THE JEDLIK LABORATORIES
RESEARCH ACTIVITY – AN OVERVIEW
2020
ANNUAL PROCEEDINGS

FACULTY OF INFORMATION TECHNOLOGY AND BIONICS
PÁZMÁNY PÉTER CATHOLIC UNIVERSITY

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PREFACE

This booklet gives an overview on the recent structure and results of the research groups of the Jedlik Laboratories at the Faculty of Information Technology and Bionics of Pázmány Péter Catholic University.

During the last 5 years the fundamental research directions remained essentially the same, but several new young colleagues joined the research groups. The research infrastructure was also significantly improved primarily in the form of new laboratories and groups equipped with state of the art instruments. Here we have to mention the "Preclinical studies on dermal barrier and blood-brain barrier" and the "Systems biology of molecular and cellular networks" research groups led by Dr. Habil. Franciska Erdő, and Prof. Attila Csikász-Nagy, respectively. The research groups at Jedlik Laboratories form the ground of successful PhD training at the Faculty, since majority of the supervising professors at the Roska Tamás Multidisciplinary Doctoral School of Science and Technology perform their daily research work there. The recently obtained research grants, student prizes and individual scholarships clearly justify that Jedlik Laboratories is a key organizational unit at PPKE-ITK for maintaining the close connection between research and education which has been one of the most important objectives of the Faculty since the beginning.

This document contains the original introduction of Prof Tamás Roska (1940-2014), founding dean of the Faculty and first director of the Jedlik Laboratories. We are committed to preserve his human and scientific heritage, and to actively develop the conditions of quality research at the Faculty.

January 22, 2020

Prof. Attila Csikász-Nagy
Vice Dean for Research, Director of Jedlik Laboratories

Prof. Gábor Szederkényi
Head of the Roska Tamás Multidisciplinary Doctoral School of Science and Technology

INTRODUCTION TO THE FIRST EDITION

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 3 joint centers and 5 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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1. SIMULATIONS OF ELECTROMAGNETIC FIELDS AND FIELD-MATTER INTERACTIONS – TOWARD ENGINEERING QUANTUM ELECTRODYNAMICS

GYÖRGY CSABA, Associate Professor; ÁRPÁD I. CSURGAY, Professor; ÁDÁM PAPP, Postdoc

MODELING AND SIMULATION OF PHOTOSYNTHETIC ENERGY TRANSFER [1]

Increasing amount of experimental data suggest that quantum effects play a role in certain physiological processes, e.g. in photosynthesis, even in the vibrant media of living matter at room temperature.

We have performed a study how undamped and especially damped intramolecular vibrational modes influence the dynamics of photosynthetic exciton energy transfer, focusing particularly on the impact of vibrational relaxation on the efficiency of the process.

To approach the problem, we proposed a new general-purpose model formulated as a Lindblad-type master equation. Solving the equation numerically, first we demonstrated on dimer model systems at zero temperature that the presence of a vibrational mode can compensate the energy mismatch of the electronic states.

Then we showed that the damping of the intramolecular vibrational mode can further promote the exciton transfer by unidirecting the energy flow. We also verified that this enhancement surpasses the enhancement that can be attributed to the dephasing effect of the vibrational relaxation. Afterwards, we investigated how these phenomena depend on various system parameters.

Finally, we investigated the afore mentioned effects at room temperature in a more realistic system, namely a heptamer inspired by the FMO complex. Our results provide insight into the role of molecular vibrations in the exciton energy transfer from a new aspect.

Understanding the high efficiency of the biological photosynthetic processes suggests that developing quantum circuits could –at least in principle—enhance the energy transfer efficiency of solar cells and bionic sensors.

NANOSCALE SPECTRUM ANALYZER BASED ON SPIN-WAVE INTERFERENCE [2]

Magnetic excitations (spin waves) are one of the promising 'alternate state variables' in electronics, due to their potentially very low energy, short wavelength, and high speed. A number of proposals and/or device demonstrations use spin-waves for realizing Boolean logic gates, or non-Boolean computing primitives.

In our studies, we presented a new class of devices and also a new application area for spin-waves. We have shown that they are very well-suited for high-frequency and extremely compact spectrum analyzer devices. Our proposed device also exemplifies how ideas from non-Boolean, optical devices can be re-invented in the domain of spin-waves, which could be much more amenable to integration than light waves.

In the studied device, the microwave signal is first converted into spin-wave excitations. The Oersted field of a simple waveguide can generate a coherent spin-wave wavefront in a magnetic thin-film. The signal processing takes place in the spin-wave domain, via linear interference, and the resulting interference pattern is picked up electrically at the output.

We used analytic calculations and micromagnetic simulations to verify and to analyze the operation of the device. The results suggest that all performance figures of this magnetoelectric device at room temperature (speed, area, power consumption) may be significantly better than what is achievable in a purely electrical system. We envision that a new class of low-power, high-speed, special-purpose signal processors can be realized by spin-waves.

MODELING AND SIMULATION OF SUPERCONDUCTING JOSEPHSON-EFFECT QUANTUM CIRCUITS [3]

Nanotechnology and cryotechnology enable engineers to develop devices and integrated circuits in which quantum phenomena have dominant way.

Macroscopic finite-state 'artificial atoms' are realized exploiting superconductive Josephson effect, and these 'atoms' exchange microwave photons in superconductive microwave circuits.

The achievements of cavity quantum electrodynamics in quantum optics are mimicked in the microwave frequency range.

We have developed modeling and simulation techniques for quantum circuits. First, we approximated the quantum circuit as a closed quantum system, then we introduced more accurate open system models for quantum devices and composite quantum systems. The effects of amplitude and phase damping are illustrated by simulation. The role of classical resistors in quantum circuits have been investigated. Special attention was given to the almost standardized technology developed for superconductive microwave quantum circuits. We identified some open problems that circuit designers face in developing computer-aided-design tools for quantum circuits.

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2. CELLULAR WAVE COMPUTING AND SPATIAL-TEMPORAL ALGORITHMS

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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).

