BREAKFAST 8:15-8:45 AM

OPENING REMARKS 8:45 - 9:00 AM,

Nabil Adam, Vice Chancellor for Research and Collaborations, Rutgers University.

SESSION 1. 9:00 - 10:45 AM, Chair John B. Kostis, Rutgers University

Clinical Trials: You Can’t Live With Them, You Can’t Live Without Them.

John B. Kostis, The Cardiovascular Institute of New Jersey, Rutgers Robert Wood Johnson Medical School.

Abstract: Patient relevant cardiovascular events include myocardial infarction (heart attack), stroke, heart failure and death. These non-communicable diseases are common in industrialized societies and are becoming prevalent worldwide. They are related to the fact that saving calories to avoid starvation, enhancing immunity to fight infections, and maintaining blood volume and blood pressure in order to survive bleeding or dehydration, conferred evolutionary advantages to our distant ancestors. The main modifiable risk factors for atherosclerotic cardiovascular disease are smoking, hypertension, hypercholesterolemia and diabetes.

Controlled clinical trials are necessary in order to establish the efficacy of interventions. Limitations of clinical trials are that they do not examine the totality of evidence on each issue, they condone imbalance between errors of commission (treating) versus errors of omission (not treating when needed) and they place undue emphasis on p values. Publication bias, patient selection, and short duration are additional problems. However, efficacious intervention may not be effective when implemented in a community. A best approach is to emphasize primordial prevention i.e. the prevention of cardiovascular disease rather than primary prevention (the prevention of an event in persons who have the disease) or secondary prevention i.e. prevent a second event among persons who have survived the first.

Randomized Clinical Trials: The stepped Wedge design.

Edwin van den Heuvel, Eindhoven University of Technology, the Netherlands.

Abstract: The stepped wedge design (SWD) originated in 1980 as a pragmatic trial, but received substantial more attention only in the last decade. In a SWD all patients start at the control treatment and switches to the new or alternative treatment during the trial. The switch moments are predefined before the trial but are typically different for (groups of) patients. Randomization is used to allocate (groups of) patients to the different switches. There are two types or categories of SWDs, namely “cross-sectional” and “longitudinal”. The SWD is however not without controversy, especially for the longitudinal types. The trial is suspected to generate “survivor bias” and may take substantially longer than more traditional trial designs like the parallel group design. The presentation will provide some history of the SWD’s,
its advantages and disadvantages with respect to other clinical trial designs, some current statistical developments, and some future research possibilities.

**Optimising Pharmaceutical Research Resource Allocation (OPRRA).**

**John Gittins**

University of Oxford, U.K.

**Abstract:** I will discuss a new software (OPRRA) for resource allocation in the discovery phase of pharmaceutical research and the associated stochastic theory, including a new approach on the quantification of risk. OPRRA models discovery in five successive stages, as follows. 1) Before screening, leading to setting up a cascade of screens. 2) Looking for a lead series. 3) Looking for a backup lead series. 4) Optimizing a lead series to find a candidate drug. 5) Looking for a backup candidate drug from a lead series which has already provided one or more candidate drugs.

The software has two main purposes: 1) to indicate profitable resource allocation rates for individual projects during discovery; 2) to help identify allocation plans for portfolios of projects which are profitable, feasible, and acceptably risky.

Its application for purpose 1. it requires data for a number of projects, or potential projects, which are currently in discovery. For purpose 2. it needs groups of projects between which resources are fairly readily transferable.

Most parameters may be entered either as point values or by means of a probability distribution. These probability distributions are designed to cope with the inevitable huge uncertainties as to how projects will progress.

Project-specific data ideally should be based on historical records, either internal to the company or industry-wide, for example from CMR, with judgmental corrections based on the characteristics of individual projects. In many cases there are reasonable default assumptions.

OPRRA also models phases 1, 2, and 3 of clinical trials, but is not concerned with their planning.

