Symposium on Emerging Topics in Control and Modeling: Biomedical Systems
Interactive Session Abstracts

Title: A hidden Markov model and analytic spatial filter for enhanced information transfer rates in EEG-based brain-computer interfaces

Authors: Martin McCormick, Rui Ma, Todd Coleman

Institution: The University of Illinois at Urbana-Champaign – Electrical and Computer Engineering

Abstract:

Brain computer interfaces (BCI) enable humans to control external devices with thoughts instead of physical movements. This allows the paralyzed to direct wheel chairs or spell sentences on a computer and soldiers to control unmanned aircraft with their imagination.This technology relies upon accurate and real-time analysis of biological signals. Recordings of weak voltages on the scalp (EEG) are relatively easy to obtain but pose challenges for robust estimation. In this study, we consider EEG signals recorded during Motor Imagery (MI) –in which the subjects reveals their intents by imagining left hand movement or right hand movement. The computer can then determine which hand the human is imagining by detecting event related de-synchronization (ERD) from reconstructed source regions in the brain. This information channel can be used to convey binary commands for complex tasks.

Title: A Portable-Powered Ankle-Foot Orthosis for rehabilitation

Authors: Alex Shorter

Institution: The University of Illinois at Urbana-Champaign - MechSE

Abstract:

Introduction: Innovative technological advancements in the field of orthotics, such as portable-powered orthotic systems, could create new treatment modalities to improve the functional outcome of rehabilitation. An ankle-foot orthosis (AFO) is used to ameliorate the impact of lower-limb neuromuscular impairments on gait. In this paper, we present a novel portable-powered AFO (PPAFO) to provide un-tethered assistance for daily at-home rehabilitation treatment.

Methods: The PPAFO provides both plantarflexor and dorsiflexor torque assistance via a bi-directional pneumatic rotary actuator. The system uses a portable pneumatic power source (compressed CO_2 bottle) and embedded electronics to control the actuation of the foot. Experimental data from one impaired and three healthy subjects were collected to demonstrate design functionality. The impaired subject had bilateral impairment of the lower legs due to cauda equina syndrome .

Results: Data from healthy walkers demonstrated that the PPAFO was capable of providing correctly timed plantarflexor and dorsiflexor assistance during gait. Healthy EMG data showed a reduction in tibialis anterior activation during stance and swing indicating functional dorsiflexor assistance. Additionally, the vertical ground reaction force data from the impaired walker demonstrated that the PPAFO was capable of provided functional plantarflexor assistance.

Conclusion: The PPAFO opens opportunities for new orthotic and clinical treatment strategies.

Title: A Universal Computational Method for Pulse Sequence Design

Authors: Justin Ruths

Institution: Washington University in St. Louis – Electrical and Systems Engineering

Abstract:

The design of innovative pulse sequences has dramatic effects on the capabilities of medical imaging. Specially designed sequences can, for example, create medical images with higher resolution, highlight binding agents targeting tumor growth, and provide methods to measure heart muscle cell metabolism. As challenging applications arise, researchers and clinicians alike seek dependable ways to developing the solutions to these pulse design problems, which can be cast as optimal control problems. We introduce a flexible numerical method based on ideas from pseudospectral approximations that transform the continuous optimal control problem to a constrained minimization problem. Orthogonal polynomial approximation yields fast convergence rates and low amounts of necessary discretization, which in turn yields less computational time. In addition, the method, especially when compared to the often used gradient method, is easily adaptable to new problems without the need to perform offline calculations and the polynomial approximation techniques inherently find smooth solutions that are easily and accurately implemented on experimental equipment. We present compelling simulations and experimental results from several areas of pulse sequence design to motivate the universal quality of the method.

Title: Adaptive Model Predictive Control of Human Promyelocytic Leukemia Cell Differentiation

Authors: Sarah Noble

Institution: Purdue University – School of Electrical and Computer Engineering

Abstract:

Cellular differentiation is a complex process largely studied experimentally. Over the past several decades mathematical models for this process have been generated, and increasingly these models are being employed to design experiments that predictably direct cell fate. This work generates and evaluates a control strategy for sustaining a desired constant level of differentiated human promyelocytic leukemia (HL60) cells. Nonlinear model predictive control is applied using a model of HL60 cell differentiation which reflects the dominant observable cell states along the known granulocyte/monocyte differentiation pathway. The experimental realization of the controller successfully achieved the target differentiation level to within ± 5%. In an effort to improve the controller's accuracy, the inherent heterogeneity of the cell population (which evokes the classical plant-model mismatch problem) must be addressed. This is done through an adaptive model predictive control strategy that performs an online adaptive identification of experiment-specific parameters from recurrent cell population measurements. Simulated experiments demonstrate that even with typical sparse and noisy experimental data, the model parameter uncertainties are sufficiently constrained to reduce the plant-model mismatch and more accurately achieve the control objective. The efficacy of this adaptive model predictive control process is currently being evaluated through laboratory experiments with HL60 cells.

