Neuromodulation: Technology at the Neural Interface

Syllabus
Pre-Conference Seminar

December 7- 8, 2007
Acapulco, Mexico

– Fundamentals of Neuromodulation
– Basics of Neural Engineering
– Creating a Neuromodulation Startup Company (Non-CME)

ins international neuromodulation society

8th world congress

North American Neuromodulation Society est. 1994

11th annual meeting

A Welcome from the Co-Chairs

Dear Colleagues,

A warm welcome to Acapulco and the Fairmont Princess Hotel, both extraordinary locations for the 8th World Congress of the International Neuromodulation Society, the 11th Annual Meeting of the North American Neuromodulation Society, and our Joint Meeting.

We have chosen the title of this event, "Neuromodulation: Technology at the Neural Interface" because this title defines our field of medical, bioengineering and manufacturing endeavor, the fastest growing field in medicine today. Neuromodulation is defined as technology that modulates the nervous system for improvement of humankind. Medical devices, today, have been engineered and used to improve psychiatric function, movement disorders, epilepsy, chronic pain, cardiac, bowel and bladder function and to improve abilities of patients that have been lost to them from various illnesses and traumas.

Our conference starts off on the 7th of December with a full day seminar, titled "Fundamentals of Neuromodulation", chaired by Joseph Pancrazio, Project Director for the National Institute of Neurologic Disorders and Stroke (NINDS) of the USA's National Institutes of Health (NIH). Dr. Pancrazio has brought together some of the leading experts in the field of the science that is fundamental to the field of neuromodulation.

On the 8th of December, we have two one-half day seminars that continue the theme of fundamentals. Professor Dominique Durand of Case Western University, Editor-in-Chief of Neural Engineering, will present "Understanding Neural Engineering," a course for non-engineers, and Christopher Coburn, Executive Director of Innovations for the Cleveland Clinic, will chair a one-half day seminar, Bringing Neurotech Innovations to Reality, a course on how to bring a neurotech idea to completion. Mr. Coburn has years of experience in the field of creating businesses from innovations and will bring representatives of neuromodulation start-up companies to talk about the process.

Our Conference Scientific Sessions start on the 9th of December and end on the 12th of December. Comprising our scientific program will be CME supported plenary sessions from leading experts in their field, open free paper presentations and CME supported breakout sessions.

Colleagues, as chairpersons, we are proud to bring this event to you. This particular event will for years to come, identify Neuromodulation, Technology at the Neural Interface.

Elliot Krames, MD, Co-chairman and President, International Neuromodulation Society (INS)
Joshua Prager, MD, Co-chairman and President, North American Neuromodulation Society (NANS)

A Welcome from Our Honorary Chairperson

Dear Colleagues,

We welcome you to this Joint Conference of The International Neuromodulation Society (INS) and the North American Neuromodulation Society (NANS) in Acapulco Mexico. These prestigious organizations have put together an ambitious program to update knowledge in the fascinating field of neuromodulation. At present, this is one of the most rapidly developing and promising fields in medicine, and provides different specialists with efficient and still minimally invasive alternatives to treat otherwise hopeless patients. As new indications for neuromodulation have been found over the years, different specialties have been impacted.

Therefore, INS and NANS have recruited a large membership to their mission and vision that includes, cardiovascular surgeons, gastroenterologists, pain doctors, neurosurgeons, pulmonologists, urologists, and more recently, psychiatrists. Also the physiology and mechanisms of action of neuromodulation, have attracted neurologists, neurophysiologist, neurochemists and biomedical engineers to the field. All these professionals will have a forum in the INS-NANS conference which promises to be a great event.

This Conference takes place here in Acapulco, one of the most renown resort towns of the Mexican Pacific coast, and specifically in the Fairmont Princess Hotel, which offers more than any visitor would expect.

I have been kindly invited to act as cochairman for this Meeting, and I can assure you that the traditional Mexican hospitality will accompany you during your visit.

