COSY

Centre of Excellence in Computational Complex Systems Research
Annual Report 2008

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Editor

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1 Introduction

2008 is in many ways very significant and historical. In the long-awaited administrative reorganization of Helsinki University of Technology (TKK), Laboratory of Computational Engineering (LCE) as the Centre of Excellence in Computational Complex Systems Research (COSY) and Laboratory of Biomedical Engineering joined forces to form the department of Biomedical Engineering and Computational Science (BECS) as part of the Faculty of Information and Natural Sciences. With this new structure COSY (as an autonomous part of BECS) keeps attacking challenging problems of complexity science while at the same time covering the teaching responsibilities for Computational Science, Cognitive Science, and Computational and Cognitive Biosciences majors in various degree programmes of TKK. In 2009 COSY is moving to the same premises with the rest of BECS that will intensify the joint strategy work.

The main goal of COSY is excellence in scientific research focussed on studies of complexity in various physical, biological, cognitive, economical, or social systems, in terms of their structure, function, and response. For this we have adopted trans-disciplinary holistic system level approach combining physical, mathematical, biological, neurocognitive or social science viewpoint with computational analysis, modelling, and simulation. Our research has been organised to four focus areas: 1. Models & Methods, including Complex networks and agent-based models, Complex dynamics and statistical physics, Statistical and information theoretic modelling methods, and Brain signal analysis; 2. Engineered and Artificial Systems, including Engineered nano-systems and Modelling of learning and perception; 3. Cognitive & Social Systems, including Cognitive systems and Structure and dynamics of social network; 4. Computational Systems Biology, including Bioimaging, Biospectroscopy and newly formed focus to Computational Health. The grouping of these focus areas is intended to be quite loose to promote research being conducted as cohesively as possible by joining the multi-disciplinary expertise within COSY.

In COSY we have continued to emphasize that our research is nationally and internationally strongly networked, as evidenced e.g. by the close ties with the Wolfson College of Oxford University in the form of an affiliate research unit. This unit of Computational Complex Systems and Network Research (CCSNR) with its own computing facilities, part-time director, two full-time researchers and a visiting scholar programme for the COSY’s researchers to network with Oxford scientists, continues to collaborate closely with Oxford’s Complex Agent-Based Dynamic Network (CABDyN) cross-departmental research cluster. COSY also cultivates a number of national and international collaborations funded nationally or by EU, which together with the Oxford link and mutual short-term visits fulfil also the role of researcher training. All these activities of COSY have borne a lot of fruit, i.e., about 46 scientific publications of which most in high impact factor journals with the average impact factor per journal article keeping to increase steadily reaching the level of 4.26, as evidence of high research quality. In terms of degrees 2008 continued to be a very productive:18 MSc’s and 5 DSc’s.!

Kimmo Kaski
Professor
2 Personnel

Professors
Kaski Kimmo Professor
Lampinen Jouko Professor
Sams Mikko Academy Professor
Tulkki Jukka Professor

Visiting Professors
Barrio Rafael Prof. (Universidad Nacional Autonoma de Mexico, Mexico)
Kertész Janós Prof. (Technical University of Budapest, Hungary)
Landau David Prof. (University of Georgia, USA)
Rauschecker Josef Prof. (Georgetown University, USA), Finland Distinguished Prof
Rissanen Jorma Prof. (USA)
Töyli Juuso Prof. (Helsinki School of Economics)

Adjunct Professors (Docents)
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Kertész Janós Prof. (Technical University of Budapest, Hungary)
Landau David Prof. (University of Georgia, USA)
Lehtokangas Mikko Docent (Tampere University of Technology)
Mouritsen Ole Prof. (Southern Denmark University, Denmark)
Oresic Matej Docent (VTT Biotechnology)
Parkkinen Jussi Prof. (University of Joensuu)
Räihä Kari-Jouko Prof. (University of Tampere)
San-Miguel Maxi Prof. (Universitat Illes Balears, Spain)
Sutton Adrian Prof. (Imperial College, London, UK)
Tirri Henry Prof. (University of Helsinki)

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Hyttinen Juha, Systems Engineer
Järvenpää Aino, Secretary
Kojonen Senja M.Sc., Project Planning Officer (18.7.2008-)
Lampinen Eeva M.Sc., Project Planning Officer (on leave 7.6.2008-)
Selonen Arto Dr.Tech, Systems Administrator
Virolainen Kaija Ph.D., Research Coordinator
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Engelhardt Peter Ph.D., Docent
Jääskeläinen Iiro Ph.D., Docent
Linna Riku Ph.D.
Saramäki Jari Ph.D.
Särkkä Simo Ph.D.

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Boxberg Fredrik Dr.Tech.
Kauhanen Laura Ph.D.

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Havulinna Aki M.Sc.
Heikkilä Oskari M.Sc.
Hulkkonen Jenni M.Sc.
Hyvönen Jörkki M.Sc.
Häyrynen Teppo M.Sc.
Jylänki Pasi M.Sc.
Jääskeläinen Pentti M.Sc.
Kauramäki Jaakko M.Sc.
Kettunen Juho M.Sc.
Kislyuk Daniel M.Sc.
Kivelä Mikko M.Sc.

Researcher in Oxford University, Oxford, UK
Onnela Jukka-Pekka Ph.D. JRF

Researcher in Harvard Medical School, Boston, USA
Ahveninen Jyrki Ph.D.

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Hänninen Jarno
Kangas Antti M.Sc.
Kivisaari Pyry
Koskela Sonja
Lehti Tuuli

Palander Kimmo M.Sc.
Peltola Tomi
Pennala Eero
Pietiläinen, Ville
Pihlaja Miika
Pihlström Kim M.Sc.
3 Boards

3.1 Centre of Excellence Scientific Advisory Board

Board Members

- Professor R Holland Cheng, University of California, Davis, USA
- Professor Alex Hansen, Norwegian University of Science and Technology, Norway
- Professor George R. Mangun, University of California, Davis, USA

Observers

- Professor Ulla Ruotsalainen, Tampere University of Technology (2006-7)
- Research Professor Tuja Pulkkinen, Finnish Meteorological Institute (2008-)
- Science Adviser Pasi Sihvonen, Academy of Finland, Programme Unit
- Senior Science Adviser Pentti Pulkkinen, Academy of Finland (2006-7)
- Science Adviser Vesa Siivola, Academy of Finland (2008-)
- Vicerector Outi Krause, Helsinki University of Technology
- Technology Manager Erkki Hietanen, Finnish Funding Agency for Technology and Innovation (Tekes), Helsinki

3.2 Internal Research Board “Oldies”

- Ala-Korpela Mika Ph.D., Docent
- Hassinen Pia M.Sc.
- Jääskeläinen Iiro Ph.D., Docent
- Kaski Kimmo Professor (Chairman)
- Kojonen Senja M.Sc.
- Lampinen Eeva M.Soc.Sc.
- Lampinen Jouko Professor
- Linna Riku Ph.D.
- Sams Mikko Professor
- Saramäki Jari Ph.D.
- Tiippana Kaisa Ph.D.
- Tulkki Jukka Professor
- Valpola Harri Dr.Tech., Docent
- Vehtari Aki Dr.Tech., Docent
- Virolainen Kaija Ph.D.
4 Teaching

Degree programmes and major subjects

Courses spring 2008
- S-114.1327 Physics III (EST) (6 cr)
- S-114.1427 Modern Physics: Computational Virtual Laboratory (Sf) (2 cr)
- S-114.2240 Seminar on Computational Engineering (3 cr) V
- S-114.2510 Computational Systems Biology (5 cr)
- S-114.3155 Business Game (3 cr) P
- S-114.4202 Special Course in Computational Engineering II (3-6 cr) P V
- S-114.4220 Research Seminar on Computational Science (3 cr) P V
- S-114.4610 Special Course in Bayesian Modelling (1-8 cr) P V
- S-114.4762 Systemic cognitive neuroscience (2 cr) L

Autumn 2008
- S-114.1100 Computational Science (5 cr)
- S-114.1310 Introduction to Modelling and Information Theory (3 cr)
- S-114.2500 Basics for Biosystems of the Cell (5 cr)
- S-114.2601 Introduction to Bayesian Modelling (5 cr) P
- S-114.3200 Sepcial course on computational engineering (6 cr)

Courses that can be taken any time
- S-114.3215 Special Project in Computational Engineering (3-8 cr)
- S-114.3520 Special Project in Computational Systems Biology (3-7 cr)
- S-114.4220 Research Seminar on Computational Science (3-6 cr) P V
- S-114.4230 Individual Studies on Computational Engineering (1-6 cr) P V
- S-114.4612 Special course in Bayesian modeling 2 (1-8 cr) L V
- S-114.4771 Special Project in Cognitive Science and Technology (3-7 cr) P V
- S-114.4772 Individual Studies in Communication and Cognition (1-9 cr) P

Abbreviations:
L & P: The course can be taken in Bachelor, Masters or Doctoral level studies
V: A course with varying content

For more information see:
Study Programme, Helsinki University of Technology
The study www-page: http://www.becs.tkk.fi/fi/opinnot/
**5 Theses**

**Doctor of Science / Philosophy**
- Kauhanen, Laura (Electromagnetic signals in noninvasive brain-computer interfaces)
- Kumpula, Jussi (Community structures in complex networks: detection and modeling)
- Nummenmaa, Aapo (Hierarchical Bayesian Aspects of Distributed Neuromagnetic Source Models)
- Segerståhl, Margareta (Developmental Biology of Sex Determination: Establishing a Basis for Systems Approach)
- Wang, Hao (Objects Extraction and Recognition for Camera-Based Interaction: Heuristic and Statistical Approaches)

**M.Sc. - Diplomas**
- Ahonen, Lauri (A computational approach to estimation of crowding in natural images)
- Blomqvist, Hanna (Enhancing the usability of a frequency converter control keypad)
- Hartikainen, Jouni (Sparse Gaussian Process Models In Bayesian Spatio-Temporal Analysis)
- Heikkilä, Oskari (Numerical modeling of high efficiency LEDs)
- Hulkkonen, Jenni (Minimum description length principle in novelty detection)
- Järvi, Noora (Improving software subcontracting process - pattern oriented approach)
- Lagerstöm, Hanna (Preliminary investigation of user and usability requirements for the production of a high-end panel)
- Leikola, Jaakko (Virtuaalisen oppimisympäristön ryhmätyöviestinnän kehittäminen)
- Luoma, Matti (Automated recognition of young conifer trees)
- Ollikainen, Antti Ilmari (Ohjelmisto pelikokemuksen tutkimiseen - peliominaisuksien sekä peliriippuvuuden vaikutus)
- Poikola, Matti (Uutispalveluiden tuottaminen hakuteknologioiden avulla)
- Ranne, Reetta-Johanna (Dementiaryhmäkodin hoitotyön toimintatilanteita tukeva työympäristö)
- Rautio, Milja (Usability evaluation of a competence solution)
- Sandholm, Niina (Virtual biological activity profiles, biological descriptors, for use in data mining applications)
- Savolainen, Petri (Tractography-guided transcranial magnetic stimulation in a working memory study)
- Tukiainen, Taru (Metabolic characterisation of mild cognitive impairment by 1H NMR spectroscopy and self-organising maps)
- Turtola, Pekka (Visual, haptic and visual-haptic perception of paper roughness)
- Villanen, Liisa (From and customer acceptability of self-service technologies to successful implementation of speech recognition services)
6 Research Projects

Models & Methods
including research on Complex networks and agent-based models, Complex dynamics and statistical physics, Statistical and information theoretic modelling methods, and Brain signal analysis;

Engineered & Artificial Systems
including research on Engineered nano-systems and Modelling of learning and perception;

Cognitive & Social Systems
including research on Cognitive systems and Structure and dynamics of social network;

Computational Systems Biology and Computational Health
including research on Bioinformatics and population-wide Health data analysis.

The general aim of COSY is to conduct transdisciplinary research on complex systems around and affecting us by using holistic system-level research paradigm and by developing new tools for studying them. In order to understand the complexity of various natural, technological, and societal systems holistic system-level research approach is needed. We have taken up the challenge to study structural and functional properties of systems from multidisciplinary perspective by using computational data analysis, modelling, and simulations.

The research of COSY (Figure 1.) is conducted by joining the expertise of its researchers in physical, biological, cognitive, and computational sciences with loose grouping into four focus areas.

Figure 1 The research is conducted in four mutually supportive fields
The main role of the **Models and Methods** research line is to facilitate the research of the other groups of the COSY. The focus is both on "fundamental" as well as on "applied" research. The former comprises theoretical and numerical work on mathematical and physical models of complex systems with one of the main focuses being on complex networks and agent-based models, and complex dynamics and statistical physics. In the latter, the focus is on computational tools and methods required for analysing and understanding experimental data of, for example brain signals and public health data.