Title: Anatomical Landmark Based Analysis of the Corpus Callosum Abnormalities in Essential Autism

Authors: Qing He

Institution: University of Missouri – Computer Science

Abstract:

Autism is a severe developmental disorder whose neurological basis is largely unknown. Autism is a subtype of autism that displays more homogeneous features within group. The aim of this study was to identify the shape differences of the corpus callosum between patients with autism and the controls. Anatomical landmarks were collected from mid-sagittal MRI of 25 patients and 18 controls. Euclidean distance matrix analysis and thin-plate spline were used to analyze the landmark forms. Point-by-point shape comparison was performed both globally and locally. A new local shape comparison scheme was proposed which compared each part of the shape in its local coordinate system. Point correspondence was established among individual shapes based on the inherent landmark correspondence. No significant difference was found in the landmark form between patients and controls, but the distance between interior genu and posterior most was found significantly shorter in patients. Thin-plate spline analysis showed significant group difference between the landmark configurations in terms of the deformation from the overall mean configuration. Significant global shape differences were found in the anterior lower body and posterior bottom, and local shape difference existed in the anterior bottom. This study can serve as both clinical reference and a detailed procedure guideline for similar studies in the future.

Title: Assessing spatiotemporally complex and coupled gait patterns using temporal cross-correlation

Authors: Kiwon Park

Institution: University of Illinois at Urbana-Champaign – Mechanical Science and Engineering

Abstract:

The spatiotemporal joint coupling patterns during gait are closely associated with musculoskeletal injury mechanics, but previous tools used to examine human gait have mainly focused on univariate measures. These tools are unable to capture the complex nature of human movement or assess correlated patterns of joint or segmental movement patterns within and between human limbs. The goal of this study was to characterize different gait behaviors (unbraced, knee braced, and ankle braced) by using cross-correlation technique to investigate spatiotemporally complex and coupled joint parameters in gait. Bracing simulated knee or ankle injuries by restricting joint range of motion. To highlight significant differences in spatiotemporally complex and coupled gait behaviors between different gait conditions, this technique was applied to the angular displacement and velocity histories across twelve lower extremity variables. This work investigated the nature of joint variable coupling for different simulated injured gait conditions. Statistical analyses of the results of a temporal cross-correlation technique were applied to characterize significant changes in the relative timing and magnitude of angular displacement and velocity profiles. More importantly, the signature diagram captured significant spatiotemporal changes and couplings not only of entries involving the affected right knee or ankle parameters, but among other joint variables.

Title: Automatic Recognition of Apoptosis in Cancer Cell Images

Authors: Liu Hailing

Institution: Chosun University – Information and Communication Engineering

Abstract:

The process of programmed cell death or apoptosis, characterized by distinct morphological characteristics and energy-dependent biochemical mechanisms, is considered a vital component of various processes including normal cell turnover, proper development and functioning of the immune system, embryonic development and chemical-induced cell death. Nowadays quantification of apoptosis in vivo or apoptosis recognition and counting are generally carried out manually which can be labor-intensive, time-consuming, and error-prone. In our poster we described the method and also demenstrate the experiment results of a software package to accomplish the automatic recognition and counting of apoptosis according to their distinct physical and morphological features. Our results show that the software can obtain a very high recognition rate and can help biomedical scientists to get the precise number of apoptosis in their biomedical experiments.

Title: Brat-mediated bi-stability and cell-competition autoregulate stem cell number in the Drosophila germarium

Authors: Michael Pargett

Institution: Purdue University – Biomedical Engineering

Abstract:

Complex organisms must maintain stable populations of stem cells to remain healthy and support somatic tissues. In the germline stem cells (GSC) of the Drosophila ovary, Bone Morphogenetic Protein (BMP) signaling regulates the decision between stem cell self renewal or differentiation. Our collaborators have elucidated key players in the intracellular network that regulates cell-receptivity to extracellular BMPs, however the interaction between the intra- and extracellular regulation of BMP distributions and interpretations remains unknown. To determine the relative contribution of intra- and extracellular control of BMP regulation we developed a local model for a single cell receiving an extracellular cue and a 3D extracellular model of the germarium. The proposed intracellular feedback mechanism exhibits bistabilty in response to levels of BMP signaling, making cells refractory to additional signal. By combining intracellular and extracellular regulation in the 3D multi-cell model, we find that cell-mediated competition for limiting amounts of ligand leads to autoregulation of stem cell number in the niche. Competition, combined with the bistable intracellular system controls the maintenance of the constrained stem cell population, causing differentiation of extraneous GSCs and repopulating if GSCs are lost.

Title: Compensating Input Delay and Muscle Fatigue during Neuromuscular Electrical Stimulation Control

Authors: Nitin Sharma

Institution: University of Florida - Mechanical and Aerospace Engineering

Abstract:

Neuromuscular electrical stimulation (NMES) is the application of a potential field across a muscle via internally or externally placed electrodes in order to produce a desired muscle contraction. It is a promising technique that has the potential to restore functional tasks in persons with movement disorders.

