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1 Introduction

Year 2006 marks for the Laboratory of Computational Engineering (LCE) its 10th anniversary as a successful research and teaching unit. It is also the first year as the Centre of Excellence (CoE) in Computational Complex Systems Research (CCSR) for 2006-2011, following the successful six year period as a multidisciplinary CoE in Computational Science and Engineering (CCSE), for 2000-2005.

Since many complex physical, biological, cognitive, economical, or societal systems, we study, show self-organisation and emergent properties in their structure, function, and response, CCSR has adopted in its research trans-disciplinary holistic system level approach. For this CCSR combines either physical, mathematical, biological, neurocognitive or social science viewpoint with its computational analysis, modelling, and simulation expertise. Therefore, we have organised our research to four focus areas: 1. Models & Methods, including Complex networks and agent-based models, Pattern formation in biological systems, 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, and Biospectroscopy. These four research areas are, however, quite loose such that the research is conducted as cohesively as possible and by joining the multi-disciplinary expertise within the CoE.

We also emphasize that our research continues to be internationally strongly networked, as evidenced by the fact that since the beginning of 2002 the CoE has had an affiliate research unit in Wolfson College of Oxford University with its own computing facilities, one part-time director, two full-time researchers and a visiting scholar programme for the CoE’s researchers to network with Oxford scientists. For 2002-2005 it operated as the affiliate unit of Advanced Computational Science and Engineering (ACSE) and for 2006-2011 as the affiliate unit of Computational Complex Systems and Network Research (CCSNR), collaborating now closely with Oxford’s Complex Agent-Based Dynamic Network (CABDyN) cross-departmental research cluster. In addition, CCSR cultivates a number of national and international collaborations funded nationally or by EU, which together with the Oxford link and mutual short-term visits up to few months fulfill also the role of researcher training.

In 2006 the activities of CCSR have in many ways borne a record amount of fruit, i.e., about 80 scientific publications of which more than 50 in high impact factor journals. Moreover, the average impact factor per journal article has been increasing steadily reaching the level of 3.25. Thus our emphasis in research is top quality. In LCE’s history year 2006 was also a record year in finished degrees and researcher training, i.e., 23 MSc’s and 9 DSc’s. One of the DSc’s, Ph.D. Jukka-Pekka Onnela won the best thesis of 2006 award at Helsinki University of Technology.

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2 Personnel

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Kaski Kimmo Academy Professor
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Häyrynen Teppo M.Sc.
Hyvönen Jörkki M.Sc.
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Kauhanen Laura M.Sc.
Kauramäki Jaakko M.Sc.
Kettunen Juho M.Sc.
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Kumpula Linda M.Sc.
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Köhler Sebastian M.Sc.

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Onnela Jukka-Pekka Ph.D.

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

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Heimo Tapio
Hokkanen Johanna
Hulkkonen Jenni
Hukkinen Janne
Kaapro Aatu
Kaarela Ilari
Kangas Antti
Kivelä Mikko
Koskentalo Katri
Kyttä Klaus
Lankinen Niko
Lilja Ville

Lindqvist Peter
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Mäkäräinen Meeri
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Palomäki Tapio
Parkkinen Juuso
Peltola Tomi
Pennala Eero
Pihlström Kim

Puharinen Hanna
Rolig Kaisa
Salminen Aino
Sandholm Niina
Seppälä Lauri
Siivola Markus
Suviitaival Tommi
Tukiainen Taru
Turtola Pekka
Tykkälä Tommi
Vanhatalo Maija
Yli-Krekola Antti
3 Boards

3.1 Scientific Advisory Board

*Board Members*
- Professor R Holland Cheng, University of California, Davis, USA
- Professor Alex Hansen, Norwegian University of Science, Norway
- Professor George R. Mangun, University of California, Davis, USA

*Observers*
- Professor Ulla Ruotsalainen, Tampere University of Technology
- Science Adviser Pasi Sihvonen, Academy of Finland, Programme Unit
- Senior Science Adviser Pentti Pulkkinen, Academy of Finland, Programme Unit
- 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
- Heikkonen Jukka Dr.Tech., Docent
- Jääskeläinen Iiro Professor
- Kaski Kimmo Academy Professor (Chairman)
- Lampinen Jouko Professor
- Linna Riku Ph.D.
- Onnela Jukka-Pekka Ph.D.
- Sams Mikko Academy Professor
- Saramäki Jari Ph.D.
- Tiippana Kaisa Ph.D.
- Tulkki Jukka Professor
- Valpola Harri Dr.Tech.
- Vehtari Aki Dr.Tech., Docent
- Virolainen Kaija Ph.D.
4 Teaching

**Degree programmes and major subjects**

<table>
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<th>Electronics and Electrical Engineering</th>
<th>Communications Engineering</th>
<th>Bioinformation Technology</th>
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<tr>
<td>• Computational Science</td>
<td>• Mathematical methods in telecommunications</td>
<td>• Computational and cognitive biosciences</td>
</tr>
<tr>
<td>• Cognitive Science</td>
<td>• User-oriented technology</td>
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**Courses spring 2006**

- S-114.1327 Physics III (EST) (6 cr)
- S-114.1427 Modern Physics: Computational Virtual Laboratory (Sf) (2 cr)
- S-114.2510 Computational Systems Biology (5 cr)
- S-114.2730 Emotions and Communication (6 cr)
- S-114.2740 Perception and Production of Speech (6 cr)
- S-114.2750 Memory and Learning (3 cr)
- S-114.3155 Business Game (3 cr) P
- S-114.4204 Modelling of Vision (5 cr) P
- S-114.4220 Research Seminar on Computational Science (3 cr) P V
  Topic: *Principles of brain evolution*
- S-114.4270 Computational Cell Biology (5-7 cr) P
- S-114.4610 Special Course in Bayesian Modelling (1-8 cr) P V
- S-114.4762 Systemic cognitive neuroscience (2 cr) L

**Autumn 2006**

- S-114.1100 Computational Science (5 cr)
- S-114.1310 Introduction to Modelling and Information Theory (3 cr)
- S-114.1710 Cognitive Neuroscience (4-5 cr)
- S-114.2500 Basics for Biosystems of the Cell (5 cr)
- S-114.2601 Introduction to Bayesian Modelling (5 cr) P
- S-114.2720 Perception and Action (4-6 cr)
- S-114.3200 Sepcial course on computational engineering (6 cr)
- S-114.3760 Measurement of electroencephalography (6 cr)
- S-114.3812 Computational Neuroscience (6 cr)
- S-114.4220 Research Seminar on Computational Science (3-6 cr) P V
  Topic: *Bayesian Estimation of Time-Varying Processes*
- S-114.4150 Complex Networks (5 cr) L

**Courses that can be taken any time**

- S-114.2801 Neuroinformatics (5 cr)
- S-114.3215 Special Project in Computational Engineering (3-8 cr)
- S-114.3520 Special Project in Computational Systems Biology (3-7 cr)
- S-114.4230 Individual Studies on Computational Engineering (1-6 cr) P 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

For more information see publication: Study Programme, Helsinki University of Technology, or the www-page [http://www.lce.hut.fi/teaching/](http://www.lce.hut.fi/teaching/)
5 Theses

Doctor of Science / Philosophy

- Kostiainen Timo Studies in Probabilistic Methods for Scene Analysis
- Kätsyri Jari Human Recognition of Basic Emotions from Posed and Animated Dynamic Facial Expressions
- Nikunen Petri Studies of surface diffusion and dissipative particle dynamics
- Oksanen Jani Modeling Transmitters, Amplifiers and Nonlinear Circuits for the Next Generation Optical Networks
- Onnela Jukka-Pekka Complex networks in the study of financial and social systems
- Pekkola Johanna Seeing and Hearing Speech, Sounds, and Signs: Functional Magnetic Resonance Imaging Studies on Fluent and Dyslexic Readers
- Särkkä Simo Recursive Bayesian Inference on Stochastic Differential Equations
- von Alfthan Sebastian Computational Studies of Silicon Interfaces and Amorphous Silica
- Zhao Wei Molecular Modeling of Charged Membrane Systems

M.Sc. - Diplomas

- Autti Henri Voxel-based morphometry (VBM): Sensitivity evaluation and application to a study of pain patients
- Hallivuori Leena Creating Tools to Import and Edit Biological Systems Data
- Heimo Tapio Spectral Properties of Correlation Matrices Derived from Financial Time Series
- Joensuu Heikki Adaptive control inspired by cerebellar system
- Joutti Johanna Digitaalinen televisio ikäihmisten ja muiden erityisryhmien näkökulmasta (in Finnish)
- Jylänki Pasi Classification of single-trial EEG for online brain-computer interface
- Kaapro Aatu Modeling gene regulatory networks with Bayesian networks
- Kalliokoski Sami Adaptiivinen käyttöliittymä kosketusnäytölle (in Finnish)
- Kettunen Juho Hierarkin todennäköisyysmalli takaisinkytkennöille näköjärjestelmässä (in Finnish)
- Kumpula Linda A general structure of lipoprotein particles: a new approach for determining lipid distributions
- Köhler Sebastian Hygiene monitoring biosensing systems in hospital environments
- Lilja Ville A Statistical Method for Automatic Image Alignment in Electron Tomography
- Lindqvist Peter RFIF monitoring of health care routines and processes in hospital environment
- Lindroos Virpi Electroencephalographic study on audiovisual integration of speech and non-speech stimuli
- Ojala Niina Stress Level of a Patient During General Anesthesia: Measurement Investigation and User Interface Designing
- Riihimäki Jaakko Bayesian modelling of the treatment chain of hip fracture patients
- Siivola Markus A GIS tool for visualization and spatial analysis of georeferenced health data
Toikkanen Maija Oppimisen tehokkuus ja luentovideot verkkoooppimateriaalina kognitiivisen neurotieteen verkkokurssilla (in Finnish)

Tuunen Juuso The Effect of Visual Speech on FM-Sweep Evoked MEG Responses

Vanhanen Ilkka Deformable Medical Image Registration Using Graphics Hardware

Vanhatalo Jarno Sparse Log Gaussian Process in Spatial Epidemiology

Vatilo Jussi Multi-objective Reconfiguration of Medium Voltage Distribution Networks

Willberg Anna Testing and Examination of Iu interface Compatibility to General Packet Radio Service Network
6 Research Projects

The Laboratory of Computational Engineering (LCE) and the Centre of Excellence of Computational Complex Systems Research (CoE) focuses on understanding complex physical, biological, cognitive or societal systems and their behaviour. The research uses computational analysis, modelling, and simulations based on data collected by selected experimental methods. The research is conducted cohesively in four mutually supportive fields of Models and Methods, Engineered and Artificial Systems, Cognitive and Social Systems, and Computational Systems Biology, as depicted in Figure 1.