In **Engineering and Artificial Systems** the research focus is twofold, on material based engineered nanosystems and on modelling of learning and perception. In nanosystems the goal is to understand the fundamental behaviour of (solid, soft or biological) materials and devices that show intrinsic complex phenomena such as pattern formation, self-organisation and self-assembly. These nanoscale systems are well-suited for computational modelling studies, which form the basis for applying them in nanoscale bioinformatics, biomedical analysis and in imaging systems. In modelling of learning and perception the research is based on computational models of various cognitive functions of humans, including learning, perception, and communication. The results are applied in computer vision and object recognition, and in robotics to study task-driven modelling of cognitive functions from computational neuroscience perspective.

In **Cognitive and Social Systems**, the research on cognition focuses on analysing and combining data obtained using complementary non-invasive neuro-imaging methods, to disclose dynamic neuronal interactions within and between brain areas. The aim is to develop an integrated computational model to predict how those interactions give rise to emotion-motivated (goal-directed) audio-visual selective attention. In Social systems research the structure and dynamics of social networks is analyzed and modelled based on complex networks and agent based approaches.

In **Computational Systems Biology and Computational Health**, the focus is to understand biological systems at various levels (molecular, cellular, tissue, organ and individual) and national health issues through computational modelling and information theoretic data analysis methods, using data gathered with bio-spectroscopic methods (e.g. NMR), genome-wide studies, and data on national health records.
**Figure 3 Centre of Excellence COSY, the total funding for the year 2008**

**Figure 2 Master of Science and Doctor of Philosophy Degrees**
Figure 4 Publications

Figure 5 Impact factor of the refereed publications
In recent years we have seen much progress in the analysis, modelling, and theoretical studies of complex systems, with the result that seemingly very different systems can be fruitfully approached with similar methods, and share sometimes similar characteristics. These findings illustrate the interplay between the different approaches, as well as the benefits of interdisciplinary work on complex systems. As an example, the existence of unexpectedly broad connectivity distributions in complex networks was originally discovered by statistical analysis of data on the World Wide Web. Then, it was theoretically and through simulations shown to result from certain types of network growth processes which also take place in several biological and social systems. Another illustrative example of a successful cross-disciplinary framework is Bayesian statistical modelling, which has during the recent years found applications across a wide range of disciplines ranging from engineering to neuroscience, and it is rapidly becoming the standard approach in statistical modelling.

The synergies of approaching complex systems from several perspectives are quite obvious and evident. In particular, theoretically oriented development of models and methods largely benefits from collaboration with researchers who have detailed knowledge and experience on particular complex systems, such as the human brain or various biomolecular systems; likewise, the researchers working on these systems are best served by modelling work which is driven by their needs. The Models and Methods group of the CoE focuses on both theoretically oriented work as well as empirical research. Theoretical studies are related to statistical and mathematical models of complex systems, as well as developing "generic" methods for complex systems research. The empirical research at Models and Methods focuses on developing computational tools and methods and applying them on various types of empirical data, such as electronic databases of mobile telephone communication, healthcare registry data, data on industrial processes, and spatial data related to epidemiology.
6.1.1 Complex Networks and Agent-Based Models

The network approach to complex systems has turned out to be very successful during the last years. It has revealed general principles applicable to a large number of systems from a wide range of disciplines -- there are surprising similarities between networks of protein interactions, the Internet, economic systems and large-scale social networks. In general, complex systems consist of large numbers of interacting elements and have highly non-trivial interaction structures. A system’s behaviour is then determined by the properties and dynamics of the elements as well as the interaction structure. The main strength of the complex networks approach is its inherent ability to provide a simplified view of this complicated picture, which is achieved by disregarding non-essential features. However, some information is always lost in such simplifications: one of the current trends is to limit this loss by including additional information about e.g. interaction strengths to the complex networks framework.

In the network approach, interacting elements are represented as vertices and their interactions by edges. Studies of network characteristics have produced novel findings such as the small-world property, the ubiquity of networks with broad degree distributions (the degree of a vertex is simply the number of connections it has), and the frequent appearance of high clustering and hierarchical structures. In other words, many statistical characteristics have been observed to be universal, i.e. similar in a large number of very different networks. Modern-day electronic databases and computational tools have been of especial importance to the development of this framework.

Lately, it has been realized that the simplest approximation, where edges either exist or not, has to be extended for a deeper understanding of the function and dynamics of complex networks. First, the interaction strengths can be taken into account in the form of edge weights – this additional degree of freedom provides deeper insight into the structural properties of networks. Second, in many cases, edges are not

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Project homepage: http://www.lce.hut.fi/research/mm/complex/

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Prof. Maxi san Miguel
Oxford University, U.K.
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University of Notre Dame, USA
Prof. Albert-László Barabási
static; there is dynamics on multiple time scales, from very fast processes of link activation-deactivation to slower processes of dynamic rearrangements of entire networks. Both of these aspects (interaction strengths, edge dynamics) are inherently linked to the mesoscopic structure of complex networks – structure beyond the scale of single vertices or their immediate neighbourhoods.

Such structure is typified by communities, which are sets of nodes with dense and strong internal connections, loosely connected to the rest of the network. Community structure is typically nested – smaller communities reside inside larger ones – and has important consequences on any dynamic processes taking place on networks. The recent activities of the Networks group are related to the above issues: our focus has been on developing the theoretical and methodological framework of weighted complex networks, initiating studies of edge dynamics and their relationship to network structure, and developing and assessing methods for detecting community structure on multiple scales.

As discussed above, in the framework of weighted complex networks, the interaction strengths of a complex system are taken into account. This is usually achieved by assigning a scalar value to each edge representing the interaction strength. As an example, in the network of world trade, vertices represent countries, an edge exists between two countries if there is mutual trade, and the weight of this edge represents e.g. the total annual trade volume – we have investigated several aspects of this interaction system using weighted network methodology (Battacharya et al, J. Stat. Mech. P02002 (2008)). Likewise, in social networks, the strengths of social ties are readily taken into account as edge weights. Incorporating this additional degree of freedom into the network picture evidently gives rise to new questions: how to measure and characterize the correlations between weights and topology? Are the weights distributed differently in different types of networks? How do the weights affect dynamic processes taking place on networks? How do the weights relate to mesoscopic properties, such as community structure?

In order to answer these questions, we have investigated several empirical weighted networks, and simultaneously developed methods for weighted network analysis. Some empirical data sets are inherently weighted networks – consider, e.g., the above-mentioned world trade network, or a large social network reconstructed from mobile telephone call records, where the total amount of time spent on the phone between two persons is a natural proxy for the tie strength. On the other hand, some systems where all elements interact with each other to a varying extent may also be recast as networks e.g. by progressively filtering out interactions of negligible strength. Such systems include stock markets, where all information is contained in correlation matrices computed from stock price time series, or genetic relationships between living entities. The latter case has been studied within the EU FP6 NEST-Pathfinder project EDEN, where the genetic relationships, evolutionary patterns, and ecological diversity of Mediterranean endangered marine plants are studied with network methods, in collaboration with institutions from Spain, Portugal and Germany. Here one of the key objectives is to detect clusters of genetically similar samples and understand their relationship with the underlying geography. In conjunction, we are developing software which allows biologists to easily utilize network-related data analysis techniques in studies of genetic relationships.

As mentioned above, communities and modules, i.e. sets of nodes with dense internal connections and higher-than-average link weights, are abundant in complex networks, and detecting and understanding such structure is one of the most important research trends in today’s network science. We have approached this problem from the methodological perspective, developing algorithms (Kumpula et al, Phys. Rev. E 79, 026109 (2008)) and mathematical methods (Heimo et al, Physica A 386, 5930 (2008), Heimo et al, J. Stat.
Mech. P08007 (2008)), as well as studied the effects of such structure on dynamic processes (Toivonen et al, Phys. Rev. E 79, 016109 (2009)). For the algorithms and methods, our main focus has been on extracting hierarchical, nested community structures from weighted networks with multilevel methods, allowing us to investigate the studied systems with multiple resolutions (see Figure 6). We have also focussed on methods which allow studies of very dense weighted networks, in practice systems described by full interaction strength matrices. Furthermore, we have also taken the first steps towards understanding the dynamics of such structures (Heimo et al, Physica A 388, 145 (2009)).

Figure 6 Modular structure of stock interactions detected using the Potts method (Heimo et al, J. Stat. Mech. P08007, 2008). The networks represent maximal spanning trees of stock interaction correlation matrices, inferred from time series of NYSE stock returns. a) The stock network together with Forbes industry classification. Prices of stocks belonging to the same industry sector typically show strong correlations, which is also reflected in the branch structure of the spanning tree. b) and c) Clusters of correlating stocks detected from the full correlation matrix using the Potts method, at two different levels of resolution. These clusters correspond well to the Forbes classification.
Polymer dynamics

The group’s research is motivated by analysis of experiments on structurally and dynamically complex systems in biology. Also non-physical complex structures, where unrestricted connectivity induces complex behaviour, are studied. Many biologically relevant structures and processes are characterised by their elasticity and rheology, whose interplay results in highly complex dynamics. In addition, the investigated structures, like the cytoskeleton, are heterogeneous, which paradoxically places a requirement of complete understanding of the object's mechanics in order to be able to interpret measurements correctly. Hence, the only way to find the correct structure and mechanics of the object is to construct a computational model that gives the experimentally observed behaviour.

Our first goal is to characterise the basic building elements of biological structures, for example actin filaments in the cytoskeleton. They are typically describable with various polymer models, which then link to form more complex structures. Since the linkage of the filaments is quite unrestricted, i.e. they can cross many neighbouring filaments without linking, the structural analysis of such a structure benefits from the methods used for analysing complex networks.

Our computational models are typically based on coarse-grained methods, such as stochastic rotation dynamics (SRD). In our hybrid algorithm the object under study follows detailed molecular dynamics while the solvent is modelled using SRD. Hence, molecular details of the solvent are not included. The coarse-grained solvent acts as a momentum conserving heat bath which can support hydrodynamic modes. Thus the method is ideal for investigating systems characterised by rheology and elasticity.

By extensive simulations using different polymer models we have shown that experiments where polymer is extended by flow can be used for detecting some characteristics of the DNA elasticity which manifest themselves clearly at large length scales but cannot be observed by mechanical force extension experiments even at very small length scales. Most notably, we have shown that the correct form of the DNA bending potential can be distinguished unambiguously from the form of the DNA extension response to flow velocity at micron length scales. The observation is remarkable, given that very precise DNA bending experiments cannot be used to determine conclusively the correct form even at length scales as short as 10 – 80 nm. By systematic analysis, the conclusiveness of different experimental methods has been evaluated. We have determined that the maximum length scale at which constant force and constant extension experiments give different results in a good solvent is ten persistence lengths, approximately 500 nm for DNA. Assessment of this length scale is
important for the correct interpretation of e.g. experiments using optical tweezers. For the worm-like chain, confirmed as the correct model for DNA, we have found an underlying scaling relation between its extension and flow velocity of the form $L_p \sim v^{0.155}$, which potentially serves as a starting point to understanding hydrodynamic interactions of semiflexible polymers.

No-slip

![Stretched wormlike DNA-chain](image)

**Figure 7** Stretched wormlike DNA-chain

Our research on complex dynamics involved in biologically relevant processes is inseparable from the above described characterisation of biopolymers. The ubiquitous process of biopolymer (e.g. DNA, RNA, and proteins) transport, or translocation, through nano-scale pores is a prototype example of a case where fairly simple constraints induce complex dynamics. Typically, for example in the protein import into intra-cellular compartments, such as mitochondria, chloroplasts, and peroxisomes, the translocation is aided by an electric pore potential. We have studied these translocation processes in order to understand the determining dynamics. We have shown that forced translocation is distinctly a non-equilibrium process even at pore potentials which barely induce translocation. We have introduced a phenomenological theory describing this process. Our results put the theory for biological translocation processes into a new perspective. Most notably, our results show that there exists no universal scaling law relating the translocation time to the polymer length, which is in clear contrast to several claims based on computer simulations using less realistic dynamics. This has significant bearing on the design of experimental setups for DNA sequence decoding.

![A snapshot from the simulation of a polymer translocation through a pore in a wall](image)

**Figure 8** A snapshot from the simulation of a polymer translocation through a pore in a wall
Our aim is to develop the computational models to encompass increasingly complex structures. At a later stage these models will be used to analyse experiments on e.g. lipid bilayer structures and viral capsids. High-quality experimental data on lipid bilayer structures will be available via collaboration with Helsinki Biophysics and Biomembrane group. Experimental data on translocation of RNA across pores on viral capsids will be available from the Molecular and Cellular Biology group in University of California Davis.

Collaboration related to actin filaments has been initiated with the experimental group led by Dr. Joachim Kappler at the Institute of Physiological Chemistry, University of Bonn. High-quality experimental data on lipid bilayer structures will be available via collaboration with Helsinki Biophysics and Biomembrane group led by Prof. Paavo Kinnunen.