Francisco Velasco, M.D., Honorary Chairperson
"Neuromodulation: Technology at the Neural Interface"

Fundamentals of Neuromodulation

Friday, December 7, 2007

La Princesa Restaurant (12)	7:00 – 7:45	Breakfast
Atlantes Center (I)	7:45 AM – 4:00 PM	Preconference Seminar: Fundamentals of Neuromodulation
	7:45 - 8:00	Welcome Joseph Pancrazio, PhD, Chairman
	08:00 - 08:45	Bioelectrical Basis for Neuromodulation Warren Grill, PhD
	08:45 - 9:30	Design and Implementation of Interfaces for Neuromodulation Dominique Durand, PhD
	09:30 -10:15	Modeling the Effects of Neuromodulation at the Single Cell and Network Levels Cameron McIntyre, PhD
	10:15 -10:30	Break
	10:30 -11:15	Safety of Electrical Stimulation Douglas McCreery, PhD
	11:15 -12:00	Material Compatibility for Neuromodulation Devices Ravi Bellamkonda, PhD
	12:00 -12:45	Surgical Considerations for Neuromodulation Devices Jaimie Henderson, MD
	12:45 - 2:00	Hosted Lunch – Non CME "Neural Engineering Partnerships: Bridging the Clinical and Engineering Divide" Ali Rezai, MD, and Hunter Peckham, PhD
	2:00 - 2:45	Principles of Drug Delivery in the Nervous System Charles Nicholson, PhD
	2:45 - 3:30	Convective Drug Delivery in the Spinal Cord – Implications for Neuromodulation Malisa Sarntinoranont, PhD
	3:30 - 4:00	Research and Funding Opportunities for Neuromodulation Joseph J. Pancrazio, PhD
	4:00 – 4:30	No Host Bar

Basics of Neural Engineering

Saturday, December 8, 2007

LaPosadita Restaurant (18)	7:00 – 7:45	Breakfast
Atlantes Center (I)	7:45 AM – 10:45 AM	Preconference Seminar: Basics of Neural Engineering
	7:45 - 8:00	Welcome Dominique M. Durand, PhD, Chairman
	08:00 - 08:30	Electrophysiological Neuroimaging of Brain Activity Bin He, PhD
	08:30 - 9:00	Interfacing Neurons with Light Karl Deisseroth, PhD
	09:00 -9:30	Useful Signals from Motor Cortex Andrew B. Schwartz, PhD
	9:30 – 9:45	Break
	9:45 – 10:15	Engineering Neural Tissue Ravi V Bellamkonda, PhD
	10:15 – 10:45	Detection, Prediction and Control of Epileptic Seizures Brian Litt, MD
	10:45	Adjourn

Creating a Neuromodulation Startup Company (non-CME)

Saturday, December 8, 2007

Atlantes Center (I)	1:00 – 1:15	Welcome Chris Coburn, Chairman
	1:15 – 1:45	Neuromodulation Market Characteristics and Investment Trends John Bowers
	1:45 – 2:15	Commercialization Pathways Chris Coburn
	2:15 – 2:30	Inventor and Conflict of Interest Issues Ali Rezai, MD
	2:30 – 3:00	Intellectual Property Benjamin Pless
	3:00 – 3:15	Issues Related to Neuromodulation as an Emerging Field Ali Rezai, MD
	3:15 – 3:45	Break
	3:45 – 4:00	Case Studies Northstar – John Bowers NeuroPace – Benjamin Pless Intelect Medical – Ali Rezai, MD
	4:00	Adjourn

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Continuing Medical Education Accreditation

Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and Standards of the Institute for Medical Quality and the California Medical Association (IMQ/CMA) through the joint sponsorship of Starfish Health Partners. Starfish Health Partners is accredited by the IMQ/CMA to provide continuing medical education for physicians.

Starfish Health Partners has applied to the European Accrediting Council for Continuing Medical Education for authorization to offer European physicians CME/CPD. European accreditation has been sought in order to allow participants to validate the credits obtained at this activity in their home European country. EACCME credits are recognized by the American Medical Association towards the Physician's Recognition Award (PRA).

Designation of CME Credit
Starfish Health Partners has designated Fundamentals in Neuromodulation a maximum of 6.75 APA PRA Category 1 Credits. Physicians should only claim credit commensurate with the extent of their participation in this activity.

Starfish Health Partners has designated Basics of Neural Engineering a maximum of 4 APA PRA Category 1 Credits. Physicians should only claim credit commensurate with the extent of their participation in this activity.

