Mathematics in Biology and Medicine

Workshop – May 11-12, 2017 – Linköping University

Thursday, May 11

8.30-8.40	Opening
8.40-9.25	C-F. Westin
	Probing the microstructural features of the human brain in vivo using multidimensional diffusion MRI
9.25-10.10	J. Hagenblad
	Reading the book of life - Statistical analysis of quarternary data
10.10-10.40	Coffee break
10.40-11.25	U. Wennergren
	Challenges in biology – opportunities to mathematics
11.25-12.10	T. Lindström
	Simulation Modeling for Foot and Mouth Disease
12.10-13.30	Lunch
13.30-13.50	C. Altafini
	Sign patterns of steady state influence matrices of biological and ecological networks
13.50-14.10	A. Eklöf
	Usage of Bayesian networks in analysing secondary extinctions in food webs
14.10-14.30	J. Nordström
	A Stable High Order Accurate Finite Difference Scheme for the Hodgkin-Huxley Equations
14.30-14.50	S. Ghersheen
	Dynamical Behavior of SIR model with coinfection of two viruses
14.50-15.20	Coffee break
15.20-15.40	U. Akram
	Logistics of organic manure for reuse in crop production: A case study in Sweden and Pakistan
15.40-16.00	N-H. Quttineh
	Systems analysis of biogas production based on animal manure - A case study of Västervik region
16.00-16.20	G. Cedersund
	Systems pharmacology: multi-level modelling for improved diagnosis and drug development
16.20-16.40	G. Barabas
	Species packing in nonsmooth competition models

All presentations will be given in lecture room Nobel (BL32).
Coffee / tea is served in Kaffematte.
We will eat lunch together in restaurant Kårallen.

Friday, May 12

8.30-8.40	Discussion
8.40-9.25	T. Ebbers
	Magnetic resonance imaging of the heart and vessels; From Fourier to Poisson
9.25-10.10	M. Karlsson
	Computational Fluid Dynamics in the Heart and the Larger Vessels
10.10-10.40	Coffee break
10.40-11.25	J. Stålhand
	Soft Tissue Modelling
11.25-12.10	T. B. Schön
	On the search for useful representations
12.10-13.30	Lunch
13.30-13.50	J. Wilzén
	Physiologically motivated Gaussian Process Priors for the Hemodynamics in fMRI
13.50-14.10	R. Jaroudi
	Source Localization of Brain Tumors via Reaction-Diffusion Models
14.10-14.30	B. Morén
	Challenges in Using Mathematical Optimization in High Dose-Rate Brachytherapy
14.30-14.50	Q. Ali
	Game Theoretical Model of Yeast Damage Retention Mechanism
14.50-15.20	Coffee break
15.20-15.40	A. Ghosh
	A one dimensional asymptotic model of blood flow through a curved, elastic blood vessel
15.40-16.00	S. A. Nazarov
	Transmission conditions in a one-dimensional model of bi-furcating arteria
16.00-16.20	G. Zavorokhin
	A fractal graph model of capillary type systems
16.20-16.40	F. Berntsson
	A one-dimensional model of a false aneurysm

All presentations will be given in lecture room Nobel (BL32).
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Abstract - Invited Speakers

Magnetic resonance imaging of the heart and vessels; From Fourier to Poisson

Tino Ebbers
Linköping University, Linköping, Sweden

Abstract

Magnetic resonance imaging (MRI) is a medical imaging technique used to acquire images of the anatomy and the physiological processes of the body in both health and disease. By combining strong magnetic fields, radio waves, and field gradients data is measured in the frequency domain, called k-space, which is transformed to the spatial domain. In cardiovascular MRI, the technique is, for instance, used to study scar tissue and perfusion in patients with known or suspected coronary artery disease, and anatomy and blood flow dynamics in complex congenital heart diseases. By adapting the pulse sequence, MRI can be used to image a large variety of parameters, ranging from relaxation times, tissue displacements, blood flow velocity vectors, and turbulence stress tensors. Data processing, analysis and visualization of these often time-resolved three-dimensional datasets can be challenging, however. In this presentation, special focus will be on four-dimensional flow magnetic resonance imaging (4D flow MRI), which enables comprehensive access to time-varying and multidirectional blood flow through the cavities of the heart and great vessels. Different visualization strategies and computation of derived flow parameters, as wall shear stress, relative pressure fields, turbulent stress tensor will be discussed.

