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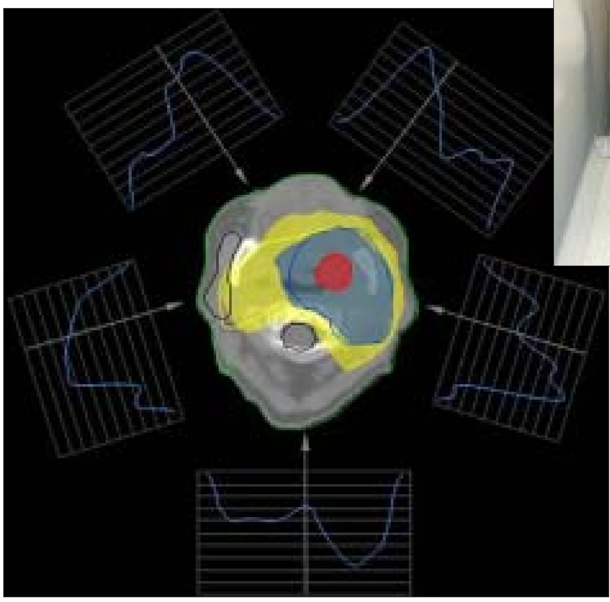
G M M C

Gothenburg Mathematical Modelling Centre



Annual Report 2006

Swedish Foundation for Strategic Research

Contents

Editors: Setta Aspström, Michael Patriksson
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GMMC members and others, photo Jan-Olof Yxell
IMRT planning, Anna Bäck
Göteborg 2007

Introduction

The Gothenburg Mathematical Modelling Centre, GMMC, started operations in January 2006. The basis was a 5-year grant from the Swedish Foundation for Strategic Research and support from Chalmers University of Technology and Göteborg University. GMMC combines four components: The Stochastic Centre, Applied Mathematics, Quality Science, and the Fraunhofer–Chalmers Research Centre for Industrial Mathematics (FCC).

Our vision is to be a role model for cooperation between mathematics and industry–society–science. We want to
– generate new exciting strategic knowledge in Reliability and Risk, Biomathematics, and Optimisation and Modelling.
– develop new closer and more mobile cooperations which connect university, industrial research institutes, industry, and society.
– sustain and develop an extensive international and industrial network and an attractive, creative, and international environment where people develop to the full of their potential, and can access a very wide range of knowledge.

Generality is at the core of mathematical modelling. The models we develop typically are useful in very many different, and often unexpected, situations. The skills a mathematical modeller learns in solving one problem makes her better at solving other problems not just in the same, but also in other quite separate areas of inquiry. Thus the single most important way for GMMC to attain its goals is to recruit and keep the best scientists and to help them perform to the best of their ability. Professor Igor Rychlik from Lund University, a leading expert in Fatigue and in Ocean Modelling, has been our top recruitment for 2006. We have also hired two postdocs in Biomathematics and a PhD student from Moscow University, and an AstraZeneca employee has joined us as a PhD student with support from AstraZeneca and GMMC. To achieve the latter goal we have experimented with new ways of working and with working in new constellations. Some examples:

A new project has collected researchers from Mathematical Statistics, Quality Science, FCC, SP and Volvo around the aim to develop an integrated approach to reliability which covers the entire spectrum of reliability problems facing a company. To keep the team together and focussed we have started regular lunch to lunch retreats and one-day meetings.

The Optimisation and Modelling groups have been joined into one team , which also includes a member from Mathematical Statistics and researchers at Sahlgrenska University Hospital and Karolinska Institute, in a new project on improving radiation treatment of cancer. What is new is not so much the way of working as consistent effort at putting this problem at the center of attention. Spurred by the advent of GMMC the team has also undertaken new projects in prostate positioning and in combustion engine optimisation.

Biomathematics requires a symbiosis of biology and mathematics. Extending earlier efforts we work with a wide range of researchers in biology, chemistry, and image analysis. Much of this is as cooperations, or participation as partners, with a number of other centres: the SSF

Strategic Center for “Cardiovascular and Metabolic Research”, the Winnex Centre “Supramolecular Biomaterials Structure Dynamics and Properties” and the Göteborg University platforms in Chemical Biology and in Theoretical Biology.

Will the new ways of working and the new projects survive and thrive? Advances build on taking risks, and we have tried to take (calculated) risks. Thus there is a possibility that not all the new projects will be successes, and that not all the new ways of working will survive. However, we are confident that the ones which succeed will make it all worth while.

We believe GMMC opens paths to ways of doing things better, safer, and more economically, for industry and for society, and want to make them widely used. The most basic way is through close cooperations with industry, society and other sciences and by presenting our results at conferences and courses for industry. FCC lives from “selling mathematics to industry”. This is to a large extent done through person to person contacts with many industries and organizations. GMMC is an important part of this. Plans for next year includes amplifying these efforts in supplementary ways, including mailings and presence at industrial fairs.

