THE JEDLIK LABORATORIES
RESEARCH ACTIVITY – AN OVERVIEW
2016

FACULTY OF INFORMATION TECHNOLOGY AND BIONICS
PÁZMÁNY PÉTER CATHOLIC UNIVERSITY

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a Pázmány Péter Katolikus Egyetem rektora

PREFACE

The present document intends to give a brief but complete overview on the research activity of the Jedlik Laboratories of the Faculty of Information Technology and Bionics, at Pázmány Péter Catholic University. The Jedlik Laboratories are formed around the research activities of the Faculty professors and PhD students of the Multidisciplinary Doctoral School. These 30+50 researchers on the field of information technology and bionics may exhibit a large research capacity if they are working in a well-focused manner. It was recognized by the title "Research Faculty" given by the Hungarian state in 2013.

The research descriptions of our laboratories are completed by some relevant publications as well.

This document contains the original introduction of Prof Tamás Roska (1940-2014), founding dean of the Faculty and first director of the Jedlik Laboratories. I try to do my best to follow his research ideas in the life of our Faculty.

Budapest, 22 December, 2015

Péter Szolgay
Director of Jedlik Labs

INTRODUCTION

In 1635, Péter Pázmány, Archbishop of Esztergom, Primate of Hungary, an outstanding preacher and the renewer of the Hungarian language, established a University that is the oldest today in Hungary. Until 1950, under various names, at that time as the Pázmány Péter University of Sciences (Pázmány Péter Tudományegyetem) has been the most important and oldest University in Hungary. In 1950, the Pázmány University was split into three parts, the Medical School, the smallest part keeping the name of Pázmány (Theology, philosophy), and the rest as the Eötvös Loránd University of Sciences.

After the collapse of the communist system, in 1991, the Pázmány University started to reextend. Today, it is a University with 8 000 students doing education and research in almost all fields of sciences: humanities, social sciences, law, and theology, as well as major fields in science and technology. Its Multidisciplinary Institute of Advanced Studies has been recently established (the Pázmány Institute) and it is a University of national excellence in Hungary.

The strong ties with the Semmelweis Medical University have been developed during the last 10 years, and last year a special alliance between the three Pázmány rooted Universities had been established in the fields of research.

On July 1, 1998, the Faculty of Information Technology was established, as a strongly research oriented Faculty, teaching and doing research in electronic and computer engineering and later on in bionic engineering. Presently, the Faculty is accredited to give doctoral degrees and habilitation in electrical engineering, information technology, and biology. Right from the beginning, may be the first in Europe, a systematic study and a synergy was developed with neurosciences, teamed up also with a few outstanding neuroscientists from the Hungarian Academy of Sciences. Finally, establishing the undergraduate curriculum in Molecular Bionics five years ago in collaboration with the Semmelweis University, the first of this kind in Europe, the special character of our Faculty has been developed. Actually, Bionics is defined by four disciplinary pillars: molecular biology, neuroscience, electromagnetics and photonics, and computer engineering.

We have started in a Department system, without the classical continental chair system, and the research laboratories forming a unit called A. Jedlik R&D Laboratories or briefly, Jedlik Laboratories were also established. Each laboratory, one of the 22 today, offers some experimental facilities, many of them with high-end technologies. In addition, during the last 10 years we have developed a close relationship with the Semmelweis Medical University forming already 2 joint centers and 4 joint research projects. A special relationship exists from the beginning with the Research Institute of Experimental Medicine of the Hungarian Academy of Sciences (HAS), our neuroscience teaching and research is based mainly by Professors with joint affiliation. Joint affiliation has also been started last year with five professors at various clinical departments of the Semmelweis University.

In addition, we have strategic partnerships with five other institutes of the HAS, as well as developing partnerships with many companies.

In this booklet, we intended to give a brief, however, quite complete picture about the activities of the Jedlik Laboratories. The details of the projects are published in each year in our Annual Research Reports.

Special thanks are due to many individuals for their generous support. First of all, to the Rector of our University in 1998, Professor Péter Erdő, by founding this Faculty, and making it to become a research faculty. We are grateful to the many outstanding colleagues joining to this intellectual adventure as professors. Special thanks are due to the directors of five Institutes of the HAS who generously offered the joint appointments of some of their excellent researchers and their laboratory use at the beginning, as well as to the three Rectors of the Semmelweis Medical University. Many seminal collaborations developed during the long tenure of Rector Professor Tivadar Tulassay. Our present Rector, Professor Szabolcs Szuromi, our Dean Professor Péter Szolgay, and Pro-Dean Professor Judit Nyékyné Gaizler provided extraordinary help in establishing and supporting the Jedlik Laboratories, and providing for a lifestyle of a research university.

The hard and dedicated works of the many colleagues of our Faculty in the Jedlik Laboratories as well as of the many outstanding graduate students are the cornerstones of the success.

Now, we are heading to a major new project, by building a Bionic Innovation Center, for serving as a catalyst for the Hungarian Bionics Industry. This is being established now, with the generous support of the Government of Hungary. This specially funded National Innovation Center, the first of its kind in Central-Eastern Europe will exploit the many young talents who are receiving their degrees in the Bionics curricula.

May 15, 2013

Tamás Roska
Director of the Jedlik Laboratories

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Joint Centers with the Semmelweis University

Various joint Research projects with the Semmelweis University

1. SIMULATIONS OF ELECTROMAGNETIC FIELDS, AND FIELD MATTER INTERACTIONS – TOWARD ENGINEERING QUANTUMELECTRODYNAMICS

ÁRPÁD I. CSURGAY, Professor
Graduate students: ÁDÁM FEKETE, IMRE JUHÁSZ, ÁDÁM PAPP

In this report we present (i) two applications of short wavelength spin-waves, (ii) a case study on excitation energy transfer between two-state atoms, and (iii) a study on stimulated emission microscopy.

To simulate micromagnetic spin-waves we use OOMMF – Object Oriented Micromagnetic Framework and electromagnetic simulations to estimate the generated wave amplitudes for different geometries and at different frequencies.

To simulate room temperature molecular systems subject to optical frequency electromagnetic excitations we introduce equivalent quantum circuit models composed of (i) two-state 'atoms', (ii) ideal lossless harmonic oscillators and (iii) transmission lines coupled to (iv) heat baths representing the environment, and illuminated by (v) electromagnetic excitation. The temporal dynamics of the system is obtained by the numerical solution of the Liouville–von Neumann master equation describing the dynamics of the reduced density operator.

(I) SHORT-WAVELENGTH SPIN-WAVE GENERATION [1], [2].

We investigate the use of microstrip lines for short-wavelength spin-wave generation in magnetic thin films. We use micromagnetic (OOMMF – Object Oriented Micromagnetic Framework) and electromagnetic simulations to estimate the generated wave amplitudes for different geometries and at different frequencies. Our results suggest that in applications where coherent wavefronts need to be generated a microstrip line might also be used instead of more complicated devices (e.g. spin-torque oscillators) with comparable efficiency.

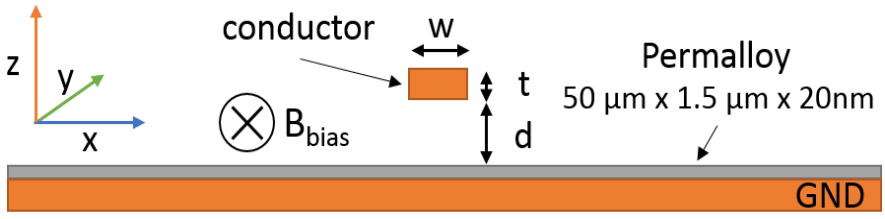

Fig. 1 *Geometry of the simulated microstrip line (cross section).*

As a first approach, we calculated the magnetic field generated by the microstrip line using Ampere's law, assuming a uniform current distribution through the wire, and ignoring the effect of the ground plane and the dielectric. For the simulations, we assumed 1 mA current. We applied the calculated spatial field distribution as an external magnetic field in OOMMF multiplied by a time-dependent sinusoidal function at microwave frequencies.

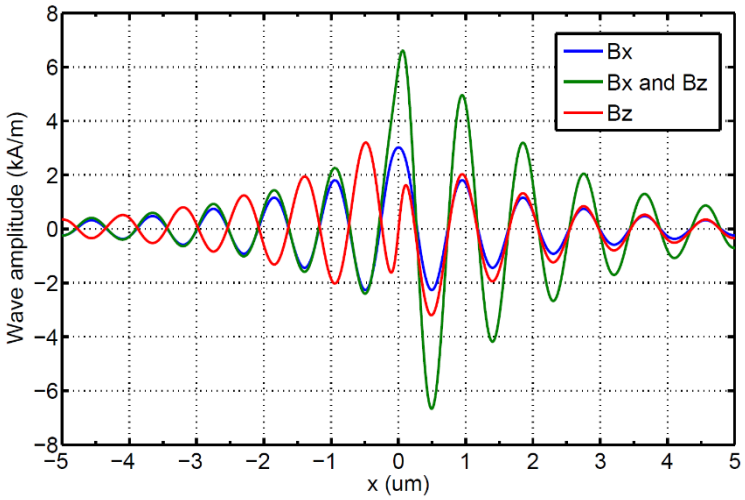

Fig. 2 *Anisotropic spin-wave generation by the microstrip line centered at x = 0 μm (green), and spin waves generated by applying only the x (blue) or z (red) field component of the line.*

We found that the wavelength of the generated spin waves is independent of the physical dimensions of the microstrip line in the investigated range of the physical dimensions, but it depends on the applied biasing magnetic field B_{bias} and the frequency f. However, there is strong correlation between the spin-wave amplitude and the physical dimensions of the microstrip line, the generation efficiency decays as the physical dimensions of the microstrip increase (for the same spin-wave wavelength).

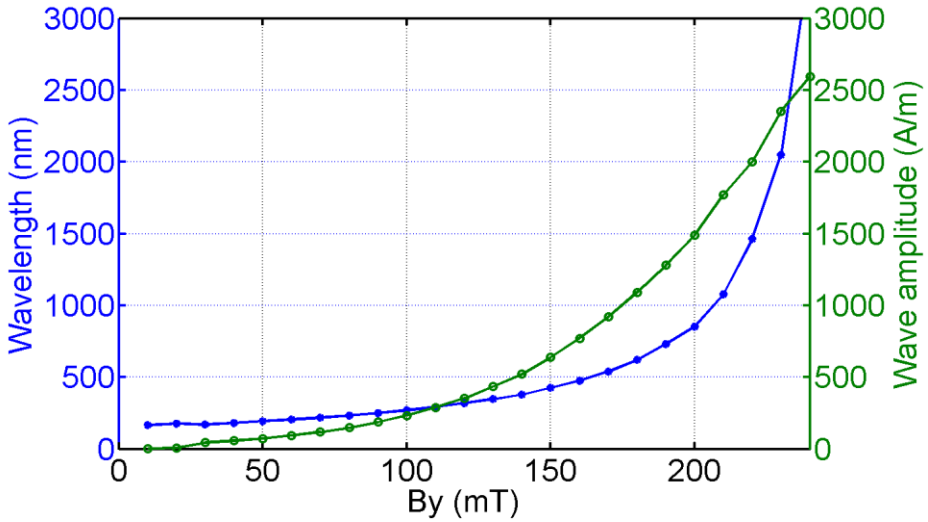

Fig. 3 *Wavelength and amplitude of the generated spin waves in function of B_{bias} (f = 15 GHz, w = 100 nm, d = 100 nm, t = 50 nm)*

We have studied the use of spin waves for computing and signal processing purposes. Spin waves are propagating excitations of the spins in magnetic materials that can represent and carry information. The idea of utilizing spin waves for computing is not new, however, it got special interest in the last decade in nanoscale devices. Spin-wave devices promise high speed, low power devices with relatively simple fabrication.

While most devices presented so far aim to create novel switches to replace transistors in logic applications, we focus on wave-based approaches where the spin waves are used to perform linear transformations on analog signals. We borrow ideas from the well-established

optical computing theory, but instead of light we use spin waves in magnetic films which can be integrated on-chip straightforwardly. We propose spin-wave elements analogous to optical elements like lenses, mirrors and gratings [2]. Using micromagnetic simulations (OOMMF) we demonstrate that although there are many differences between light and spin waves, it is possible to redesign the optical computing concepts to be realized on magnetic medium. One of the most important concept in optical computing is the Fourier transform property of a lens which is the basis of many optical algorithms, like signal filtering and pattern matching. We show that a spin-wave lens can also realize these functions. We design a GRIN lens for spin waves and demonstrate the Fourier transformation with the GRIN lens using micromagnetic OOMMF simulations.

Our calculations suggest that in both speed and power consumption multiple orders of magnitude improvement is achievable (not including the supporting circuitry). Although there are many proposed devices for spin-wave generation and readout, these are still the bottleneck of the energy consumption of the envisioned system, but even considering these losses our proposed device has a significant gain compared to state-of-the-art CMOS realizations.

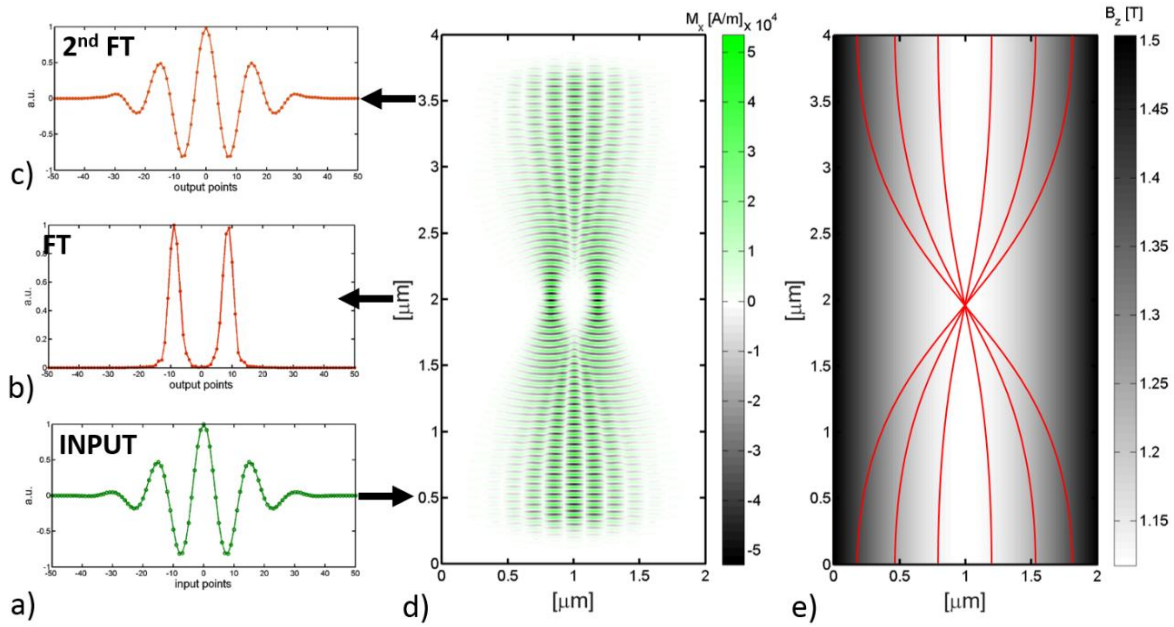

Fig. 4 *Micromagnetic simulation of a GRIN lens performing Fourier transform. a) Morlet wavelet as input. b) Fourier transform performed by the GRIN lens @ ½ pitch length. c) 2nd Fourier transform performed by the GRIN lens @ 1 pitch length. d) Snapshot of the waves propagating in the magnetic film. e) Applied magnetic field distribution to realize GRIN lens.*

(II) SIMULATION OF EXCITATION ENERGY TRANSFER BETWEEN COUPLED TWO-STATE ATOMS [3], [4]

We developed a quantum mechanical model and implemented a simulator program using Quantum Toolbox in Python (QuTiP) to investigate the energy transfer between coupled atoms. The simulator solves the Lindblad master equation of a system consisting of N coupled two-state atoms, defined by energy, coupling and dissipation parameters.

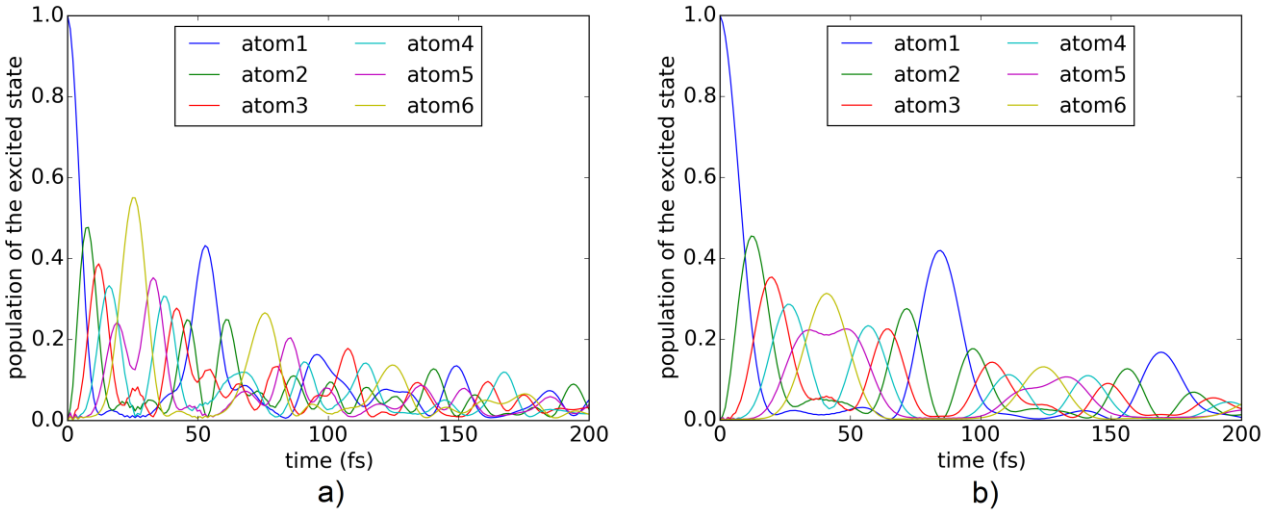

Fig. 5 *Energy transfer in a chain built up of six linearly coupled two-state atoms. The curves depict the population of the excited state of each atom over time. At the beginning of the simulations, the first atom was in the excited state, while all the other atoms were in the ground state. The site energies of the atoms were 1.08, 1.06, 1.04, 1.02, 1.00, and 0.98 eV, respectively; that is, they formed a decreasing sequence. The decay rate characterizing the irreversible energy transfer from the excited state of the atoms towards the environment was 0.01 fs^{-1}. The coupling strengths between the adjacent atoms were set to a) 0.1 or b) 0.06, which resulted in a faster (a) or a slower (b) energy transfer.*

(III) MODELING AND SIMULATION RELATED TO STIMULATED EMISSION MICROSCOPY [5]

We illustrate the modeling and simulation of a published measurement by developing a new QED model and comparing the measured data with simulations. The experiment demonstrated the principle of a new stimulated emission microscope which can perform label-free detection of non-fluorescent molecules forcing them to emit stimulated photons (“seeing in the dark”).

In the experiment a non-fluorescent bio-chromophore (crystal violet) molecule was subject (i) to a strong short laser pulse generating excitation by absorption. (ii) Then photon emission was stimulated by a second weak laser pulse, and the spectrum of relative excitation as a function of stimulating wavelength was measured.

We created a quantum-electrodynamic QED model and computationally feasible simulation program to understand the dynamics of stimulated emission microscopy.