Neural Engineering Partnerships: Bridging the Clinical and Engineering Divide is a non-CME lecture (12/7/2007).

Creating a Neuromodulation Startup Company is a non-CME seminar (12/8/2007).

Content Validity
Starfish Health Partners and INS have reviewed this program to ensure it is scientifically-based, accurate, current, objectively presented, and independent of commercial influence; and that all suggestions for patient care are valid, conform to standards of care, and provide benefits that outweigh risks.

Faculty Disclosure
Consistent with the policy of Starfish Health Partners, faculty for this activity will disclose any economic or other personal interests that create, or may be perceived as creating, a bias related to the material presented. Any conflicts of interest determined have been resolved prior to the start of the pre-conference sessions. Faculty will also disclose to you any product mentioned during their presentation that is not labeled for the use under discussion or is still investigational. These policies are intended to allow you to form your own judgments about content presented during this activity.

Faculty Listing

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Saturday December 8, 2007 Basics of Neuromodulation
Saturday December 8, 2007 Creating a Neuromodulation Startup Company

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CME Faculty Disclosures

All faculty invited to participate in this conference completed and signed a policy statement form attesting to their understanding of, and agreement to comply with, the following standards for CME independence and content validity.

Fair Balance
I will prepare a fair and balanced presentation(s) that is objective and scientifically rigorous and will disclose to the audience when I am reporting results of industry-based scientific research.

Best Available Evidence
Recommendations involving clinical medicine in this CME activity will be based on the best available evidence that is accepted within the profession of medicine as adequate justification for their indications, contraindications, and risks in the care of patients.

Sources and Limitations of Data
To the extent practical, recommendations involving clinical medicine in this CME activity will be substantiated by peer-reviewed sources. I will make meaningful disclosure to the attendees if products or procedures I discuss are off-label, unlabeled, experimental, and/or investigational (not FDA approved), and any limitations on the information that I present, such as data that are preliminary or that represent ongoing research, interim analyses, and/or unsupported opinion.

Scientific Integrity
All scientific research referred to, reported or used in support or justification of a patient care recommendation will conform to generally accepted standards of experimental design, data collection and analysis.

Free of Commercial Bias
CME content presented to learners will be free of commercial bias. No product, service, or therapeutic option will be over-represented when comparing competing products, services, and therapeutic options. I will use scientific or generic names as much as possible rather than brand names in my presentation(s). Should it be necessary to use a trade name, then trade names of all similar products or those within a class will also be mentioned. A singular brand name will be used only if the audience is unlikely to recognize the generic name or if the brand is the only one of its kind.

Payments
I have not and will not accept an honorarium, additional payment, or reimbursements except for payments from the International Neuromodulation Society's authorized representatives for my participation in this activity.

The following faculty disclose that neither they, nor their spouse/partner, have any relevant financial relationships with commercial interests whose products or services are in anyway associated with the content of this presentation.

Ravi V. Bellamkonda, PhD
Karl Deisseroth, PhD
Dominique Durand, PhD
Warren M. Grill, PhD
Douglas B. McCreery, PhD
Charles Nicholson, PhD
Joseph J. Pancrazio, PhD
Malisa Sarntinoranont, PhD
Andrew B. Schwartz, PhD

The planners and faculty of Preconference Seminars: Fundamentals of Neuromodulation and Basics of Neural Engineering listed below have disclosed that either they, or their spouse/partner, have a relevant financial relationship with a commercial interest. The relationships were reviewed by INS, Starfish Health Partners and the planning committee, and any conflicts of interest were resolved prior to the activity.

Faculty Name	Speaker Programs	Consultant/ Advisory Board	Investigator (i.e. contracted research grants)	Stockholder	Company Employee
Bin He, MD					Medtronic
Jamie Henderson, MD	Medtronic	Medtronic			
Brian Litt, MD		NeuroVista Corp.		NeuroPace, Inc.	
Cameron McIntyre, PhD		IntElect Medical Advanced Bionics	IntElect Medical	IntElect Medical	

Preconference Seminar: Fundamentals of Neuromodulation
Friday December 7, 2007

Restaurant Princesa
7:00 – 7:45

Breakfast

Atlantes Center (I)
7:45 – 8:00

Welcome

Joseph J Pancrazio, PhD, Chairman
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Email: pancrazj@ninds.nih.gov