Holger Rootzén, centre leader

People

Leaders

Holger Rootzén, centre leader
Michael Patriksson, deputy centre leader

Members

Leif Arkeryd, Mathematics
Marina Axelson-Fisk, Mathematical Statistics
Jöran Bergh, Mathematics
Bo Bergman, Quality Sciences
Olle Häggström, Mathematical Statistics
Peter Jagers, Mathematical Statistics
Mats Jirstrand, Fraunhofer–Chalmers Centre
Bo Johansson, Mathematics
Stig Larsson, Mathematics
Jacques de Maré, Mathematical Statistics
Olle Nerman, Mathematical Statistics
Uno Nävert, Fraunhofer–Chalmers Centre
Michael Patriksson, Mathematics
Holger Rootzén, Mathematical Statistics
Mats Rudemo, Mathematical Statistics
Aila Särkkä, Mathematical Statistics
Bernt Wennberg, Mathematics
Nanny Wermuth, Mathematical Statistics

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Lena Carlsson, Göteborg University
Anders Hynén, Bombardier
Tomas Morsing, Second AP Fund

Secretary

Setta Aspström

Guests

Anders Brahme, Karolinska Institute: to define a cooperation plan and give a Colloquium talk

Gou Chengjun, Key Lab for radiation physics and technology, Sichuan University China: to discuss different mathematical modelling aspects of radiation therapy and give talks in GMMC/Kinetic theory and Computational Mathematics seminars

Malin Hollmark, Karolinska Institute: to give a talk in GMMC/Kinetic theory seminar and to discuss a joint cooperation plan with Gou

Johanna Kempe, Karolinska Institute: to give talks in GMMC/Kinetic theory seminar and to discuss a joint cooperation plan with Gou

Luo Zhengming, Key Lab for radiation physics and technology, Sichuan University China: to define cooperation plan and give a talk in GMMC/Kinetic theory seminar

Calendar 2006

Seminar
Chris Glasbey, Edinburgh: Image restoration and segmentation using generalisations of dynamic programming, January 12

Defence of doctoral thesis
John Gustafsson: Unwarping and Analysing Electrophoresis Gels, January 12

Seminars
Katja Schladitz: Geometric modelling and flow simulation for non-woven, February 16

Claudia Lautensack: Modelling of sintered structures, February 16

Seminar
Bo Markussen, Veterinary and Agricultural University, Denmark: Statistical analysis of image warps using stochastic differential equations, February 28

Seminar
Alexander Atamas: Monte Carlo Techniques for Pricing Path-dependent Cliquet Options, April 25

Seminar
Ursula Gather, Dortmund: Analysing Online Monitoring Data in Intensive Care, May 4

Seminars
Dieter Prätzel- Wolters: Mathematics as a technology – Projects and Research at Fraunhofer ITWM, May 16

Holger Rootzén: GMMC – people and projects at our new Gothenburg Mathematical Modelling Centre, May 16

Meeting
GMMC and Scientific Board, May 16

Seminar
Sören Asmussen, Århus: Tail Probabilities for a Computer Reliability Problem, May 18

Seminar
Anastassia Baxevani: Lamperti transformed fractional Brownian motion, May 23

Defence of licentiate thesis
Cilla Persson: Aspects of Missing Information in Genetic Linkage and Association Studies, May 30

Defence of licentiate thesis
Viktor Olsbo: Analysis and Modelling of Epidermal Nerve Fiber Patterns: a Point Process Approach, May 31

Seminar
Luo Zhengming: Algorithm Investigation in Phoenix Treatment Planning system, August 7

Seminars
Jim Matis, Texas A&M University: On New Cumulative-Size Dependent Mechanistic Models for Describing Insect Population Growth, August 29

Eric Renshaw, University of Strathclyde: The Generation of High-Intensity Space-Time Growth-Interaction Processes: Inferring Structure from Partial Observations, August 29

Defence of doctoral thesis
Erik Svensson: Computational Characterization of Mixing in Flows, September 1

Seminar
Anders Brahme, Karolinska Institute: From the transport theory of charged particles to biologically optimized ratiation therapy, September 25

Seminar
Nanny Wermuth: On distortions of effects, September 26

Seminar
Peter Jagers and Serik Sagitov: The path to extinction, October 5

Seminar
Lauren Lissner and Kirsten Mehlig, Public Health and Community Medicine: Statistical applications in longitudinal population research – example on alcohol and dementia, October 26

Defence of doctoral thesis
Gwenaëlle Genet: A Statistical Approach to Multi-input Equivalent Fatigue Loads for the Durability of Automotive Structures, October 27

Meeting
GMMC scientific meeting, November 14

Course
Failure mode avoidance, November 22–23. Arranged by UTMIS (The Swedish Fatigue Network) and GMMC. Lecturers: Tim Davis, Ford Motor Company, and Bo Bergman, Chalmers University of Technology. 70 participants of which 19 were from universities, 12 were from institutes and 39 were from industry.

Meeting
Board meeting, November 29

Seminars
Aila Särkkä, Modelling of the space-time structure of a forest stand, November 30

Johanna Kempe: Mean energy and range in light ion beams, November 30

Seminar
Guo Chengjun, Sichuan University, China: Electron transport bipartion model and its application in tumor radiotherapy, December 13

Seminar
Malin Hollmark, Medical Radiation Physics, Karolinska Institute and Stockholm University: Fast semi-analytical algorithm for narrow beam dose distri-butions in ion therapy, December 14

Meeting
GMMC scientific meeting, December 15

Positions announced

Post Doc in applied mathematics, last application date September 18. Two persons will begin during 2007

Assistant professor in optimisation with application to medicine and simulation, last application date October 19

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 2006, and tentative plans for 2007, in four GMMC projects: cancer treatment through the IMRT technique: Modelling and biological optimisation; Positioning system optimisation; Combustion engine optimisation; and Designing for optimal risk exposure.