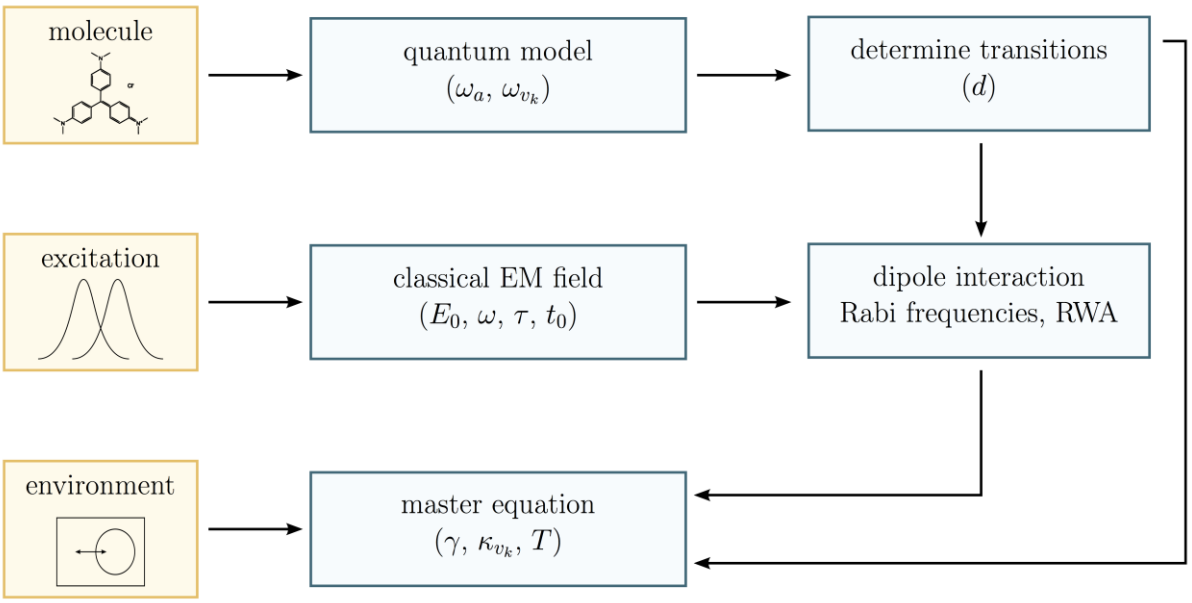

Fig. 6 *Block diagram of the main parts of model and the corresponding variables.*

Based on the new model we have performed simulations verifying the published experimental results. Entanglement between vibrational states turned to be significant. We could reproduce the experimental results of spectroscopic measurements by taking into account entanglement between two vibrational states. High correlation between calculated and measured data confirmed the validity of the proposed model.

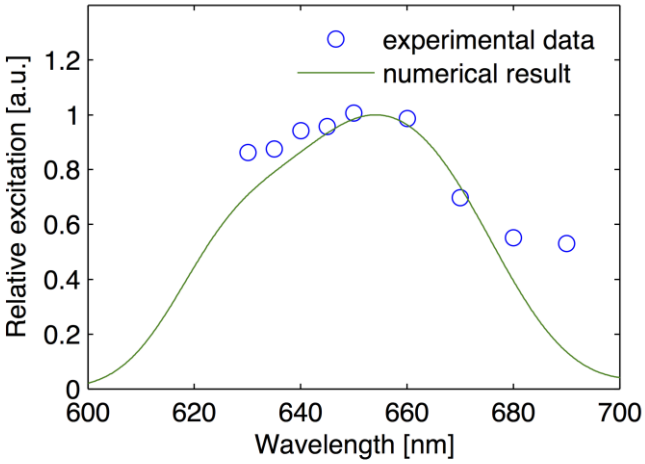

Fig. 7 *Numerical results of spectrum calculation shows the relative excitation as a function of wavelength in the simulation model compared to the experimental data presented by Min at al.*

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2. CELLULAR WAVE COMPUTING AND SPATIAL-TEMPORAL ALGORITHMS

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Graduate students: TAMÁS FÜLÖP, ATTILA STUBENDEK

The Cellular Wave Computing paradigm emerged as a new kind of computer, an algorithmically programmable spatial-temporal computer. Its spatial-temporal elementary instruction was the dynamics of a Cellular Nonlinear Neural Network (CNN) composed of simple nonlinear dynamic cells and local interaction patterns. These elementary instructions were combined algorithmically to form the CNN Universal Machine. Soon, a broader class of cell dynamics and local interaction patterns were introduced. A new kind of algorithmic thinking has developed and the first mixed-signal integrated circuit implementations appeared.

Right at the beginning of this new kind of computing principles, the neurobiological inspiration, in particular the retinal research and the visual pathway, was important. Actually, several cellular wave computing models had been developed following the new discoveries in retinal research.

The formal description of the algorithms on a Cellular Wave Computer had been defined as the alpha-recursive functions.

The arrival of commercially available cellular visual microprocessors (Eye-RIS of AnaFocus Ltd., Bi-i of Eutecus Inc., and Smart Photo Sensor of Toshiba Corp.) make this new computing paradigm a practical alternative for very low power, small form factor, and high computing power, high frame rate applications.

Nano-scale electronics technologies, both CMOS and beyond CMOS, provide the means to fabricate massively parallel systems with thousands or millions of processors/cores in a small package, as well as in low-power versions. Most of these architectures contain cellular or multi-cellular architectures where the precedence of geometric and logical locality is a must. The cells might vary both in function as well as in their modes of operation, including arithmetic or analog, logic, and symbolic cells, as well as integrated sensory elements. In the whole operation, the interplay between local dynamics and global dynamics plays an increasingly important role. The maturity of 3D integration technologies provides another mechanism for complexity and efficiency increase.

In addition to the architectural innovations and algorithmic mappings, the basic spatial-temporal dynamics in the Cellular Wave Computers are becoming more complex *leading to surprisingly new theoretical and practical results*, as well. This means that even the elementary spatial-temporal instructions of the CNN dynamics become more complex. In particular,

i) the spatial-temporal input will be dynamic even in a Cellular Automaton,

ii) one or more spatial-temporal waves defined by templates is used for a continuous

dynamic input without breaking it into discrete-time frames, and the qualitative differences of the spatial-temporal output will code the input features (frameless computing), and

iii) oscillatory cells are used in a global synchronization mode, where the elementary computational primitive is a spatial-temporal synchronization effect.

In addition to these theoretical challenges, practical challenges emerge:

i) the implementation of non-topographic problems (like particle filters),

ii) the sense and avoid problems in avoiding the collision of a UAV and a bigger airplane,

iii) the architectural solutions for beyond CMOS nano-electromagnetic technologies, e.g. informing associative memories, the specific use of nanomagnetic components and integrated systems (like Spintronic Oscillators and static nanomagnets).

REFERENCES AND A FULL RECENT OVERVIEW CAN BE FOUND IN

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3. VIRTUAL AND PHYSICAL MACHINES WITH MEGA-PROCESSOR CHIPS – THEORETICAL AND EXPERIMENTAL RESULTS

PÉTER SZOLGAY, Professor; ANDRÁS KISS, Assistant Professor; ZOLTÁN NAGY, Associate Professor, ISTVÁN REGULY, Assistant Professor
Graduate students: ENDRE LÁSZLÓ

Many core computers are the current approach to the solution of computationally intensive problems. At the present day, many core may mean 1000 but soon few 100000 or even more processing elements will be available on a desktop machine.

New ideas and new methods are required in algorithm development for these types of architectures. Using the cellular architecture of processors and memories new kind of parallel algorithms have to be developed. For the same Physical multi-cellular machine architecture different Virtual Machines can be defined, the latter is serving for algorithmic and software development. However, all virtual machines are to be uniquely mapped to a specific Physical Machine (a chip or chip set, etc.). Hence all computing element has a geometrical position on the Physical Machine and a geometric or topographic address on the Virtual Machine. In this new scenario of computer science and computer engineering computational complexity, computing power is a multi-parameter vector, any algorithm solving a problem will have a speed-power-area-bandwidth-accuracy metric. These parameters and this metric should be handled simultaneously and optimized.

Some new principles are summarized below.

First of all, we do not have efficient compilers though many examples are solved daily. In some of our problems we have used the CNN Universal Machine as an intermediate platform for compiling algorithms. Namely, we have developed an efficient CNN Universal Machine simulator on the FPGA or GPU and if an algorithm is described by as a cellular wave computing algorithm defined on a CNN Universal Machine, the compiling problem is solved.

We emphasize that due to the topographic nature of the Physical machine, an optimal *partitioning and placement is also needed* on the virtual machine, or on the intermediate "compiler prototype" (like the CNN Universal Machine). A Field Programmable Gate Array (FPGA) based framework has been described to accelerate simulation of a tough topographic problem, a nonlinear wave problem that is a complex physical spatio-temporal phenomenon, such as fluid dynamics (the hard test-problem since the invention of the digital computer). We have studied this problem since a while to develop a prototype virtual machine platform for them.

i) In the course of the design of an arithmetic unit which consists of locally controlled groups of floating point units both *partitioning and placement* aspects have to be considered. To solve this problem a framework has been elaborated in which the partitioning is based on an initial floor-plan of the vertices of the layered data-flow graph of the algorithm solving a given PDE or another problem. We have formulated this problem as a method for *implementing data-flow graphs on FPGAs*. The algorithm can minimize the number of cut nets and guarantee deadlock-free partitions.

ii) In case of topographic problems, *complicated geometries require unstructured spatial discretization, which results in irregular memory access patterns* severely limiting computing performance. *Data locality* is improved by mesh node renumbering technique, which results in predictable memory access pattern. Additionally, *storing a small window of node data in the on-chip memory* of the FPGA can increase data reuse and *decrease memory bandwidth requirements*.

iii) As one example, in numerical solution of fluid flows the generation of the floating-point data path and control structure of the arithmetic unit containing dozens of operators is a very challenging task when the goal is high operating frequency. Efficiency and use of the framework is described by a case study solving the Euler equations on an unstructured mesh using finite volume technique. On the currently available largest FPGA the generated architecture contains three processing elements working in parallel providing two orders on magnitude (90 times) speedup compared to a high performance microprocessor.

iv) Numerical algorithms can be implemented by using fixed –point or Floating point arithmetic with different precision. The selection of the *optimal data precision* to the different steps of an algorithm is *NP complete*. As an example, the solution of the advection equation was analyzed by using first and second order discretization methods. For this example if the resources are on an FPGA, and power dissipation or processing speed is prescribed, we have developed and algorithm for determining an optimal bit width.

v) A Fermi NVIDIA GPU based implementation of a CNN Universal Machine was also developed, and was analyzed and compared to a multicore, multithreaded CPU. The basic goal of this project is to get a clear picture about the capabilities and limits of GPUs.

vi) Key algorithms are the different Kalman filter implementations in trajectory estimation of the intruder airplane. To increase the speed of computation of unscented nonlinear Kalman filter was implemented on Xilinx Spartan 6 LX45 FPGA. The speed of this implementation is approximately 1000 iteration /s. It would be important if we want to follow multiple targets.

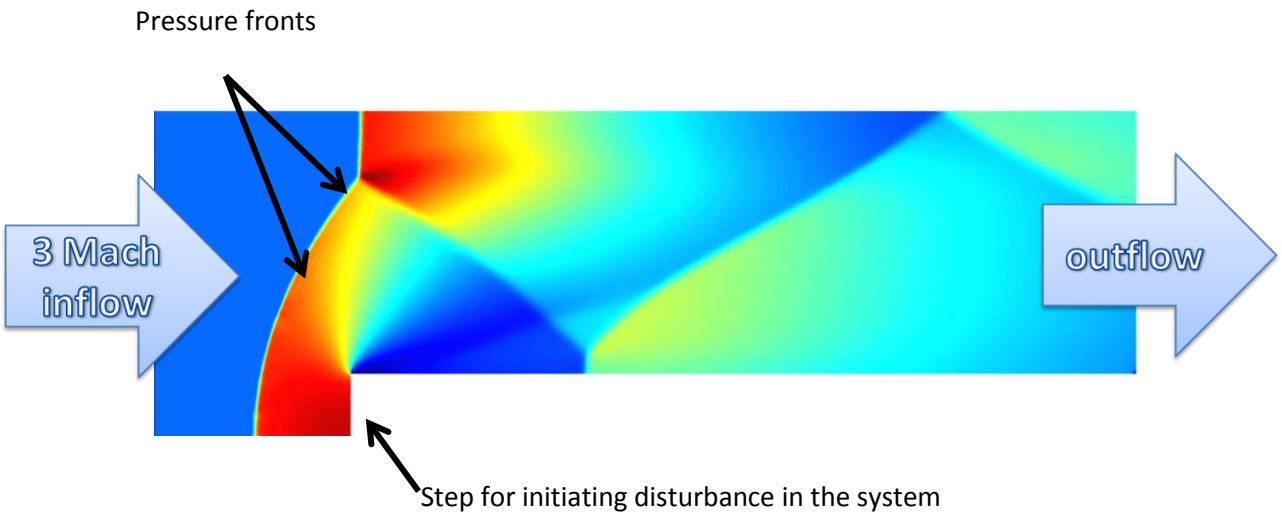

Fig. 1 *A two dimensional flow analysis was implemented on different array computing architectures*

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4. NATURAL LANGUAGE PROCESSING

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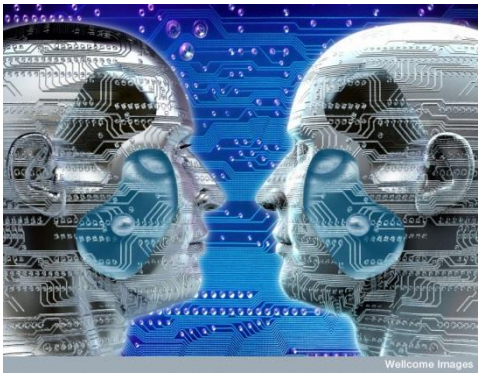
PhD Students: ISTVÁN ENDRÉDY, BALÁZS INDIG, GYŐZŐ ZIJIAN YANG



SHORT DESCRIPTION OF THE ACTIVITIES

The Natural Language Processing Group consists of faculty researchers, post-graduate researchers, PhD students, undergraduate students and programmers who work together developing algorithms that enable computers to process and understand human languages. Our research interest covers:

- corpus linguistic applications
- statistical machine translation
- syntactic parsing
- medical text mining
- morphologies
- spelling correction
- part-of-speech tagging

One of the most ambitious aims of the research group is to develop new methods and algorithms for syntactic parsing of the Hungarian language. Such a method must handle grammatically possible, but not correct analyses. That is why to deal with problems efficiently, *parallelism* is necessary. In practice for a human understanding is cooperatively done by several parts of the brain. To incorporate this knowledge the consideration of current state of the neurolinguistics and psycholinguistics is indispensable. The model that is to be researched is characterized by *performance*, while the state-of-the-art research results are considered from various field of applied linguistics. Since the current state of research does not provide any deeper understanding of how the ambiguous phrases are understood, in our project we incorporate parallel corpora to handle these—not necessarily multilingual—problems. With this, *new aspects of corpus linguistic* research are being revealed. The developed new methods are adapted to many aspects of Hungarian language. For using it for medical text processing tasks, we expect growing performance and precision. The developed algorithms are also planned to be adapted to other agglutinating languages and are expected to behave similarly well.

SELECTED PUBLICATIONS

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5. DISCOVERY RESEARCH IN NEUROBIOLOGY

Department of Neuroscience, adjunct location at the Institute of Experimental Medicine of the Hungarian Academy of Sciences
TAMÁS FREUND, Professor, head of department (cellular and network neurobiology); ZSOLT LIPOSITS, Professor (endocrine neurobiology); IMRE KALLÓ, Associate Professor; SZABOLCS KÁLI, Associate Professor; BARBARA VIDA, Assistant Professor
Graduate students: ERZSÉBET FARKAS, ATTILA JÁDY

RESEARCH ACTIVITY

Cellular and Network Neurobiology Group

Research in the group aims to identify the cellular and network mechanisms of the generation of characteristic cortical (mainly hippocampal) activity patterns using *in vitro* electrophysiology and computer simulations.

1. A hippocampal slice preparation, which exhibits spontaneous repetitive sharp waves under control conditions, and which can be induced to generate gamma oscillations by the application of cholinergic drugs, has been developed. In parallel, a large-scale network model of the CA3 area based on experimentally determined cellular and network parameters has been constructed, which consists of interacting pyramidal cell and interneuron populations, and exhibits repetitive sharp waves (including accompanying high-frequency ripple oscillations) very similar to their experimental counterparts. (Figure 1) (*Káli et al., 2012*). The model also made explicit predictions concerning the mechanisms which contribute to the generation of sharp waves: it suggested that the initiation of sharp waves relies on random fluctuations of population activity, while the termination of sharp waves probably requires some novel form of slow negative feedback.

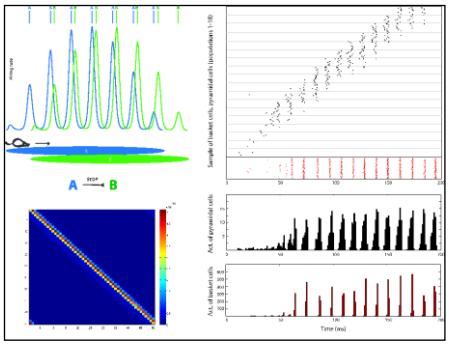

Fig. 1 *(top left) activity during exploration of two CA3 pyramidal cells with overlapping place fields, showing theta phase precession; (bottom left) matrix of synaptic weights between pre- and postsynaptic populations, ordered by place field location, which formed during exploration as a result of spike-timing-dependent plasticity; (right) spontaneous replay of learned sequences of activity during sharp-wave-associated ripple oscillation.*

2. The effects of neuronal morphology and voltage-gated conductances on the frequency-dependent impedance of neurons are also investigated.

Endocrine Neurobiology Group

A major long-term goal of the group is the elucidation of neuronal and hormonal mechanisms acting centrally in the neuroendocrine control of reproduction. One particular focus is on central actions of estrogen on estrogen-receptive neuronal systems throughout the brain. Further, hormonal and afferent neuronal control of gonadotropin-releasing hormone (GnRH) neurons is studied, with special regard to negative and positive estrogen feedback to these cells which underlies reproductive cyclicity in the female. In addition to rodents,

neuronal networks innervating human GnRH neurons are also in the scope of studies using post-mortem human brain samples. The impact of diminishing estradiol signaling on diverse brain functions during menopause is also under exploration in rodent models of menopause by means of gene expression profiling. This translational research supports drug discovery targeting the safe and novel way of hormone replacement therapy for menopausal women.

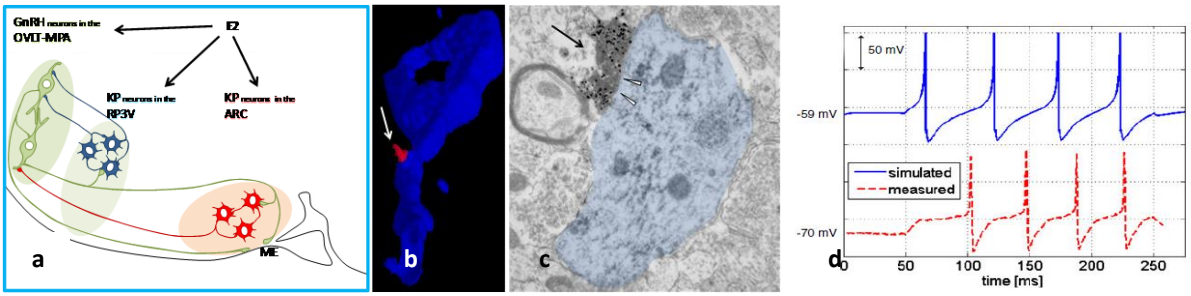

Fig. 2 *Interaction of key neuronal elements of the hypothalamic regulatory center for reproduction. (a) Network model of kisspeptin (KP) and gonadotropin-releasing hormone (GnRH) neurons. Traditional synaptic (b,c), as well as, non-synaptic mechanisms (direct hormonal, volume and retrograde transmission) act within the network, which ultimately determine the firing (d) and secretory activity of the GnRH neurons.*

Another line of discovery research is dedicated to obtain integrated knowledge from structural, functional and molecular aspects of the complex hypothalamic mechanisms that regulate stress, adaptation and metabolism. A special emphasis is placed on the neuronal circuitry involved in the central regulation of the hypothalamic-pituitary-adrenal and thyroid axes, and the crucial role of type-2 deiodinase in thyroid hormone actions in the brain. These studies use cutting-edge light and electron microscopic techniques, a wide repertoire of molecular biological techniques and slice electrophysiology. The translational value of these efforts is manifested in the better understanding of the role of the brain in development of obesity and addiction, and the dissection of molecular mechanisms of thyroid hormone actions.