Reading the book of life - Statistical analysis of quarternary data

Jenny Hagenblad
Linköping University, Linköping, Sweden

Abstract

Of all the biological sciences genetics is arguably the one that is most tractable mathematically. At its foundation are the four "letters", or bases, of the DNA - A, T, G and C - resulting in a quarternary data system. At each variable position in the DNA, each of the two bases present in an individual will, on average, be interited to half of the offspring, and the probability of different outcomes can easily be calculated as shown by Mendel and others more than 100 years ago.

During the past couple of decades the ease with which genetic data can be acquired has experienced a revolution that more than matches the development of the computational capacity of computers. The resulting amounts of data have required new mathematical approaches to the analysis and interpretation of genetic data. This has allowed us to understand the evolutionary history of species at a much finer detail than before. In this talk I will present both classical and more recent mathematical approaches to the analysis of genetic data within an evolutionary framework.

Computational Fluid Dynamics in the Heart and the Larger Vessels

Matts Karlsson
Linköping University, Linköping, Sweden

Abstract

Combining computer simulations and imaging to create individualized models of the human cardiovascular system has for a long time been a goal in clinical medicine and biomedical engineering. We seek to create such patient specific models of the heart and the arterial tree in order to perform intervention planning as well as follow-up and possibly develop these tools as a diagnostic aid. With the introduction of different imaging techniques such as CT, MRI and 3D ultrasound it is now possible to make more precise 3D geometrical depictions of a specific patient vascular system, this goal has come closer. With a very detailed geometrical model at hand there should a short step towards performing computer simulations, either with fixed or moving walls. However, such models can only be achieved if we utilize the basic principles of fluid dynamics as well as the modelling and simulation capabilities from computational engineering and high performance computing in combination with modern imaging modalities and image processing in unison. In this presentation, we are discussion the fluid mechanics of the flow in the heart and the larger vessels as well as derived or modelled parameters such as wall shear stress and low density lipoproteins (bad cholesterol) together with visualization of invariants of the Reynolds stress tensor.

Simulation Modeling for Foot and Mouth Disease: Overcoming Challenges for Applied Epidemiological Modeling.

Tom Lindström
Linköping University, Linköping, Sweden

Abstract

Stochastic simulation models are powerful tools that can be used to inform policy decisions regarding control actions, identify spatial hotspots, or predict the course of an outbreak. I will discuss some of the challenges involved when developing and implementing such models. I will focus on two projects that primarily considers outbreaks of foot and mouth disease (FMD), a viral disease that infects all cloven hooved animals and is of major concern for the livestock industry. First, I will talk about our ongoing project with the aim of building a disease spread model for continental scale outbreaks in the US (United States Disease Outbreak Simulator, USDOS [1]), and the related model for animal shipments (United States Animal Movement Model, USAMM [2]). I will bring to attention some of the challenges this undertaking has faced, including dealing with data constraints, as well as some computational issues. Secondly, I will discuss a project focused on ensemble modeling (EM) for epidemiology. This work was motivated by the fact that there are several models available for FMD, and they sometimes provide conflicting recommendations. EM offers the ability to use multiple disease spread models collectively [3]. I will present a Bayesian method for this purpose [4], and present some preliminary results that indicate that disease predictions can be improved by using EM rather than a single model.

Keywords: Disease spread modeling, Foot and mouth disease, Animal movement, Bayesian statistics, Ensemble modeling.

References

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On the search for useful representations

Thomas B. Schön[1], Manon Kok[2] and Jeroen D. Hol[3]
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[2]University of Cambridge, Cambridge, United Kingdom.
[3]Xsens Technologies B.V., Enschede, the Netherlands.

Abstract

I will discuss how we can develop useful *representations* (models) capable of explicitly summarizing and explaining the situation at hand based on sensor measurements. The problem of automatically *learning* these representations lies at the heart of this problem. One of the key lessons from modern machine learning is that flexible models often give the best performance. I will show two strategies in how we can find these representations; 1. We derive the entire representation and find the unknown parameters using the measured data. 2. The machines automatically discover the representations that are necessary to solve a particular task (*deep learning*).