Cancer treatment through the IMRT technique: modelling and biological optimisation

Team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Mohammad Asadzadeh, Leif Arkeryd, Marina Axelson-Fisk, Christoffer Cromvik, Michael Patriksson
Sahlgrenska University Hospital: Thomas Björk-Eriksson (Department of Oncology), Anna Bäck and Caroline Olsson (Department of Radiation Physics, Göteborg University), Karl-Axel Johansson and Niclas Pettersson (Department of Therapeutic Radiation Physics)

Mathematical modelling and numerical analysis of radiation therapy planning

In clinical treatment of cancer tumors diverse types of radiation, treatment modalities, such as photons, electrons, protons, neutrons, and ions, play a central role. Background particles can be set in rapid motion as a result of interactions with radiation particles, thereby becoming radiation particles themselves. The transport of the radiation particles through the background is described by a system of coupled Boltzmann transport equations. A solution of this system is a vector of phase space number densities, that is, number of radiation particles per unit volume in phase space, i.e., position-direction-energy space. Even if the beam aimed at the tumor consists of only one particle type (for instance photons, as in X-ray), interactions between radiation particles and background will set in motion other types of particles. Careful calculations always require consideration of several types of particles. Interactions of radiation particles with each other are negligible in this context, so the relevant transport equations are linear. Also, the relevant transport equations contain no time derivatives. Information obtained through imaging, such as the locations of soft tissue, bone, or air gaps, yields coefficients in these equations.

Our aim is to develop mathematical models and construct fast approximation techniques for optimization of physical and biological models that describe the treatment outcome. In this context we plan to model a light ion-beam problem and approximate it by using deterministic bi-partition and finite element techniques. (Equally detailed probabilistic approaches by e.g. Monte-Carlo simulations would be slower and more costly.)

The energy deposition of both electrons and light ions is quite accurately described by the generalized Fermi-Eyges version of the Boltzmann equation. An analytic solution would here be ideal to describe the physical characterization of therapeutic pencil beams for dose delivery calculation with narrow pencil beam scanning which is expected to become an ultimate way to treat patients in the future. This however, is not a generally achievable task. Therefore, to insure reliable and efficient clinical treatment plans using light ions, our focus will be on constructing optimal deterministic, schemes for this type of transport phenomena with test results based on clinical data from actual dose measurements. These data, for some pencil beams will be provided in the framework of our cooperation with the Karolinska Institute in Stockholm and Sichuan University in China.

During 2006 we have established contacts with the division of radiation physics in the Karolinska Institute as well as the department of nuclear radiation physics in Sichuan University. We have invited scientists from both research centers for short and long terms visits to Math Department in Chalmers in order to cooperate with them and to be able to identify the nature of mathematical questions in this field.

Biological models and optimization for IMRT planning

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 in 750 patients, including many treated with the IMRT technique.

During 2006 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 begun the work towards the construction of such an objective function. Work has in particular been initiated on the gathering of information on cellular radiosensitivities, on validation studies of biological criteria, as well as on convex optimization models and methods based on a combination of biological and physical measures.

Future research plans include a stronger focus on the construction and evaluation of therapy plans that are near-optimal with respect to the treatment goals but also practical. Therefore, we intend to devise and investigate models that allow for multi-planar beams, and also plans that may restrict the complexity of the dose delivered in order to make the plan more robust and less time consuming ("smoothing"). Further, we intend to expand all models devised to include the possibility of using electron and ion beams through a collaboration across all members of the team.

Combustion Engine Optimisation

Team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Michael Patriksson
Fraunhofer–Chalmers Centre: Stefan Jakobsson, Ann-Brith Strömberg
Volvo Car Corporation: Mattias Ljungqvist
Volvo Powertrain: Dimitri Lortet, Johan Wallesten

This project is a cooperation among GMMC, Volvo Car Corporation (VCC) and Volvo Powertrain (VP). The work done by GMMC is performed at Fraunhofer–Chalmers Centre (FCC). The goal of the project is to develop best practice and a software demonstrator for combustion engine optimisation based on computational fluid dynamics.

It is nowadays possible to simulate the physical and chemical processes inside combustion engines by appropriate software and high performance computers. These simulations can predict, for example, fuel consumption and emission of soot and nitrogen oxides; see Figure 1. By varying the design parameters of the engine, different configurations of these can be simulated and their performance compared. In this project we use global and local optimisation algorithms in combination with the simulations to find optimal design parameters with respect to a goal function. 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 optimisation. Moreover, since an engine simulation can consume several days of computer time, it is clear that very efficient optimisation algorithms are required.

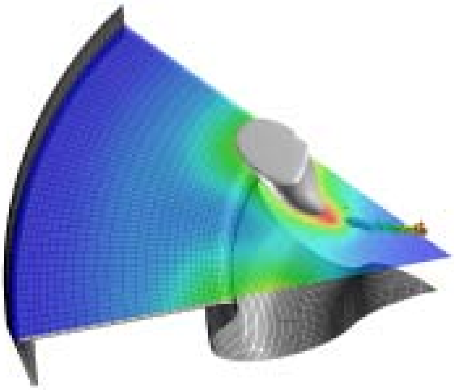


Figure 1: A sector calculation of a combustion engine. The droplets consists of fuel and their colours indicate their temperature. The grey object is an isosurface for the concentration of soot and the plane with a coloured contour plot illustrates the fuel concentration (illustration from VCC).

At VCC an initial optimisation study was made during 2006 with the following characteristics: Three load cases were considered (1500, 2000, and 4200 rpm) with different values of the torque; six parameters were used to define the cylinder design and control (swirl number, spray angle, tip protrusion, hole diameter, hole length, and flow number); and four objectives for each load case were considered: maximise efficiency and minimise NO_x, soot, and the maximal time derivative of the pressure (the latter is used as a measure of the noise and harshness of the engine).