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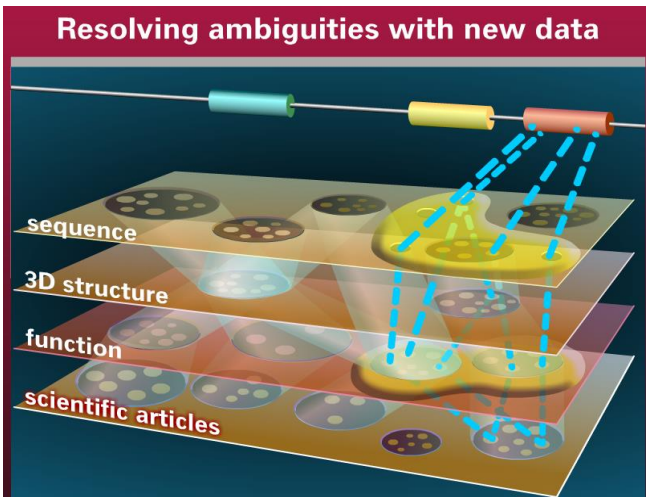
6. BIOINFORMATICS LABORATORY

SÁNDOR PONGOR, Professor
Graduate students: BALÁZS LIGETI, JÁNOS JUHÁSZ, JÓZSEF HEGEDŰS, DÁNIEL VARGA

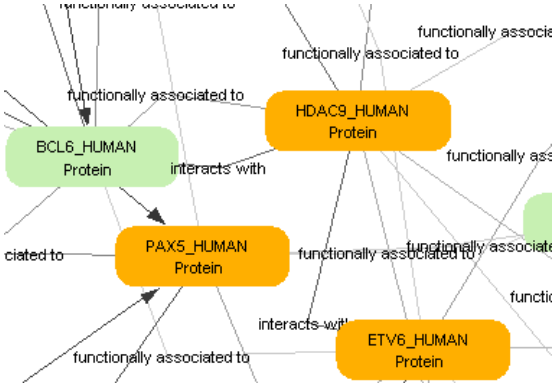
While traditional bioinformatics has evolved from simple data management to data-interpretation, the emphasis today has shifted to high-throughput data collection, personal medicine and the analysis of complex systems. This tendency is accompanied by an unprecedented development of new computer architectures and cloud computing that bring the power of supercomputers within arm's reach of bench scientists and clinical practitioners.

BIOINFORMATICS OF NEXT GENERATION SEQUENCING DATA



Interpretation of next generation sequencing data is a highly challenging task, because extracting information useful for medical researchers and practitioners requires advanced data mining methods, simultaneously applied to high throughput data linked to a continuously updated network of molecular databases and medical publications. In this fast evolving scene of new technologies, integrating heterogeneous data is perhaps one of the most challenging tasks. Our current interest includes development of marker databases, new algorithms for analyzing metagenomics data, including medical hypothesis generation and prediction of useful drug combinations. . In this project we are concerned with developing new, hardware-accelerated pipelines for these purposes, making use of the in house knowledge of new computer architectures such as FPGA and GPU, which allow us to increase computer power by orders of magnitude. We are also collaborating with the Technical University of Graz where one of the strongest FPGA-based bioinformatics infrastructure of Central Europe is being built.

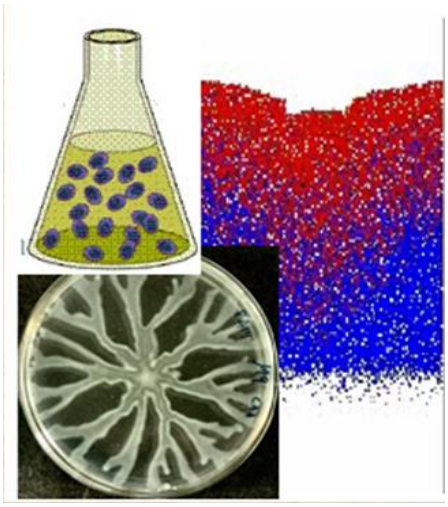
HIGH THROUGHPUT DATA/MINING OF PROTEOMICS DATA



High throughput mass spectrometry analysis produces large amounts of noisy data that have to be filtered and preprocessed with computational tools before subjected to detailed analysis and interpretation. Our strategy uses principles borrowed from cognitive psychology for identifying network patterns in mass spectra. Namely, the human mind is able to capture holistic features in complex sensory inputs, and we trust that similar principles can be applied to abstract data structures. The bioinformatics support of proteomics research is a central theme in our projects. We develop new tools capable of filtering and processing large data streams characteristic of high throughput analysis workflows.

MICROBIOME BIOINFORMATICS: BACTERIAL COMMUNICATION NETWORKS

Microbial communities play fundamental roles in health and disease as well as the stability of the ecosystem. A better understanding of these systems may provide insights into the mechanisms of infections, epidemics as well as environmental and social processes. Our group uses bioinformatics tools as well as agent based models to understand how signals contribute to colonization and infection. We showed that signal sharing allows several bacterial species to cross barriers that the single species can not which may provide important clues to polymicrobial diseases.



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Prof. Ines Mandic-Mulec, University of Ljubljana, Ljubljana, Slovenia

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Prof. Christoph Sensen, Graz University of Technology, Graz, Austria

Prof. Vittorio Venturi, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

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7. STRUCTURAL BIOINFORMATICS & PROTEOMICS

ZOLTÁN GÁSPÁRI, Associate Professor; ANNAMÁRIA F. ÁNGYÁN, Postdoctoral researcher
Graduate students: DÁNIEL DUDOLA, ANNAMÁRIA KISS-TÓTH, ANETT KORAI, BERTALAN KOVÁCS

The two main projects in the laboratory are

i. Generation and analysis of dynamic protein conformational ensembles

ii. Experimental investigations of selected proteins of the postsynaptic density

Proteins are the most versatile biomolecules responsible for a number of tasks on living organisms. Their efficiency is conventionally attributed to their geometric and physicochemical complementarity with their partners that can be e.g. other proteins, nucleic acids or small molecules like drugs. However, proteins are not static entities but display dynamics on time scales spanning 14 orders of magnitude. In the last decade, the exact mode of action is linked to internal dynamics and its changes for an increasing number of proteins. In spite of this, atomic-level descriptions of experimentally determined internal protein motions are not routinely generated and used for explaining biological phenomena. Our aim is to use and further develop an approach that synergistically puts together conventional molecular dynamics calculations and restraints determined with experimental techniques, primarily NMR spectroscopy. The calculations result in an ensemble of conformations that reflect the internal dynamics of the molecule on a given time scale and are in agreement with experiments. Such ensembles can be used to investigate the role of dynamics in partner molecule binding, catalysis and regulation and are expected to lead to a deeper understanding of the nature of intra- and intermolecular interactions. Molecules studied at the moment include the antifungal protein PAF with potential therapeutic value, a DNA polymerase involved in DNA repair the small prolyl isomerase parvulin and selected domains of proteins of the postsynaptic density.

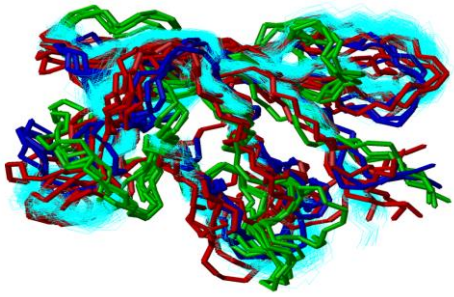

Fig. 1 *Structural ensembles of different conformational states of the antifungal protein PAF. Cyan: native-state observable ensemble representing ps-ns timescale dynamics, blue: conformers characteristic at 265 K, red: conformers characteristic at 344 K, green: normally "invisible" conformers in exchange with the observable state at 273 K*

In 2015 we have completed the setup of a novel biotechnology laboratory where we aim to initiate experimental investigation of selected proteins of the postsynaptic density. We are particularly interested in the detailed organization of the interaction network between these proteins.

Fig. 2 *Views of the interior of the recently equipeed biotechnology laboratory at PPCU FIT.*

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8. ANALYSIS AND CONTROL OF DYNAMICAL SYSTEMS

GÁBOR SZEDERKÉNYI, Professor; DÁVID CSERCSIK, Assistant Professor
Graduate students: ZOLTÁN A. TUZA, BERNADETT ÁCS, PÉTER POLCZ

SCIENTIFIC BACKGROUND: THE SYSTEM THEORETIC POINT OF VIEW

Although models are "really nothing more than an imitation of reality", their widespread utilization not only in research and development but also in the everyday life of developed societies is clearly indispensable. Due to the complexity of system components and their possible interactions, without building, analyzing and simulating appropriate models, we could not predict the outcome of common events, not to mention the operation of involved technological or living systems. When we are interested in the evolution of certain quantities usually in time and/or space, we use dynamic models. The deep understanding and the targeted manipulation of such models' behaviour are in the focus of *systems and control theory* that provides a common framework for handling dynamical models from different application fields and thus supports to form an interdisciplinary viewpoint on electrical, mechanical, thermodynamical or biological systems.

RESEARCH TOPICS

Computational analysis and synthesis of quantitative biological models

The key importance of dynamics in the explanation of complex phenomena occurring in living systems is now a commonly accepted view. Besides the sufficient maturity of systems and control theory, the accumulation of biological knowledge mainly in the form of reliable models and the recent fast development in computer and computing sciences converged to the birth of a new discipline called systems biology, which can hopefully address important challenges in the field of life sciences in the near future. For modeling biological processes, we primarily use two related canonical nonnegative system classes that have clear biological relevance, good dynamical descriptive power, and a computationally advantageous algebraic structure: the quasi-polynomial system class and the kinetic system class coming originally from biochemistry.

The structural non-uniqueness of biochemical reaction network models is an intensively studied area with applications in the structural and parametric identification (inference) of biological networks. We have been developing optimization-based computational procedures for the determination of network structures that are dynamically equivalent or similar to a given initial kinetic system [1]. The existence or non-existence of reversible, weakly reversible, complex, detailed balanced or deficiency zero structures has important consequences regarding the qualitative dynamical properties of the modeled network [2, 3, 4]. Moreover, the developed optimization framework is suitable for the algorithmic building of chemical network structures corresponding to a given dynamics.This framework has been extended for the treatment of rational kinetic systems in [11].

Our other important research topic is the modeling and parameter estimation of biological systems based on real measurement data. We have given an effective method for the parameter estimation of a human blood-glucose dynamics model [7]. The mathematical model of a cell-free transcription/translation process suitable for identification was developed and analyzed in [5].

Nonlinear control

The main question in our work related to the design of controllers for nonlinear systems is how the physical/chemical properties of these models can be used for effective control. In [6] we propose a hierarchically structured model for process systems that gives rise to a distributed controller structure that is in agreement with the traditional hierarchical process control system structure where local controllers are used for mass inventory control and coordinating controllers are used for optimizing the system dynamics. In [8] we give a computational solution for obtaining a closed loop nonlinear polynomial system that corresponds to a weakly reversible deficiency zero network and thus satisfies robust stability properties.

PUBLICATIONS

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9. ELECTROPHYSIOLOGY – INVASIVE AND NON-INVASIVE BIONIC INTERFACES

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Graduate students: EMÍLIA TÓTH, KATHARINA HOFER, BÁLINT PÉTER KEREKES, ÁGNES KANDRÁCS, MILÁN SZEKERKA, PATRÍCIA BEREGSZÁSZI, GERGELY CSÁNY, TAMÁS ZÖLDY, RICHÁRD FIATH, DOMOKOS HORVÁTH, GERGELY MÁRTON, BÁLINT FILE, ZOLTÁN KÁRÁSZ ZALÁN RAJNA, DOMOKOS MESZÉNA, KINGA KOCSIS, EDIT GYŐRI, TAMÁS MOLNÁR, TIBOR NÁNÁSI, ZSUZSANNA KŐVÁRI, CSILLA SZABÓ, VIRÁG BOKODI, BARBARA FRANCZ

The Electrophysiology Laboratory was established by the University as a research and education facility, located in the Jedlik building. The Laboratory heavily collaborates with the Institute of Cognitive Neuroscience and Psychology, Institute of Technical Physics and Materials Science (RCNS HAS), Institute of Experimental Medicine (HAS) and the National Institute of Neurosciences. The Laboratory integrates several disciplines including electrophysiology, materials science, chip- and micro electromechanical systems (MEMS) research, computational research, neurology research and optical imaging research in order to investigate the physiological and pathological functions of the central nervous system.

Two rooms are assigned to the Laboratory one for conducting experiments and the other for data processing. In the experimental room there are two computers capable of acquiring and analyzing bioelectrical signals, a stereo-microscope and stereotaxic device essential for animal experiments and several supplementary tools (oscilloscope, amplifiers, sterilization tools, electrical and mechanical stimulators and animal keeping chamber). In the data processing room there are three computers with software necessary to analyze the large volume of data generated in the experimental room.

The Laboratory is involved in bionic probe research by designing and validation of various probe structures realized by the partners. These probes are usually brain implantable devices, which can detect electrical activity of cortical and sub-cortical structures in animals. We are also providing histology studies to verify the biocompatibility of the devices developed. Besides Hungarian partners, the Laboratory is also involved in probe design and testing at IMEC (Belgium) and IMTEK (Germany) in the scope of an EU FP7 project. We also take leading role in the research and development of active probes used in the study of of multi-scale interactions in the thalamo-cortical system in animal models.

The Laboratory is also involved in the investigation of the cortical generators of event related potentials, spontaneous and epileptic activity in animal models and in humans. A number of collaborative research projects are running on the field of in vivo and in vitro electrophysiology and optical imaging in epileptic and tumor patients and in animal models. In particular, one of our current main research interests is the functional characterization of the thalamo-cortical neural networks responsible for the sensory information processing.

Recently, in collaboration with our partners we investigated the cortical sources of slow sleep oscillations in humans. We described several unique characteristics of neocortical neural networks during depolarized and hyperpolarized phases of the sleep slow oscillation. Our results showed that in the generation of slow oscillation the superficial cortical layers played a leading role, in contrast to animal models, where the deep layers were more involved. In addition, we have shown that human cortical neurons fire substantially less than neural cells

of animals and this firing pattern may have an important role in memory consolidation during sleep.

We have also characterized the function of cortical neural networks in animal models during the sleep-wake cycle concentrating on the cortical acoustic information processing. We have found that acoustic stimuli can induce either depolarized or hyperpolarized state transition of cortical slow oscillation during deep sleep, which may be instrumental in triggering both arousal and sleep preservation mechanisms.

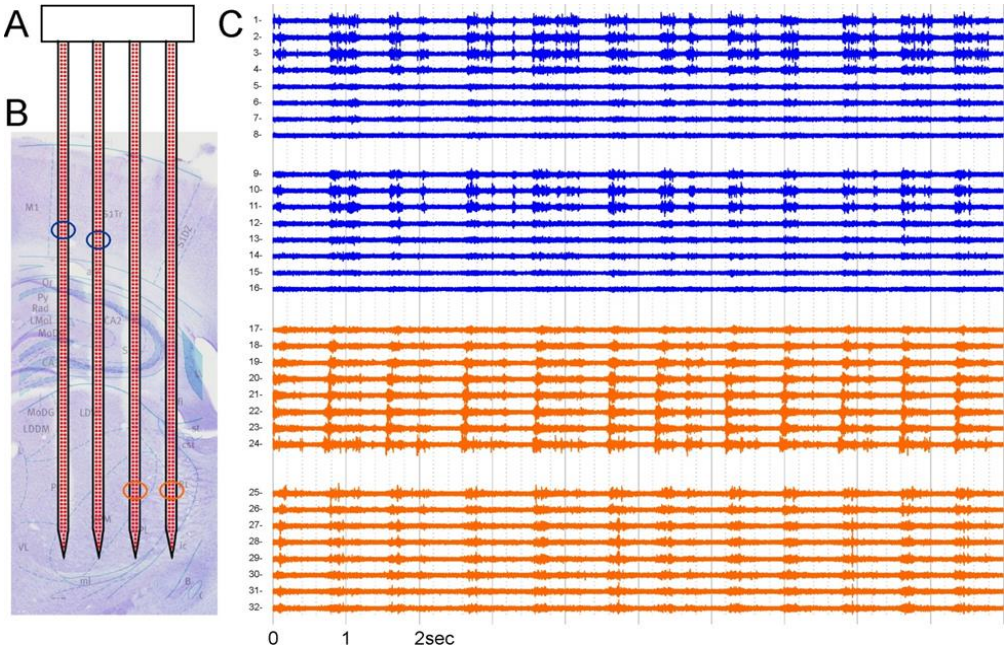

Fig. 1 ***A:*** *Schematic picture of the electronic depth control probe developed in an EU FP6 collaboration. The innovative feature of the probe is the electronically addressable recording site selection that allows the experimenter to change registration areas without physically moving the probe in the brain. The lack of movement is beneficial in the preservation of neural activity.* ***B:*** *The anatomy of the thalamo-cortical system with schematic drawing and actual histology.* ***C:*** *Action potential activity during anesthesia with slow waves. Cortical action potential activity is marked in blue, thalamic action potential activity is marked in red.*

Since 2014 the Laboratory is involved in the Hungarian Brain Research Program, with the Institute of Cognitive Neuroscience and Psychology, Institute of Technical Physics and Materials Science (RCNS HAS), Institute of Experimental Medicine (HAS) and the National Institute of Neurosciences.

In this program the Laboratory is involved in the designing and testing of foil based electrodes fitting on the brain surface, useable in Elecrtocorticography studies, and with electrodes implanted in the brain tissue the activities of the neurons near the electrodes are recordable. The fusion of the two technique gives a new insight to the connection of the signals detected on the brain surface, and the laminar recordings. These MEMS based electrodes were tested with electrochemical impedance spectroscopy in vitro and in vivo, and their biocompatibility is also promising.

The Laboratory is involved in the development of MR compatible and /or multichannel

amplifiers useable in human or animal studies. Two photon imaging, and analysis methods are developed, for human and animal studies, of the evoked rhythmic population activity. The fusion of the electrophysiologycal and optical imaging in vitro and in vivo is under development in the Laboratory. The cortical and hippocampal, epileptic and physiological population activities are under investigation in human and animal model. There are brain computer interface studies for registratory, and intervening EEG, EOG, EMG and eye movement following algorhythms.

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10. MULTI-PHOTON MICROSCOPY

BALÁZS RÓZSA, Professor; BALÁZS CHIOVINI, Head of the laboratory; DÉNES PÁLFI PhD, GÁBOR JUHÁSZ PhD, MIKLÓS MADARÁSZ labmembers; GERGELY KATONA PhD, Supervisor

IN VITRO 2D TWO-PHOTON MEASUREMENT OF NETWORK ACTIVITY (PPKE)

Sharp wave-ripples (SPW-R) activity is involved in the process of memory consolidation. We investigate spontaneous single cell neuronal activities during SPW-R in the hippocampus CA3 region under *in vitro* conditions. Fast spiking (FS), PV+ basket cells (BCs) as the clockworks for neuronal oscillations are important elements of hippocampal neuronal networks. Thus, we focus on PV+ interneurons to reveal the dendritic calcium dynamics during SPW-R. Recently we have extended our interest of these measurements with the principal, pyramidal neurons to the better understand of the spontaneous neuronal network activity.

To achieve this, we combine two-photon microscopy, local field electrophysiology, single cell electrophysiology, and dendritic patch clamp recordings. To measure the pharmacological background of calcium dynamics in single cell dendrites, we use focal synaptic stimulation and two-photon uncaging of novel, own developed glutamate and GABA caged compounds.

