Workshop
on
Optimization in Medicine

Center for International Mathematics

Thematic term on Optimization

July 20-22, 2005
IBILI (Institute of Biomedical Research in Light and Image)
University of Coimbra, Portugal

http://www.mat.uc.pt/tt2005/om

Workshop on Optimization in Medicine

Center for International Mathematics

Thematic term on Optimization

July 20-22, 2005

IBILI (Institute of Biomedical Research in Light and Image)

University of Coimbra, Portugal

http://www.mat.uc.pt/tt2005/om

Scope: The study of computing in medical applications has opened many challenging issues and problems for both the medical computing and mathematical communities. This workshop is intended to foster communication and collaboration between researchers in the medical computing community and researchers working in applied mathematics and optimization.

Mathematical techniques (continuous and discrete) are playing a key role with increasingly importance in understanding several fundamental problems in medicine.

For instance, mathematical theory of nonlinear dynamics and discrete optimization has been used to predict epileptic seizures. Next to stroke, epilepsy is among the most common disorders of the nervous system. Measures derived from the theory of nonlinear dynamics and discrete optimization techniques are used for prediction of impending epileptic seizures from analysis of multielectrode electroencephalographic (EEG) data.

Several examples of the use of mathematics in medicine can be found in recent cancer research. Sophisticated mathematical models and algorithms have been used for generating treatment plans for radionuclide implant and external beam radiation therapy. With Gamma Knife treatment, for example, optimization techniques have been used to automate the treatment planning process.

Optimization has been used to address a variety of medical image registration problems. In particular, specialized mathematical programming techniques have been used in a variety of domains including the rigid alignment of primate autoradiographs and the non-rigid registration of cortical anatomical structures as seen in MRI.

The technical part of the conference will be organized around seven invited talks, describing recent relevant applications of optimization to medicine. These talks will describe the state-of-the-art about the use of optimization in medicine and outline open research avenues in this field. The invited presentations will be complemented by sessions of contributed talks.

Organizers

Carlos J.S. Alves (Tech. Univ. Lisbon, Portugal)
Ana Luísa Custódio (New Univ. Lisbon, Portugal)
Panos M. Pardalos (Univ. Florida, USA)
Luís Nunes Vicente (Univ. Coimbra, Portugal)

Sponsors

Centro Internacional de Matemática

Centro de Matemática da Universidade de Coimbra

Centro de Matemática e Aplicações do IST

Fundação Calouste Gulbenkian

Fundação para a Ciência e a Tecnologia

Instituto Biomédico de Investigação da Luz e da Imagem

Other Events

Workshop on Optimization in Finance
School of Economics, University of Coimbra, July 5-8, 2005
`http://www.mat.uc.pt/tt2005/of`

Summer School on Geometric and Algebraic Approaches for Integer Programming
Faculty of Science, University of Lisbon, July 11-15, 2005
`http://www.mat.uc.pt/tt2005/ss`

Workshop on PDE Constrained Optimization
Tomar, July 26-29, 2005
`http://www.mat.uc.pt/tt2005/pde`

PROGRAM AT GLANCE

Wednesday 20

9:00–9:45	Registration
9:45–10:00	Opening Remarks
10:00–11:00	Invited Speaker I1
11:00–11:30	Coffee Break
11:30–12:30	Invited Speaker I2
12:30–14:00	Lunch
14:00–15:00	Invited Speaker I3
15:00–15:30	Coffee Break
15:30–17:30	Session S1
18:00	Visit to (Old) University of Coimbra

Thursday 21

9:00–10:00	Invited Speaker I4
10:00–10:30	Coffee Break
10:30–12:30	Session OS1
12:30–14:00	Lunch
14:00–15:00	Invited Speaker I5
15:00–16:00	Invited Speaker I6
16:00–16:30	Coffee Break
16:30–18:30	Session S2
19:30	Conference Dinner

Friday 22

9:30–10:30	Invited Speaker I7
10:30–11:00	Coffee Break
11:00–12:30	Session OS2
12:30–14:00	Lunch
14:00–16:00	Session S3
16:00–16:30	Coffee Break
17:00	Visit to Roman Ruins (Conimbriga)

Wednesday 20

9:00–9:45 **Registration** – Foyer

9:45–10:00 **Opening Remarks** – Auditorium

Invited Speaker I1 – Auditorium

10:00–11:00 **Michael C. Ferris**, Univ. Wisconsin, USA
Optimization of gamma knife radiosurgery

11:00–11:30 **Coffee Break**

Invited Speaker I2 – Auditorium

11:30–12:30 **Jari P. Kaipio**, Univ. Kuopio, Finland
Optimization and optimal control in high intensity ultrasound surgery

12:30–14:00 **Lunch**

Invited Speaker I3 – Auditorium

14:00–15:00 **Alfred K. Louis**, Univ. Saarbrücken, Germany
Optimal reconstruction kernels in medical imaging