The main role of the Models and Methods research line is to facilitate the research activities of the other groups of the CoE. The focus is both on "fundamental" as well as "applied" research. The former comprises theoretical and numerical work on mathematical models of complex systems with one of the main focuses being complex networks, which are rapidly becoming a standard framework to analyze and understand complex interactions. In the latter, the focus is computational tools and methods required for analysing and understanding experimental data, such as state-of-the-art statistical modelling methods (e.g. Bayesian modelling), with applications in several fields, in particular brain signal analysis and bioimaging. In Engineering and Artificial Systems the research focus is two fold, on material based engineered nanosystems and on information processing model of systems. In nanosystems there is need to understand the fundamental behaviour of materials (solid, soft or biological) and devices, which show intrinsic complex phenomena such as pattern formation, self-organisation and self-assembly. These nanoscale systems are well-suited for computational modeling studies, which form the basis for applying them in nanoscale bioinformatics, biomedical analysis and in imaging systems. In the area of
information processing systems, the research is based on computational models of cognitive functions, such as learning and perception, which are central issues in many research topics throughout the CoE. The results are applied in computer vision and object recognition, and in robotics to study task-driven modeling 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 neuroimaging methods, to disclose dynamic neuronal interactions within and between brain areas. Based on the data and its analysis, 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 will be analyzed and modelled based on complex networks and agent based approaches.

**Computational Systems Biology** is a new and rapidly developing field of research with focus to understand structure and processes of biological systems at molecular, cellular, tissue and organ level, through computational modeling and novel information theoretic data- and image analysis methods. With the break-through in deciphering the human genome using 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 (bioinformatics), its expression to proteins, protein structures (proteomics), metabolic pathways and networks, intra- and inter-cell signalling, and the physico-chemical mechanisms involved in them (biophysics).

Currently there is wide interest in biology and biomedicine in structures, relations and functions of biological systems, which we study with a wide at-site-arsenal of state-of-the-art information theoretic analysis and multiscale modelling methods. One of our main interests is high density lipoprotein particles, the carriers of good cholesterol in the blood stream, and reverse cholesterol transport related to the particle structure and function. In addition, the structural aspects of low density lipoprotein particles, the carriers of bad cholesterol, will be tackled via spectroscopy (NMR) and imaging (cryo-electron microscopy) experiments. In the systems biology research LCE’s wide repertoire of information theoretic data and image analysis methods serve as key approaches.

![Figure 2: CoE is total budgeted with LCE, the total funding for the year 2006.](image)
6.1 Models and Methods

In the 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 sometimes also share 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 with 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 is rapidly becoming the standard approach in statistical modelling.

The synergies of approaching complex systems from several perspectives are 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 at LCE 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.

Figure 3: Models and Methods
6.1.1 Complex Networks and Agent-Based Models

Senior researchers: Jari Saramäki, Jukka-Pekka Onnela, János Kertész and Kimmo Kaski
Researchers: Tapio Heimo, Jörkki Hyvönen, Jussi Kumpula and Riitta Toivonen

The network approach to complex systems has turned out to be very fruitful during the last years, revealing general principles applicable to a large number of systems, ranging from the Internet to genetic regulation. Generally speaking, complex systems typically consist of large numbers of interacting elements and have highly non-trivial interaction structures. A system’s behaviour is then determined both by the properties of the elements as well as the interaction structure. The key strength of the complex networks approach is its inherent ability to simplify this complicated picture by disregarding non-essential features and considering only the "skeleton" of the interacting system. It should be noted, however, that sometimes even some essential features are discarded. Some information is always lost in such simplifications. It should be noted, however, that sometimes even some essential features are discarded. Some information is always lost in such simplifications. In the network approach, the 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. This approach has led to a number of paradigmatic models, providing a holistic framework in which the details of the interactions between the constitutions are discarded and only their scaffolds are considered. Modern-day electronic databases and computational tools have been of especial importance to the development of this framework.

In the early days of complex networks research (late 1990’s to early 2000’s) complex networks research mainly focused on statistical characterization of networks, together with modeling efforts to explain the variety of network structures observed in nature. Many statistical characteristics were observed to be universal, i.e. similar in a large number of very different networks ranging from the Internet to protein interaction networks. Lately, the focus of research has been shifting towards functionality-related aspects and dynamics of processes taking place on networks, as well as understanding the functional role of "mesoscopic" network structures such as groups of vertices forming highly connected communities. In addition, it has been realized that the "first-order" approximation, where edges either exist or not, has to be extended by incorporating information on the interaction strengths in the form of edge weights. The recent activities of the Networks group at LCE are related to the above issues: our focus has been on developing the theoretical and methodological framework of weighted complex networks and studying dynamics and the role of cliques/communities on such networks.

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. 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?
In order to answer these questions, we have investigated several empirical weighted networks, and simultaneously developed methods for weighted network analysis. These data sets include a large social network reconstructed from mobile telephone call records, scientific collaboration networks, the network of world trade, and networks inferred from financial time series. Figure 4. depicts a small sample of the large telephony network, where vertices represent mobile phone users, and edge weights are defined as the total amount of time two persons have spend talking with each other. It is clear that the structure of this network is far from random - "communities" with dense internal connections exist, and the edges within these communities have typically larger weights than those connecting the communities. In order to quantify these structural features, several new analysis methods have been developed (see the section on Cognitive and Social Systems for more). The observed weight-topology correlations together with the community structure also give rise to unexpected effects in the flow of information on social networks. Community structures, i.e. tight "circles of friendship" have also been observed to radically alter the dynamics of sociodynamic models. As an example, in a language-related model, where each the language "spoken" by each vertex (i.e. person) depends on peer pressure and bilingualism is allowed, the existence of communities in a model network has been observed to drastically change the way the dynamics proceeds to equilibrium.

The existence of communities with dense internal connections evidently plays a major role in the functionality of complex networks - in social networks they appear to "localize" information and regulate dynamic processes, in biological systems such as metabolic networks the communities serve as functional modules, and in networks of stock market interactions, communities are related to industry sectors (see Figure 5). However, detecting and characterizing such communities in large networks is a difficult task, and related methods are currently a major focus of attention of network researchers. We have recently shown that one methodology based on global energy minimization suffers from serious limitations. Furthermore, we have shown that in the context of networks constructed from correlation matrices of financial time series, eigenvector-based analysis, which has been
viewed as one alternative method, provides no straightforward way of detecting strongly interacting clusters. The above findings, as well as some recent results by other groups, indicate that there is a need for novel community detection methods – especially for the case of weighted networks.

Figure 5: Network of stock market interactions, reconstructed by thresholding a correlation matrix calculated for stock return time series. Vertices correspond to selected New York Stock Exchange stocks, and edges to high correlations between them. Four industry sectors clearly emerge.
6.1.2 Complex Dynamics in Biological Systems

Senior researchers: Riku Linna and Kimmo Kaski
Junior researchers: Kim Pihlström

Computational models for generic systems that form a basis for addressing specific biological systems have been implemented. Many of the biological systems fall into a category called complex fluids. Here rheology, if not dominating, at least contributes to the overall dynamics. Typically, there is interplay between elasticity and rheology, and there exists dynamic regimes in which either of the two dominates. This interplay results in dynamics of high complexity. In order to be able to simulate systems large enough an insight on what can be approximated without violating the essential characteristics of the dynamic system is required. Models for simulating dynamics of a single polymer and an elastic membrane formed by cross-linked polymers have been implemented using a coarse-grained method coined stochastic rotation dynamics (SRD). In SRD the dynamics of the filament chains are modelled exactly by a molecular dynamics (MD) solution of Newton’s equations of motion, but the solvent is described by a stochastic rotation dynamics algorithm, a particulate flow solver which reproduces the thermohydrodynamic equations of motion by following the behaviour of particles which move in discrete time, but in continuous space. Molecular details of the solvent are not included: it acts as a momentum conserving heat bath which can support hydrodynamic modes. The method is ideal for investigating systems characterised by the interplay of rheology and elasticity. Specifically, hydrodynamics can be switched off in the dynamics leaving the elastic filaments in a Brownian heat bath. The role of rheology can thus be pinned down and the aforementioned regimes defined.

Figure 6: (a) Polymer extended by flow: The ratio of the projected length $z$ and the contour length $L$ as a function of $v \times L^{0.59}$, where $v$ is the flow velocity. Contour lengths (number of beads) are 50 (+), 100 (x), and 200 (+). (b) Polymers extended by force exerted on the end bead: AP (arbitrary bending potential), WLC (worm-like chain), FJC (freely jointed chain). N is the number of beads (polymer lengths) and $z$ is the measured length projected along the direction of the pulling force.

Generic models for the dynamics of DNA in a confined geometry, whose dimensions are of the order of the polymer’s radius of gyration, have been implemented and simulated. Comparing simulations to available experimental results clearly show that the current paradigm that the DNA can elastically be characterised by a worm-like chain, i.e. a chain having a harmonic bending potential, does not necessarily hold. The models validity was
checked by reproducing the experimentally obtained scaling behaviour for a DNA extended by flow, Figure 6 (a).

Figure 6 (b) shows the mechanical extension of a freely-jointed (FJC), worm-like and an arbitrary chain, which has a linear bending potential. Only FJC response differs somewhat from the others due to the lack of orientational preference of the individual segments. Preliminary simulations of a membrane crumpling in confined geometry have been performed and compared with some available experimental and theoretical results to validate the model. The model will be further developed for simulating a curved cytoskeleton network relevant for example in red blood cell motility. A so called N-fold Monte Carlo method was used for simulating a nanoscale droplet exhibiting a transition from diffusive to ballistic dynamics with a surface step potential as a control parameter. The droplet dynamics could be fully characterised. An anisotropic finitesize scaling analysis for the system is underway.
Complex phenomena may have complex structure or apparently simple structure with a large number of elements producing emergent complexity. Modeling is challenging if known structural information is incomplete or if there is a large number of unknown parameters compared to the amount of observations available. Bayesian approach provides consistent and flexible way to combine available structural information and uncertain observations.

Bayesian approach can be used to combine simpler modeling blocks to form more elaborate models, which are called hierarchical models. After dividing the phenomenon to simpler parts, there may still be such complex interactions that flexible generic modeling tools are needed. In our group we have used, for example, hierarchical, spatial, spatio-temporal and dynamic models to combine simpler parts, and non-parametric approaches such as Bayesian neural networks and Gaussian processes to model non-linear effects with complex interactions.

Although sometimes complex model may be divided in very simple parts, just the large number of those parts and interactions between them make the computations challenging. The complex models may have a large number of unknown parameters, for example, thousands in brain signal analysis or tens of thousands in spatial epidemiology or in modeling of human visual perception. To approximate the required high-dimensional integrals, we have used both Monte Carlo methods (e.g., Markov chain Monte Carlo, importance sampling, particle filters), which provide generic approach easy to adapt for new models, and analytic approximations (e.g., variational, expectation propagation, Rao-Blackwellization) which need more work in construction, and may not always be appropriate, but may give huge reductions in computation time. In addition to efficient integration techniques, sometimes a model can be replaced with a computationally simpler approximation by ignoring the weakest interactions. We use this kind of approach, for example, in sparse approximations of Gaussian processes. Development of the efficient methods is important for making the required computations feasible in applications with large scale data.