**Percolation and fragmentation of complex networks**

Methods for analysing complex networks are studied. These generic methods have much in common with those needed for understanding complex structures in biology. Contrary to random structures having a finite dimension, the studied complex networks have no topological restrictions to the connectivity, i.e. any site can have an unlimited number of connections (links) to other sites.

Presently, we are studying how the concepts of percolation and fragmentation can be used in analysing networks. We have adopted different parametrisations for studying data from a mobile phone network of 3.9 million nodes. We have investigated further the percolation-like transition of this network and refined quite substantially the picture of the percolation-like transition related to the weight distribution of this network.

![Cluster size distribution of the network](image)

**Figure 9** Cluster-size distributions of the network when 30, 60, and 80 % of the weakest links are removed. The scale-invariant distribution is obtained at the assumed percolation threshold (80 % of the links removed).
6.1.3 Bayesian Modelling and Applications

Analysis of healthcare data

Focus of the project is to develop methods for healthcare data analysis. The goal is to create tools to aid healthcare agents (e.g. doctors and administration) to produce and evaluate regional healthcare key figures, and anticipate the expected cost effect of a treatment for a single patient or a treatment process. The emphasis is in development of methods for analysis of large scale healthcare data, for example, available in patient registries and mortality records. The project is a part of Tekes FinnWell - Healthcare technology programme.

Bayesian hierarchical methods make it possible to combine group-level and individual-level information in a flexible way, and nonlinearities and possible interactions between covariates can be automatically learned from the data, for example, with Gaussian process models. Implicit interactions allow also characterizing some of the hierarchical structures that are often modelled explicitly. Due to high-dimensional data and difficulties in interpreting and explaining the results of the complex models, one of the objectives is to obtain clear and understandable visualisations for the results. Pilot projects for the analysis of large scale patient data are analysis of institutionalisation of the elderly in city of Vantaa and the treatment of hip fracture patients in various hospital districts in Finland.

In Vantaa pilot the goal was to predict institutionalization and find groups with relatively high risk. The data set included different care events (nursing home periods, physician visits, home care etc) from registers of Vantaa city and Stakes. The data were modeled using Gaussian processes, after which an informative subset of covariates was chosen with variable selection. Using a smaller set of covariates made it easier to visualize the data and study combinations of factors which affected risk. As expected, institutionalization was predicted more accurately by register data than mere age and gender which are traditionally used. Groups with different risk levels were found. In groups with no care events or no events except home care, the risk is low and increases with age and with number of daily home care visits. Higher risk groups are described by different risk factors, e.g. functional capacity, number of hospital days and having nursing home periods, and age and home care has less effect.

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Project homepage: http://www.lce.hut.fi/research/mm/model/
In the hip fracture pilot, the objective is to research the prediction accuracy for the lengths of stay in sequential states of the treatment chain after a fractured hip. The project is conducted in co-operation with National Research and Development Centre for Welfare and Health (Stakes). In modelling the length of stay, parametric models such as the Coxian phase-type distributions and Weibull mixture models were considered first. The results showed that these parametric models did not capture well the characteristics in the data, and therefore a nonparametric Bayesian multilayer perceptron (MLP) model was used as a flexible alternative to predict the patient length of stay. Since there were nonlinearities and interactions in the model, average predictive comparisons were studied to assess the relevances of covariates in the prediction. The current development focuses on using Gaussian processes instead of the MLP model, and implementing a variable selection method for the Gaussian processes to increase the interpretability of the models.

Figure 10 In Vantaa pilot, groups of elderly with high institutionalization risk were found with help of visualizations where the high-dimensional covariate set was mapped into two-dimensional space. The colors show values of different covariates.
Figure 11  The evolution of spatial distribution of relative risk to female lung cancer in Finland during 1953-2003. Clear high risk areas can be identified from the northern and southern parts of the country, while clear low risk areas tend to be located around the central areas. The general temporal increase of risk to lung cancer can also be seen from the maps. The inference of the model parameters also suggests that time is a strong factor with this data set.
**Spatial and spatio-temporal epidemiology**

Spatial epidemiology seeks to reveal geographical variations in health outcomes and risks to health. The objective has been to create computationally efficient tools that provide accurate and easily interpretable results for the use of healthcare authorities.

In the first phase of the project, we created a customized GIS (Geographical Information Systems) tools to estimate and visualize geographical variations in relative risk of death. The adaptive binned kernel estimation method involved the use of circular computation areas operated on a grid with a maximum resolution of 250 m x 250 m allowed by the data. Risk estimates were based on comparing area-specific expected numbers of deaths to actual death counts within an averaging moving window.

The exploratory method featured fast and interactive creation of disease maps due to a simple algorithm and graphical interface. Its primary purpose will be to provide preliminary analysis over large scopes of data, but it does not facilitate the inclusion of explanatory variables aiding further understanding of the detected phenomena. For this reason the focus of the research has moved towards Bayesian spatial methods that provide an improved control on smoothing and statistical significances, and the flexible use of explanatory variables.

The Bayesian models studied utilize Gaussian processes, whose advantage is the flexibility in choosing the spatial covariance structure. The challenges with using Gaussian processes in spatial modeling are the inference time and memory requirements that scale unfavorably as a function of number of data points, and that the models are analytically intractable. These difficulties lead to a need of approximate computational methods that have been the main focus of the research for few years.

The methods under study include sparse Gaussian processes and analytical approximations for high dimensional integrals. The sparse Gaussian processes utilize special kind of covariance functions that lead to computationally faster implementation compared to traditionally used covariance functions. The approximate integration has been implemented using Laplace approximation and expectation propagation algorithm. The approximations are very fast to evaluate, and give very accurate results in the spatial models.

We have also extended the Gaussian process based disease mapping models from spatial to spatio-temporal domain. This enables the investigation of temporal dynamics of the spatial distribution of disease risk, and thereby extends the potential scope of disease mapping analysis. The covariance structure of the model is formulated such that the risk is assumed of being composed of independent spatial and temporal components as well as a component, in which space and time are coupled. Currently using the developed methods allow inference for data sets exceeding 20000 data points. The constructed models were tested with three municipal level cancer data sets with interesting results. While the temporal component was strongly present in each data set, clear spatial and spatio-temporal patterns were also identified.

*Project homepage: http://www.lce.hut.fi/research/mm/gp/*
The constructed spatio-temporal models were also applied to life expectancy estimation by replacing the time component with age group component, and then using the smoothed death rate estimates in traditional life table calculations. This approach has the advantage that it induces correlations among space and age dimensions, whereas traditional life table analysis usually assumes them to be independent, and provides realistic uncertainty estimates for the life expectancies.

Figure 12 Estimated relative risk of death caused by cerebral vascular diseases between 1995 and 2000. A zoomed-in image from Turku region. The resolution is 250 m x 250 m.
6.1.4 Statistical Brain Signal Analysis

The expertise of both Bayesian Methodology group and Cognitive Science and Technology group meet in the statistical brain signal analysis project. The work is done in collaboration with Massachusetts General Hospital–Harvard Medical School NMR Center.

Localising the neural currents indicating brain activity based on non-invasive magnetoencephalog-raphic (MEG) and electroencephalographic (EEG) measurements (i.e., solving the electromagnetic inverse problem) is most naturally formulated in probabilistic terms and thus becomes a problem of statistical inference. Because of the ill-posedness of the inverse problem, reliable inference cannot be made relying on the data only. Some additional a priori information must be provided in order to obtain sensible results, motivating a Bayesian treatment of the problem.

The overall aim of this project is to apply the methods of Bayesian data-analysis to the study of cognitive brain functions as revealed by MEG, EEG, and functional Magnetic Resonance Imaging (fMRI). We employ a variety of state-of-the-art estimation techniques from Markov chain Monte Carlo (MCMC) to Variational Bayesian (VB) methods. The models are evaluated and validated by using both empirical MEG datasets and simulated data.

One of the aims is to provide an automated procedure for localising MEG sources with the freshly introduced hierarchical minimum-norm estimation (hMNE). The progress of the VB-method is demonstrated in Figure 13. In this approach every possible source current has its own variance whereas in the traditional MNE every current has the same variance. Another focus of the research is on developing data-analysis techniques for combining MEG and fMRI. The rationale behind this is that MEG has excellent temporal resolution, but obtaining inverse estimates with high spatial specificity is hampered by the possibility of several distinct current patterns producing very similar MEG measurements. On the other hand, conventional fMRI provides direct spatial information about the possible locations of brain activity, but with limited temporal resolution.
Figure 13 A schematic illustration of the Variational Bayesian algorithm iterations in the MEG source localization procedure. Instead of several small current sources, only a few prominent sources pop up as a result of the algorithm.

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6.2 Engineered and Artificial Systems

Modern technology research is building novel artificial systems. In nanotechnology this emphasizes the need to understand the fundamental behaviour of materials fields and devices, which show intrinsic complex phenomena such as pattern formation, self-organisation and self-assembly. In the area of information technology, we develop computational models of cognitive functions, such as learning and perception, which are central issues in many research topics throughout the COSY. We apply the results in computer vision and object recognition, and in robotics to study task-driven modelling of cognitive functions from computational neuroscience perspective.
6.2.1 Engineered Nanosystems

The research of micro- and nanoelectronic materials, photonics and devices is getting a wider interface with problems of molecular and cell biology and medicine. This offers a manifold of new challenges for multidisciplinary theoretical research and computational science. At micro- and nanoscale the interaction of semiconductor, polymer and metallic surfaces with molecular level biosystems and the modulation of this interaction with microscopic voltage probes, light or chemical agents will be subject of extending research in the next years.

Information storage and communication systems utilizing quantum and all-optical devices are areas where nanomaterials and their technological applications are being worked out. In these areas we have continued to work on photonics applications. A new project has been started on developing very high efficiency light emitting devices that can be applied for white light luminaire as well as for specific thermophotonic devices.

In nonlinear materials we have studied carrier dynamics in quantum dots excited simultaneously by terahertz radiation from a free electron laser and an Ar-ion laser. The theoretical model and simulations are used to analyze recent experiments at UCSB. This work involves also collaboration with University of Tokyo. As a highlight of our work in this area we have proposed a new radiation based cooling mechanism of quantum dot excitons.

Recently started project on photonic biomorphic neural circuits has been continued. In this research area we work on stochastic properties of thermal and coherent photon fields. The photon bunching in partially coherent light is analyzed using dynamic quantum kinetic models in order to develop a quantum optical model of the network eye.

Project homepage: http://www.lce.hut.fi/research/eas/nanosystems/
Solid state lighting based on wide bandgap semiconductors and LEDs is expected to provide a viable way to high efficiency (up to 70-80 %) lighting solutions in the next 5-10 years. Lighting is the largest single user of electric energy with a 20 % share of global electricity consumption and large electrical energy savings will be possible using LED based lighting solutions. Currently, however, the performance of LEDs is still insufficient for use in general lighting applications and further advances are required. The research of this project is conducted as a part of the 5-year research program, 'High Efficiency Solid State Lighting Enabled by New Technologies' (HighLight), started in 2008 and lead by Prof. Harri Lipsanen, Department of Micro and Nanosciences. The HighLight program is a part of the Multidisciplinary Institute of Digitalisation and Energy (MIDE) of TKK and concentrates on the development of high efficiency LED structures for general illumination.

A part of the HighLight project will be dedicated for the study of novel nanometer scale light emitting structures (quantum dots and wires) and novel semiconductor/air interfaces for optimal photon extraction. This includes studies of photon extraction by patterning the semiconductor surfaces by nanoparticles or photonic crystals.

This project also studies the thermodynamics of light emission in semiconductors and the effect of the materials and device geometries on the efficiency of LEDs. This far the project has concentrated on studying the differences of conventional LED structures and new lateral LED geometries, as well as on studying the temperature dependence of the efficiency of LEDs and the thermodynamics of optically coupled LED structures. The modeling of LEDs and other light emitting devices is based on complex groups of nonlinear differential equations, which include the semiconductor equations, transfer equation for photons and heat, the interaction between photons and matter as well as models for the dielectric optical cavities of LEDs. The phenomena described by the models include the current, heat and photon transfer in the devices and provide valuable insight in the operation and loss mechanisms of LEDs and light emission in general. Special interest in the analysis has been paid in the temperature dependence of the light emission properties of the LEDs.