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3. VIRTUAL AND PHYSICAL MACHINES WITH MEGA-PROCESSOR CHIPS

Péter Szolgay, Professor; Zoltán Nagy, Associate Professor; András Kiss, Assistant Professor; István Reguly, Assistant Professor
Graduate students: Attila Fejér, Sam Khozama, Levente Márk Sántha

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. One example of fine grained cellular architectures are Field Programmable Gate Arrays (FPGA), which composed of more than a million logic elements, more than 10,000 coarser DSP blocks and thousands of 4kB on-chip SRAM blocks. Virtual machines equipped with these huge FPGA devices are available from the major cloud vendors making widespread availability of programmable logic devices for various users and application fields.

Traditionally, developing circuits for FPGA implementation required the knowledge of special hardware description languages (VHDL, Verilog). Complex algorithms described in common programming languages must be translated manually to create an FPGA based accelerator circuit, which is an error prone and time consuming process taking several months. Designer productivity can be improved by using the C/C++ based High Level Synthesis tools which appeared around 2010 and become a mature development methodology today. Some integrated tools support hardware/software co-design where the designer can mark computationally intensive functions for automatic FPGA implementation.

In most cases HLS tools are able to reduce design time only. To efficiently use these types of architectures new ideas and new methods are required in algorithm development. To utilize the cellular architecture of heterogeneous processing elements and memories new kind of parallel algorithms have to be developed. In this new scenario of computer science and computer engineering computational complexity, computing power is a multi-parameter vector where 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. C to FPGA compilers and FPGAs provide an excellent tool and platform for experiments to create and evaluate radically different architectures in a short time for several challenging computational problems.

Some new principles and examples are summarized below.

ELECTROPHYSIOLOGICAL SIGNAL ANALYSIS

The extracellular measurement of brain electrical activity contains local field potentials and mixtures of action potentials generated by the neurons. It is essential to determine which individual neuron produces the recorded unit activity, so spike sorting methods are used. High channel-count neural probes are capable of recording the activity of large neural ensembles from up to more than hundred individual brain positions simultaneously, pose an even greater challenge for spike sorting applied on general-purpose hardware. Real-time clinical applications could greatly benefit from a hardware-accelerated data processing, especially in the case of Field-Programmable Gate Arrays (FPGAs) or Application Specific Integrated

Circuits (ASICs), which are energy-efficient compared to traditional CPUs or GPUs, and can significantly reduce the computation time required to process large amounts of high-dimensional data. OSort is an online unsupervised template-matching spike sorting algorithm, which works on the detected spikes and uses them as features. Important parts of the algorithm are the automatically computed clustering and merging thresholds, which are calculated based on the standard deviation of the signal.

The algorithm works as follows: When the first spike is received from the detector, the mean of this spike is stored as the first cluster. The next incoming spike is compared to the cluster mean using squared difference as distance metric. If this distance is below the cluster threshold, then the spike is assigned to this cluster, if not then a new cluster is formed. This process is applied to all spikes. When the cluster assignment is done the mean of the cluster is updated and the merging begins. In this process the distance between the stored means and the new cluster mean are calculated. When the cluster with the lowest distance is below the merging threshold, then it is merged with the updated cluster.

The original version of the OSort algorithm works with a single-channel. The multi-channel version of the algorithm is similar to the original one, but the data flow and structure is completely redesigned. The original MATLAB algorithm is translated to C/C++ taking into account the special requirements of Xilinx Vivado HLS (High Level Synthesis) compiler. The spike input and cluster number outputs are mapped to an AXI-Stream bus while the threshold can be set via an AXI-Light connection. The full system requires additional blocks such as AXI interconnect, AXI-DMA engine, memory, Ethernet, ADC interface to connect to peripheral devices and an ARM processor to control the high level operation of the system. Due to the relatively low operand bit width the system can operate on 200MHz clock frequency on a Xilinx Zynq XC7Z020 device. If the number of clusters is maximized to 128 one spike (5x4x64 data points) can be clustered in 18,127 clock cycles in the worst case, which results in 90.635us clustering time for a spike or more than 11,000 spike/s. According to our measurements it is 40 times faster than the identical algorithm running offline on the PC (i7-4770, 3.4GHz, 8GB DDR3) in MATLAB.
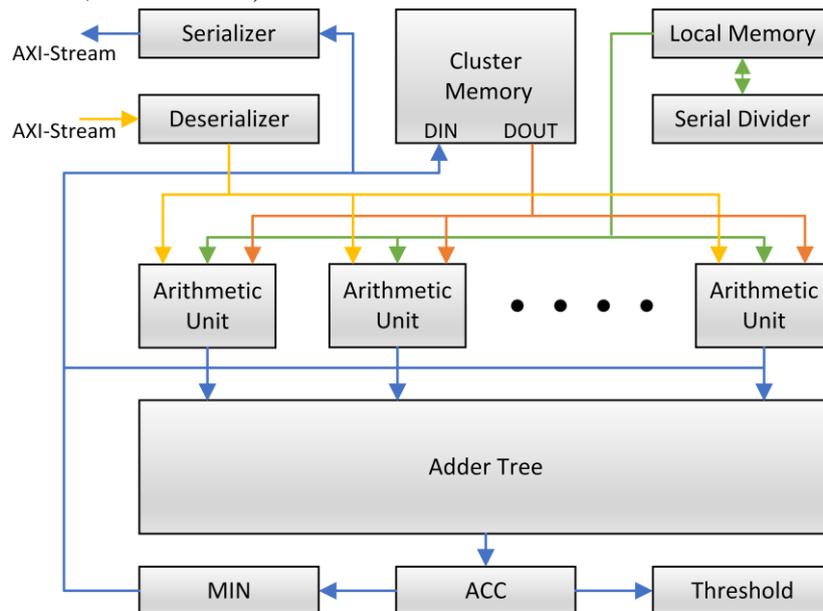

Fig. 1   Architecture of the Clustering Module of the OSort algorithm

SCALE-INVARIANT FEATURE TRANSFORM COMPUTATION

Feature detection implementation on FPGA has been the focus of the research community of vision research, due to the growing need in real-time performances in various tasks such as object matching, 3D reconstruction, and action recognition. Popular feature extraction algorithms such as Scale-Invariant Feature Transform (SIFT) have been successfully implemented. Nevertheless, the problem still remains important as for wearable devices one needs lower energy consumption than for stationary ones. A wearable computing framework has been developed for wearers of vision-assisted neuro-prostheses. In this scenario the amputee wears glasses with an eye-tracker and a stereo camera system is fixed on the upper-limb prosthesis. After the recognition of an object to grasp in the glasses' field of vision, it is necessary to locate the object of interest in the view of prosthesis-mounted cameras. This is fulfilled by detection of characteristic points and matching of cameras' views using these points. To do this SIFT point detection and matching has to be fulfilled to calculate Homography Matrix.