15:00–15:30 **Coffee Break**

Contributed Session – S1 – Auditorium

15:30–16:00	**Matthias Ehrgott**, Univ. Auckland, New Zealand *Beam selection in radiotherapy design*
16:00–16:30	**Anton Schiela**, Konrad Zuse Inst., Berlin, Germany *A function space oriented interior point optimization algorithm for hyperthermia treatment planning*
16:30–17:00	**Gonçalo Valadão**, Inst. Telecomunicações, IST, Portugal *Discontinuity preserving phase unwrapping using graph cuts*
17:00–17:30	**Andrzej Cegielski**, Univ. Zielona Gora, Poland *Projection methods for large scale inconsistent linear split feasibility problems*

18:00 **Visit to (Old) University of Coimbra**

Thursday 21

Invited Speaker I4 – Auditorium

9:00–10:00	**Leon D. Iasemidis**, Arizona State Univ., USA *Optimization in epilepsy*

10:00–10:30 **Coffee Break**

Organized Session – **OS1** – Auditorium

Organizer: **Tuong Ha-Duong**, Univ. Tech. Compiègne, France

10:30–11:00	**Abdel El Badia**, Univ. Tech. Compiègne, France *On an inverse EEG problem*
11:00–11:30	**Carlos J.S. Alves**, CEMAT, Tech. Univ. Lisbon, Portugal *A note on the determination of dipolar sources in EEG and complex root finding*
11:30–12:00	**Sylvain Baillet**, Cognitive Neuroscience & Brain Imaging Lab., France *Tackling complexity in brain functional imaging with high-temporal resolution*
12:00–12:30	**Bilal Atfeh**, INRIA Sophia Antipolis, France *Bounded extremal and Cauchy-Laplace problems on 3D spherical domains*

12:30–14:00 **Lunch**

Invited Speakers I5, I6 – Auditorium

14:00–15:00	**Anand Rangarajan**, Univ. Florida, USA *Optimization in medical imaging registration*
15:00–16:00	**Eva K. Lee**, Georgia Inst. Technology, USA *Integer programming in radiation therapy*

16:00–16:30 **Coffee Break**

Contributed Session – **S2** – Auditorium

16:30–17:00	**Karine Deschinkel**, PRiSM Laboratoire d'Informatique, France *Overview of optimization problems in HDR brachytherapy*
17:00–17:30	**François Galéa**, PRiSM, Univ. Versailles, France *A continuous tabu search method for catheter placement optimization in HDR brachytherapy*
17:30–18:00	**Anand Srivastav**, Univ. Kiel, Germany *LP based randomized re-construction of seeds in brachytherapy*
18:00–18:30	**Abderrahmane Habbal**, INRIA, Univ. Nice, France *Tumoral angiogenesis modeled as a Nash game*

19:30 **Conference Dinner** – Quinta das Lágrimas

Friday 22

Invited Speaker I7 – Auditorium

9:30–10:30 **Horst W. Hamacher**, Univ. Kaiserslautern, Germany
Multicriteria optimization in radiation therapy

10:30–11:00 **Coffee Break**

Organized Session – OS2 – Auditorium

Organizer: **Ariela Sofer**, George Mason Univ., USA

11:00–11:30 **Michael C. Ferris**, Univ. Wisconsin, USA
Fractionation in radiation treatment planning

11:30–12:00 **Fredrik H. Carlsson**, Royal Inst. Technology (KTH), Sweden
Iterative regularization in IMRT optimization

12:00–12:30 **Ariela Sofer**, George Mason Univ.
Optimization of radiofrequency ablation for the treatment of tumors

12:30–14:00 **Lunch**

Contributed Session – S3 – Auditorium

14:00–14:30 **Paula Lopes**, Univ. Coimbra, Portugal
On the application of the rough set approach in medicine: Corticotherapy into sarcoidosis

14:30–15:00 **Giandomenico Mastroeni**, Univ. Pisa, Italy
Some remarks on separation methods for classification problems

15:00–15:30 **Antonio Fuduli**, Univ. Calabria, Italy
Semi-supervised classification by nonsmooth nonconvex optimization

15:30–16:00 **Mario Rosario Guarracino**, ICAR-CNR, Italy
A classification method based on generalized eigenvalue problems

16:00–16:30 **Coffee Break**

17:00 **Visit to Roman Ruins (Conimbriga)**

Titles and Abstracts – Invited Talks

Optimization of gamma knife radiosurgery

Michael C. Ferris

The Gamma Knife is a highly specialized treatment unit that provides an advanced stereotactic approach to the treatment of tumors, vascular malformations, and pain disorders within the head. Inside a shielded treatment unit, beams from 201 radioactive sources are focused so that they intersect at the same location in space, resulting in a spherical region of high dose referred to as a shot of radiation. The location and width of the shots can be adjusted using focusing helmets. By properly combining a set of shots, larger treatment volumes can be successfully treated with the Gamma Knife. It is therefore possible to automate the treatment planning process. For each patient, an optimization seeks to produce a dose distribution that conforms closely to the treatment volume. The variables in the optimization can include the number of shots of radiation along with the size, the location, and the weight assigned to each. Formulation of such problems using a variety of mathematical programming models is described, and the solution of several test and real-patient examples is demonstrated.