Practical applications of the models include new LED geometries and photonic heat pumps. The photonic heat pumps are devices where heat is transfered by photons instead of the more conventional working fluids of mechanical heat pumps or charge carriers of Peltier elements. The photonic heat pumps show promise for exceeding the performance of conventional solid state heat pumps based on Peltier effect. At best the structures may even compete with compressor based heat pumps on special applications.
Figure 14  A schematic picture of the band diagram of a double heterojunction light emitting diode illustrating the electron and hole transport, phonon absorption and light generation in the active region. The electrons (holes) flowing to the active region through the n-type (p-type) semiconductor absorb energy from the phonons as they climb over the potential gradients. When the electrons and holes recombine the absorbed heat contributes to the energy of the emitted photon. The black and white color gradient describes the electron distribution in the structure; black corresponds to a filled electron state and white to an empty electron state. The small curly arrows represent phonons and the large curly arrows represent photons.
Quantum trajectory approach to photon counting

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Usually photon detection statistics of the electro-magnetic field are calculated assuming that the field remains unchanged by the photon measurement process. For high intensity fields the changes may be neglected but for low intensity fields the measurement back action to the electromagnetic field must be taken into account. An appropriate interpretation of this phenomenon is related to the fundamental quantum measurement theory.

The instantaneous changes in quantum systems are modelled using the quantum jump superoperators. The quantum jumps produce interesting phenomena. For example with selected initial conditions for the electro-magnetic field an absorption process can increase the expectation value of the number of the photons in the field.

We have modelled the photon subtraction using the quantum trajectory theory and derived operators for absorption of exactly one photon and at least one photon based on the Srinivas and Davies (SD) model [J. Mod. Optic. 28, 981, 1981]. These operators correspond to experimental setups with resolving and nonresolving detectors, respectively. Calculated coincidence photon counting probabilities for the Fock state, thermal field, and coherent field are shown in Fig. 1. Furthermore, we have shown how the operators are applied consistently within the quantum trajectory theory.

![Figure 15](image)

(a) The coincidence probabilities of counting $k$ photons one at each measurement interval using the quantum jump operator $\hat{J} \hat{\rho} = \hat{a} \hat{a}^\dagger \hat{\rho}$, where $\hat{\rho}$ is the density operator of the electromagnetic field and $\hat{a}$ ($\hat{a}^\dagger$) is boson annihilation (creation) operator. Operator $\hat{J}$ gives count rate $\gamma \Pi$, coupling constant times number of photons. Note that in this example the measurement duration $\Delta t$ is chosen so that $\gamma \Pi \Delta t$ can become bigger than unity due to the measurement back action. Therefore more complicated operators corresponding resolving and nonresolving detectors must be used.

(b) The coincidence probabilities of counting exactly one photon at each measurement interval (resolving detector).

(c) the coincidence probabilities of counting at least one photon at each measurement interval (nonresolving detector). The results are calculated using the SD model based operators for the Fock state, the thermal field and the coherent field. The initial expectation value of the number of photons is 10.

Figure 15 The coincidence probabilities of counting photons
Modelling of cognitive functions is central issue in many research topics in the COSY – both to model the human cognitive functions, and to build artificial systems with those capabilities. In general perception can be seen as a signal processing or a state estimation problem. In the signal processing view, the sensory signals are processed in the system in order to detect the signal from noise, and to make classification and recognition based on the signal. Another view is that the system maintains a state space representation of the outside world, and the sensory signals are used to update the state. The signal processing view leads to bottom up, or data driven, processing, possibly with top-down feedback from context modulating the classifier operation. The state estimation view is a top-down, or model driven, scheme, where the current system state produces predictions for the sensory signals, and the prediction residual is a novelty signal used to update the system state.

The signal processing view is appropriate for many machine vision applications, like quality inspection, identification and limited surveillance applications. For generic perception skills, it is not clear how some required properties can be implemented in this view. These include fusing the information from several sensors, integrating different cues from one sensor modality, integrating temporal cues, and the specific role of context and background information in the processing.

In the state estimation view there is a latent representation for the world, giving prediction to the sensory signals. Thus all the sensory signals or cues that are predicted from a state variable can be readily used to update the variable. Mathematically the uncertainty in the state estimate and predictions can be represented as probability distributions, leading to Bayesian inference. In this scheme all the previously learnt or perceived information together with all the context information in the current task form the prior probabilities for the state variables and sensory signal predictions, and the Bayes’ rule is used to update the state after the sensory signal is observed.

From the engineering point of view, the Bayesian state space approach brings together classification, dynamic state estimation and inverse modelling as different parts of the perception task. There are also evidentially supported theories for modelling the brain functions as Bayesian inference (e.g. see the works of David Mumford and Karl Friston).

In our group we are developing object recognition and scene analysis methods based on Bayesian inference approach. Often in top-down object recognition a major problem is the weak influence of the data to the process. We are using Monte Carlo methods for the latent state representation, so that the recognition is done by sampling from the complex posterior distributions determined by the prior probabilities (from the context) and the likelihood function linking the state variables to the sensory signals. We have been developing sampling methods where the sensory signals are used efficiently in the proposal distributions. In the following we review results of Bayesian object matching.

Project homepage: http://www.lce.hut.fi/research/eas/vision/
Bayesian object matching

Object recognition and scene analysis are inherently ill-posed problems, as the visual information projected on the image plane (camera or retina) is not sufficient for inferring the 3D world characteristics. Thus some kind of prior knowledge of the world and the objects must be included in the process. Probability theory (i.e., Bayesian inference) provides one approach, which is theoretically consistent, and applies to recognition of objects given the image, as well as to learning of the world characteristics given a set of known samples.

We have been developing an object and scene analysis approach based on Bayesian inference. The feature part of the system is based on Gabor filters, which resemble the simple cells on primary visual cortex. On these primitive features, the system learns the variability of shapes of known objects (such as faces) and also the variability of individual details (such as the corner of the left eye). For recognizing an unknown object in a novel image, the object is modelled by the learned shape model and individual random effects, and the matching of the objects is carried out by evaluating the posterior distribution of all the unknown model parameters, including the feature positions on the image. This replaces the search, or model fitting, in traditional error-minimization techniques. The developed approach is rather generic, based directly on the probability theory with little ad hoc elements, which makes it easy to extend the model. For example, a difficult problem with flexible shape models (such as elastic graph matching, which represent state-of-the-art in face recognition) is partial occlusion of the object by other objects.

Figure 16 Sequential feature matching. The black circles mark the drawn locations of the current feature, while the green circles are the previously drawn features. The shape (yellow lines) represent the mean of the shape prior.
We have developed an occlusion model yielding joint estimation of the visibility and the position of the features, which can handle even serious occlusions (see Figure 16). We have also developed an efficient MC-method, based on sequential Monte Carlo sampling that requires no initialization and can handle any number of visible features. The sampling roughly corresponds to matching the features sequentially, starting from the most significant features in each image, automatically without any predetermined order. Special novelty in the system is a near-optimal proposal distribution for the feature positions, which takes into account both the likelihood (‘where the feature is seen on the image’) and the shape prior (‘where the feature would be given the other features’). Figure 16 shows an example of the sequential matching process and Figure 17 illustrates matching when the target objects are occluded.

Figure 17 Matching in the presence of occlusion. Even though the target objects are heavily occluded, the system is able to find the approximate locations of the features.
**Steerability properties of Gabor filters**

Gabor filters are information-theoretically optimal oriented bandpass filters which have been traditionally used in pattern recognition as a generic framework for the representation of visual images. Gabor-based features are widely used in face recognition, for example. Neurological studies have found Gabor-type structures on the visual cortex of mammals. This fact suggests that the Gabor representation is an efficient one in pattern recognition tasks.

We have derived analytical steering equations for Gabor filters, which enable Gabor filters to be used as approximately steerable filters, whose responses can be interpolated to arbitrary orientation, eliminating time-consuming recomputation of the Gabor transform with a rotated image. Some families of steerable filters are quite close to Gabor filters in terms of impulse responses, and the steering performance of Gabor filters can be understood via this connection.

Steerability can be used in object matching for explaining variation in features due to plane rotations. We have successfully applied Population Monte Carlo methods for rotation-invariant matching problems, where steerability can also be used for choosing efficient proposal distributions for the rotation parameter, leading to faster convergence.

![Figure 18 Probabilistic object matching without and with filter steering, with their average feature similarity scores shown on top of the images. Steering corrects the effect of rotation and the similarity scores remain almost constant](image-url)
Finding novel objects and object classes

We have built a probabilistic model that aims in locating instances of a common object, appearing in a set of unannotated images. The approach is sequential; the images are processed one at a time, and each matched instance is used as training data for the upcoming images. The used object representation is sparse, consisting of grid of nodes, which are matched in a novel image. Simple automatism is used to select the nodes in the first image. Along the sequence, the system learns the representation of the object, i.e. typical appearances of the nodes with certain arrangement. Only the nodes that correspond with the training nodes should be associated with the object, which is an issue that we have lately been studied. The probability distribution of the nodes is sampled with Sequential Monte Carlo methods, which we also have revised lately.

Figure 19 The matching results of a sequence of 30 images, containing a dog. Top row shows the first three images of the sequence, and bottom row the last three. The means of the SMC samples are marked with dots, and the sizes of the dots are proportional to the prior association probabilities and the colours to the posterior association probabilities, so that the greener the dot, the higher the probability. On the right, the evaluation of the prior association probabilities are illustrated.
The computational neuroscience group in LCE studies the system-level organization of the brain. In the brain, there are several interacting subsystems, which work in concert and each contribute to generation and adaptation of behaviour. In order to understand the brain, our group is building computational models of these subsystems and studying the complex, emergent behaviour and learning of an agent, which interacts with its environment. This type of research is called embedded computational neuroscience and it requires a body and environment to interact with. To this end, we have used a physics simulator platform. In other words, we have worked on simulated robots but in the future we also aim at verifying the results with real robotic platforms. ZenRobotics Ltd., a spin-off company of the group, already applies the methods for real robots.

Overview of the brain architecture – an evolutionary perspective

During evolution, the brain has always been part of a complete autonomous system. We are roughly following the evolutionary path of mammalian brain development and that is why our first embodied model—a complete brain which controls an autonomous robot—was cerebellar motor control. Cerebellum is an evolutionarily old system and is shared by all vertebrates and is critically involved in motor control. However, it is also known that cerebellum is involved in sensory processing, sensorimotor integration and cognitive functions. Algorithmically, a simple description of cerebellum is that it is a predictor. We have shown how a simple predictor can assist in motor control and it is also easy to see how a predictor can assist in the other tasks, in which cerebellum is known to be involved.

Our development of the computational models for different parts of the brain is by no means strictly serial. Rather, we are developing and testing computational models of various parts of the brain before they get integrated in autonomous agents. The point in building a complete autonomous agent is that we get a better intuition about what kind of processing is needed by the already existing integrated components in order to improve motor performance and ability to tackle more complex environments. We can then tune the hypotheses about the computational role of different parts of the mammalian brain.

Apart from the cerebellar model, the main topics of our research have so far been the basal ganglia and the mammalian neocortex. Basal ganglia are thought to assist in selection of behaviours and learning through trial and error. Evolution has determined a set of fixed reflexes and action patterns for an animal. Now, the basal ganglia can learn similar patterns. Thus, they make the agent adaptive to an unknown world.

As opposed to cerebellum, neocortex appeared quite late in evolution and is shared by modern mammals. Neocortex is the most complex part of the brain and tremendously enlarged in humans. It is the site of high-level cognition, consciousness and imagination.
Dorsal cortex, the evolutionary precursor of neocortex is much older and simpler, though. It seems that one of the first tasks the precursor of neocortex solved was development of behaviourally meaningful representations. As an example, consider a balancing robot which is riding an uneven terrain and has cameras enabling depth vision—in principle; it is by no means a trivial task to extract depth information from the images of two cameras. We are investigating how motor signals can bias the development of perceptual systems and dynamic selection of useful information (selective attention) such that perception will be optimized for the behavioural needs of motor control.

We have already started to integrate the models of different brain modules. We have noticed that the interplay between the cerebellum and the basal ganglia enhances learning of both of the modules. We have also noticed how crucial it is for the neocortex to be able to represent different contexts for the cerebellum.

Other systems that we plan to incorporate in the model later include the hippocampal formation. This module appears to have developed to assist navigation and is able to compress, store and replay sequences of events.

Although the different modules of the mammalian brain seem to have evolved to serve the needs of basic motor control, these mechanisms have later been adopted by higher-level cognition. For instance, when we plan, we in a sense navigate through options and select promising paths of thinking. This can be considered as internalised navigation where basal ganglia help us make choices and hippocampal formation enables us to remember the paths of thinking. It is easier to study and understand navigation, manipulation and sensory associations than planning, reasoning and symbolic language, but the same underlying mechanisms are at work.

**Cerebellar learning for motor control**

The cerebellum is responsible for timing, fine-tuning and coordinating the motor system. By learning in a self-supervised fashion from error signals generated by other parts of the brain and body, the cerebellum is able to rapidly execute and accurately time motor actions in response to external stimuli.

The learning algorithm executed by the cerebellum is efficient and simple: if a reflex is triggered in response to an event, the system will associate the action of the reflex with the system states that preceded the event. The next time a similar state is observed, the system will anticipate the reflex by performing the reflex action beforehand. With suitably chosen reflexes, the cerebellum learns to be a stable controller that can, for instance, keep a dynamically balanced robot upright.