Whatever way the model is constructed, we should be able to evaluate how well it can model the phenomenon. Our research on model evaluation is based on decision theoretic approach of examining predictive distributions and the relative values of consequences of using the models.

The research results can be applied widely in many application areas. In our group, current applications are analysis of large scale patient data, modeling of health-care processes, spatial epidemiology, analysis of MEG and fMRI data, dynamic state estimation and reliability analysis of sensor networks, analysis of NMR metabonomic data, modeling of continuous casting of steel, object recognition, computer vision, and modeling of human visual perception. In these applications there is potentially substantial structural knowledge of the phenomena, but there is also a lot of unknown uncertainties which are difficult to model. Assessment of models in these applications is challenging, since some of the interesting quantities are not directly observable or the measurements are difficult to make.

Some of the applications are presented in following sections: dynamic state estimation for surveillance, analysis of health-care data, brain signal analysis and computer vision. In
addition, modeling of human visual perception, and analysis of NMR metabonomic data are presented elsewhere in this report.

**Dynamic State Estimation**

The goal of the research is to develop new estimation methods for challenging applications. Methodological development includes new algorithms for multiple target tracking and continuous-discrete filtering and smoothing. The new methods have been applied to target tracking, estimating the spread of a disease and to estimation of state of a physical phenomenon from indirect sensor measurements.

In Tekes project Development of Management Systems for Infrastructure Maintenance in Infra Technology Programme, the goal was to develop new estimation methods for remote surveillance of tunnels and physical processes, which are indirectly observed through inaccurate sensors. The methods are applicable to detection of sensor failures and malfunction, and modeling other abnormal behaviour of the sensors. This allows, for example, automatic detection and compensation of broken sensors, which opens possibility for using cheaper but less reliable sensors.

The problem in remote surveillance is much related to multiple target tracking and for this reason the recently developed new sequential Monte Carlo (particle filtering) based methods for multiple target tracking are directly applicable. The methods that have been developed for clutter modeling and estimation can be also used for detection of the sensor failures, malfunction and abnormal behaviour. These methods would allow also classification of different time-dependent events based on multiple sensors, like, detection of human movement in buildings or sudden temperature changes in tunnels. Figure 7 shows the estimation result in case of unknown number of 2D signals (tracking).

In some applications the dynamic model can be naturally described with stochastic differential equations. In our research, the emphasis is in stochastic differential equations with non-linear drift terms and measurement models with non-linear and non-Gaussian components, where the classical linear Kalman filter cannot be used. These kind of non-linear continuous-discrete filtering problems have been previously solved using Taylor series expansion based approximation methods (extended Kalman filters), but other types of methods have been less developed for the continuous-discrete case.

By taking the formal limit of the unscented Kalman filter and the unscented Kalman smoother when the prediction time step size goes to zero the *continuous-discrete unscented Kalman filter and smoother* have been derived. By taking the formal limit, when both the prediction and measurement time step sizes go to zero the *unscented Kalman-Bucy filter*, which is a continuous-time version of the unscented Kalman filter, have been derived.
Novel Girsanov theorem based methods for performing continuous-discrete sequential importance resampling, that is, continuous-discrete particle filtering have been derived. Also a Rao-Blackwellized continuous-discrete particle filter has been developed.

Figure 8 shows the results of applying the continuous-discrete particle filter to the classical Bombay plague data. Bombay plague data consist of the number of deaths occurred weekly during the period December 1905 to July 1906. These filtered estimates are conditional to the previously observed measurements only. The estimate on week $t$ is the estimate that could be actually computed on week $t$ without any knowledge of the future observations.

![Figure 8: The result of applying the continuous-discrete particle filter to the classical Bombay plague data.](image)

**Analysis of healthcare data**

Focus of the project is to develop healthcare data analyzing systems. 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.

In research developing methods for the analysis of large scale patient data, pilot projects are analysis of institutionalisation of the elderly in city of Vantaa and the treatment of hip fracture patients in various hospital districts in Finland (see Figure 9). The aim in the Vantaa pilot is to study factors predicting the final placement in a care institution, and possibly recognise groups with different patterns of institutionalisation behaviour. In the second 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. Also analysing the effects of numerous explanatory variables and considering area level indicators, such as home region statistics, are in concern. The hip fracture pilot project is conducted in co-operation with National Research and Development Centre for Welfare and Health (Stakes).

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. 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. The final assessment of the utility of the results is done in co-operation with health services specialists.

Demographic data registers in Finland provide accurate coordinates for each individual. Consequently, information from several data registries can be linked to geographical locations through personal identification numbers. This can be utilized in the study of spatial epidemiology, which seeks to reveal geographical variations in health outcomes and risks to health.

We have 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. An example image illustrating variations in the death risk due to cerebral vascular diseases is presented in Figure 10 and Figure 11.

The results showed that geographical variations exist. 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. Current development concentrates on implementing Bayesian spatial methods for an improved control of smoothing and statistical significances, and the flexible use of explanatory variables. Due to large scale data, we have studied approximate methods to overcome the computational limitations of Gaussian processes. The methods studied include reduced rank approximations of the covariance matrix and expectation propagation for marginalizing over latent values.
Figure 10: Estimated relative risk of death caused by cerebral vascular diseases between 1995 and 2000. The estimates were based on a standard population of 4.8 million and around 18000 deaths.

Figure 11: A zoomed-in image from Turku region. The resolution is 250 m x 250 m.
Statistical brain signal analysis research is a multidisciplinary project combining the expertise of both Bayesian Methodology group and Cognitive Science and Technology group, in collaboration with Massachusetts General Hospital–Harvard Medical School NMR Center (Dr. John W. Belliveau and Dr. Matti S. Hämäläinen).

Localising the neural currents indicating brain activity based on non-invasive magnetoencephalographic (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.

The current 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. Due to the different physical origins of MEG and fMRI signals (and noise), there can be MEG false positives or negatives in the fMRI activation map, and consequently a hard fMRI location constraint leads to suboptimal MEG inverse estimates (see Figure 12). Our latest approaches utilise fMRI data for MCMC proposal distributions, algorithm initialisation, or as a priori probability weights.

Figure 12: A schematic illustration of MEG and fMRI data-analysis with empirical data. Identical experimental paradigm with visual stimuli was carried out in MEG and fMRI. Auranen, Nummenmaa, Vanni et al., unpublished data.
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 (solid, soft or biological) and devices, which 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 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 CoE. 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.

Figure 13: Engineered and Artificial Systems
6.2.1 Engineered nanosystems

The research of micro- and nanoelectronic materials 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. Accordingly we are extending our research to biosensing systems and other fields combining information and communication technologies and systems biology. 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 fundamentally new nanomaterials and their technological applications are being worked out. In these areas we have continued to work in the field of fast all-optical devices. Research on nonlinear optical materials, coherent nonlinear systems and light-induced quantum effects will be crucial in the development of future all-optical information processing. Related to optical communications, we have introduced a new fast coherent all-optical flip-flop memory. 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 during 2006 we have proposed a new radiation based cooling mechanism of quantum dot excitons.

Recently we started research of low power biomorphic neural circuits based on floating gate MOS and SET transistors has been continued. In this research area neuro-MOS and neuro-SET based neural networks are developed and studied, especially for fast and power efficient signal processing. In 2006 we have started a new research project on quantum optical modeling of the network eye.
Cooling of radiative quantum dot excitons by THz radiation

Researchers: Fredrik Boxberg and Jukka Tuukkan

We have studied strain-induced quantum dots (SIQDs), which are formed in a near-surface InGaAs quantum well (QW) as a result of the strain field, induced by superficial InP stressor islands. The electronic structure and photonic properties of SIQDs have been analyzed using electro-elastic strain models and multiband effective mass models. Our simulations are based on an effective continuum description of the atomic structure and the envelope function model of the carrier eigenstates. We have focused on a particular experiment on SIQDs and the modulation of the charge carriers using THZ radiation. We have performed master equation simulations of the time-evolution of the QD electron-hole populations using a combination of advanced electron structure simulations and experimental estimates of governing carrier life times.

It was found that the piezoelectric potential induces strong potential minima in the valence band and is able to confine several holes in exterior, optically dark states. These potential minima play a considerable role in the carrier relaxation and recombination. The piezoelectric potential enables a THz radiation-activated exciton cooling, by providing an additional mechanism of carrier relaxation into the QD ground state. The piezoelectric potential enables also the emission of a delayed PL flash, even in the absence of any carrier generation. Figure 14 shows the analyzed experiment and a comparison between the experimental and simulated QD PL.

![Diagram](image)

Figure 14: (a) Experimental setup, that was theoretically analyzed. The strain-induced quantum dots were simultaneously pumped by an Ar+ (or Ti-Sap) laser and excited by a free electron laser. It was seen that the THz radiation increases the ground state QD PL, at the same time decreasing the PL of the excited QD transitions and of the QW. The experimental (b) and simulated (c) PL are in good qualitative agreement.
Modelling optical components for access networks

Researchers: Jani Oksanen and Jukka Tulkki

In the long haul network backbone where complex logical operations, like routing, are not needed, electrical components have been superseded by optical ones during the last decade. This has enabled an enormous boost in the data rates of the backbone, but left the electronic solutions in the metropolitan area and access networks outdated. However, to date there are no technologically viable solutions for replacing all the electronics by optics. This project concentrates on constructing models and ideas for new all-optical devices, with the needs of the access networks in mind.

In the project we have this far investigated 1) the differences of the quantum well and dot lasers with respect to their chirp under direct current modulation, 2) the operation of an optical amplifier linearized using gain clamping in vertical direction (also known as linear optical amplifier, or LOA), 3) the use of quantum cascade lasers in free space optical communications 4) all-optical signal regeneration using partly coherent laser networks and 5) all-optical flip-flop memories and decision circuits essentially based on coherent feedback between two laser amplifiers. These topics have been studied using analytical and numerical models ranging from band structure calculations to stochastic rate equations.

In addition to modeling the nonlinear components of optical networks, the project is gradually shifting towards more diverse topics. These include for example building a model of the compound eye of insects and developing new, more efficient led structures for general illumination.

Figure 15: (a) A schematic representation of a modified flip-flop circuit and building block of an optical logic gate realized with laser amplifiers and coherent feedback. (b) The output of an AND gate realized using two flip-flop circuits. (c) The output of a corresponding OR gate.
If electrons move through a conducting device without scattering the transport of electrons is ballistic. Ballistic transport is observed when the length of the channel is small compared to the mean free path of an electron. In the ballistic transport regime a device can be modelled in terms of transmission probabilities which are calculated for different combinations of source and drain eigenmodes.

