Gothenburg Mathematical Modelling Centre

Annual Report 2007

Swedish Foundation for Strategic Research

UNIVERSITY OF GOTHENBURG

CHALMERS

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Göteborg 2008

Contents

Introduction

Highlights:

- New mathematical models for biological processes in cells and for the interaction between cells are developed at a high rate. But is it possible to control if the models agree with measurements? This question led us to new and unexpected results on (non)identifiability of systems of differential equations with delay terms. The results are of interest also outside of biology. (Milena Angeuolva, Bernt Wennberg).

- A continued effort of many GMMC researchers to improve methods for finding out how genes work led to a new method for the analysis of affymetrics type microararrays. On spike-in data the method is shown to be superior to established and widely used methods such as LIMMA (Magnus Åstrand, Mats Rudemo).

- A new factor model of Black-Scholes type for financial portfolio optimization may circumvent the dominating problem of traditional portfolio optimization: the estimation (or guessing) of mean returns of financial instruments (Carl Lindberg).

- A book manuscript on our new approach to reliability improvement has been accepted by Wiley. The approach is able to treat all three major sources of uncertainty: statistical uncertainty, parameter uncertainty, and model uncertainty, within the same framework. The approach has been implemented at Volvo Aero.

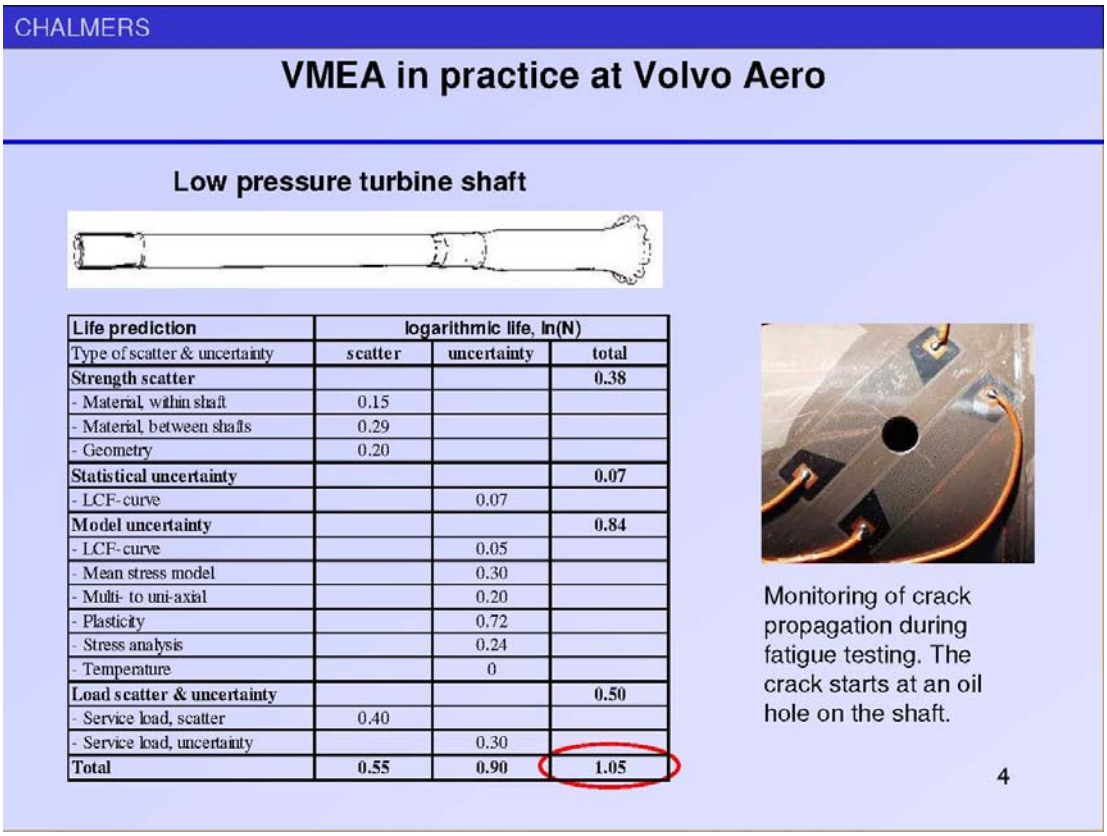
The year has been one of consolidation and of creating new links inside projects and over project boundaries – and of hard work – for the three main projects embarked upon at the beginning of GMMC.

One major new subproject, Ocean Engineering, started in 2007. In this, we try to model and predict extreme properties of the global ocean wave climate using satellite data. We also study the shapes of individual very large waves, and how their impact is transmitted through ship hulls. Goals include the assessment of metal fatigue in ships and planning of ship routes to decrease fatigue damage and risks of capsizing. Part of the work and the financing is in cooperation with the SEAMOCS EU project.

GMMC receives direct support from the founding organization, SSF, and from Chalmers and University of Gothenburg. Throughout, we try to make these grants last longer by sharing costs. The Stochastic Centre, funded by the Swedish Research Council, is the major contributor. Other important components are the SSF-funded Cardiovascular Disease Center and the Vinnova funded SUMO Centre. A final component is to use GMMC funds for "guarantees", which can lead to the results we want without any costs at all. One example is Sven Nelander, who was recruited to Gothenburg from New York with the help of a guarantee to get a job, given by us, the SSF Cardiovascular Disease Centre, and Chalmers Biocentre. Nelander returned in 2007 and now has a research associate position paid for by the Swedish Science Research Council. But, efforts of cost sharing notwithstanding, funding constraints now are substantial: exciting projects compete for more funds than we have.

Mathematics is “generic” and it is not easy to predict what will become influential. Here two examples, one from the past and one (we hope) form the future. First the past: Sture Holm, now retired, but part of the GMMC risk analysis effort, in 1979 wrote a paper on testing many different scientific hypotheses at the same time. In the first five years after its publication the paper attracted little attention – measured by the Thompson Scientific citation count, a mere 2 citations. But, spurred by needs from gene technology where such situations are standard fare, interest started to grow exponentially, and at the time of writing the paper has a citation count of 2,952. This makes it the by far most cited paper on stochastic theory in Scandinavia, and is exceptional also by world standards. The future: for 2008 we are, on a quite small budget, planning for a workshop on “Society and social dilemmas: game theoretic and other mathematical modeling”, which will mix mathematics with social science, biology, psychology and philosophy. Perhaps results from this workshop could come to have a similar impact in the distant – or not so distant – future?

Holger Rootzén, centre leader



A basic scheme for reliability measurement

People

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Michael Patriksson, deputy centre leader

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Johan Segers, Université catholique de Louvain
Fima Klebaner, Monash University
Ross Leadbetter, University of North Carolina
Massoud Asgharian, McGill University

Calendar 2007

Workshops and courses

Mathematical Aspects of Systems Biology, Gothenburg, March 21–24

Radiobiology and Radiobiological modelling in radiotherapy, Clatterbridge, May 8–11

Stochastic Approaches to Evolution, Gothenburg, 26–30 May (co-sponsored by Stochastic Centre and the Platform for Theoretical Biology of the University of Gothenburg)

Recent results for graphical Markov models, Mainz, Germany, September 1–5

Spatio-Temporal Stochastic Models in Geophysical Sciences, Gothenburg and Varberg, September 26–28 (co-sponsored by Stochastic Centre)

Asset Liability Management and SimIns, Stockholm, November 15

Robust Multiobjective Design Optimization with Simulation, Gothenburg, December 3–4

Seminars

Gilles Guillot: A statistical genetical model, March 1

Nadia Lalam: A quantitative approach for Polymerase Chain Reaction based on a Hidden Markov Model , March 20

Tom Britton, Stockholms universitet: Random graphs, epidemics and vaccination, May 24

J. Deasy, St. Louis: The CERR and ORART environments for radiotherapy research, May 29

Fredrik Edelvik: Finita Elementmetoder för elektromagnetiska problem (in Swedish), at Chalmers Kontaktdag Högskola–industri, May 31

Mats Kvarnström: Gel Structures from Transmission Electron Micrographs, June 8

Aila Särkkä: Some Space-Time Models for Tree Growth, June 8

Claudia Lautensack: Random Laguerre Tessellations with Application to Foam Modelling, September 4

N. Yanev, Sofia: Limiting distributions in multitype branching processes, September 20

David Cox, Nuffield College, Oxford: Some Special Models Arising in a Study of an Infectious Disease, October 18

Niels Richard Hansen, Köpenhamn: Point process models in genome analysis, October 23

Serik Sagitov: Reduced branching processes with very heavy tails, November 1

Timo Koski, Stockholm, On probabilistic predictive detection of DNA motifs, December 6

Defences of doctoral theses

Magnus Karlsson: Load Modelling for Fatigue Assessment of Vehicles – a Statistical Approach, February 23

Erik Brodin: Extreme Value Statistics and Quantile Estimation with Applications in Financs and Insurance, March 9