The optimisation was carried out with the software *STORM* and the simulations were performed using *starCD*. As goal function a weighted mean of all objectives was used. At VP a similar study was made with two load cases. Instead of treating the emission of NO_x and soot as goal functions they were bounded to be lower than some reference values. Mathematically this means that the emissions were treated as boundary conditions. The study setup was made with design of experiments (DoE) and data analysis with neural networks, see Figure 2.

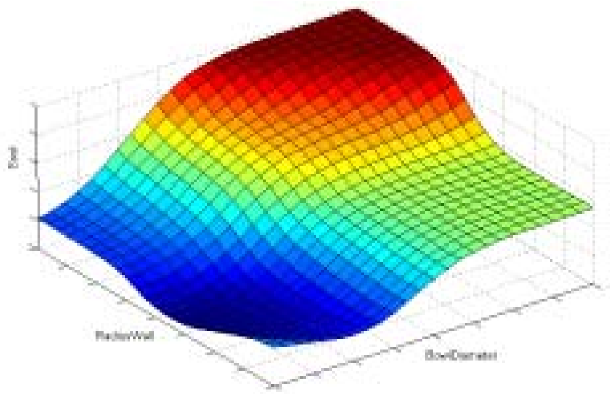


Figure 2: Neural network approximation of the soot function with respect to two of the six design and control parameters defining the cylinder (illustration from VP).

At FCC the work so far has been to continue VCC:s initial study together with VCC, analyse simulation data from both VCC and VP, and to develop new optimisation algorithms suitable for the present problem. In the continued project with VCC, FCC has used RBFSolve from the Tomlab optimisation toolbox to generate new input data. To avoid unphysical results we had to transform the objective function for the noice and harshness. We have analysed data from VCC and VP using linear regression, interpolation with minimal Frobenius norm, and analysis of response surfaces using interpolations with radial basis functions. We have also studied the results with respect to Pareto optimality of objective values. Moreover, multiobjective optimisation of response surfaces has been performed.

The algorithm RBFSolve is designed for optimisation of a single goal function and the boundary conditions are expected to be cheap to evaluate. However, in the VCC application there are multiple objective functions grouped into several load cases and in the VP application the boundary conditions are expensive to evaluate. In addition, all numerical computations contain errors due to approximations. Therefore an appropriate optimisation method should not be too sensitive to simulation errors. This can be accomplished by replacing exact interpolations with approximations. We currently work on an algorithm for the combustion engine optimisation application based on radial basis functions and which takes the above remarks into account. This work is the topic of a current masters thesis at FCC. The group also plans to have a workshop at the end of 2007 on the topic of robust multiobjective optimal design, with emphasis on combustion engines.

Adaptive finite element methods for optimal control in automotive applications

Team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Karin Kraft, Stig Larsson
Vehicle Safety, 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 applications 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 the modelling 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 implemented in computer code and used in control systems for heavy vehicles.

Positioning System Optimisation

Team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Michael Patriksson
Fraunhofer–Chalmers Centre: Fredrik Edelvik, Stefan Jakobsson
Micropos Medical AB: Tomas Gustafsson, Roman Iustin

This project is performed in close cooperation with 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.

A main 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 tumours to support efficient radiation therapy. Ultimately the goal is to develop an integrated optimization tool for radiation therapy using accurate position in 4D.

The software that is used is the hybrid time-domain solver (Edelvik, PhD Thesis, Dept of Information Technology, Uppsala University) developed within the General Electromagnetic Solvers (GEMS) 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 is 13.56 MHz and until recently only the amplitude of the signal was used to locate the prostata. However, in this project the phase difference of the signal is also to be used which is believed to facilitate a more accurate positioning. Routines have been added to the software to enable the calculation of the phase difference and an 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.

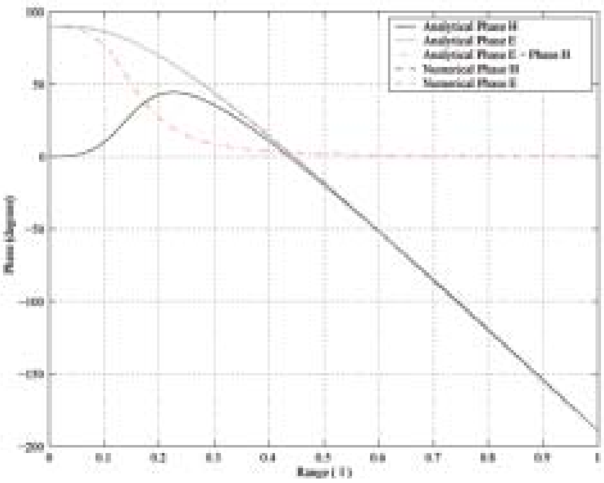


Figure 1: The difference in phase between source and receiver in a homogeneous medium as a function of distance in wavelengths.

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 is almost negligible. At this frequency it is impossible to calculate, or measure, the phase difference accurately enough to make it useful for finding the tumour 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 tumour.