We have used the mode matching (MM) method within the Landauer-Büttiker formalism to calculate the conductance of a silicon on insulator (SOI) quantum point contact (QPC). We have calculated how the strain affects to the conductance in the QPC due to the changes in the electron eigenstates (see Figure 17 and Figure 16).

![Figure 16: (a) The total conductance of the non-strained QPC as a function of the Fermi energy measured from the Si conduction band edge. (b) The total conductance of the QPC when the strain-induced potential is included in the calculations of transverse eigenstates.](image1)

![Figure 17: The effect of oxidation-induced strain on the conductance of the QPC. The strain-induced potential profile of the QPC. (a) The potential for electrons in 001 minimum at 7 nm above the bottom. (b) The cross-sectional potential in the middle of the QPC. (c) The cross-sectional potential at the end of the QPC](image2)
Biomorphic devices

Senior researchers: Jukka Tulkki
Junior researchers: Teppo Häyrynen

Our goal is to enhance the computational power with the circuit models that imitate the systems in nature. Distributed parallel systems may offer noise robust and fault tolerant signal processing with low energy consumption. In Figure 18 we show a voltage characteristics of a single electron A/D/A circuit which can be used for signal level restoration and noise reduction after analog computing stages.

Figure 18: The voltage characteristics of the single electron A/D/A converter.

Currently we are investigating how interference and correlation may be used in optical detection. We are trying to imitate the detection and the signal processing capabilities of the compound eye.
Structure of twist grain boundaries in silicon

Researchers: Sebastian von Alfthan, Adrian Sutton and Kimmo Kaski

Grain boundaries (GBs) are interfaces between crystalline grains of different orientation. They exist in polycrystalline silicon, which is widely used for solar cells and thin-film transistors. In pure twist GBs the axis around which the crystals are rotated, is perpendicular to the interface. The minimum-energy structure of such boundaries is still considered controversial as one cannot measure it experimentally. In this work we attempt to settle the question if the structure of twist GBs is disordered or crystalline.

Using molecular dynamics methods we have found crystalline minimum energy structures for several twist grain boundaries in silicon. These structures comprise the same two structural units in different combinations. We recognized that the key to finding these minimum energy structures is to allow the number of atoms at the boundary to change. The results are supported by experimental evidence since the studied periodic GBs have been measured to have a lower energy than non-periodic boundaries. We have also validated the model by calculating the energy for some structures using ab initio methods. We are now turning our attention to the behaviour of these boundaries at temperatures up to the melting point. Preliminary results show that the structural units are stable up to the glass transition point but the pattern of structural units comprising the boundary fluctuates. Above the glass transition temperature the structural units are metastable and the boundary undergoes a continuous melting transition.

Figure 19: The lowest energy \( \Sigma 5 \) boundary. The colour of atoms and bonds indicates the position perpendicular to the boundary. Structural units in the plan view are indicated by shading the 5 membered rings (thick bonds).

Figure 20: Four low energy \( \Sigma 13 \) boundaries with different atomic densities. Only bonds forming five-membered rings are shown. We have indicated structural units in the
6.2.2 Modelling of Learning and Perception

Researchers: Jouko Lampinen, Timo Kostiainen and Ilkka Kalliomäki
Junior researchers: Miika Toivanen and Juho Kettunen

Modelling of cognitive functions is central issue in many research topics in the CoE – 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 some of the results.
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.

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 below). 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 21 shows an example of the sequential matching process and Figure 22 illustrates matching when the target objects are occluded.

![Figure 21: 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.](image-url)
Image segmentation by MCMC methods

The goal of this work is to develop computationally efficient techniques for the division of natural colour images into meaningful segments. Segmentation is an essential step in image interpretation and computer vision. The slowness of many segmentation methods has been an obstacle to their use in many computer vision applications.

Our approach is based on statistical models for the textures of the segments. We use a probabilistic Markov chain Monte Carlo (MCMC) algorithm to determine how to divide an image such as a natural photograph into segments. The MCMC approach requires the processing of a large number of different sample segmentations. The computational cost depends critically on the quality of these samples. In this work we develop efficient methods to generate good samples for the algorithm by taking advantage of many types of information contained in the images, such as edges.

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.

Figure 22: 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 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.

**Finding novel objects and object classes**

The object matching system described above has an occlusion model for dealing with the feature points that are not visible. By extending this model we are studying an algorithm for finding an unknown object from a set of images, where the shape, or the variation of the shape, or the variation of the feature appearance between the images are not known.

Figure 23: Examples of segmentation results.

Figure 24: 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.
The localization and recognition proceed in sequential manner. A rectangular grid of node points is set on the first image of the sequence, hopefully covering the object (foreground) and probably some background. Each nodes’ prior probability to belong to the foreground object (‘node visibility’) is 0.5. The grid is localized in a novel image using Sequential Monte Carlo to find the modes of the posterior, so that the background nodes are regarded as being in occlusion. The prior information on the node visibilities are updated into posterior information in a Bayesian fashion, so that they reflect the current knowledge about which nodes belong to the object.

Next the grid is localized in a third image, using the Gabor responses of first image grid and matched second image grid, and so on. Ideally, the foreground node visibilities converge to one and the background visibilities to zero. It is to be noted, that no manual pre-annotation of the images is needed. Figure 25 shows an example of the matching process. The current research is on finding a robust likelihood parametrization needed in classifying the nodes into foreground and background points, and on improving the SMC sampling.

Figure 25: The matching result of a sequence of three images. The means of SMC samples are marked with crosses. The prior node visibility probabilities are shown above each node and the posterior probabilities below each node, in percents.
6.2.3 Computational Neuroscience

Researchers: Harri Valpola, Tuomas Lukka, Iina Tarnanen, Harm Aarts, Janne Hukkanen, Heikki Joensuu, Antti Yli-Krekola, Ville Mannari
Project homepage: http://www.lce.hut.fi/research/eas/compneuro/

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 behavior 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 Webots 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.

During evolution, brain was always 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 topic of our research has so far been the mammalian neocortex. As opposed to cerebellum, neocortex has 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 (described in more detail in the next section) 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.

Other systems that we plan to incorporate in the model later include basal ganglia and hippocampal formation. Basal ganglia are thought to assist in selection of behaviours and learning through trial and error. Hippocampal formation 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 at the same time powerful and simple: if a reflex is triggered in response to an event, the system will associate the action of the reflex with the 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.

For example, Figure 26 shows a simple system where the reflex only uses the current state of the robot (including velocities) and where the goal of the reflex is to keep the robot upright. Occasionally, footballs are launched towards the robot and it is given some inputs to be able to tell when a football is coming. Due to the reflex, the robot learns to anticipate the incoming football in advance and to lean towards it, in order to regain upright posture as soon as possible. The robot does not have sufficient power to recover from a hit of the football if it only stays upright and reacts after the football has hit it.

Figure 26: A simple reflex that tries to keep the robot upright but that knows nothing about the environment has taught the robot to respond to an environmental stimulus. Since the cerebellar algorithm predicts from the inputs giving the position of the ball that the reflex would soon (after the impact) cause it to try to lean towards the left, it leans towards the left already in preparation and manages to avoid falling down.
Having such lifelike behaviour (anticipating an impact and leaning towards it) emerges from a simple rule and a simple learning system is a good demonstration of the potential of cerebellar control. A more complicated example where the system has learned to use visual information is shown in Figure 27.

The animations shown in the right-hand margin demonstrate this experiment: in the topmost animation, the robot has not yet learned to respond to the ball and falls over when the ball hits. In the middle animation, the robot has learned to respond to the ball by leaning towards it and is able to stay upright. In the bottom animation, the ball has been made massless: expecting a collision, the robot leans towards the ball but when the ball has no mass, it stumbles. In ongoing development at the end of the year were systems such as the ones shown in Figure 28. The goal of the system is to keep the multi-jointed robot arm at a given position.

![Figure 27: A robot that learns to make use of visual cues from a virtual camera in order to anticipate and compensate for the roughness of the terrain, modelled as a kind of drag on the robot's wheel.](image)

![Figure 28: (a) A variation of the basic pole balancing problem where the robot balances in two dimensions using a ball, just like the real-life Ballbot robot of CMU (http://www.msl.ri.cmu.edu/projects/ballbot/). (b) A three-joint arm where the joints have learned to coordinate with each other by predicting each other’s effects on themselves. In both figures the extra boxes are animated bar graphs that visualize various dynamic variables.](image)
With a sensory delay, this is not an easy task: the different degrees of freedom interact
and righting one segment will cause the others to experience more force and can easily lead
to chaotic and unstable states. The cerebellar controller is able to coordinate the arm by
taking into account the positions of all joints and anticipating the motion of the other joints
and compensating for it proactively.

**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 also 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 29 with one of the units shown in the enlargement. Each unit receives bottom-up input vectors (solid black arrows) and represents their
regularities (features in machine learning terminology) by neural activation levels (the plots
with blue curves) which are the outputs of the unit. 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. Implicitly the units make Bayesian inference about the identity of
their bottom-up inputs using contextual inputs as background information to refine their
judgement. The units also implicitly evaluate the importance of the bottom-up information
they are receiving and decide whether to represent and broadcast it.

In practice the contextual information is processed by an associator module which looks
for correlations between the context and the input features. Those bottom-up features that
are supported by the context are highlighted. In Bayesian terms, the context mediates
the prior probabilities and bottom-up connections mediate the likelihood of different features
being present in the world.

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.

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 guiding learning. We have shown that in a hierarchical model like the one shown in Figure 29, 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.

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 other 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.
6.3 Cognitive and Social Systems

In our cognitive systems research, we focus on understanding neural basis of active hearing. Making sense of our acoustic environment is a vital and highly complex task. Our brain converts the stream of sound signals into features and objects, prioritizing relevant information while maintaining the ability to quickly react to unexpected, novel events. Consider yourself at a cocktail party. In the midst of social noise, you can, with relative ease, select a discussion you want to follow. Such selection is based on the various acoustic features related to, for example, a speaker’s location, voice quality and sound intensity. In addition, selection is strongly enhanced by seeing the speaker, especially his/her articulatory and other communicative gestures. Although our understanding of the mechanisms underlying selective listening has progressed rapidly during the past decades, the functional brain architecture underlying human active hearing (in contrast to passively responding to acoustic stimuli) still remains elusive. Our research utilizes advanced, non-invasive human brain imaging methods, such as combined fMRI, MEG, and EEG, and linear causality modeling techniques, to investigate the functional brain organization subserving active hearing. 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. 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.