A pervasive problem with current NMES technology is the rapid onset of the unavoidable muscle fatigue during NMES. In closed-loop NMES control, disturbances such as muscle fatigue are often tackled through high-gain feedback which can over stimulate the muscle which further intensifies the fatigue onset. A neural network-based NMES controller is developed that incorporates the effects of muscle fatigue through an uncertain function of the calcium dynamics. The developed controller is proven to yield uniformly ultimately bounded (UUB) stability for an uncertain nonlinear muscle model in the presence of bounded nonlinear disturbances.

Another impediment in NMES control is the presence of input or actuator delay. Control of nonlinear systems with actuator delay is a challenging problem because of the need to develop some form of prediction of the nonlinear dynamics. The problem becomes more difficult for systems with uncertain dynamics and bounded disturbances. Motivated to address the input delay problem in NMES control, a predictor-like method is developed to address the time delay in the control input. A Lyapunov-Krasovskii functional is used within a Lyapunov-based stability analysis to prove semi-global UUB tracking.

Title: Constrained Kalman Filtering for IMRT Planning

Authors: Isuru Dasanayake

Institution: Washington University in St. Louis - Department of Electrical & Systems Engineering

Abstract:

We develop a new optimization algorithm for Intensity Modulated Radiation Therapy (IMRT) planning using a dynamical systems approach. In IMRT, radiation beams are optimized to deliver highly localized 3D conformal radiation dosage to a targeted tumor while avoiding surrounding critical structures, then the optimized dose delivered in several steps (treatment fractions) to achieve the prescribed dosage. Modeling and optimizing an IMRT plan is a challenging task since tumors can change in size, shape, and position during the course of fractionated treatment. Accordingly, re-optimization of radiation beam weights is generally needed for each treatment fraction, which is computationally expensive and practically inefficient. We establish a recursive algorithm, which is based on the development of a constrained Kalman filter, to develop a complete treatment plan that takes changes in the tumor geometry into account.

Title: Contribution of passive properties of muscle-tendon units to the metacarpophalangeal joint torque of the index finger

Authors: Pei-Hsin Kuo

Institution: University of Maine – Mechanical Engineering

Abstract:

Purpose: Muscles and soft tissues across the index finger MCP joint are addressed to dominate the passive net joint torque. The purpose of the study was to investigate the contribution of MTUs to the passive net torque of the index finger MCP joint in flexion and extension.

Method: The seven Hill-type model was built to investigate the MTUs torques. The MCP joint was simulated moving passively from neutral position (50 degree) to full extension (100 degree) and full flexion (-70 degree). The study adopted the moment arms from the ACT`hand to calculate the muscle length change and MTUs torques. Net MTU contribution was investigated based upon the net joint torque from subject results.

Results and Discussion: The results showed that the MTUs did not provide most contribution for the MCP joint (<50%). This meant that the soft tissues might provide larger contribution to the passive property at the ends of ROM of the MCP joint. The extrinsic flexors and extensors provided most of the passive contributions to the net MTU torque although the intrinsic MTUs demonstrated small counterbalance to the net MTU torque in extension. The study separated the musculotendons and soft tissues explicitly and enabled to investigate the passive behaviors of the extrinsics and intrinsics.

Title: Electromyographic analysis of the pelvic limb muscles of healthy Labrador Retrievers

Authors: Mei Kuen Hsu, Chantal Ragetly

Institution: University of Illinois at Urbana-Champaign – Mechanical Engineering

Abstract:

Electromyography (EMG) allows for detection and quantification of the muscular activity and is commonly used in human movement studies. Yet in veterinary literature, there is a paucity of work characterizing muscular activation patterns in canine limbs during gait. Our goal is to quantify the duration of muscle activation, ratio of activated/resting muscle duration and determine the timing of muscle activation during a gait cycle.

Twelve healthy adult Labrador Retrievers were tested with surface EMG (sEMG) electrodes attached bilaterally over the quadriceps, hamstring and gastronemius muscle groups. The EMG resting potential were recorded at standing, left and right lateral recumbencies. The tested subjects trotted on a dual-belt treadmill at 2m/s. The EMG signals were synchronized with force data . The EMG signals were rectified and filtered with 4th order butterworth filter at cutoff frequency of 18Hz before analysis. The average value of 4 gait cycles of the right hind leg was analyzed.

These data will be used to establish reference normal EMG pattern in dogs that could be used to detect abnormal muscle activities in future studies.