One of the main attractions of the cerebellar model of control is its robustness: the system can quickly learn to respond to new conditions, and can learn to anticipate changes in the external world that place demands on the motor system (for example, knowing that a heavy weight will shortly be placed in one’s hands, a person will automatically prepare by assuming a more solid posture). The cerebellar algorithm is also able to make use of any contextual data from the rest of the brain that happens to be available.

Our work concerns the application of the cerebellar control model into robotics using a simulation environment; the ability of the cerebellar controller to take advantage of extraneous inputs for adaptation and the mathematical aspects of the cerebellar controller itself.
Figure 20 A simulated wheeled robot using the cerebellar algorithm for stabilizing itself. A reflex tells the robot when it is about to fall over. The small images show the robot in a situation when its dynamics change due to the heavy weight atop of it moving in vertical direction.

Figure 20 shows a simple simulated wheeled robot using the cerebellar algorithm for stabilizing itself. The robot is able to stay upright even when its sensory inputs (tilt, velocity etc.) are delayed. The robot has thus learned to anticipate its future state with the help of a reflex telling it when it is or was about to fall over.

The cerebellar algorithm was also proven to be able to coordinate a system with several degrees of freedom. The goal of the system was to keep the multi-jointed robot arm at a given position (Figure 21). The segments interact and righting one segment will cause the others to experience more force and can easily lead to unstable states. By taking into account the positions of all joints and anticipating the motion of the others the cerebellum learned to compensate for them proactively.

Our ongoing cerebellar research focuses on contextual inputs. The small images in Figure 20 show an example of changed dynamics. When the heavy weight the robot is carrying moves in vertical direction, the dynamics of the system change, and the controller needs to account for the changes. We are now investigating ways to convey information about the changed context to the cerebellum.
**Model of neocortex**

As its name suggests, neocortex has evolved relatively recently, some time after mammalian lineage departed from reptiles. The neocortex has expanded the most during evolution and with its numerous folds and gyri is the largest structure in the human brain. The neocortex processes inputs from all the senses and is the seat of high-level cognitive functions such as decision making, imagination, planning and consciousness. It learns regularities, rules, abstractions and relations from the world using the sensory inputs it receives. Thus, it forms a model of the world where the animal is living. It also supports attention by deciding which aspects of the world are relevant at each moment.

The neocortex has a stereotypical six layered organization. Although many details vary, the overall structure is still recognisable throughout different cortical areas and species. This suggests that the neocortex can do all of its functions with variations of the same basic algorithm. This algorithm must be quite general and widely applicable because over the course of evolution, neocortex has expanded enormously and taken over many functions of other specialized, subcortical brain structures. For instance in human motor control, the motor cortex is a necessary executive organ without which we become paralysed. In contrast, in many other mammals such as rats, the whole neocortex can be removed without critically impairing motor behaviour.

So far our model of the neocortex supports learning and attention. The model consists of a large number of similar, interconnected information processing units, which interpret their inputs and make decisions about what information to broadcast based on the contextual inputs they receive from their neighbours. In such a network, global attention emerges from the units’ individual decisions to broadcast information (see “Complex networks and agent-based models” and “Cognitive Systems” for other related research).

The model is depicted in Figure 22. Each local neural population, or neural unit, learns and represents a set of different features from its inputs. Each unit receives bottom-up input vectors (solid blue arrows) and represents their regularities (features in machine learning terminology) by neural activation levels. In addition to the bottom-up inputs, the units receive information about other units through contextual inputs (dashed purple arrows). The units use the contextual information to improve their estimate about the identity of their bottom-up input and to make a decision about which features are the most relevant at the
moment. The units make Bayesian inference about the identity of their bottom-up inputs implicitly, using contextual inputs as background information to refine their judgement.

The context-based associations are also used to assess the value of representing different features. So far we have experimented with evaluating the features based on their coherence with the context. The motivation is that it is better to represent those features which belong to the same object or event rather than represent features which belong to different objects or events. In practice this is achieved by highlighting context-supported features even more than Bayesian probability theory would suggest and then selecting only the most active features. In a network of processing units, this type of selection quickly singles out the features belonging to the most prominent object. The network automatically learns to perceive objects based on the associations between the context and the bottom-up inputs. This corresponds to finding Gestalt shapes.

Since it is usually beneficial to process and represent more than one object, we have added a mechanism to switch between different objects. Again, this process relies on a very simple habituation mechanism distributed among the processing units: the active output neurons gradually get “tired”. After a while some of the units start to make decisions to represent the features of another object and due to the context connections between units, this change escalates rapidly through the network and the network switches its attention to another object (Figure 23).

One of the most intriguing aspects of neocortex is its ability to come up with abstract, meaningful concepts. Our model uses so called competitive learning where the output neurons learn to respond even stronger to those inputs for which they became active. Since the contextual inputs modulate the activations strongly, they also have an important role in

![Figure 22 An example architecture of the neocortex](image-url)
guiding learning. We have shown that in a hierarchical model like the one shown in Figure 22, the upper layers develop meaningful abstract representations. Moreover, since the emergent selection process in the network is able to attend to one object at a time, learning is faster because the features of different objects do not mix up.

![Input vs What the cortex sees](image)

Figure 23 Jumping attention emerges in the cortex model. When the model was fed with the static image on the left, the network represented different images on different time instants: its attention focused on different objects in the image.

So far we have not embedded the model into a larger cognitive architecture but this has been the goal in the design of the model. We are planning to include inputs from other “subcortical” modules as contextual inputs in order to bias attention and learning in the neocortical model. There are also various interesting possibilities to improve the model’s evaluation of important bottom-up inputs. For example, it is usually important to represent bottom-up inputs which are predictive of changes in context whereas the reverse temporal order indicates that the corresponding bottom-up inputs are not important. When receiving context from a motor system, such as the cerebellar model discussed in the previous section, and bottom-up inputs from sensors, such as cameras, the model could then learn to represent those visual features which are important for the motor behaviour of the system.

**Integrating basal-ganglia and cerebellar models**

Basal ganglia are an evolutionarily old system, and its homolog is found for example from all vertebrates. It is well conserved in evolution, suggesting a fundamental role in the brain function. Two main functions of basal ganglia are action selection and learning voluntary actions by trial and error.

Our research aims to combine the abovementioned model of cerebellar predictor, and a reinforcement learning model accounting of trial and error learning of new actions. Teaching a cerebellar predictor always needs an error signal, which from the biological view point can be thought of as a reflex. In this scheme, learning new tasks would require a new handcrafted reflex signal every time. Moreover, designing workable reflex signal becomes increasingly tedious with the growing task complexity. This can be circumvented by using a reinforcement learner model of basal-ganglia to learn a coarse version of the required reflex from reward signal coming from environment. Moreover, addition of the cerebellar model can speed up the learning in a typically slow reinforcement based algorithm.

Actor-critic algorithms and cerebellar models have traditionally been studied separately. In a combined model, the role of cerebellum overlaps with the actor part of the reinforcement learning algorithm. Our goal is to learn, how the division of labour between the modules could be optimized.
6.3 Cognitive and Social Systems

Cognitive systems

In cognitive systems research, we have focused on studying the neural basis of active perception as a system with many interacting mechanisms, studying also the role of emotions in active perception, and have recently expanded our approach to study the brain in more naturalistic stimulus and task paradigms such as when viewing movies.

In our active perception research, we have continued our efforts to elucidate how the brain converts the stream of acoustic energy into features and objects, seamlessly combines auditory and visual information, memorizes the immediate past, predicts what is going to happen next, and prioritizes processing of relevant stimuli while maintaining capability to react quickly to unexpected events. As an everyday example, in a crowded cocktail party, one can selectively attend to a given conversation despite interference from multiple overlapping conversations, especially when seeing the lip movements of the speaker. Yet background noise and other conversations are automatically analyzed to some extent, as evidenced by attention being drawn to unexpected (i.e. unpredictable) events, such as one’s name being brought up in a background conversation. Further, the brain quickly adjusts to an unfamiliar accent of a new conversation partner, with such perceptual learning effects persisting over long periods of time, even up to a lifetime. In our theoretical framework (Jääskeläinen et al. 2007), we aim to unify aspects of task-relevant modulation (i.e., short-term plasticity) along the entire auditory pathway, from cortex to auditory periphery. Emotions, on the other hand, fundamentally shape our goals, and how stimuli are evaluated/processed in the brain (for a recent theoretical paper from our laboratory on this topic, see Alexandrov and Sams (2005).

Our research utilizes advanced, non-invasive human brain imaging methods, such as combined fMRI, MEG, and EEG, and linear causality modelling techniques. Our research scope is deliberately broad, ranging from bottom-up, largely stimulus-drive processes in auditory cortex to extra-acoustic influences on auditory processing, including selective attention and multisensory perception, with the use of both more traditional highly controlled and reduced stimulus/task settings as well as novel naturalistic stimulus/task paradigms and the associated new types of signal/data analysis approaches. We believe that this holistic approach is crucial for understanding the highly interactive and dynamic process of how internal and external contexts guide active hearing. In addition, our basis research has extended to studying Brain-Computer Interfaces in tetraplegic and healthy subjects. We collaborate intensively with our colleagues in Harvard Medical School, Boston, Georgetown University, Waschington DC, and Northwestern University, Chicago, USA, to achieve our research goals.
Social systems

In social systems we focus on understanding how "microscopic" social interactions between a large number of individuals give rise to the "macroscopic" structure - the society. Consider, as an example, your everyday social life. You are likely to have repeated social interactions with a relatively small number of people (friends, colleagues, family members). It is also likely that many of these people are also bound to each other by social ties – your friends are very likely to be each other’s friends as well. In addition, these social ties surrounding you most probably form some kind of community structure, where you participate in several cliques, such as those consisting of your colleagues or friends sharing a same hobby. Zooming out of this local picture, these cliques and communities are in turn interconnected by social ties between their members as well as shared participants. Zooming out even further, we reach the societal level, where even larger-scale structures start to become visible - those formed by ties within and between socioeconomic classes, professional, political and scholarly communities, etc. You are part of a very, very large network of social ties.

Social networks have been the subject of intensive study since the 1930’s. In this framework, social life consists of the flow and exchange of norms, values, ideas and other social and cultural resources, and social action of individuals is affected by the structure of the underlying network. The structure of social networks is important then not only from the perspective of the individual, but also from that of the society as a whole. However, uncovering the structure of social networks has been constrained by the practical difficulty of mapping out a large number of individuals. Here, modern electronic databases offer unprecedented opportunities to uncover and explore large-scale social structures. Furthermore, by combining expertise in various fields such as social sciences, statistical physics, and computer science, we can simulate and study processes taking place on these enormous networks, such as diffusion of ideas and opinions. Our team was recently the first to show that very large social networks are, contrary to popular belief, not particularly optimal for unconstrained random flow of information. Rather, the structure tends to localize information within cliques. For any information to spread across the network, the "weak ties" connecting cliques have to be actively utilized. Currently, we are focussing on the dynamics of social networks inferred from communication records. Such dynamics takes place on several time scales, from the short-term time scale of communication events and patterns to the longer time scale of network rearrangement. Our first observations indicate clear traces of "causal" sequences of communication events where information is passed (e.g. from A to B to C). Furthermore, the observed short-term dynamics appears to slow down processes taking place on the level of the entire network, as compared to randomized reference dynamics with no short-term correlations.
Continuing our efforts to elucidate the neural basis of audiovisual integration, we tested for the feature specificity of adaptation of auditory-cortex magnetoencephalographic N1m responses to phonemes during lipreading. We presented eight healthy volunteers with a simplified sine-wave first-formant (F1) transition shared by /ba/, /ga/, and /da/, and a continuum of second-formant (F2) transitions contained in /ba/ (ascending), /da/ (level), and /ga/ (descending), during lipreading of /ba/ vs. /ga/ vs. a still-face baseline. N1m responses to the F1 transition were suppressed during lipreading, further, visual /ga/ (vs. /ba/) significantly suppressed left-hemisphere N1m responses to the F2 transition contained in /ga/. This suggests that visual speech activates and adapts auditory cortex neural populations tuned to formant transitions, the basic sound-sweep constituents of phonemes, potentially explaining enhanced speech perception during lipreading.

**Thematically related EEG study**

In a thematically related EEG study, we combined the McGurk effect with mismatch negativity (MMN), a response that is elicited in the auditory cortex at a latency of 100-250 msec by any above-threshold change in a sequence of repetitive sounds. An "odd-ball" sequence of acoustic stimuli consisting of frequent /va/ syllables (standards) and infrequent /ba/ syllables (deviants) was presented to 11 participants. Deviant stimuli in the unsensory acoustic stimulus sequence elicited a typical MMN, reflecting discrimination of acoustic features in the auditory cortex. When the acoustic stimuli were dubbed onto a video of a mouth constantly articulating /va/, the deviant acoustic /ba/ was heard as /va/ due to the McGurk effect and was indistinguishable from the standards. Importantly, such deviants did not elicit MMN, indicating that the auditory cortex failed to discriminate between the acoustic stimuli. Our findings show that visual stream can qualitatively change the auditory percept at the auditory cortex level, profoundly influencing the auditory cortex mechanisms underlying early sound discrimination.