The main goal of our research is to study the systemic mechanisms of active auditory perception. A system is a dynamic organization of activity of components in different anatomical areas. Interaction of components provides an adaptive result for an organism. In our theoretical framework, a system-creating factor is the result of a system, its goal. Most human auditory neuroscience research has concentrated on the processing of auditory information within the classically defined auditory cortex, with little consideration of other fundamental components of the auditory system. In contrast, our research aims to unify aspects of task-relevant modulation along the entire auditory pathway, from cortex to auditory periphery. Indeed, our research team was among the first to persuasively show that visual information processing can have a profound effect on the auditory-neural processing. Recently, we have also shown that visual processing of speech already influenced auditory processing at a so-called "low" brainstem level. The emerging hypothesis that we are investigating contends that the auditory system is constantly and rapidly reorganizing on the scale of milliseconds to seconds, in order to meet the specific demands of the task the subject is performing. We believe that this reorganization involves a multi-directional flow of context-related information between both central and peripheral brain regions, as well as areas located outside the classical auditory pathway that are involved in multi-sensory integration, attention, planning, and expectation. The unique expertise in psychology, neurophysiology and computational modeling in our multidisciplinary research environment has positioned us well to investigate this challenging and important auditory perceptual hypothesis.

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.

Figure 30: Cognitive and Social Systems
Our recent research has concentrated on neurocognitive mechanisms of multisensory perception, especially of audiovisual speech perception. In real life, visual information of objects normally precedes in time the sounds made by the object (e.g. in audiovisual speech lip movements are visible before the acoustic signal is heard). This led us to conclude that processing of visual information often helps us to create quite specific expectations of the nature of the following acoustic event. Therefore, our research naturally extended to the mechanisms of selective auditory attention.

Attention is crucial in integrating audiovisual speech perception. In our pioneering behavioural study we showed that the direction of visual spatial attention influences how strongly auditory and visual speech are perceptually integrated. In a later study, utilizing a modification of Posner’s attention paradigm, we showed that the direction of visual spatial attention almost exclusively determines which source of visual information is integrated with auditory information. In this study, the subjects fixated between two faces articulating consonant-vowel syllables. The degree of integration was indicated by the strength of the McGurk effect. In a subsequent experiment, we showed that the direction of visual attention influences the strength of perceptual audiovisual integration, and that this influence is correlated with modification of the auditory cortex activity. We extended these results to the field of auditory attention, manipulating subjects’ expectations by varying the probability at which the auditory stimulus appears in one of five spatial locations.

Processing visual speech influences activity in the primary and secondary auditory cortex and the auditory brainstem: In our pioneering MEG study utilizing the mismatch (odd-ball) paradigm we showed that processing of visual speech information has access to the human auditory cortex. In our more recent studies we showed that the amplitude of N1 deflection, generated in the auditory cortex 100 ms after the onset of the auditory stimulus, is also influenced by processing of visual speech. In our fMRI study we defined the anatomical location of the primary auditory cortex from the subjects’ structural MRIs. Our results showed that even the primary auditory cortex, in addition to other auditory cortical areas, is sensitive to the processing of visual speech.

The neural basis of human auditory discrimination can be studied accurately and noninvasively by recording "mismatch responses" to infrequent changes in physical properties of the acoustic stimulus. Almost any distinguishable change in a sequence of repetitive sounds generates mismatch negativity (MMN) at a latency of about 100-250 ms in the auditory cortex. Auditory perception is not isolated from other sensory modalities but can be modified by simultaneous processing of visual information. An intriguing example is the "McGurk effect": Acoustic syllable /ba/ presented simultaneously with a mouth articulating /ga/ is typically heard as /da/. In our EEG experiment, an odd-ball sequence of acoustic stimuli consisting of frequent /va/ syllables (standards) and infrequent /ba/ syllables (deviants) was presented to 11 subjects. Deviant stimuli in the unisensory 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 thus phonologically indistinguishable from the standards. Importantly, such deviants did not elicit MMN, indicating that the auditory cortex failed to discriminate...
between the acoustic stimuli. Our finding persuasively shows that processing visual information that is relevant for the perceptual task can profoundly influence the auditory-cortex mechanisms underlying early sound discrimination (Figure 31). Intriguingly, in our recent EEG recordings, we demonstrated that processing of visual speech influences auditory processing very early, already at brainstem level.

An experienced car mechanic can often deduce what’s wrong with a car by carefully listening to the sound of the ailing engine, despite the presence of multiple sources of noise. Indeed, the ability to select task-relevant sounds to awareness, whilst ignoring irrelevant ones, constitutes one of the most fundamental of human faculties. Several models suggest that selective attention increases gain in the neurons processing relevant stimulus features. Alternative models have claimed that selective attention enhances feature selectivity of cortical receptive fields in visual cortex. Our recent study suggest that such mechanisms may govern selective attention in human auditory cortex: selective attention to sound location enhanced stimulus specificity of adaptation in the posterior "where" pathway of auditory cortex, while attending to phonetic content of sounds resulted in analogous changes in the anterior "what" pathway. No evidence for overall enhancement of neuronal responses was found, supporting the idea that attentional modulation of neuronal adaptation also involves short-term plasticity of neuronal receptive fields in the auditory cortex. This interpretation is in line with recent studies in behaving ferrets, showing that attending to a certain sound frequency results in gradually evolving short-term plastic changes in the spectrotemporal receptive fields of primary auditory cortex neurons.

Figure 31: (Left) The stimuli presented in different experimental conditions. (Right) ERPs to the standard and deviant stimuli in different conditions. Deviant stimuli elicited a significant typical mismatch response in the Auditory and Ellipse conditions. In the McGurk condition, when subjects viewed /va/ articulations which rendered the standards indistinguishable from the deviants, the deviants did not elicit a mismatch response, indicating that auditory cortex did not discriminate between the different acoustic stimuli.
In our recent EEG study, we showed further evidence that increased gain alone cannot explain auditory selective attention in the human auditory cortex, but that enhanced frequency selectivity in the underlying tonotopically organized neurons additionally contributes to filtering of task-relevant stimuli from noise. We quantified the neural frequency tuning of auditory cortex in 20 healthy subjects by masking 1000-Hz tones by continuous white noise with parametrically varying frequency notches around the tone frequency. When the subjects selectively attended slight increments in tone frequency (1020 Hz), the global field power of event-related brain responses at 100 ms from the stimulus onset to the 1000-Hz tones increased, but as a non-multiplicative function of the width of the notch. Our results suggest that modulation of receptive fields of primary auditory cortex neurons observed in lower animals during classical conditioning constitutes the neural basis of enhanced perception during selective attention in humans (Figure 32 and Figure 33).

Figure 32: (Left) A schematic illustration of the used task paradigm. Target tones, indicated in red colour, were either higher in frequency or longer in duration. The background grey represents the noise masker, while the white area represents the gaps in the noise.

Figure 33: (a) Grand average global field power (GFP) of electrical activity as a function of time vs. width of the noise gap. Results of paired t-test comparisons between the conditions demonstrate the largest attention effects at the N100 peak latency and the similarity of the two Attend conditions. (b) Global Field Power amplitudes at N100 peak latency show the non-multiplicative suppression in amplitude with narrower notches during selective attention.
Our recent research has concentrated on the structure of large-scale social networks and the effects of this structure on processes taking place on such networks. 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 Notre Dame (USA), and Harvard University (USA).

As discussed in the introduction, uncovering the 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. Social scientists have ordinarily based their studies on questionnaire data, typically reaching the order of N 100 individuals. Although the spectrum of social interactions that may be probed in this approach is wide, the strength of an interaction is often based on recollection and, consequently, is highly subjective. However, in the late 1990’s a change of paradigm took place. The availability of electronic databases from emails to phone records attracted the interest of (statistical) physicists. These databases provide unprecedented opportunities for social network analysis. In this scheme the order of N 106 individuals may be handled, and although the range of social interactions is evidently narrower, information on them 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.

We have performed detailed analysis of a network consisting of the mobile phone call records of approximately seven million individuals over a period of 18 weeks. The call records have been extracted from the customer data base of a mobile network operator, whose customer base is approximately 20% the population of its undisclosed country of operation. For the purpose of privacy and anonymity, each subscription is identified only by a surrogate key in our data set. 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. We consider the links as weighted, such that the total amount of time two individuals have spend talking to each other is considered as a proxy of the strength of their social tie.

Our key results so far can be summarized as follows: i) we have presented a large-scale verification of the Granovetter hypothesis, which states that the overlap of the circles of friendship around two individuals increases as function of the strength of the tie connecting these two individuals. Although this hypothesis is very commonsensical and has been widely accepted in sociology, there has been no direct large-scale proof until now. ii) We have shown that strong and weak social ties play an altogether different role in the overall connectivity of the network. If all social ties are "severed", i.e. removed from the network in ascending order from the weakest to the strongest, the network becomes fragmented when roughly 80 percent of the links have been removed. In contrary, if links are removed in descending order starting from the strongest tie, the network appears very robust to the procedure and becomes fragmented effectively only when all links have been removed. In practical terms, the weak links are crucial for the overall connectivity of the network - they are the "glue" which keeps society together - while strong ties are related to local, small
The above structural properties, especially the correlation between tie strength and network structure, give rise to unexpected information transmission properties. In particular, in simulations of random, unconstrained spreading of information, we have observed that the strong within-community tie strengths tend to trap information within the communities. If tie strengths are not taken into account, information flows faster and reaches a larger number of recipients. Hence, contrary to popular belief, the underlying structure of social networks is not particularly well "optimized" to random information spreading. Rather, if information is to spread through the network, active participation and activation of the "weak ties" connecting different communities is required from those forwarding the information.

Figure 34: A schematic example of simulated information spreading on a small sample of the empirical social network. (a) Information flow when tie strengths affect the process such that the probability of spreading through a link depends on its strength. (b) Control case, where the tie strengths do not affect the process. The colour of a link indicates the total number of transmission events through that link in multiple simulations.
6.3.3 Brain Computer Interface

Senior researchers: Jukka Heikkonen and Mikko Sams
Researchers: Pasi Jylänki, Laura Kauhanen, Janne Lehtonen and Tapio Palomäki

Brain Computer Interfaces (BCIs) enable motor disabled and healthy persons to operate electrical devices and computers directly with their brain activity. Our BCI recognizes and classifies different brain activation patterns associated with real movements and movement attempts made by tetraplegic persons. One of our aims is to examine whether subjects with no previous experience of BCIs could achieve satisfactory performance after a short training period. Feedback plays an important role when learning to use a BCI. The most commonly used feedback modality is visual feedback. Visual attention, however, might be needed for application control: to drive a wheelchair, to observe the environment, etc. Subjects may also be blind. During 2006, we started to teach subjects with other feedback modalities. In two studies we tested the short-term learning of subjects imaging left and right hand movements. Twelve untrained subjects learned to use a BCI for the first time, receiving either haptic or visual feedback. In the second study the subjects were given more time to get accustomed to the feedback and a robot simulator program was included to mimic a distracting environment. We only used the tactile and visual stimuli as information about the output of the BCI.