Anders Sjögren: Weighted Analysis of Microarray Experiments, May 24

Johan Svensson: Assessment of residual life for opportunistic maintenance, June 1

Alexander Herbertsson: Pricing Portfolio Credit Derivatives, September 14 (at the School of Business, Economics and Law, University of Gothenburg)

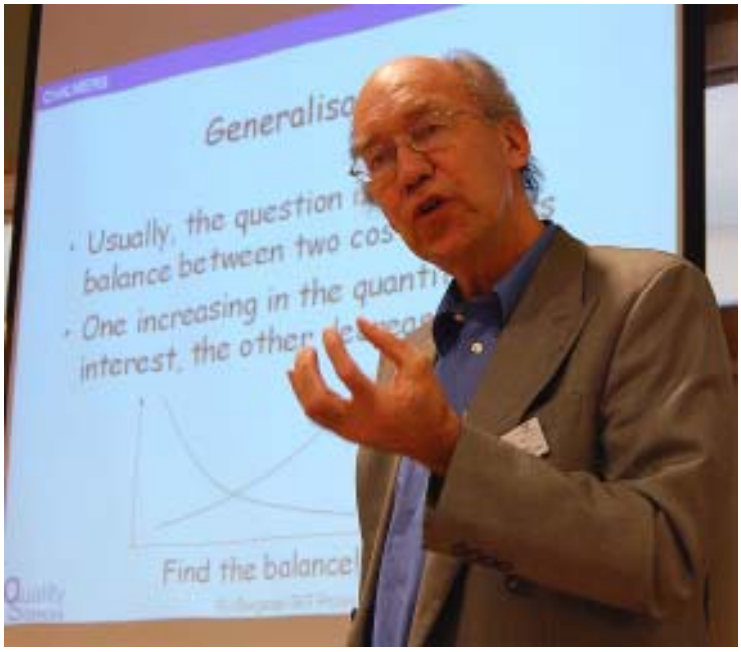
Milena Anguelova: Observability and identifiability of nonlinear systems with applications in biology, November 30

Erik Kristiansson: Statistical Analysis of Gene Expression Data, December 7

Defences of licentiate theses

Christoffer Cromvik, Matematik:
Numerical Folding of Airbags Based on Optimization and Origami
Supervisor: Stig Larsson

Fardin Saedpanah, Matematik: The Continuous Galerkin Method for Fractional Order Viscoelasticity



Bo Bergman at the workshop ***Robust Multiobjective Design Optimization with Simulation****, Gothenburg, December 3–4*

Optimisation and modelling

Modern engineering optimisation often includes the combination of simulation tools with efficient traditional engineering techniques. This demands an efficient platform of optimisation tools that integrate the simulation models that together describe the system. Several GMMC projects are of this variety, where the core is in optimisation but where the entire GMMC capability, from statistical analysis to differential equation modelling and solution, is utilized.

We describe below some achievements in this area during 2007, and tentative plans for 2008, in four GMMC projects: Cancer treatment through the IMRT technique: modelling and biological optimisation; Antenna optimisation; Combustion engine optimisation; and Optimal control of heavy vehicles.

Cancer treatment through the IMRT technique: modelling and biological optimisation

Mathematical modelling of particle transport with applications in radiation oncology

Team members:
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Mohammad Asadzadeh, Leif Arkeryd

In the medical discipline of radiation oncology, collimated beams of high-energy radiation are directed toward malignant tumor sites. The objective is twofold: (i) to deliver a sufficiently strong dose to the tumor to ensure with high probability that it is "controlled," and (ii) to deliver a sufficiently weak dose to the surrounding healthy tissue to ensure with high probability that complications will not arise. In solving this optimization problem, oncologists use a sequence of computer-generated 3-D transport (or, dose) calculations that simulate the effect of radiation beams penetrating through human tissue. These calculations are based either on Monte Carlo simulations or empirical and ad-hoc experimental data analysis. Accurate mathematical models for the reconstruction problems are of vital importance not only for early tumor diagnosis but also for target definition, dose planning systems and therapy. In this regard we focus on dose calculations in electron and ion beams which are involved in a major part of radiations treatment plans. Dose calculations in electron beam therapy planning are frequently based on pencil beams formulas such as Fermi-Eyges formula. The Fermi-Eyges formula is an exact solution of the Fermi equation. The Fermi equation equation can be derived in two steps from the linear Boltzmann equation modeling electron transport. First, the linear Boltzmann equation is approximated by the Fokker-Planck equation. Second, the Fokker-Planck equation is approximated by the Fermi equation.

In the framework of our project, we study the accuracy of these approximations. Our main conclusions are: 1. The discrepancy between the linear Boltzmann and Fokker-Planck equations is more important than that between the Fokker-Planck and Fermi equations. 2. The inaccuracy of the Fokker-Planck approximation is primarily due to the neglecting of large-angle scattering,

which is significant in radiotherapy dose calculations. In this regard certain aspects, considering narrowly focused pencil beams in 2-D model media, are studied in Asadzadeh and Larsen (2008).

Our future goal is to study the more realistic 3-D problem as well as to consider the ion beam (energy dependent, broad beam) calculations related to some recent clinical applications. To better understand the ion transport we (joint work with P. Kowalczyk, from department of mathematics, University of Warsaw) plan to consider a discrete Vlasov-Poisson model based on a Galerkin approach. In collaborations among Johanna Kempe (Karolinska Institute), Jiping Xi (project student) and Changjun Gou (Key Lab. of Radiation Physics, Sichuan University, China), the streamline diffusion method will be compared to the bipartition model for electron transport and to the Fourier transform for ion transport, respectively.

Biological models and optimization for IMRT planning

Team members:
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Marina Axelson-Fisk, Christoffer Cromvik, Michael Patriksson
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Department of Mathematics, Linköping University: Torbjörn Larsson
Department of Radiation Physics, Lund University Hospital: Per Nilsson
Department of Oncology, Umeå University Hospital: Björn Zackrison

The project's main purpose is to design and evaluate a new optimisation strategy for IMRT (Intensity Modulated Radiation Therapy) planning. The goal in radiation therapy is to maximise tumour control and minimise complications in organs-at-risk and normal tissues. In order to further improve the quality of life for patients treated with this technique we will include biological parameters into the objective function that take into account the risk of different long-term complications in the patient (including both severe and minor ones). This involves providing statistically valid biological descriptions of dose absorbtion both in organs-at-risk and in normal tissues. The resulting objective function for use in clinical treatment of cancer patients will therefore have terms based on patient-specific data as well as terms based on aggregated meaures of the effect of IMRT treatments in the past. While the former data can be adjusted during treatment, such as from repeated measurements of tumour growth speed, the latter provides "damping terms" from aggregated data that ensures that previous clinical experience from complications are also taken into account.

At our disposal we will have the results of the recently completed national study ARTSCAN on tumour effect and side effects after conformal radiotherapy in 750 patients, including many treated with the IMRT technique. A particular strength of the ARTSCAN study is the assembled data on side effects in multiple degrees which normally are hard to come by. Access to such data will open up new possibilities to account for less severe side effects in the treatment planning process.

Until now work has been performed on two main tasks. An ideal (as well as physically realistic) objective function for use in IMRT is given by voxel-based target ordinations based on a known biological distribution in the tumour such as the tumour's doubling time as well as the cellular radiosensitivity, density of clonogenic cells, and degree of hypoxia. Its optimization provides controls for the treatment machine such that it produces the best possible radiation to each voxel. In many cases the information necessary can be obtained through direct measurements in the patient (PET, MRSI, etc.). Our team has decided on a construction of such an objective function, and have gathered information on the relevant cellular biology.

Because of intrinsic uncertainties in the above-mentioned data as well as in parameters of a biological objective function, 2007 saw the development of a new optimization framework. It is based on previous research on robust optimization by team members, and essentially extends the biological optimization model with a stochastic one, such that we optimize an expectation of the original objective function. The formulation is convex and has been established to yield treatment plans that are robust to data variations; these may include uncertainties in the objective function's biological parameters and in the ordination, as well as in the the dose delivered by the treatment machine.

Research plans for 2008 and onwards include a stronger focus on the construction and evaluation of therapy plans that are near-optimal with respect to the treatment goals but also are practical. Therefore, we intend to devise and investigate models that may restrict the complexity of the dose delivered by accounting for treatment delivery limitations determined by the treatment machines. We expect that such therapy plans will be less time consuming to derive and easier to implement in the clinic. Since the inverse problem for IMRT has many competing objectives which often are in conflict, an appealing way to solve such problems is by a multi-objective approach. Because of this, we will gradually conduct our work towards a multi-objective optimization model. Finally, we intend to expand all models devised to allow for multi-planar beams as well as to include the possibility of using electron and ion beams through a collaboration across all members of the team.