As a concrete example where it is very natural for us humans to derive the entire representation is the application of human motion capture using measurements from *inertial sensors* [1, 2]. We have worked on this problem for more than a decade now. I will show how to solve the problem and mention medical applications of this technology like rehabilitation of stroke patients.

In many other applications it is very hard (if not impossible) for us humans to derive competitive representations. For example, when it comes to analyzing images or vast datasets it is currently better to give this task to the machines. Deep learning has *revolutionized* computer vision and machine learning. Based on numerous examples (training data), a deep neural network can, in theory, learn virtually any function, with applications such as describing the content of diverse images, playing games (chess, Go, Poker) or understanding speech. Deep learning is producing the best solutions on many tasks like this at the moment and I will provide a brief introduction to deep learning and show a few intriguing medical results published over the last months [3, 4].

Keywords: Human motion capture, inertial sensors, deep learning.

References

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Soft Tissue Modelling

Jonas Stålhand
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Abstract

Mechanical modelling of soft tissue is a field which is attracting much interest and has been fast growing since the 1970's. The interest is not only driven by the intriguing complex non-linear properties shown by the soft tissue, it is also linked to the realisation that the onset and development of many common diseases are associated with alterations in the tissue mechanics[1].

Tissue modelling is a unique branch of engineering because it concerns living matter which evolves over time and adapts to its environment. The evolution and adaptation are linked to alterations in the micro-structural composition as well as to changes in the organ geometry[2]. The tissue response is controlled by time-dependent and coupled multi-physics processes involving both mechanical, chemical and electro-physiological stimuli. As a consequence, tissue models are usually quite complex and generally solved using numerical methods, e.g. finite elements[3]. In addition, the models typically include a large number of parameters which need to be identified from experiments. The amount of information contained within measurements on human organs are limited, either because the registration must be made in vivo or because it is hard to isolate the tissue response to a single model parameter. This often makes it necessary to use non-linear parameter identification techniques to identify model parameters[4].

This talk will exemplify and elaborate on some of the difficulties in soft tissue modelling based on the authors research. It will also try outline some future challenges within the field.

Keywords: Soft tissue, Model, Multiphysics, Parameter identification

References

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Challenges in biology – opportunities to mathematics

Uno Wennergren
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Abstract

The complexity that appears in biological systems have always been a challenge to understand and to formalize into models, regardless if formulated as mathematical models or symbolic. Yet these biological systems are crucial for us humans since they range from physiology, medicine, epidemiology, food production, animal welfare, species extinctions, biodiversity, pollution and climate change. The last decades, and probably even more so the coming ones, there have been a large shift in how we can perceive and handle such biological systems. Several technological advances have generated tons of data that can feed into models that deal with these biological complexities. It ranges from DNA and cell data, data stored by governments, industry and organisations, satellite data, meteorological data, etc. Hence our perception of how biological systems works do change as well as the possibility to predict, regulate and adapt the systems. Given this mathematics will play a fundamental role. Firstly, our understanding of the dynamics must increase and evolve. It's not only a philosophical question whether biodiversity promotes stability or not. Since we have tons of data we can predict and manage systems and hence our knowledge must evolve in at least the same rate as the technological advances. Secondly, the enormous amount of data and complexity of the models creates a challenge in applied settings and hence statistics, numerical methods, optimizations algorithms, etc. also must evolve to keep up with the technological advances. Finally, human population have increased enormously during the last century and the per capita energy consumption as well. This inevitably emphasize our need to better understand complex biological systems such that we can to predict and manage them to form a sustainable future. Examples will be given on large scale systems.

Probing the microstructural features of the human brain in vivo using multidimensional diffusion MRI

Carl-Fredrik Westin
Harvard Medical School, Boston, USA

Abstract

Diffusion magnetic resonance imaging (dMRI) is an imaging method that uses the diffusion of water molecules to generate contrast in MR images. It allows the mapping of the diffusionprocess of molecules, mainly water, in biological tissues, in vivo and non-invasively. Molecular diffusion in tissues is not free, but reflects interactions with many obstacles, such as macromolecules, fibers, and membranes. Water molecule diffusion patterns can therefore reveal microscopic details about tissue architecture, either normal or in a diseased state. A special kind of dMRI, diffusion tensor imaging (DTI), has been used extensively to map white matter connectivity in the brain.