For efficient BCI control, we have to select subject specific features from the EEG signals. We developed a feature selection method based on Bayesian inference. We tested the method (during the breaks). Figure 35 shows the setup of study where the subject received either tactile stimuli to the lower neck or visual feedback on the screen while learning to control a robot wheelchair in a simulated environment.

In the experiments, the classifier was adapted to the user’s brain activity using information about the subject’s intent. Thus the subjects could receive feedback from the beginning of the experiments. High classification accuracies were possible in both experiments. No differences were found between training with vibrotactile or visual feedback. These results show that vibrotactile feedback could be used as an alternative to visual feedback when starting to learn to use a BCI. The choice of feedback modality is therefore largely dependent on subjects’ preferences, intended environment of use and the application. During 2006 we also further developed our EEG-based online BCI system which uses MATLAB in data analysis. It is now capable of classifying EEG signals and giving subjects feedback as often as every 20 ms.

Our research is funded by European Union (MAIA project) and the Finnish Graduate School in Electronics, Telecommunications and Automation.
Computational systems biology is a new and rapidly developing field of research with focus to understand structure and processes of biological systems at molecular, cellular, tissue and organ level, through computational modeling and novel information theoretic data- and image analysis methods. With the break-through in deciphering the human genome using the most up-to-date computational approaches and modern experimental biotechnology, it has become possible to understand the structure and functions of bio-molecules, information stored in DNA (bioinformatics), its expression to proteins, protein structures (proteomics), metabolic pathways and networks, intra- and inter-cell signaling, and the physico-chemical mechanisms involved in them (biophysics).

There is currently wide interest in biology and biomedicine in structures, relations and functions of biological systems, which we study with a wide at-site-arsenal of state-of-the-art information theoretic analysis and multiscale modelling methods. One of our main interests is high density lipoprotein particles, the carriers of good cholesterol in the blood stream, and reverse cholesterol transport related to the particle structure and function. In addition, the structural aspects of low density lipoprotein particles, the carriers of bad cholesterol, will be tackled via spectroscopy (NMR) and imaging (cryo-electron microscopy) experiments. In the systems biology research LCE’s wide repertoire of information theoretic data and image analysis methods serve as key approaches.
Bioimaging has a central role in computational systems biology for understanding the structure and functions of small scale biological objects (e.g., viruses, mitochondria and cells), information stored in DNA (bioinformatics), and its expression to proteins and protein structures (proteomics). There are many imaging modalities that can be used for the purpose, such as (cryo-)electron tomography, single particle and light microscopy techniques even in computing reconstructions of living cells.

Microscopy tomography based light or electron microscopy is a valuable tool for structural analysis 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 at LCE. 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. A newest line of research has directed towards reconstructing living cells from light microscopic projections in EU project "AUTOMATION" coordinated by Pasteur Institute, France.

Figure 37: 3D reconstruction of the N protein of hantavirus with our modified MDL filtering.
Multi-Dimensional Reconstructions from Microscopic Biological Objects

A novel imaging system, aiming at high-content high-throughput multi-dimensional analysis of microscopic biological structure inside non-adherent living cells, is developed in the AUTOMATION consortium, which is financially supported by the Sixth Framework Programme of the European Union. Three-dimensional imaging methods are developed to be used with the novel cell-manipulator technology to facilitate the study of structural relationships among biomolecules. By the novel technology, non-adherent individual living cells can be rotated in suspension which provides a possibility to make a multi-dimensional reconstruction of the micro-structure inside the cells. The project is coordinated by Dr. Spencer Shorte, Institut Pasteur, France.

Our research group develops methodology for computing multi-dimensional reconstructions from image streams. The research problem has been divided into two parts. First, in order to compute the reconstruction, the pose, and possibly deformation, of the object has to be automatically recovered. This is a geometry estimation problem, which is in many ways similar to the image alignment problem in electron tomography, where computer vision methods can be used. Second, the actual reconstruction methods are considered for living cells, where the problems are closely related to the inverse problems especially from the view points of statistical inversion theory and tomography. One future plan of ours is to consider the geometry estimation and reconstruction methods for dynamically deforming, individual living cells.

Figure 38: A stereo view from the reconstruction interphase nuclei of lymphocytes, where nuclear lamina is stained with the green fluorescent protein. The original image set was acquired by Olivier Renaud, Institut Pasteur.
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 is the reconstruction of bacterial S-Layer protein using electron crystallography methods.

Figure 39: Stereo pairs of tilted side views of the reconstructed N-protein trimer showing the docking of three dsRNA, to the three symmetrically joint cavities of the trimer in (a), and docking of three ssRNA, (b) to the same cavity locations.
**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 which may be obtained by tilting the specimen stage by small angular increments. The reconstruction can be then computed from the TEM tilt series using tomographic methods. 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 seven 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 (c.f. Figure 40) 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 of a conventional critical-point-dried sample.

Figure 40: (a) Immuno electron tomography (IET) stereo pair of prefixed chicken fibroblast cell. Vinculin is shown by 3.5 nm and FAP52 with 1.4 nm immunogold conjugates. A delicate knotty fiber-like cluster that sticks out from the filopodia surface is densely labeled by 1.4 nm gold (black arrows on the fiber-like structure, a white arrow points to a knotty cluster). The insertion (c) shows the filopodia protruding from a cell at low magnification.
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 41: (a) The original cryo-EM image of a PRD1 virus. (b) The result of MDL based denoising.
Gene regulatory network modeling

In a single organism almost all cells contain the same genetic material; nevertheless cells are differentiated for different purposes and functions. While the difference in genome between man and chimpanzee is around one percent, both species are totally different in terms of appearance and capabilities. It is clear that we cannot understand how cells and organisms work by just looking at the nucleotide sequence in the DNA. It is the regulatory systems that determine which genes are expressed, when and where, and to what extent. One way of describing these regulatory systems are gene regulatory network models. These models are usually networks of genes that directly affect each other. Such networks do not explicitly represent the proteins and metabolites that actually mediate gene interactions. Understanding, describing and modelling such gene regulation networks is one of the most challenging problems in functional genomics.

 Recovering gene regulatory networks from biological data is a very difficult problem, but when succeeds, offers a wealth of information, applicable to for example drug development. These networks have usually been inferred from gene expression measurements that describe the activity of genes at certain stage or condition. However, gene expression data alone is not sufficient for reliable recovery of gene network structures. Our research has concentrated on how the learning process and the quality of the results can be improved by incorporating information from additional sources in Bayesian network modeling framework. Bayesian networks are probabilistic graphical models that are one of the most popular frameworks for learning gene regulatory networks.

 Several different sources of biological information exist that can be used for improving the learning of Bayesian network models of gene regulatory networks. For example known network structures, protein-DNA interactions and DNA sequence information can be used for improving the learning results. Information from these sources can be applied to the learning process through informative structure priors, search space restrictions and model refinements. The obtained results show that without prior information, the recovery of networks is very unreliable. Introducing informative structure priors and restrictions for learning improve the quality of recovered networks.
6.4.2 Biospectroscopy

Group leader: Mika Ala-Korpela
Senior researchers: Jukka Heikkonen, Kimmo Kaski and Aki Vehtari
Researchers: Johanna Hokkanen, Antti Kangas, Vibhor Kumar, Jussi Kumpula, Linda Kumpula, Niko Lankinen, Ville-Petteri Mäkinen, Jaakko Niemi, Tomi Peltola, Aino Salminen, Teemu Suna and Taru Tukiainen

Collaborators: Tuulia Tynkkynen, Pasi Soininen, Reino Laatikainen (Department of Chemistry, University of Kuopio); Matti Jauhiainen (Department of Molecular Medicine, National Public Health Institute, Helsinki); Marja-Riitta Taskinen (Division of Cardiology, Department of Medicine, University of Helsinki); Petri Ingman (Department of Chemistry, Instrument Centre, University of Turku); Sanna Mäkelä, Antti Nissinen, Minna Hannuksela, Markku Savolainen (Department of Internal Medicine, Clinical Research Center, University of Oulu); Per-Henrik Groop (Folkhälsan Institute of Genetics, Folkhälsan Research Centre, University of Helsinki); Olli Gröhn, Timo Liimatainen, Juhana Hakumäki (A. I. Virtanen Institute, Biomedical NMR Research Group, University of Kuopio); Petri Sipola (Department of Clinical Radiology, Kuopio University Hospital); Katarina Lähdesmäki, Katarina Öörn, Petri T. Kovanen (Wihuri Research Institute, Helsinki); Sarah Butcher (Institute of Biotechnology, Electron Microscopy Unit, University of Helsinki); Tuula Pirttilä (Department of Neurology, Kuopio University Hospital); Hannu Maaheimo (National Biological NMR Laboratory, Institute of Biotechnology, University of Helsinki); Risto Kauppinen (School of Sport and Exercise Sciences, Faculty of Medicine, Imperial College, London, UK); Jesus Brezmes-Llecha, Xavier Correig-Blanchar (Department of Electronic, Electrical and Automation Engineering, Universitat Rovira i Virgili, Tarragona, Spain); Rajiv Jalan (Liver Failure Group, Institute of Hepatology, London, UK); Michael Hardey (HYMS – The Hull York Medical School, UK)

The genomics, transcriptomics and proteomics represent the genome-oriented main discipline in life sciences. Physiology constitutes the triggering of specific functional pathways by environmental signals and thereby, the phenotype of a biological system is largely reflected by its metabolite composition and their interactions. An essential and complementary 'omics'-approach in understanding of biomolecular function is therefore metabonomics - the quantitative measurement of the time-related multiparametric metabolic responses of multicellular systems to pathophysiological stimuli or genetic modification. We are applying metabonomics, using mainly $^1$H NMR spectroscopy of serum, in atherothrombosis related diseases. We aim to develop analytical and data analysis aspects of NMR-based metabonomics as well as to reveal and understand biochemical pathways. In addition, we study lipoprotein metabolism, including the structure and function of lipoprotein particles.

$^1$H NMR Metabonomics

Measuring metabolites is not new. For decades, clinicians have charted chemistries in blood, urine, and other body fluids - e.g., using glucose to track diabetes and cholesterol to monitor heart disease. 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. We could also talk about ‘global biochemistry’. The ultimate goal of metabonomics is to be able to distinguish between an individual who is healthy and someone who has (diagnosis) - or might develop (risk assessment) - a disease. In the field of metabonomics, mass spectrometry and NMR spectroscopy have
become the two key technologies. An appealing feature of NMR spectroscopy for metabonomic applications is its specific yet non-selective nature (see Figure 43). Particularly, $^1$H NMR has the advantage of efficiently obtaining information on large numbers of metabolites in biofluids in vitro as well as in various tissues ex vivo and in vivo.