Title: Encoding and Decoding Finger and Wrist Movements from M1 Neurons in 1 Primate using Point Process Models

Authors: Liang-hui Chu

Institution: The Johns Hopkins University – Institute of Computational Medicine, Dept. of Biomedical Engineering

Abstract:

In this poster, we first present preliminary results on the finger and wrist movement information encoded in individual cortical neurons. The dynamics or cortical neuronal activity are characterized using point process models (PPMs) estimated from single-unit recordings recorded sequentially from a population of 115 neurons in the M1 hand area of one trained rhesus monkey during flexion and extension movements of each finger and the wrist. The PPMs showed significant differences in temporal dynamics of spiking activity during movement for different neurons and different movement types. We then used the PPMs to develop a decoding algorithm, for which we used different ensembles (different numbers of neurons in each ensemble) of the 115 neurons to decode each test trial, assuming that movement onset has been detected (synchronous decoding). Average decoding accuracies were as high as 100%. Future work entails employing asynchronous decoding using PPMs, which would take an important step towards the development of a brain machine interface for direct neural control of a state-of-the-art, multi fingered hand prosthesis.

Title: Evolutionary Game Theoretical Approach for Controlled Drug Delivery: Theory and Experimental Results

Authors: Jing Wu

Institution: The University of Tennessee - Department of Mechanical, Aerospace and Biomedical Engineering

Abstract:

In this study, we show how evolutionary game theory can be embedded into a traditional optimal control framework in order to predict strategies for time-dependent drug dosages in the context of a growing pathogen population that exhibits the capacity to evolve in direct response to the level of applied drug. To illustrate our method for integrating evolutionary games with optimal control systems, we consider a simplified model that describes a generic trade-off between viral replication rate and drug resistance. Experiments on in vitro *Giardia lamblia* drug delivery were done to verify the theoretical prediction. The technique that we outline, however, is readily extendable to more complicated models that account, in more detail, for the specific biology of a particular pathogen of interest.

Title: Image Driven Modeling of Neuromuscular Control of Speech

Authors: Thomas Paine

Institution: University of Illinois at Urbana-Champaign - Bioengineering

Abstract:

Speech is a complex product of the neuromuscular system. Our goal is to develop a neuromuscular control model of speech using MRI derived physiological measurements. Key to developing such a model is assuring that neural inputs are paired with their resulting speech articulator response. For this purpose we have designed a multimodal MRI acquisition that captures simultaneous images of brain function and dynamic muscle movement. Functional images are acquired with timing typical of fMRI experiments, approximately 1 brain volume per second. The dynamic portion provides 14 fps video of mid-sagittal articulator movement. To our knowledge, this is the first time dynamic images of articulation have been captured during functional neuro-imaging, providing an exciting opportunity to examine neural control of speech.

The neural representation of speech production has previously been modeled as a complex system involving feed-forward motor commands, as well as acoustic and articulator feedback. These models do not account for the physiology of the neuro-motor control system. By extending such models to include patient physiology, metrics for healthy speech production can be developed along with quantitative determination of differences found in normal aging and impairments such as traumatic brain injury and stroke.

Title: Integrative systems modeling identifies novel drug targets for Tuberculosis

Authors: Sriram Chandrasekaran and Nathan D. Price

Institution: The University of Illinois at Urbana-Champaign - Biophysics

Abstract:

Systems biology seeks to understand the cell by studying interactions between its various components and the properties that emerge from these interaction networks. The integration of these diverse network types would enable us to better predict how genetic mutations and transcriptional perturbations are translated into metabolic changes, and has several important applications including diagnosing metabolic disorders and discovering novel drug targets. We have developed a new method called Probabilistic Regulation of Metabolism (PROM) which achieves this synthesis by integrating the transcriptome and metabolome for use in constraint based modeling. The PROM approach is an amalgam of modeling tools like Probabilistic Boolean Networks for modeling transcriptional regulation and Constraint - based analysis and optimization for modeling metabolism.

Tuberculosis is a major cause of death in the third world, yet much remains to be learned about this pathogen especially with respect to its regulatory and metabolic networks. We applied our method to build the first genome-scale integrated metabolic–regulatory model for *Mycobacterium tuberculosis (M.tb)*, a critically important human pathogen. This systems-level analysis incorporates data from over 1500 microarrays, 2000 transcription factor–target interactions regulating 3300 metabolic reactions, and 2150 knockout phenotypes for E.coli and M.tb. By reconstructing and modeling the M.tb network, we show that PROM can make accurate predictions of cellular phenotype, identify functions of less studied regulatory genes and discover transcriptional hubs that control cellular metabolism. Importantly, identifying such key genes that control vital steps in metabolism could help us predict better drug targets for therapy.

Title: Inverse dynamics gait analysis of the pelvic limbs of healthy Labrador Retrievers

Authors: L. Michaela Klump, Chantal Ragetly and Elizabeth Hsiao-Wecksler

Institution: University of Illinois at Urbana-Champaign – General Engineering

Abstract:

Most canine gait analysis studies have been performed while walking overground; however, the use of instrumented treadmills is becoming more common in humans. The objective was to compare the movement and forces around the hind limb joints during treadmill and overground trotting trials.

Twenty healthy Labrador Retrievers trotted overground across an embedded force plate and over a split-belt treadmill with force plates. Skin motion markers identified thigh, shank, and foot. Kinetic and kinematic data were computed.