Atlantes Center (I)
8:00 – 8:45

Bioelectrical Basis for Neuromodulation

Warren M Grill, PhD
Department of Biomedical Engineering, Duke University
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Outline

I. Introduction

- There exists a sound biophysical basis for electrical neural stimulation
- Empirical observations can be understood using the underlying bio physics
- This understanding provides basis on which to design, implement, and tune therapies

II. Stimulation of Nerve Fibers

- Profile of polarization generated by point source stimulation
- Anodic vs. cathodic stimulation, and the basis for the threshold difference
- Influence if fiber diameter
- Influence of fiber location
- Therapeutic Implications
  - Origin of the Recruitment (input-output) Curve
  - Considerations for the Selection of Stimulus Pulse Duration
  - Regulated Voltage vs. Regulated Current Stimulation

III. Stimulation of Central Neurons

- Profile of polarization generated by point source stimulation
- Anodic vs. cathodic stimulation, and the basis for the threshold difference
  - Stimulation within the brain
  - Stimulation from the surface of the brain
- Therapeutic Implications
  - What elements are excited during CNS stimulation?
  - Direct vs. synaptic effects of stimulation

Atlantes Center (I)

Learning Objectives

Upon completion of this presentation, participants will be able to:
1. Describe the coupling between electric fields and neural stimulation
2. Explain the impact of changes in stimulation parameters
3. List the effects of stimulation waveform

References

Grill, WM (2004) "Electrical Stimulation of the Peripheral Nervous System: Biophysics and Excitation Properties. in Neuroprosthetics: Theory and Practice, KW Horch, G Dhillon, Eds.,, World Scientific Publishing, pp. 319-341.

Grill, WM (2004) "Electrically Excitable Nerve Elements: Excitation Sites in Peripheral and Central Stimulation" in Brain Stimulation and Epilepsy, H Lüders, Ed., Martin Dunitz Publishers, Ltd., London, pp. 55-66.

Grill WM, McIntyre CC (2001) Extracellular excitation of central neurons: Implications for the mechanisms of deep brain stimulation. Thalamus and Related Systems 1(3):269-277.

Gustafsson B, Jankowska E (1976) Direct and indirect activation of nerve cells by electrical pulses applied extracellularly. Journal of Physiology 258(1):33-61.

Kuncel AM, Grill WM (2004) Selection of stimulus parameters for deep brain stimulation. Clinical Neurophysiology 115(11):2431-2441.

McIntyre CC, Grill WM, Sherman DL, Thakor NV (2004) Cellular effects of deep brain stimulation: model-based analysis of activation and inhibition. Journal of Neurophysiology 91:1457–1469.

Ranck JB Jr (1975) Which elements are excited in electrical stimulation of mammalian central nervous system: a review. Brain Research 98(3):417-440.

Acknowledgements

Preparation of this material was supported in part by grant R01 NS40894 from the NIH.

8:45 – 9:30

Design and Implementation of Interfaces for Neuromodulation

Dominique M Durand, PhD
Biomedical Engineering, Case Western Reserve University
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8:45 – 9:30

Abstract

Neural Interfacing is an essential component of an effective neuromodulation system. Significant progress and breakthroughs in interfacing have been made in several areas in the central nervous systems such as the brain machine interface, the retinal prosthesis for blind patients and deep brain stimulation for Parkinson's patients. Progress has also been made in the area of neural interfacing in the peripheral nervous system. By reshaping or maintaining the nerve into an elongated shape, it is possible to place multiple electrodes in the vicinity of a nerve generate selective stimulation, selective recording and fiber diameter selectivity. This design is being applied to the control of femoral nerve for standing and the hypoglossal nerve for obstructive sleep apnea.