Our biomedical focus is understanding atherothrombosis - the various complex life long processes of harmful lipoprotein particle elevation and their modifications leading to lipid accumulation and potentially to a thrombus formation and a subsequent heart attack. Applications of $^1$H NMR metabonomics to study human serum are experimentally rather fast and straightforward. Measuring lipoprotein subclass profiles by $^1$H NMR therefore contrasts favourably to other lipoprotein measurement protocols and is currently receiving wide academic and commercial interest. The independent role of lipoprotein subclasses for the risk assessment and development of atherothrombosis is currently well recognised. We have indeed recently illustrated the inherent suitability of $^1$H NMR metabonomics for automated studies of lipoprotein subclass related metabolic interactions in a clinically relevant context and demonstrated the power of self-organising map (SOM) analysis in an extensive and representative case of $^1$H NMR metabonomics (see Figure 44).

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 in Figure 44. 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 $^1$H NMR metabonomics of serum equipped with a chemometric classifier, e.g., a SOM. On the left in Figure 44 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

Figure 43: Illustration of characteristic $^1$H NMR molecular windows for a type 1 diabetic (T1DM) patient. 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.
green line within the SOM) alongside the interplay between metabolic pathways and their consequences.

It is our aim to perform extensive metabonomic NMR studies in various clinically relevant sets of serum samples and to develop as well as to apply data analysis approaches capable of detecting differences in the biomolecular status of the individuals in relation to disease risk assessment and diagnosis. We have started our clinically oriented NMR metabonomic applications within two projects: i) alcohol related anti-atherogenic processes and diseases and ii) type 1 diabetes and the risk of diabetic nephropathy and vascular complications. The studies involve systematic linking of various biochemical and methodologies to study atherothrombosis and lipoprotein related phenomena. Within these studies we will put particular effort towards a comprehensive systems biology approach and we will be integrating complementary metabolic data from NMR spectroscopy with all available other data of clinical significance (including various clinically utilised biochemical markers, diagnostic data, other spectroscopic data and genetic information).

Figure 44: A schematic simplification of the challenge related to the risk assessment and diagnosis of atherothrombosis.

Our first results demonstrate that $^1$H NMR metabonomics clearly distinguishes metabolic characteristics of T1DM and appears approximately as good means to diagnose diabetic nephropathy from serum as an advanced set of biochemical variables.

Along the $^1$H NMR experimentation, we have also focused on developing biochemistry based signal models for the key metabolites in human serum and setting up a software allowing to simulate sets of $^1$H NMR spectra corresponding to various biomedical conditions, such as different lipoprotein subclass profiles and metabolic pathways, related to the risk assessment of coronary heart disease. We have also designed a potential scheme for the utilisation of MR methodologies in the assessment of long-term and short-term risk for atherothrombosis events. 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.

Our recent results have shown that the new $^1$H NMR metabonomics approach, combined with newly developed multi-factorial statistical analysis methods, is capable of finding clear metabolite alterations in the serum samples of various patient groups. The spectra contain an unforeseen wealth of information on serum metabolites, for example, in relation to type 1 diabetes and diabetic nephropathy. These data provide a systems biology view on metabolism, an aspect that cannot be captured by a handful of conventional clinical
variables. It is our intention to develop NMR metabonomics towards increased biomolecular understanding and thereby to improve individual disease risk assessment and to develop more specific molecular markers for the detection and follow-up of atherothrombosis.

The work in the near future will focus on collecting more clinically relevant data via $^1$H NMR metabonomics of serum and on related spectral analyses. We will study the role of $^1$H NMR spectroscopy in lipoprotein subclass quantification and the performance of various data analysis methods in biomedical spectroscopy applications.

**Molecular Structure of Lipoprotein Particles**

Lipids are carried in the circulation in water(blood)-soluble lipoprotein particles that consist of a hydrophobic core consisting mainly of esterified cholesterol and triglycerides, and a hydrophilic surface of mainly unesterified cholesterol, phospholipids and apolipoproteins. Apolipoproteins (i.e., the protein molecules in various lipoprotein particles) maintain the structural integrity of lipoprotein particles and direct their metabolic interactions with cellsurface receptors, hydrolytic enzymes, and lipid transport proteins. The low density lipoprotein (LDL) particles are the major cholesterol carriers in circulation and their physiological function is to carry cholesterol to the cells. In the process of atherogenesis these particles are modified and they accumulate in the arterial wall. Although the composition and overall structure of the LDL particles is well known, the fundamental molecular interactions and their impact on the structure of LDL particles are still not well understood. The HDL particles are the key cholesterol carriers in the reverse cholesterol transport, i.e., transfer of accumulated cholesterol molecules from the arterial intima to liver for excretion. HDL particles have several documented functions, although the precise mechanism by which they prevent atherosclerosis still remains partly uncertain.

Using proton NMR we have recently been able to identify and quantify lysophosphatidylcholine (lysoPC) (in addition to PC and sphingomyelin) in LDL particles. This finding is particularly important concerning studies of LDL particle modifications in various pH conditions. Recent evidence suggest that atherosclerotic plaques and plaque vulnerability are related to acidic pH and recent results have also pointed out remarkable differences in the LDL particle modifications at different pH after enzymatic modifications. LysoPC may also induce various cell related phenomena in the intima since it is known to have some functions in cell signalling.

Recently we have also been developing a computationally optimised, general structural model for spherical lipoprotein particles. Our preliminary modelling, based on extensive biochemical data on the molecular compositions of different lipoprotein particles, indicates new aspects in relation to the distribution of hydrophobic lipid molecules, such as triglycerides and cholesterol esters, in the particles. The obtained molecular distributions seem to be a characteristic of each metabolic lipoprotein category revealing a molecular rationale for the lipoprotein metabolism.

In the current multidisciplinary collaboration we will study the molecular structures of lipoprotein particles, focusing on HDL particles in relation to reverse cholesterol transport as well as on native and modified LDL particles in relation to early atherosclerotic lesion formation. On the biophysical side the role of optimised structural modelling in the studies of lipoprotein structure will be evaluated further. The applications of SOM analysis and the Bayesian methodology for NMR data as well as for clinical biochemistry data are to be extended. To reach the general goal - detailed molecular understanding of lipoprotein structure and dynamics - we will be applying and combining various experimental and computational approaches.
**Sterol Interaction with Membrane Lipids**

Researchers: Tomasz Róg, Ilpo Vattulainen and Mikko Karttunen

‘Laboratory of Physics and Helsinki Institute of Physics, HUT

Cholesterol (Chol) is an important constituent of eukaryotic cell membranes where it accounts for up to 50 mol% of the membrane lipids. The biological roles of Chol involve maintenance of proper fluidity, formation of glyco-sphingolipid-Chol-enriched raft domains, reduction of passive permeability, and increasing the mechanical strength of the membrane. The Chol molecule consists of a planar tetracyclic ring system with the 3β-hydroxyl group and a short 8-carbon atom chain. The planar tetracyclic ring system of Chol is not symmetric about the ring plane. The sterol ring has a flat side with no substituents (α-face) and a rough side with two methyl substituents (β-face). In natural and model membranes, Chol effectively increases the order of saturated alkyl chains of phospholipids (ordering effect) and the membrane surface density (condensing effect). Chol analogues, whose molecular structures often differ little from that of Chol, affect membrane ordering and condensation much less. Thus, the molecular structure of Chol seems to be optimal for its biological membrane functions. The main goal of these studies has been to elucidate the relationship between the Chol structure and its effect on the bilayer made of saturated and unsaturated PC molecules. In this aim ten models of lipid bilayer were constructed - three composed of DPPC (dipalmitoylphosphatidylcholine), and three of DOPC (dioleoylphosphatidylcholine). To the pure PC bilayer cholesterol, desmosterol, ketosterol and modified cholesterol were added (structure of the cholesterol molecule and its analogues is shown in figure). 100 ns of the molecular dynamics simulation of these systems were performed using GROMACS software. In the modified cholesterol molecules both methyl substituents were removed from the α-face, so the molecule has two flat faces. Analyses of obtained trajectories will provide information about the role of α and β-faces of cholesterol as well as help to understand the evolutionary pathway of sterol family on which we observed removal of methyl group.

![Figure 45: Cholesterol structure with sites of modifications, thus leading to a set of sterols studied here.](image)
Glycolipids

Researchers: Tomasz Róg, Ilpo Vattulainen and Mikko Karttunen
Laboratory of Physics and Helsinki Institute of Physics, HUT

Glycolipids belong to a heterogeneous class of lipids - about 300 different oligosaccharide head groups connected with 60 different hydrophobic parts have already been characterized. Glycolipids play a major role in a variety of cellular functions, such as cell-cell recognition, cell adhesion, signal transduction, and protein sorting. In cell membranes, glycolipids are mainly found in rafts, which are lipid domains comprised, for example, of saturated sphingolipids, glycolipids, and cholesterol. Rafts are thought of as highly ordered, nano-sized domains floating in fluid-like membranes composed of phosphatidylcholine (PC) molecules and smaller amounts of cholesterol. One of the reasons why rafts are so fascinating is that they have been suggested to provide specific environments for membrane proteins. In other words, rafts, and thus glycolipids, would be involved in governing protein functioning.

In order to understand the role of glycolipids in biological membranes, we performed series of molecular dynamics simulations of lipid bilayers composed of glycolipids. In our studies we used two sugar headgroups glucose and galactose attached to the glycerol (dipalmitoyl) and sphingo moiety. Phosphatidylcholine and phosphatidylethanolamine headgroups were used as reference systems. All simulations were performed using GROMACS software. All bilayers were composed of 128 lipid molecules hydrated with 3600 water molecules. To parameterize lipid molecules we used all atom OPLS parameterization which was already validated against experimental data for 1,2-di-O-palmitoyl-3-O-?-D-glucosyl-sn-glycerol. The simulations were performed at constant pressure and constant temperature 343, 358, and 368 K. The temperature and pressure were controlled using the Berendsen methods. For electrostatic interactions PME methods was used. The simulation protocol used in this study has been success fully applied in various molecular dynamics simulation studies of lipid bilayers.

Figure 46: Structure of two h bonded glycolipid molecules extracted from MD simulated lipid bilayer.
The Oxford affiliate unit of Complex Systems and Network Research (CSNR) functions as a framework for collaborations between LCE and researchers at Oxford University, especially those in the cross-departmental CABDyN research cluster. CABDyN is a multi-disciplinary team involving Physics Department (Prof. N. Johnson), Said Business School (Dr. Felix Reed-Tsochas), Department of Engineering Sciences (Prof. Janet Efstathiou), and Mathematics Institute (Prof. Philip Maini). LCE 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.

Since September 2006 CSNR has been locally headed by Dr. Jukka-Pekka Onnela, a Junior Research Fellow at Wolfson College, Oxford University. One of the aims is to work on projects that combine the competence developed at LCE 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. As a case study we have implemented a simple model of woodland fungal growth. Together with biologists in Oxford, we aim to develop the model further and test its predictions experimentally.