Our solution is implemented in C++ language using the Xilinx Vivado Design Suite HLS compiler to speed up development process and quickly explore various architectures for accelerating SIFT. The realized IP accelerator can be used in PYNQ project. PYNQ is an open source project from Xilinx which helps to design embedded systems with Xilinx Zynq Systems on Chips (SoCs) and supports the use of Python language and Python libraries.

We made some modifications on the original code and separated it into two different parts the Gaussian filter calculations and the keypoint detector and filtering parts. The Gaussian Filter unit can compute the Gaussian blurred image and the Difference of Gaussian blurred images, which is the first step of the SIFT computation. The second stage is the Scale Space Extrema maximum search unit which can calculate whether the current pixel is a maximum in its 3x3x3 range when it is saved as a candidate keypoint.

The proposed system is implemented on the TUL PYNQ-Z2 FPGA board and operating on 220Mhz clock frequency which makes it possible to process a FullHD (1920x1080@60FPS) video in real time. The generated hardware uses ~36% of the available FPGA resources therefore there are enough space left to implement further SIFT steps and implement more algorithms. The power dissipation of the current partial SIFT module is very low, just 1.672W which is acceptable for our system. The dissipation of the embedded ARM processor is 1.256W, while the FPGA programmable logic consumes only 0.274W.

FLUID FLOW SIMULATION

Numerical simulation of complex computational fluid dynamics problems evolving in time plays an important role in scientific and engineering applications. Accurate behavior of dynamical systems can be understood using large scale simulations, which traditionally requires expensive supercomputing facilities. Simulating complicated geometries requires unstructured spatial discretization which results in irregular memory access patterns severely limiting computing performance.

To accelerate the computation irregular memory access patterns should be hidden by temporally storing the relevant grid points in the on-chip memory of the FPGA or CPU cache. Therefore the cells should be reordered to get a banded adjacency matrix with bandwidth BW (for example by using the well-known Reverse Cuthill-McKee (RCM) matrix bandwidth

reduction algorithm). When cell i is processed only volumes in the [i-BW,i+BW] index range must be stored on-chip. After cell i is updated the center of the window is moved to the next cell. The oldest cell (i-BW) can be discarded and the new cell (i+1+BW) can be loaded. Computation is started by loading serial sequence of state values into the Memory unit until it is half filled. In this phase value of the first cell is loaded to the Current node register and the Neighborhood memory is filled by its neighbors using the incoming connectivity descriptors. When all neighbors are loaded valid stencil data can be send to the arithmetic unit in each clock cycle.

The proposed framework was tested by creating an FPGA based architecture to solve the 2D Euler equations describing motion of inviscid, adiabatic, compressible fluid flows. Performance of our architecture implemented on a Xilinx Virtex-6 XC6VSX475T FPGA is compared to a high performance Intel Xeon E5620 microprocessor running on 2.4GHz clock frequency. During the comparison various mesh sizes are used with 7,063 to 394,277 triangles. The measured performance of the FPGA is 325million triangle update/s or equivalently 69.22GFLOPs. According to our measurements performance of our architecture does not depend on the size of the mesh in the test cases. Comparison of the performance of the two architectures shows that the FPGA based system can outperform the Intel Xeon processor by computing 90 times faster.

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4. MTA-PPKE HUNGARIAN NATURAL LANGUAGE PROCESSING GROUP

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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 and quality estimation

- medical text mining

- syntactic parsing

- morphologies

- part-of-speech tagging

- spelling correction

- neural word embedding

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 necessarily correct input. In practice, human understanding is cooperatively done by several parts of the brain to deal with such problems efficiently, which can be modelled by introducing *parallelism* to our computational model. To incorporate such knowledge, state-of-the-art results of neurolinguistics and psycholinguistics are indispensable. The model that is to be created is also characterized by *performance*, thus methods of various fields of applied linguistics also meet in our research. Since current theories of computational text processing do 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.

Moreover, one of the most recent fields of natural language processing is using *neural networks* to represent and process various levels of written texts. We also aim at creating such models that are to be integrated into our parser but can also be used as standalone tools for

representing and analyzing syntactic and semantic aspects of words, phrases and larger bodies of texts.

We also apply our methods to *social media texts*, which provide an extreme test environment, since these texts include a very high ratio of noise. As a result, our methods are evaluated from the aspect of robustness against noise and once being able to process such texts, we are also working on creating the largest annotated Hungarian web corpus.

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5. COMPUTATIONAL NEUROSCIENCE

(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); SZABOLCS KÁLI, Associate Professor; ZSOLT LIPOSITS, Professor (Endocrine Neurobiology)
Graduate students: SÁRA SÁRAY, MÁTÉ MOHÁCSI, LUCA TAR
Students: ORSOLYA NÉMETH, DÁNIEL TERBE

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 major effort is now underway to construct large-scale data-driven models of the mouse hippocampus in the context of the European Human Brain Project. Experiments in the laboratory of Tamás Freund at the Institute of Experimental Medicine have resulted in a large database of neuronal morphologies, single cell electrophysiological recordings and synaptic properties for many identified cell types of the hippocampus. Neuronal and circuit models are then built based on these data using reproducible, automated workflows. To create morphologically and biophysically detailed models of various hippocampal cell classes, the densities of ion channels are tuned using advanced evolutionary algorithms. The electrophysiological behavior of the resulting cell models is validated against a variety of experimental findings using a battery of automated, quantitative tests implemented in the HippoUnit software package developed in the lab. The validated neuronal models are placed in the hippocampal volume, the connectome is derived, and the network is simulated on supercomputers. Data, tools, and models are made available to the research community via the platforms of the Human Brain Project.
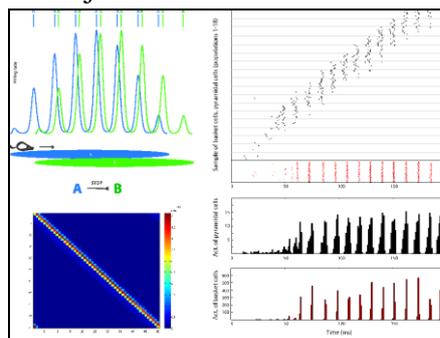
Fig. 1 *(top left) activity during exploration of two CA3 pyramidal cells with overlapping place fields, showing theta phase precession; (bottom left) matrix of synaptic weights between pre- and postsynaptic populations, ordered by place field location, which formed during exploration as a result of spike-timing-dependent plasticity; (right) spontaneous replay of learned sequences of activity during sharp-wave-associated ripple oscillation.*

2. The dynamics of hippocampal networks are also investigated using a combined experimental-modeling approach which uses simplified (point neuron) models and takes advantage of an improved hippocampal slice preparation that can generate several characteristic activity patterns of the hippocampus, either in control conditions or as a result of pharmacological or optogenetic manipulations. Investigations have revealed the

mechanisms of hippocampal sharp wave-ripple events, and the cellular and synaptic changes underlying switching between different types of network dynamics, which are mediated by subcortical inputs, and are normally associated with changes in animal behavior.