**Break.**

**SESSION 2.A 11:00 - 1:00 PM, Chair Sanjay Mehrotra**

Northwestern University

Contour approximation of spatial data.

**Adi Ben-Israel**

Rutgers University.

**Abstract:** Given a set $S$ of points in $\mathbb{R}^n$, a contour approximation of $S$ is a function that captures most points of $S$ in its lower level sets. A concrete application is the home-range of a species, the territory in which the animals live and travel, shown experimentally by Dixon and Chapman [2] to involve the harmonic mean of certain distances, a result since then confirmed for hundreds of species. The harmonic mean of distances also appears in inverse distance weighted interpolation [3], clustering [4], and elsewhere. The unique role of the harmonic mean in contour approximation was established by Arav [1], through a list of desirable properties expected of such an approximation. This lecture gives an axiomatic framework, and a probabilistic optimization model that unifies the above results, a model applied successfully to clustering and classification.

*Joint work with Tsvetan Asamov and Cem Iyigun.*

**References:**


**Applying Stein’s Method: Probability Approximations and Simulation.**

**Sheldon M. Ross**

University of Southern California.

**Abstract:** We will give some improvements to the usual Chen-Stein bound for the probability of a union of events, and also show how Stein’s Method can be applied in simulation.

**Dynamic Learning in Strategic Pricing Games.**

**John Birge**

Chicago Booth.

**Abstract:** In monopoly pricing situations, firms optimally vary prices to learn demand. The variation must be sufficiently high to ensure complete asymptotic learning. In competitive situations, however, varying prices provides information to competitors and may reduce the value of learning. This talk will discuss how this effect can be strong enough to stop learning so that firms optimally reduce any variation in prices and choose not to learn demand. The result can be that the selling firms achieve a collaborative outcome instead of a competitive Nash equilibrium.
The many-interacting-worlds interpretation of quantum mechanics and Stein’s method.

Ian McKeague, Columbia University.

Abstract: It has been conjectured that quantum effects arise from the interaction of finitely many classical worlds. The wave function is then thought to be recoverable from observations of particles in these worlds without knowing the world from which any particular observation originates. In this talk we discuss how Stein’s method can be used to obtain such results as the number of worlds goes to infinity. For a parabolic potential well, we show that the ground-state particle configuration is asymptotically Gaussian, thus matching the ground-state solution of Schroedinger’s equation. We also discuss how higher energy solutions of Schröedinger’s equation can be interpreted in the same way.

SESSION 2.B 11:00 - 1:00 PM, Chair Eugene A. Feinberg, Stony Brook University

Partially Observable Markov Decision Processes (POMDPs) to Personalize Cancer Screening: An Example from Mammography Screening.

Oguzhan Alagoz, University of Wisconsin-Madison.

Abstract: Cancer, the second leading cause of death in the US, is an asymptomatic disease but is curable especially if detected early. Although many screening technologies are effective for early diagnosis of cancer, cancer screening has several potential risks, including a high rate of false positives and overdiagnosis. Therefore, the balance of benefits and risks, which depend on personal characteristics, is critical in designing a cancer screening schedule. In this presentation, we will describe the use of partially observable Markov decision processes (POMDPs) for optimizing cancer screening decisions. POMDP models can be used to address several controversial open research questions in cancer screening, such as when to start and stop screening and how often to screen. POMDP models provide a well-suited framework to optimize screening decisions because they allow the representation of the unobservable true health condition of a patient and testing that provide partial information about the true health condition. We will use a previously developed POMDP model for mammography screening to demonstrate the development and application of a POMDP model for cancer screening. In contrast to prior research and existing guidelines which consider population-based screening recommendations, we propose a personalized cancer screening policy based on the prior screening history and personal risk characteristics of women. Our POMDP model incorporates two methods of detection (self or screen), age-specific unobservable disease progression, and age-specific mammography test characteristics. We use a validated micro-simulation model based on real data in estimating the parameters and solve this POMDP model optimally for individual patients. Our results show that our proposed personalized screening schedules outperform the existing guidelines with respect to the total expected quality-adjusted life years, while significantly decreasing the number of mammograms. We further find that the mammography screening threshold risk increases with age. We derive several structural properties of the model, including the sufficiency conditions that ensure the existence of a control-limit policy.