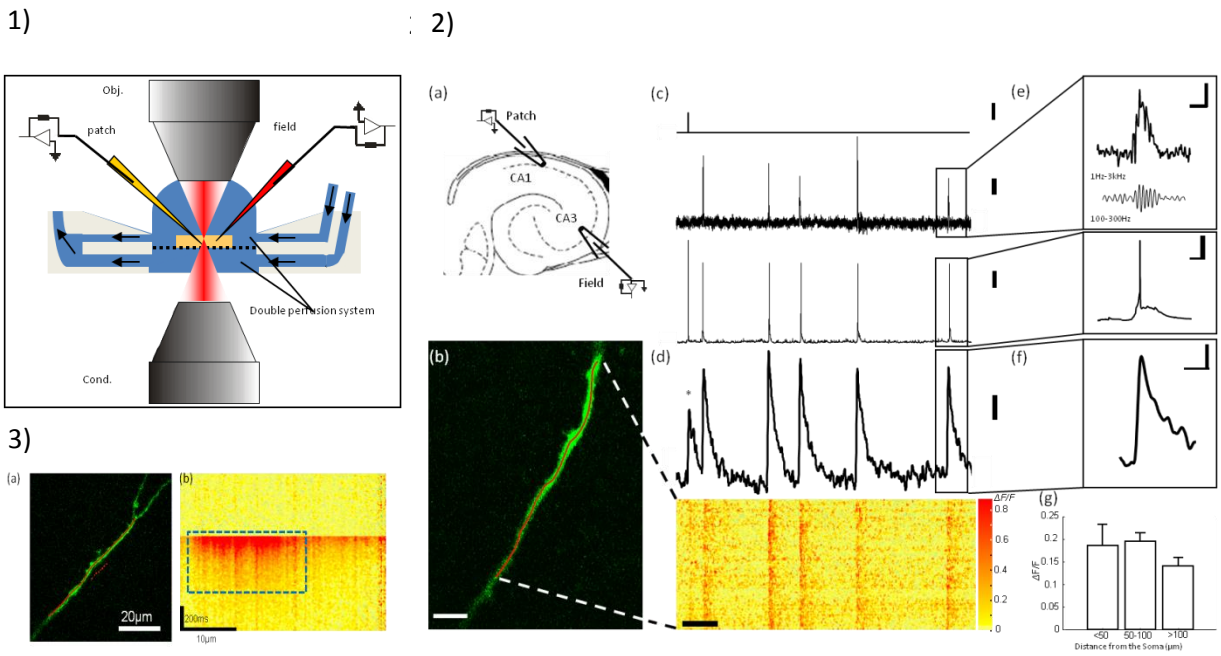


Fig. 1 ***1)*** *Experimental arrangement to generate spontaneous network activity in in vitro conditions.* ***2)*** *Simultaneous two-photon calcium imaging, whole cell patch clamp recording and local field potential recording in in vitro measurement.* ***3)*** *Two-photon uncaging and calcium imaging. (Chiovini B et al. 2010 Neurochem Res.)*

IN VIVO 3D TWO-PHOTON MEASUREMENT OF NETWORK ACTIVITY

To understand the fast computational mechanisms of the brain, one needs to be able to perform rapid measurements at several sites along a single neuron as well as to image large populations of neurons. Traditional two-dimensional measurements are severely limited for such kinds of endeavors since neurons are located in three dimensions. To overcome this problem, we have developed new solutions to perform three-dimensional functional imaging with large scanning ranges along the z direction. With our three-dimensional microscopes we are able to maintain random access point scanning with a short pixel dwell time. The speed and scanning volume of our technique in combination with the ~ 800 μm penetration dept of two-photon technology makes our methodology very convenient for *in vivo* measurements of neuronal populations, too.

Populational activity has long been studied in the visual cortex. We conduct *in vivo* two-photon imaging of the V1 area after using multicell bolus loading of a calcium indicator dye. Neuronal network responses are followed after visual stimulation using a moving bar or moving grating protocol. In addition, active cells are selected based on the previously recorded somatic activity and their dendritic responses are followed along with the network activity in three dimensions by using whole-cell patch clamp techniques.

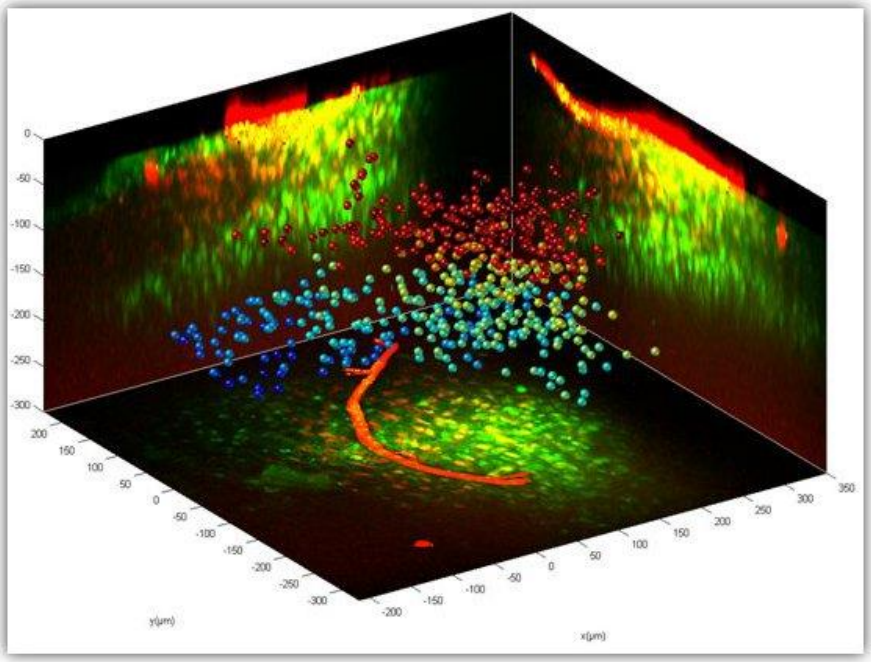


Fig. 2 *Projection of the 3D volume with multicell bolus loading of a calcium indicator dye. Points represents 251 simultaneously measured cells.*

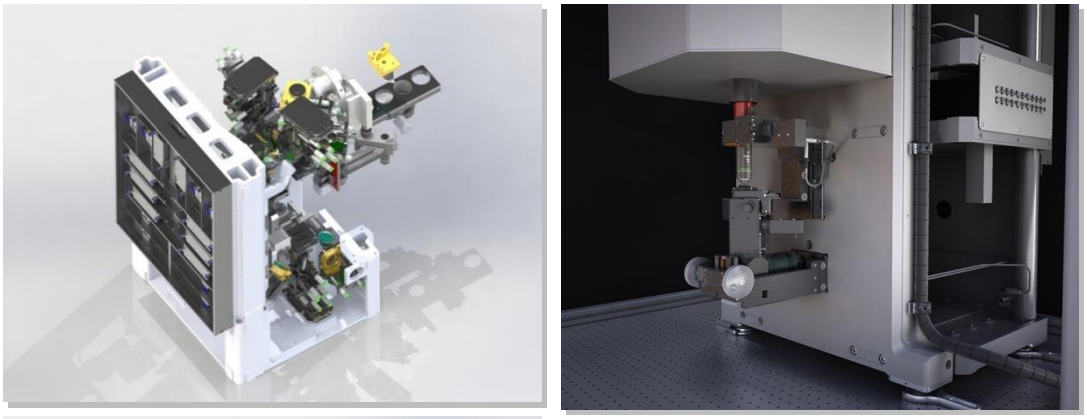
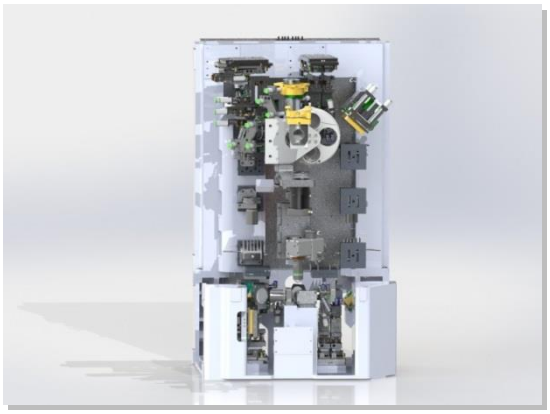


Fig. 3 *The plan of the new 3D microscope will be developed for the simultaneous measurement and photo-stimulation of multiple brain areas*



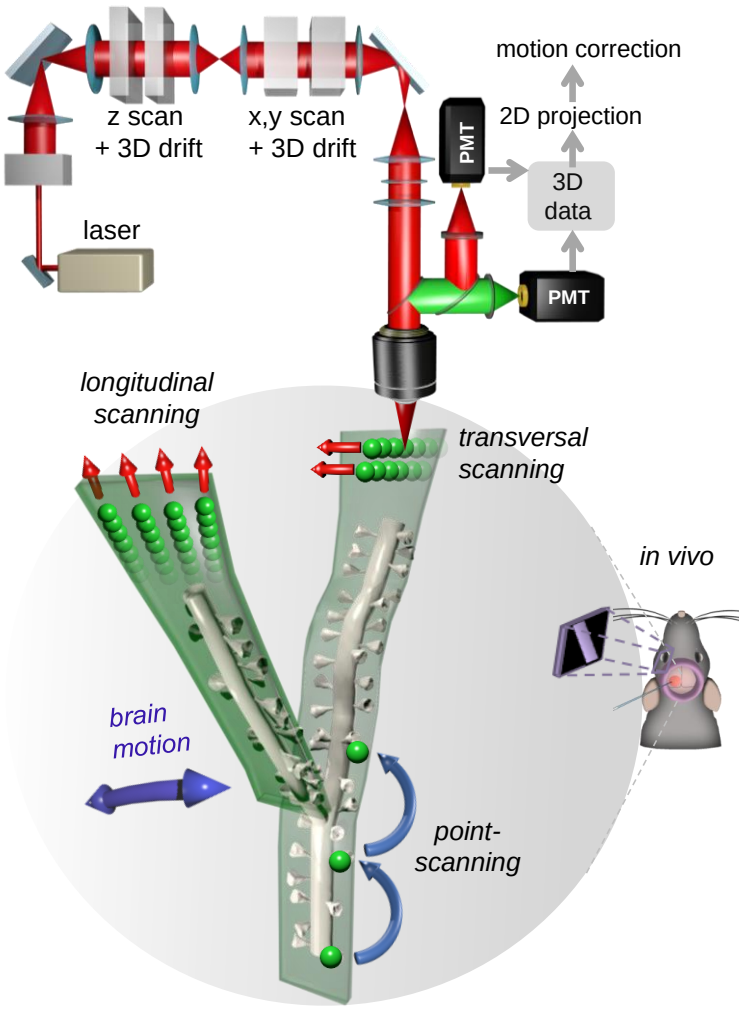


Fig. 4 *New microscope technologies were developed for the 3D measurements of the moving brain of behaving animals.*

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11. PROGRAMMABLE OPTICS

SZABOLCS TŐKÉS, Associate Professor; MIKLÓS GYÖNGY, Associate Professor; KRISTÓF IVÁN, Associate Professor
Graduate students: ANDRÁS JÁNOSSY

We are working in several aspects of programmable optics combining different imaging modalities: Computational Optics, Optoacoustical Imaging, Digital Holographic Microscopy

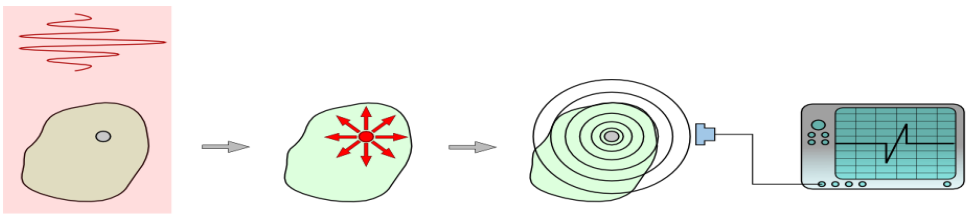
i. Our recent field of research is Photo- (or Opto-) Acoustical Microscopy Its main advantage is that deep living tissues can be imaged for clinical diagnostic purposes. However, it usually requires multispectral optical exciting. Moreover surgeons can look under the surface before cutting into the tissue.

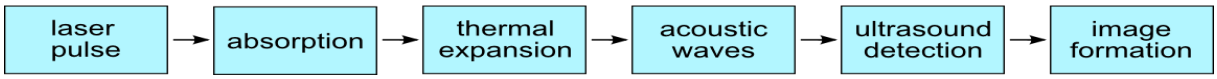
ii. Our traditional and renewable field is building equipment to digitally capture complex wave-fields, which are holograms and reconstruct the wave-field and 3D objects by wave propagating algorithms. We use highly parallel GPUs to produce real-time 3D reconstructions. Its main applications are in biological digital holographic microscopy (DHM), especially in microfluidics. It is promising that infrared DHMs can look deeply inside human tissues.

iii. Different optical, opto-acoustical, acoustical imaging modalities will be combined simultaneously to get deep tissue information that was not possible before.

iv. It is possible to combine multiphoton microscopy with photoacoustic microscopy.

How we generate and capture optoacoustic signals:





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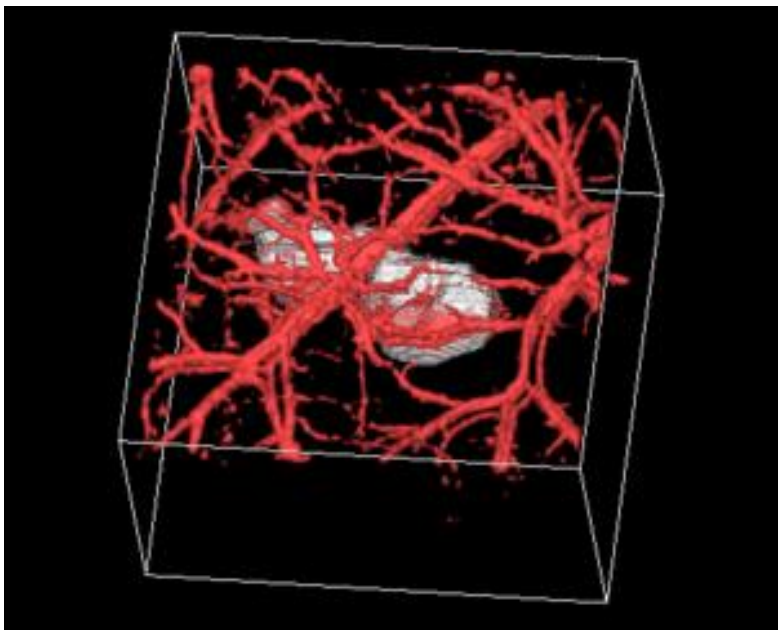

Fig. 1 *Photoacoustic imaging of vasculature around tumor tissue (Lihong V. Wang)*