In this talk I will describe a novel diffusion MR framework for imaging and modeling of microstructure in the brain that we call q-space trajectory imaging (QTI). The QTI framework consists of two parts: encoding and modeling. First we propose q-space trajectory encoding, which uses time-varying gradients to probe a trajectory in q-space, in contrast to traditional pulsed field gradient sequences that attempt to probe a point in q-space. Then we propose a microstructure model, the diffusion tensor distribution (DTD) model, which takes advantage of additional information provided by QTI to estimate a distributional model over diffusion tensors. I will describe how to derive rotationally invariant scalar quantities from the estimated DTD, describing intuitive microstructural tissue features of the human brain, including size, shape, and orientation coherence measures.

Abstract - Contributed Speakers

Logistics of organic manure for reuse in crop production: A case study in Sweden and Pakistan

Usman Akram, Nils-Hassan Quttineh and Uno Wennergren
Linköping University, Linköping, Sweden

Abstract

Sustainable use and reuse of nutrients (nitrogen, phosphorous and potassium), for agricultural productions, are essential for both ecosystem health and food security. Spatio-temporal changes as a result of specialized farming and urbanization have caused a spatial separation of crops, livestock, and humans. The logistic constraints have led to a reduced reuse of organic manure (livestock manure and human excreta). As a result, there are areas of intensive use of mineral fertilizers as well as areas having a surplus of nutrients from the organic manure. This process has given rise to, or risk of, severe eutrophication and food depletion. A high-resolution spatial information of these surpluses and demands lacks in the scientific literature. To eradicate the nutrient emission, and the shortage, the high-resolution spatial analysis is necessary. The analysis forms a baseline for the transport and system solution for a complete reuse of organic manure. In this study, we use high-resolution spatial data on (i) crop areas (ii) livestock numbers and (iii) human population in Sweden and Pakistan. We combine these data with data on crop demand, soil types, nutrient content in manure and human excreta in grids: 5km*5km in Sweden and 10km*10km in Pakistan. Our estimate reveals a surplus or shortage of organic manure -related to the nutrient need of crops- in the grids. Using a mathematical model, we analyze the transports of manure and human excreta to achieve an increased spatial balance in nutrient demand and supply. The results show that the transports and reuse of organic manure reduce the losses of nitrogen, phosphorus, and potassium by; 69%, 100%, 2% in Pakistan and 56%, 100%, 7% in Sweden. Accordingly, the use of mineral fertilizers is reduced by; 30%, 67%, 17% of nitrogen, phosphorus and potassium in Sweden, and 60% of nitrogen in Pakistan.

Keywords: Organic manure, eutrophication, logistics, recycling, food security

Game Theoretical Model of Yeast Damage Retention Mechanism

Qasim Ali and Marija Cvijovic
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Abstract

Damage retention is a crucial step during the division process of a yeast cell. Each cell grows in size to reach a threshold that is followed by its asymmetrical division into a mother and a daughter cell. The division process of the cell is known as budding. Each mother cell has the capacity to bud several daughters during its life time depending upon its efficacy of retaining damage. An efficient damage retention results in a short lifespan of the yeast mother cell. However it ensures a healthy cell progeny. This work is intended to develop a game theoretic model to find a maximum payoff function that is based on reproduction success as well as optimal number of healthy daughters. Two damage retention strategies are introduced, each one is followed by a group of cells. An altruism parameter is introduced to allow each group of cells to decrease their selfless behavior in case of loosing the game. The decrease in the altruism will allow mother cells to show more selfish attitude and therefore decrease the retention capacity of their progeny. This evolutionary mechanism will potentially reach a stable equilibrium state by having desired outcome. The analysis and the experimental validation will be the future focus of the work.