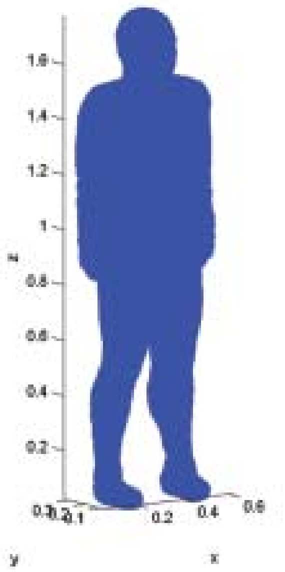


Figure 2: The Zubal human body phantom

In Figure 2 a phantom model of a human is shown. The model, known as the Zubal phantom (http://noodle.med.yale.edu/zubal/), 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 will be used to produce results of the type shown in Figure 1 for the real case. Such results are very interesting since they can for instance be used to find a suitable frequency for the antenna system. A good choice is a frequency for which a small movement in the implant results in a large, and therefore easily measurable, 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, see Edelvik and Abenius (2006) and Edelvik (2007). The thin sheet model avoids resolving the thickness of the coating with the grid and therefore reduces the number of grid cells substantially. The choice of frequency and the material properties of the treatment table are good candidates for optimization that will be considered during 2007. Another interesting issue to investigate is if a high level of detail model of the human is needed or if simpler models can be used.

Reliability and Quality

The manufacturing and insurance industry has since long put substantial efforts into systematic and quantitative methods for reliability improvement and risk control. A similar endeavor has come much later to the rest of the financial sector. However now also there quantification of risk, and methods, ranging from options to insurance, to reduce risks are very much at the center of attention.

Risk results from a combination of uncertainty and exposure to loss. Loss may take many forms, such as adverse consequences for human health and life, damage to property or the environment, or economic losses. Uncertainty may come from lack of information or because a phenomenon is inherently random. A remarkable achievement of science has been the development of stochastic techniques which allow risk to be treated quantitatively, and to some extent controlled. Many of the methods used in manufacturing are important for finance, and vice versa, and transmission of knowledge is important. We work in both areas, and try to exploit the synergies.

Core team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Jacques de Maré, Holger Rootzén, Igor Rychlik
Quality Sciences, Chalmers University of Technology: Martin Arvidsson, Bo Bergman
Fraunhofer–Chalmers Centre: Pär Johannesson, Joachim Johansson, Sara Lorén, Thomas Svensson
Volvo Car Corporation: Åke Lönnkvist

Risk and Quality

Reliability is an important quality aspect for consumers as well as for producers. The root of unreliability is uncertainty caused by variation in the material, in the production and in the use of products.

To be able to improve reliability it is essential to have a systematic and rational approach to estimate the importance of the different sources of variation. This is the starting point in the work to reduce their impact on products in service.

There are different methods in use and a new unified way is developed based on robust design projects (Variation Mode and Effect Analysis) as well as a number of industrial projects to improve fatigue life prediction.

Mathematical modelling is an important tool in improving reliability and reducing the effect of uncertainties. It is noted that complex models tend to increase rather than decrease the prediction uncertainties and a principle to choose an optimal complexity of the models is included in the unified approach.

A theoretical basis for our common approach is presented in "Detecting, Identifying and Managing Sources of Variation in Production and Product Development" (2006) by Alexander

Chakhunashvili in a PhD thesis in Quality Sciences. This basis is combined with the work carried out at FCC and Volvo Aero where a guideline for reliability prediction is formulated.

In order to incooperate the different ideas within a common frame a number of internal meetings and seminars were organized during 2006. Also to spread our ideas to the industrial and scientific society is important. A course was given and papers submitted and presented.

Our current plan includes collecting our ideas in a book, organizing conference sessions in 2007, delivering courses for industry in 2007 and hosting the ENBIS conference in 2009.

Financial Risk

We work on the complementary problems: Catastrophic Risk, Credit Risk, ALM, and Portfolio management.

The picture shows damage caused by the storm Gudrun which struck Sweden in 2005 and caused economic damages in excess of SEK 3 billion. Can the size of losses due to storms like Gudrun be predicted? Should Gudrun cause insurance companies to change their thinking about risks associated with storm losses? In collaboration with the Länsförsäkringar group we have developed new methods to answer such questions. A focus has been on situations where there is one “mechanism” (say losses to buildings) which is important in itself and rather frequent, and another one (say forrest losses) which is more rare but also even more costly.

Credit derivatives are used to manage default risk. The market for simple instruments, e.g. CDSs, is growing very rapidly and more complicated instruments such as CDOs and trance CDOs which depend on a basket of bonds are now also liquidly traded. To price the risk associated with these instruments one needs dynamic models for the dependence between defaults of different firms. We have developed a class of Markov based models for this, and methods to make the models computationally tractable.

Efficient simultaneous management of all risks lies at the heart of the insurance industry. But complexity rapidly increases with the interplay between all of a company’s assets and liabilities. For solvency purposes, e.g. as stipulated under pillar one of the Solvency II-accord, full Asset Liability Modeling is needed. We have participated in the development of a state of the art commercially available ALM/DFA modeling tool, SimIns.

Standard Markowitz-like methods for optimising portfolios of stocks are unrealistically sensitive to assumptions and estimates of growth rates. An exciting development is a new optimisation model which avoids this problem. In collaboration with the Second AP Fund we have participated in the implementation of the model into an Excel plug-in, RoPOX. RoPOX both computes optimal portfolio weights and judges portfolio stability.

Biomathematics

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

Core team members:
Mathematical Sciences, Chalmers University of Technology and Göteborg University: Peter Jagers, Olle Nerman, Mats Rudemo, Aila Särkkä, Bernt Wennberg, Nanny Wermuth
Fraunhofer–Chalmers Centre: Mats Jirstrand, Mats Kvarnström

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 comes 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. Viktor Olsbo defended his licentiate thesis in May 2006.