Multicriteria optimization in radiation therapy

Horst W. Hamacher

Radiation therapy is one of the most frequently used tools in fighting cancer. Several mathematical optimization problems need to be solved to find for each patient the best possible therapy, include the following:

- At which angles should the radiation gantry stop (geometry or angle problem)?
- Which kind of intensity should be sent off at each of the angles to achieve a conformal radiation (intensity problem)?
- How should the radiation be implemented using multileaf collimators (MLC problem)?

All of these problems are at this point of time only partially solved. Since the evaluation of the decisions is in all of these cases dependent on more than one objective, it is obvious, that a multicriteria approach is useful in many instances. The mathematical challenge in this approach is that one is dealing with large scale problems and that a finite representative set of all Pareto optimal solutions is needed in order to help the radiation planner. In the talk, recent results in solving radiation problems in a multicriteria environment will be presented.

Optimization in epilepsy

Leon D. Iasemidis

Epileptic seizures are manifestations of intermittent spatio-temporal transitions of the human brain from chaos to order. These transitions can be quantified by measures from nonlinear dynamics, namely Lyapunov exponents and correlation integrals, estimated from the electrical activity (EEG) of the brain over time at electrode sites overlying the epileptogenic zone as well as normal brain areas. By analysis of the above nonlinear dynamical measures, it has been shown that the core of these transitions is the progressive entrainment of critical brain sites by the epileptogenic focus long prior to the occurrence of an epileptic seizure. The use of optimization techniques (i.e., quadratic integer programming) for the selection of the critical brain sites can lead to long-term prediction of impending epileptic seizures, as well as to the localization of the epileptogenic focus. Both issues are of tremendous clinical and scientific importance. The combination of techniques from nonlinear dynamics and optimization can be used for prediction of upcoming transitions in other complex biological and physical systems that undergo intermittent spatio-temporal transitions.

Optimization and optimal control in high intensity ultrasound surgery

Jari P. Kaipio

High intensity focused ultrasound (HIFU) has been long planned to be used in treating tumors. This is to be distinguished from hyperthermia, in which the tissue is moderately heated to enhance the effect of radiotherapy. In HIFU the tissue is heated to 60 - 95 degrees so that the thermal dose produces a lesion. The treatment is carried out by placing from tens to hundreds of ultrasound transducers around the relevant part of the patient boundary. Then the phases and the amplitudes of the transducers are controlled in such a fashion that ideally only the tumor is destroyed while the healthy tissue is not harmed. The associated optimization problem for temporal transducer evolutions under a number of constraints is heavily nonlinear and involves thousands of unknowns. We treat both the feedforward optimization problem as well as the feedback problem with magnetic resonance imaging based state observations.

Integer programming in radiation therapy

Eva K. Lee

In recent years, technical advances in medical devices have led to improved delivery of radiation therapy treatment to cancer patients. These advances call for a renewed emphasis on developing sophisticated methods for designing treatment plans. In this talk, we will give an overview of the issues involved in treatment planning, and describe the use of sophisticated mathematical models and algorithms that have been demonstrated to be effective for treatment planning.

Brachytherapy is a radiation treatment that involves the placement of encapsulated radionuclides (“seeds”) within or near a tumor. We will illustrate the use of mixed integer programming (MIP) in designing clinically relevant brachytherapy treatment plans, and demonstrate the challenges in the solution process. We also will highlight how tumor shrinkage and movement can be managed efficiently in the planning process.

In contrast to brachytherapy, external beam radiotherapy involves the use of radiation beams that traverse from a source external to the body, through healthy tissue, to access the tumor site. An advanced form of external beam radiation therapy, known as intensity-modulated radiotherapy (IMRT), allows each radiation beam to be subdivided into tiny "beamlets". This enables a high degree of variation/modulation of the intensity within each beam. Appropriate use of IMRT has the potential to lead to substantially better treatment than was previously possible. However, the high level of variation leads to challenging issues in treatment planning. We will describe large-scale MIP models for IMRT treatment planning designed to find the "optimal" configuration of beam angles and beamlet intensities so as to deliver a necrotic dose of radiation to the tumor itself, while limiting radiation to healthy tissue.

Optimal reconstruction kernels in medical imaging

Alfred K. Louis

In medical imaging like x-ray tomography or MRI the searched-for information has to be recovered from the measured data. Nowadays typically one reconstructs the object, either in two or three dimensions and displays the images on a screen. The evaluation is completely left to the physician. We present a technology to derive reconstruction algorithms for different imaging technologies like 3D cone beam tomography and EPRI. To speed up the computation special features of the data assembling are used. Furthermore we consider the fact that for analyzing the images only moments of them are sometimes used. We present optimal strategies for their reconstruction. Real data applications in 3D x-ray CT are presented.