Eugene A. Feinberg, Stony Brook University.

Abstract: Medical decisions are often based on incomplete information. This talk describes sufficient conditions for the existence of optimal policies for Partially Observable Markov Decision Processes (POMDPs) with Borel state, observation, and action sets, when the goal is to minimize the expected total costs over finite and infinite horizons. For infinite-horizon problems, one-step costs are either discounted or assumed to be nonnegative. Action sets may be non-compact and one-step cost functions may be unbounded. The introduced conditions are also sufficient for the validity of optimality equations, semi-continuity of value functions, and convergence of value iterations to optimal values. The talk is based on joint papers with Pavlo Kasyanov and Michael Zgurovsky from the National Technical University of Ukraine “Kyiv Polytechnic Institute”

Optimal Learning in Health Care and Medical Research.

Warren Powell, Princeton University.

Abstract: Health care and medical research represents an endless array of opportunities for collecting information, from laboratory experiments to medical tests to the results of hospital procedures and the administering of drugs. In each setting, collecting information is time consuming and expensive, as well as risky. Professionals draw heavily on their domain knowledge, but it can be quite easy to fall in the trap of doing what appears to be best, especially when it involves decisions that involve actual patients. We describe the knowledge gradient policy, and show how it can handle both offline experimentation (in the laboratory) and online learning (from diagnostic testing and the results of actual procedures). The talk focuses on the ability of the knowledge gradient to handle a variety of belief models. We describe settings that exploit correlated beliefs, linear and nonlinear parametric models, as well as high-dimensional sparse additive models. We contrast the use of multivariate normal priors on unknown parameters against discrete priors, which offer significant strengths but with some limitations.

Aditya Mahajan, McGill University, Canada.

Abstract: Remote estimation refers to a system that consists of a sensor and an estimator. The sensor observes a discrete-time Markov process and, at each time step, decides whether or not to transmit the state of the process to the estimator. When the sensor does not transmit, the estimator uses prediction to estimate the state of the process. We consider the problem of optimally designing the transmission and the estimation strategies to minimize the expected estimation error when there is a constraint on the expected number of transmissions. This is a constraint decentralized control problem. The solution approach consists of four steps. In the first step, we use the common-information approach of Nayyar Mahajan Teneketzis (2013) to transform the decentralized control problem into a centralized partially observed Markov decision problem. In the second step, we use majorization theory to identify the structure of optimal transmission and estimation strategies. In the third step, we use renewal theory to identify the performance of a generic strategy that has the specified structure. Finally, in the fourth step, we identify the optimal strategies with the specified structure. We present numerical results for symmetric birth-death Markov chains and for first-order auto-regressive Gaussian process.

These results represent an example of decentralized stochastic control where complete numerical results are obtained.

Lunch Break.

SESSION 3.A 2:15 - 4:15 PM. Chair Sanjay Mehrotra, Northwestern University Room 5085


Madhu Mazumdar, Institute of Healthcare Delivery Science, Mount-Sinai Health System.

Abstract: The ever increasing burden of US healthcare costs - currently 18% of gross domestic product - remains a priority for policymakers. Particular focus has been given to overuse of healthcare resources. In 2012, the American Board of Internal Medicine Foundation, together with Consumer Reports and medical specialty societies launched the so-called “Choosing Wisely” campaign. Each participating society announced evidence-based lists of five tests or procedures in its clinical domain that are over-utilized (http://www.choosingwisely.org/doctor-patient-lists/). Since the launch of this initiative an increasing number of single institutional studies have been published that describe efforts to reduce overuse of particular “Choosing Wisely” tests or procedures such as diagnostic imaging, pharmacological interventions or blood transfusions. Particularly the use of clinical decision support tools embedded in the electronic medical record system appears to be promising as an effective intervention if executed and evaluated properly. I will discuss an ongoing randomized control trial of diagnostic imaging at Mount-Sinai Health System and illustrate utilization of a variety of methods such as meta-analysis, segmented regression analysis, and simulated power analysis for its initiation.