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6. NEUROENDOCRINE RESEARCH GROUP

(Department of Neuroscience, adjunct location at the Institute of Experimental Medicine of the Hungarian Academy of Sciences)
ZSOLT LIPOSITS, Professor; IMRE KALLÓ, Professor; IMRE FARKAS, Professor; CSABA VASTAGH, Professor
Graduate student: VERONIKA CSILLAG

RESEARCH ACTIVITY

The Neuroendocrine Research Group investigates primarily the neural- and hormonal regulation of the endocrine- and autonomic functions of rodents by using a combination of functional neuroanatomical, molecular biological and neurophysiological techniques in wild-type and genetically modified experimental animals.

The functions, activity and the signal transmission of the gonadotropin-releasing hormone (GnRH) producing neurons, which provide the primary output of the neuronal network, show significant changes during the cyclic operation of the ovaries, as well as, after the cessation of the cycles, during menopause.

The sex- and estrous cycle phase-dependent gene expression profile is mapped with single cell high throughput assays and validated in the key cellular elements regulating reproduction, including the GnRH neurons. The highly relevant regulatory genes and signaling pathways are identified by using bioinformatical and analytical approaches. The molecular biological, neuroanatomical and functional data produced establish a base for modelling the consequences of the pathological and potential therapeutic changes in endogenous levels of gonadal hormones.

The major research topics are the followings:

- Examination of the mutual regulatory inputs between the GnRH neurons and their afferent neuronal systems during the different phases of the ovarian cycle and in pathophysiological conditions.

- Investigation of the age-dependent reduction of estrogen-signaling, studying its consequences in the central nervous system, and providing data for prevention and establishing new therapeutic approaches.

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7. BIOINFORMATICS LAB

SÁNDOR PONGOR, Professor; JÁNOS JUHÁSZ, Postdoc; BALÁZS LIGETI, Postdoc
Graduate students: REGINA KALCSEVSZKI
*Students*: ÉVA MERCÉDESZ KISTÓTH, PÉTER KOVÁCH, BÁLINT STELLEK, DILAN DANIAL, MÁRTA 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.
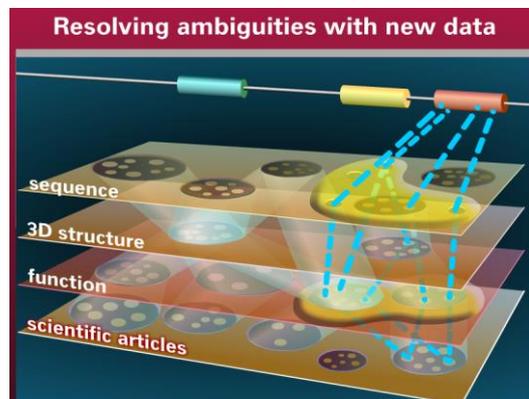
HIGH THROUGHPUT DATA/MINING OF PROTEOMICS DATA
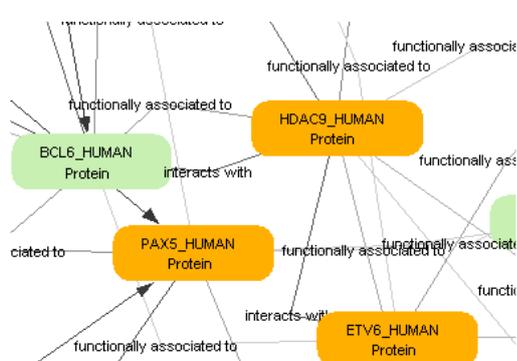
High throughput mass spectrometry analysis produces large amounts of noisy data that have to be filtered and preprocessed with computational tools before subjected to detailed analysis and interpretation. Our strategy uses principles borrowed from cognitive psychology for identifying network patterns 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 cannot which may provide important clues to polymicrobial diseases.
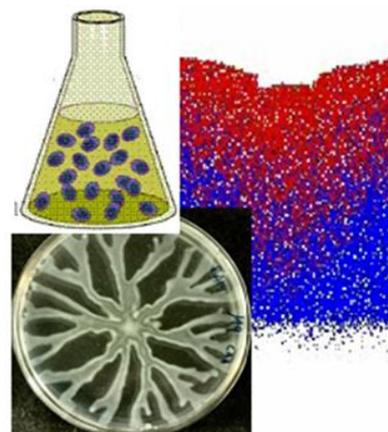
COLLABORATIONS:

- Prof. Balázs Győrffy, Semmelweiss University and Research Centre for Natural Sciences, Hungarian Academy of Sciences, Budapest, Hungary

- Prof. Attila Kertész-Farkas, National Research University Higher School of Economics, Moscow, Russia

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

- Prof. Dóra Szabó, Semmelweiss University, Budapest, Hungary

- 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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8. STRUCTURAL BIOLOGY AND PROTEOMICS

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Students: FANNI FARKAS, BRIGITTA MARUZS, ANDRÁS LÁSZLÓ SZABÓ