Optimization in medical imaging registration

Anand Rangarajan

Registration refers to the process of aligning two or more images with minimum shape difference being the alignment criterion. In medical imaging, the problem of registering multiple images frequently arises. Since the images can be acquired from different modalities (PET, fMRI) or from different subjects, the task of medical image registration can be quite challenging. Due to the natural shape differences that are manifest across subjects, inter-subject image registration forces us to use non-rigid alignment criteria. In our formulation of this problem, we first select a set of shape features resulting in two sets of features, one from each image. Then we try to find the smallest shape deformation that can approximately take one set of shape features onto the other. If we knew the counterpart in set two of each shape feature in set one, the estimation of the minimum shape difference would be reasonably straightforward. Since this information is unknown a priori, we attempt to discover the feature counterparts while minimizing the shape difference. The result is an integrated optimization algorithm which simultaneously estimates the feature counterparts and the shape deformation that lead to best alignment. We demonstrate the application of this algorithm in a variety of domains including the rigid alignment of primate autoradiographs and the non-rigid registration of cortical anatomical structures as seen in MRI.

Titles and Abstracts – Talks

A note on the determination of dipolar sources in EEG and complex root finding

Carlos J.S. Alves

In a recent work [El Badia and Ha-Duong 2000], El Badia and Ha-Duong presented new techniques to solve an inverse problem in potential theory that consisted in the determination of the intensity and location of dipolar sources, with applications in electroencephalography. In this talk we establish a connection between the methods presented in [El Badia and Ha-Duong 2000] and numerical methods that have been developed by Kravanja et al. (e.g. [Kravanja and Van Barel 1999]), in the context of complex root finding, which are developments of the work by Delves and Lyness [Delves and Lyness 1967].

Bounded extremal and Cauchy-Laplace problems on 3D spherical domains

Bilal Atfeh

When facing the inverse EEG problem of locating current sources in the brain, one first has to solve the issue of propagating the available measures from a part of the scalp to the cortex. This raises a Cauchy problem for Dirichlet-Neumann data and Laplace operator, which can be handled in spherical domains and for which we propose a regularization scheme based on the resolution of an approximation problem. We consider the preliminary case of the unit sphere $\mathbb{S}$, where the issue is to approximate in ℓ_2 norm a $\mathbb{R}^3$-valued vector field defined on one hemisphere by (the trace of) the gradient of a function that is harmonic in the unit ball $\mathbb{B} \subset \mathbb{R}^3$, where its norm is majorised on the other hemisphere. We will make precise the links with the EEG problem. Then we will provide and explain well-poisedness and constructive results concerning the above extremal problem, and show a number of numerical experiments.
Joint with: L. Baratchart, J. Leblond, and J.R. Partington

On an inverse EEG problem

Abdel El Badia

In this talk we consider an inverse EEG problem. A uniqueness result is established and a local Lipschitz stability is discussed. Assuming the number of dipoles bounded by a given integer M, we propose an algebraic algorithm which allows us to estimate the number, the locations and moments of dipoles. Using special functions, we propose a global Lipschitz stability estimate for dipolar sources.

Tackling complexity in brain functional imaging with high-temporal resolution

Sylvain Baillet

Recent advances in brain functional imaging allow the estimation of the cortical distribution of neural currents from EEG and MEG scalp recordings. Because this problem is highly underdetermined, this poses quite a few issues in terms of modeling, estimation and optimization. We will discuss several of these aspects by introducing compact parametric multipolar models of distributed brain activity and adapted procedures for statistical inference. As a consequence to high-temporal resolution, large sequences of brain activation images need to be subsequently explored. We will also introduce feature extraction and analysis approaches to this problem.

Iterative regularization in IMRT optimization

Fredrik H. Carlsson

In beamlet-based intensity-modulated radiation therapy optimization, the machine settings are determined from a conversion of the optimal fluence profiles. The inherent ill-conditioning of the problem, resulting in jagged optimal profiles, is a disadvantage in the conversion step. We utilize iterative regularization of a quasi-Newton method to create high-quality non-jagged profiles suitable for conversion. For the five clinical cases considered, we found that converting the smooth profiles generated with our regularization scheme produces plans that outperform the plans obtained by converting the jagged optimal fluence profiles.