Network Granger Causality with Inherent Grouping Structure and its Applications to Biological Systems.

George Michailidis, University of Michigan.

Abstract: The problem of estimating high-dimensional network models arises naturally in the analysis of many biological systems. In this work, we aim to learn a network structure from temporal panel data, employing the framework of Granger causal models under the assumptions of sparsity of its edges and inherent grouping structure among its nodes. To that end, we introduce a group lasso regression regularization framework, and also examine a thresholded variant to address the issue of group misspecification. Further, the norm consistency and variable selection consistency of the estimates are established, the latter under the novel concept of direction consistency. The proposed methodology is illustrated on a data set coming from functional genomics.

Designed Sampling from Large Databases for Controlled Trials.

Sanjay Mehrotra, Northwestern University.

Abstract: The increasing prevalence of rich sources of data and the availability of electronic medical record databases and electronic registries opens tremendous opportunities for enhancing medical research. For example, controlled trials are ubiquitously used to investigate the effect of a medical treatment, perhaps dependent on a set of patient covariates, and traditional approaches have relied primarily on randomized patient sampling and allocation to treatment and control group. However, when covariate data for a large cohort group of patients have already been collected and are available in a database, one can potentially design a treatment/control sample and allocation that provides far better estimates of the covariate-dependent effects of the treatment. We develop a new approach that uses optimal design of experiments concepts to accomplish this objective. The approach selects the patients for the treatment and control samples upfront, based on their covariate values, in a manner that optimizes the information content in the data.

Dynamic Abandon/Extract Decisions for Failed Cardiac Leads.

Lisa Maillard, University of Pittsburgh.

Abstract: Pacemaker and defibrillator lead wires fail stochastically, requiring the surgical implantation of a new lead. Whenever a lead fails, it may be beneficial to extract one or more of the failed leads currently implanted, including previously abandoned leads.
Extracting a lead carries life-threatening risks that increase in the dwell time of the lead. However, there are situations in which extraction is not optional: the total number of implanted leads (both failed and functioning) is subject to a maximum limit, typically five, and infections can occur requiring the mandatory extraction of all implanted leads. To study the tradeoff between avoiding risky extractions and maintaining space for future leads, we develop Markov decision process models to determine patient-specific extraction policies for various types of cardiac devices as a function of patient age and the age of every implanted lead. We use clinical data to calibrate the model and present insightful numerical results, including comparisons to heuristics commonly used in practice.

**SESSION 3.B 2:15 - 4:15 PM, Chair Javier Cabrera, Rutgers University**

**Model Selection for Bayesian Survival Models Using Bregman Divergence Measure.**

Lynn Kuo, University of Connecticut, Daoyuan Shi, University of Connecticut.

**Abstract:** Related to the Cox’s proportional hazards model, we consider several semi-parametric Bayesian models used for survival analysis. The inference is feasible due to the recent advance in Bayesian computation. Then we explore the predictive approach of model selection using the Bregman divergence criterion. The Bregman divergence criterion includes a general class of loss functions defined by squared Euclidean distance, squared Mahalanobis distance, generalized Kullback-Leibler divergence, and the Itakura-Saito distance. We illustrate our method based on a real data set. We will further compare our results to that selected using Akaike, deviance, and Watanabe-Akaike information criteria.

**MAP inference for MRI Reconstruction.**

Ramin Zabih, Cornell University.

