Haifa, Israel)

16. **Neural Information Flow Networks in Songbirds**
Alexander Hartemink (Duke University)

17. **Tracking Spatio-Temporal Changes in ECOG**
Anant Hegde (University of Florida)

18. **Adaptations of Stationary Analytics Techniques to Understand the Nonstationary Neural Activity Underlying Performance of a Complex Cognitive Task**
Linda Hermer-Vazquez (University of Florida)

19. **Change Detection of Synchrony in Oscillatory Neurophysiologic Signals**
Qiang Huang (University of South Florida)

20. **Shape Analysis for Automated Sulcal Classification and Parcellation of MRI Data**
Monica K. Hurdal (Florida State University)

21. **Resetting of Brain Dynamics by Epileptic Seizures**
Leonidas D. Iasemidis (Arizona State University)

22. **Parallel Image Clustering using Level Set Methods**
Moongu Jeon (Gwangju Institute of Science and Technology, Korea)

23. **Development of a Rodent Seizure Control System using Intracerebroventricular Injections of Midazolam**
Kevin M. Kelly (Drexel University)

24. **Neural Networks, Monte Carlo Methods, and Real-world Neurons**
Jeff Knisley (East Tennessee University)

25. **Computational Evaluation of Mixed Integer Programming Models for Discrimination and Classification**
Fang Liang (University of Colorado)

26. **Distinguishing Independent Bi-Temporal from Unilateral Onset in Epileptic Patients by the Analysis of Nonlinear Characteristics of EEG Signals**
Chang-Chia Liu (University of Florida)

27. **A New Brain Mapping Based on the Visualization and Modeling of the Short Term Maximum Lyapunov Exponent**
Nadia Mammone (Reggio Calabria, Italy)

28. **A Simulation Tool Using Discrete Integrate and Fire Neurons: Modeling the Influence of Anatomy on Information Flow in Very Large Simulated Networks**
Maya Maimon (University of Haifa, Israel)

29. **Dynamical State Dependent Electrical Stimulation for Seizure Control in a Chronic Limbic Epilepsy Model**
    Sandeep P. Nair (University of Florida)

30. **Biomarker Discovery in Ischemic Stroke - A Neuroproteomic Study**
    Andrew K. Ottens (Univesity of Florida)

31. **Visual Analysis for Comparing Structure, Timing and Synchronization Properties of Neural Populations**
    Kay A. Robbins (Univsersity of Texas at San Antonio)

32. **Group Sensing with Electroencephalograms (EEG)**
    David Rosenbluth (Telecordia)

33. **Hyperplane-Based Decision Trees and Their Optimization**
    Michele Samorani (Università degli Studi di Bologna, Italy)

34. **Choosing the Appropriate Level of Abstraction for Brain Machine Interfaces: Data Collection and Analysis Insights**
    Justin C. Sanchez (University of Florida)

35. **Kernel Based Methods Applied to Single Trial Neural Signals**
    Onur Seref (University of Florida)

36. **Graph Theory-Based Data Mining Techniques to Study Similarity of Epileptic Brain Network**
    Wichai Suharitdamrong (University of Florida)

37. **A Feedback Control Systems View of Epileptic Seizures**
    Kostas Tsakalis (Arizona State University)

38. **Differential Proteomic Analysis of Traumatic Brain Injury Biomarker Study**
    Keving K.W. Wang (University of Florida)

39. **MEG in Dyslexia: A Power and Coherence Study**
    Yan Zang (University of Florida)

Tabu Search Enhanced Graphical Models for Classification of High Dimensional Data

Xue Bai and **Rema Padman**

Heinz School of Policy, Management, and Information Management
Carnegie Mellon University

Data sets with many discrete variables and relatively few cases arise in health care, ecommerce, information security, text mining, and many other domains. Learning effective and efficient prediction models from such data sets is a challenging task. In this paper, we propose a Tabu Search enhanced Markov Blanket (TS/MB) procedure to learn a graphical Markov Blanket classifier from data. The TS/MB procedure is based on the use of restricted neighborhoods in a general Bayesian Network constrained by the Markov condition, called Markov Blanket Neighborhoods. Computational results from real world data sets drawn from several domains indicate that the TS/MB procedure is able to find a parsimonious model with substantially fewer predictor variables than in the full data set, and provides comparable prediction performance when compared against several machine learning methods.

Dynamical EEG Properties in the Limbic Epilepsy Rat Model

P.R. Carney[1,2,6,9,10], **S.P. Nair**[2,10,11], **D-S. Shiau** [2,5,10,11], **W.M. Norman**[1,10], **P.M. Pardalos**[2,3,4,9,10], **Z. Liu**[1,6,10] , **J. Principe**[2,8,10], **J.C. Sackellares**[1,2,5,6,7,10,11]

[1]Pediatrics, [2]Biomedical Engineering, [3]Industrial and Systems Engineering, [4]Computer and Information Science and Engineering, [5]Neuroscience, [6]Neurology, and [7]Psychiatry, [8]Electrical Engineering, University of Florida, Gainesville, FL 32611, USA
[9]Center for Applied Optimization, [10]McKnight Brain Institute, University of Florida, Gainesville, FL 32611
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We have previously reported preictal transitions, detectable in the spatiotemporal characteristics of the EEG signal in human mesial temporal lobe epilepsy (MTLE) using short term largest Lyapunov exponent (STL_{max}) and average angular frequency ($\bar{\Omega}$). These results have prompted us to apply the quantitative nonlinear methods to a chronic limbic epilepsy rat (CLE) model, as this model has several important features of human MTLE. The present study tests the *hypothesis* that the rat EEG is being generated by a nonlinear system and that the preictal dynamical changes, similar to those observed in humans, exist in the CLE model. Test data sets include twenty-eight, 2-hr data sets from 4 CLE rats (mean seizure duration 78±21 sec) are analyzed, each containing a seizure and intracranial data beginning 1 hr before the seizure onset, and twenty-eight 2-hr epochs far away from each seizure analyzed. The signal was tested for the presence of nonlinearities using the correlation integral measure falsified with surrogate datasets. Two measures, the short term largest Lyapunov exponent and average angular frequency, are used to study dynamical state changes in the model. Short term largest Lyapunov exponent values show a significant drop and average angular frequency values show a significant peak during the ictal period. Convergence of these indices among electrode sites is also observed in both STL_{max} and $\bar{\Omega}$ values before seizure onset. Results indicate that there are characteristic spatiotemporal changes in the EEG signal that precede and accompany seizures in rat CLE.