A current problem is the inability to compute accurately enough the dose delivered to tissue; this is due to the fact that we still have to use CERR's rather simple pencil beam calculator using large voxels. In order to sufficiently well compare plans previously calculated by software used by clinics with those that can be calculated with the new robust model, it is necessary to either find means to utilize the clinic's software or write our own.

Plans for 2008 also include the recruitment of an assistant professor (role: assist in leading research work on biological optimization) and a postdoc (role: assist in work on software development) to the research team, and a masters project together with the Department of Radiation Physics with emphasis on algorithms for the conversion of an optimal dose plan to an implementable one by the treatment machine. In 2008 we will also be involved in the organization of a workshop on IMRT prior to the large conference ESTRO 27 in Göteborg, held September 14-18, with distinguished guest lecturers; moreover, M. Patriksson will give an invited presentation, "Biologically based IMRT optimization including uncertainties of input parameters", at the symposium on "Treatment plan optimisation" within the conference.

Combustion Engine Optimisation

Team members:
Fraunhofer-Chalmers Centre for Industrial Mathematics (FCC): Stefan Jakobsson, Fredrik Edelvik
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Michael Patriksson
Volvo Car Corporation: Mattias Ljungqvist
Volvo Powertrain: Dimitri Lortet, Johan Wallesten

The goal of the project is to develop best practice and a software demonstrator for combustion engine optimization based on computational fluid dynamics. It is nowadays possible to simulate the physical and chemical processes inside combustion engines using appropriate software and high-performance computers. These simulations can predict, for example, fuel consumption, and emission of soot and nitrogen oxides (NOx). By varying the design parameters of the engine, different configurations of these can be simulated and their can be performance compared.

Evidently, it is favourable for combustion engines to have a low fuel consumption as well as a low emission of soot and nitrogen oxides. The goal function, defined by the designer, combines these different goals. Since the engine must work well in certain ranges of load and speed conditions, it is necessary to take several such conditions into account in the optimization. Moreover, since an engine simulation can consume several days of computer time, it is clear that efficient and specialized optimization algorithms are required.

During 2007 we have developed and implemented a multiobjective optimization algorithm based on interpolation/approximation with radial basis functions (RBF). The initial implementation has been completely revised in order to speed up the algorithm and also include more objectives. The algorithm has been evaluated on a large number of test problems and also successfully applied to antenna optimization (see below). During the autumn the algorithm has been coupled to simulations of combustion engines in collaboration with a masters thesis student from the automotive engineering program at Chalmers. The simulation case has been provided by Mattias Ljungqvist at VCC and represents the Volvo D5 diesel engine. The engine speed is 2000 rpm and the operating conditions corresponds to an engine torque of 122 Nm. The three objectives to be optimized for are emissions of soot, NOx and IMEP (Indicated Mean Effective Pressure, a measure of the performance of the engine). Up to now 138 cases have been simulated where each takes approximately 20 hours. Results from the algorithm include an approximate set of Pareto points and also coefficients for the RBF approximations of the objectives. This makes it possible to do further postprocessing of the data afterwards. An illustration of a multiobjective optimization of the response surfaces to find the Pareto set for NOx and soot with constraints on IMEP is shown in Figure 1.

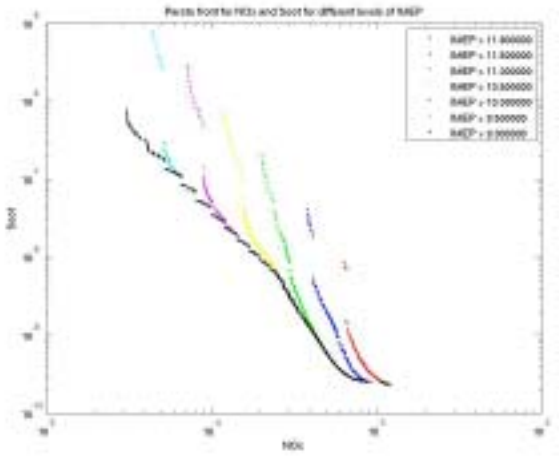


Figure 1: Pareto fronts for emissions of NOx and soot with constraints on IMEP

A problem with these kind of simulation based optimizations with very long simulation times is the risk for getting corrupted data into the optimization (the optimization campaign may take several months). What may happen is that the simulation software is updated or there are other changes of the computer system that may cause the simulations to produce false output. It is then important to identify these errors and rerun the corresponding cases. We developed a two-point cross validation technique in combination with RBF approximation to find these erroneous points. Figure 2 shows the result of such a validation. The dip in the curve indicates that the data for this point is likely to be corrupted. The l^2 line for IMEP suggests that the cases 64 and 67 are incorrect, which they indeed are.

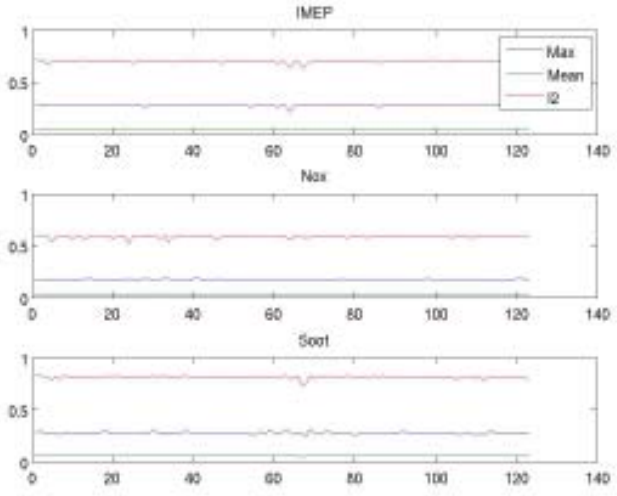


Figure 2: Results from a two-point cross validation of simulation data for combustion engines

When we have coupled the algorithm to simulation of combustion engines, we have identified a number of key points which we want to improve and develop further. During the course of optimization the algorithm tries to improve the approximation, especially near the Pareto front. The new evaluation point is chosen so that it maximizes a quality function which is a weighted integral over the parameter space and involves the distance to the Pareto front and the uncertainty of the approximation measured by the distance to an already evaluated point. In a continued project, we would like to improve this idea and also study other variants of it and compare their performance on multiobjective simulation problems. Other points to be improved include: finding reasonable convergence criteria for the algorithm, developing the approximation method for RBF further (currently we use uses cross validation to a free parameter for the approximation; some problems show up when the density of evaluated points are low and in combination with transformations of the objective functions), develop parallel versions, and to tune the algorithm so that it focuses more on the interesting areas of the Pareto front. We have experienced that the low soot region of the Pareto front is overemphasized in our optimization.

Antenna optimization

Team members:
Fraunhofer-Chalmers Centre for Industrial Mathematics (FCC): Stefan Jakobsson, Fredrik Edelvik
Micropos Medical AB: Tomas Gustafsson, Roman Iustin

This project is performed in close cooperation with the company Micropos Medical that develop a patent pending automatic system for high precision four-dimensional radiotherapy, 4DRT. The system includes an active positioning marker for each patient based on a tailored system of antenna, receivers, and signal analysis. The goal is to develop methodology and software for computational electromagnetics simulation (CEM) of wave propagation in the human body, to develop methodology and software for CEM-based optimal design, and to apply the result to the design of an antenna system for accurate positioning of cancer tumors to support efficient radiation therapy. The software that is used is the hybrid time-domain solver developed within the General Electromagnetic Solvers project. This solver combines a finite-element time-domain solver on unstructured grids with a finite-difference time-domain solver on a Cartesian grid. The choice of solver is motivated by the fact that the human body is strongly heterogeneous and very large computational grids with millions of degrees of freedom are expected.

The Micropos positioning system is based on an antenna system with an implant attached to the prostata. The implant is modeled as a magnetic dipole. An antenna array integrated in the treatment table is used to receive the signal. Currently the frequency 13.56 MHz is used and only the amplitude of the signal to locate the prostata. However, in this project the phase difference of the signal is used which is believed to facilitate more accurate positioning. Routines have been added to the software to enable calculation of the phase difference and accurate modeling of the source. In Figure 1 results are shown for a case where the source and receiver are located in a homogeneous medium and an analytical solution is known.

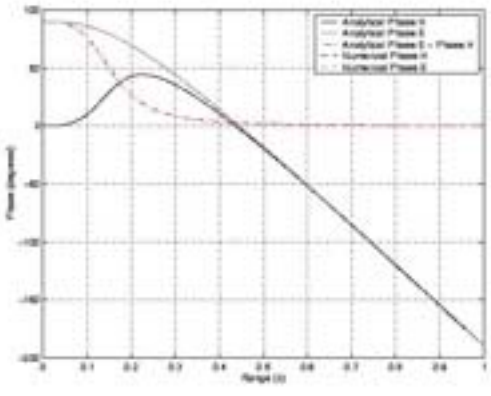


Figure 1: The difference in phase between source and receiver in a homogeneous medium as a function of distance in wavelengths

A major difficulty is that the frequency 13.56 MHz implies a wavelength in vacuum of roughly 22 meters. Since the distance between source and receiver is on average 0.32 meters we are to the very far left on the x-axis in Figure 1, where the curves are flat and therefore the phase difference almost negligible. At this frequency it is impossible to calculate, or measure, the phase difference accurately enough to make it useful for finding the tumor position. On the other hand, if the frequency is too large there will be a lot of internal reflections of the signal in the human body and the noise level makes it impossible to accurately localize the tumor.