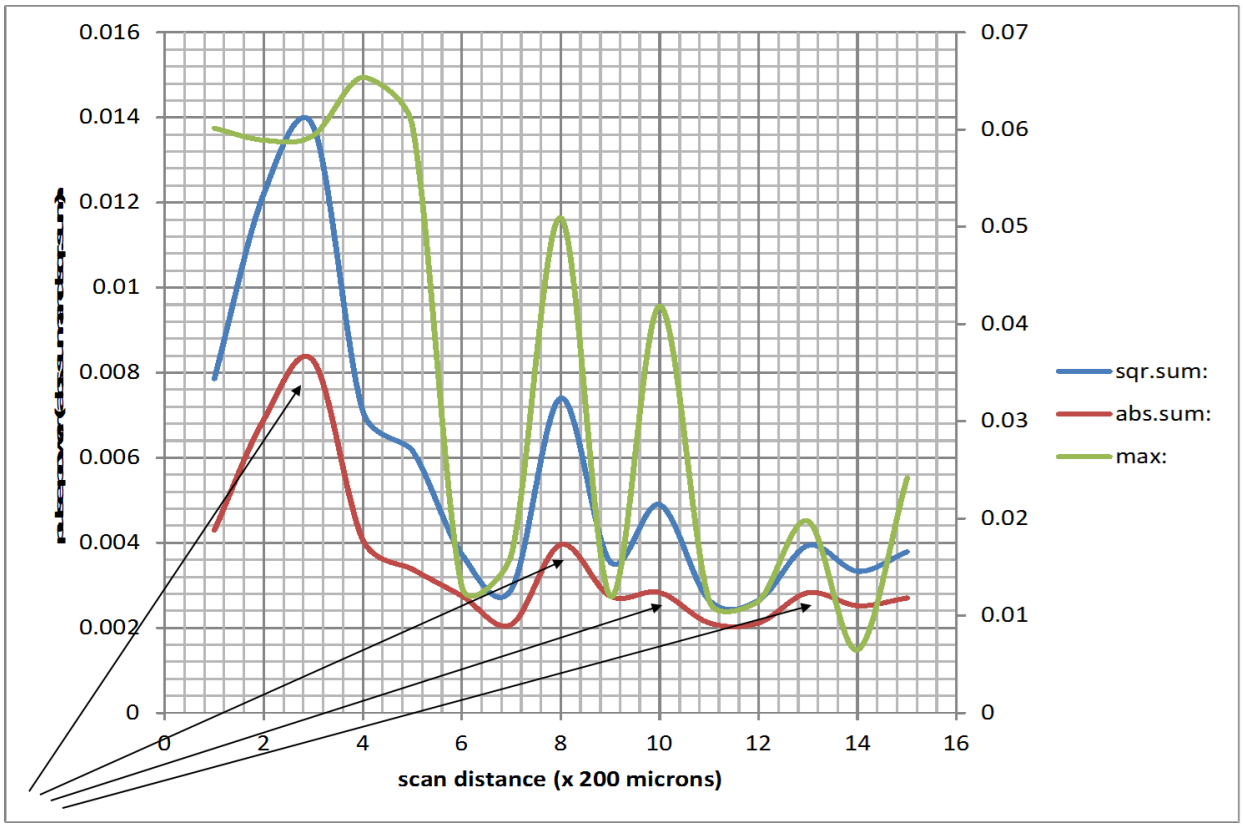

Fig. 2 *Photoacoustic imaging of vasculature of mouse muscle (our result)*

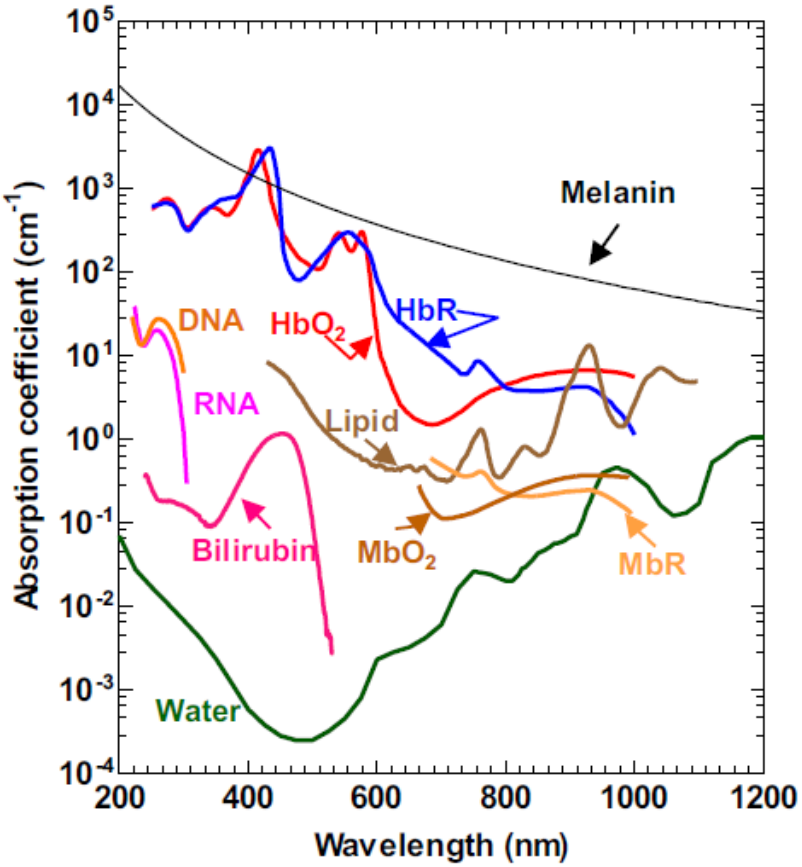

Fig. 3 *Absorption coefficient of different endogen tissue elements*

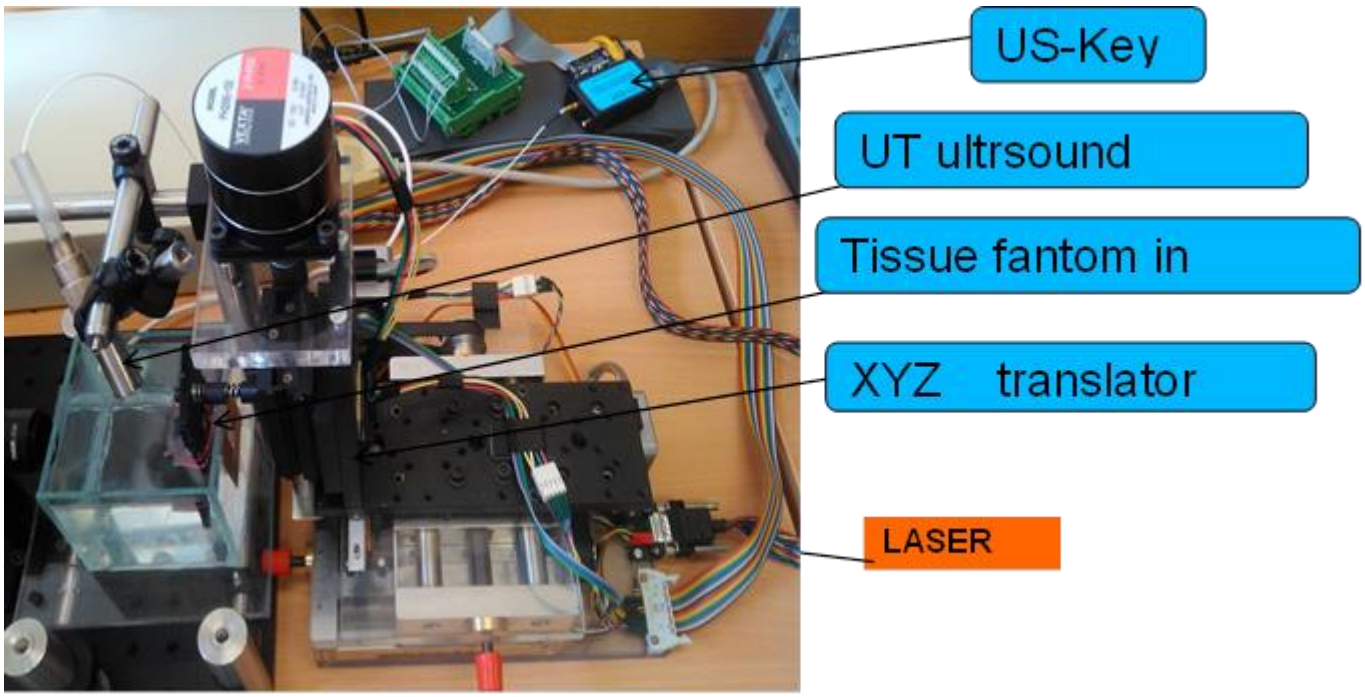

Fig. 4 *Our photacoustic setup*

12. MOVEMENT REHABILITATION

JÓZSEF LACZKÓ, Associate Professor; PÉTER SZOLGAY, Professor; RÓBERT TIBOLD, Assistant Professor; BENCE BORBÉLY, ÁDÁM VÁLY
Graduate students: LILLA BOTZHEIM

MEDICAL REHABILITATION ACTIVITY OF THE LABORATORY

Research in the Movement Rehabilitation Laboratory deals with the questions how the nervous system interacts with parts of the body and the environment to produce well coordinated movements like cyclic limb movements or reaching movements as reaching and transporting and object held in the hand. How external forces, resistances, practice, learning or fatigue does effect movement execution? How the central nervous system chooses particular solutions for a motor task that has theoretically an infinity of different solutions. Based on measured movements, we aim to reveal the contributions of muscle properties, limb geometry and neural activation in the control of limb movements.

Applying an ultrasound based movement analyzing system (ZEBRIS, Ivry, Germany) we record kinematic parameters of human movements. We place ultrasound emitting markers on anatomical landmarks of the body and record their position as function of time during human movements. Simultaneously we record muscle activities applying surface electromyograms (EMG) and we study muscle synergies.

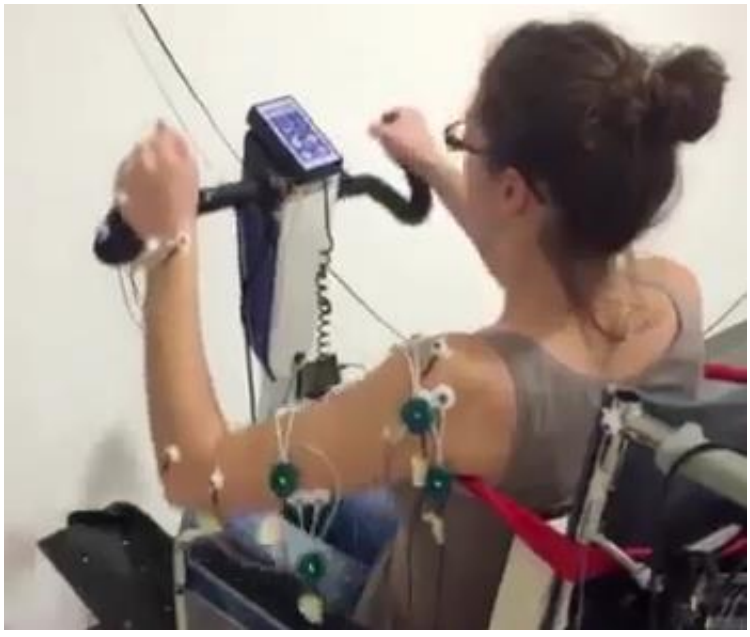

Fig. 1 *Cycling arm movements of an able bodied participant while muscle activities (EMG) and kinematic variables are measured.*

We measure and analyze multi-joint movements in able-bodied individuals and our aim is to apply our research in medical rehabilitation for people with movement disorders.

The goal of our research in the laboratory is to use biomedical engineering methods and biomechanics to investigate and understand how humans use and control their movements. The main motivation is to improve abilities (e.g. limb movements) of people who partly lost their motor and sensory functions. Beside basic research our aim is to reactivate paralyzed

muscles and to restore lost motor functions for people who suffered accidents or neurological disorders as stroke, spinal cord jury or other neural based movement dysfunctions.

Based on measured and averaged kinematic parameters and muscle activities (Electromyograms) of able bodied people we define muscle activity patterns that can be applied for controlling functional electrical muscle stimulation (FES) for people with paralysed limbs. FES is a technique to generate muscle activities by transferring electrical signals to muscles via electrodes to evoke limb movements. In cooperation with the National Institute for Medical Rehabilitation and the the University of Physical Education we trained 26 spinal cord injured patients whose lower limbs were paralyzed to perform lower limb cycling movements on a recumbent bike (ergometer) using their own muscles. Otherwise these people would not be able to generate active muscle forces.

A general interest of the laboratory is human-machine interface. This includes functional electrical stimulation, when an artificial device sends the control signals to muscles. Another field of human-machine interface is the use of bioelectrical signals recorded from the human body for controlling movements of external objects. We study how information can be changed between the human body and artificial instruments. Our research can be applied in neuromorphic control of prosthetic devices designed for paralysed patients (neuroprostheses).

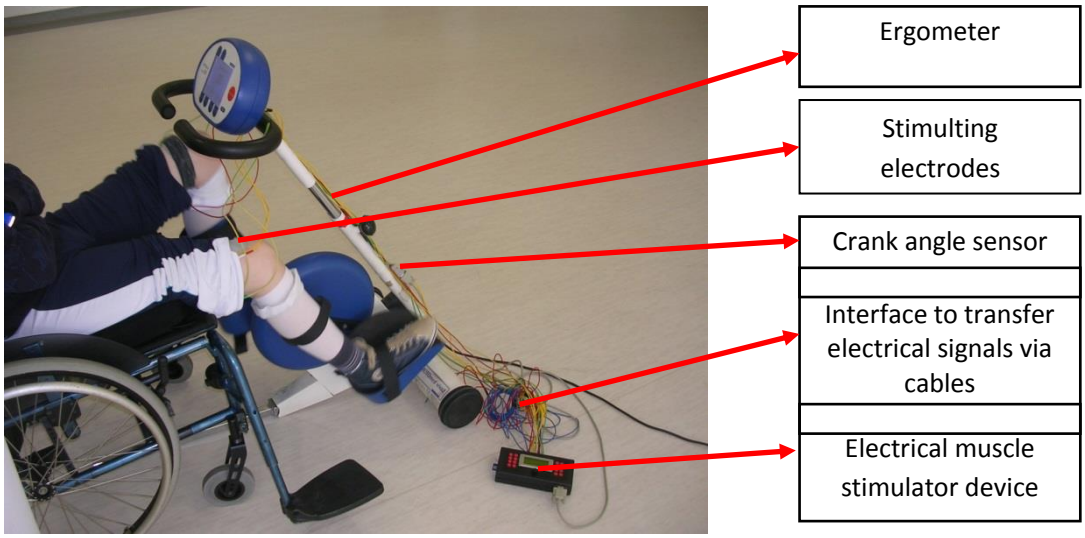

Fig. 2 *Training set up as paralyzed patients are cycling on an ergometer in the National Institute for Medical Rehabilitation using an 8 channel electrical stimulator device developed at the Pázmány Péter Catholic University.*

SOME STEPS TOWARD DESIGN OF AN ARM PROSTHESIS

Measurement and analysis of wrist movements with inertial and biopotential sensors were integrated based on commercially available inertial sensor systems. In addition to hardware considerations current sensor fusion algorithms were compared on the basis of implementation complexity hardware requirements and effectiveness to support the design decision s in the proof of concept implementation.

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13. ULTRASOUND BIONIC TECHNOLOGIES

MIKLÓS GYÖNGY, Associate Professor

LABORATORY OVERVIEW

The activities of the laboratory are primarily motivated by the current ability and future potential of ultrasound technology to help in the early diagnosis of cancer. The scope of the research is wide in the sense that fundamental as well as applied research is being conducted, the aim always being that these ends be integrated with each other. On the fundamental end of the spectrum, the question of how ultrasound images arise is studied. This activity is summarised in the next section of the document. One of the possible fruits of this research is the understanding of how the microstructure of various pathologies such as skin cancer is mapped to certain quantitative parameters and qualitative features on ultrasound images. This leads to research about how skin cancer can be diagnosed using ultrasound and what devices are suitable for this. Since this research is carried out in collaboration with the Department of Dermatology, a summary of this research can be found towards the end of this book, under the title "Ultrasound Technology in Dermatology" *(see pp. 89)*

MODELLING OF ULTRASOUND IMAGE FORMATION

Although many models exist for describing the formation of ultrasound images, the validation of these models is lacking in the literature. The laboratory has conducted research that suggests that based on histology slides, the first-order statitistics of different ultrasound tissue types can be predicted [1]. It has also shown that the ultrasound image produced by distributions of inanimate scatterers can be correctly predicted (Figure 1, [3]).

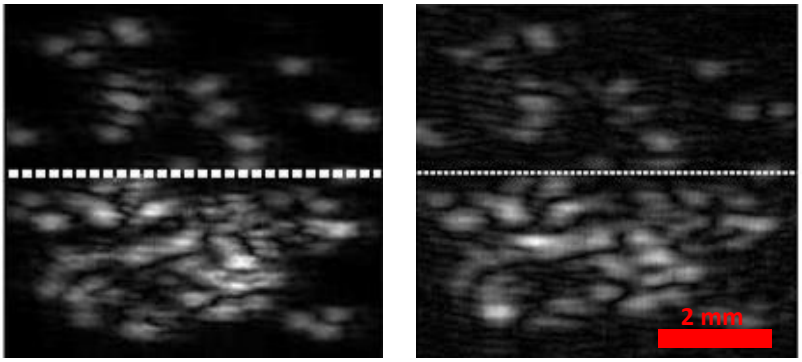

Fig. 1 *Comparison of simulated (left) and experimentally obtained (right) ultrasound images of a distribution of 49-μm-diameter polystyrene microspheres. Note that – despite the presence of noise in the experimentally obtained image – the features of both images show substantial agreement with each other. This agreement is particularly interesting in the case of the speckle pattern seen in the bottom half of the images that is produced by a high concentration of interfering scatterers. Work with Ákos Makra [3].*

The research of ultrasound scattering by inanimate scatterers helps two strands of research. Firstly, it is related to the aforementioned research of modelling scattering by tissue samples. This is helped by the construction of an acoustic microscope in our laboratory (Figure 2), where we are currently working to make scanning an order of magnitude faster,

reducing typical 3D scanning times from 6 hours to 10 minutes. Once this is achieved, we will be able to validate our research regarding how to use tissue-based scattering models to achiever super-resolution images.

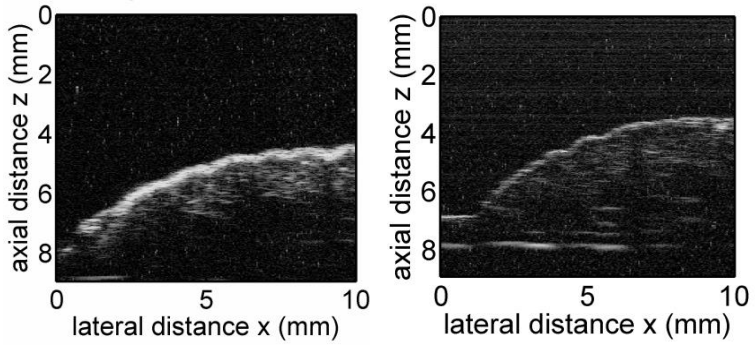

Fig. 2 *Acoustic microscope images of porcine skin using two different transducers. Left: 35 MHz. Right: 75 MHz.*

The second strand of research concerns the development of cost-effective and durable ultrasound phantoms that can be used to calibrate ultrasound imaging systems (Figure 3).

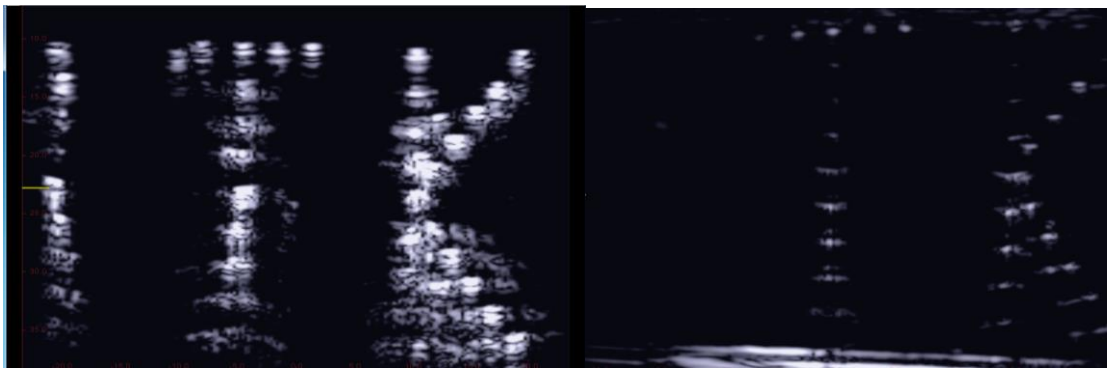

Fig. 3 *Phantoms with the abbreviation of our Faculty, "ITK". Left: phantom printed with fused filament printing. Right: phantom printed with DLP printing. It can be seen that DLP printing potentially provides higher resolution phantoms, however the lack of the letter "I" underscores the need for ensuring good focussing of the projected pattern. Work with Krisztián Füzesi.*

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14. BIOMICROFLUIDICS AND POLYMER OPTOELECTRONIC TECHNOLOGIES

KRISTÓF IVÁN, Associate Professor; ANDRÁS J. LAKI, PhD
Graduate students: ESZTER LEELŐSSYNÉ TÓTH, MÁRTON HARTDÉGEN, ÁDÁM GYÖRGY SZÉLIG

RESEARCH TOPICS

Food safety diagnostic rapid tests

- Sensitive detection of pathogens based on DNA fingerprint
- Foodborne parasitology

Diagnostic devices for human healthcare applications

- Circulating Tumor Cells (CTC)
- Blood analysis

Sample preparation methods for downstream processing

- Particle separation methods: hydrophoresis and acoustophoresis

The main aim of our Biomicrofluidics Laboratory is to design and fabricate devices for medical, veterinary and industrial applications. We are focusing on the miniaturization of bioanalytical processes into microfluidic devices. Fundamental and applied research is carried out in collaboration with research institutes and industrial partners.

Food safety diagnostic rapid tests

Food safety describes handling, preparation and storage of food in ways that prevent foodborne illnesses. We are developing novel methods to detect foodborne pathogens in order to aid medical doctors, veterinarians and laboratory attendants. Also, foodborne pathogen testing and detection is a major concern for food industries. Our highlighted ongoing research project is to combine traditional sample preparation techniques with genotype sequencing within a single microfluidic device. Our lab developing tests for common foodborne parasitoses and Listeria.

Diagnostic devices for human healthcare applications

Our work in this field is focused on the analysis of serological samples. We are developing tools for the separation and analysis of extracellular microvesicles/exosomes secreted during cell-to-cell communication and tumor development; also, applications in circulating tumor cell (CTCs) separation are investigated. CTCs are thought to be responsible for a majority of cancerous metastases.

Particle separation

The separation of sub-micron and micron-sized particles is a challenging research area in microfluidics. The advancements in microfluidics enable sorting technologies that combine the benefits of continuous operation with small-sized scale suitable for manipulation and probing of individual particles or cells. Continuous separation and sorting of microparticles can be managed using external forces (acoustophoresis, electrophoresis, magnetophoresis, applying mechanical forces and optophoresis) or using exquisite geometric microchannels (hydrophoresis). Our work is focused on label-free, continuous and effective methods:

hydrophoresis and acoustophoresis. Hydrophoresis is achieved by varying the geometry of the microfluidic channels, which in turn effectively manipulates the particles (transport, separation and sorting). Acoustophoresis is an ultrasound-based manipulation of microparticles, where mechanical and acoustic particle properties (size, shape, density, and compressibility) determine the manipulation effects.

Particle recognition and classification is crucial for the verification of separation techniques. We use high-fps camera systems (e.g. Cellular Nonlinear Network based machines) for real-time recognition, classification and counting of different objects (particles, cells or debris).

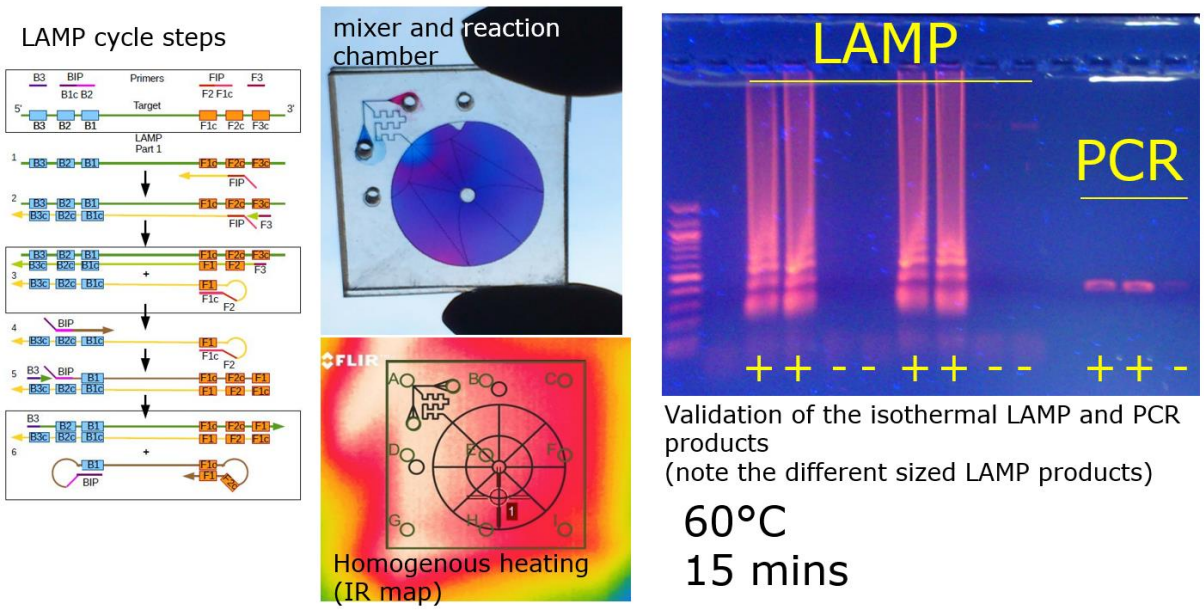

Fig. 1 *Detection of a specific gene from L. monocytogenes by the isothermal PCR method (LAMP) – amplification and detection*

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[4] A. J. Laki, L. Botzheim, K. Iván, V. Tamási, and P. Civera, “Separation of Microvesicles from Serological Samples Using Deterministic Lateral Displacement Effect,” *BioNanoScience*, vol. 5, no. 1, pp. 48–54, 2014.