Joint with: Anders Forsgren

Projection methods for large scale inconsistent linear split feasibility problems

Andrzej Cegielski

Let $C \subset \mathbb{R}^n$ be a closed convex subset, A – an $n \times m$ real matrix and $b \in \mathbb{R}^m$. Consider the following linear split feasibility problem (LSFP):

$$\text{find } x \in C \text{ such that } A^\top x \leq b, \tag{1}$$

if such x exist. The problem has lot of applications, e.g., computed tomography and intensity modulated radiation therapy can be modeled as a large scale inconsistent LSFP. We study projection methods for the LSFP which generate a sequence (x_k) by the following iterative scheme:

$$x_{x+1} = T(x_k), \tag{2}$$

where $T : \mathbb{R}^n \to \mathbb{R}^n$,

$$T(x) = P_C(x - \mu\gamma(x)Aw(x)), \tag{3}$$

where $\mu \in [0, 2]$ is a relaxation parameter, $\gamma : C \to \mathbb{R}_+$ is a step size function and $w : C \to \mathbb{R}^m_+$ is a weight operator. The simultaneous projection method ([Butnariu and Censor 1990] and [De Pierro and Iusem 1985]), the surrogate constraints method ([Yang and Murty 1992]) and the CQ -method ([Byrne 2002]) applied to problem (1) are special cases of our method. We study the Fejér monotonicity of method (2)-(3) with respect to Fix T and the convergence of the method in dependence of the step size γ and of the weight operator w.

Overview of optimization problems in HDR brachytherapy

Karine Deschinkel

Brachytherapy is a medical treatment process, based on the use of radioactive sources, which are placed within the patientś body, in order to submit a curative radiation dose to a cancerous tumor. High dose rate brachytherapy makes use of devices called remote afterloader which are able to place a single radioactive source along catheters or applicators. The source may be stopped at many locations (dwell positions) within a catheter during a given time called dwell time. The problem is to determine the optimal position and the number of catheters, and jointly the optimum dwell times at each dwell positions of each selected catheters such that the resulting dose distribution fulfills the clinical criteria prescribed. These criteria include constraints on the prescribed dose to the tumor, dose uniformity, maximal dose to organs at risk, and falloff dose to the normal tissue around the tumor. After a short description of the different steps of the treatment process, this talk gives an critical overview of models and optimization methods involving in HDR brachytherapy. First we present the type of constraints that are used to express the clinical criteria, and the type of indexes that are proposed to measure the quality of the resulting dose. Then we discuss on the two main optimization problems in HDR Brachytherapy: catheters placement and dose optimization. Finally we analyze the implemented methods in the HDR brachytherapy treatment planning systems and deduce directions of future works.
Joint with: François Galéa and Catherine Roucairol

Beam selection in radiotherapy design

Matthias Ehrgott

The optimal design of a radiotherapy treatment depends on the collection of directions from which radiation is focused on the patient. These directions are manually selected by a physician and are typically based on the physiciansś previous experiences. Once the angles are chosen, there are numerous optimization models that decide a fluency pattern (exposure times) that best treats a patient. So, while optimization techniques are often used to decide the length of time a patient is exposed to a high-energy particle beam, the directions themselves are not optimized. The problem with optimally selecting directions is that the underlying mixed integer models are well beyond our current solution capability. We present a rigorous mathematical development of the beam selection problem that provides a unified framework for the problem of selecting beam directions. This presentation provides insights into the techniques suggested in the literature and highlights the difficulty of the problem. Second, we compare several techniques head-to-head on clinically relevant, two-dimensional problems.
Joint with: Allen Holder

Fractionation in radiation treatment planning

Michael C. Ferris

Radiotherapy treatment is often delivered in a fractionated manner over a period of time to increase the probability of controlling the tumor and decrease damage to normal tissues surrounding the tumor. However, movement of the patient or the internal organs during or between treatment sessions can result in failure to deliver adequate radiation to the tumor (leading to recurrence of the disease) or to painful and debilitating damage to surrounding tissues. Even before the treatment starts, the physician faces uncertainty in prescribing the radiation dose, because the extent of the cancerous cells is often not known with complete precision.

Emerging delivery devices are able to determine the actual dose that has been delivered at each stage facilitating the use of adaptive treatment plans that compensate for errors in delivery. In our work we attempt to take uncertainty into account at the planning stage, and develop a technique that allows fractionation to decrease errors, rather than increase them.

We formulate a model of the day-to-day planning problem as a stochastic program and exhibit the gains that can be achieved by incorporating uncertainty about errors during treatment into the planning process. Due to size and time restrictions, the model becomes intractable for realistic instances. We show how heuristics and neuro-dynamic programming can be used to approximate the stochastic solution, and derive results from our models for realistic time periods. These results allow us to generate practical rules of thumb that can be immediately implemented in current planning technologies.

Joint with: Meta M.Voelker

Semi-supervised classification by nonsmooth nonconvex optimization

Antonio Fuduli

The goal of semi-supervised classification is to use unlabeled data to improve the generalization. Most of the learning models apply inductive inference where a decision function is derived from input data (training set) and this function is further applied to predict output values for new input data. The model is created without taking into account any information about new data (testing set). This is the case of a standard Support Vector Machine (SVM).