Cluster Analysis of Epileptic Brains

W. Art Chaovalitwongse
Department of Industrial and Systems Engineering
Rutgers University

We attempt to extract insightful characteristics of the brain dynamical connectivity preceding epileptic seizures through an optimization-based cluster analysis of electroencephalogram (EEG) data. The brain clustering problem can be formulated as a quadratic program. The experimental results in this study suggest that the proposed cluster analysis may be able to differentiate normal and abnormal (pre-seizure) EEGs.

Probability Distribution Function and Optimal Strategy for Natural Selection

Su-Shing Chen
Computer and Information Science and Engineering
University of Florida

The probability distribution function of optimal score of global alignment of biomolecular sequences will be shown to be a three-parameter gamma function. Thus the natural selection search can be described by a simulated annealing process with the temperature as one parameter of the gamma function.

Evolution as the Blind Engineer: Wiring Minimization in the Brain

Dmitri Chklovskii
Cold Spring Harbor Laboratory

The human brain is a network containing hundred billion neurons, each communicating with several thousand others. Neuronal communications are implemented by biological wiring, which draw on limited resources such as space, time and energy. This suggests that evolution must have solved optimal design problems. We analyzed multiple features of brain architectures, from neuronal placement to neuronal shape, and found that they could be explained as solutions to optimal design problems. Such an approach leads to a systematic view of the brain architecture, which should help understand brain function.

Current Source Density Analysis of Ongoing Neural Activity: Theory and Applications

Mukesh Dhamala

Department of Biomedical Engineering
University of Florida

Current source density (CSD) analysis of spatial local field potentials provides information about the local neural activity in terms of current sources and sinks. The signal-to-noise ratio in an evoked response potential (ERP) can be enhanced simply by averaging of repeated measurements. However, averaging suppresses the underlying ongoing or spontaneous neural activity in the average evoked response. Ongoing oscillations require a different treatment to estimate the overall activity. We propose a technique to perform CSD analysis from the trials of ongoing neural activity. Our method employs estimation of phases and amplitudes from single trials by a least squares fit to sinusoidal waveforms. CSD profiles are estimated from phase-realigned trials and also from reconstructed average waveforms. We test these methods on simulated data and also on an experimental dataset consisting of intra-cortical local field potentials recorded on multicontact depth electrodes from monkeys performing intermodal selective attention task.

Statistical Modeling of Neurobiological Data

Mingzhou Ding
Department of Biomedical Engineering
University of Florida

Neural data are complex. Understanding this complexity lies at the center of contemporary neuroscience research. In this talk I will discuss modeling multi-channel neural data in typical cognitive paradigms. A generative data model is presented first which includes ongoing neural activities and acknowledges trial to trial variability of evoked responses. Then a statistical procedure is introduced that deals with various aspects of this generative model. Examples of neural recordings from monkeys performing cognitive tasks will be used to illustrate the approach.

Sourcing Organizing Concepts for Neocortical Dynamic Data from Many-Body Physics

Walter J. Freeman
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Neural activity patterns related to behavior occur at all scales in time and space from the atomic and molecular to the whole brain. Patterns form through interactions in both directions, so that the impact of transmitter molecule release can be analyzed upwardly through synapses, dendrites, neurons, populations and brain systems to behavior, and control of that release can be described step-wise through top-down transformations. We explore the feasibility of organizing and interpreting neurophysiological data in the context of many-body physics by using tools that physicists have devised to analyze comparable hierarchies in other fields of science. We focus on a mesoscopic level that offers a multi-step pathway between the microscopic functions of neurons and the macroscopic functions of brain systems revealed by hemodynamic imaging. We apply the Hilbert transform to electroencephalographic (EEG) recordings from high-density electrode arrays fixed on epidural surfaces of primary sensory and limbic areas in rabbits and cats trained to discriminate conditioned stimuli in the various modalities. The resulting high spatiotemporal resolution of EEG signals gives evidence for diverse intermittent spatial patterns of amplitude (AM) and phase modulations (PM) of carrier waves that repeatedly re-synchronize in the beta and gamma ranges at near zero time lags over long distances. The dominant mechanism for neural interactions by axodendritic synaptic transmission should impose distance-dependent delays on the EEG oscillations owing to finite propagation velocities. It does not. EEGs instead show evidence for anomalous dispersion: the existence in neural populations of a low velocity range of information and energy transfers, and a high velocity range of the spread of phase transitions. This distinction labels the phenomenon but does not explain it. We explore the this and related phenomena using concepts of energy dissipation, the maintenance by cortex of multiple ground states corresponding to AM patterns, and the exclusive selection by spontaneous breakdown of symmetry of single states in cinematographic sequences.

- Freeman W.J. (2005) Origin, structure, and role of background EEG activity. Part 3. Neural frame classification. Clin. Neurophysiol. 116 (5): 1118-1129. http://authors.elsevier.com/sd/article/S1388245705000064
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- Kozma R, Puljic M, Balister P, Bollabás B, Freeman WJ. (2005) Phase transitions in the neuropercolation model of neural populations with mixed local and non-local interactions. Biol. Cybern. 92: 367-379.
- Freeman WJ, Vitiello G (2005) Nonlinear brain dynamics and many-body field dynamics. http://www.arxiv.org/find [Freeman] q-bio.OT/0511037
- Freeman WJ, Vitiello G (2005) Nonlinear brain dynamics as macroscopic manifestation of underlying many-body field dynamics. http://www.arxiv.org/find [Freeman] q-bio.OT/0511037

Dyslexia: An Example of Natural Variation in Large-Scale Neural Network Organization

Richard E. Frye
Department of Neurology, College of Medicine
University of Florida

Janet McGraw Fisher
Department of Psychology, Boston University

Seppo Ahlfors, Athinoula A. Martinos
Center for Biomedical Imaging, Charlestown, MA