**Abstract:** Fast inference algorithms for computing the MAP estimate of a Markov Random Field are widely used in computer vision. I will describe the challenges and opportunities involves in applying these techniques to a very different problem, namely the reconstruction of high quality MR images. The main goal is to significantly reduce scan time and increase resolution, which in turn would have substantial clinical benefits. Technically, the problem centers on an over-determined linear inverse system. I will present some promising preliminary results using graph cut inference methods that use a more realistic prior than classical Tikhonov-style regularization.

**Acoustic Feedback Cancellation: a Kalman filter approach.**

George V. Moustakides, Rutgers University & University of Patras, Greece.

**Abstract:** We consider the problem of acoustic feedback cancelation occurring in digital hearing aids. By modeling the speech signal as an AR process with coefficients that are assumed known and applying the Kalman filter theory, we develop a prototype feedback estimation/cancellation algorithm capable of reducing, significantly, the acoustic echo effect. Motivated by this prototype version, we then propose a variant that not only performs the necessary feedback estimation/cancellation but also estimates, concurrently, the AR coefficients which are now regarded as unknown. Using stochastic approximation theory we can show convergence of our final algorithm while simulations demonstrate that its performance is only slightly inferior to the prototype algorithm which, as pointed out, requires exact knowledge of the AR model.

**Personalized Disease Networks (PDN) for Understanding and Predicting Cardiovascular Diseases and Other Complex Processes.**

Javier Cabrera, Rutgers University.

**Abstract:** We develop a novel method for building patient level personalized disease networks for prediction of medical outcomes. Standard Bayesian network models have been used in the past for building disease networks from data corresponding to a patient population and producing a single network. But for cardiovascular diseases Bayesian network models do not fit individual patient data because of the diversity of pathways corresponding to multiple symptoms and diseases that each individual may have. Thus, one single Bayesian network cannot capture the inter-individual variability. We propose a methodology which begins by building personalized disease networks, one for each patient or case. Then we analyze these data as a dataset of networks, one per observation.

We develop cluster methodology for the generated PDN’s data and ways to summarize the clusters and study the within cluster variability. In addition we develop data visualization technics, to display, compare and summarize the network data. Finally we analyze a cohort dataset of African American patients with heart diseases a New Jersey statewide database (Myocardial Infarction Data Acquisition System, MIDAS) of cardiovascular disease outcomes. We use the MIDAS data to apply our network methodology and build patient predictive networks for cardiovascular diseases. And we show that the network data improves on the prediction of patient outcomes such as death or cardiovascular death, when compare with the standard statistical analysis.

Collaborators: Fei Wang, Nabil Adam, Dhammika Amaratunga, John Kostis, Willian Kostis, Jaideep Vaidya

**Break.**
Bagging in the Real World.
Periklis Papakonstantinou, Rutgers University.

Abstract: Bagging is one of the most successful heuristics in Machine Learning (as of now > 13,000 references). Part of its success is its generality: given any method for learning predictors from data, Bagging aims to produce an ensemble of predictors that combined together outperform in accuracy the single one. However, Bagging is a heuristic thus occasionally fails. We ask in what sense can we develop theory for improving and analyzing Bagging and other very successful practical heuristics. To that end, we provide a new framework and mathematical tools, and then by adapting ideas from Derandomization and Pseudo-randomness (areas at the frontiers of Computational Complexity) we construct the first, provably universally better than Bagging heuristic.

This is joint work with Jia Xu and Cao Zhu.

Will Clinical Trials Prove Fatal to Big Pharma?
Paul Jeffrey, NJEDA Commercialization Center for Innovation and Technology.

Abstract: As healthcare costs rise, pressure to reduce the cost of pharmaceuticals intensifies. However, at the same time, the world continues to demand new medicines to improve and prolong life – and clinical trial data to provide meaningful outcomes data to prove it. The result is huge pressure on the pharmaceutical industry and squeezed profits. Examples of the increasing burden of clinical trials will be presented, including review of recent clinical trials of PCSK-9 inhibitors to lower LDL cholesterol and potentially reduce cardiac events and death. Possible solutions to the staggering cost of outcomes trials will be discussed. But, in the end, can big pharma survive or will all of our new medicines be developed by small companies targeting orphan diseases?