Learning Objectives At the completion of this presentation, participants should be able to:

1. Describe the relationship between nerve anatomy and interfacing
2. Discuss the concept of selective stimulation of nerve
3. Examine the possibility of selective recording
4. Apply the concept of neural interfacing to neural prosthetic design

9:30 – 10:15

Modeling the Effects of Neuromodulation at the Single Cell and Network Levels

Cameron McIntyre, PhD
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Abstract

Deep brain stimulation (DBS) is an effective clinical treatment for several medically refractory neurological disorders. However, the clinical successes of DBS are tempered by our limited understanding of the effects of the stimulation on the nervous system, and scientific definition of the therapeutic mechanisms of DBS remains elusive. In addition, it is presently unclear what electrode designs and stimulation parameters are optimal for maximum therapeutic benefit and minimal side effects. This presentation will describe our attempts to integrate neuroanatomical, neurophysiological, and electrical data to create a computational framework that enhances our understanding of the effects of DBS and provides a virtual testing ground for new stimulation paradigms.

Learning Objectives At the completion of this presentation, participants should be able to:

1. Quantify the electric field generated by deep brain stimulation
2. Characterize the neural activation that occurs as a direct result of applied electric fields

3. Simulate the response of stimulation induced activity in large scale neural networks
4. Identify techniques to experimentally validate detailed theoretical models of neuromodulation

10:15 – 10:30

Break

10:30 – 11:15

Safety of Electrical Stimulation

Douglas B McCreery, PhD
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Abstract

Electrical stimulation (ES) is an effective means of activating or otherwise modulating the activity of neurons and axons in the central and peripheral nervous system. However, ES does convey a risk of injury to the neurons and axons, and also may induce reversible but long-lasting changes in the electrical excitability of the neural elements. The neuronal injury and/or persisting depression of neuronal excitability may be caused by toxic products produced during the charge injection process, and/or by the physiological stresses associated with prolonged excitation of individual neurons and populations of neurons. An understanding of these physiological and electrochemical mechanisms is essential to the design of neural implants, and for the development of safe and effective stimulation protocols.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Identify the potential risks associated with neurostimulation and understand the concept of the "therapeutic window" for safe and effective electrical neurostimulation and neuromodulation.
2. Identify the electrochemical and physiological mechanisms that un derlie stimulation-induced tissue injury.
3. Appreciate the distinction between "electrochemically prudent" and "functionally safe" electrical stimulation of neural tissue.
4. Identify procedures for designing protocols for electrical stimulation that will minimize the risk of tissue injury.
5. Describe the problems (and also the potential benefits) associated with stimulation protocols that induced prolonged changes in neuronal excitability.

11:15 – 12:00

Material Compatibility for Neuromodulation Devices

Ravi V Bellamkonda, PhD
Georgia Institute of Technology/Emory University
Neurological Biomaterials and Therapeutics Department of Biomedical Engineering
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Wallace H Coulter and George McConnell, MS contributed significantly to this presentation.

Abstract

Focal neuromodulation made possible by implanted devices has the potential to address several pathologies of the nervous system. However, implanted devices cause injury akin to a small and controlled stab wound. In this talk, the precise meaning of 'biocompatibility' as it applies to implanted medical devices will be examined. The difference in tissue reaction between an implant that remains in the brain chronically Vs. one that is removed immediately after implantation will be examined using a rat model of electrode implantation. The paradox of how an implanted electrode might be 'compatible' for neuro-stimulation but not compatible for neuro-recording will be examined. The spatio-temporal response of microglia, astrocytes and extracellular matrix moieties such as chondroitin sulfate proteoglycans will be presented after implantation of neuromodulatory devices in rat models. Also examined will be the molecular basis of tissue reaction and the potential ways to modulate tissue reaction to implanted electrodes either due to mechanical properties of implanted devices, or by modulating the susceptibility of neural tissue to local inflammation from implanted devices. Lastly, the particular conditions for 'biocompatibility' of implanted chronic recording electrodes such that they remain functional will be examined.

Learning Objectives

1. Define 'biocompatibility' from the perspective of implanted, neuro modulatory devices.
2. Describe the relationship between acute and chronically implanted neuromodulatory devices and resultant tissue reaction in the brain
3. Explain the implications of tissue reaction to 'recording' Vs. 'stimula tion' applications of neuromodulatory devices
4. Summarize materials based strategies to modulate the local tissue response to implanted neuromodulatory devices.