**Project homepage:** [http://www.lce.hut.fi/research/css/systems/](http://www.lce.hut.fi/research/css/systems/)

We also used whole-head magnetoencephalography (MEG) to record changes in neuromagnetic N100m responses generated in the left and right auditory cortex as a function of the match between visual and auditory speech signals. Stimuli were auditory-only (AO) and auditory-visual (AV) presentations of /pi/, /ti/ and /vi/. Three types of intensity matched auditory stimuli were used: intact speech (Normal), frequency band filtered speech (Band) and speech-shaped white noise (Noise). The behavioural task was to
detect the /vi/ syllables which comprised 12% of stimuli. N100m responses were measured to averaged /pi/ and /ti/ stimuli. Behavioural data showed that identification of the stimuli was faster and more accurate for Normal than for Band stimuli, and for Band than for Noise stimuli. Reaction times were faster for AV than AO stimuli. MEG data showed that in the left hemisphere, N100m to both AO and AV stimuli was largest for the Normal, smaller for Band and smallest for Noise stimuli. In the right hemisphere, Normal and Band AO stimuli elicited N100m responses of quite similar amplitudes, but N100m amplitude to Noise was about half of that. There was a reduction in N100m for the AV compared to the AO conditions. The size of this reduction for each stimulus type was same in the left hemisphere but graded in the right (being largest to the Normal, smaller to the Band and smallest to the Noise stimuli). The N100m decrease for the Normal stimuli was significantly larger in the right than in the left hemisphere. These results suggest that the effect of processing visual speech seen in the right hemisphere likely reflects suppression of the auditory response based on AV cues for place of articulation.

We used functional MRI (fMRI) to examine activation of the during strictly controlled auditory attention tasks to show that selective auditory attention modulates neural activity in the human inferior colliculus (IC) in addition to the human auditory cortex (AC). The IC is an obligatory midbrain nucleus of the ascending auditory pathway with diverse internal and external connections. The IC also receives a massive descending projection from the AC, suggesting that cortical processes affect IC operations. In this study, 21 subjects selectively attended to left-ear or right-ear sounds and ignored sounds delivered to the other ear. IC activations depended on the direction of attention, indicating that auditory processing in the human IC is not only determined by acoustic input but also by the current behavioral goals. In another study, subjects looked at emotion-evoking pictures taken from the International Affective Picture System database while 32-channel EEG evoked responses (ERPs) to an unchanging auditory stimulus ("danny") were collected. Effects of viewing negative emotion pictures were seen as early as 20 msec. Thus, it appears that emotion can also affect auditory function early in the sensory processing stream.

**Cognitive style in autism spectrum disorders**

As a clinical research extension of our basic research efforts, we tested the detail-focused cognitive style in autism spectrum disorders, which implies that persons with autism spectrum disorders (ASDs) have a perceptual bias for local but not for global stimulus features. The recognition of emotional facial expressions representing various different levels of detail has not been studied previously in ASDs. We analyzed the recognition of four basic emotional facial expressions (anger, disgust, fear and happiness) from low-spatial frequencies (overall global shapes without local features) in adults with an ASD. A group of 20 participants with Asperger syndrome (AS) was compared to a group of non-
autistic age- and sex-matched controls. Emotion recognition was tested from static and dynamic facial expressions whose spatial frequency contents had been manipulated by low-pass filtering at two levels. The two groups recognized emotions similarly from non-filtered faces and from dynamic vs. static facial expressions. In contrast, the participants with AS were less accurate than controls in recognizing facial emotions from very low-spatial frequencies. The results suggest intact recognition of basic facial emotions and dynamic facial information, but impaired visual processing of global features in ASDs.

**Brain-computer interface studies**

Continuing on our brain-computer interface studies, we investigated whether inexperienced subjects could control a BCI accurately by means of visually-cued left versus right index finger movements, performed every 2 s, after only a 20-min training period. Ten subjects tried to move a circle from the center to a target location at the left or right side of the computer screen by moving their left or right index finger. The classifier was updated after each trial using the correct class labels, enabling up-to-date feedback to the subjects throughout the training. Therefore, a separate data collection session for optimizing the classification algorithm was not needed. When the performance of the BCI was tested, the classifier was not updated. Seven of the ten subjects were able to control the BCI well. They could choose the correct target in 84%-100% of the cases, 3.5-7.7 times a minute. Their mean single trial classification rate was 80% and bit rate 10 bits/min. These results encourage the development of BCIs for paralyzed persons based on detection of single-trial movement attempts.

In 2008, we also developed a BCI, which tetraplegic subjects could control only in 30 minutes. Six such subjects (level of injury C4-C5) operated a 6-channel EEG BCI. The task was to move a circle from the centre of the computer screen to its right or left side by attempting visually triggered right- or left-hand movements. During the training periods, the classifier was adapted to the user's EEG activity after each movement attempt in a supervised manner. Feedback of the performance was given immediately after starting the BCI use. Within the time limit, three subjects learned to control the BCI. We believe that fast initial learning is an important factor that increases motivation and willingness to use BCIs. We have previously tested a similar single-trial classification approach in healthy subjects. Our new results show that methods developed and tested with healthy subjects do not necessarily work as well as with motor-disabled patients. Therefore, it is important to use motor-disabled persons as subjects in BCI development.

**Neurocinematics study**

During 2008, we also took our first significant steps towards using more naturalistic stimulus paradigms in our neurocinematics study published in the Open Neuroimaging Journal by Jääskeläinen and colleagues. Specifically, hemodynamic activity in occipital, temporal, and parietal cortical areas were previously shown by others to correlate across subjects during viewing of a 30-minute movie clip, however, most of the frontal cortex lacked between-subject correlations. Here we presented 12 healthy naïve volunteers with the first 72 minutes of a movie ("Crash", 2005, Lions Gate Films) outside of the fMRI scanner to involve the subjects in the plot of the movie, followed by presentation of the last 36 minutes during fMRI scanning. We observed significant between-subjects correlation of fMRI activity in especially right hemisphere frontal cortical areas, in addition to the
correlation of activity in temporal, occipital, and parietal areas (see Figure 24). It is possible that this resulted from the subjects following the plot of the movie and being emotionally engaged in the movie during fMRI scanning. We further showed that probabilistic independent component analysis (ICA) can be used to reveal meaningful activations in individual subjects during natural viewing conditions.

Figure 24 We observed significant between-subjects correlation of fMRI activity in especially right hemisphere frontal cortical areas, in addition to the correlation of activity in temporal, occipital, and parietal areas. The inter-subject correlation maps are overlaid on A) sagittal, coronal and axial MRI slices and, B) on inflated cortical surfaces of left and right hemispheres.
6.3.2 Structure and Dynamics of Social Networks

Our focus areas are empirical analysis of data on large-scale social networks, the effects of observed structural features on processes taking place on such networks, as well as modelling the emergence of these features. This research has been closely related to the activities of the Complex networks and agent based models group (see Models & Methods), and also involves international collaborators from Budapest University of Technology (Hungary), University of Oxford (UK), University of Notre Dame (USA), and Harvard University (USA). In terms of complex network science, the main focus of the empirical research line is on linking social tie strength and communication patterns of individuals to the overall network structure.

Uncovering structural properties of large social networks has been so far constrained by the practical difficulty of mapping out interactions among a large number of individuals. Hence, most social science studies deal with analyzing questionnaire data, typically only reaching the order of N=100 individuals. The benefit of this approach is that the spectrum of social interactions accessible to studies is wide. However, as a downside, the strength of an interaction is harder to quantify; in questionnaire-based data, it is based on recollection and, consequently, is highly subjective. However, the availability of electronic databases from emails to phone records has recently attracted the interest of both sociologists and (statistical) physicists. These databases provide unprecedented opportunities for modern social network analysis – social networks as large as millions of individuals may be handled, and although the range of social interactions is evidently narrower (e.g. email or phone communication), all information is objectively quantifiable. Although both approaches have their merits, studying large scale networks may better shed light on how individual microscopic interactions translate into macroscopic social systems. In addition to this being one of the key questions as posed by social scientists, it is also the one to which statistical physics in general, and the science of complex networks in particular, can make a contribution.

In 2008, we have continued studies of social networks inferred from mobile phone call records, where the first results were published in 2007 (see Onnela et al., Proc. Natl. Acad. Sci. (USA) 104, 7332 (2007); Onnela et al., New J. Phys. 9, 179 (2007)). The (anonymized) call records have been extracted from the customer data base of a mobile network operator, whose customer base is approximately 20th of the population of its country of operation. In the network analysis, the subscriptions (i.e. mobile phone users) are represented as the network’s nodes. They are interconnected by a link if the two users have both called each other during the investigated period, and we use the aggregated call minutes between people as a proxy of the social tie strength. Our first results concerned the relationship of tie strengths to network topology, verifying the Granovetter hypothesis. In 2008, we have
extended our studies to include communication patterns – each call or text message in the database is time-stamped, so we have full knowledge of how frequently and when people communicate. Our first results indicate clear causal behaviour – incoming calls trigger outgoing calls within a relatively short time (see Lauri Kovanen, Structure and dynamics of a large-scale complex social network, Master’s Thesis, 2009) and there are clear traces of even longer chains of communication events. We have also identified inherent biases in calling behaviour – many social relationships appear such that one party tends to initiate communication. Our next target is to move on from communication patterns between individuals to communication patterns within social groups, and attempt to link observed patterns with the nature of the groups.

In addition to empirical analysis, we have studied a number of social network models, proposed in the complex networks literature, and analyzed their features and connections to traditional network models in the social sciences (Toivonen et al, A comparative study of stochastic algorithmic models for social networks, submitted (2008)). Special attention has been paid to features such as emergent formation of social groups. Related to the latter, we have also continued our studies of the dynamics of opinion formation processes on networks containing community structure, published in Toivonen et al, Phys. Rev. E 79, 016109 (2009). Here the focus has been the nature of “trapping” effects associated with dense social groups which are only sparsely interconnected (see Figure 25).

Figure 25  The mobile communication network employed in social network studies contains communities, i.e. groups of people with frequent and dense social ties. The above figure displays a large community detected in this network. The arrows indicate phone calls taking place within this group, at around 2 AM on New Year’s night, 2007.
Computational systems biology focuses to understand biological systems at various levels (molecular, cellular, tissue, organ and individual) through computational modelling and information theoretic data and image analysis methods. With the most up-to-date computational approaches and modern experimental biotechnology, it has become possible to understand the structure and functions of biomolecules, information stored in DNA, its expression to proteins, protein structures, metabolic pathways and networks, intra- and intercellular signalling, and the physico-chemical mechanisms involved. COSY has been concentrating mainly to various computational approaches and method development of systems biology in close collaboration with researcher of medicine and biology.
6.4.1 Bioimaging

Bioimaging plays an important role in computational systems biology for understanding the structure and functions of microscopic objects (e.g., chromosome, mitochondria, cell nucleus and cell membrane), genetic information in DNA (bioinformatics), and protein expression from their structures (proteomics). Numerous imaging modalities can be applied for the imaging purpose, for instance (cryo) electron tomography, single-particle reconstruction and optical fluorescence microscopy.

Microscopic tomography based light or electron microscopy is an essential tool for analysing 3D structure of biological objects. Especially electron tomography has gained a lot of interest due to its ability to provide methods of 3D reconstruction of macromolecular assemblies and cellular structures providing potential insights to qualitative and quantitative spatial comprehension of structures versus function at the molecular level. In electron tomography, we have developed new methods for 3D reconstruction in COSY. This has involved automatic image alignment and efficient minimum description length based denoising methods before reconstruction. In addition to axial tilt series based electron tomography, we have also worked with single particle reconstruction issues for protein structure determination for those proteins that cannot be crystallised, but also recently for LDL particles. One of the research directions has been focus towards on reconstructing non-adherent living cells from a micro-rotation image series.

Figure 26 A stereo view from 3D reconstruction of C. elegans embryo with a Histone-GFP marker by using expectation-maximization algorithm. The raw data image set was acquired by Olivier Renaud, Institut Pasteur.
4D-Dimensional Reconstructions of non-adherent live cells in suspension

A novel optical imaging system, aiming at high-content high-throughput multi-dimensional analysis of non-adherent living cells in suspension, has been developed under the AUTOMATION consortium of the Sixth Framework Programme of the European Union. Three-dimensional imaging employs the novel cell-manipulator technology to facilitate high-resolution 3D imaging of non-adherent live cells. By this technology, living cells are rotated in suspension that provides us new potential tools to achieve also 4D-dimensional (structure + time) reconstructions of living cells.