The model known as the Zubal phantom was constructed from CT images of a male and consists of 498x192x96 voxels of resolution 3.6 mm. A total of 128 different tissue types are included in the model and a tissue type is attached to each voxel. Each tissue type has certain electric properties that in general also depends on frequency. This model has been used as input for simulations to calculate a database of phase differences for different source and receiver positions. This result is useful for Micropos to improve the understanding of the system and obtain information on suitable receiving positions. A good position is such that a small movement in the implant results in a large, and therefore measurable, phase difference. Furthermore, it is important that different implant positions do not produce the same phase difference.

The treatment table has been shown to have a large impact of the result. A thin sheet model has been developed that can be efficiently used to model different thin coatings of the table (Edelvik, 2007b). The thin sheet model avoids resolving the thickness of the coating with the grid and therefore reduces the number of grid cells substantially. Substantial effort has been made in 2007 to simulate the receiving antenna of RFID type. It consists of a metallic patch on top of a lossy dielectric substrate (Figure 2). Routines for handling lumped circuit elements have been implemented for this purpose.

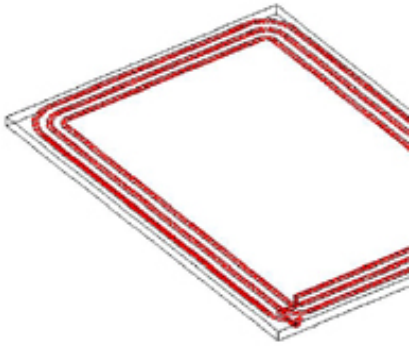


Figure 2: The Micropos receiving antenna element

The complexity of the Micropos system and the low frequency imply very long simulation times, in the order of several days. To make optimization feasible we have therefore studied a different patch antenna (Jakobsson et al, 2007) at a larger frequency. Patch antennas are popular in wireless communication systems such as cell phones, WLAN and GPS. The objective is to transmit as much electromagnetic energy as possible at some defined frequency or a band of frequencies in order to have a more broad banded antenna. The optimization is carried out with respect to three design parameters L, W and x, see Figure 3. As objective functions we choose the return loss at two frequencies 2600 and 3000MHz. We have developed a general, multi-objective, optimization algorithm based on radial basis functions which is also used in the combustion engine optimization project (see above). The patch antenna will also be included in a survey paper, where different optimization algorithms are compared (Strömberg et al, 2007).

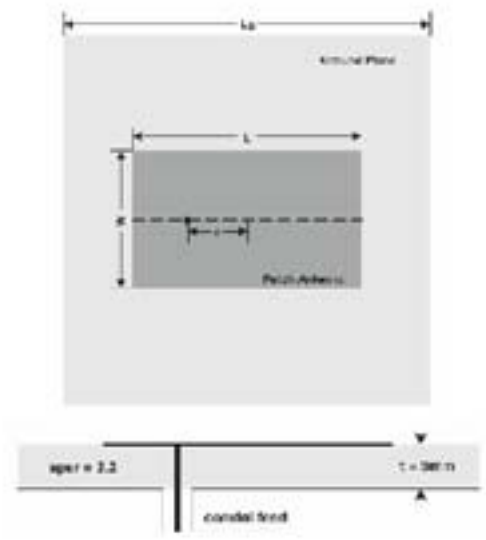
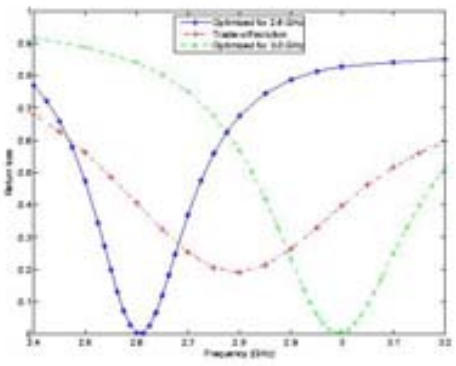


Figure 3: A probe fed patch antenna with feed position at x



In Figure 4 the return loss as a function of frequency is shown for three configurations, one optimized for 2600MHz, one for 3000MHz and one trade-off solution which is chosen to be approximately in the middle of the Pareto front. It is clear how the dip in the return loss is smeared out in the trade-off solution in order to be a good compromise for both frequencies.

Figure 4: Return loss as a function of frequency

Antenna optimization using electromagnetic simulations for Ericsson Together with researchers at Ericsson's Antenna Research Centre we will apply the optimization algorithm algorithms developed in the above projects in order to study communication performance possibilities and limitations for multiple antennas within a limited area, such as a handheld terminal. The efield software for EM simulations, partly developed by FCC, is very well suited for such applications and will be used for the simulations.

Optimal control of heavy vehicles by means of an adaptive finite element method

Team members:
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Karin Kraft, Stig Larsson
Applied Mechanics, Chalmers University of Technology: Mathias Lidberg

This research is concerned with numerical methods for optimal control of differential equations with applications in the automotive industry. This involves the development of theory and algorithms as well as application to anti-skid systems for heavy vehicles. The project is done in cooperation with Vehicle Safety at Chalmers. We develop numerical methods for solving the differential and algebraic equations that arise in connectin with optimal control of the dynamics of heavy vehicles. The stiff boundary value problems that occur are usually solved by shooting methods. Our approach is to use adaptive finite element methods which allow error control and adaptive computational meshes. The algorithms are to be implemented in computer code and used in control systems for heavy vehicles.

During 2007 we have derived an adaptive finite element method with error control based on a posteriori error estimates. This method controls the error in an arbitrary linear functional (or a norm) of the state variables and it requires the solution of an additional adjoint problem. The method was implemented in Matlab and tested on a collision avoidance manoeuvre.

If you only want to control the error in the functional to be minimized, then it is more effective to use the methodology of dual weighted residuals, which uses only the equations already introduced by the calculus of variations and no extra adjoint equation is needed. We have adapted this methodology to optimal control problems. The algorithm has been implemented for problems with quadratic goal functional and linear state equation.

Risk, Reliability and Quality

Core team members:
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Sofia Åberg, Anastassia Baxevani, Jacques de Maré, Holger Rootzén, Igor Rychlik
Quality Sciences, Chalmers University of Technology: Bo Bergman, Torben Hasenkamp
Fraunhofer-Chalmers Centre for Industrial Mathematics (FCC): Pär Johannesson, Sara Lorén
SP Technical Research Institute of Sweden: Thomas Svensson
Volvo Car Corporation: Åke Lönnkvist
Weavering Capital: Carl Lindberg

Our Risk, Reliability and Quality is aimed at three application areas:
– Reliability and Quality
– Ocean Engineering
– Management of Economic Risks

Ocean Engineering is new to us. It is lead by Igor Rychlik together and Sofia Åberg who were recruited to Gothenburg in 2007 and by Anastassia Baxevani who came to us earlier. Two new graduate students have been employed. One of them is supported and advised in cooperation with Bretagne University and the French ocean research institute IFREMER (Institut Français de Recherche pour l'Exploitation de la Mer). The other student is similarly part of our collaboration with Norske Veritas in Oslo and the division of Ship design at Chalmers. Much of our work is under the auspices of a new EU project, SEAMOCS. One part of this was a workshop organized by us. A further workshop, on Spatio-Temporal Modeling, was a joint project for two of our three main projects: Risk Reliability, Quality and Biomathemathics.

Work on Reliability and Quality continues using the model for cooperation which was started in 2006. An important part is recurring two day meetings outside of Gothenburg. During the year two new major partners, SP Technical Research Institute of Sweden and Volvo Cars, was included in our team. Our main goal remains to be to formulate and implement an approach for reliability engineering which takes all sources of variations and uncertainties into account, but still is simple to apply. Last year we presented our ideas in a number of workshops and conferences. This was continued in 2007 with a workshop with industry which was centered on our approach. We have prepared a preliminary version for a book: "Robust design methodology for reliability" where our approach is presented in a collection of essays. A contract offer for the book was received from Wiley in December. The target date for the complete manuscript is October 2008.

A reliability course for industry was given at Volvo Trucks by Pär Johannesson and Jacques de Maré. The course consists of four half-days that were driven by problems from the industry. A major event in the planning is that we next year will arrange the ENBIS-conference (European Network of Business and Industry Statistics) in Gothenburg.