12:00 – 12:45

Surgical Considerations for Neuromodulation Devices

Jaimie M Henderson, MD
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Abstract

The use of surgically implanted devices to modulate the function of the nervous system is expanding rapidly. Implantable drug delivery systems and electrical stimulators have been used since the mid-20th century to treat pain, spasticity, and movement disorders. With the advent of new technologies such as multi-channel neuronal ensemble recording, optical stimulation, and "smart" systems incorporating real-time feedback, surgical considerations for safe and accurate delivery have taken on increasing importance. An overview of state-of-the-art surgical techniques for neuromodulation will be presented, including both current and future innovations. The important interface between clinicians and engineers will be discussed, with emphasis on designing devices which will minimize surgical complexity and maximize safety and efficacy.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Describe state-of-the-art techniques for implantation of neuro modulatory devices
2. Analyze the strengths and weaknesses of current surgical approaches
3. Discuss design considerations for new devices from the standpoint of surgical ease and safety

12:45 – 2:00

Hosted Lunch (Non-CME)

Neural Engineering Partnerships: Bridging the Clinical and Engineering Divide

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2:00 – 2:45

Principles of Drug Delivery in the Nervous System

Charles Nicholson, PhD
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Abstract

This presentation will focus on the routes and impediments to drug delivery in the central nervous system (CNS). The talk will emphasize the role of the blood-brain barrier as an impediment to drug delivery, means of circumventing this to varying degrees and the subsequent transport of drugs in the CNS. Diffusion plays a major role in this transport along with the geometry of the extracellular space and the binding properties of the extracellular matrix and other drug-specific sites. The influence of the size of the drug vector will be discussed and the potential utility of modeling.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Describe the major routes for drug administration in the CNS
2. Following the talk participants will be able to describe the fundamental role of diffusion in drug transport within the CNS
3. Following the talk participants will be able to describe how different classes of drug vector interact with extracellular geometry and binding sites.

2:45 –3:30

Convective Drug Delivery in the Spinal Cord – Implications for Neuromodulation

Malisa Sarntinoranont, PhD
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Abstract

With the development of promising therapeutic agents for chronic pain, spinal injury, and other neurodegenerative diseases, local drug delivery methods are increasingly being considered as a solution to overcoming transport barriers encountered by macromolecular, slow-diffusing drugs. For example, convection-enhanced delivery (CED) relies on infusion-driven flow to transport drugs significant distances through the extracellular space. Design of such regional therapies will require new tools to evaluate drug transport issues specific to nervous tissue physiology. Medical image-based *computational* models of tissue transport may be used to determine the influence of anatomical boundaires, tissue structure, interstitial (extracellular) fluid flow, and diffusive transport in white and gray matter regions. For example, a novel application of *diffusion tensor imaging* (DTI) technology predicts preferential flow and transport directions along white matter tracts.

Models that predict the local tissue distribution of an injected macromolecular tracers in the spinal cord will be presented. Successful physiologically-based tracer transport models may be used for feasibility studies and improved infusion protocols. Ultimately, image-based transport modeling provides an important step toward computer-aided chemical surgery and patient-specific therapeutic treatment.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Identify the advantages of local delivery methods such as CED
2. Discuss the use of DTI in computational models.
3. Differentiate convective (bulk flow) transport from diffusional transport.
4. Understand the influence of hydraulic conductivity on extracellular transport.

3:30 – 4:00

Research and Funding Opportunities for Neuromodulation

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National Institute of Neurological Disorders and Stroke, Specialty Biomedical Engineering
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Abstract

The National Institute of Neurological Disorders and Stroke (NINDS) has the mission to relieve the burden of neurological disease. Devices enabling neuromodulation have been a vital and productive component of the NINDS mission. For over 30 years, the NINDS has supported grants and contracts on a number of areas within the neuromodulation including: neural prosthesis, deep brain stimulation, biocompatibility of neural interfaces, and brain/computer interfaces. NINDS is particularly interested in seeing the resulting technologies reach translation to the clinical. To this end, the NINDS supports not only academic efforts, but those of the private sector as well. This presentation will describe various funding mechanisms used to support basic, applied, and clinical efforts for neuromodulation research. Features of successful teaming relationships will be identified with an emphasis on multidisciplinary research. Participants will be provided with a description of web-based tools and approaches for evaluating the scientific opportunities in neuromodulation. Potential emergent areas that are likely to impact the future of neuromodulation, such as nanotechnology and computational methods, will be presented and discussed.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Recognize the research and development topics that various NIH Institutes emphasize for neuromodulation
2. List funding mechanisms available for supporting research and development projects in neuromodulation through the National Institutes of Neurological Disorders and Stroke
3. Choose teaming relationships most effective in advancing interdisciplinary research.
4. Apply tools and approaches to identify scientific gaps in NIH support for neuromodulation research and development
5. Describe emergent research and development opportunities for neuromodulation