Large Scale Analytics for Medical Applications.
Dimitris N. Metaxas, Rutgers University.

Abstract: Over the last 20 years, we have been developing a general, scalable, computational framework that combines principles of computational learning with sparse methods, mixed norms, learning, dictionaries, CNNs and deformable modeling methods. This framework has been used for resolution of complex large scale problems in medical image analysis. Our methods allow the discovery of complex features, shapes and learning-based analytics. We will present these methods and their applications to several medical applications which include feature discovery for segmentation and recognition of body parts, cardiac MRI image reconstruction and cardiac analytics including blood flow, large scale histopathological image analysis and retrieval, body-part recognition from images and body fat estimation.

Sponsors: Rutgers Business School, Applied Probability and Data Analytics Laboratory
Institute for Data Science, Learning, and Applications, Department of Management Science & Information Systems
The Cardiovascular Institute of New Jersey, the Center for Dynamic Data Analytics, the Rutgers Center for Operations Research

Prediction of Thrombus-Prone Regions in Abdominal Aortic Aneurysms Using Hierarchical Bayesian Spatial Models.
Ioannis Kamarianakis, Arizona State University.

Abstract: Intraluminal Thrombus (ILT) is present in almost all abdominal aortic aneurysms (AAAs), with several studies trying to identify its association with the risk of rupture. Prediction of ILT growth is of interest, as clinical studies have demonstrated that it might indicate AAA rupture risk. Near wall hemodynamics, described by wall shear stress (WSS), oscillating shear index (OSI) and relative residence time (RRT) have been identified as significant determinants for ILT deposition. This work associates flow dynamic conditions at the AAA wall with ILT deposition distribution using Hierarchical Bayesian Spatial Regression models. Parameter estimation is based on integrated nested Laplace approximations, a deterministic algorithm which has proven capable of providing accurate and fast results.

Dynamic Learning of Patient Response Types: An Application to Treating Chronic Diseases.
Diana Negoescu, University of Minnesota.

Abstract: Currently available medication for treating many chronic diseases is often effective only for a subgroup of patients, and biomarkers accurately assessing whether an individual belongs to this subgroup do not exist. In such settings, physicians learn about the effectiveness of a drug primarily through experimentation, i.e., by initiating treatment and monitoring the patient’s response. Precise guidelines for discontinuing treatment are often lacking or left entirely at the physician’s discretion. We introduce a framework for developing adaptive, personalized treatments for such chronic diseases. Our model is based on a continuous-time, multi-armed bandit setting, and acknowledges that drug effectiveness can be assessed by aggregating information from several channels: by continuously monitoring the (self-reported) state of the patient, but also by (not) observing the occurrence of particular infrequent health events, such as relapses or disease flare-ups. Recognizing that the timing and severity of such events carries critical information for treatment design is a key point of departure in our framework compared with typical (bandit) models used in healthcare. We show that the model can be analyzed in closed form for several settings of interest, resulting in optimal policies that are intuitive and have practical appeal. We showcase the effectiveness of the methodology by developing a treatment policy for multiple sclerosis.
When compared with standard guidelines, our scheme identifies non-responders earlier, leading to improvements in quality-adjusted life expectancy, as well as significant cost savings.

**A Review of Binary Independent Component Analysis Applied to Molecular Features.**

**Phillip G. Bradford**, University of Connecticut.

**Abstract:** This talk gives an introduction to binary Independent Component Analysis (ICA). It focuses on several example applications using the R-language to identify molecular features. These molecular features are not independent, however variations of ICA still offer predictive value. A discussion of the algorithms landscape for variations of ICA completes the discussion. This is joint work with John D. MacCuish, President Mesa Analytics & Computing, Inc.