Eric Halgren
University of California at San Diego

Jacqueline Liederman
Department of Psychology, Boston University

The decoding, production and understanding of oral and written language are some of the most complex cognitive processes. Such processes involve the rapid integration and coordination of neural activity in widely distributed cortical areas. The organization and dynamics of the brain's language processing system is still being investigated, although the basic large scale structure of the system is well known in individuals without language deficits. However, the neural basis of language processing maybe fundamentally different in individuals with developmental language disorders such as dyslexia. Functional neuroimaging studies over the past two decades have demonstrated differences in the distribution and connectivity between important cortical areas involved in reading in individuals with developmental phonological dyslexia as compared to normal readers. A recent functional MRI (fMRI) study suggests that different patterns of large-scale neural system organization in developmental phonological dyslexic individuals are dependent on the eventual ability of such individuals to acquire adequate reading skills (Shaywitz et al., Biol Psychiatry 54:25, 2004). However, fMRI primarily provides information pertaining to where the brain is activated but not how neural activity dynamically changes on a millisecond time scale. Thus, in order to better understand patterns of large-scale neural organization in dyslexia, we have used magnetoencephalography (MEG) to study the evolution of spatiotemporal patterns of neuronal activity and the dynamics that occur between important cortical areas in normal and dyslexic individuals during a visual phonological decoding task. Different patterns of large-scale neural network organization are revealed in dyslexics as compared to normal readers. For example, whereas normal readers tend to lateralize cortical interactions to the left hemisphere after a short time, the neural activity in some dyslexic individuals tends to oscillate between the two hemispheres for an extended period of time. However, not all dyslexic readers activate the brain in the same manner. In addition, our MEG results suggest that these differences may go beyond the organization of the large-scale neural networks. It appears that some dyslexic individuals may have a fundamental difference in the type of communication that occurs between different cortical areas. Some dyslexic individuals demonstrate stepwise linear activation of cortical areas with restricted interactions between activated areas, whereas normal individuals tend to demonstrate simultaneous activation of widely distributed areas with multiple interactions between activated areas. At this point we are still investigating and understanding individual variation in large scale-scale organization of neural activation patterns in individuals with normal and abnormal language abilities. MEG is a tool that can provide this information and dyslexia provides a well studied model of abnormal language processing that can be utilized to understand the potential natural variations in neural organization.

Fuzzy Hyperplane Clustering Algorithm and Applications to Sparse Representations

Pando Georgiev and **Anca Ralescu**
ECECS Department
University of Cincinnati
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We develop a fuzzy hyperplane clustering algorithm based on finding a skeleton (a union of hyper-planes) of a given set of data points. The resulting algorithm has a direct application to the following sparse representation problem: represent a given data matrix $\mathbf{X} \in \mathbb{R}^{m \times N}$ in the form $\mathbf{X} = \mathbf{AS}$, where $\mathbf{A} \in \mathbb{R}^{m \times n}$, $\mathbf{S} \in \mathbb{R}^{n \times N}$, as a priori is known that such a representation exists and the matrix $\mathbf{S}$ is sparse in the sense that each column of it has at least $n - m + 1$ zeros. Applications to fMRI data analysis are considered.

Discrimination and Classification by Mixed Integer Programming

Fred Glover
Leeds School of Business
University of Colorado, Boulder

Gary Kochenberger
Business School
University of Colorado, Denver

Several mixed integer programming models have been proposed for discrimination and classification based on the objective of minimizing the number of misclassified points. Two recent models by Glen (2003,2005), respectively involving single and multiple hyperplane separations, embody the computational state-of-the-art. We analyze Glen's models and show that a superior single hyperplane model results from an earlier formulation by Glover (1993), which reduces the set of weight variables by half and further eliminates discrete special-ordered-set restrictions applicable to these variables. By extension, we provide a new model for multiple hyperplane classification that not only has comparable advantages but also handles more general problem structures by removing an implicit "partial convexity" assumption required by Glen's model. Computational implications of these new models are explored in a companion paper.

Online Analysis of Device-Tissue Interactions - Modeling Tissue Impedance Spectra

Aparna Gupta
Department of Decision Sciences and Engineering Systems
Rensselaer Polytechnic Institute

W. Shain
Wadsworth Center, Albany, NY

J. William
Department of Biomedical Engineering
University of Wisconsin, Madison, WI

K.L. Smith and **C.S. Bjornsson**
Wadsworth Center, Albany, NY

Effectiveness of implanted neural prosthetic devices is governed by the level of continued access the devices maintain with targeted neurons in the brain. One major cause for lack of long-term function is the development of reactive responses around the implanted devices. Development of these biological responses coincides with changes in the electrical properties of the tissue adjacent to the inserted devices, often results in increased resistivity compared to normal tissue. For successful recording and stimulation of neural tissue using prosthetic devices, an understanding of the tissue-electrode impedance properties as reactive responses progress around the implanted device is necessary. This understanding of correlations between changes in device-tissue impedance will lead to developing on-line methods for modulating stimulation parameters or controlling drug delivery intervention strategies, thus help improving effectiveness of the devices. In this research, we develop finite-element method (FEM) based models for different initial cell and vascular geometries obtained from in-vivo tissue slices. The FEM models are used to assess the impedance spectrum due to change in initial geometries. Based on an initial geometry, we develop modified cell and vascular configuration geometries for 1 to 20 days after device insertion. FEM analysis is conducted of the impedance spectrum for the modified geometries. A validation of initial and modified impedance spectra is done with experimental data.

Reading the Mind: fMRI Analysis Via One-Class Machine Learning Techniques

David R. Hardoon
School of Electronics and Computer Science
South-Hampton University

Larry M. Manevitz
Department of Computer Science
University of Haifa

One-Class Machine Learning techniques (i.e. "bottleneck" neural networks and one-class support vector machines (SVM)) are applied to classify whether a subject is performing a cognitive task or not by looking solely at the raw fMRI slices of his brain. "One-class" means that during training the system only has access to positive (i.e. task performing) examples. "Two-class" means it has access to negative examples as well. Successful classification of data by a system trained under either of the one-class systems was accomplished at close to the 60% level. (In contrast, an implementation of a standard two class SVM succeeds at around the 70% level.) These results were stable over repeated experiments and for both motor and visual tasks. Since the one-class neural network technique is naturally related to dimension reduction, it is possible that this mechanism may also be used for feature selection.

Neural Information Flow Networks in Songbirds

Alexander Hartemink
Department of Computer Science
Duke University

Songbirds are one of very few organisms to exhibit vocal learning: the ability of an organism to learn to produce new utterances on the basis of what it hears in its environment. As such, they make an excellent model system for understanding human language acquisition and use. Vocal learning involves the auditory cortex for processing of sensory input, the motor cortex for generation of new vocal output, and interconnections between the two. In collaboration with Erich Jarvis in Duke's neurobiology department, we are starting an effort to map out how various regions of the auditory and motor cortices are communicating with one another to enable vocal learning to arise in the songbird. While much of traditional computational neuroscience has focused on the behavior of and interactions between single neurons, we are trying to work at a slightly higher level of brain organization, investigating how collections of neurons in certain brain regions, taken together, are communicating with collections of neurons in other brain regions, taken together. We are using multi-unit electrophysiological recordings and network inference algorithms to reverse-engineer these neural information flow networks; I will show fairly preliminary results revealing the kinds of things we can learn through this approach.