Differing amplitudes in kinematic parameters were apparent between overground and treadmill trials. The hock (ankle) and stifle (knee) reaction forces in the horizontal direction during breaking were greater for treadmill trials. The stance time was shorter for treadmill trials. Hock velocity during flexion and extension, stifle velocity during flexion, stifle flexor and hip extensor moments, power generation and absorption around the hock, and power generation around the stifle were greater compared to overground trials.

On the treadmill, dogs moved their hock and stifle joints faster to unload their limb faster. This lead to larger energy generation and absorption around these joints.

This study highlighted the differences in canine overground and treadmill gait, which may be due to real difference between overground and treadmill gait or an inadequate habituation to treadmill trotting.

Title: L1 Adaptive Methods for Control of Patient Response to Anesthesia

Authors: Matthew Ralph

Institution: The University of Illinois at Urbana-Champaign - Industrial & Enterprise Systems Engineering

Abstract:

We examine the application of recently developed L_1-adaptive control methods for the closed-loop control of anesthesia delivery during surgery. Our objective is to design controllers that are robust to inter-patient variability, such that patients follow a pre-specified Bispectral Index profile. The controllers are designed using identification-based models constructed using clinical trial data. We examine four different identified patient models, design L_1-adaptive controllers for each, and apply them to all four patients. Examples of the closed-loop system performance are given and evaluated based on tracking error and amount of anesthesia administered to the patient.

Title: Learning-Reasoning Lattices in Telehealth

Authors: Stanley Jointer II, Dr. Lakshman Tamil, and Dr. Gopal Gupta

Institution: The University of Texas at Dallas – Dept. of Computer Engineering

Abstract:

Telehealth is imperative to provide anytime, anywhere care and to reduce healthcare costs. Providing a cognitive support system that brings together various medical sensor data with the patient's health records leads to improved diagnosis and care in telehealth environments. We realize the system by the development of a dependent mixture of experts system called a Learning-Reasoning Lattice (LRL). An LRL is capable of taking sensor classifications from a machine learning classifier (MLC) and inject the information into a probabilistic reasoning (PRR) system developed by medical professionals. This poster describes the foundations for the system.

Title: Modeling and Control of A Pneumatic Power Ankle Foot Orthosis

Authors: Yifan Li

Institution: The University of Illinois at Urbana-Champaign – Mechanical Science and Engineering

Abstract:

A preliminary design for a portable powered ankle foot orthosis (PPAFO) was previously developed using off-the-shelf pneumatic components to explore new opportunities for fluid power in human assistive devices. The untethered pneumatically powered PPAFO provides both motion control and external torque assistance at the ankle via a binary, event-based control scheme that uses solenoid valves. While stable, this design approaches results in limitations to the overall performance of the system. Here we present a modeling and control approach that seeks to address the limitations of the current method. Hardware and control configurations were evaluated using simulations of the modeled PPAFO and ankle/foot system during three functional gait tasks: (1) velocity control of the foot at the start of the gait cycle, (2) assistive propulsive torque during the end of stance, and (3) position control of the foot during swing. The use of computational models of the PPAFO/leg system, combined with the introduction of a proportional valve and new control architecture, resulted in performance and efficiency improvements for the PPAFO in simulation.

Title: Modeling and Simulation of Intravascular Drug Delivery from a Drug-Eluting Stent

Authors: Xiaoxiang Zhu

Institution: The University of Illinois at Urbana-Champaign – Chemical and Biomolecular Engineering

Abstract:

Stents are widely used in coronary angioplasty procedures to prevent vessel remodeling. However, patients very often experience a high risk of in-stent restenosis because of the low effect of systematic drug in-take. Drug-eluting stents are constructed to serve as a local drug delivery tool to ensure a continuous release of drug at the target vascular site. Our work uses multi-dimensional mathematical modeling and simulation to describe the intravascular drug delivery from a drug-eluting stent with hydrophobic drug and biodurable polymeric coating, taking into account the geometry of a stent strut and drug-tissue interactions.

Title: Modeling Mitochondrial Permeability Transition at the Mitochondrial Population Bioenegetics Level

Authors: Jason Bazil

Institution: Purdue University – Weldon School of Biomedical Engineering

Abstract:

An extremely important phenomenon relative to human physiology is mitochondrial permeability transition (MPT). MPT is a type of ischemia/reperfusion injury that leads to organ dysfunction. When no intervention is available, MPT ultimately leads to cell death; therefore, mitochondria can serve as the final arbiters of cell viability. In order to help facilitate a better understanding of this phenomenon, a model of MPT was developed. The model encodes the three basic necessary conditions for MPT: a high calcium load, alkaline matrix pH and circumstances which favor de-energization. The MPT induction model was able to reproduce the expected bioenergetic trends observed in a population of mitochondria subjected to conditions which favor MPT. Specifically, the model reproduced the change in MPT induction rate and extent when regulatory cations and pH were varied. The model was also used to show that in an acidic potassium-salt based environment, the mitochondrial potassium-hydrogen exchanger plays an important role during the MPT induction process. The model serves as a tool for investigators to use to understand the MPT induction phenomenon, explore alternative hypotheses for mitochondrial permeability transition pore regulation, as well as identify endogenous pharmacological targets and evaluate potential therapeutics for MPT mitigation.