**Computational Phenotyping using Tensor Factorization and Tensor Network.**

**Jimeng Sun**, Georgia Institute of Technology.

**Abstract:** Computational phenotyping is the process of converting heterogeneous electronic health records (EHRs) into meaningful clinical concepts (phenotypes). Tensor factorization has been shown as a successful unsupervised approach for discovering phenotypes. However, tensor methods have some major limitations for phenotyping: 1) unable to incorporate existing medical knowledge; 2) fail to handle high-order tensors (e.g., order > 5).

We will talk about two of our recent developments in addressing these challenges: First, we proposed Rubik, a constrained non-negative tensor factorization and completion method for phenotyping. Rubik incorporates 1) guidance constraints to align with existing medical knowledge, and 2) pairwise constraints for obtaining distinct, non-overlapping phenotypes. Rubik also has built-in tensor completion that can significantly alleviate the impact of noisy and missing data. We evaluate Rubik on two large EHR datasets. Our results show that Rubik can discover more meaningful and distinct phenotypes than the baselines.

Second, we extended a theoretical framework called tensor networks for analyzing high-order tensors. We developed an efficient sparse hierarchical Tucker model (Sparse H-Tucker) for finding interpretable tree-structured factorizations from sparse high-order tensor. Sparse H-Tucker scales nearly linearly in the number of non-zero tensor elements. We applied Sparse H-Tucker on a real EHR dataset for learning a disease hierarchy. The resulting tree structure provides an interpretable disease hierarchy, which is confirmed by a clinical expert.

**Asymptotically Optimal Multi-Armed Bandit Policies under Side Constraints.**

**Odysseas Kanavetas**, Sabancı University, Turkey, **Apostolos N. Burnetas**, National and Kapodistrian University, Greece, and **Michael N. Katehakis**, Rutgers University.

**Abstract:** We develop asymptotically optimal policies for the multi armed bandit (MAB) problem, under side constraints. Such models are applicable in situations where each sample (or activation) from a population (bandit) incurs a known bandit dependent cost. We consider the class of feasible uniformly fast (f-UF) convergent policies, that satisfy sample path wise the cost constraint. We first establish a necessary asymptotic lower bound for the rate of increase of the regret function of f-UF policies. Then we construct a class of f-UF policies and provide conditions under which they are asymptotically optimal within the class of f-UF policies, achieving this asymptotic lower bound. We provide the explicit form of such policies for the case in which the unknown distributions are Normal with unknown means and known variances.

**SESSION 4.C 4:30 - 6:30 PM, Chair Floske M. Spieksma**, University of Leiden, the Netherlands

**Markov Processes: parametrization and continuity.**

**Floske M. Spieksma**, University of Leiden, the Netherlands.

**Abstract:** Structures of optimal policies in Markov decision processes can be derived by a value iteration argument, provided the jump rates are bounded in the state variable. If the jump rates are unbounded, a perturbation has to be performed, which keeps structure of the optimal policy intact. A consecutive limit has to be taken, in order to obtain the desired result for the non-perturbed process. This requires certain continuity properties to hold.

It appears that standard conditions for studying discounted Markov decision processes imply continuity properties in the wider setting of a parametrized Markov process. Similar results holds as well for strong drift conditions imposed on a parametrized Markov process, when the objective is to maximize the average expected reward.

**A Hybrid Stochastic Model for Self-Regulated Biochemical Systems.**

**Felisa Vazquez-Abad**, City University of New York, **Alexey Nikolaev**, City University of New York.

**Abstract:** Some biological processes follow cycles (notably circadian) where the concentration of proteins changes periodically. For example, “activators” and “repressor” molecules may alternate in cycles completing a full cycle every 24 hours or so. Self-regulation is the result of complex interactions involving gene expression and protein production. It is known that aberrant cycles may cause tumorigenesis and other important deceases.