Tracking Spatio-Temporal Changes in ECOG

Anant Hegde and **Jose C. Principe**
Department of Electrical Engineering
University of Florida

It is widely believed that the dynamics of the brain are characterized by continual temporal changes in its spatial organizations. Such spatio-temporal changes could eventually lead to certain clinical manifestations. For an epileptic brain, in particular, changes associated with epileptic events could possibly be reflected in their overall spatial connectivities. Therefore, tracking the ongoing temporal changes in spatial networks of an epileptic ElectroEncephalogram (ECOG) might provide useful clinical insights on the occurrence of seizures.

In this study, we propose a simple statistical approach to quantify the temporal changes in spatial patterns of an ECOG. Previously, we developed a non-linear synchronization measure, called the SOM-Similarity Index, to quantify mutual associations between various brain regions. We propose to apply the mantel test statistics on the SOM-similarity indices to track the temporal changes of the spatial patterns. Statistical comparisons between inter-ictal and pre-ictal states suggest significant changes in the spatial connectivity prior to a seizure. Results confirm 5 out of 6 complex-partial seizures exhibited significant changes, anywhere between 1.5 hours before seizure and the seizure.

Adaptations of Stationary Analytics Techniques to Understand the Nonstationary Neural Activity Underlying Performance of a Complex Cognitive Task

Linda Hermer-Vazquez
Behavioral Neuroscience Program, Dept. of Psychology
University of Florida

One of the main goals of our lab is to understand the flow of information across task-related, cortical and subcortical brain sites during the performance of decision-making and other executive tasks. With multisite, multielectrode recordings of action potentials and local field potentials, we have extensively studied an olfactory GO/NO-GO task that rats perform in <350 ms/trial. During each trial's brief, ~340 ms duration, we have found that at least 5 task phase-specific and brain area-specific firing rate modulations occur, indicating a high degree of nonstationarity in the neural spike data underlying task performance. Our adaptations of stationary analysis techniques applied to the spike and LFP data have revealed the following types of neural modulation leading to successful task performance: (1) Upon recognition of the GO cue, a subpopulation of neurons in each task-related, olfactory or motor brain area undergoes transient spike firing inhibition just prior to the initiation of the voluntary move; (2) at the same time, task-related cortical and subcortical sites display cross-area coordination in the form of transient, broadband coherence in their LFPs and increased beta-frequency (12-30 Hz) spiking in a different subpopulation of units; (3) task-related brain areas perform convergent roles upon recognizing the GO cue, and then perform divergent processing roles during motor execution; and (4) during performance of the motor sequence, cortical areas guide the activity of subcortical motor execution systems involved in obtaining the reward, likely maintaining cross-area coordination.

Change Detection of Synchrony in Oscillatory Neurophysiologic Signals

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Synchronization, a phenomenon describing the adjustment of rhythms of interacting oscillatory objects like that of neurons, has been related to several central issues of neuroscience. In this study, we focus on detecting the changes of synchrony (rather than the synchrony itself) among oscillatory neurophysiologic signals.

Shape Analysis for Automated Sulcal Classification and Parcellation of MRI Data

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Parcellation and labeling of cortical features are important, often manually intensive processes in visualization and interpretation of neuroimaging data. Labeling cortical structures is critical for cartography and conveying pertinent information to compare individual subjects or different populations. As the number of subjects in studies increases and larger data sets are acquired, it is critical to have automated tools. Large sample sizes mandate the use of automated procedures that are sensitive to relevant anatomical features. Additionally, such automated procedures can be used as valuable tools in teaching and training medical students. Due to the variability in folding patterns of each individual cortex, it is often a challenging task for the novice (and sometimes expert!) to identify and label cortical features.

Mathematically, properties of the shape of curves and surfaces in 3D space can be described by features such as their velocity fields, writhe, extremal length, principal curvatures, and Gaussian curvatures. For parcellation, additional information such as the location of cortical features is also of interest; these can be described by simpler features such as position and mathematical moments. We present a variety of geometric invariants to quantify properties of the shape of the cortical surface on a global as well as local level.

In our preliminary studies, topologically correct cortical surfaces representing the white matter and gray matter have been reconstructed using freeware software that is available to the neuroscience community (for example, FreeSurfer (Fischl et al., 1999) and BrainVisa (Mangin et al., 2001)). Curves of maximal and minimal principal curvature have been traced on 15 cortical surfaces. A user identifies a start and end point of a sulcus or gyrus and dynamic programming methods are used to automatically compute the path of principal curvature between these two points, thus tracking the ridge of a gyrus of the fundus of a sulcus. Five curves on each hemisphere, resulting in 150 curves from 15 subjects have been traced. Kernel Optimal Component Analysis was applied to moments, writhe invariants and their higher order analogues to extract features for parcellation and labeling. We were able to classify sulcal and gyral curves into left and right hemispheres, as well as distinguish the type of curve (i.e. central sulcus, occipital sulcus). These results indicate that the selected features vectures represent promising characteristics for automatically parcellating sulcal curves.

Probing Brain Function Across Different Spatial and Temporal Scales with Tomographic Analysis of Magnetoencephalographic Signals

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Magnetoencephalography (MEG) has always been associated with excellent temporal resolution. It is now becoming apparent that tomographic analysis of MEG signals can provide accurate localization, at least for places a few centimeters away from the center of the head [1]. It is therefore becoming possible to explore brain function by accurately mapping activity over the entire cortical mantle and probing interactions between areas across timescales ranging from milliseconds to minutes in the same run, for example when a piece of music is played [2]. Longer timescales can also be probed by repeating experiments, days, months or years apart. Recent MEG results will be used to demonstrate a variety of methods, each designed to highlight different aspects of brain function across different spatial and temporal scales.

In the first experiment the MEG signal was recorded following visual stimulation with simple checkerboard stimuli confined to one quadrant of the visual field. The responses were analyzed using tomographic analysis of the average data and the results were compared with responses to identical stimuli on the same subjects using fMRI. The loci of activation within V1 for MEG and fMRI agreed to within a few millimeters, which was as good as the coregistration of the data would allow [3]. The same data were analyzed in a completely data driven approach. Pattern analysis principles were used to analyze time courses of single-trial activity extracted from a spatial filter matching the dominant MEG signal topography established about 70 milliseconds after stimulus onset. Distinct response modes were identified by a novel scheme for detecting and organizing the structure in single-trial recordings. The interpretation of variability in terms of regional dynamics showed only a relatively weak activation in primary visual cortex. The main contribution to the polymorphic response across single trials was traced to activity in polymodal areas and cooperative activity in striate and extrastriate areas [4].