Keywords: yeast, damage retention, evolutionary game theory

Sign patterns of steady state influence matrices of biological and ecological networks: from qualitative to quantitative criteria

Claudio Altafini[1] and Giulia Giordano[2]
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Abstract

In biological and ecological networks, the steady-state influence matrix gathers the signs of steady-state responses to step-like perturbations (or press perturbations, as they are called in the ecological systems literature) affecting the variables. Such signs are difficult to predict a priori, because they result from a combination of direct effects (deducible from the Jacobian of the network dynamics) and indirect effects [1]. We show that for stable monotone or cooperative networks, the sign pattern of the influence matrix can be qualitatively determined based exclusively on the sign pattern of the system Jacobian [2]. For other classes of networks, we propose criteria to assess whether the influence matrix is fully positive: we show that a semiqualitative approach yields sufficient conditions for Jacobians with a given sign pattern to admit a fully positive influence matrix [3], and we also provide quantitative conditions for Jacobians that are translated eventually nonnegative matrices [4]. We present a computational test to check whether the influence matrix has a constant sign pattern in spite of parameter variations, and we apply this algorithm to quasi-Metzler Jacobian matrices, to assess whether positivity of the influence matrix is preserved in spite of deviations from cooperativity.

Keywords: Ecological networks, Biological networks, Press perturbations, Community matrix, Influence matrix, Qualitative approach, Quantitative approach

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Species packing in nonsmooth competition models

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Abstract

Despite the potential for competition to generate equilibrium coexistence of infinitely tightly packed species along a trait axis, prior work has shown that the classical expectation of system specific limits to the similarity of stably coexisting species is sound [1]. A key reason is that known instances of continuous coexistence are fragile, with a tiny alteration of the parameters leading back to the classical limiting similarity predictions. Here we show that robust continuous coexistence can arise if competition between species is modeled as a nonsmooth function of their differences?specifically, if the competition kernel, giving the degree of competition between two phenotypes as a function of their trait values, has a nondifferentiable sharp peak at zero trait difference. We explain the mathematical reasons behind why such kernels lead to such inflated coexistence patterns, and investigate what mechanisms would give rise to nondifferentiability in the first place. The reason turns out to be discontinuous resource use, and we argue that such sudden jumps in the utilization of resources are unrealistic and therefore one should expect kernels to be smooth in reality.

Keywords: competition kernel, continuous coexistence, limiting similarity, trait axis

References

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A one-dimensional model of a false aneurysm

Fredrik Berntsson[1], Vladimir Kozlov[1], Matts Karlsson[1] and Sergey A. Nazarov[2]
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[2]St Petersburg State University, St Petersburg State Polytechnical University, and Institute of Problems of Mechanical Engineering RAS, Russia.

Abstract

A false aneurysm is a hematoma, i.e. collection of blood outside of a blood vessel, that forms due to a hole in the wall of an artery. This represents a serious medical condition that needs to be monitored and, under certain conditions, treated urgently. In this work a one-dimensional model of a false aneurysm is proposed. The new model is based on a one-dimensonal model of an artery previously presented by the authors[1] and it takes into account the interaction between the hematoma and the surrounding muscle material. The model equations are derived using rigurous asymptotic analysis for the case of a simplified geometry.

Even though the model is simple it still supports a realistic behaviour for the system consisting of the vessel and the hematoma. Using numerical simulations we illustrate the behaviour of the model. We also investigate the effect of changing the size of the hematoma. The simulations show that our model can reproduce realistic solutions. For instance we show the typical strong pulsation of an aneurysm by blood entering the hematome during the work phase of the cardiac cycle, and the blood returning to the vessel during the resting phase. Also we show that the aneurysm grows if the pulse rate is increased due to, e.g., a higher work load.

Keywords: False Aneurysm, Elastic Vessel, Asymptotic Analysis

References

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Systems pharmacology: multi-level modelling for improved diagnosis and drug development

Gunnar Cedersund
Linköping University, Linköping, Sweden

Abstract

I will in this presentation give an overview of the different modelling projects I am involved at LiU, ranging from basic biology in different cell types, to diagnosis of diseases in specific organs, monitoring of patients in the intensive care unit, and to improved drug development for autoimmune diseases and type 2 diabetes. All of these models are done using a similar multi-level modelling methodology, involving a systematic testing of mechanistic hypotheses for each sub-system, and a subsequent integration into multi-level models. I will also explain how we identify uniquely identified properties in unidentifiable models, and how this ability is what makes the difference between modelling for its own sake, and usefulness in biomedical applications.