The two main projects in the laboratory are

i. Computational analysis of protein structure and dynamics

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, members of the small prolyl isomerase parvulin family and selected PDZ domains of proteins of the postsynaptic density.
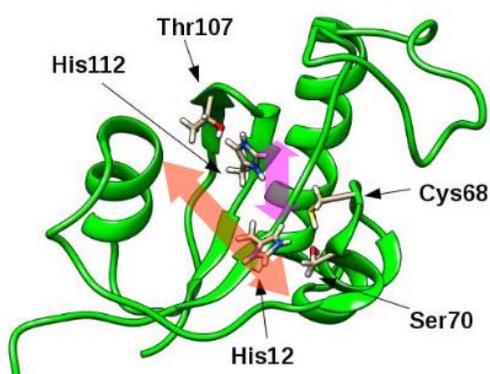
Fig. 1 *Structure of the parvulin fold with the identified motions: opening.closing of the substrate binding cleft (salmon) and residues of the conserved hydrogen-bonding network (purple) indicated.*
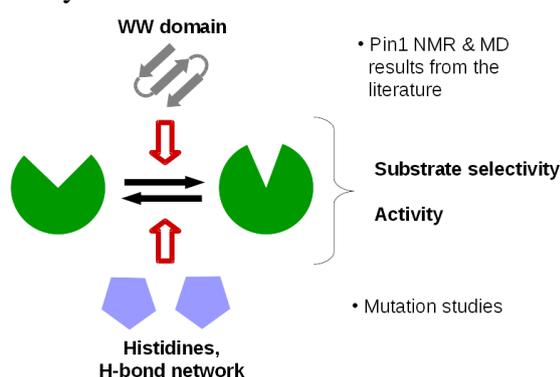
Fig. 2 *Proposed general regulatory mechanism of the parvulin PPIase family. The exnent and dynamics of the opening of the substrate-binding cleft can be modulated by interactions with the WW domain (if present) and the exact configuartion of the hydrogen.bond network centered around two conserved histidine residues.*

Single alpha helices (SAHs, also known as charged single alpha helices, CSAHs) represent a unique structural motif that contradict the long.standing pradaigm of the instability of isolated alpha-helices in aqueous solution.These segments exhibit a charectristic repeating pattern of charged residues (Glu,Arg and Lys). We have set up a web service for the detection of such motifs, available at csahserver.itk.ppke.hu and have also implemented the most computer.intensive detection algorithm, FT_CHARGE of FPGA boards in collaboration with Dr. Zoltán Nagy. Using this implementation, we are able to provide monthly releases of CSAHDB, a database of SAHs predicted from the full UniProt protein sequence database. Curiously, SAHs are abundant in RNA.binding proteins although their direct involvement in RNA binding is unlikely. We have built architectural models of the paraspeckle, a large supramolecular structure binding long noncoding RNA molecules and having a conserved SAH segment. We found that the position of the SAH is compatible with its role as a ruler to properly position the RNA-binding domains upon the assembly of the ribonucleprotein complex.

Fig. 3 *Architectural model of the protein scaffold of the paraspeckle ribonucleoprotein complex found in eukaryotes.*
SAH segments may be responsible for the exact positioning of dimers of the constituent proteins (NONO and PSPC1) relative to each other

The postsynaptic density is an elaborate network of proteins capable of dynamic rearrangement. We have successully produced several selected domains of postsynaptic proteins, for which NMR investigations are under way in collaboration with prof. Gyula Batta, University of Debrecen. Our aim is to characterize the structural and dynamical changes in these proteins upon interaction with their partners.
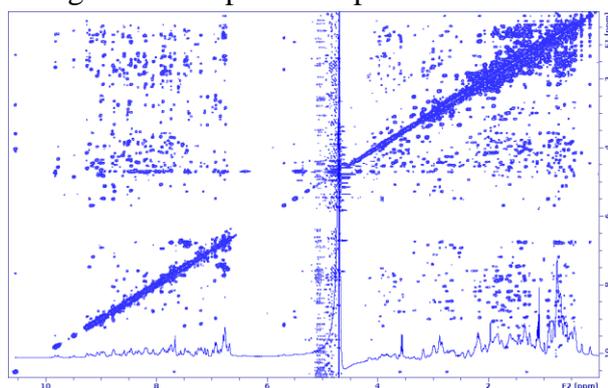
Fig. 4 *Homonuclear NOESY spectrum of human PSD95-PDZ3 at 700 MHz obtained at the University of Debrecen. The spectrum is characteristif of a well-folded protein as expected for the globular PDZ domain.*

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9. ANALYSIS AND CONTROL OF DYNAMICAL SYSTEMS

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Students: BALÁZS CSUTAK, MIHÁLY VÁGHY, GERGELY HORVÁTH, HALA JABBOUR
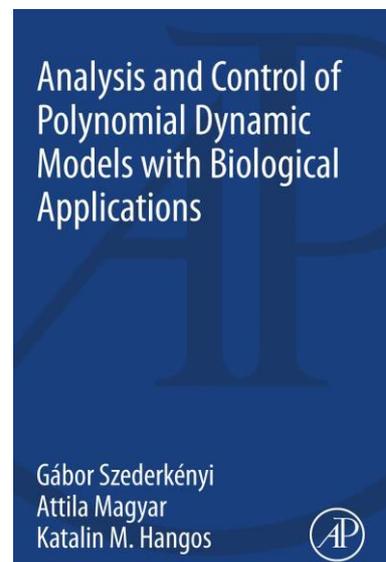
SCIENTIFIC BACKGROUND: THE SYSTEM THEORETIC POINT OF VIEW

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 control of biologically motivated nonlinear systems

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 polynomial nonnegative system classes that have clear biological relevance, good dynamical descriptive power, and a computationally advantageous algebraic structure.

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 known dynamical system. In [1], the first solution in the literature is given to determine all possible structurally different linearly conjugate realizations (i.e., reaction graphs) of a given kinetic polynomial dynamical system. This approach is extended to uncertain kinetic models in [2]. The stability notions known for complex balanced kinetic models are extended for time-delay models in [3]. The notion of stoichiometric compatibility class is generalized, and it is shown that complex balanced equilibria are at least locally stable in delayed models. Our research results on kinetic and quasi-polynomial systems are summarized in [4].

Analysis and Control of Polynomial Dynamic Models with Biological Applications

Gábor Szederkényi
Attila Magyar
Katalin M. Hangos

Computing or approximating the domain of attraction (DOA) is a fundamental task in control theory. An improved method for computing a bounded estimate of the DOA of locally asymptotically stable uncertain rational nonlinear system models is proposed in [5].