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15. EXPERIMENTAL MATHEMATICS

BARNABÁS GARAY, Professor; MIKLÓS KOLLER, Assistant Professor; MIKLÓS RUSZINKÓ, Professor

MATHEMATICAL ANALYSIS AND COMPUTATION

In collaboration with *Mauro Di Marco, Mauro Forti* and *Luca Pancioni* (all of Siena University), *Barnabás Garay* and *Miklós Koller* started an extensive research in explaining the emergence of long transient oscillations, i.e., of metastable patterns of periodic orbits in one--dimensional cellular neural networks with periodic boundary conditions and two--sided nearest--neighbor interconnections [6], [7], [8]. Oscillations of this type were observed in electrical circuit experiments performed in Siena and in Budapest.

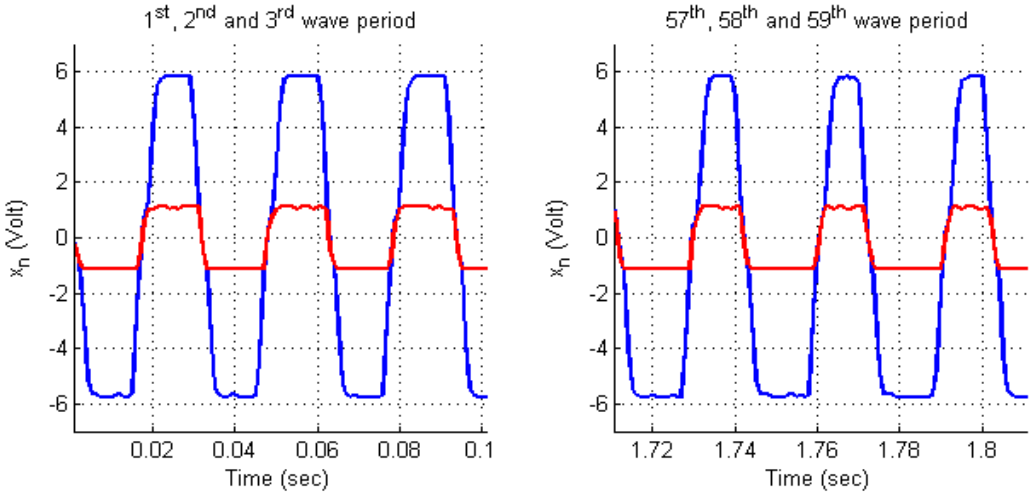

Fig. 1 *Case N=16. The metastable periodic rotating wave as shown on the oscilloscope. (Inner state in blue, output in red.) The circuit experiments were made in the bistable parameter region.The oscillation collapses after 74 wave periods and settles down suddenly to an asymptotically stable equilibrium.*

The phenomenon is robust with respect to the non-idealities of the circuit implementation. The underlying mathematical model is the coupled system of differential equations

$$\tau \dot{x}_n = -x_n + \alpha\, \sigma(x_{n-1}) + \beta\, \sigma(x_{n+1}), \qquad n = 1, 2, \ldots, N$$

where the activation function is chosen for $\sigma(x) = 2^{-1}(|x+1| - |x-1|)$, τ is the time constant, and the variables x_0 and x_{N+1} are identified with x_N and x_1, respectively. For a large domain of real parameters α, β, the duration of the transient phase (as a function of N) is exponentially long. Experimental and numerical findings were confirmed by analytic estimates on the Floquet eigenvalues of the periodic rotating wave with maximal symmetry [10]. Metastable and multistable behavior (which, for other parameter regions, is also present in the simple system of equations above) have an important role in Kelso's coordination dynamics modeling cognitive and decisional tasks performed by neurons and neural networks.

Barnabás Garay and PhD student *Balázs Indig* coauthored a computer-assisted proof for chaos in Vallis' conceptual model for El Niño [9], a variant of the 3D Lorenz system without symmetry.

COMBINATORICS AND COMPUTATION

With their six joint papers in distinguished international journals, *Miklós Ruszinkó* is a regular collaborator of the 2012 Abel Prize winner, *Endre Szemerédi*. In all of these papers exemplified by [1], a method called Szemerédi's Regularity Lemma has been used. For the first view, because of the enormous combinatorial bounds, this approach seems to be entirely `out of the world'. On the other hand recent models in brain research suggest that maybe this approach can be useful in more applied topics as well. Also the latest work by Miklós Ruszinkó [5] on phase transitions in mean-field approximation was motivated by recent results of brain research.

One of the hot topics using methods from discrete mathematics is coding theory. During our research we improved several bounds on parameters of certain codes frequently used. Maybe our most important results in this area are those we got on bounds on codes for multiple access communication channels. Multiple access channel models usually assume a large number of non-cooperating users trying to get an access to the limited resources of a given channel [2]. Even more applied research is going on FPGAs [3], [4]. The attempt is to accelerate unstructured finite volume computations on FPGAs. The novelty in our investigations, with a larger group around *Péter Szolgay*, is that we are trying to combine algebraic non-elementary clustering methods to achieve a better computational performance.

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16. SOFTWARE DEFINED ELECTRONICS AND VIRTUAL INSTRUMENTATION

GÉZA KOLUMBÁN, Professor
Graduate students: TAMÁS KRÉBESZ, CSABA JÓZSA

ACTIVITY OF THE SDE-VI LAB, A BRIEF DESCRIPTION

Recent research topics of the Software Defined Electronics (SDE) and Virtual Instrumentation (VI) laboratory:

Reconfigurable physical layers

- Elaboration of CS-GCSK/GCS-DCSK modulation schemes
- Derivation of analytical expression for the BER performance of these new modulation schemes
- Elaboration of a step-by-step method for the derivation of detection algorithms assuring optimum solution for different applications

Application-oriented protocols for PHY layer

- Elaboration of UWB FM-DCSK protocol which improves by an order the coverage of the already published Gaussian UWB Impulse Radio (IR)
- Elaboration of UWB Chirp IR TR protocol which improves by an order the coverage of Gaussian UWB IR but which preserves the channel dispersion suppression capability of Gaussian one

SDE conform BaseBand (BB) WND models

- Elaboration of a step-by-step method for the derivation of equivalent BB models of WLAN and BioMed devices
- By integration of BB simulators into the SDE platform we have elaborated a software defined research platforms for the generation and analysis of real physical signals (see photo below

Detection algorithms on GP-GPU platform suitable for WLAN applications

- We have shown that with appropriate parallel algorithms the GP-GPU platforms can be used to implement detectors
- Elaboration of PSD algorithm which implements the ML detection on GP-GPU platform

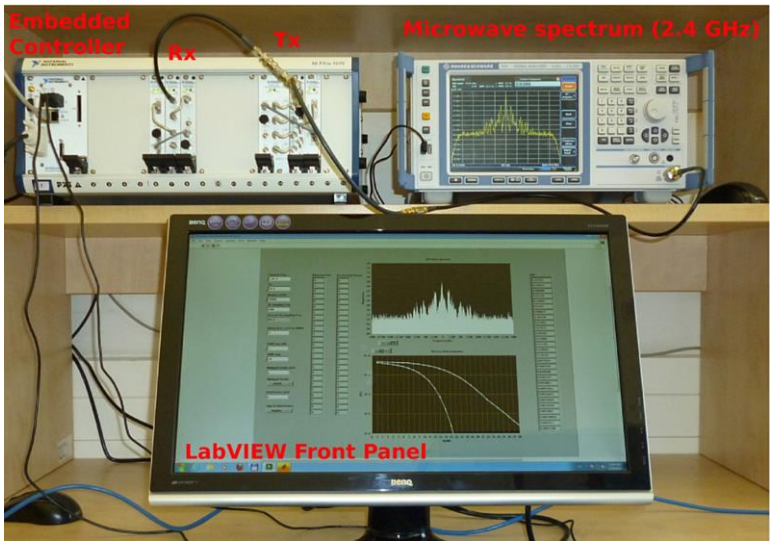

Fig. 1 *Photo of the PXI based SDE research and development platform installed in the SDE-VI lab. The "Embedded Controller" that is responsible for running the application software and controlling the modular units, the "Rx" unit that performs the transformation between the RF and baseband domains, and the "Tx" unit that performs the inverse transformation, are in the same PXI chassis. The "LabVIEW Front Panel" that appears on the PC monitor shows the graphical user interface of the software that is run by the "Embedded Controller". The real physical signals generated by software are measured by a Rohde & Schwarz spectrum analyser.*

INTERNATIONAL RECOGNITION OF OUR LABORATORY

Our SDE-VI Lab has been playing a leading role worldwide in the research of software defined electronics. This leading role had been recognized by IEEE CAS Society and we were asked to write a tutorial on SDE for the IEEE CAS Magazine in 2012. See item [9] in the publications list. Our contribution to this area has attracted the attention of the scientific community even more. As a consequence Prof. Kolumbán has been elected as a speaker in the 2013-2014 Distinguished Lecturer Program (DLP) by the IEEE-CAS.

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[11] W. K. Xu, L. Wang, Géza Kolumbán: A Novel Differential Chaos Shift Keying Modulation Scheme, *International Journal of Bifurcation and Chaos*

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17. ARTIFICIAL INTELLIGENCE AND SPATIAL-TEMPORAL SEMANTICS

KRISTÓF KARACS, Associate Professor
Graduate students: MIHÁLY RADVÁNYI, ATTILA STUBENDEK, ANNA HORVÁTH, GÁBOR ORBÁN

FOCUS OF THE LABORATORY

The lab mainly deals with intelligence problems related to sensory processing. As sensors have become miniaturized and ubiquitous in modern information technology, remotely processing all acquired data is not feasible any more. Remote does not necessarily refer to the cloud, but in this sense another processor, or even the other side of the same topographic processor, may also count as a remote location. Local processing requires appropriate knowledge and architectural organization. A key principle we developed is semantic embedding that refers to the process of injecting background information into the hierarchical recognition process at appropriate levels.

RESEARCH TOPICS

Scene understanding of 3D scenes

We consider 2D image flows containing the projection of 3D environments with other related information from other modalities. Specific scenes are described using a multimodal semantic language including spatiotemporal events, signatures of canonical views of typical objects, as well as spatial relationships of the objects and/or events. Semantic embedding during the recognition process is built on the knowledge in this representation.

The most important applications are autonomous local navigation and orientation tasks, either for personal or robot navigation. We developed a mobile framework for cell phones that serves as a basis for a guide helping blind and visually impaired people in their daily tasks.

Visual learning

Recognizing objects in a visual environment is a nontrivial task mainly because of the huge number of looks (imprints) how an object can be perceived from different viewpoints under various lighting conditions. Visual learning aims to find characteristic signatures (features and feature groups) that are invariant to rotation across multiple scales and adaptive clustering methods that are able to identify which signatures belong to the same, and which ones to different semantic categories.

Offline handwriting recognition

Recognition of handwritten cursive scripts is a much more difficult task than optical character recognition. The latter already has widespread commercial solutions, but the former is still an actively researched area. The main difference between the two fields is besides the fact that letter shapes greatly depend on individual writers is that touching characters pose a much more complex recognition scheme due to their ambiguous separation borders.

Semantic embedding is realized through a holistic word recognition technique that detects features on the word level without binding them to characters and a special linguistic engine that can find all proper linguistic forms that match a given holistic description.

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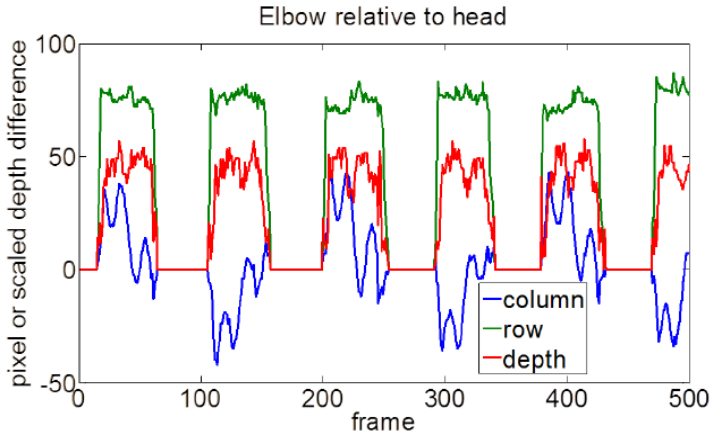
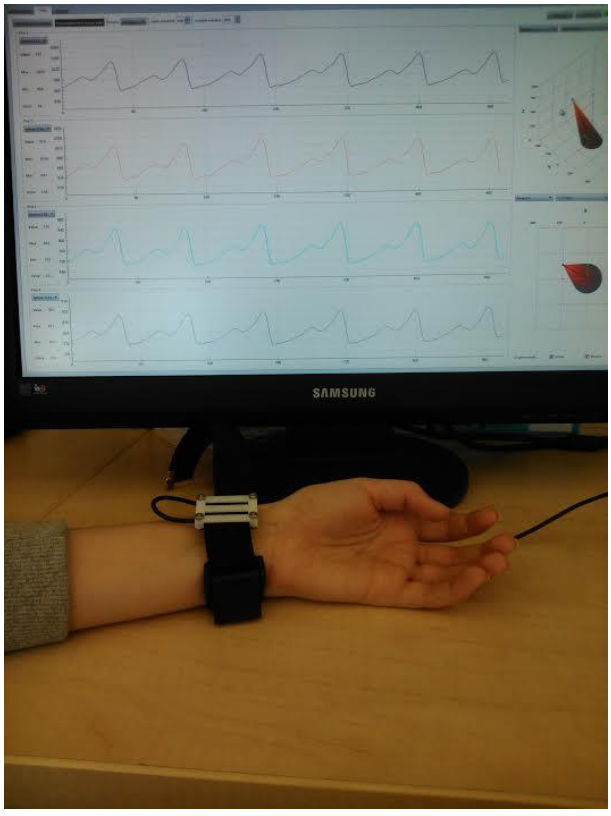
18. SENSING-ACTUATING ROBOTICS

GYÖRGY CSEREY, Associate Professor; MIKLÓS KOLLER, Assistant Professor
Graduate students: SÁNDOR FÖLDI, Balázs Jákli, NORBERT SÁRKÁNY

LATEST RESULTS

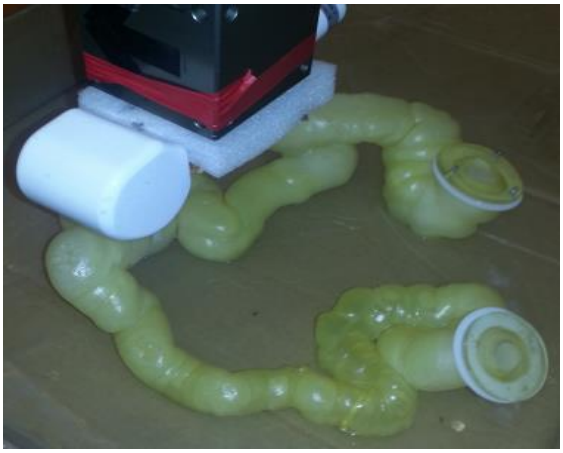


Nonintrusive human recognition techniques promise the ability to distinguish people by their biological traits without their active participation. The technique pursued in this research is gait recognition, identifying someone by the unique way he or she walks. This is of natural interest in security applications, but other endeavors also stand to benefit from increased access to information about gait. Examples of these include walking rehabilitation and shoe design. A pilot study was conducted with 12 subjects walking repeatedly in both directions past the Kinect, which sampled at approximately 17 frames per second. The walking environment had some daylight present but was mostly dark for the sake of the Kinect image quality. Certainly real environments will not satisfy this condition and may have large windows and the like; however, it was desired to reach the best-case performance for this version of the algorithm. An example of the result quality is shown in Figure. We are using siamese network deep learning for distinguish between gait patterns.

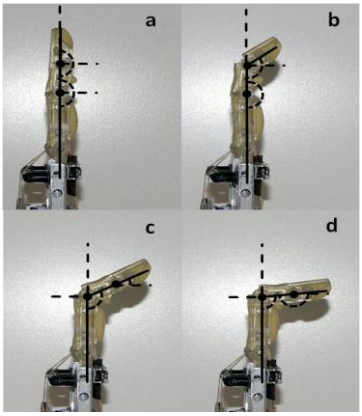


The principle of pulse diagnosis is that the vascular system is connected to all inner organs and, by this, carries information about them. This information can be read from the propagation of pulse wave, the so called pulse characteristic. This pulse wave is usually measured on the radial artery. With the help of this method some cardiovascular and inner organ diseases could be diagnosed by only one examination. The basics of this method were introduced in the Traditional Chinese Medicine. The main diasadvantages of the traditional method are the following: it's really hard to learn, and it's also subjective, the accuracy of diagnosis depends on the qualifications and concentration state of the practicioner. This is why an objective, automatized pulse diagnostic system is required. In our

laboratory we try to develop an automatized pulse diagnostic system based on our 3D tactile sensors, which was also developed here. Using this sensor, the pulse waveform can be measured non-invasively, without pain and side effects on the radial artery at the wrist. We have a clinical TUKEB license to make our measurements, record information of participants and publish our results.



Capsule endoscopy is a completely painless, non-invasive procedure, which gives the doctor images, similar in quality to those of conventional endoscopic techniques, of the gastrointestinal tract, including the esophagus and the whole small and large intestine. During development a 3D printed model of the intestine, obtained from a CT scan, was used in a robotics environment as a trajectory for the capsule to be led along by an automated algorithm. Our purpose was to improve and to automate the movement mechanism of the capsule, so that it could be moved to its appointed position and tilted by a given angle (with the speed of conventional endoscopic techniques). In our case the whole intestinal tract is monitored during a given trajectory, further on the capsule is expected to be able to examine selected regions in more detail, if needed. One of our long-term aims is to enable the user to control the capsule with the device from another room in real time via a robotic hand.



This work presents a design of an anthropomorphic biomechatronic hand, focusing on the design of the fingers and its bio-inspired flexor-extensor like low-level control. The kinematic description, the detailed explanation and presentation of the 3D CAD design are included. The description of the applied 3D tactile and magnetic sensors is also detailed in the article. Matlab simulation results and also the first experiments of the hardware prototype gave promising results and show that the approach can be an effective solution for the need of a hand-like actuator in robotics.

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19. MOBILE SENSING NETWORKS

ANDRÁS OLÁH, Associate Professor; KÁLMÁN TORNAI, Assistant Professor; ISTVÁN REGULY, PhD
Graduate students: DÁVID TISZA

INFRASTRUCTURE OF THE WIRELESS SENSOR NETWORKS LABORATORY

USRP sw radios, Xbow Mica development kits, TI CC2420 development kits, Amber AMB8423 wireless target boards, sensors

ACTIVITIES

One of the central issues in the development **Wireless Sensor Networks** (WSNs) is to devise new protocols under the constraint of limited resources (e.g. energy, size, available bandwidth, computational power…etc.). The most important characteristics of WSN are as follows:

- since the sensors are installed over a large area, a direct link between the information source and destination does not exist, hence the communication protocols to be developed have to support reliable multi-hop operation;
- sensor nodes needs only a low data rate (LR) communications link where some latency time is tolerated;
- channel conditions including both the propagation conditions and inner and outer radio interference (coexistent wireless system) are varying continuously;
- ultra low power consumption: using the same AAA battery, one node should operate for at least a few years, since regular maintenance (including battery changing) would make the system impractical.