In the second experiment eye movements were studied in different states (awake state and sleep) [5] and in a complex GO/NOGO paradigm [6]. Tomographic analysis of single trial activations and follow up connectivity analysis showed that REM saccades correlated with bilateral pontine and FEF activity some 250 to 400 ms before REM saccade onset, which in turn was preceded 200 ms earlier by reciprocal activation of the pons and FEF [5]. In the GO/NOGO study MEG data were analyzed following visual cues to define planning, preparation and execution or inhibition of saccades. Tomographic reconstructions of activity identified spike-like responses that were widely distributed across the cortex, cerebellum and brainstem during cue presentations and saccades. The properties of these “MEG spikes” were influenced by the stimuli and task demands. The MEG spikes were organized into feed-forward and corollary discharge sequences that could, when combined with the slower activity-linked processing in discrete brain areas over long periods, lasting hundreds of milliseconds. allowing competing motor programs for as yet undecided future actions to be maintained until cues with new information resolved the uncertainty.

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Resetting of Brain Dynamics by Epileptic Seizures

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Epileptic seizures occur intermittently as a result of complex dynamical interactions among many regions of the brain. By applying signal processing techniques from the theory of nonlinear dynamics and global optimization to the analysis of long-term, continuous multi-channel electroencephalographic (EEG) recordings from epileptic patients, we will present evidence that epileptic seizures appear to serve as dynamical resetting mechanisms of the brain, that is the dynamically entrained brain areas before seizures disentrain faster and more frequently ($p<0.05$) at epileptic seizures than any other periods. We expect these results to shed light into the mechanisms of epileptogenesis, seizure intervention and control, as well as into investigations of intermittent spatiotemporal state transitions in other complex biological and physical systems.

Parallel Image Clustering using Level Set Methods

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This paper presents a parallel hierarchical image-pixel clustering (segmentation) method for multi-phase images based on a level set method and a semi-implicit Additive Operator Splitting (AOS) scheme which is stable, fast, and easy to implement. The method successively segments image sub-regions found at each step of the hierarchy using a decision criterion based on the variance of intensity across the current sub-region. The segmentation continues until a specified number of levels has been reached. The segmentation information for sub-images at each stage is stored in a tree data structure, and is used for reconstructing the segmented images. The method avoids the complicated governing equations of the multi-phase segmentation approach, and appears to converge in a fewer iterations. Most PDE-based image segmentation algorithms employ an explicit scheme to solve the system equations. However, an explicit scheme has a time step constraint and also when parallelized, data dependency is unavoidable at the boundary of the region assigned to processors, which requires communication between neighboring processors to share the boundary information. AOS is a semi-implicit scheme that effectively decomposes a multi-dimensional system into a series of independent one-dimensional systems, which is composed of multiple tri-diagonal systems. Functional parallelism is made possible by this decomposition and within each one-dimensional processing step, data parallelism is achieved by solving the independent tridiagonal systems, resulting in a nested parallelism. Thus, implementation of parallelism is straightforward, and the parallel program will be subject to less communication overhead than explicit schemes. In this paper, we employ the AOS scheme for a level set formulation of the segmentation problem, and its parallelization will be examined for a couple of brain and other images with MPI and OpenMP.

Development of a Rodent Seizure Control System Using Intracerebroventricular Injections of Midazolam

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Epileptic seizures that originate from the neocortex of the brain often do not respond to current medical or surgical therapies. Our recent studies in rats have focused on the development of a novel closed loop feedback control system for use in the treatment of poststroke seizures, a type of neocortical epilepsy. This control system is intended to ultimately interface with a patient's brain and includes EEG sensors and a processor that mathematically converts EEG signals to dynamical properties (spatiotemporal characteristics), analyzes these dynamical properties to anticipate seizure onset, and activates a medication delivery device to prevent seizure occurrence. Dynamical properties of interest include neuronal synchrony, assessed by the short-term maximum Lyapunov exponent (STLmax), and neuronal complexity, assessed by the pattern match regularity statistic (PMRS). Changes in neuronal synchrony and complexity can be recognized during the transition periods from pre-seizure to seizure to post-seizure states. Transition from the pre-seizure period to seizure occurrence may be prevented by infusing a fast-acting benzodiazepine, midazolam, into the brain and altering its dynamical state. In order to achieve this objective, we have begun a comprehensive evaluation of the pharmacological requirements of the system using an arterial occlusion model of poststroke epilepsy. Initial studies of the concentration-response characteristics of EEG signal dynamics in response to single intracerebroventricular (ICV) injections of midazolam have been conducted to determine the optimal concentration for effecting detectable changes in STLmax and PMRS while causing minimal disturbance of the animal's behavior. An optimal midazolam concentration will be used to determine whether the direction and magnitude of the change of STLmax or PMRS in response to a single ICV injection of midazolam vary as a function of the value of that property at the time of dosing. We anticipate that successful completion of these studies will enable the development of mathematical models to explain and predict dynamical changes in response to drug administration in an epileptic brain.

Neural Networks, Monte Carlo Methods, and Real-world Neurons

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Although artificial neural networks (ANN's) can be used for data mining and analysis of large data sets, the use of ANN's may be complicated by slow convergence, spurious states, and other confounding factors. Incorporating Monte-Carlo methods can partially ameliorate these factors, especially in the analysis of microarray data. Additional features can be incorporated by comparison with dendritic electrotonic models with Hodgkin-Huxley ion channels (Glenn and J. Knisley, 2005). Such features include the use of ANN's not only as universal classifiers (Cybenko, 1989), but also as tools for estimating the significance of parameters in models of biological systems. In this presentation, the incorporation of Monte-Carlo techniques and concepts from models of real neurons will be described. In addition, an algorithm for combining Monte-Carlo methods with ANN's to analyze gene expression in microarray data will be given. A similar algorithm has been used in conjunction with graph-theoretic invariants in protein-folding and RNA identification (D. Knisley, Haynes, and Seier, submitted).