Two theses on Management of Economic Risk were defended during the year. The problems treated included wind storm insurance, methods for analysis of high frequency stock price data and credit risk. The latter area gained increased attention during the year through the

subprime loan crisis in the USA. At FCC we completed the development of two program packages for industry use. One, SimIns which was developed in cooperation with Svenska Försäkringsföreningen and is a state-of-the-art Asset-Liability-Management/Dynamic Financial Analysis tool for insurance companies. The other one, RoPox is the result of a joint project with the Second Swedish national Pension fund. It implements Carl Lindberg's new ideas on portfolio optimization.

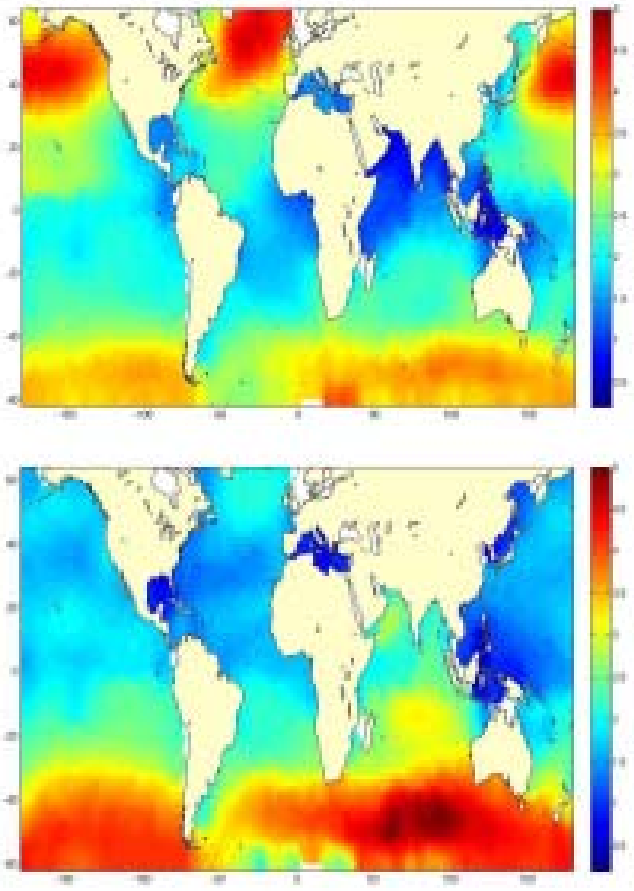


Figure 1 and 2: These figures show the median of the logarithmic values of significant wave height (a measure of the variability of the ocean surface) during the month of February the first and during August the second. It can be seen that the areas were the highest values occur during the winter are in the north hemisphere with values reaching the 4.5 m. There is also a region below -30 degrees in latitude with high energy. The median values of significant wave height reach the 3-3.5 m. The situation, as you can see, changes in the summer. Then the areas of high energy move to the south hemisphere. In the south of the Indian ocean the median values of the significant wave height reach up to 5 m. It is also interesting to notice that at least during August the median values of the significant wave height are higher in the south hemisphere than those of the north hemisphere during the month of February.

Biomathematics

The biomathematical theme has several main directions: systems biology, image analysis, statistical analysis of e.g. microarray data, and spatial statistical modelling. As e.g. the dose optimisation project shows, work in this direction is also carried out within other main themes of the GMMC.

Core team members:
Mathematical Sciences, Chalmers University of Technology and University of Gothenburg: Peter Jagers, Olle Nerman, Mats Rudemo, Aila Särkkä, Bernt Wennberg, Nanny Wermuth
Fraunhofer–Chalmers Centre for Industrial Mathematics (FCC): Mats Jirstrand, Mats Kvarnström
Chemical and Biological Engineering, Chalmers University of Technology: Magnus Nydén
Sloan-Kettering, New York: Sven Nelander
SIK: Niklas Lorén

Spatial modelling

Preliminary neurologic studies indicate qualitative differences in the spatial patterns of epidermal nerve fibers (ENF) based on pathophysiological conditions in the subjects. Our PhD student Viktor Olsbo (with Aila Särkkä as main advisor) is trying to quantify differences in the spatial pattern of ENFs in subjects without neuropathy (diabetes in our case) from the patterns in subjects with neuropathy. This is joint work with Lance Waller at Emory University, Atlanta, and neurologists William Kennedy and Gwen Wendelschafer-Crabb at University of Minnesota. The data come from the Kennedy Laboratory. We have applied second order methods of spatial point and fibre processes to the ENF data and according to our preliminary results the ENF pattern becomes more clustered as the neuropathy advances. We have also suggested some models for the ENF patterns, and studied the properties of the models.

Polar ice consists of compacted snow. The ice in deeper layers is compressed by the weight of newly fallen snow. The gain due to snowfall is balanced by a drift sidewards keeping the total height of the ice shield nearly constant. During this process, air pores are isolated within the ice. The question posed in this study is whether the spatial arrangement of the pores can tell us something about the interaction of the compaction and the drifting process. We investigate the point pattern of centers of the air pores which are extracted from 3d tomographic images of pieces of ice cores. Our postdoc Claudia Lautensack together with Aila Särkkä, Katja Schladitz (Fraunhofer ITWM, Kaiserslautern, Germany) and Johannes Freitag (Alfred Wegener Institute for Polar and Marine Research, Bremerhaven, Germany) introduced some directional summary statistics in 3d based on the nearest neighbour distance function and Ripley's K function. Furthermore, these summary statistics were used as the basis in order to test whether the ice is compressed, in other words whether the spatial pattern of the air pores in z direction differs from the pattern in x-y direction.

Systems biology and bioinformatics

Research in systems biology is carried out in collaboration with the research platform Quantitative Biology at the Faculty of Science, University of Gothenburg (and in particular with Stefan Hohmann and Anders Blomberg), and with the SSF-funded Sahlgrenska Center for Cardiovascular and Metabolic Research (CMR).

The Second Workshop on the Mathematical Aspects of Systems Biology was organised in collaboration with the Stochastic Centre. Around 70 participants from nine countries met at a successful three-day meeting at Nya Varvet.

The collaboration with the Quantitative Biology platform also extends to a long-running collaboration with Carl-Johan Franzén at the Department of Chemical and Biological Engineering. The work aims at understanding metabolic and signalling pathways in cells, in particular yeast cells (S. Cerevisiae). In some cases, models for signalling pathways consist of delay differential equations. The theory parameter identification is more complicated in this case, and the theory is far from being complete. A number of results pertaining to this project were presented in Milena Anguelova's thesis defence in November 2007.

In the collaboration with the CMR, a new PhD-student, Martin Berglund (financed by the University of Gothenburg via CMR), has started to work on models for the lipid metabolism. Part of the work consists of analysing and extending existing multi-compartmental models, and a particular focus will be to investigate how to use experimental data of many different kinds (e.g. data for individuals v.s. population data).

The research conducted at the Department of Systems Biology and Bioimaging at the Fraunhofer–Chalmers Centre (FCC) is focused on the application and development of computational methods, software tools, and dynamic models of biological systems on different levels of abstraction utilizing time resolved measurement data. The computational tools and algorithms developed at the department can be divided into four main areas: system identification, model reduction, quantitative bioimaging, and software tools ~V to support the model building process and computational analysis of the obtained models. FCC has extensive experience in developing methods and computational tools in systems biology, such as the systems biology toolbox for Matlab, which features a wide range of functions for analysis and simulation of biological systems. During 2007 this toolbox has been further extended, in particular for high performance computing (SBaddon) and connectivity to the model description language SBML (a GUI facilitating SBML export).

Together with professor Bernt Wennberg we have initiated a common project within GMMC entitled 'A Joint Systems Biology Research Platform for FCC and MV', which focus on methods for system identification of biological and biochemical systems. An integral part of this project has been a series of joint seminars. In 2007 the subjects under study in this project have been parameter estimation in biochemical systems using prediction error minimization, parameter estimation in nonlinear mixed effects models described by stochastic differential equations, and model reduction based on time scale separation and state aggregation. We have also initiated work on applying the developed methods in an applied modeling project regarding the RAS/cAMP/PKA pathway in S. cerevisiae, which also involves quantitative bioimaging.