In the transductive inference methods, instead, the decision function is derived utilizing also additional information related to the testing set. This is the case of the Transductive Support Vector Machine (TSVM) where some knowledge on the testing set is taken into account during the training procedure.

In this talk we propose to use TSVM to solve semi-supervised classification problems. In particular in the TSVM we looks for a hyperplane which is far away from the labeled and unlabeled points. The objective function of TSVM seems to be appropriate but it is nonconvex and nonsmooth and thus difficult to minimize. We optimize this function using nonsmooth techniques.

Finally we present some preliminary numerical results obtained by running the proposed method on some standard test problems drawn from the binary classification literature.

Joint with: Annabella Astorino

A continuous tabu search method for catheter placement optimization in HDR brachytherapy

François Galéa

Catheters placement in high dose rate (HDR) brachytherapy still relies on the application of the rules determined by outdated dosimetry systems, such as the Paris system. Most of the recent research has been focused on the optimization of dwell times, whereas the catheter placement determination schemes still do not take into account the use of modern techniques, and particularly the use of HDR remote afterloaders.

In this talk, we present a methodology for determining a suitable placement of the catheters, making use of a tabu search method with continuous variables.

The major difficulty for implementing metaheuristics with continuous variables concerns the unavailability of a simple neighborhood function. This is due to the fact that in most cases, the objective function cannot be written as a simple analytic expression. After a characterization of the difficulties specific to continuous problems, we describe the algorithms proposed within the framework of a Tabu search method.

Joint with: Gilbert Boisserie

A classification method based on generalized eigenvalue problems

Mario Rosario Guarracino

Binary classification refers to supervised techniques that permit to split a set of test points in two classes, starting from a training set of points whose membership is known. Binary classification plays a central role in the solution of many medical and biological problems. Examples are the detection with high accuracy of tissues that are prone to cancer, or the tracking down of new DNA sequences or proteins to their origins. Many methods are available, which give good results in terms of accuracy of the computed classification. This work shows how a binary classification problem can always be expressed in terms of a generalized eigenvalue problem. A new regularization technique is proposed which gives results that are comparable, in terms of classification accuracy, to other techniques in use. Its advantage relies in its lower computational complexity with respect to existing techniques based on generalized eigenvalue problems and the possibility to use it on very large data sets. Finally, the method is compared with others, using benchmark data sets.

This work has been founded by "Matematica e Diagnosi Medica", joint project of Center for Research "Enrico Fermi" and University of Pisa.

Tumoral angiogenesis modelled as a Nash game

Abderrahmane Habbal

An original approach based on game theory framework is proposed to model antiangiogenesis. It relies on a competition between two density functions which are intended to represent respectively activators and inhibitors of angiogenesis. To illustrate our approach, we define a porous media versus structural linear elasticity theoretic game. The problem is formulated as a topology design static with complete information game, for which existence of a Nash equilibrium was proved. We assume that activators would act in order to provide the tumor with an optimal drainage network, while the inhibitors would try to keep the structural compliance of the extracellular matrix as low as possible (or try to minimize the drainage of the blood vessels network in the case of zero-sum version). The numerical results clearly characterize the multiplicity of feeding channels as an optimal response of the activators to optimally distributed inhibitors

On the application of the rough set approach in medicine: corticotherapy into sarcoidosis

Paula Lopes

Sarcoidosis is a multisystem disorder of unknown cause. The symptoms and/or findings that necessitate corticosteroids therapy remain controversial but most physicians feel that progressive symptomatic disease should be treated. Over the last years, the application of rough set methodology in medicine has open many challenges. In this paper we propose a methodology based on rough set approach to induce a set of rules that can support medical decisions. Rough set approach deals with an information expressed in a data table in which the data related to some decision attributes are supposed depending from the data related to some condition attributes. In case of medical application, the decision attribute may be the proposed therapy which depends on the condition attributes that can be data about symptoms. Rough set methodology gives indications with respect to the relevance of attributes and set of attributes. Moreover it expresses the knowledge contained in the data table in terms of in the form of "if ... then..." decision rules. The decision rules are derived after computing the solution of a Boolean function which requires the use of logical techniques, optimization algorithms, or meta-heuristics like genetic algorithms. In case of the above medical example the decision rules are of the form "if these symptoms, then this therapy". In our application condition attributes are the following: clinical features, laboratory findings, diffusion capacity, radiological stage, CT scan, BAL, Ga scan, extra pulmonary involvement, and histology. The decision attribute is related undergo or not undergo corticotherapy.

Joint with: Sara Freitas, José Figueira, Salvatore Greco, and Carlos Cordeiro

Some remarks on separation methods for classification problems

Giandomenico Mastroeni

We consider the problem of separating two discrete point sets in a finite dimensional Euclidean space. In particular, we focus our attention on (piecewise) linear and spherical separation. It is known that such problems can be approximated by means of suitable linear optimization problems. This is the case, for example,of a spherical separation with fixed center. The use of kernel transformations, in the Support Vector Machines approach, allows us to extend the analysis to further types of nonlinear separation.