Game theoretic analysis and design of complex networks

The game theoretic approach for investigating networks and routing problems have been among the intensively studied fields in recent decades. The application area is really wide including electrical, telecommunication, economic and biological networks. Our latest contributions in this field are the following. A cooperative game-theoretic framework is introduced in [6] to study the behavior of cooperating and competing electrical-energy providers in the wholesale market considering price-preference rational consumers. It is shown that cooperation of generators may be necessary to divert consumers from their previous providers. In [7], we consider a wireless contextualization of the local routing protocol on scale-free networks embedded in a plane and analyze how cooperation affects network efficiency, and also the stability of cooperation structures. It is shown that the proposed cooperation model enhances the network performance in the sense of reduced passage time and jamming. A discrete time probabilistic model of depositor behavior is proposed in [8] which takes into account the information flow among depositors. The optimal offers of the bank can be computed as a result of a suitably constructed nonlinear optimization problem.

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10. INTEGRATIVE NEUROSCIENCE GROUP

ISTVÁN ULBERT, Professor; GYÖRGY KARMOS, Professor Emeritus; LÚCIA WITTNER, Postdoc; RICHÁRD FIÁTH, Postdoc; GERGELY MÁRTON, Postdoc; DÁNIEL HILLIER, Assistant Professor
Graduate students: BÁLINT FILE, BEÁTA TÜNDE SZABÓ, ÁGNES KANDRÁCS, CSILLA SZABÓ, CSABA KÖLLŐD, FADEL WARD, WAHDOW MOUTZ, ANDRÁS ADOLF, GERGELY MÉSZÁROS
Students: HUDA YOUSEF, ANDRÁS BOHN, ADRIENN LILLA MÁRTON, MELINDA RÁCZ, DOROTTYA SZÁSZ, TIBOR NÁNÁSI, CSABA LIBER, ZSÓFIA VIRÁGHALMY, KINGA RÉKA TASNÁDY, VIOLA MATUSZ, ÁDÁM JUHÁSZ, ÁDÁM DEBRECENI, SOMA NYÁRI, MÁRTON VOLOSIN
Research Assistant: DOMONKOS HORVÁTH

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 (RCNS HAS), Institute of Technical Physics and Materials Science (CER HAS), Institute of Experimental Medicine (HAS) and the National Institute of Clinical 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 multi-scale interactions in the thalamo-cortical system in animal models. We have successfully validated the two-dimensional electronic depth control silicon probe in vivo (see Fig 1.).

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.
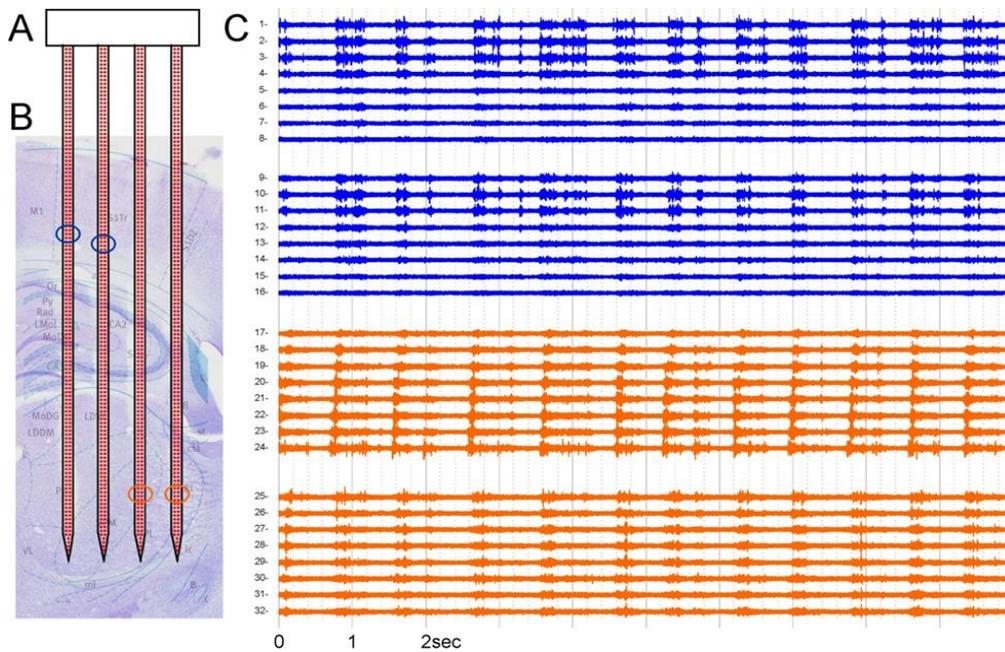

Fig. 1   *A: Schematic picture of the electronic depth control probe developed in an EU FP6 collaboration. The innovative feature of the probe is the electronically addressable recording site selection that allows the experimenter to change registration areas without physically moving the probe in the 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 (RCNS HAS), Institute of Technical Physics and Materials Science (CER 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 electrophysiological 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 registration, and intervening EEG, EOG, EMG and eye movement following algorithms.

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11. MULTI-PHOTON MICROSCOPY

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Graduate student: ZSOLT MEZRICZKY
Students: ANNA MIHÁLY, BENEDEK SZMOLA
Research assistant: DÉNES PÁLFI