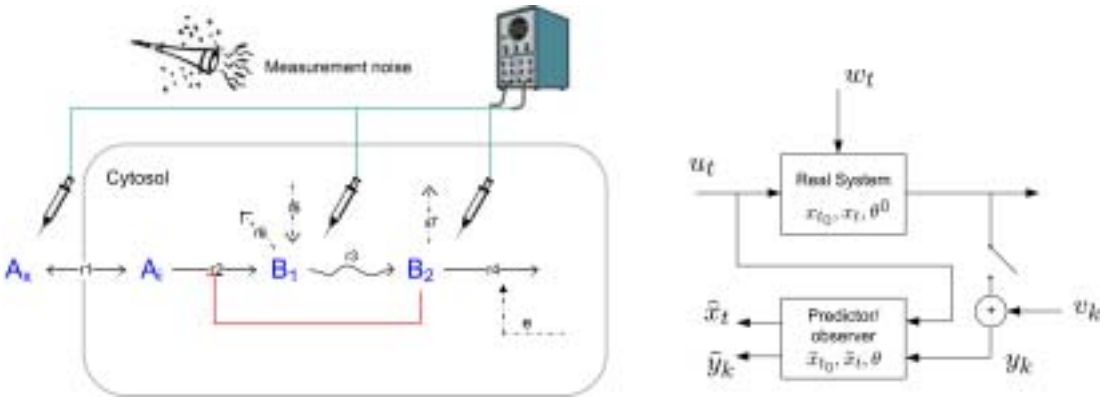


Figure 1: Parameter estimation in biochemical systems using prediction error minimization. Both time resolved measurement data and perturbations applied to the system is used as input to a predictor (parametrized in terms of unkown model parameter) to generate predicted outputs. In the prediction error minimization (PEM) framework parameter estimates are computed by minimizing an objective function given by some norm or measure of the prediction errors (the difference between measured and predicted output). The maximum likelihood estimate can be shown to be a special case of PEM corresponding to an objective function that consists of a weighted sum of squares of the prediction errors and log det terms of covariance matrices for the predicted output.

The research in statistical models and methods in bioinformatics, genomics and systems biology in the group lead by Olle Nerman has been quite intensive in 2007, despite Nerman himself being quite active in adapting to the new role as head of the division of Mathematical Statistics. The two most important scientific events were the organisation of a workshop in statistical methods in systems biology organised in collaboration with Bernt Wennberg's group with financial support by Chalmers Biocenter, Stochastic Centre and GMMC, and the successful dissertation of Erik Kristiansson in December.

During 2007 the group has also established close relations with Joachim Larsson's research group in Eco-toxicogenomics at Sahlgrenska Academy, University of Gothenburg, and most of Erik Kristianssons research has been directed torward this group. Kristiansson will make a two year postdoc period in the Eco-toxicogenomic research environment in the University of Gothenburg, starting in January 2008.

The long collaboration of Nerman and Kristiansson with Markus Tamas' group in the Department of Cell- and Molecular Biology (CMB) about analyses of molecular level effects of Arsenic stress has resulted in one published article and a submitted manuscript.

Ongoing collaboration performed by Olle Nerman, Holger Rootzén, Peter Gennemark and Dmitrii Zholud with Anders Blomberg's genomics group in the CMB is likely to result in several publications during 2008.

Similarly the partly EU-supported collaborations performed by the two young PhD students Alexandra Jauhiainen and Janeli Sarv with Per Sunnerhagen's group in the University of Gothenburg and Edda Klipp's group in Berlin, concerning posttranscriptional regulation will result in publications in 2008.

Statistical modeling for polymerase chain reactions

The Polymerase Chain Reaction (PCR) is a major DNA amplification technology from molecular biology. Quantitative analysis of PCR (Q-PCR) aims at determining the initial amount of DNA molecules from the observation of (typically several) PCR amplifications curves. This may be important in areas like gene expression analysis, virology, or food quality control, just to name a few.

The mainstream observation scheme of DNA amplification during PCR involves fluorescence intensity measurements. Under the classical assumption that the measured fluorescence intensity is proportional to the amount of DNA molecules present, and under the assumption that these measurements are corrupted by an additive Gaussian noise, we analyzed a single amplification curve using a Hidden Markov Model (HMM). The unknown parameters of the HMM may be separated into two parts. On one hand, the parameters from the amplification process are the initial number of the DNA molecules and the replication efficiency, which is the probability of one molecule to be duplicated. On the other hand, the parameters from the observational scheme are the scale parameter allowing to convert the fluorescence intensity into the number of DNA molecules and the mean and variance characterizing the Gaussian noise. We applied maximum likelihood estimation procedures to infer the unknown parameters of the model, the main parameter of interest for quantitative PCR being the initial number of DNA molecules, and we proposed to rely on the Expectation-Maximization(EM) algorithm to derive the parameter values.

We also considered a binary-splitting population-size-dependent branching process for which the offspring from generation n + 1, conditionally on the past of the process up to generation n, follows a Bernoulli distribution with probability of success depending on the population size at generation n according to a Michaelis-Menten type model. The aim was to determine the initial population size of the process based on consecutive observations of it. An estimator using the method of moments was proposed and its behaviour, using a finite number of observations, was deduced. The model might be used to represent DNA amplification by PCR.

We also performed numerical simulations to support the PhD project of Annelie Persson, from the Department of Cell and Molecular Biology, University of Gothenburg. This study is related to the population dynamics of two types of C. Elegans, one wild-type and one mutant. One would like to assess whether one population shows significantly better growth than the other, when they are reproducing in competition in the same environment. The problem is that one cannot let the two populations grow infinitely because, after some time, they would exceed the container in which they grow together. Therefore, the experimenter should extract samples of the populations. The problem that we have analyzed consists in determining how many extractions one needs in order to observe a significant difference in growth that one would expect.

This work was performed by Nadia Lalam, Paris, as a visiting post-doctoral fellow at the GMMC, January–June 2007.

Microarray data analysis

Two PhD theses on the analysis of microarray data have been completed during 2007 by Anders Sjögren, supervised by Mats Rudemo and Erik Kristiansson, supervised by Olle Nerman. An important part of these theses is the development of the WAME algorithm that accounts for varying accuracies for different microarrays and also covariation between the arrays; see the two PhD theses and the papers by Kristiansson et al. (2006) and Sjögren et al. (2007).

Together with AstraZeneca GMMC has co-financed graduate studies for Magnus Åstrand who will defend his PhD thesis 14 February 2008. Magnus has been supervised by Mats Rudemo and Petter Mostad. He has pursued development of the WAME algorithm introduced earlier at the Mathematical statistics department, Chalmers. In Åstrand et al. (2007a) the WAME method is considerably improved by use of the EM algorithm, which makes the WAME algorithm much faster. In Åstrand et al. (2007b) the WAME method is extended for use with multiple probe arrays, in particular for the current de facto industry standard, the Affymetrix platform. Two algorithms, PLW and LMW, are introduced and compared to 12 existing methods from the literature for five published spike-in data sets (with known sets of differentiably expressed genes). The algorithm PLW comes out as number one for four of these five data sets. It may well turn out that PLW will become the standard for analysis of Affymetrix type data.

Image analysis

Gel structure modeling

A method, described in Nisslert (2007), for identifying the three-dimensional gel microstructure from statistical information in transmission electron micrographs has been developed in cooperation betweeen Department of Mathematical Statistics, Chalmers, Department of Chemical and Biological Engineering, Chalmers, SIK (the Swedish Institute for Food and Biotechnology) and FCC.

The gel strand network is modelled as a random graph with nodes and edges, and parameters in the model are estimated by a Markov chain Monte Carlo method. The three-dimensional network may be simulated from the model. During 2006 and 2007 we have had a project on simulation of diffusing particles and molecules in complex 3-D geometries such as gel networks estimated from the TEM images. For this we have developed an adaptive time-stepping solver for stochastic differential equations (SDE). The surrounding geometry acts as obstructing medium for the diffusing molecule and the solver can take care of more general kinds of particle-structure interactions using interaction potentials, as well as reflection and adsorption. Here, it is of interest to be able to predict the diffusive behavior (e.g. mobility, stability) of the molecule-structure pair, where either one, or both, is designed for a specific purpose. The estimated diffusion coefficients are validated by comparing with diffusion coefficients measured via an experimental method called NMR diffusometry. Two manuscripts based on the developed adaptive simulation method have been submitted for publication.

Particle tracking

Control of the microscopic characteristics of colloidal systems, primarily the interaction and diffusion coefficients, is critical in a wide range of application areas, including food products and pharmaceuticals. These characteristics determine the macroscopic properties of the system, such as whether the particles will coagulate or remain freely diffusing. For example, in milk, interactions between the small (100 nm to 1000 nm in diameter) fat particles and proteins suspended in the fluid determine whether it coagulates into cheese or yoghurt. In pharmaceutical drugs, the active substances must remain stable in tablet or liquid form for several months between production and medication. When finally delivered to the body, these substances have to be released in a controlled fashion in order for them to be effective.

Sequences of microscope images obtained at AstraZeneca of diffusing polystyrene particles of diameter 500 nm have been analyzed. Suspensions of polystyrene spheres are a common test system for colloidals since by varying the solvent and salt concentration we can emulate features of a wide variety of more intricate colloidal systems. This system is used as a model for describing release of medical drugs in pharmacy, where the understanding of interaction and mobility of the active drug substances is of crucial importance. The positioning methods developed can be used for 3-D tracking from sequences of 2-D images of diffusing particles and the accuracy of the position estimates goes well beyond sub-pixel accuracy, see Kvarnström and Glasbey (2007). The same principle for tracking can be used in virtually any application where the depicted objects are roughly rotationally symmetric.