A function space oriented interior point optimization algorithm for hyperthermia treatment planning

Anton Schiela

We consider optimization in local hyperthermia, a cancer therapy, in which the tumor is heated by application of microwaves. This procedure is controlled by the adjustment of the phases and amplitudes of the microwave antennas.

Our optimization task is to compute the optimal antenna parameters, such that the tumor is heated as much as possible, while the healthy tissue does not exceed a certain maximal temperature.

This leads to an optimal control problem subject to a stationary heat equation and constraints on the temperature. This problem is solved by a function space oriented primal interior point method. We will present the key features of this method and show numerical results.

Optimization of radiofrequency ablation for the treatment of tumors

Ariela Sofer

Radiofrequency ablation is a minimally invasive technique for killing tumors. A needle is placed near the tumor and heat is applied. Temperatures above 50C kill tissue. The treatment plan is to determine the number of needles and their positions to guarantee that the entire tumor is killed while vital tissue is spared. The spread of heat is governed by the bio-heat PDE equation. We present an approach that approximates the burn lesions by ellipsoids, resulting in a nonlinear set covering problem. We present the formulation, solution approaches and computational results.

Joint with: Bradford J. Wood

LP based randomized re-construction of seeds in brachytherapy

Anand Srivastav

Brachytherapy for various cancers like prostate, lung and breast is widely used. At the Universitaets Klinik in Kiel the brachytherapy of prostate cancer is the standard treatment. Here about 80 radioactive seeds are implanted in the prostate. Due to movement of patient, the organ and blood circulation, seeds can move in the organ and change their original position. For the quality control of the treatment it is most important to locate the seeds days or weeks after the implantation. This is usually done taking three x-ray films of the organ from three different angles. So, each film shows the seed images from a different 3-dimensional perspective. The task is to determine the location of the seeds in the organ by matching seed images of the three films (reconstruction problem). By taking an appropriate geometrical measure as a cost function for matching three seed images from each film, the problem reduces to the NP-hard three-dimensional assignment (or matching) or AP3 problem.

In the literature, heuristics of different flavor have been applied to the problem (e.g [Narayanan, Cho, and Marks 2004], [Altschuler and Kassaee 1996], [Balas and M.J. Saltzman 1991], [Brogan 1989], [Siddon and Chin 1984], [Amols and Rosen 1980]). Usually, their performance cannot be proved, but is supported by experimental success.

In this paper we present the first efficient randomized algorithm for the problem, which approximately solves the integer, linear program modeling of AP3, and prove its approximation guarantee. For data sets of about 80 seeds an extension of the basic algorithm was able to find the real seed locations within a few minutes on a SUN workstation.

Joint with: Helena Fohlin

Discontinuity preserving phase unwrapping using graph cuts

Gonçalo Valadão

In several imaging techniques such as magnetic resonance imaging (MRI), Interferometric Synthetic Aperture Radar (InSAR), and Interferometric Synthetic Aperture Sonar (InSAS), phase plays a crucial role. Namely, in MRI phase knowledge is needed to determine magnetic field maps that are then used to correct geometric distortions in echo-planar systems [Jezzard and Balaban 1995]; other examples are the water and fat separation [Glover and Schneider 1991] and dynamic range increasing of phase contrast measurements.

However, in all of the mentioned applications only modulo-2π (wrapped) noisy observations are available. Phase unwrapping is the process of inferring absolute phase from the wrapped and noisy observed phase.

In this communication we present a new phase unwrapping (PU) algorithm of the minimum L^p norm type for $p > 0$. This generally leads to computationally demanding algorithms to which much attention has been devoted in the last years [Ghiglia and Pritt 1998], [Dias and Leitão 2002]; in particular for $p < 1$ this is a NP-hard problem [Chen 2001].

Our approach follows the idea introduced in [Dias and Leitão 2002] of an iterative binary optimization scheme, the novelty being the casting onto a graph max-flow/min-cut formulation, for which there exists efficient and more general scope algorithms. That graph formulation is based on recent energy minimization results via graph-cuts [Kolmogorov and Zabih 2004]. Accordingly, we term this new algorithm PUMF (for phase unwrapping max-flow) for which performance with $p \geq 1$ has been shown in [Bioucas-Dias and Valadão 2005]. This approach allows us to handle the full $p > 0$ range of ℓ_p norm minimization tasks which constitutes a novelty here illustrated. PUMF is an exact energy minimizer for $p \geq 1$. In the range $p < 1$, where handling of discontinuities in the absolute phase is particularly enhanced, PUMF acts as an approximate minimizer, building on recent results published in [Rother, Kumar, Kolmogorov, and Blake 2005].

A set of experimental results illustrates the effectiveness of the PUMF for $p \geq 0$.