![Figure 27 Time snapshots of the 4D-spatio-temporal reconstruction of a Jurkat cell with GFP marker.](image)

The research group of COSY has been developing methodology for computing multi-dimensional reconstructions from micro-rotation image streams. The research problem is divided into two parts. First, in order to compute the reconstruction, the orientation of microscopic object has to be accurately estimated. This is a geometry estimation problem that is closely related to the image alignment problem in electron tomography. Second, once the object orientation has been solved, we compute the actual reconstruction of the living cells, where in this case the reconstruction problems are closely related to the inverse problems especially from the viewpoints of statistical inversion and tomography. Finally, the geometry estimation and 4D reconstruction methods for dynamical configuration changes in living cells have been developed and achieved during the past year (Figure 27). Also solid 3D prints (Figure 28) of nuclear lamina have been produced including a solid "4D print", i.e. superimposing of 3D reconstruction snapshots.
CryoEM Single Particle Reconstruction

The current paradigm for structure determination of macromolecules is shifting towards fields that are different from X-ray crystallography and NMR spectroscopy. Single particle reconstruction (SPR) from cryo-electron microscopic (cryoEM) images is an efficient addition to axial electron tomography methods (ETM). SPR can also be used to complement and confirm the X-ray crystallographic structure of proteins. For 3D reconstruction using cryoEM images of the specimen many (some hundred thousands) projection images are needed. Solving irregular (asymmetric) or varied, i.e. micro- and macro-heterogeneous samples is still an undeniable challenge in the field of SPR.

We have developed methods to denoise micrographs. Embedded filtering processes in the SPR method to improve resolution of 3D volumes are integrated. 3D reconstruction of N protein of Hantavirus has also been accomplished to understand its structure and function. We are now finding new and efficient way to do high-resolution 3D reconstruction for heterogeneous samples. For this we have already proposed filtering of cryoEM images and in order to find a good method for finding orientations of the specimen images and reconstruct 3D electron density maps we are looking some alternatives like maximum likelihood methods and probabilistic SPR. We are currently working to present LDL (low density lipoprotein) at near atomic resolution.

A new project has been added that is the reconstruction of bacterial S-Layer using many different methods e.g. SPR, ETM together with electron crystallography tools.
**Image Alignment in Electron Tomography**

Electron tomography is used in reconstructing three-dimensional objects such as macromolecules, viruses, and cellular organelles to learn their three-dimensional structures and properties. The reconstruction is made from a set of transmission electron microscope (TEM) images that are obtained by tilting the specimen stage, by small angular increments. The reconstruction can be then computed from the TEM tilt series using our maximum entropy (MEM) axial tomographic method. However, in order to successfully compute the 3D reconstruction, TEM images have to be accurately aligned or registered. This is essentially a geometric problem that can be solved by computer vision methods.

We have investigated the automatic image alignment problem for electron tomography over several years. Currently, we are able to align conventional critical-point-dried samples with similar accuracy level that was previously achieved only by using fiducial gold markers. Our state-of-the-art marker-less, feature-based alignment method is based on tracking interest points on the intensity surface of the images by utilising the geometric constraints among the subsets of three views (trifocal alignment). The related robust parameter fitting procedure is able to reliably utilise hundreds of thousands of point measurements from a tilt series in a conventional critical-point-dried (CPD) sample.

**Signal denoising with Minimum Description Length principle**

The need for high-throughput assays in molecular biology places increasing requirements on the signal processing and modelling methods. However, meaningful information cannot be extracted from the measurements if the effects of noise in the data are not removed. An efficient denoising method enables smaller details to be extracted reliably in high-
throughput applications, where extreme conditions reduce the signal quality or cost effectiveness demands minimization of the reaction volumes.

Denoising can be done in a quite elegant and efficient way by the Minimum Description Length (MDL) principle, which treats and separates noise from the useful information as that part in the data that cannot be compressed. In other words, noise is defined to be the part in the data in which the given statistical model class cannot find any regular features. Ideally, this definition of noise does not include any ad hoc assumptions about the noise distribution.

Our research concentrates on improving the MDL denoising method in several different ways. In addition to dealing with the theoretical aspects of the MDL model selection principle, we also work with practical applications. On practical side we are developing denoising methods for cases where the common Gaussian noise assumption does not hold, and also methods which, in addition to removing noise, could separate components having different statistical qualities from the data.

Our analysis of the denoising problem in 1-D signals such as mass spectrometry, capillary electrophoresis genotyping and DNA sequencing signals as well as in 2-D cryo-EM images shows that the MDL denoising method produces robust and intuitively appealing results sometimes even in situations where competing approaches perform poorly.

Figure 30 Isolated CPD chromosome mounted on a holey-carbon-Au grid. The tomography tilt series was automatically registered using "trifocal alignment" method and the chromosome was reconstructed with MEM. A rim of the carbon hole is visible as an arch on the top of the chromosome. The 3D configuration of chromosome coiling emerges extensively clearly only with stereo viewing.

Figure 31 left) The original cryo-EM image of a PRD1 virus. (right) The result of MDL based denoising.
6.4.2 Computational Medicine

The projects that were previously termed as “Biospectroscopy” have clearly progressed and focused towards using a metabonomics approach, mainly 1H NMR spectroscopy of serum, in atherothrombosis related diseases. We have termed this area now as “Computational Medicine”, a concept which indicates the growing biomedical and clinical connections in this area of our research. For example, the collaboration and connections with the clinical research groups studying type 1 diabetes (Department of Diabetes Genetics, Institute of Genetics, The Folkhälsan Research Center & Department of Medicine, Division of Nephrology, Helsinki University Central Hospital, Helsinki, Finland), reverse cholesterol transport and lipoprotein metabolism (Department of Internal Medicine, Clinical Research Center, University of Oulu, Oulu, Finland) and liver-related diseases (Imaging Sciences Department, Division of Clinical Sciences, Faculty of Medicine, Imperial College, London, UK) have been significantly strengthened. This work aims for the development of analytical and data analysis aspects of NMR-based metabonomics in combination with revealing and understanding biochemical pathways related to disease diagnostics and risk assessment. Also, the combined use of various ‘omics data is of increasing interest. In addition, we are interested in lipoprotein metabolism at the subclass level, including the structure and function of the lipoprotein particles as complex molecular entities.

Multidisciplinary organisation

The Group was launched from scratch in summer 2004 at the Laboratory of Computational Engineering (LCE and now COSY) at Helsinki University of Technology. Currently the Group and its scientific research are a joint endeavour of COSY and the Department of Diabetes Genetics at the Folkhälsan Research Center, Biomedicum, Helsinki. The Group is also part of the Academy of Finland Centre of Excellence in Computational Complex Systems Research (2006-2011) COSY. The Group has been lead by Dr Mika Ala-Korpela in collaboration with Prof Kimmo Kaski (Head of COSY) and Dr Per-Henrik Groop (Head of the Department of Diabetes Genetics at Folkhälsan).

Towards personalised medicine

Understanding the factors that influence human health and cause diseases has always been a driving force of research. With the exciting progress in high-throughput analytical techniques and the profound integration of experimental and computational approaches, medicine has newly got hold of new technological and conceptual tools for holistic investigations of living organisms at the system level. The still young discipline of systems
biology has mostly been applied to study well-characterised model organisms. However, the first human studies also report on tremendous opportunities that combined molecular and computational technologies can have for the progress of personalised and predictive medicine.

**Metabonomics – a new field of ‘omics’**

Genomics, transcriptomics and proteomics, represent the ‘genomistic’ main discipline in life sciences. The phenotype of a biological system, however, is principally reflected by its metabolite composition and their interactions. Therefore, a key ‘omics’ in understanding of biomolecular function is metabonomics: the measurements of multi-metabolic responses to pathophysiological stimuli or genetic modifications. Mass spectrometry (MS) and $^1$H nuclear magnetic resonance (NMR) spectroscopy (Figure 32 Error! Reference source not found.) have become the two key technologies in this area.

![Characteristic $^1$H NMR spectra of serum for the LIPO and LMWM windows](image)

Figure 32 Illustration of representative 1H NMR molecular windows for a control individual (blue), for a patient with type 1 diabetes with normoalbuminuria (green), for a patient with type 1 diabetes with macroalbuminuria, i.e., diabetic nephropathy (red), and for an alcoholic individual (black). The assignments for the LIPO window resonances refer to fatty acids in triglycerides, cholesterol compounds and phospholipids in various lipoprotein particles, the cholesterol backbone –C(18)H3 and the –N(CH3)3 groups of surface phospholipids. The LMWM resonances marked gp are from the N-acetyl protons of mobile N-acetylated carbohydrate side-chains of glycoproteins.
Measuring metabolites is not new. For decades, clinicians have charted chemistries in blood, urine, and other body fluids — using glucose to track diabetes and cholesterol to monitor heart disease, for example. What is new in the metabonomics approach is that we are now casting a wider net, attempting to gather an unbiased sample of metabolites that can serve as a snapshot of an organism's physiology. The ultimate goal of metabonomics is to be able to distinguish between an individual who is healthy and someone who has (the diagnostic dimension) — or might develop (the risk assessment dimension) — a disease (Figure 33).

**Figure 33** Atherosclerosis is a diffuse systemic disease that is characterised by the local build-up of lipid-rich plaques within the walls of large arteries. The atherothrombotic processes are multigenetic, being influenced also by dietary and environmental components, and are apparent as early as the second decade in life with an increased incidence in the elderly. Atherothrombosis involves inflammatory processes with an array of metabolic, molecular and cellular manifestations in tissues, e.g., those depicted within the arterial wall. A varying degree of these intimal processes are reflected by the biochemistry of body fluids, such as serum. The biological heterogeneity as well as the slow development and progression of pathological conditions make the borderline between 'health' and 'disease' indistinct. One option to approach the problem, as previously presented by us, is 1H NMR metabonomics of serum equipped with a chemometric classifier, e.g., a SOM. On the left in Figure 34 a hypothetical SOM is shown together with four overlapping clusters that are thought to represent the metabolic changes in the arterial intima. While definite classification as 'healthy' and 'diseased' may not be available by nature, the metabonomics approach with a holistic look at the multidimensional metabolic changes may prove useful in the assessment and follow up of an individual 'health path' (represented by the light green line within the SOM) alongside the interplay between metabolic pathways and their consequences.
Towards new technological platforms

One of the great challenges for 21st century medicine is to deliver effective therapies that are tailored to the biological state of an individual to enable personalised healthcare solutions. We have recently outlined the advantages of magnetic resonance (MR) technologies in detecting molecular and cellular processes related to developing coronary heart disease (CHD): lipoprotein subclass analytics by *in vitro* $^1$H NMR metabonomics of serum is used for risk assessment and *in vivo* MR imaging for direct detection of plaque composition and vulnerability (Figure 34). This would clinically facilitate early individual primary prevention and also give a personal rationale to comply with lifestyle modifications and potential drug therapies.

Figure 34 A potential scheme utilising MR methodologies in the risk assessment of long-term risk for atherothrombotic events (non-symptomatic individuals) and of short-term risk for recurrent cardiovascular events after an experienced acute coronary syndrome (ACS) (symptomatic patients). At risk assessment point I the molecular constituents of serum, including lipoprotein subclasses, could be assessed by *in vitro* $^1$H MRS metabonomics for non-symptomatic individuals. If high long-term risk for atherothrombotic events is indicated, non-invasive in vivo MRI could follow for the potential detection of plaque (risk assessment point IIa) and subsequent compositional evaluation of the vulnerability of the detected plaque(s) for rupture or erosion (IIb). Depending on the outcome from the plaque detection and assessment by MRI the individual could accordingly be directed for further actions. If vulnerable plaque at point IIb would be detected, considerations for aggressive drug therapy or invasive therapies such as angiographic stenting or bypass surgery would be needed. In the case of an individual with an experienced ACS (III) *in vitro* $^1$H MRS metabonomics could be used to complement the clinical protocols when evaluating the risk for recurrent cardiovascular events and the proper individual treatment options. For some symptomatic patients *in vivo* MRI might also be feasible at point III for direct assessment of plaque composition and vulnerability. This scheme can be seen as one option to elucidate the potential of MR in detecting individual intermediate atherothrombotic end points and utilising their prognostic value before the occurrence of a definite end point. The recent MR findings and developments awaken confidence that this kind of schemes might be operational in the near future saving both human suffering and societal health costs.
The Oxford affiliate unit of Complex Systems and Network Research (CSNR) functions as a framework for collaborations between COSY and researchers at Oxford University, especially those in the cross-departmental CABDyN research cluster. CABDyN is a multi-disciplinary team involving Physics Department, Said Business School, Department of Engineering Sciences, and Mathematics Institute. COSY and CABDyN share a common interest in studying complex networks and agent based models, including modelling network formation and collective dynamics and developing novel structural characteristics for weighted complex networks.