We would like to examine the elementary units and the functionality of learning and memory with our experiments. Our aim is to understand how the brain can encode the information acquired from learning in its cells. We measure learning related neuronal responses of different brain areas of behaving mice with the help of our high-efficiency, high resolution microscope.
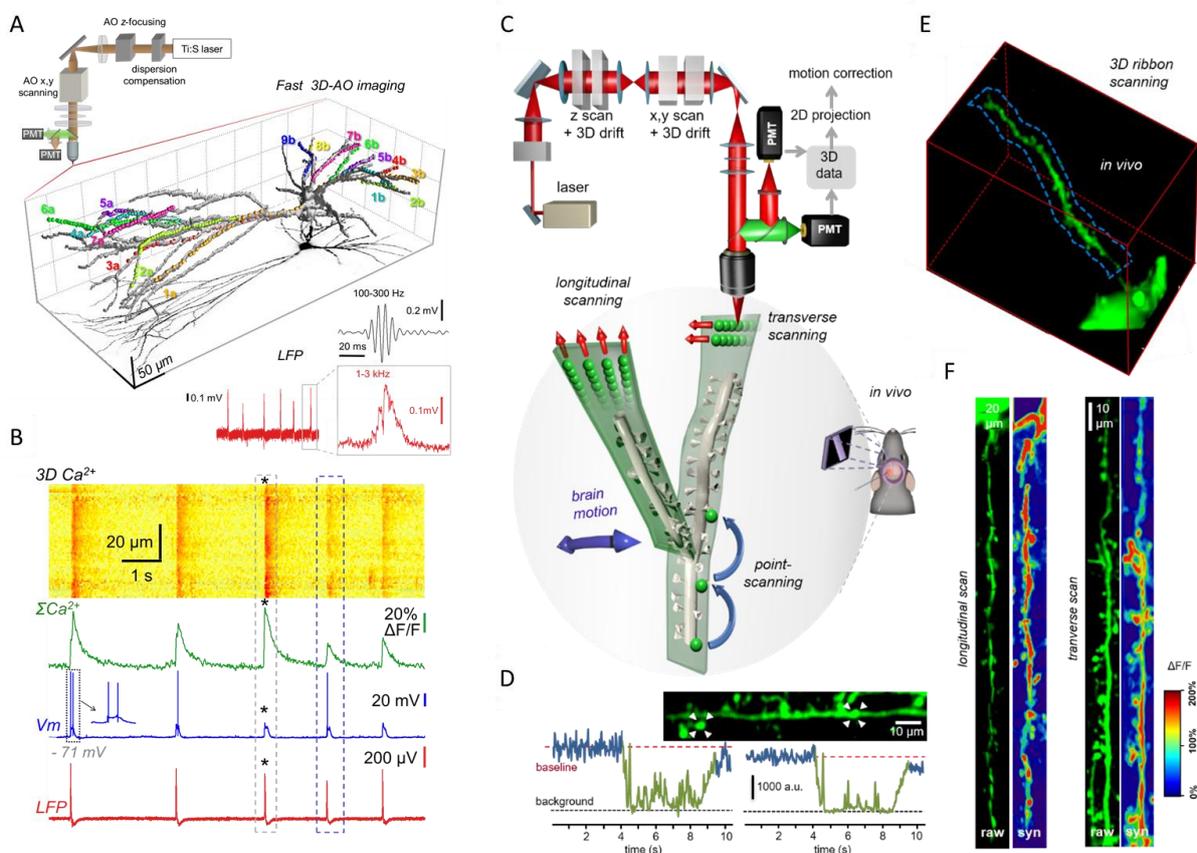
Fig. 1 *In vitro and in vivo Ca^{2+} imaging of neuronal activities in single cell level. (A-B) SPW-R associated dendritic spikes in vitro (see: Chiovini, Turi et al. 2014). (C-F) In vivo imaging of spiny dendritic segments with 3D DRIFT AO microscopy in behaving animals (see: Szalay, Judák et al. 2016).*

RESEARCH TOPICS

Test and apply newly synthetized uncage materials *in vitro* and *in vivo*

Caged compounds are excellent tools to simulate and modulate neuronal activity patterns from subcellular to network level. We introduced DNI-Glu-TFA and MNI-Glu-TFA cage compounds with high two-photon action cross section. We have developed a new enzymatic elimination method with a broad application range in one and two-photon uncaging experiments which eliminates the side effects of the continuously escaping neurotransmitters.

We demonstrated the efficiency of the new method by examining two salt of glutamate materials in neurophysiological experiments, one of which, DNI-Glu-TFA, has more than 7.2 times higher two-photon uncaging efficiency and a smaller GABA receptor blocking effect than MNI-Glu-TFA (see: Pálfi, Chiovini et al. 2018). Although highly efficient excitatory caged molecules have already been synthesized, the development of inhibitory caged molecules for two-photon microscopy has proven to be difficult. Therefore, here we ready to develop a new, more effective caged GABA material.

2D two-photon measurement of single cell and neuronal network activities *in vitro and in vivo*

Sharp wave-ripples (SPW-Rs) activity is involved in the process of memory consolidation. We investigate spontaneous single cell and neuronal network activities during SPW-Rs in the hippocampus CA3 region under *in vitro* and *in vivo* conditions. In our previous work, we have evinced dendritic regenerative activities, calcium spikes and interneuronal ripple oscillations in fast spiking parvalbumin containing interneurons *in vitro* (Chiovini et al. 2010, Chiovini, Turi et al. 2014). These results support the idea of the existence of dendritic supralinear signal integrations during SPW-R oscillations *in vitro*. Recently we have extended our interest of these *in vitro* and *in vivo* experiments with the measurement of pyramidal neurons to the better understand of the global and spontaneous neuronal network activities.

3D two-photon measurement of single cell and neuronal network activities *in vivo*

Understanding brain function requires novel imaging methods such as 3D randomaccess point scanning that can simultaneously read out neural activity on both the dendritic and somatic scales. Our 3D AO scanning method can increase measurement speed and signal-to noise ratio by up to 6-9 orders of magnitude, but suffers from one main disadvantage: fluorescence information is lost during brain movement in awake, behaving animals as the amplitude of brain motion is much larger than the diameter of a single excitation spot. We developed a novel fluorescent imaging technology, which can extend each scanning point to small 3D lines or surface or volume elements, preserving fluorescence information for fast off-line motion correction. Our method effectively eliminates *in vivo* motion artefacts, allowing fast 3D measurement of over 100 dendritic spines with 3D lines, over 100 somata with squares and cubes, or multiple spiny dendritic segments with surface and volume elements in moving animals. We used the new technology to record activity of inhibitory neurons in the moving brain of behaving animals. We revealed a new, broadcasted signalling pathway which activates learning mechanism through the entire neocortex during reward and punishment.

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12. MOVEMENT ANALYSIS AND MOTOR CONTROL LAB

JÓZSEF LACZKÓ, Associate Professor
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Student: BALÁZS RADELECZKI
Research assistant: MÁRTON BESE NASZLADY

The Movement Rehabilitation Laboratory studies how human limb movements are controlled to execute well-coordinated movements. Such movements are, for instance, reaching an object with the arm or transporting an object held in the hand; lower limb and upper limb cycling movements as bicycling or am cranking. 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. The laboratory cooperates with the Department of Computational Sciences of the Wigner Research Centre for Physics (HAS Wigner RCP) and with the Department of Information Technology and Biorobotics, Faculty of Science, University of Pecs.

In the laboratory we apply an ultrasound based movement analyzing system (ZEBRIS, Ivry, Germany) for recording kinematic and muscle activity signals during human limb movements. We place ultrasound emitting markers on anatomical landmarks of the body and recorded their positions. Simultaneously we record muscle activities by surface electromyography (EMG).