Usage of Bayesian networks in analysing secondary extinctions in food webs

Anna Eklöf
Linköping University, Linköping, Sweden

Abstract

Ecological communities are composed of populations connected in tangled networks of ecological interactions. Therefore, the extinction of a species can reverberate through the network and cause other (possibly distantly connected) species to go extinct as well. The study of these secondary extinctions is a fertile area of research in ecological network theory.

However, to facilitate practical applications, several improvements to the current analytical approaches are needed. In particular, we need to consider that (i) species have different 'a priori' probabilities of extinction, (ii) disturbances can simultaneously affect several species, and (iii) extinction risk of consumers likely grows with resource loss. All these points can be included in dynamical models, which are, however, difficult to parameterize.

Here we advance the study of secondary extinctions with Bayesian networks. We show how this approach can account for different extinction responses using binary – where each resource has the same importance – and quantitative data – where resources are weighted by their importance. We simulate ecological networks using a popular dynamical model (the Allometric Trophic Network model) and use it to test our method.

Dynamical Behavior of SIR model with coinfection of two viruses

Samia Ghersheen, Vladimir Kozlov, Vladimir Tkachev and Uno Wennergren
Linköping University, Linköping, Sweden

Abstract

Viral diseases such as AIDS/ HIV, Dengue fever, Hepatitis B and C are the great threats to human lives and multiple strains of these viruses made it more complicated to control. Multiple viruses are widely studied because of their negative effect on the health of host as well as on whole population. The dynamics of coinfection is important in this case. We formulated a SIR model that describes the coinfection of two viruses in a single host population with logistic growth term. The model describes four classes of population: Susceptible, infected by first virus, infected by second virus, infected by both viruses and completely immune class. We analyzed and proved that all solutions are bounded and all equilibrium points are positive and locally stable except trivial equilibrium. We are investigating the dependence of risk of infection and intensity of infection on carrying capacity. Increase in carrying capacity can lead to increase in infected population without affecting the susceptible population.

Keywords: SIR model, coinfection, carrying capacity, stability

A one dimensional asymptotic model of blood flow through a curved, elastic blood vessel

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Abstract

We derive a one dimensional model of blood flow through an arbitrarily curved blood vessel having anisotropic, laminar and elastic wall structure. The blood vessel is assumed to have a circular cross section of varying radius along its length while having a general curvature and torsion for its given centre line. The vessel wall has several anisotropic layers of variable thickness. We take into account the reaction of the surrounding tissue on the vessel wall and the blood flow. We formulate a suitable moving frame of reference in order to better suit the geometry in consideration to have simpler expressions. For modeling the wall, constitutive relations of elasticity and Newton's second law are used to obtain the partial differential equation system for the displacement vector field of the wall material. A dynamic boundary condition and a kinematic no-slip boundary condition are assumed on the inner surface of the wall which help in coupling the equations with the linearized Navier-Stokes equation governing the blood flow within the vessel. We assume the thickness of the wall of the vessel to be small compared to the radius of any cross section, while the radius is also taken to be small compared to the length of the vessel. Under such assumptions, we perform dimension reduction twice to obtain a one dimensional model for the blood flow.

Keywords: Haemodynamics, Elasticity, Fluid mechanics, Asymptotic analysis.

Source Localization of Brain Tumors via Reaction-Diffusion Models

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Abstract

In this work we discuss a mathematical method for the inverse problem of locating the brain tumor source (origin) based on the reaction-diffusion model. Our approach consists in recovering the initial spatial distribution of the tumor cell density starting from a later state, estimated from a medical image. We use a regularization method posing the inverse problem as a sequence of well-posed forward problems. Simulations with synthetic data demonstrate the accuracy of our approach for locating brain tumor sources. We illustrate our results with 3-dimensional simulations of the tumor at different stages of its growth for two types of data i) the 3d Shepp-Logan phantom and ii) an MRI T1-weighted brain scan from the Internet Brain Segmentation Repository (IBSR). These simulations are numerically implemented using a standard finite difference discretization of the space and time-derivatives, generating a simplistic approach that performs well.

This work is a joint collaboration with George Baravdish (Linköping University), B. Tomas Johansson (Linköping University) and Freddie Åström (Heidelberg University). [1]

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Challenges in Using Mathematical Optimization in High Dose-Rate Brachytherapy

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Abstract

High dose-rate brachytherapy is a method of radiation therapy, used in cancer treatment, where the radiation source is placed inside or close to a tumour. In addition to give a high enough dose to the tumour it is also important to spare nearby organs and healthy tissue. Mathematical optimization is used increasingly at clinics in the planning of the treatment. Commonly, the planning is done while the patient is anesthetised which makes it important to be able to solve the optimization model fast.