Symposium on Emerging Topics in Control and Modeling: Biomedical Systems
Interactive Session Abstracts

Title: Modeling of Cellular Differentiation upon Hematopoietic Stem Cell Transplantation

Authors: Serena Pearce and Ann Rundell

Institution: Purdue University – Biomedical Engineering

Abstract:

Standard treatment of leukemic diseases employs chemotherapy to reduce the number of mature and malignant cells followed by hematopoietic stem cell (HSC) transplantation to reconstitute the circulating mature blood cells. Mathematical modeling can contribute new understandings of the complicated hematopoietic reconstitution process. An ordinary differential equation mathematical model is constructed to reflect the differentiation process of the transplanted HSCs into eosinophils, lymphocytes, monocytes, and neutrophils. Compartments of the model represent each stage of the differentiation process and cells transition from one compartment to the next as they differentiate; select compartments support self-renewal. The solutions of the model reproduce trends observed in clinical data following myeloablative transplantation. The main complication of HSC transplantation is graft-versus-host disease, an immunological disorder that leads to serious morbidity and mortality. Some alternative strategies developed, such as nonmyeloablative transplantation, lessen the adverse effects of this disease. The model will be extended to study the emergence of graft-versus-host disease upon HSC transplantation following myeloablative and nonmyeloablative chemotherapy and used to design and evaluate potential chemotherapeutic and immunosuppressive strategies to prevent its onset as well as mitigate its severity.

Title: Neuromuscular control adaptation in gait due to injury: A motivating study using a simplified dynamic model

Authors: Louis DiBerardino

Institution: The University of Illinois at Urbana-Champaign – Mechanical Science and Engineering

Abstract:

Changes to the neuromuscular control system due to injury are difficult to measure or interpret. The goal of this work is to motivate the study of neuromuscular control adaptation due to injury using a simplified dynamic model. A hypothesis of this work is the existence of isolated discontinuous changes in the actuation strategies deployed by the neuromuscular control system in response to continuous changes in musculoskeletal physiology.

This work considers a multi-degree-of-freedom mechanical system that shares certain features with gait (periodicity, symmetry, coupled DOFs, distinct phases of motion, and intermittent mechanical contact). The model's basic structure allows the possibility to study a periodic system response using simple inputs and equations of motion, while still capturing many of the advanced dynamical features found in gait.

Preliminary numerical simulations prove that discontinuous control changes do in fact take place during small perturbations to the system parameters. The system also does not return to the same actuation strategy once the parameter is returned to the baseline state. This work establishes that such phenomena may exist in dynamic systems sharing certain characteristics found in gait, and should be further explored to better understand the relatively unknown mathematics behind neuromuscular control with regard to injury.

Title: Point Process Modeling of Cortical Spiking Activity in Normal and MPTP Primates during Deep Brain Stimulation

Authors: Sabato Santiniello

Institution: The Johns Hopkins University – Institute of Computational Medicine, Dept. of Biomedical Engineering

Abstract:

Deep Brain Stimulation (DBS) is an effective electrical therapy for the treatment of movement disorders in Parkinson's Disease (PD). DBS restores motor skills by delivering regular high frequency (>100 Hz) trains of pulses within the basal ganglia, a set of subcortical nuclei involved in movement selection. Though effective, the mechanisms and impact of DBS on motor cortex are still unknown. We propose a point-process input-output model to describe the effects of stimulation on the cortical activity in normal and PD conditions, and investigate the influence of the stimulation frequency on the neuronal activity. Our models are estimated from single unit recordings from the sensorimotor cortex of 2 primates, before and after a neurotoxin is administered to develop stable Parkinsonian motor symptoms. Our models suggest that subcortical DBS impacts the cortical activity by changing the spiking pattern (spikes and rebounds antidromically elicited) and increasing the synchronization of neurons at the stimulation frequency both in normal and PD conditions. Our models show a difference in the modulation of the spike propensity in the different conditions: in normal primates, neurons quickly recover after each pulse and fire independently, while in PD spike propensity is time-locked with the stimulation and no post-stimulus modulation occurs.

Title: Point Process Models show Temporal Dependencies of Basal Ganglia Nuclei under Deep Brain Stimulation

Authors: Shreya Saxena

Institution: Johns Hopkins University – Biomedical Engineering

Abstract:

Deep Brain Stimulation (DBS) is an effective treatment for patients with Parkinson's disease, but its impact on basal ganglia nuclei is not fully understood. DBS applied to the subthalamic nucleus (STN) affects neurons in the globus pallidus internus (GPi) through direct projections, as well as indirectly through the globus pallidus externus (GPe). Since traditional statistical analyses of electrophysiological data provide too coarse a view of circuit dynamics, and mesoscopic biophysical dynamic models contain an intractable number of state variables for small populations of neurons, we apply a modular approach and treat each region in the STN-GPe-GPi circuit as a multi-input multi-output point process system. We use microelectrode recordings of a normal primate with DBS applied to STN at 100 and 130 Hz to estimate point process models (PPMs) for recorded regions in GPi. Our PPMs uncovered distinct dependencies between regions of GPe and GPi neurons, separated by the position of the GPi neurons, and showed normal refractory periods, inhibition from projecting neurons in the GPe, and DBS-induced oscillatory effects. The PPMs also showed the relative impact of the above factors, which traditional statistics fail to capture. Our PPM framework suggests a useful approach for understanding dynamics of complex neural circuits.