As opposed to traditional networking protocols, these limitations pose new challenges to algorithmic protocol design. A great deal of researches has been pursued into developing novel communication protocols and distributed signal processing algorithm.

In our earlier research, we have developed several novel routing and MAC protocols which significantly increased the lifespan of the WSN under constraint of reliable packet reception at the BS (e.g. correct packet arrival at the BS is guaranteed by a given probability). These protocols were adapted and implemented in our test network.

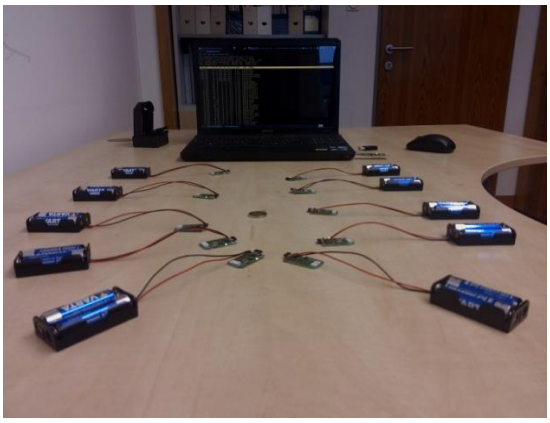

Fig. 1 *The AMB8423 development kit*

Our WSN group has a seven-year experience in research and development. The corresponding projects, education activities are as follows:

- *Development and Implementation of Wireless Indoor Climate Monitoring System* (completed project with EnerG Kft. sponsored by Hungarian Scientific Research Fund)
- *Signal processing and wireless device design and prototyping for analog sensors* (currently running project for Research Institute for Technical Physics and Materials Science (MFA) of the Hungarian Academy of Sciences)
- In the recent years we have published book chapters, journal papers and conference papers in the field.
- In this area 4 PhD were awarded and 2 PhD students are just before the thesis defense and more than 15 BSc and MSc students were working on the field.
- Recently we have developed a WSN based survivor detection system which is going to be implemented in AMB8423 wireless boards.

20. MICROELECTRONIC SYSTEMS AND INTEGRATED CIRCUITS

FERENC KOVÁCS, Professor; PÉTER FÖLDESY, Associate Professor
Graduate students: ZOLTÁN KÁRÁSZ, DOMONKOS GERGELYI, LÁSZLÓ KOZÁK, ANNA MEDGYESI, ÁDÁM LUTZ

FOCUS OF THE GROUP

- Application of advanced microelectronic technologies to sense, measure, and process physical and biological electrical phenomenon.
- Microwave and Terahertz range sensing and imaging
- Integrated circuit Neural interfaces

The group has a long time experience in deep submicron integrated circuit (IC) design. We conduct research in a field, in which the physical quantities are hardly measurable with off-the-shelf components. Hence, the need for custom designed integrated circuits is unavoidable. Our group is the only academic team in Hungary with daily routine of using advanced IC technologies.

We have participated in several international grants targeting integrated vision systems. One of the most promising directions is the usage of 3D technology to merge image sensing, multi processor image analysis, and high level target recognition and identification in a single IC. The used 3D SOI technology is provided by the MIT Lincoln Laboratory and supported by the Office of Navy Research to form an integrated three layer compact vision system for UAV (unmanned aerial vehicle) surveillance and reconnaissance.

Through cooperation with MTA Research Centre for Natural Sciences and Institute of Microelectronics of Seville, Spain we are developing a complex, multi channel neural sensor interface using very low noise BiCMOS technology. Flexible deep brain electrodes with electrically selectable sensors and integrated amplifiers open new possibilities in understanding low frequency behavior of the brain, long term memory, and adaptation processes.

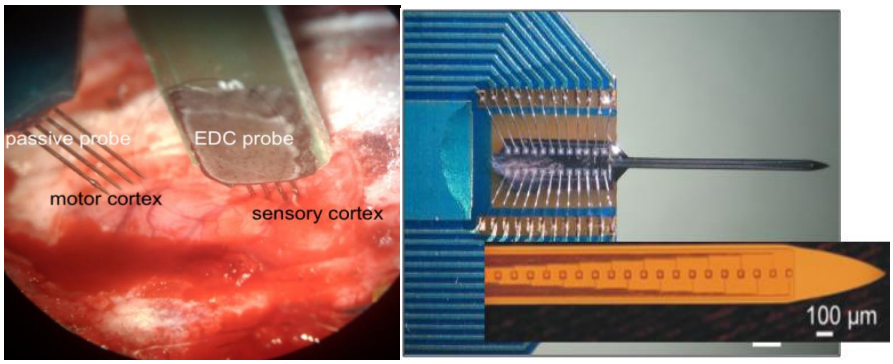

Fig. 1 *Brain electrodes with multiple contacts.*

We also work with very high frequency electromagnetic waves. In the recent decade, the so called Terahertz (>300 GHz) waves come into the center of attention as the last unutilized

region of the electromagnetic spectrum. This radiation is not ionizing, hence, in principle does not harm living tissues, meanwhile provides information of material, moisture, biomarker content undetectable by other non invasive methods. We are a leading group in highly integrated CMOS sub-THz imagers.

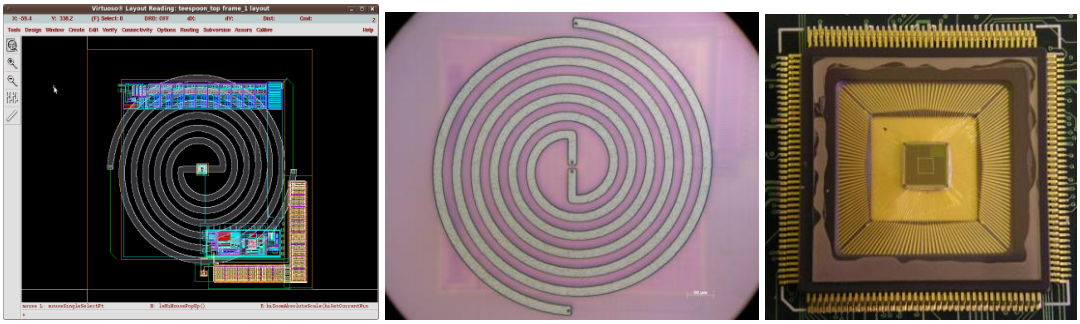

Fig. 2 *Different stages of development of a sub-THz imager: design, microphoto, and complete IC.*

Beside theoretical work and consequent development, we focus as well on real life THz applications, such as skin cancer diagnostics in cooperation with Semmelweis University.

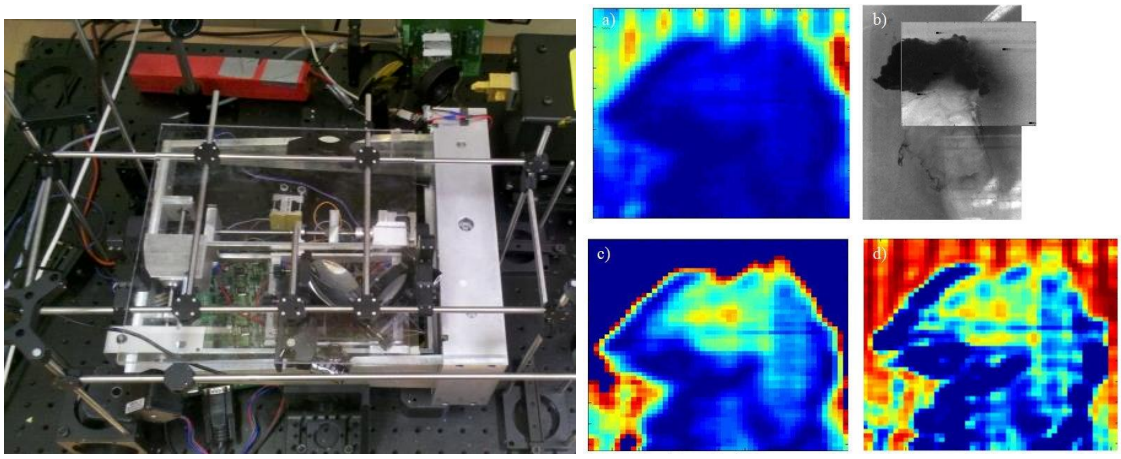

Fig. 3 *Experimental skin scanner and in vitro sample images captured at 460 GHz.*

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21. PROGRAMMING LANGUAGES AND SOFTWARE TECHNOLOGY

JUDIT NYÉKYNÉ GAIZLER, Associate Professor; ISTVÁN VETŐ, Associate Professor; GERGELY FELDHOFFER, Assistant Professor

PROGRAMMING LANGUAGES

The importance of reliability of the programs has come to the centre of interest with the development of large systems. The aim is to write "correct" programs which exactly perform their tasks, as defined by the requirements of the specification.

A theory, i.e. a methodology which supports the programmer perform his practical work to be well-considered is very important. Abstraction - as a technique of thinking - is substantial in the education of professional programmers of the future. In the same time, we have to agree with Bertrand Meyer that the “language independent methodology” is “as useful as a bird without wings”, and: “In software perhaps more than anywhere else, thought is inseparable from its expression. To obtain good software, a good notation is not sufficient; but it is certainly necessary.” That’s the reason why we try to balance in our teaching already at BSc level between methodology and tools – programming languages, environments, etc.

Algorithm and software correctness are often discussed and educated separately. We look for ways to blend concepts as weakest precondition into the use of debuggers and static analyzers. Usual solutions like precondition assertion by logic-error exceptions and its analysis by debugger are part of our MSc education program.

GPU SUPPORT IN COMPILERS

There are quite a number of research and development projects on GPU programming in these years since the raw computational power of GPUs is in general higher than CPU by a magnitude. Most of the publications in this topic used to describe the application of a given algorithm to GPU architecture. The problem of algorithm application to a given architecture contains multiple layers of abstraction. The higher level of abstraction used to describe the parallelization scheme, and the lower level is the actual GPU code which determines the memory mapping (coalescing), the use of shared memory, CPU-GPU transfer, etc. Solutions of lower level abstraction tasks are often commonly known as best practice on the given problem. This situation is similar to low level CPU programming techniques, which are today highly automated in optimizers used by compilers. Our concept is to introduce a compiler which is capable to generate GPU enabled code from standard high level programming language.

A GPU enabled compiler should generate GPU code, such as OpenCL, which is a high level programming language. It should take care of memory transfer and representation. We succeed to create a proof-of-concept compiler plugin which is capable of these features, and is integrated into GCC. The higher level of abstraction is encoded here as a lambda function which is a C++ feature in the latest standard. The programmer has to use a custom template function library to access the GPU features in this version. Each template function represents a high level parallelization scheme, such as for_each() or cumulate(). The supported features inside the lambda function include (non-recursive) function call, operator overloading, and many more. Examples of not supported features are the recursion, polymorphism and pointer

aliasing based tricks.

SOFTWARE TECHNOLOGY

The category of Software Technology includes different disciplines, related to each other, but having its own specialties. The staff of PPCU Faculty of IT carries on numerous theoretical works on the fields of sciences concerned by the following subjects, included in the education program at our Faculty:

Basics of software technology: requirements engineering, software development processes and methodologies, project planning, basic questions of software quality and standards.

Software design and evaluation: methods and tools for software design and implementation, OO analysis and design, modeling tools and practices, agile software development methodology (Extreme Programming, SCRUM, etc.), software reengineering, configuration management, as well as evaluation of software systems.

Integration of information systems: disciplines of integrated information systems, models and architectures, classes and handling of heterogeneity, the goals of integration, systems integration strategies, types of integration, middleware and integration standards, integration architectures, like SOA.

Design patterns: Types and role of the classical OO design patterns in Java and C++, architectural patterns in software development.

Our activity is extended to study the architecture, structure and functions of complex data processing application systems, like ERP, CMS and different types of eBusiness software. We are also dealing with the standards and tools of Business Process Modeling.

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22. DATA MANAGEMENT, DATA MINING AND MEDIA TECHNOLOGIES FOR COMMUNITIES

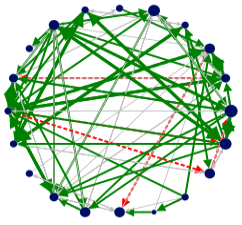
GERGELY LUKÁCS, Associate Professor; GYÖRGY TAKÁCS, Professor; MÁTYÁS JANI, Ph.D. student
Graduate students: MÁRTON HUNYADY, DÁNIEL TÓTH, ANDRÁS MATOLCSY, ÁKOS SONKOLY, ZSÓFIA SIPOS, DOROTTYA SZILÁGYI

We are working on laying the foundations for small community media using the latest available technologies such as smartphones, the mobile internet, big data and data mining. The primary goal is strengthening viable communities, supporting their self-organization on a practical level and promoting community members' mental health. Multidisciplinary cooperation with media experts, sociologists and psychologists as well as close cooperation with several communities allow us to concentrate on the technical issues while also focusing on our primary goal.

Technically, the following areas are covered:

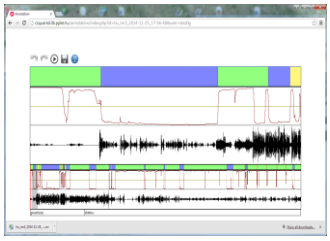
Audio data, i.e. speech and music play a central role in our approach. New challenges, such as mixed speech and music playlist generation are to be met (pure music playlist generation has been extensively handled over the past few years in the IEEE and ACM literature). There is also cooperation with the human language technology group.

Scalable database management and data mining approaches are required both for (a) analysing media content, (b) customizing the data based on individual profiles and on actual context information utilizing value-based (or dual goal) and serial recommender systems, (c) analysing usage patterns, (d) investigating data on personal connections and travel trajectories.

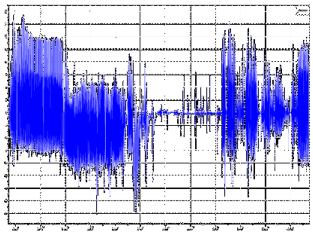


(a) Social network data

(b) Trajectory data on persons' journeys



(c) Mixed speech-music playlist



(d) Sensor data

Fig. 1 *Data sources/forms related to audio media for communities*

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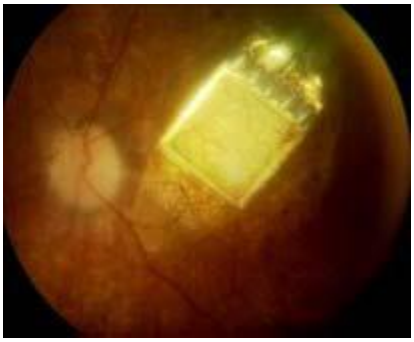
JOINT CENTERS WITH THE SEMMELWEIS UNIVERSITY

A. HUNGARIAN BIONIC VISION CENTER

B. CENTER OF NEUROMODULATION

A. HUNGARIAN BIONIC VISION CENTER

Directors: KRISTÓF KARACS PHD, Associate Professor; ÁKOS KUSNYERIK PHD
Advisers: JÁNOS NÉMETH MD, DSC, Professor, ILDIKÓ SÜVEGES MD, DSC, Professor, BOTOND ROSKA PHD, Head of Laboratory, Friedrich Miescher Institute, Basel, ÁKOS ZARÁNDY DSC, Professor
Graduate students. MIHÁLY RADVÁNYI, ATTILA STUBENDEK



The goal of the Hungarian Bionic Vision Center is to restore vision of visually impaired patients to the maximum extent and to improve the quality of their lives through using medical and technological aids. We run programs to study promising medical and engineering technologies under active research.

CURRENTLY ACTIVE PROGRAMS

I. Research, development and testing of universal electronic devices for visually impaired people

II. Taking part in international clinical studies for retinal implants and establishing these practices in Hungary (control, preoperative and postoperative follow up)

III. Optogenetic techniques

The main focus of Program I is the development and testing of the bionic eyeglass in cooperation with organizations representing visually impaired people. In the framework of Program II we mostly deal with subretinal implants. Program III concentrates on the very promising research in optogenetics.

The operation of the center is based on the cooperation between the Dept. of Ophthalmology of the Semmelweis University and the Jedlik Laboratories at the Faculty of Information Technology of the Pázmány Péter Catholic University. The center is scientifically supervised by Prof. János Németh, director of the Dept. of Ophthalmology, and Prof. Tamás Roska, founding dean of the Faculty of Information Technology. We put a strong emphasis on partnership with blind organisations. Our most important partner is the IT for visually impaired foundation.

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B. CENTER OF NEUROMODULATION

Directors: LORÁND ERŐSS MD, PHD, Associate Professor, neurosurgeon, neurologist, fellow of interventional pain practice; DANIEL BERECZKY MD, PHD, DSC, Professor
Senior clinicians in the different treatment groups of the center:
Epilepsy Surgery Program: DR. DÁNIEL FABÓ; PROF. DR. PÉTER HALÁSZ; DR.LORÁND ERŐSS
Pain Program: DR. EDIT RÁCZ; DR.LORÁND ERŐSS
Deep Brain Stimulation Program for movement disorders: DR. ANNAMÁRIA TAKÁCS; DR. ANITA KAMONDI; DR. MAGDOLNA BOKOR; DR. GERTRÚD TAMÁS; DR. LORÁND ERŐSS
Intrathecal Drug Delivery Program: DR.LORÁND ERŐSS; DR. LÁSZLÓ ENTZ
Psychologists: DR. NOÉMI CSÁSZÁR; CSABA BORBÉLY
Psychiatrist: DR. ÉVA CSIBRI
Neuromodulation nurses: KATALIN KIRÁLY; BARBARA KOVÁCS
Senior researchers: DR. ISTVÁN ULBERT; DR.GYÖRGY KARMOS; DR. LUCIA WITTNER
PhD student: DR. LÁSZLÓ ENTZ

In biotechnological context neuromodulation is a field of science, medicine and bioengineering that encompasses implantable and non-implantable technologies, electrical and chemical with the aim to improve the quality of life for humans suffering from neurological disorders.

The reason of initiation of the first neuromodulation center in Hungary was to create an interdisciplinary hub where clinical medicine, research and medical and infobionic education meets in the field of neuromodulation. In the center, research can have direct influence on medical practice and education on the graduate and postgraduate level in medical school and in information technology.

This will be a place for technology of the neural interface for doctors, bioengineers and the neuromodulation industry.

Our aim is to be a center of excellence in neuromodulation for a broad spectrum of patients with different neurological disorders in Hungary and in the Central European region:

- to support the clinical work of physicians in neuromodulation to create a center of excellence,
- to introduce neuromodulation in the medical and bionic education at graduate level,
- to promote animal research in neuromodulation and clinical investigations in the field of neuromodulation,
- to develop existing and new neuromodulation devices,
- to give the opportunity to join international multicenter clinical trials and initiate external research sites for neuromodulation companies,
- to support incubate spin-off and start-up companies in the field of neuromodulation.

The center was initiated by Loránd Erőss and founded by Professor Tamás Roska from the Pázmány Péter Catholic University and Professor Miklós Réthelyi, Minister of National Resources. The members of the Advisory Board are Gabor Racz the founder of the International Pain Center at Texas Tech University Health Sciences Center, the Dean of the Pázmány Péter Catholic University, Faculty of Information Technology, the Professor of neurology and the Professor of neurosurgery from Semmelweis University. In the supervisory board there are Hungarian and foreign specialists in the field of neuromodulation. The director of the center is Loránd Erőss.

The center incorporate the Pázmány Péter Catholic University, Faculty of Information Technology, the National Institute of Clinical Neurosciences, Functional Neurosurgical Department and the Semmelweis Medical University, Institute of Neurology, Department of Movement Disorders

This is the youngest collaborative center of the Pázmány Péter Catholic University, Faculty of Information Technology. The first research and development project is "Remote telemetrical programming of neuromodulation devices". The Neuromodulation Center is expanding the remote telemetrical programming of various IPGs and implantable pumps. With help of this new platform and device, the service can be provided regardless the physical location of the patient or the physician. It is important in cases of movement impaired, elderly, or very poor patients who cannot afford to travel for regular clinical controls or in cases of emergencies like pump EOL.