4:00 – 5:00 **No Host Bar**

Preconference Seminar: Basics of Neural Engineering
Saturday December 8, 2007

Restaurant Posadita
7:00 – 7:45

Breakfast

Atlantes Center (I)
7:45 – 8:00

Welcome

Dominique M. Durand, PhD, Chairman
Biomedical Engineering, Case Western Reserve University
Cleveland, Ohio USA
Email: dxd6@case.edu

8:00 – 8:30

Electrophysiological Neuroimaging of Brain Activity

Bin He, PhD, IEEE Fellow, AIMBE Fellow
Professor and Interim Director
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Abstract

It is of great importance to image brain activity with high resolution in both the space and time domain. We will discuss the approach of electrophysiological neuroimaging aimed at developing a high-resolution spatio-temporal imaging modality for brain research and aiding clinical applications. Electrophysiological neuroimaging reconstructs brain activity from non-invasively measured EEG. We demonstrate that electrophysiological neuroimaging can provide significantly enhanced spatial resolution as compared with scalp EEG. Brain electrical activity is represented by distributed surface or volume sources and reconstructed from EEG measurements by solving the inverse imaging problem. Examples will be provided for locating epileptogenic foci with potential applications to surgical planning in epilepsy patients. The electrophysiological neuroimaging techniques may have wide applications in neuron-modulation.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Discuss concept of EEG source imaging
2. Acquire an understanding of the basics of EEG forward and inverse problem
3. Contrast the ability and limitation of EEG source imaging

8:30 – 9:00

Interfacing Neurons with Light

Karl Deisseroth, PhD
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Abstract

Neuropsychiatric disorders arise from a combination of genetic, epigenetic and environmental influences that affect specific cell types within the brain. Elucidation and treatment of these diseases will benefit from understanding how specific brain cell types are interconnected and signal in neural circuits. New neuroengineering tools we have developed based on two microbial opsins, channelrhodopsin-2 (ChR2) and halorhodopsin (NpHR), enable the investigation of neural circuit function with cell-type-specific, temporally accurate and reversible neuromodulation using light. In combination with fast circuit imaging and behavior, these tools could lead to the development of precise neuromodulation technologies for animal models of disease and clinical neuropsychiatry.

Learning Objectives

1. Discussthe importance of cell type targeting in studying disease
2. Explain how new optical technology in prinicple can solve the problem of cell type targeting
3. Describe the recent advances in applying these optical technologies in disease models.

9:00 – 9:30

Useful Signals from Motor Cortex

Andrew B. Schwartz, PhD
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Abstract

Over the years, we have shown that detailed predictive information of the arm's trajectory can be extracted from populations of single unit recordings from motor cortex. Using drawing movements as a behavioral paradigm, these signals have been shown to contain instantaneous velocity information and many of the invariants describing animate movement. Furthermore, this technique can be used to study visuo-perceptual processes taking place as objects are drawn. By developing techniques to record these populations and process the signal in real-time, we have been successful in demonstrating the efficacy of these recordings as a control signal for intended movements in 3D space. Having shown that closed-loop control of a cortical prosthesis can produce very good brain-controlled movements in virtual reality, we have been extending this work to robot control.

We are using an anthropomorphic robot arm with our closed-loop system to show how monkeys can control the robot's movement with direct brain-control in a self-feeding task. The animals control the arm continuously in 3D space to reach out to the food and retrieve it to their mouths. Since the recorded signals are a high fidelity representation of the intended behavior and contain features of animate movement, neural prosthetic devices derived from this technology are capable of producing agile, natural movement.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Motor cortex neurons encode direction of hand movement
2. Populations of many cells are active simultaneously
3. Information from the population can be used to generate skilled arm movement

9:30 – 9:45 **Break**

9:45 – 10:15 **Engineering Neural Tissue**

Ravi V Bellamkonda, PhD
Department of Biomedical Engineering, Georgia Institute of Technology
Atlanta, Georgia, USA
Email: ravi@gatech.edu

Young-tae Kim and Wallace H Coulter contributed significantly to this presentation.