Sintering is a process for production of porous metals of ceramics in very complex shapes. First, powdered or granular material is compressed in a die. Then the material is heated to a temperature close to the melting point which makes the particles stick together resulting in porous yet strong material. Mathematical models for the geometry of sintered structures are of interest in material science, since they allow a systematic design of materials and production processes and therefore, an optimization of properties of materials and components. Aila Särkkä together with Claudia Lautensack and Katja Schladitz, both at the Fraunhofer Institute in Kaiserslautern, have used methods from spatial statistics and proposed a model based on a random dense packing of spheres for the microstructure of sintered copper in the early stages of sintering process.

Systems biology and bioinformatics

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

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. Cerevisieae). We have analysed established models of yeast glycolysis with respect to identifiability and parameter estimation, and found that in several models, the parameters cannot be identified uniquely. This can be detected using available software based on differential algebra techniques, but the particular kind of models that are studied here allow for a more elementary kind of analysis, which have been implemented in a computer code.

In some cases, models for signalling pathways consist of delay differential equations. The parameter identification is more complicated in this case, and the theory is far from complete. There are practical methods for computing approximations of the parameters, including the delay parameter itself (one class of methods are the shooting methods). We have developed a method based on so-called Ore algebra, to give criteria for determining whether a delay differential system is identifiable or not.

In 2006 we have recruited two postdocs in the field of systems biology, both of whom will start their work in 2007: Gunnar Cedersund and Peter Gennemark. Their recruitment is part of the collaboration with the Quantitative Biology platform.

Olle Nerman has in recent years focused his research and supervision on statistical genetics, bioinformatics and systems biology. In the bioinformatics area several graduate students and postdocs are working with the planning, analysis and development of analysis tools for DNA-microarrays. A recent EU-funded graduate student, Janeli Sarv, works with an interdisciplinary project that besides microarrays also considers system biology modelling of stress responses in yeast. The graduate student Alexandra Jauhiainen also works partly with this project.

Various bioinformatics questions related to stress responses to arsenic is the main topic in a collaboration between the graduate student Erik Kristiansson and researchers at microbiology at Göteborg University. Another long term collaboration with microbiologists concerns modelling and analysis of yeast growth curves derived from screening of single gene deletion mutant strains in a spectrum of environments. From autumn 2006 GMMC cofunds an Ukrainian research fellow, Dimitri Zholud, who applies modern extreme value techniques to derive properties of the screening tests used today, and to design better approaches for the future.

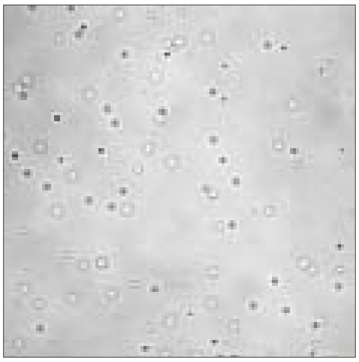
GMMC also co-finance a graduate student at Mathematical Sciences with AstraZeneca, the biostatistician Magnus Åstrand. Magnus already around 10 years ago received a licentiate degree from Chalmers in Mathematical Statistics and works now on a thesis concerning normalisation and optimising the analysis of affymetrix type microarrays using auxiliary experimantal information. The dissertation is planned to take place before the end of 2007. Magnus is supervised by Mats Rudemo and Petter Mostad.

Other research collaborations in bioinformatics concern array studies of cancer tumours, designing and developing arrays and experiments concerning adverse effects of drugs on wildlife, in particular fishes, database construction for sequence analysis based species and phylogenetic studies of fungi. Many of those collaborations are the result of an extraordinary large interaction network created by the National Graduate School in Genomics and Bioinformatics, and are initiated by the graduate students themselves.

Image analysis

Particle tracking

Since more than five years the research group on spatial statistics and image analysis at Mathematical statistics, Chalmers, have a cooperation with AstraZeneca on colloidal particle tracking and diffusion estimation using microscopy. This has e.g. resulted in the PhD thesis Kvarnström (2005) and the recent paper Kvarnström and Glasbey (2006). The data modelled and analysed are sequences of microscope images obtained at AstraZeneca of diffusing polystyrene particles of diameter 500 nm. This system is used as a model for describing the 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. The same principle for tracking can be used in virtually any application where the depicted objects are roughly rotationally symmetric.

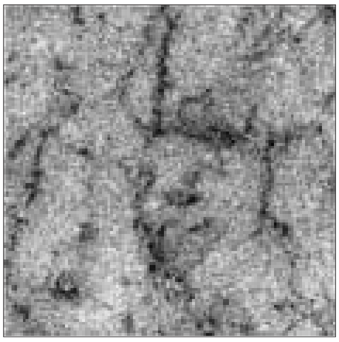


During 2007, we are planning to engage a student or two, for a diploma work involving the implementation of the methods presented in Kvarnström (2005) into a demonstrator software with a GUI for particle tracking.

Figure 1: An image from a video sequence of diffusing polystyrene particles. The particles are all of the same size; their differences in appearance is due to an out-of-focus effect, which is used for depth estimation.

Gel structure modeling

A method, described in Nisslert et al. (2006), for identifying the three-dimensional gel microstructure from statistical information in transmission electron micrographs has been developed in cooperation with SIK (the Swedish Institute for Food and Biotechnology), Department of Mathematical Statistics and Department of Chemical and Biological Engineering, Chalmers. The micrographs, see the left part of Figure 2, are projections of stained strands in gel slices.