Improved design and analysis of FRAP experiments

The FRAP (flourescence recovery after photo bleaching) technique is an efficient and versatile method for estimating diffusion coefficients. Sequences of images are obtained with a confocal microscope after bleaching with a high energy laser in a cylindric beam orthogonal to the image plane. The current project is a cooperation with the VINNOVA supported excellence center SuMo, Supramolecular biomaterials: structure dynamics and properties. Post-doc Jenny Jonasson, jointly supported by GMMC, Stochastic centre and SuMo, has developed a new likelihood-based framework for diffusion coefficient estimation, see Jonasson (2007). This framework opens up possibilities (i) to obtain localised diffusion coefficient estimates in both homogeneous and heterogeneous materials, (ii) to account for time differences between the registrations at the pixels within each image, and (iii) to plan experiments optimised with respect to the number of replications, the number of bleached regions for each replicate, pixel size, the number of pixels, the number of images in each series et cetera.

Publications and talks

Published or accepted journal articles

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M. Anguelova, B. Wennberg: State elimination and identifiability of the delay parameter for nonlinear time-delay systems, Automatica (to appear)

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A. Baxevani and I. Rychlik: Fatigue Life Prediction for a Vessel Sailing the North Atlantic Route. Probabilistic Engineering Mechanics 22, 159–169

A. Baxevani, S. Caires and I. Rychlik: Spatio-temporal statistical modelling of significant wave heigth. Environmetrics (to appear)

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B. Bergman: Conceptualistic Pragmatism, A framework for Bayesian Analysis. IIE Transactions (to appear)

L. Fernandez-Ricaud, J. Warringer, E. Ericson, K. Glaab, P. Davidsson, F. Nilsson, G.J. Kemp, O. Nerman, A. Blomberg: PROPHECY – a yeast phenome database, update 2006. Nucleic Acids Res. 2007 Jan;35 (Database issue): D463–7

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M. Josefsson and M. Patriksson: Sensitivity analysis of separable traffic equilibria, with application to bilevel optimization in network design, Transportation Research, B, 41 (2007), 4–31

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T. Larsson, J. Marklund, C. Olsson, and M. Patriksson: Convergent Lagrangian heuristics for nonlinear minimum cost network flows. European Journal of Operational Research (to appear)

C. Lindberg: News-generated dependence and optimal portfolios in a market

of Barndorff-Nielsen and Shephard type. Mathematical Finance 16, 549–568

C. Lindberg: Portfolio optimization and a factor model in a stochastic volatility market. Stochastics 78, 259–279

C. Lindberg: The estimation of a stochastic volatility model based on the number of trades. To appear in Applied Stochastic Models in Business and Industry

G. M. Marchetti and N. Wermuth: Matrix representations and independencies in directed acyclic graphs. Annals of Statistics 36 (to appear)

R. Nisslert, M. Kvarnström, N. Lorén, M. Nydén and M. Rudemo: Identification of the three-dimensional gel microstructure from transmission electron micrographs. Journal of Microscopy 2007:225, 10–21

V. Olsbo: On the correlation between the volumes of the typical Poisson-Voronoi cell and the typical Stienen sphere. Adv. Appl. Prob. 39, 4, 883–892

M. Patriksson: A survey on the continuous nonlinear resource allocation problem, European Journal of Operational Research, 185 (2008), 1–46

M. Patriksson: Robust bilevel optimization models in transportation science. Philosophical Transactions of the Royal Society, A: Mathematical, Physical & Engineering Sciences (to appear)

M. Patriksson: guest editor of Springer journal Optimization & Engineering, which will publish GMMC contributions from the GMMC Workshop on Robust Multiobjective Design Optimization with Simulation, Göteborg, December 3–4

H. Schmidt: SBaddon: High Performance Simulation for the Systems Biology Toolbox for MATLAB. Bioinformatics 23(5), 646–647.

H. Schmidt, G. Drews, J. Vera, Wolkenhauer: QSBML Export Interface for the Systems Biology Toolbox for MATLABR. Bioinformatics 23(10), 1297–1298

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M. Arvidsson, B. Bergman: The Bergman-Hynén Method for Dispersion Effects Identification. Encyclopedia of Statistics in Quality and Reliability (to appear)

B. Bergman, J. de Maré, T. Svensson (eds.): Robust Design Methodology for Reliability. A collection of essays. Book proposal accepted by Wiley

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N. Wermuth and R. Streit: Einführung in statistische Analysen. Fragen beantworten mit Hilfe von Daten. Berlin: Springer, 2007

Published or accepted conference proceedings papers

M. Anguelova, B. Wennberg: Identifiability of the time-lag parameter in delay systems with applications to systems biology. Proceedings of FOSBE 2007 (Foundations of Systems Biology in Engineering), Stuttgart, Germany, September 9–13

M. Anguelova, B. Wennberg: State elimination and identifiability of delay parameters for nonlinear systems with multiple time-delays. Proceedings of IFAC Workshop in Time Delay

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A. Baxevani, C. Borget and I. Rychlik: Spatial Models for the Variability of the Significant Wave Height on the World Oceans. Proceedings of the 17th ISOPE conference

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P. Johannesson, T. Svensson and L. Samuelsson: Probabilistic Variation Mode

and Effect Analysis: A Case of an Air Engine Component. 10th QMOD Conference (Quality Management and Organizational Development), Helsingborg, Sweden, 18–20 June

Å. Lönnqvist: Evolution of Reliability thinking. 10th QMOD Conference (Quality Management and Organizational Development), Helsingborg, Sweden, 18–20 June

F. Edelvik and E. Abenius: Time domain finite element modeling of thin sheets and coatings using shell elements. Fourth Conference on Electromagnetic computations (EMB 07), Lund, Sweden, 35–41

S. Jakobsson, F. Edelvik and B. Andersson: Multiobjective optimization in computational electromagnetics. Fourth Conference on Electromagnetic computations (EMB 07), Lund, 99–104

K. Kraft, S. Larsson, and M. Lidberg: Using an adaptive FEM to determine the optimal control of a vehicle during a collision avoidance manoeuvre. Proceedings of The 48th Scandinavian Conference on Simulation and Modeling (SIMS 2007) (to appear)

I. Rychlik and M. R. Leadbetter: Estimating capsize risk for a vessel in a following sea. ISI 2007 meeting in Lisbon, 1–4

Published computer packages

SimIns – an ALM/DFA modeling platform, hosted by FCC, http://www.fcc.chalmers.se/risk/products/simins-for-asset-liability-management/

RoPOX – Robust Portfolio optimization, hosted by FCC, http://www.fcc.chalmers.se/risk/products/ropox-for-robust-portfolio-optimisation/

WAFO – Wave Analysis for Fatigue and Oceanography, hosted by Mathematical Statistics, Lund, we are major contributors http://www.maths.lth.se/matstat/wafo/index.html

Submitted articles or reports

T. Almgren, N. Andréasson, D. Anevski, M. Patriksson, A.-B. Strömberg, and J. Svensson: Optimization of opportunistic replacement activities: A case study in the aircraft industry. Report, Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

M. Asadzadeh, A. Schatz and W. Wendland: A non-standard approach to Richardson extrapolation in the finite element method for second order elliptic problems. Preprint 2007:22 Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

M. Asadzadeh, A. Schatz and W. Wendland: Asymptotic error expansions for the finite element method for second order elliptic problems in R_N, N>=2, I: Local interior expansions. Preprint 2007:24 Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

K. Bengtsson and I. Rychlik: Uncertainty in fatigue life prediction of structures subject to Gaussian loads

K. Bogsjö and I. Rychlik: Vehicle fatigue damage caused by road irregularities

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M. Daneva, M. Göte-Lundgren, T. Larsson, M. Patriksson, and C. Rydergren: A sequential linear programming algorithm with multi-dimensional search: Derivation and convergence. Report, Department of Mathematics, Linköping University, Linköping

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A. Herbertsson and H. Rootzén: Pricing k-th-to default swaps under default contagion: The Matrix-Analytic Approach

A. Herbertsson: Pricing Synthetic CDO Tranches in a Model with Default Contagion Using the Matrix-Analytic Approach

A. Herbertsson: Modelling Default Contagion Using Multivariate Phase-Type Distribution. Under revision for International Journal of Theoretical and Applied Finance

S. Jakobsson, M. Patrikson and A. Wojciechowski: A method for simulation based optimization using radial basis functions. Report, Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

P. Johannesson, T. Svensson, L. Samuelsson, B. Bergman and J. de Maré: Variation Mode and Effect Analysis: an application to fatigue life prediction

J. K. Jonasson, N. Lorén, P. Olofsson, M. Nydén and M. Rudemo: A pixel-based likelihood framework for analysis of FRAP data

M. Kvarnström, A. Westergård, N. Lorén and M. Nydén: An Adaptive time-stepping algorithm for Brownian dynamic simulation

M. Kvarnström, A. Westergård, N. Lorén and M. Nydén: Brownian dynamic simulations in hydrogels using an adaptive time stepping algorithm