Abstract

Axonal pathways may be disrupted in the peripheral or central nervous system due to trauma. In the first half of the presentation, strategies to 'engineer' the regeneration of peripheral nerves, either with 3D hyrogels, or with oriented nanofibers will be presented. The critical design factors that govern 'optimal' peripheral nerve bridge design will be examined, and the current state of the art in research will be compared to autografting or to nerve guidance channel (entubulation). In particular concepts of 2D Vs. 3D scaffolds the implications of scaffold design for peripheral nerve regeneration will be examined. In particular, the critical role of Schwann cell migration and differentiation in peripheral nerve regeneration will be examined.

In the CNS, the thesis that a multi-factor approach that modulates the spatio-temporal course of post injury response to the spinal cord in a manner that is beneficial will be examined. The critical cellular and molecular impediments to regeneration in the CNS will be presented. In particular the effect of local delivery of anti-inflammatory agents will be compared to systemic delivery to investigate if any specific advantages exist with local drug delivery after spinal cord injury. A novel in situ geling hydrogel-nanoparticle system to modulate the tissue response immediately after spinal cord injury will be presented.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Explain what is meant by 'Neural Tissue Engineering'
2. Describe the strategies by which regeneration of peripheral nerves can be attained
3. Design criteria for 3d peripheral nerve 'bridges' will be presented.
4. List the differences in the critical design of engineering interventions between the PNS and CNS
5. Examine potential role of nanotechnology for peripheral and central nerve regeneration

10:15 – 10:45

Detection, Prediction and Control of Epileptic Seizures

Brian Litt, MD
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Abstract

Spurred on by the success of similar devices to treat cardiac arrhythmias, there has been tremendous interest in devices to detect, predict and control epileptic seizures. Approaches range from open loop devices that stimulate in regular duty cycles, independent of cerebral activity, to closed-loop, feedback-control systems that interpret the intracranial EEG "on the fly." Different methods for detecting seizures are being employed to control these closed loop systems, though more promise may rest in understanding seizure generation and identifying periods of increased periods of seizure onset. New understanding of the networks involved in seizure generation, particularly at high spatial and temporal resolutions, may hold the key to the success of antiepileptic devices.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Convey the spatial and temporal complexity of seizure generation in epileptic networks on multiple scales
2. Explain the different systems currently being considered for antiepileptic devices, and how targets for intervention are picked
3. Consider other solutions not currently embodied in antiepileptic devices
4. Relate developments in this area to Translational Neuroengineering, and similar devices under development for other neurological conditions.

12:00 - 1:00

Lunch

Preconference Seminar: Creating a Neuromodulation Startup Company
Friday December 8, 2007

Atlantes Center (I) 1:00 – 1:15	**Welcome** Chris Coburn, Chairman CCF Innovations, Executive Director Cleveland Clinic
1:15 – 1:45	**Neuromodulation Market Characteristics and Investment Trends** John Bowers Northstar Neuroscience Seattle, Washington USA Email: jbowers@northstarneuro.com
1:45 – 2:15	**Commercialization Pathways** Chris Coburn Cleveland Clinic CCF Innovations Cleveland, Ohio USA Email: coburnc@ccf.org
2:15 – 2:30	**Inventor and Conflict of Interest Issues** Ali Rezai, MD Cleveland Clinic, Center for Neurological Restoration Cleveland, Ohio USA Email: REZAIA@ccf.org
2:30 – 3:00	**Intellectual Property** Benjamin Pless Tracks Design Lab Email: bpless_tdl@earthlink.net
3:00 – 3:15	**Issues Related to Neuromodulation as an Emerging Field** Ali Rezai, MD Cleveland Clinic, Center for Neurological Restoration Cleveland, Ohio USA Email: REZAIA@ccf.org
3:15 – 3:45	Break
3:45 – 5:00	Case Studies Northstar – John Bowers NeuroPace – Benjamin Pless Intelect Medical – Ali Rezai, MD
5:00	Adjourn