Title: Preliminary investigations into multiple-model input design for controlling intracellular signaling dynamics

Authors: Jeffrey Perley, Maia M Donahue, Gregery T Buzzard, and Ann E Rundell

Institution: Purdue University – Biomedical Engineering and Dept. of Mathematics

Abstract:

Intracellular signaling pathways are crucial for the transmission and processing of biochemical information needed for the continuation of normal cellular processes. The complex nature of intracellular signaling pathways and their abstracted mathematical models challenges the design of control inputs for obtaining desired responses. In addition, these models do not exist uniquely for each intracellular pathway. Diversity in the mathematical models that support quantitative control input design arises from the selective inclusion of participating biochemical species and the choice of mathematical representation of their action (structural uncertainty) as well as model initial conditions and other parameter values (parametric uncertainty). As a result, the most effective control input design may be derived considering several mathematical models of a given signaling pathway with differing structures and parameter values. These preliminary investigations design open loop control inputs for an intracellular signaling system to reach a desired system behavior based on predictions from multiple models. The approach utilizes sparse grids for rapid and efficient screening of the input space to identify a set of controller inputs that are robust to the effects of model structure and parameter uncertainties. This multiple-model predictive controller design approach will be demonstrated in mock experiments utilizing ordinary differential equation models of the mitogen activated protein kinase pathway.

Title: Quantitative Ultrasound for Monitoring and Assessment of Thermal Therapy

Authors: Jeremy Kemmerer, Goutam Goushal, William Ridgway, and Michael Oelze

Institution: The University of Illinois at Urbana-Champaign – Dept. of Electrical and Computer Engineering

Abstract:

The quantitative ultrasound (QUS) imaging technique based on ultrasonic backscatter has proven potential for animal and human tissue characterization. Currently, new techniques are being developed in the Bioacoustics Research Laboratory in order to bring this imaging modality closer to clinical applications. New algorithms and signal processing techniques have been developed to improve the estimation of parameters based on the backscattered power spectrum and the backscattered envelope. In particular, the feasibility of detecting structural and acoustical changes in tissue due to thermal treatment of tissue is being investigated. A novel technique was developed to construct biophantoms, which were instrumental in performing controlled experiments with living cells. Results suggest that QUS has the potential to be used for noninvasive monitoring of temperature changes in tissues. QUS is also being evaluated as a means to assess tissue damage from High-Intensity Focused Ultrasound (HIFU) treatment. Results from HIFU experiments with liver samples suggest that QUS may be used to detect HIFU lesions.

Title: Real-time Heart Model for Implantable Cardiac Device Validation and Verification

Authors: Zhihao Jiang

Institution: The University of Pennsylvania – Computer and Information Science

Abstract:

Designing bug-free medical device software is difficult, especially in complex on-body and implantable devices that may be used in unanticipated contexts. Safety recalls of pacemakers and implantable cardioverter defibrillators due to firmware (i.e. software) problems between 1990 and 2000 affected over 200,000 devices, comprising 41% of the devices recalled and are increasing in frequency. The goal of this project is to develop a real-time platform to model the heart function to enable testing, validation and verification of implantable cardiac devices such as pacemakers and defibrillators. The hardware-based platform will be capable of emulating and synthesizing electrical signals (i.e. electrograms) of the functioning (i.e. during normal sinus rhythm) and malfunctioning (i.e. during arrhythmia) heart. It will be able to react to internal (i.e. premature stimuli) or external (i.e. artificial voltage like pacing signals) stimuli, as well as be adaptive to external factors like metabolic processes and medication (i.e. different type of anti-arrhythmia drugs). The model will be progressively developed starting with a set of specific capabilities and goals. The structure will be easy-to-use by surgeons and electrophysiologists so that they can contribute to the platform by easily modifying or adding new features to the existing system. The platform will then be used for functional validation, and potentially for formal verification of real and virtual medical devices for speedier FDA certification.