The recommended way to clinically evaluate dose plans is based on the concept of dosimetric indices, which is related to dose-volume histogram. A dosimetric index quantifies the discretised portion of the tumour that gets at least (or for organs, at most) the prescribed dose. One can construct optimization models for dose planning which explicitly constrains the values of dosimetric indices, but such models include a large number of binary indicator variables and become very hard to solve to optimality within the time limit with standard software [1, 2]. A promising alternative is to make nonlinear continuous approximations of the indicator functions [3].

Most optimization models for dose planning are based on the average dose to volumes, such as the tumour and organs, and no model takes locality of the dose into account explicitly. Clinically, this aspect is however a reason of concern becuase of risk for complications caused by locally high doses (which can cause necrosis). The dose plan is therefore manually adjusted if the contiguous volumes with a high dose (e.g. 200% of the prescribed dose) are too large. We will discuss how locality of the dose distributions can be included into an optimization model.

Keywords: Brachytherapy, Mathematical Optimization, Mixed Integer Programming, Dosimetric Index, Dose Volume Histogram, Dose Heterogenity

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Transmission conditions in a one-dimensional model of bifurcating arteria

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Abstract

This work was done in cooperation with V.A. Kozlov.

Development of adequate one-dimensional models of circulatory blood system meets several serious obstacles and we will discuss one very particular question related to bifurcation nodes of the arterial tree. Although the blood vessel walls are strongly elastic [3] and blood is a viscoelastic liquid [4], we consider the Stokes (or Navier-Stokes) equations in a junction of three ($\alpha = 0, \pm$) thin, of radius h, finite tubes with rigid walls meeting each other inside a small, of diameter $O(h)$, node. Neglecting the elastic properties of walls for a while, see discussion of those in [5], we employ the standard Reynolds one-dimensional model of flow in the tubes, that is, a second-order ordinary differential equation on the intervals $\Upsilon_\alpha = (0, L_\alpha) \ni z_\alpha$. The necessary transmission conditions at the junction point with the local coordinates $z_\alpha = 0$ are found with the help of the method of matched asymptotic expansions and by means of the pressure drop matrix [2] describing the boundary layer phenomenon in the vicinity of the three-dimensional bifurcation node of the arteria. As a result, we obtain transmission conditions which provide the error estimate of order $e^{\delta/h}$, $\delta > 0$, but differ from the classical Kirchhoff conditions supporting only a poor proximity order h. At the same time, based on the concept [1] of one-dimensional asymptotic images of thin spacial objects, we introduce the effective length $L^h_\alpha = L_\alpha + hl_\alpha$ of vessels such that solving the Reynolds equations in the intervals $\Upsilon^h_\alpha = (0, L^h_\alpha)$ with the Kirchhoff transmission conditions keeps the same approximation order $e^{\delta/h}$. The length increments hl_α are expressed in terms of the above-mentioned matrix of pressure drops and a computational scheme for this matrix will be discussed as well.

Keywords: Blood vessel, bifurcations of blood vessel, transmission condition

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A Stable High Order Accurate Finite Difference Scheme for the Hodgkin-Huxley Equations

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Abstract

A novel approach for simulating potential propagation in neuronal branches with high accuracy is developed [1]. The method relies on high-order accurate difference schemes using the summation-by-parts operators with weak boundary and interface conditions [2]. This work is the first demonstrating high accuracy for that equation. Several boundary conditions are considered including the non-standard one accounting for the soma presence, which is characterized by its own partial differential equation. Well-posedness for the continuous problem as well as stability of the discrete approximation is proved for all the boundary conditions. Gains in terms of CPU times are observed when high-order operators are used, demonstrating the advantage of the high-order schemes for simulating potential propagation in large neuronal trees.