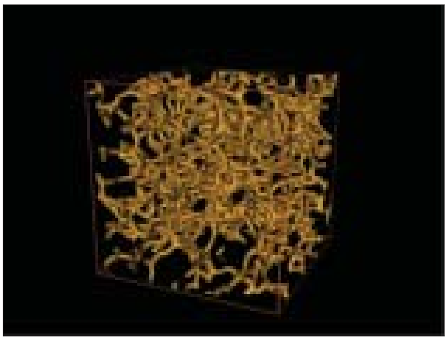


Figure 2: Left: part of a TEM micrograph from a stained Sepharose gel. Right: screen shot from a 3D rendering of the simulated gel network

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 and the right part of Figure 2 shows a 3D rendering from such a simulation. It would be of considerable interest to actually try to reconstruct the underlying 3D network from the micrographs. Development of MCMC algorithms for such a reconstruction is a challenging research problem. However, it would decrease the effort of arriving at a 3D network from TEM experiment of a microstructure. Presently, several steps of this process have to be guided manually. Also, this identification (or reconstruction) process would also largely benefit from having some kind of GUI.

During 2006 we have had a project on the 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 an 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. Among the interested industrial partners are SCA and AstraZeneca. The estimated diffusion coefficients are validated by comparing with diffusion coefficients measured via an experimental method called NMR diffusometry.

So far, this project has resulted in a MSc-thesis (Westergård, 2006) and during the autumn we have conducted more experiments and simulations and we are currently preparing two manuscripts for publication. We are also looking for students interested in a diploma work involving the design and implementation of a demonstrator for the SDE-solver, equipped with a GUI. This would enable faster testing of modifications, even for non-specialists in simulation and programming.

Improved design and analysis of FRAP experiments

The FRAP (fluorescence recovery after photo bleaching) technique is an efficient and versatile method for estimating diffusion coefficients. Figure 3 shows images obtained with a confocal microscope at three times after bleaching with a high energy laser in a cylindric beam orthogonal to the image plane. It is clearly visible how the fluorescent diffusing molecules are invading the area heavily bleached in the leftmost image. By use of maximum likelihood techniques applied to sequences of images we are presently refining available computational techniques to acquire higher accuracy. The project is a cooperation with SIK, and with Department of Mathematical Statistics and Department of Chemical and Biological Engineering, Chalmers. The methods developed will also be used to design new types of experiments that will allow study of transient structures.

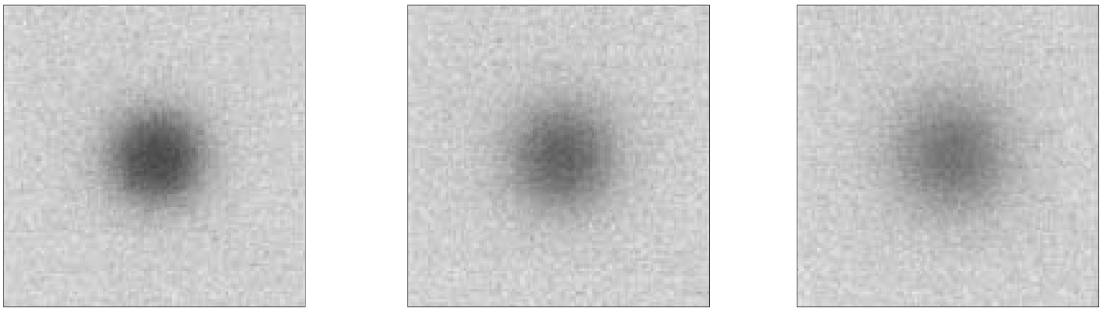


Figure 3: Images from a FRAP experiment with FITC molecules diffusing in a solution of Polyethy-lene glycol of average weight 400 g/mol and water at times 0.34 s, 3.40 s and 6.46 s after bleaching.

Publications

Published or accepted journal articles

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M. Arvidsson and I. Gremyr: Principles of Robust Design Methodology. To appear in Quality and Reliability Engineering International

A.L. Fougeres, S. Holm, H. Rootzén: Pitting corrosion: Comparison of treatments with extreme value distributed responses. Technometrics 48, 262–272

P. Johannesson, T. Svensson, L. Samuelsson, B. Bergman, J. de Maré: VMEA in Practice

M. Kvarnström and C. A. Glasbey: Estimation of centres and radial intensity profiles of spherical nano-particles in digital microscopy. To appear in Biometrical Journal

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

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K. Adolfsson, M. Enelund, S. Larsson, M. Racheva: Discretization of integro-differential equations modeling dynamic fractional order viscoelasticity. I. Lirkov, S. Margenov, and J. Wasniewski (Eds.) Proceedings of Large-Scale Scientific Computations, 2005, Sozopol, Bulgaria, LNCS vol. 3743, Springer, 76–83

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C. Cromvik and K. Eriksson: Airbag folding based on Origami mathematics

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A. Herbertsson and H. Rootzén: Pricing k-th-to-default swaps under default contagion: the matrix-analytic method

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J. Johansson: An estimate of the mean for m-dependent heavy-tailed distributions

J. Johansson: Some ideas from statistics for efficient front calculations under uncertainty

E. Kristiansson, A. Sjögren, M. Rudemo, O. Nerman: Quality Optimised Analysis of General Paired Microarray Experiments. Preprint 2006:6, Mathematical Sciences, Chalmers University of Technology and Göteborg University

T. Larsson, J. Marklund, C. Olsson, M. Patriksson: Convergent Lagrangian heuristics for nonlinear minimum cost network flows