Computational Evaluation of Mixed Integer Programming Models for Discrimination and Classification

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We perform a computer study of mixed integer programming models for discrimination and classification proposed by Glen (2003, 2005) and by Glover and Kochenberger (2005). For the objective of minimizing the number of misclassified points, one version of these models seeks a single separating (or "partially separating") hyperplane, while another version seeks multiple hyperplanes as a basis for conditional (sequential) classification. Relative efficiency and effectiveness of the alternative models are analyzed on benchmark problems for classifying patients with breast cancer and for classifying banks with different solvency levels. We show that mixed integer programming is indeed effective in these applications, and identify the qualities that characterize the superior models.

Distinguishing Independent Bi-Temporal from Unilateral Onset in Epileptic Patients by the Analysis of Nonlinear Characteristics of EEG Signals

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Purpose: To investigate the difference in electroencephalographic (EEG) characteristics between epileptic patients with independent bi-temporal seizure onset zone (BTSOZ) and those with unilateral seizure onset zone (ULSOZ).

Methods: Eight adult patients with temporal lobe epilepsy were included in the study, five patients with ULSOZ and three patients with BTSOZ. The method was based on the test of nonlinear characteristics, defined as the distinction from a Gaussian linear process, in intracranial EEG recording signals. Nonlinear characteristics were tested by the statistical difference of the short-term maximum Lyapunov exponent (STLmax), a discriminating nonlinear measure, between the original EEG signals and its surrogate data sets. Distributions of EEG nonlinearity over different recording brain areas were investigated and were compared between two groups of patients.

Results: Results from the five ULSOZ patients showed that the nonlinear characteristics of EEG recordings are significantly inconsistent ($p < 0.01$) over six different recording areas (left and right temporal depth, subtemporal and orbitofrontal). Further, the signals recorded from the temporal depth area on focal side consistently exhibited higher degree of nonlinearities than on the homologous contralateral areas. On the other hand, the nonlinear characteristics of EEG are uniformly distributed over recording areas in all three BTSOZ patients.

Conclusions: The results of this preliminary study suggest that it is possible to efficiently and quantitatively determine whether an epileptic patient has ULSOZ based on the nonlinear characteristics of their EEG recording signals. For the ULSOZ patients, it is also possible to identify the focal area by utilizing this method. However, these results will have to be validated in a larger sample of patients. Success of this study can provide more essential information to patients and epileptologists to increase the chances of successful surgery.

A New Brain Mapping Based on the Visualization and Modeling of the Short Term Maximum Lyapunov Exponent

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In this paper, a new kind of brain topography is introduced and applied to data from two patients affected by intractable epilepsy. The epileptic brain can be modeled as a non-linear dynamic system and the largest Lyapunov exponent is a measure of the chaoticity of a dynamic system, the short term maximum Lyapunov exponent (STLmax) is a robust parameter optimized for the analysis of the chaoticity embedded in the Electroencephalographic (EEG). The objective of this work is to map and to model the spatial distribution of STLmax over the head. The STLmax is estimated from segments of each channel of long term continuous scalp EEG recordings, and a movie of the STLmax segment estimates is created over the head. The movie allows a visualization of the changes of the brain dynamics over time. Moreover, a Gaussian mixture model approximation of the STLmax spatial distribution was constructed. From the centers of the fitted model quantitative information about the spatial distribution of STLmax can be extracted. Analyzing the data segment preceding each seizure, we could automatically pick up which electrodes were been related to the highest or lowest chaoticity for the longest time and we found out that the epileptogenic region was been related to the highest chaoticity. The STLmax mapping seems to be a promising tool for monitoring the evolution of the dynamics of the epileptic brain and the Gaussian mixture model showed to fit very well the spatial distribution of STLmax and to provide precious information about the spatial organization of the epileptogenic focus dynamics.

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A Simulation Tool Using Discrete Integrate and Fire Neurons: Modeling the Influence of Anatomy on Information Flow in Very Large Simulated Networks

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Formal models of neurons and neural networks provide a way to understand information processing principles in the brain. Currently, such models are usually based on differential equations and are numerically too intensive to be used in very large network simulations. Nonetheless, the Integrate and Fire model has proved particularly useful in elucidating the properties of large neural networks and the implications of large numbers of synaptic connections in such networks. However, using a temporally discretized Integrate and Fire model is simpler both logically and computationally. If all the important information from a computational perspective is represented in such temporally discrete neurons the computational challenges are mitigated and this allows us to experiment on very large artificial networks with different parameters, different architectures and different encoding techniques in a reasonable time.

To pursue this approach, we present here a computational tool following these ideas. Current capabilities allow us to run networks of up to 50 million such neurons in a reasonable time and the methods are scalable. In this tool, an information theory approach is used to quantify the flow and amount of information for various simulated stimuli. This enables us to test theories and ideas about the importance of architecture elements in the cortex, in terms of information flow in the brain. Changing the architecture of the network (which generates the spike history of the neurons) can be done by simply changing parameters during the processing of the model. Another software component measures the information of the results over time. Currently, this is done by implementing the ideas of Treves, Panzeri et al. The aim is to learn how different encoding methods and architectures change the rate and the flow of information in the brain through time. Analyzing the changes of information flow in those sequences provides a way to measure anatomical changes and to evaluate how it affects the computational capabilities.

A Novel In-Vivo Model of Basal Frontal Forebrain Origin Seizures in Anolis Lizards

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Epilepsy is a group of brain disorders characterized by spontaneous, recurrent stereotyped behaviors and a wide range of psychiatric conditions, including disturbances of mood, thought, and personality. In order to better understand basic mechanisms underlying the physiological and behavioral disturbances of specific types of epilepsies, it is important to develop animal models that closely approximate the human conditions. Most seizure and epilepsy models have been produced in rodents or other mammals. Currently, we are investigating a novel reptile model for complex partial seizures.

Anolis lizards possess 3 characteristics which are desirable for an epilepsy model. 1) Anolis have easy to describe and quantitative behavioral social rituals. Pentylenetetrazol (PTZ)-induced activation of basal frontal forebrain (BFB) circuitry can be easily observed by excessive aggressive behavior such as push-ups, throat, dew-lap and crest inflation, and eyespot darkening. Depending of circuits activated, other behaviors may be seen. 2) The Anolis brain has a well-defined homology to the mammalian BFB-systems, in terms of receptor pharmacology and neuronal circuitry. 3) Anolis posses a natural split brain. There are no commissures (corpus callosum, etc.) in the telencephalon. The lack of interhemisphereic connections allows for the use of the contralateral brain as a control for experimental interventions in one cerebral hemisphere, as we have done to date in a few animals with seizure-genic visual stimuli to low-dose PTZ treated animals with one eye covered.