Keywords: potential propagation, neuronal branches, large neuronal trees, Hodgkin-Huxley equations, soma, high-order accurate, well-posed, stability, summation-by-parts, weak boundary conditions, weak interface conditions

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Systems analysis of biogas production based on animal manure – A case study of Västervik region

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Abstract

Biogas is a flexible source of renewable energy which can provide many ecological and social benefits. It can be produced by anaerobic digestion of different types of biomass, e.g. household organic waste ("gröna påsen"), waste from food processing industry and from crops such as maize. Another source of substrate for biogas plants is animal manure that is produced in the agricultural sector. It is considered advantageous to treat the manure anaerobically before the nutrients are recycled back to farmland, as the digestion results in a reduction of the volume to be transported, the nutrients become more available for the crops and potential greenhouse gas emissions from the manure storage and spreading can be reduced. In addition, a renewable fuel is produced.

In Västervik municipality, the existing biogas plant needs to be expanded to meet the need for renewable fuel in the region. In addition, there are several animal farms in the region which produce a lot of manure. Hence, a decision has been made to plan for a new biogas plant in order to utilize the manure that exists in the municipality. Besides a biogas plant, we consider the possibility of building so called Ensy plants. Ensy plants make use of an interesting technique for processing manure; basically, the nutrients are separated from the liquids, and the result is a more compact (dryer) fertilizer which is easier and cheaper to distribute.

The objective here is to identify the optimal location for the new biogas plant, and we propose a mathematical optimization model for this problem where several important criteria are considered; For example, the size of the biogas plant, where should we build Ensy plants, amounts of manure that are going to be processed at the biogas plant and Ensy plants, as well as relevant aspects related to environmental performance.

Keywords: Organic manure, logistics, recycling, optimization, MIP

Physiologically motivated Gaussian Process Priors for the Hemodynamics in fMRI

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Abstract

The hemodynamic system that relates neural activity and BOLD fMRI signal is not known. The problem of jointly estimate the hemodynamics and the activity in task based fMRI is called joint detection estimation (JDE). We propose a new Bayesian model for task fMRI data with the following features:

- joint estimation of brain activity as well as the underlying hemodynamics
- the hemodynamics is modelled with an Gaussian process (GP) prior with physiological information
- predicted BOLD is not necessarily a linear time-invariant (LTI) system

Previous literature in the field use a LTI system where the activity paradigm is convolved with an estimated hemodynamic response function (HRF) [1, 2, 3]. The unknown HRF is assigned a GP prior with zero mean. In our model, a GP prior is placed directly on the predicted BOLD time series, where the mean function of the GP is a chosen physiological model for the BOLD response. The prior mean function may be a standard LTI system based on a canonical HRF, or a more elaborate physiological model such as the Balloon model [4]. The posterior distribution for the predicted BOLD can deviate from the prior if data is not in agreement with the prior mean.

Results on simulated data show that even if we use an erroneous prior for the GP, the proposed model is still able to discriminate between active and non-active voxels in a satisfactory way and is able to discover the true functional form of the underlying hemodynamics. The usefulness of the proposed model is demonstrated on real fMRI data, where our Gaussian process model finds activity where a baseline model does not. The discovered hemodynamics shows a time varying behavior, which cannot easily be captured with traditional JDE models which are based on LTI system.

Keywords: fMRI, Hemodynamics, Gaussian processes

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A fractal graph model of capillary type systems

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Abstract

We consider blood flow in a vessel with an attached capillary system. The latter is modeled with the help of a corresponding fractal graph whose edges are supplied with ordinary differential equations obtained by the dimension-reduction procedure from a three-dimensional model of blood flow in thin vessels. The Kirchhoff transmission conditions must be satisfied at each interior vertex. The geometry and physical parameters of this system are described by a finite number of scaling factors which allow the system to have self-reproducing solutions. Namely, these solutions are determined by the factors' values on a certain fragment of the fractal graph and are extended to its rest part by virtue of these scaling factors. The main result is the existence and uniqueness of self-reproducing solutions, whose dependence on the scaling factors of the fractal graph is also studied. As a corollary we obtain a relation between the pressure and flux at the junction, where the capillary system is attached to the blood vessel. This relation leads to the Robin boundary condition at the junction and this condition allows us to solve the problem for the flow in the blood vessel without solving it for the capillary system.

The present work is supported by Linköoping University and RFBR grant 16-31-60112.

Keywords: fractal graph, blood vessel, capillary system, Reynolds equation.

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