The neuromodulation activity in clinical practice started in 1999 implanting the first ITB pump. 2004 a regular neuromodulation program was introduced and in 2010 the first Functional Neurosurgical Department of Hungary was founded by dr Erőss. In the last 8 years since the neuromodulation program is active in the National Institute of Clinical Neurosciences 120 patient got intrathecal pumps for spasticity and pain, 77 patients went through SCS tests for chronic pain syndromes. The center introduced first in Hungary several new techniques like motor cortex stimulation for thalamic in 2008, and the first Gasserian ganglion stimulator for neuropathic facial pain and a retrograde C1 surgical lead was implanted here for drug resistant atypical facial pain. The Neuromodulation Center is increasing its activity in Deep Brain Stimulation in different movement disorders, since 2004 vagus nerve stimulation and from 2012 DBS in epilepsy.

At present this is the only Neuromodulation Center in Hungary which incorporated a Functional Neurosurgical Department and has a background of bionic research and takes part of the combined graduate and postgraduate medical and bionic education.

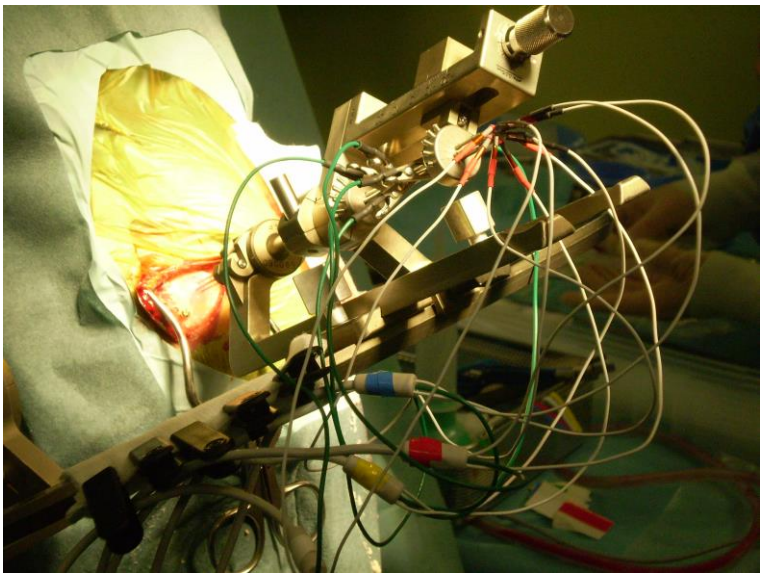

Fig. 1 *Intraoperative electrophysiological recording, during Deep Brain Stimulator implantation in a Parkinson's disease patient (Institute of Clinical Neurosciences, Budapest)*

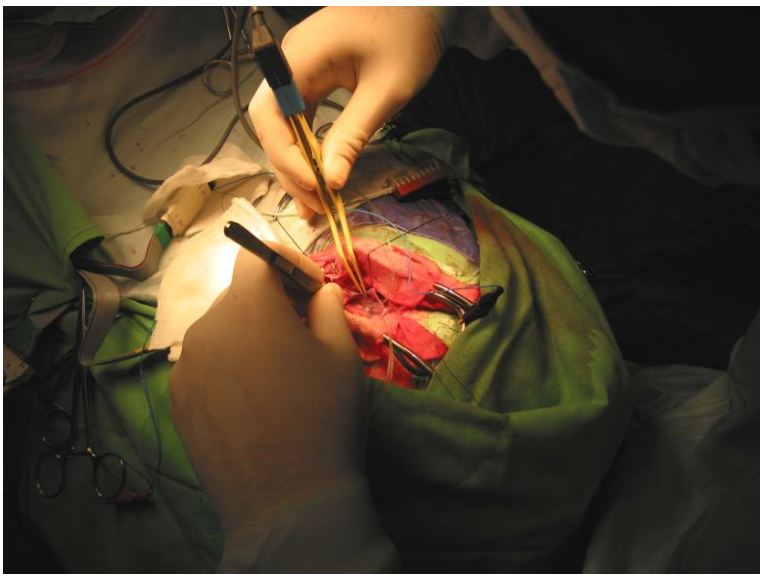

Fig. 2 *Strip electrode implantation in epilepsy surgery (National Institute of Clinical Neurosciences)*

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VARIOUS JOINT RESEARCH PROJECTS WITH THE SEMMELWEIS UNIVERSITY

I. ON-LINE PERSONALIZED GENETIC ANALYSIS FOR TUMORS

II. OPTICALLY CONTROLLED SELF ORGANIZING AMYLOID NETWORK

III. ULTRASOUND IN DERMATOLOGY

IV. DIGICON (DIGITAL MEDICAL CONSULTATION)

I. ON-LINE PERSONALIZED GENETIC ANALYSIS FOR TUMORS

SÁNDOR PONGOR, Professor; BALÁZS GYŐRFFY, Associate Professor
Graduate student: BALÁZS OLÁH

MEDICAL DATA MINING, DATA-DRIVEN HYPOTHESIS GENERATION IN CANCER RESEARCH

Research in life sciences is only possible today with access to online literature databases. Extracting information useful for medical researchers and practitioners is possible now with the methods of parallel data mining, simultaneously applied to medical publications and molecular databases. Hypothesis generation refers to generating surprising, non-trivial suppositions and explanations based on information extracted from textual resources. From a data-mining perspective, text-based hypothesis generation is a case of link discovery, i.e. a hypothesis can be considered as an undiscovered relation between pre-existing knowledge items. Early success stories include the discovery of therapies for Raynaud's disease and migraine. In the genomics era, hypotheses are often formulated as relations involving molecular entities, such as genes, proteins, drugs, metabolites, etc., so the use of textual resources needs to be combined with molecular databases, and often, with new experimental data generated by the user. A typical example of application is finding undiscovered links and synergisms between approved pharmaceuticals, as drug combinations can reach the applications phase much faster than novel drugs. A promising area is the study of synergisms that may exist between generic and targeted therapeutic agents or the design of cocktail therapies for complex diseases.

The emphasis of current cancer therapy is shifting from traditional chemotherapy to targeted drugs. Such therapies rest on two fundamental motives: i) the use of targeted pharmacons that act on one or a few molecular targets specific to tumor cells, and ii) identification of biomarkers suitable for the prediction of drug response. High throughput technologies provide massive amounts of data that can be processed from many viewpoints; the average research groups however lack the necessary and sometimes very extensive, bioinformatics repertoire. Our aim is to develop on-line facilities that are able to integrate high throughput data with a complex algorithmic procedure that allow identification of biomarkers or statistical targets. An additional goal is to create prediction systems that can help point of care diagnostics applications.

COLLABORATORS:

Dr. Balázs Győrffy, Research Laboratory of Pediatrics and Nephrology, Hungarian Academy of Sciences, Semmelweis University, Budapest, Hungary

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II. OPTICALLY CONTROLLED SELF ORGANIZING AMYLOID NETWORK

MIKLÓS KELLERMAYER, Professor; SZABOLCS OSVÁTH, Associate Professor; KRISTÓF IVÁN, Associate Professor

AMYLOID ARRAY FOR NANOELECTRONIC APPLICATIONS

The general objective of our project is to investigate whether an amyloid-fibril based oriented network can be developed into a nanoelectronic array. The array, with its nanometer-scale dimensions, may, in principle, be utilized for novel electronic applications. Specifically, we plan to 1) develop a microchip (nanoarray) from oriented network of mutant amyloid beta 25-35 (Aß25-35) fibrils organized on the surface of mica; 2) transform the amyloid fibrils into conductive nanowires via nano-gold labeling and silver enhancement; 3) assign optically modulated switches in the nanoarray by using recombinant photosynthetic reaction centers; 4) acquire high-resolution, spatially resolved conductivity map of the nanoelectronic array under optical modulation; 5) analyze conductivity data in terms of computational models.

The professional, scientific and economic significance and importance of our project is enormous even by modest estimates. The significance stems on one hand from the particularly advantageous properties of the amyloid nano-network, and on the other hand from the great general interest in the development of nanoelectronic technologies. Because of the structural features of the amyloid network the spatial resolution is truly on the nanometer scale, which represents three orders of magnitude improvement over that of the current microarray technologies and nearly two orders of magnitude improvement over that of current silicon wafer technologies. Our project may lead to the development of novel computational methodologies. In addition, technologies such as super-resolution CCD, direct-readout analytical chips, and computational nanochips may eventually be achieved.

COLLABORATORS

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III. ULTRASOUND IN DERMATOLOGY

MIKLÓS GYÖNGY, Associate Professor; KLÁRA SZALAY, Senior Physician

GROUP OVERVIEW

The working group is a joint venture between the Ultrasound Bionic Technologies laboratory of the Jedlik Laboratories *(see pp. 51)* and the Department of Dermatology at Semmelweis University. The group enables an interdisciplinary collaboration between clinical dermatologists with well-established experience in ultrasound-based diagnosis and bionic engineers with the knowledge of ultrasound biophysics. The aim of the group is to help develop an ultrasound imaging platform that can be used by dermatologists and other doctors to help them perform differential diagnosis on skin lesions. Such work has two main aspects, namely the research of appropriate differential diagnosis algorithms and the development of a suitable medical device on which these algorithms may run. These activities are considered in the corresponding sections below.

DIFFERENTIAL DIAGNOSIS

Skin lesions come in many forms, from benign nevi to malignant (but rarely fatal) basal cell carcinoma (BCC) to malignant melanoma (MM) – even between these diagnoses, many subtypes and stages of disease progression present themselves, which ultrasound imaging, given suitable expertise, can distinguish between [1]. The aim of our research is to try and represent the knowledge of an expert radiologist in a form that can be algorithmicised to enable computer-aided diagnosis (CAD). Our previous research has shown that quantitative descriptors such as the Nakagami parameter may potentially be used to perform differential diagnosis between MM and BCC melanoma and basal cell carcinoma. However, the performance of the differential diagnosis algorithms is very sensitive to choosing the correct region of interest (ROI) and to low signal to noise ratio (SNR), therefore research is ongoing to find ways to create robust Nakagami estimators.

In finding suitable algorithms to help differential diagnosis, the group took a step back and started looking at semi-quantitative scores of different ultrasound features, as provided by radiologists and medical practitioners of various levels of experience. The question is how these scores correlate with gold standard histology diagnoses. Based on these results, candidate scores may be selected that could be used by medical practitioners without radiology qualifications. Furthermore, the questions arises how the semi-quantitative scores can be translated into fully quantitative parameters (such as the Nakagami parameter) that can be calculated by (semi-)automatically using a computer, potentially enabling use of the differential diagnosis algorithms by non-professionals.

MEDICAL DEVICE DEVELOPMENT

Although diagnostic ultrasound devices are abundant on the market and are often cost-effective compared to diagnostic imaging modalities, relatively few have the capability to transmit and receive at frequencies high enough (over 15 MHz) for dermatological applications. Moreover, even ultrasound systems or transducers specifically designed for

dermatological investigation lack cost-effectiveness, portability and non-expert usability. For this reason, the Ultrasonic Bionic Technologies group of the Jedlik Laboratories *(see pp. 51)* has undertaken to develop a user-friendly ultrasound device specifically aimed for dermatological applications, with the aim of evaluating its effectiveness within the currently discussed working group. In order to enable a manually scanned transducer to create pictures from a series of so-called A-lines whose spatial location is unknown, we developed an algorithm based on the decorrelation of A-lines during manual scanning [5].

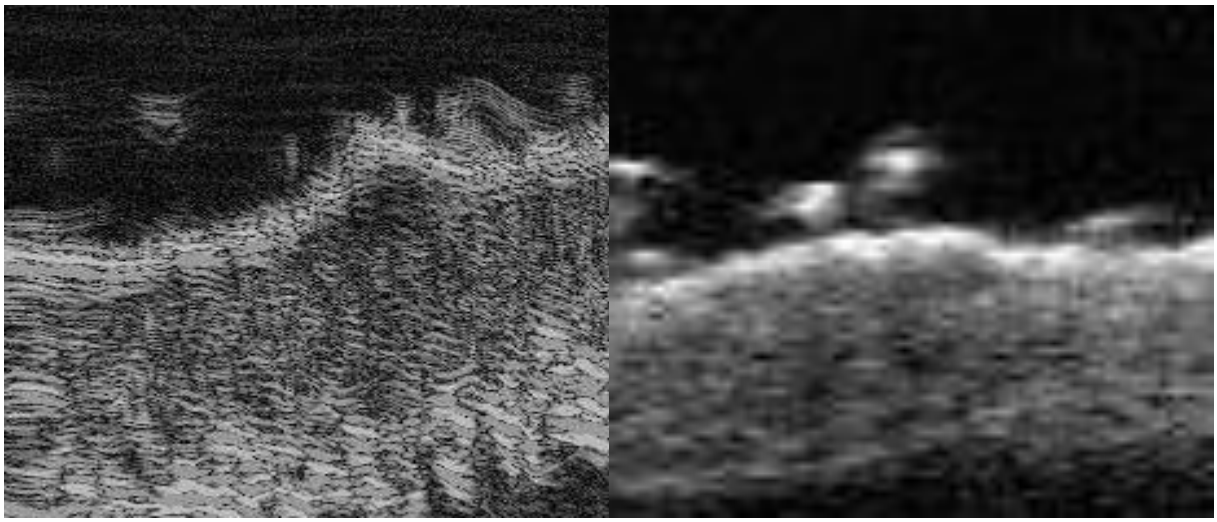

Fig. 1 *Ultrasound images of a nevus. Left: imaged using our own UltraDerm device. Right: imaged using a competitor (Draminski/Interson). Work with Gergely Csány and Helga Feiszthuber.*

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IV. DIGICON (DIGITAL MEDICAL CONSULTATION)

GÁBOR PRÓSZÉKY DSC, Professor, principal investigator; JÁNOS NÉMETH MD DSC, Professor; BORBÁLA SIKLÓSI *Assistant Professor*; GYÖRGY OROSZ PhD, LÁSZLÓ, LAKI PhD, ATTILA NOVÁK PhD
PhD student: BALÁZS INDIG

SHORT DESCRIPTION OF THE ACTIVITIES

Every day vast amount of clinical documents are gathered in hospitals in different countries containing great amount of valuable hidden information. Although this information is available in textual format, there are a number of pre-processing stages that need to be employed before the valuable data is condensed to a frame-based knowledge for the purpose of automated DDS utilization. Clinical documents likely contain some errors of the following types therefore this pre-processing stage requests robust and complex natural language analysis tools:

- typing errors: these errors occur during text input mainly by accidentally swapping letters, inserting extra letters, or just missing some
- misuse of punctuation marks
- non-standard spelling
- medical terminology errors: These errors arise from non-standard use of special medical language that can be a mixture of the Latin and the local languages (e.g. *tensio/tenzió/tenzio/tensió*).

The result of the pre-processing is a noise-*reduced* text, which still contains many ambiguities. Basic steps required for a normalized representation are:

- resolving abbreviations
- grammatical annotation (POS tagging, syntactic parsing)
- named entity recognition: doctors, drugs, diseases, dates, scores and measures, treatments and other health concerns
- explore semantic relations (synonyms, lexical semantics, etc.)
- concept matching: mapping variable lexical and surface representations of the same concept to a unique identifier with the use of a knowledge base.

After basic normalization, the resulting expanded data is to be stored in a uniform representation where the units of information are clearly separated. A higher level of structuring analyses the records on the line of each patient's medical history. Since raw texts do not necessarily include information about it, the timeline will be recognized automatically.

Both the patient's medical history (describing a patient's run in the medical history) and the history of a certain case is recognized and linked.

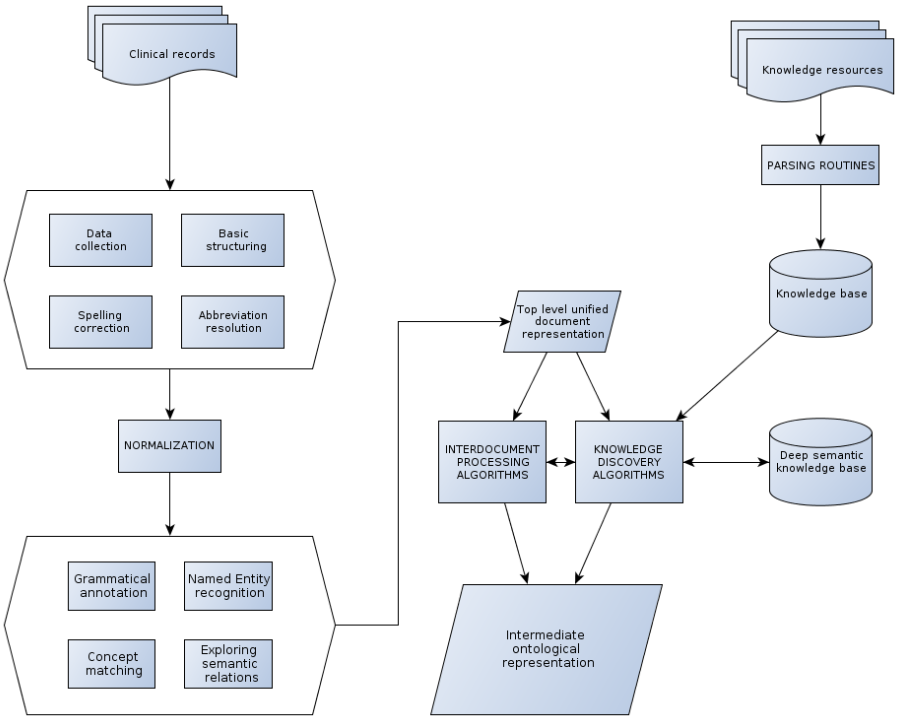

Fig. 1 *The preprocessing modules applied to the raw clinical documents in order to achieve a higher-level and normalized representation and ontological mappings.*

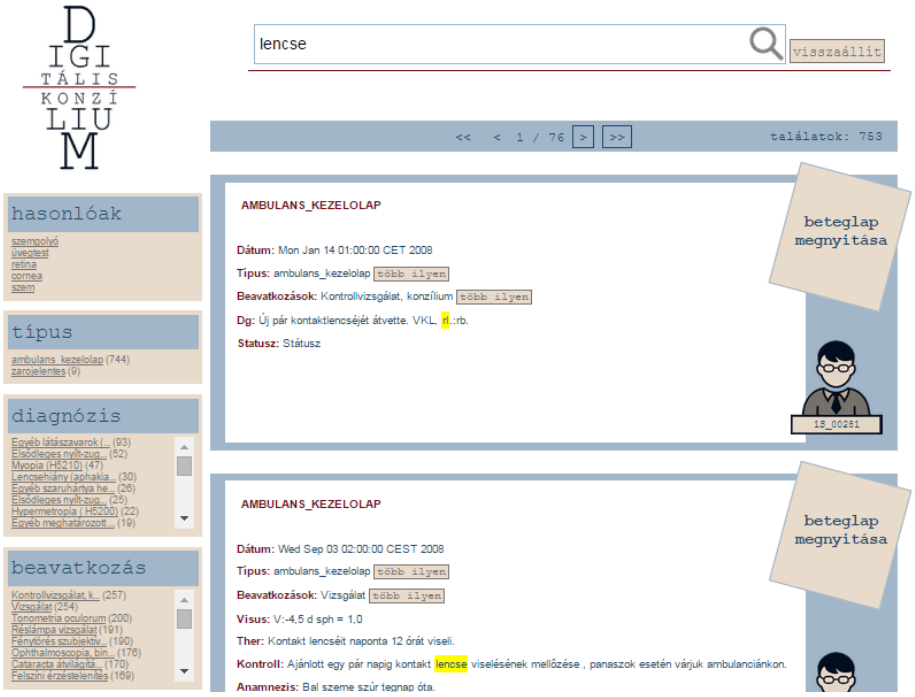

Fig. 2 *The screenshot of the pivot implementation of the ophthalmology search engine providing doctors advanced search possibilities in the database of the enhanced documents*

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