There are two main mathematical models that describe chemical interactions: the ODE model approximates the concentration of each protein as is believed to be accurate when there is a large number of molecules (fluid approximation). At the
other end, a multi-dimensional birth and death process (B&D) models the (discrete) number of molecules assuming that
the events of creation and destruction take exponential times with rates equal to the rates of the corresponding chemical
equations. This is a model used for simulations.

Our first result established the conditions under which the ODE model describes exactly (without approximations) the
expected number of molecules. Using this result we were able to propose a hybrid model that combines ODE and simulation
to acculturate the estimation of the cycle time by at least one orders of magnitude.

Besides estimating the cycle time, we aim to estimate the gradient of the cycle time with respect to the various chemical
rates. First, this will provide a method for identifying which of the chemical processes are more relevant for the cycle
time control and perhaps help to identify possible treatment when cycles become aberrant. Secondly, efficient gradient
estimation can be used in stochastic approximation to find the optimal rates for restoration of the cycle. We will present
a new result that establishes the conditions for IPA and MVD gradient estimators to be unbiased. We will discuss the
implications of these results in terms of real time computation.

Optimal Liver Cancer Surveillance In Hepatitis C-infected Populations.

Turgay Ayer, Georgia Institute of Technology.

Abstract: Hepatocellular carcinoma (HCC) is the most common type of liver cancer and the fastest-growing cause of
cancer-related deaths in the United States. Most HCC cases are attributed to chronic hepatitis C virus infection, which has
become endemic affecting nearly 3 million Americans. Although surveillance for HCC in hepatitis C patients can improve
survival, the optimal surveillance policies remain unknown. In this study, we first develop a probabilistic natural history
model to capture the natural disease history and then propose a mixed-integer programming (MIP)-based framework to
systematically analyze a rich set of HCC surveillance policies and determine the most cost-effective HCC surveillance
policies with the maximum societal net benefit. We theoretically analyze the HCC surveillance problem and a) identify the
sufficient conditions under which additional surveillance improves the cost-effectiveness of a policy, b) characterize when
the surveillance policies should be adapted to populations with different disease progressions, and c) quantify the trade-off
between decreasing HCC incidence and increasing treatment outcomes. We carefully parameterize our model using a large
clinical trial data, a previously validated simulation model, and published clinical studies. Our numerical analyses lead to
two main results with important policy implications. First, we find that, unlike the current one-size-fits-all type policies,
the optimal HCC surveillance interval should be stratified based on the stage of hepatitis C infection and age. Second,
we find that, in addition to cirrhotic patients, expanding surveillance to patients in earlier stage of hepatitis C infection
improves the cost-effectiveness of HCC surveillance.

Radiation Therapy Design via Stochastic Orders.

Constantine Alexander Vitt, Rutgers University.

Abstract: Radiation therapy design optimizes the radiation dose delivery for the treatment of cancer. We propose a new
design approach based on a probabilistic interpretation of the problem. We consider several stochastic orders for expressing
the medical requirements regarding the dose distributions. The problem formulation facilitates the application of convex
optimization tools and methods while keeping close control on the dose delivery. We propose specialized decomposition
methods for solving the resulting optimization problems and report on the numerical results.

DINNER 6:45 - 9:15 PM Share your memories of Lee Papayanopoulou, Michael N. Katehakis, coordinator.

Organized by: Michael N. Katehakis (Chair), John B. Kostis, Dimitris N. Metaxas
Program Committee: David Dobrzykowski, Kemal Gursoy, Stella Kappodistria, Spiros Papadimitriou, Andrzej Ruszczynski, Flora Spieksma, Yao Zhao
Conference Coordinator: Ms. Luz Kosar luz@andromeda.rutgers.edu

Sponsors: Rutgers Business School, Applied Probability and Data Analytics Laboratory
Institute for Data Science, Learning, and Applications, Department of Management Science & Information Systems
The Cardiovascular Institute of New Jersey, the Center for Dynamic Data Analytics, the Rutgers Center for Operations Research