T. Larsson, A. Migdalas, M. Patriksson: A generic column generation scheme

C. Lindberg: The estimation of a stochastic volatility model based on the number of trades

C. Lindberg: Robust portfolio optimization

Å. Lönnqvist: Including noise factors in Design-FMEA

Å. Lönnqvist: Evolution of Reliability thinking, Reliability Engineering response to some technical issues

P. Marcotte and M. Patriksson: Traffic Equilibrium

V. Olsbo: On the Correlation Between the Volume of the Typical Cell of a Poisson-Voronoi Tessellation and the Volume of the Typical Sphere in the Stienen Model

M. Patriksson: A survey on the continuous nonlinear resource allocation problem

H. Rootzén: Weak convergence of the tail empirical function for dependent sequences

E. Svensson and S. Larsson: Pointwise A priori Error Estimates for the Stokes Equations in Polyhedral Domains. Preprint 2006:19, Mathematical Sciences, Chalmers University of Technology and Göteborg University

T. Svensson and J. de Maré: Differential quotients versus partial derivatives for prediction intervals

PhD theses

E. Svensson: Computational characterization of mixing in flows
Supervisor: S. Larsson, Mathematical Sciences

G. Genet: A Statistical Approach to Multi-input Equivalent Fatigue Loads for the Durability of Automotive Structures
Supervisor: J. de Maré, Mathematical Sciences

J. Gustafsson: Unwarping and Analysing Electrophoresis Gels
Supervisor: M. Rudemo, Mathematical Sciences

Licentiate Theses

H. Martinsson: Model-Based Localization of a Three-Dimensional Object from Images
Supervisor: B. Johansson, Mathematical Sciences

V. Olsbo: Analysis and Modelling of Epidermal Nerve Fiber Patterns: a Point Process Approach
Supervisor: A. Särkkä, Mathematical Sciences

Master Theses

C. Andersson: Solving optimal control problems using FEM
Supervisors: S. Larsson, Mathematical Sciences and M. Lidberg, Applied Mechanics, Chalmers University of Technology
Examiner: S. Larsson, Mathematical Sciences

K. C. Batchu and M. Tuohetahuntila: Implementation of methods to estimate the growth curves of yeast
Supervisor: O. Nerman, Mathematical Sciences

F. Eriksson: Identifying non-transcriptional molecular pathways
Supervisor: O. Nerman, Mathematical Sciences

H. Folin: Randomized Hypergraph Matching Algorithms for Seed Reconstruction in Prostate Cancer Radiation
Supervisor: P. Jagers, Mathematical Sciences

M. Gillstedt: Dynamiken hos rotationer av cirkeln
Supervisor: B. Wennberg, Mathematical Sciences

E. Gudfinnsson and N. Sigfússon: Construction of an Optimal Linkage Arm Using Structural Optimization
Supervisor: A.-B. Strömberg, Fraunhofer–Chalmers Centre
Examiner: M. Patriksson, Mathematical Sciences

A. Hall: Finite element methods for parabolic stochastic PDEs
Supervisor: S. Larsson, Mathematical Sciences

B. K. Huy: Automatisk beräkning av antal celler i musögon i mikroskopbilder
Supervisor: M. Rudemo, Mathematical Sciences

T. Jansson: Resursutnyttjande i en fleroperationsstation
Supervisor: M. Patriksson, Mathematical Sciences

D. Lamazhapova: Bayesian Network for Learning from Biological Data
Supervisor: O. Nerman, Mathematical Sciences

J. Lindblad: Strukturerade produkter i portföljoptimering
Supervisor: H. Rootzén, Mathematical Sciences

G. Lövgren and O. Westerdahl: Optimal allokering i aktieindexobligationer
Supervisor: H. Rootzén, Mathematical Sciences

K. Mehlig: Alkohol och demens: Kvinnoundersökningen i Göteborg, 1968–1992
Supervisor: N. Wermuth, Mathematical Sciences

H. A. Noor: Network Identification and Regulatory Inference from Systematic Gene Perturbation Experiments
Supervisor: O. Nerman, Mathematical Sciences

L.-O. Olsson: Objektidentifiering i IR-bilder med utnyttjande av nyckelpunkter
Supervisor: M. Rudemo, Mathematical Sciences

J. Sarv: Normalisation and analysis of a post-transcriptional mRNA assay
Supervisor: O. Nerman, Mathematical Sciences

M. Sunnåker: New Approaches to Model Reduction of Biochemical Reaction Systems
Supervisor: H. Schmidt, Fraunhofer–Chalmers Centre
Examiner: K. Lindgren, Physical Resource Theory, Chalmers University of Technology

A. Westergård: Simulating diffusion with Brownian dynamics using an adaptive time-stepping algorithm
Supervisor: M. Kvarnström, Fraunhofer–Chalmers Centre
Examiner: M. Nyden, Chemical and Biological Engineering, Chalmers University of Technology

Financial Report GMMC 2006

	in 1000 SEK
Income	
The Swedish Foundation for Strategic Research	3021
Chalmers University of Technology	319
Total income	**3340**
Expenses	
Personnel expenses	
Reliability and risk	710
Biomathematics	305
Optimisation and modelling	440
Management and coordination	400
Project initiation	50
Rendering our results	70
Fellowships	68
Other personnel expenses	20
Total personnel expenses	**2063**
Other expenses	
Travelling and accomodation for guests	19
Travelling, workshops, conferences	122
Miscellaneous	31
Total other expenses	**172**
University levy ("högskolemoms")	**238**
University overhead University administration, computer support, premises etc.	**867**
Total expenses	**3340**

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http://www.chalmers.se/math/EN/research/gmmc