In this model, seizures are induced by intra-peritoneal (i.p.) injection of PTZ to activate the basal forebrain bundle in Anolis lizards (A. carolinensis, A. equestris and A. garmani) which vary in size and several key behaviors. This drug-induced activation of the basal forebrain typically produces seizures characterized by a tonic-clonic generalized fit of approximately 5 minutes in duration. Following the clonic phase is usually a series of distinct behavioral displays including; ambulation in a fore-limb strut posture with head cocked and dewlap partly distended (characteristically seen in dominant anoles when socially confronted), multiple simple motor tics of the head, limbs, and torso, occasional tail lashing, and often scores of forelimb pushups. In the case of A. euqestris, a display of tonic-clonic activity was followed by motor tics. During these behavioral displays the animals do not respond to visual stimuli (e.g. waiving a red-tipped pen). Without intervention, such activity lasted > 1 hr. When such animals were given 1 mg/Kg pentobarbital i.p., the behavioral displays ceased within several minutes. Several animals have survived multiple inductions of such seizures over several days without apparent ill-effect.

To confirm the presence of brain electrical activity characteristic of seizures, simple surface EEGs have been recorded from bilateral scalp electrodes located ~1 mm superior to the anole's ear. In one A. garmani showing only partial seizure activity, paroxysmal rhythmic delta activity (1-2 Hz) was seen. More animals will be done with electrodes implanted in the brain itself to allow correlation of regional EEG activity with specific behaviors.

Dynamical State Dependent Electrical Stimulation for Seizure Control in a Chronic Limbic Epilepsy Model

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Epilepsy represents a group of heterogeneous syndromes affecting at least 2 million people in the USA and Canada and about 0.8% of the total world population (Hauser, 1997). Despite many advances in the treatment of epilepsy, there continue to be a large number of individuals who do not respond to currently available therapeutic interventions and have to resort to alternative methods of seizure control which include electrical stimulation of deep brain structures and related bodies such as the vagus nerve. Current applications of electrical stimulation as targeted therapy for chronic condition such as temporal lobe epilepsy do not take into the potential improvements that could be achieved by taking into account the state of the epileptic brain. The goal in this research is to use strategic stimulus delivery to affect brain dynamics and define conditions necessary for directing the brain towards a desired state. A systematic approach was taken to address the question at hand. First, a chronic limbic epilepsy (CLE) animal model that captures many of the hallmarks of the human condition was utilized to test whether dynamical descriptors of intracranial EEG (iEEG) behave in a similar fashion as observed in humans. Second, the ability of these dynamical descriptors to warn of a seizure susceptible state was investigated. Third, a seizure warning and intervention scheme (based on state space regional coupling) was designed and implemented to study the effect of state dependent electrical stimulation. Promising results of the state dependent stimulation scheme are presented including effects on EEG dynamics as well as seizure frequency.

Biomarker Discovery in Ischemic Stroke - A Neuroproteomic Study

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Stroke is a leading cause of death and disability among the elderly. Over 700,000 incidents occur annually resulting in 275,000 deaths in the US alone. Ischemia through blood vessel occlusion in the brain comprises over 80% of stroke incidents. Ischemia is characterized by loss of oxygen and nutrients resulting in extensive oncotic cell death followed by neuronal remodeling and recovery. Techniques in neuroproteomics have been applied to characterize molecular changes as a result of ischemic stroke that may be useful as putative biochemical markers.

Visual Analysis for Comparing Structure, Timing and Synchronization Properties of Neural Populations

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The cortex has a rich structure of neurons inter-connected by excitatory and inhibitory synapses. Advances in recording and modeling technology have made it possible to measure response of a spatially distributed population of neurons at high temporal resolution. However, once acquired, analysis or comparison of such data sets remains a challenge. We have developed several analysis techniques and supporting visualization tools to elucidate structure and timing of space-time data such as those obtained from neural models, voltage sensitive-dye imaging or multi-electrode array experiments. These tools are designed to help scientists explore their data and to make side-by-side comparisons of structure as parameters or experimental conditions are varied. The tools are implemented in Java as part of Davis (Data Viewing System), a general-purpose data viewer designed for the simultaneous display and comparison of dynamic data sets. Davis allows scientists to study the detailed behavior of individual elements and the interaction of these elements to achieve cortical function. We demonstrate how Davis can be used to understand and compare the dynamic behavior across models, as well as to reveal relationships between underlying variables. We examine in particular detection of waves and synchronization properties in experimental and model data sets.

Group Sensing with Electroencephalograms (EEG)

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Low signal to noise ratio of single-trial surface EEG signals makes the dynamic detection of event-related potentials (ERP) a challenging task. Traditional trial averaging methods for enhancing the signal-to-noise ratio of ERP signals are inappropriate for realtime spatio-temporal analysis of neuro-physiological dynamics. We propose and present analysis results for a novel method of improving signal-to-noise of single trial EEG that is based upon averaging of EEG signals over individuals rather than over trials. This technique, while not relevant for clinical applications, is relevant for BCI applications in which the objective is to detect, interpret, and act on neuro-physiological signals. We call this approach Group EEG. This paradigm is used in the simple task of detecting visual evoked potentials (VEPs) simultaneously witnessed by multiple observers (Group Sensing).

In this paper we present several techniques that compensate for inter-subject variation in EEG signal characteristics and neuro-physiological responses to stimuli, enabling combination of signals across subjects. We compare the performance of several different approaches to improving the signal-to-noise of surface VEPs including: averaging multiple trials from a single subject; averaging multiple channels from a single subject; and averaging single trials over multiple subjects. These results were obtained for 64 Channel EEG data recorded from 11 subjects performing a visual target detection task. Our results show that combining single-trial EEG signals from pairs of subjects improved the detectability of ERPs by up to 20% (average 10%) over single subject detection when using simple threshold detection algorithms.

Hyperplane-Based Decision Trees and Their Optimization

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Several approaches have been proposed for discriminating (classifying) the elements of two or more data sets based on generating successive hyperplanes, following an original proposal by Glover (1990). Many of the corresponding algorithms are greedy algorithms, since they do not change a hyperplane after building it. Our multi-hyperplane approach produces a tree which is a particular case of Decision Tree. We show how it is possible to modify this tree using heuristic and meta-heuristic algorithms in order to create a clearer separation between the groups and improve the performance of the classifier.