Joint with: José M. Bioucas-Dias

E-Mail List

Carlos J.S. Alves
(calves@math.ist.utl.pt)
CEMAT, Tech. Univ. Lisbon, Portugal

Paula Amaral
(paca@fct.unl.pt)
New Univ. Lisbon, Portugal

Annabella Astorino
(astorino@icar.cnr.it)
ICRAP, CNR, Italy

Bilal Atfeh
(bilal.atfeh@sophia.inria.fr)
INRIA Sophia Antipolis, France

Abdel El Badia
(abdellatif.elbadia@utc.fr)
Univ. Tech. Compiègne, France

Sylvain Baillet
(sylvain.baillet@chups.jussieu.fr)
Cognitive Neuroscience & Brain Imaging Lab., France

Pedro Baptista
(pbaptista@aibili.pt)
AIBILI, Portugal

Rui Bernardes
(rcb@aibili.pt)
AIBILI, Portugal

Mounir Bouter
(boutermou@yahoo.fr)
Univ. Algiers, Algeria

Francisco Caramelo
(fcaramelo@ibili.uc.pt)
Univ. Coimbra, Portugal

Fredrik H. Carlsson
(fcar@math.kth.se)
Royal Inst. Technology (KTH), Sweden

Andrzej Cegielski
(a.cegielski@wmie.uz.zgora.pl)
Univ. Zielona Gora, Poland

Lucileida Cruz
(lregina25@yahoo.com.br)
Univ. Coimbra, Portugal

Ana Luísa Custódio
(alcustodio@fct.unl.pt)
New Univ. Lisbon, Portugal

Karine Deschinkel
(desk@prism.uvsq.fr)
PRiSM Lab. d'Informatique, France

Matthias Ehrgott
(m.ehrgott@auckland.ac.nz)
Univ. Auckland, New Zealand

João Ferreira
(jfilipe@aibili.pt)
AIBILI, Portugal

Nuno Ferreira
(nuno@ibili.uc.pt)
IBILI, Univ. Coimbra, Portugal

Michael C. Ferris
(ferris@cs.wisc.edu)
Univ. Wisconsin, USA

Helena Fohlin
(hef@numerik.uni-kiel.de)
Univ. Kiel, Germany

Antonio Fuduli
(antonio.fuduli@unical.it)
Univ. Calabria, Italy

François Galéa
(galea@prism.uvsq.fr)
PRiSM, Univ. Versailles, France

Mario Rosario Guarracino
(mario.guarracino@na.icar.cnr.it)
ICAR-CNR, Italy

Abderrahmane Habbal
(habbal@unice.fr)
INRIA, Univ. Nice, France

Tuong Ha-Duong
(tuong.ha-duong@dma.utc.fr)
Univ. Tech. Compiègne, France

Horst W. Hamacher
(hamacher@mathematik.uni-kl.de)
Univ. Kaiserslautern, Germany

Leon D. Iasemidis
(Leon.Iasemidis@asu.edu)
Arizona State Univ., USA

Jari P. Kaipio
(kaipio@venda.uku.fi)
Univ. Kuopio, Finland

Eva K. Lee
(evakylee@isye.gatech.edu)
Georgia Inst. Technology, USA

Paula Lopes
(pac_lopes@netcabo.pt)
Univ. Coimbra, Portugal

Alfred K. Louis
(louis@num.uni-sb.de)
Univ. Saarbrücken, Germany

Pedro Coimbra Martins
(pmartins@iscac.pt)
Inst. Politécnico Coimbra, Portugal

Giandomenico Mastroeni
(mastroen@dm.unipi.it)
Univ. Pisa, Italy

Maria Teresa Monteiro
(tm@dps.uminho.pt)
Univ. Minho, Portugal

Panos M. Pardalos
(pardalos@cao.ise.ufl.edu)
Univ. Florida, USA

Anand Rangarajan
(anand@cise.ufl.edu)
Univ. Florida, USA

Catherine Roucairol
(Catherine.Roucairol@prism.uvsq.fr)
PRiSM Lab. d'Informatique, France

Anton Schiela
(schiela@zib.de)
Konrad Zuse Inst. Berlin, Germany

Renata Silva
(renata@mat.uc.pt)
Univ. Coimbra, Portugal

Ariela Sofer
(asofer@gmu.edu)
George Mason Univ., USA

Paula Sousa
(phfs19@yahoo.com.br)
Univ. Coimbra, Portugal

Anand Srivastav
(asr@numerik.uni-kiel.de)
Univ. Kiel, Germany

Georg Stadler
(ge.stadler@uni-graz.at)
Univ. Graz, Austria

Gonçalo Valadão
(gvaladao@lx.it.pt)
Inst. Telecomunicações, IST,
Portugal

Luís Nunes Vicente
(lnv@mat.uc.pt)
Univ. Coimbra, Portugal