N. Lalam: A quantitative approach for Polymerase Chain Reaction based on a Hidden Markov Model. Preprint 2007:20 Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

N. Lalam: A moment estimator of the initial number of individuals from a population-size-dependent branching process used to model Polymerase Chain Reactions. Preprint 2007:19 Department of Mathematical Sciences, Chalmers University of Technology and University of Gothenburg

C. Lindberg: Robust portfolio optimization

C. Lindberg, F. Espen Benth and M. Groth: The implied risk aversion from utility indifference option pricing in a stochastic volatility model

M. Patriksson: On the applicability and solution of bilevel optimization models in transportation science: A study on the existence, stability and computation of solutions to SMPEC models

K. Podgorski and I. Rychlik: Envelope Crossing Distributions for Gaussian Fields. Under revision for Probabilistic Engineering Mechanics

M. Åstrand, P.Mostad and M.Rudemo: Empirical Bayes models for multiple probe type arrays at the probe level

PhD theses

M. Anguelova: Observability and identifiability of nonlinear systems with applications in biology
Supervisor: B. Wennberg, Mathematical Sciences

E. Brodin: Extreme Value Statistics and Quantile Estimation with Applications in Financs and Insurance
Supervisor: H. Rootzén, Mathematical Sciences

A. Herbertsson: Pricing Portfolio Credit Derivatives (School of Business, Economics and Law, University of Gothenburg)
Supervisor: H. Rootzén, Mathematical Sciences

M. Karlsson: Load Modelling for Fatigue Assessment of Vehicles – a Statistical Approach
Supervisor: J. de Maré, Mathematical Sciences

E. Kristiansson: Statistical Analysis of Gene Expression Data
Supervisor: O. Nerman, Mathematical Sciences

A. Sjögren: Weighted Analysis of Microarray Experiments
Supervisor: M. Rudemo, Mathematical Sciences

J. Svensson: Assessment of residual life for opportunistic maintenance
Supervisor: D. Anevski, Mathematical Sciences

Licentiate theses

Christoffer Cromvik, Matematik: Numerical Folding of Airbags Based on Optimization and Origami
Supervisor: Stig Larsson

Fardin Saedpanah, Matematik: The Continuous Galerkin Method for Fractional Order Viscoelasticity
Supervisor: Stig Larsson

Master theses

J. Almquist and N. Lämås: Mathematical modeling of a Xenopus laevis oocyte expressing the NBC and MCT membrane transporters – towards a better understanding of the neuron-glial interplay
Supervisor: H. Schmidt, FCC
Examiner: M. Wahde, Vehicle Safety, Chalmers and C. Breitholtz, Automatic Control, Chalmers

J. Rudholm and A. Wojciechowski: A method for simulation based optimization using radial basis functions
Supervisor: S. Jakobsson, FCC
Examiner: M. Patriksson, Mathematical Sciences, Chalmers

M. Saif Ul Hasnain: Simulation based multiobjective optimization of diesel combustion engines
Supervisor: S. Jakobsson, FCC
Examiner: S. Andersson, Applied Mechanics, Chalmers

N. Skaar: Parameter Estimation Methods for Continuous Time Dynamic Systems given Discrete Time Measurements
Supervisor: M. Jirstrand, FCC
Examiner: B. Mehlig, Complex Systems, Department of Physics

P. Zarrineh: Development of Parameter Estimation Methods for Biochemical Reaction Systems
Supervisor: M. Jirstrand, FCC
Examiner: O. Nerman, Mathematical Statistics, Chalmers

Invited talks

M. Arvidsson: An operationalization of robust design methodology. 10th international QMOD conference (Quality Management and Organisational Development), Helsingborg

B. Bergman: chaired a special session on Reliability, Countermeasures, Quality Excellence, Robust Design. 10th international QMOD conference (Quality Management and Organisational Development), Helsingborg

B. Bergman: On the relationships between a continuous improvement perspective and an optimisation perspective. Workshop: Robust Multiobjective Design Optimization With Simulation, Gothenburg

B. Bergman: Healthcare Improvement Initiatives. Middle East Quality Association (MEQA-2007) conference, Dubai

B. Bergman: Summary: Lean or Six Sigma. Teknikföretagens kvalitetsråd, Göteborg

B. Bergman: Reliability and Robustness. Meiji University, Tokyo

B.Bergman: speaker, ISBIS-2007, Azores

B. Bergman: invited panelist Six Sigma – A Management Fad? Pros and Cons, ISI, Lisbon

C. Cromvik: An approach for the robust optimization of a biological objective in Intensity Modulated Radiation Therapy. Workshop on Robust Multiobjective Design Optimization with Simulation, Gothenburg

F. Edelvik: Time domain finite element modeling of thin sheets and coatings using shell elements. Fourth Conference on Electromagnetic computations (EMB 07), Lund

F. Edelvik: Multi-objective optimization for antenna design. Workshop on Robust Multiobjective Design Optimization with Simulation, Gothenburg

P. Jagers: seminar, Monash University, Melbourne

P. Jagers: speaker, Stochastic modelling in population dynamics, Centre Internationel des Rencontres Mathematiques, Luminy, Marseille

P. Jagers: lecture, 6-th Congress of Romanian Mathematicians, Bucharest

P. Jagers: main lecture, Advanced School and Conference on Statistics and Applied Probability in the Life Sciences, Abdus Salam International Centre for Theoretical Physics, Trieste

P. Jagers: seminar, University of Oxford

P. Johannessson: Probabilistic Variation Mode and Effect Analysis: A Case Study of an Air Engine Component. 10th international QMOD conference (Quality Management and Organisational Development), Helsingborg

P. Johannesson: Variation Mode and Effect Analysis: A Case Study of an Air Engine Component. Mathematical Statis-

tics, Lund University with Lund Institute of Technology

P. Johannesson: Statistical analysis of constant and different variable amplitude spectra. Fatigue 2007, Cambridge, UK

S. Lorén: Skattning av utmattningsgränsens fördelning under inhomogena spänningsvillkor. UTMIS nätverksmöte, Braås, Sweden

S Lorén: Skattning av inklusionsfördelning med och utan direkta inklusionsmätningar. Stål 2007, Borlänge, Sweden

Å. Lönnqvist: Evolution of Reliability thinking – Countermeasures for technical issues. 10th international QMOD conference (Quality Management and Organisational Development), Helsingborg

M. Patriksson: On the applicability and solution of bilevel optimization models in transportation science. Symposium on Networks: Modelling and Control organised by the Royal Society, London

M. Patriksson: On the existence and computation of robust solutions in hierarchical optimization. Workshop on Robust Multiobjective Design Optimization with Simulation, Gothenburg

H. Rootzén: speaker, CLAPEM 11, Lima, Peru

H. Rootzén: speaker, Extremes V, Bern, Switzerland

H. Rootzén: speaker, Levy Processes, Copenhagen, Denmark

H. Rootzén: speaker, ISI, Lisbon, Portugal

H. Rootzén: speaker, SAMSI opening workshop on Risk Analysis, Research Triangle Park, North Carolina

T. Svensson: Complexity versus scatter in fatigue modelling. Division of Electronic Devices, Department of Electrical Engineering, Linköping University

T. Svensson and Å. Lönnqvist: presentations, workshop arranged together with ENBIS (European Network for Buissness and Industrial Statistics), Glasgow

M. Ul Saif al Hasnain: Combustion engine optimization: A multiobjective approach. Workshop on Robust Multiobjective Design Optimization with Simulation, Gothenburg

N. Wermuth: lecture, American Mathematical Institute, Palo Alto, USA

N. Wermuth: lecture, Technion, Haifa, Israel

A. Wojciechowski: A method for simulation based optimization using radial basis functions. Workshop on Robust Multiobjective Design Optimization with Simulation, Gothenburg

Financial Report GMMC 2007

	in 1000 SEK	
Income		
The Swedish Foundation for Strategic Research	4843	1) 2)
Chalmers University of Technology	600	
University of Gothenburg	91	
Total income	**5534**	
Expenses		
Personnel expenses		
Reliability and risk	969	
Biomathematics	968	
Optimisation and modelling	475	
Management and coordination	385	
Project initiation	50	
Rendering our results	25	
Fellowships	408	
Guests	14	
Other personnel expenses	5	
Total personnel expenses	**3299**	
Other expenses		
Travelling and accomodation for guests	21	
Travelling, workshops, conferences	349	
Equipment	155	
Miscellaneous	33	
Total other expenses	**558**	
University levy ("högskolemoms")	**265**	
University overhead		
University administration, computer support, premises etc.	**1412**	
Total expenses	**5534**	

1) Of this 1 580 000 SEK was received during 2006.

2) Additionally GMMC received 1 387 000 SEK during 2007for use in January and February 2008. This amount is not included above.

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