Choosing the Appropriate Level of Abstraction for Brain Machine Interfaces: Data Collection and Analysis Insights

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Brain Machine Interface (BMI) experimental paradigms offer a new avenue to study and understand brain function because they provide functional electrophysiological and behavioral data that is synchronized over time. The choice of available brain signals and recoding methods can greatly influence the ability to extract control features, ease of implementation, and operating performance. Several hypotheses for the level of BMI performance can be attributed to selection of electrode technology, choice of model, and methods for extracting rate, frequency, or timing codes. Review of the state of the art in BMI design, clearly indicates a need for rethinking the fundamental techniques used to record and quantify the interactions of ensembles of neurons (namely which activity to sample, what information to extract, and how to preprocess the information). We will discuss the relative capacities and limitations of non-invasive (i.e., EEG from scalp electrodes), minimally invasive (ECoG activity from subdural electrode arrays), and maximally invasive (single neuron activity or local field potentials (LFP) from multi-electrode intracortical implants) techniques. We will explore the ongoing research at the University of Florida to analyze the BMI control capacities of ECoG, LFPs, and single neuron intracortical signals, the stability of invasive recordings, and the clinical recording challenges associated with human implants.

Kernel Based Methods Applied to Single Trial Neural Signals

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Analyzing single-trial data is one of the most common ways of studying neural signals. In this study, we use kernel based classification and feature selection algorithms to study the spatiotemporal interactions between different cortical sites of the brain on two different neural data sets. In the first set, we analyze local field potentials (LFPs) collected from macaque monkeys as they performed a visual discrimination task. We use classification to distinguish the temporal phases of the task, and feature selection to determine the relative contribution of the cortical sites to the classification. A similar methodology is applied on a second set of neural signal data set, which comprises EEG recordings from dyslexic and normal brains to study the spatiotemporal differences between them.

Graph Theory-Based Data Mining Techniques to Study Similarity of Epileptic Brain Network

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In the study of epileptic brain, the similarity measure among pairs of two electrodes has been studied for years. However, the study of pair-wise similarity on several pair of electrodes is limited due to a large number of combinations among electrode pairs which exponentially increase as the number of electrodes increases. With this large amount of information from several electrodes pairs, we cannot visually examine each individual electrode pair to find the significant pattern. In this work, we applied spectral partitioning and maximum clique to study the pattern of similarity network in epileptic brain. From constructing brain similarity network (BSN) of electrodes site, we can study the result of spatial connection from all electrodes in BSN to learn the connectivity pattern among different brain areas. After that, we use this information to construct spatio-temporal patterns to understand the pattern of epileptic seizure efficiently.

A Feedback Control Systems View of Epileptic Seizures

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Networks of coupled chaotic oscillators offer interesting possibilities to investigate functional mechanisms of seizure-like phenomena and potential control strategies for their suppression. In search of such a model and a mechanism to explain the observed behavior of the epileptic brain, the authors in [1] followed Freeman's approach (e.g., see [2]) of representing the brain as interconnections of nonlinear chaotic oscillators, connected with each other via diffusive coupling. They showed that an increase in the strength of coupling results in progressive synchronization between the oscillators, that is consistent with the preictal entrainment behavior of the epileptic brain [1], [3].

While this coupled oscillator model can exhibit chaos-to-order-to-chaos transitions, changes in the employed diffusive coupling do not produce the explosive growth of signals observed during seizures. Using a similar network of oscillators with varying coupling, we demonstrate that a plausible cause of seizures is pathological feedback. Although far from being a model for epilepsy, the presented mechanism has interesting semi-physical interpretation and close ties with a variety of recent practical observations and theories from adaptive systems, optimization, and chaotic systems. We classify “network seizures” depending on the number of paths and location of the pathological feedback and we discuss structural requirements of seizure suppression strategies. In particular, we show that for a single pathological path, seizure suppression can be achieved by stimulating the focus. But when seizures involve multiple pathological feedback paths, distributed sensing and stimulation is necessary to suppress seizures. Offering an intriguing interpretation of the observed behavior, this result is consistent with clinical studies of electrical stimulation in epileptic patients, e.g., [4], [5], [6].

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Differential proteomic analysis of traumatic brain injury biomarker study

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Traumatic brain injury (TBI) has an annual incidence of approximately 2 million persons in the United States, yet no affective treatment is available despite many clinical trials. The absence of diagnostic endpoints in the form of biochemical markers of brain injury hampered assessment of therapeutic trials. In this study, a neuroproteomics approach was utilized to characterize differential protein changes after controlled cortical injury to develop potential biomarkers of TBI. Proteins from control and injured rat cortical samples were separated by cationic-anionic exchange chromatography - polyacrylamide gel electrophoresis (CAX-PAGE). Differential targets were subsequent analyzed by reverse phased liquid chromatography tandem mass spectrometry (RPLC-MSMS) for semi-quantitative confirmation and protein identification. (Leave out experimental details from abstract) Results were analyzed to produce a concise list of 90 differential protein components: 35 decreased and 53 increased after TBI. In addition, we also identified at least 4 proteins that might be subjected to proteolysis. Differential data of the more interesting proteins were confirmed by western blot analysis as potential biochemical markers of TBI. Further, some of the results provide insight into mechanisms brain injury, and provide an avenue into understanding TBI pathology to facilitate therapeutic evaluation by monitoring severity and progression of disease.

MEG in Dyslexia: A Power and Coherence Study

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Magnetoencephalography (MEG) offers high temporal and spatial resolution and has attracted a great deal of interest in neuroscience. The goal of this study is to compare properties of MEG power and coherence between normal and dyslexia readers. Whole head MEG signals were recorded with a NeuroMag VectorView system (306 SQUID detectors) from six right-handed adults and six dyslexic patients performing a non-word rhyme matching task. Power and coherence spectra were calculated by a MultiVariate AutoRegressive (MVAR) modeling approach. We focused on three important language areas: Broca's, Wernicke's, and angular gyrus. Our results showed that mu- and beta-band oscillations are strongest and most coherent in the Wernicke's area. During the prestimulus time interval, mu and beta band synchronized activities in the left lateral frontal cortex are stronger and more coherent in normal readers than in dyslexic reader, whereas dyslexic readers show stronger and more coherent alpha band synchronizations in left occipital cortex. Our findings supported the hypothesis that mu and beta oscillations in lateral frontal cortex are related to high-order sensory signal processing, while alpha band oscillations in occipital cortex may be related to "idling".