Figure 48: The functional dynamic network framework allows one to specify a fixed number of microscopic rules that govern the behaviour of the system. The colours correspond to nutrient concentrations from high (red) to low (blue). One can clearly see the emergence of canalized flux channels, which have been observed experimentally in a wide class of real biological fungi. (David M.D. Smith, Jukka-Pekka Onnela, Chiu Fan Lee, Mark Fricker, and Neil F. Johnson, Network automata and the functional dynamic network framework, arXiv:physics/0701307v1)
7 Research Activities

7.1 Visits to the Laboratory

- Prof. Yuri Alaxandrov, Russian Academy of Science, Moscow, Russia
- Prof. Rafael Barrio, Universidad Nacional Autónoma de Mexico UNAM, Mexico
- Prof. Holland Cheng, University of California, Davis, USA
- Associate prof. Chris Davis, University of Melbourne, Australia
- Prof. Michael Finnis, Imperial College, U.K.
- Prof. Alex Hansen, Norwegian University of Science, Norway
- Prof. Janos Kertesz, Budapest University of Technology, Hungary
- Prof. David Landau, University of Georgia, USA
- Prof. Claudio Mirasso, Mediterranean Institute of Advanced Studies, Mallorca, Spain
- M.Sc. Francesco Orabona, University of Genoa, Italy
- Prof. Josef Rauchecker, Georgetown University, USA
- Prof. Jorma Rissanen, IBM, California, USA
- Assistant Prof. Dr. Neslihan Serap Sengör, Istanbul Technical University, Turkey
- Prof. Adrian Sutton, Imperial College, U.K.
- M. Sc., Gergely Tibely, Budapest University of Technology, Hungary
- Prof. Alessandro Vespignani, School of Informatics, Indiana University, USA

7.2 Visits by Laboratory Personnel

Kimmo Kaski
- Universidad Nacional Autónoma de Mexico, Instituto de Fisica, Mexico City, Mexico, 29.5. - 5.6.2006.

Mika Ala-Korpela
- Hamilton Institute, National University of Ireland, Maynooth, Ireland. 26. – 29.7.2006
- Imaging Sciences Department, Hammersmith Hospital, Division of Clinical Sciences, Faculty of Medicine, Imperial College, London, UK. 9. – 12.12.2006

Tapio Heimo
- Budapest University of Technology and Economics, Budapest, Hungary 4.-15.12.2006

Jussi Kumpula
- Summer school on complex systems, Chamonix, France, 4.7.-28.7.2006

Riku Linna
- Wolfson College & Theoretical Physics, Oxford, UK.

Tomasz Róg
- Jagiellonian University, Faculty of Biotechnology, Krakow, Poland, March 2006
- Durham University, Faculty of Chemistry, United Kingdom, August 2006
7.3 Participation in Conferences and Seminars

Kimmo Kaski
- Physics of Risk, Vilnius, Lithuania, 13.5. -16.5.2006
- Computational Physics, Xián, China 11. – 15.11.2006
- Computational Physics, Hangzhou, China 16. – 19 .11.2006
- ECCS'06 Conference, Oxford 25.9. – 29 .9.2006
- The Conference on Complex systems, Lisbon 22.11. – 25.11.2006

Jouko Lampinen
- The 8th Valencia meeting on Bayesian Statistics, June 2-6, Benidorm, Spain NordStat 2006, the 21st Nordic Conference on Mathematical Statistics.
  Talk: Bayesian model for object localization and recognition. (Invited)

Mikko Sams
- International Cerebral Palsy Conference, Oulu, Finland, 2-5.2.2006.
  Talk: Neurocognitive mechanisms of multisensory integration. (Invited)
- Brain Awareness Week, Helsinki Collegium for Advanced Studies, Helsinki, Finland, March 16th, 2006.
  Talk: Neurocognition of audiovisual speech perception. (Invited)
- Cross-modal interaction in natural and artificial cognitive systems (CINACS), Hamburg, Germany, September 28, 2006.
  Talk: Neurocognition of audiovisual speech perception. (Invited)
  Talk: Valence and intensity of emotions. (Invited)

Sami Brandt
- Statistical Methods in Multi-Image and Video Processing Workshop, in conjunction with ECCV 2006, Graz, Austria, May.
Talk: Camera Motion Recovery without Correspondence from Micro-Rotation Sets in Wide-Field Light Microscopy

- 18th International Conference on Pattern Recognition (ICPR 2006), Hong Kong, China, August.

Mika Ala-Korpela
- The 28th Finnish NMR Symposium, June 7–9, Kuopio, Finland, 2006.

Talk: NMR Metabonomics as a potential recipe against natural fuzziness in the borderline of health and disease.


Talk: (in tandem with Ville-Petteri Mäkinen): A novel Bayesian approach for uncovering potential spectroscopic counterparts for clinical variables in $^1$H NMR metabonomic applications.


Talk: The role of metab*omics in biomedicine: $^1$H NMR spectroscopy in disease risk assessment and diagnostics. (Invited)

- The 23rd Annual Scientific Meeting of the European Society for Magnetic Resonance in Medicine and Biology (ESMRMB), September 21–23, Warsaw, Poland, 2006.

Talk: Metabolic changes in simulated and clinical $^1$H NMR data sets of serum by means of sample correlation spectroscopy and covariance analysis.

- Laboratory seminar at the Department of Molecular Medicine, Biomedicum, National Public Health Institute, November 28, Helsinki, Finland, 2006.

Talk: $^1$H NMR as a high-throughput metabonomic tool? (Invited)

Tapio Heimo
- The Econophysics Colloquium '06, Tokyo, Japan, 21.11.-26.11.2006

Danai Laksameethanasan
- IEEE International Symposium on Biomedical Imaging (ISBI 2006), April.

Jukka-Pekka Onnela
- Physics of Risk, Vilnius, Lithuania, 13.5.-16.5.2006
- The Econophysics Colloquium '06, Tokyo, Japan, 21.11.-26.11.2006

Tomasz Róg
- Physics Days, Tampere, Finland, 9.-11.3.2006.

Jari Saramäki
- Physics of Risk, Vilnius, Lithuania, 13.5.-16.5.2006

Talk: Characterizing Weighted Complex Networks in Economics and Society

Riitta Toivonen
- Physics of Risk, Vilnius, Lithuania, 13.5.-16.5.2006

Harri Valpola
- Computational and Systems Neuroscience, 5-10.3. 2006, Salt Lake City, Utah, USA.
- Adaptation in Artificial and Biological Systems, April 3-6, 2006, Bristol, UK.
• International Symposium on Computational Neuroscience, May 8-9, Montreal, Canada.
• Fifteenth Annual Computational Neuroscience Meeting, 16.-20.6.06, Edinburgh, UK
• TransVision06, August 17-19, 2006, Helsinki, Finland.
  \textit{Talk:} Designing Artificial Minds, the Ninth International Conference on the Simulation of Adaptive Behavior, September 25-30, 2006, Rome, Italy.
• The Ninth Scandinavian Conference on Artificial Intelligence, 25-27.10.06, Espoo, Finland.
  \textit{Talk:} Learning anticipatory behaviour using a simple cerebellar model.

Ville-Petteri Mäkinen
• Atherosclerosis Club Annual Meeting, March 17-18, Oulu, Finland, 2006.
  \textit{Talk:} $^1$H NMR metabonomics of serum: introduction of molecular windows and assessment of indicators of metabolic complications in type 1 diabetic patients.
• The 19th Annual Meeting of the European Diabetic Nephropathy Study Group (EDNSG), May 19-20, Helsinki, Finland, 2006.
  \textit{Talk:} $^1$H NMR metabonomics of diabetic kidney disease. (invited)
  \textit{Talk:} Detection of metabonomic features from $^1$H NMR spectra of serum: A molecular view of diabetic nephropathy.
• The 28th Finnish NMR Symposium, June 7–9, Kuopio, Finland, 2006.
  \textit{Talk:} Associating $^1$H NMR spectra with clinical variables: metabonomics of diabetic kidney disease.
  \textit{Talk:} (in tandem with Mika Ala-Korpela): A novel Bayesian approach for uncovering potential spectroscopic counterparts for clinical variables in $^1$H NMR metabonomic applications.
• The 23rd Annual Scientific Meeting of the European Society for Magnetic Resonance in Medicine and Biology (ESMRMB), September 21–23, Warsaw, Poland, 2006.
  \textit{Talk:} Diagnosing diabetic nephropathy by $^1$H NMR metabonomics of serum. (2nd prize in the Young Investigator Award Finals)

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

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

Sami Brandt
• The Institute of Electrical and Electronics Engineers (IEEE)
• The Computer Society of the IEEE
• The International Association for Pattern Recognition (IAPR)
• The Pattern Recognition Society of Finland
• The Finnish Inverse Problems Society

Ilkka Kalliomäki
• Member of HATUTUS, Pattern Recognition Society of Finland
• Member of the International Association for Pattern Recognition (IAPR)

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
• Awards:
  Suomen Valkoisen Ruusun 1 luokan ritarimerkki
• 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

Jouko Lampinen as acted as
• Member of the program committee of
  NordStat 2006, the 21st Nordic Conference on Mathematical Statistics, and organizer
  of a special session Statistics in information engineering
  VIE 2006, Visual Information Engineering
  ESANN 2006, European Symposium on Artificial Neural Networks

Mikko Sams
• Member of the Editorial Board in journals:
  Tiede
  Polysteekki

Mika Ala-Korpela
• Reviewer in journals:
  Biochemistry
  Chemistry and Physics of Lipids
  Journal of Magnetic Resonance
  BMC Bioinformatics
  Critical Reviews in Clinical Laboratory Sciences
• A member of the management group of a Tekes project for Neste Oil Ltd
• Chaired session in a scientific meeting:
• Awards: The Best Poster Presentation
  The Faculty of Medicine Science Day, University of Oulu, 14.2.06, Oulu, Finland,
  (Sanna Mäkelä et al.)
  The 28th Finnish NMR Symposium, 7–9.6.06, Kuopio, Finland, (Niko Lankinen et al.)
  2nd prise in the Young Investigator Award competition of the European Society for
  Magnetic Resonance in Medicine and Biology (ESMRMB) annual meeting in
  Warsaw, Poland, September 2006 (Ville-Petteri Mäkinen et al.)

Sami Brandt
• Reviewer in journals:
  Pattern Recognition Letters
• Reviewer in conferences:
  18th International Conference on Pattern Recognition (ICPR 2006)

Harri Valpola
• Member of Editorial Board:
  Neurocomputing
• Reviewer in journals, book series and international conferences:
  Neural Computation
  IEEE Transactions on Neural Networks
  IEEE Transactions on Signal Processing
  The Ninth Scandinavian Conference on Artificial Intelligence
8 Publications