CSNR is locally run by Dr. Jukka-Pekka Onnela, a Junior Research Fellow of Wolfson College, Oxford University (spending the last third of 2008 at Harvard University as Fulbright Fellow) and staffed by M.Sc. Phillip Staniczenko as graduate student in physics. In addition, professor Kimmo Kaski as Supernumerary Fellow of Wolfson Collage is in CSNR as part time head. One of the aims is to work on projects that combine the competence developed at COSY in dealing with weighted complex networks with the application domain specific knowledge of different researchers in Oxford.

One such example is a project related to developing a mathematical framework that allows coupling network structure and function. More specifically, the topology of the network evolves according to some specified microscopic rules and there is a dynamic process taking place on the network that both depends on its structure but is also capable of modifying it. As such it is a generic framework for dealing with the types on systems in which network structure, dynamics, and function are interrelated. The fruits of this type joint research with Oxford scientists is the analysis and modelling studies of social networks, more specifically mobile communication based social network.
7 Research Activities

7.1 Visits to the Laboratory

- Dr. Jyrki Ahveninen, Harvard Medical School, Massachusetts, USA
- Dr. Sophie Arnaund-Haond, The Center of Marine Sciences (CCMAR), Portugal
- Prof. Rafael Barrio, Universidad Nacional Autónoma de Mexico UNAM, Mexico
- Dr. Daniel Baumann, Bruker Ltd., Rheinstetten, Germany
- Dr. Jesus Brezmes, Departament d'Enginyeria Electronica, Electrica i Automàtica, Universitat Rovira i Virgili, Spain
- Prof. Sir Roger Elliott, Oxford University, U.K.
- Prof. R. Holland Cheng, the Department of Molecular and Cellular Biology, University of California, Davis, CA, USA
- Dr. Lin Fa-Hsuan, Institute of Biomedical Engineering, National Taiwan University, Taiwan
- Dr. Victor Eguiluz, Institute for Cross-Disciplinary Physics and Complex Systems IFISC, University of Balearic Islands, Spain
- Dr. Santo Fortunato, Complex Networks Lagrange Lab, Institute for Scientific Interchange (ISI), Torino Italy
- Prof. Alex Hansen, Department of Physics, Norwegian University of Science and Technology, Trondheim, Norway
- Prof. Harry Holthöfer, Centre for Bio-Analytical Sciences, Dublin City University, Ireland.
- Prof. Marjo-Riitta Järvelin, Department of Epidemiology and Public Health, Imperial College London, Norfolk Place, St. Mary’s Campus, UK.
- Prof. Janos Kertesz, Budapest University of Technology, Hungary
- Dr. Konstantin Klemm, the Bioinformatics Department at Leipzig University, Germany
- Prof. Olav M. Kvalheim, Department of Chemistry, University of Bergen, Norway.
- Prof. David Landau, The University of Georgia, USA
- Prof. Gerald Langner, Neuroacoustics, Darmstadt University of Technology, Marburg, Germany
- Dr. Eduardo Lopez, Saïd Business School, University of Oxford, UK
- Prof. Andrejz Nowak, Department of Psychology, University of Warsaw, Poland
- Prof. Howard Nusbaum, Department of Psychology, The University of Chicago, USA
- Dr. Gareth Pearson, The Center of Marine Sciences (CCMAR), Portugal
- Dr. Tarja Rajalahti, Department of Chemistry, University of Bergen, Norway.
- Prof. Jorma Rissanen, IBM, California, USA
- Dr. Alex Rozenfeld, University of Balearic Islands, Spain
- Ass. Prof. Baillet Silvain, Medical College of Wisconsin, Milwaukee, WI, USA
- Prof. Jacques Vervoort, Laboratory of Biochemistry, Wageningen University, The Netherlands
- Prof. David Wharam, Institute of Applied Physics, University of Tübingen, Germany
## 7.2 Visits by the Laboratory Personnel

Kimmo Kaski
- IFISC, Universitat de les Illes Balears, Spain
- Trinity College, The University of Dublin, Ireland
- Tallinn University of Technology, Estonia
- International Institut of Mathematics, Chennai, India
- University of Oxford, UK

Mikko Sams
- Institute of Psychology of Russian Academy of Sciences, Russia

Jukka Tulkki
- Laser Infrarouge d'Orsay, France

Mika Ala-Korpela
- Wageningen EU NMR Centre, University of Wageningen, The Netherlands
- Imaging Sciences Department, Hammersmith Hospital, Division of Clinical Sciences, Faculty of Medicine, Imperial College, UK
- Bruker BioSpin GmbH, Germany
- Department of Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Denmark
- Bruker BioSpin GmbH, Germany
- Unilever R&D, The Netherlands
- Physics Department, Universidad de los Andes, Columbia
- National Research Council Canada, Institute for Information Technology, Scientific Park, Canada
- Department of Pharmaceutics and Analytical Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Denmark
- NMR Laboratory, Department of Chemistry, Moscow State University, Russia
- The Silesian Centre for Heart Diseases, Cardiology Department, Poland

Iiro Jääskeläinen
- Massachusetts General Hospital - Harvard Medical School - Massachusetts Institute of Technology Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, Massachusetts, USA

Jari Saramäki
- The Bioinformatics Department at Leipzig University, Germany
- Université Catholique de Louvain, Belgique
- University of Oxford, U.K.
7.3 Participation in Conferences and Seminars

Kimmo Kaski
- COST P10 Physics of risk, Slovenia
  *Invited paper: Modelling of complex social networks.*
- Statistical Physics of complex systems, Guwahati, India 7.-12.1.2008
- Sociophysics, Torino, Italy 25.5.-29.5.2008
  *Plenary paper: Modelling of social systems.*
- COST P10 Physics of risk, Zurich, Switzerland 26.-29.10.2008
  *Plenary paper: Social systems: analysis and modelling.*

Jouko Lampinen
- Paris, France 21.-26.4.2007 *(Invited lecture)*

Mikko Sams
- Acoustics’08 kokous, Paris, France, 27.6.-5.7. 2008
  *Chairman of the session.*
- International Organization of Psychology annual meeting, St. Petersburg, Russia, 11.-13.9.2008.
- Christian Benoit Muistosymposium, Crenoble, France 27.-31.10.2008
  *Invited paper*

Jukka Tulkki
- HIGHLIGHT, Universitete Montpellier II, France 10.9.-12.9.2008
- The FinnDiane Study Group Research Seminar, Biomedicum Helsinki, Finland, *Invited paper*
  *Invited paper*
- The European Diabetic Nephropathy Study Group (EDNSG) meeting, Hanover 16.-17.5.2008
- The 4th Atlantic Omics Symposium, Moncton, NB, Canada, 18.–20.8.2008
  *Invited paper*
  *Invited paper*
- Bruker Biospin Users Meeting, Stockholm, Sweden, 30.9.-1.10.2008
  *Invited paper*
  *Invited paper*
- The European Association for the Study of Diabetes (EASD) Young Scientists Training Course, Helsinki, Finland, 13.-17.10.2008
Jouni Hartikainen
- Royal Statistical Conference, Nottingham, U.K.
- Bayesian Research Kitchen, Grasmere, U.K.

Oskari Heikkilä
- HIGHLIGHT, Universitète Montpellier II, France 10.9.-12.9.2008

Iiro Jääskeläinen

Riku Linna

Janne Ojanen
- ICML/UAICOLT Workshop (Recent Breakthroughs in Minimum Description Length Learning), Helsinki, 9.7.2008
- 2008 Workshop on Information Theoretic Methods in Science and Engineering (WITMSE 08), Tampere, 18.-20.8 2008

Jaakko Riihimäki

Jari Saramäki
- Sigma Phi 2008 - International Conference on Statistical Physics, ORTHODOX ACADEMY OF CRETE, Kolymbari, Chania, Greece, 13.-20.7.2008

Simo Särkkä

Jarno Vanhatalo

Mikko Viinikainen
- ARVO 2008, Fort Lauderdale, FL, USA, 27.4. - 1.5.2008
7.4 Memberships in Scientific Societies

Kimmo Kaski
- Fellow by invitation of the American Physical Society, USA
- Member of Association for Computing Machinery
- Fellow by invitation of the Finnish Academies of Technology
- Fellow and Chartered Physicist by invitation of the Institute of Physics, UK
- Member by invitation, Academica Europaea
- Member of American Association for the Advancement of Science (AAAS), USA
- Fellow by invitation of the Finnish Academy of Science and Letters
- Supernumerary Fellow, Wolfson College, University of Oxford, UK
- COST (European Cooperation in Science and Technology) Committee member

Jouko Lampinen
- Board member of Brain Research Society of Finland (BRSF)
- Member of International Neural Network Society (INNS)
- Member of Pattern Recognition Society of Finland, Hatutus (member of IAPR)

Mika Ala-Korpela
- American Heart Association
- American Society for Biochemistry and Molecular Biology
- European Society for Magnetic Resonance in Medicine and Biology
- Finnish Atherosclerosis Society

Harri Valpola
- Board member of Finnish Artificial Intelligence Society
- Member of Pattern Recognition Society of Finland, Hatutus (member of IAPR)

Aki Vehtari
- Board member of Pattern Recognition Society of Finland, member-society of IAPR (International Association for Pattern Recognition)
- Fellow of the Royal Statistical Society
- Member of the International Society for Bayesian Analysis
- Member of the European Network for Business and Industrial Statistics
7.5 Other Activities

Kimmo Kaski
- Opponent Trinity College Dublin, Ireland
  Ricardo Coelho
- Member of Committee on the development of computational Science in Finland, Ministry of Education
- The Editorial Board in International Journal of Modern Physics C
- Reviewer for European Science Foundation - Review of Self-organized nanosystems
  (SONS) programme Science Foundation Ireland - Programme Review
  Belgian Science Policy Office: Interuniversity Attraction Poles network review
- Reviewer in Journals
  Physical Review Letters
  Physical Review E
  Physica A
  International Journal of Modern Physics C

Mikko Sams
- Board member (representing Helsinki University of Technology) of the BioMag laboratory
- Vice chairperson of the board of CICERO learning network
- Expert member in the Board of the Advanced Magnetic Imaging Center, Helsinki University of Technology
- Member of the Editorial Board in journals:
  Tiede
  Polysteekki

Jukka Tulkki
- Pre-examiner of a doctoral thesis
  Anna Sankari, Oulu University
  Jaime Zaratiegu, Oulu University
  Hannu-Pekka Komsa, Tampere University of Technology
- Opponent of a doctoral thesis
  Anna Sankari, Oulu University

Iiro Jääskeläinen
- Reviewer in journals, book series and international conferences:
  Journal of Neurophysiology
  Brain and Cognition

Jari Kätsyri
- Reviewer in journals, book series and international conferences:
  Emotion
Jari Saramäki
- Member of Scientific Advisory Board, Xtract Ltd.
- Reviewer in journals, book series and international conferences:
  - Physical Review Letters
  - Physical Review E
  - Physica A
  - European Physical Journal B

Harri Valpola
- Member of Editorial Board:
  - Neurocomputing
- Board member
  - Finnish Artificial Intelligence Society
- Reviewer in journals, book series and international conferences:
  - New Journal of Physics

Jarno Vanhatalo
- Fellow of
  - The Royal Statistical Society

Aki Vehtari
- Reviewer in journals, book series and international conferences:
  - Scandinavian Journal of Statistics
  - IEEE Transactions on Neural Networks
  - International Journal of Engineering Simulation
  - International Journal of Computer Systems Science & Engineering

Antti Yli-Krekola
- Reviewer in journals:
  - Neurocomputing
8 Publications

8.1 Publications in Refereed Journals


Mäkelä, Sanna M.; Jauhiainen, Matti; Ala-Korpela, Mika; Metso, Jari; Lehto, Tiina M.; Savolainen, Markku J.; Hannuksela, Minna L.: HDL2 of heavy alcohol drinkers


8.5 Book Chapters


Ojanen, Janne; Heikkonen, Jukka; Kaski, Kimmo: Towards the multicomponent MDL denoising. In: Grünewald, Peter; Myllymäki, Petri; Tabus, Ioan; Weinberger, Marcelo; Yu, Bin, Festschrift in Honor of Jorma Rissanen on the Occasion of his 75th Birthday. Tampere 2008, Tampere International Center for signal Processing, 205-212.

8.3 Conference Proceedings


**8.4 Conference Abstracts**


Saalasti, Satu; Tiippana, Kaisa; Laine-Hernandez, Mari; Kätsyri, Jari; von Wendt, Lennaul; Sams, Mikko: Audiovisual speech perception in Asperger syndrome. IMRF’08, Hamburg, Germany, July 16-19, 2008. *(talk)*


Vanhatalo, Jarno; Vehtari, Aki: Modelling local and global phenomena with sparse Gaussian processes. 24th Conference on Uncertainty in Artificial Intelligence, July 2008. *(talk)*