Title: Remote Teleoperation of an Unmanned Aircraft with a Brain-Machine Interface

Authors: Abdullah Akce, Miles Johnson, Or Dantsker, and Timothy Bretl

Institution: The University of Illinois at Urbana-Champaign

Abstract:

We present an interface that enables a human pilot to remotely teleoperate an unmanned aircraft with input only from an electroencephalograph (EEG). We formulate the problem of interface design as the problem of constructing an optimal communication protocol that allows the pilot to specify desired paths for the aircraft. Desired paths are smooth curves that we represent as strings in an ordered symbolic language. The pilot specifies a string in this language by giving binary commands ("turn left" or "turn right"), just like he or she would search for words in a dictionary by turning pages forward or back. The binary commands, interpreted from the EEG signals, reflect whether the pilot is providing left- or right-motor imagery in their brain (for ex. by thinking about clenching their left or right hand). A graphical display provides visual feedback to the pilot by showing annotated video from the aircraft's onboard camera. These design choices allow us to model the EEG sensor and the graphical display as a noisy binary channel with noiseless feedback. With this abstraction, we derive an optimal communication protocol using tools from feedback information theory. Our approach uses arithmetic coding as a method of lossless data compression and posterior matching as a closed-loop feedback policy. We demonstrate the feasibility of this approach with physical hardware in a perimeter surveillance task.

Title: Restoring the Basal Ganglia in Parkinson's Disease to Normal via Multi Input Phase shifted Deep Brain Stimulation

Authors: Rahul Agarwal

Institution: Johns Hopkins University – Biomedical Engineering

Abstract:

Deep brain stimulation (DBS) injects a high frequency current that effectively disables the diseased basal ganglia (BG) circuit in Parkinson's disease (PD) patients, leading to a reversal of motor symptoms. Though therapeutic, high frequency stimulation consumes significant power forcing frequent surgical battery replacements and causing widespread influence into other brain areas which may lead to adverse side effects. In this paper, we conducted a rigorous study to assess whether low frequency signals can restore behavior in PD patients by *restoring* neural activity in the BG to the normal state. We used a biophysical-based model of BG nuclei and motor thalamus whose parameters can be set to simulate the normal state and the PD state with and without DBS. We administered pulse train DBS waveforms to the subthalamic nucleus (STN) with frequencies ranging from 0-150Hz. For each DBS frequency, we computed statistics on the simulated neural activity to assess whether it is restored to the normal state. In particular, we searched for DBS waveforms that suppress pathological bursting, oscillations, correlations and synchronization prevalent in the PD state and that enable thalamic cells to relay cortical inputs reliably. We found that none of the tested waveforms restores neural activity to the normal state. However, our simulations led us to construct a novel DBS strategy involving low frequency multi-input phase-shifted DBS to be administered into the STN. This strategy successfully suppressed all pathological symptoms in the BG in addition to enabling thalamic cells to relay cortical inputs reliably.

Title: Unmatched muscle power: mapping physiological control to virtual world physics

Authors: Bradly Alicea

Institution: Michigan State University – Computer Science

Abstract:

Unmatched muscle power is a theoretical and experimental technique intended to incorporate electrophysiological and adaptive properties of skeletal muscle into virtual environment control. In everyday settings where movement-related activities seem to be effortless, the production of muscle power is hypothesized to be perfectly matched to that activity. The requirement of a mapping between the real and virtual worlds provides an opportunity to intentionally distort control parameters important to perception and action in a human-machine interface. By understanding the neural response to distorted feedback, better control strategies can be devised for applications relevant to rehabilitation technologies and non-standard populations.

The amount of force output relative to that required for optimal control during a given physical activity can be under- or over-produced in cases of pathology or injury, or when the control imperative is poorly defined. In this submission, amplitude components of the EMG signal for selected arm muscles and object displacement in the virtual environment are used to parameterize aspects of this decoupling. Experimental results utilizing various forms of force-feedback conditioning in a motion-controlled virtual environment will be briefly discussed. Using these findings and principles, biologically-realistic control policies can be formulated to enhance purely statistical or symbolic descriptions of real-world activities.

Title: Using Point Process Models to Describe the Cortico-Striatal and Pallido-Striatal Dependencies in Healthy Primates

Authors: Sabato Santiniello

Institution: The Johns Hopkins University – Institute of Computational Medicine, Dept. of Biomedical Engineering

Abstract:

The basal ganglia (BG) are subcortical nuclei modulating motor-related cortical activity. They integrate and relay motor information to cortex and a pathological change in their activity typically results in movement disorders. Striatum is the first stage in the BG motor loop and, by interacting with globus pallidus externus (GPe) and subthalamic nucleus (STN), plays a pivotal role in modulating input from motor cortex. The dynamical behavior of striatum under cortical, pallidal and subthalamic influence is still unclear, although dramatically impacts the motor loop. We propose a point-process input-output model to describe how striatum combines cortical input and feedback projections from GPe and STN. The relative impact of the inputs, temporal dependencies, and effects of electrical stimulation are modeled and estimated from striatal single unit recordings from 2 non human primates, recorded before and during stimulation of the STN (several patterns are considered). The model suggests that GPe and cortex affect striatum on different time scales, i.e., the striatal spike propensity goes up within 2-3 ms from a cortical spike but 10 ms from a pallidal one, and goes down 18-20 ms after the pallidal spike (feedback reactivation). Stimulation of STN masks pre-existent dynamics and entrain neurons at the stimulation frequency.