Fig. 1 *Arm cranking movements of an able bodied participant. Muscle activities (EMG) and kinematic variables are measured while the participant is arm cranking on an arm-cycle ergometer.*

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. We use biomedical engineering methods and biomechanics to investigate and understand how humans use and control their movements and to discern hidden features of multi-joint limb movements.

Our motivation is to improve physical abilities of people who partly lost their motor and sensory functions. Beside basic research our aim is to help to reactivate paralyzed muscles and to restore lost motor functions for people who suffered accidents or neurological

disorders as spinal cord injury. One particular field of research and application is Functional Electrical neuromuscular Stimulation (FES).

Based on measured and averaged kinematic parameters and muscle activities (Electromyograms) of able bodied people we define muscle activity patterns that are applied for controlling FES for spinal cord injured persons with paralyzed limbs. FES is a technique to generate muscle activities by transferring electrical signals from a controller to muscles via electrodes to evoke limb movements. During the last several years, in cooperation with the National Institute for Medical Rehabilitation and the University of Physical Education we trained more than 40 spinal cord injured patients whose lower limbs were paralyzed to perform lower limb cycling movements on a cycle-ergometer using their own muscles. Otherwise these people would not be able to generate active muscle forces.

Fig. 2 *Spinal cord injured, lower limb paralyzed patient is cycling on an ergometer in the National Institute for Medical Rehabilitation using a multichannel electrical stimulator device developed at the Pázmány Péter Catholic University.*

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13. SUPERRESOLUTION IN OPTICAL AND ULTRASONIC DETECTION (SOUND) LABORATORY

Miklós Gyöngy, Associate Professor
Graduate students: Janka Hatvani, Ákos Makra, Péter Marosán

LABORATORY OVERVIEW

The aim of the imaging group is to understand various wave processes and phenomena to map the properties of various objects, including biological tissue. Primarily ultrasound is used, however other modalities such as optics and CT are also of interest. We develop models that allow us to go beyond the classical resolution limits imposed by the diffraction limit.

IMAGING

We are developing a portable ultrasound device to image skin using ultrasound, using high frequencies (~ 20 MHz) to provide high-resolution (< 1 mm) images.
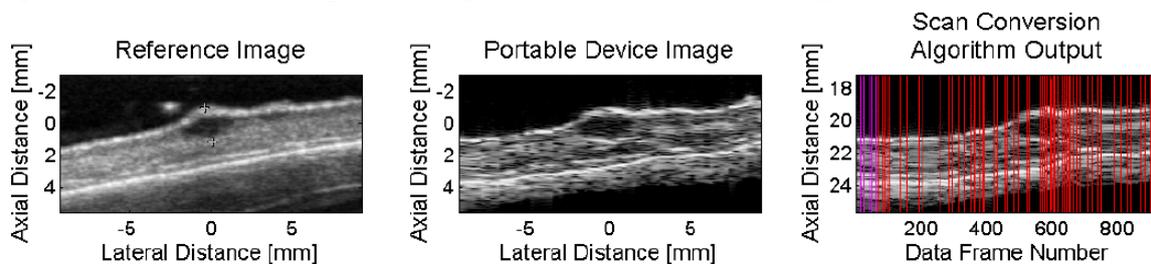

Fig. 1   *Comparison of ultrasound images of a skin lesion. Left: commercial device. Centre: own portable device. Right: scan conversion algorithm in action, with red lines showing scan lines that are selected by our algorithm based on our real-time data-based scan reconstruction algorithm. Image source: [1].*

We have found that for ultrasound images, processing in the axial (or depth) direction enhances image resolution even in cases where the point spread function is depth-dependent.
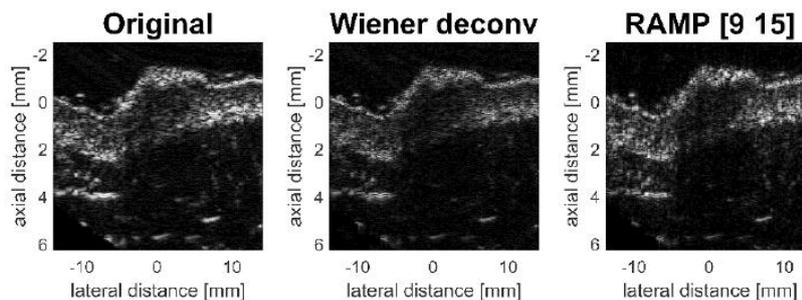
Fig. 2   *Resolution enhancement of a skin image using axial processing. Left: original image. Centre: result of Wiener deconvolution in the axial direction. Right: result of ramp filtering in the axial direction. Both approaches improve not only the depth resolution, but also (counterintuitively) the lateral resolution. Image source: [2].*

In order to test our approaches on experimental data while having access to the ground truth, we have developed a methodology to print 3D phantoms with known scatterer distributions.

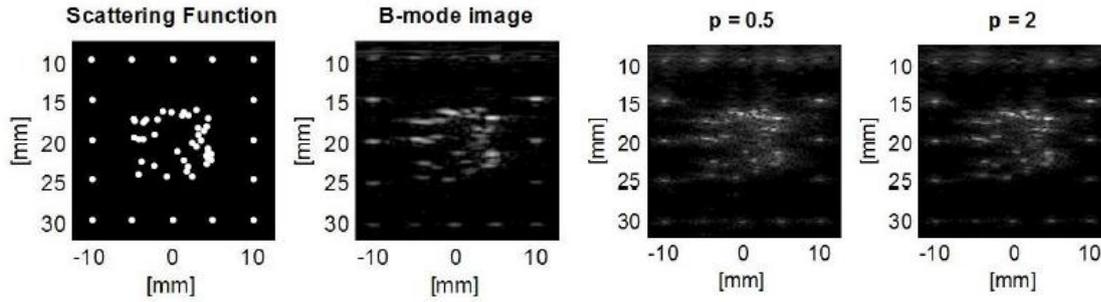**Fig. 3** *3D Printing methdology to test deconvolution algorithms. From left to right: original scattering function design; resulting B-mode image; result of lp deconvolution with p=0.5; result of lp deconvolution with p=2. Image source: [3].*

Our research into image resolution enhancement also spans CT imaging, where our recent results suggest the potential superiority of CNN approaches over classical deconvolution methods.
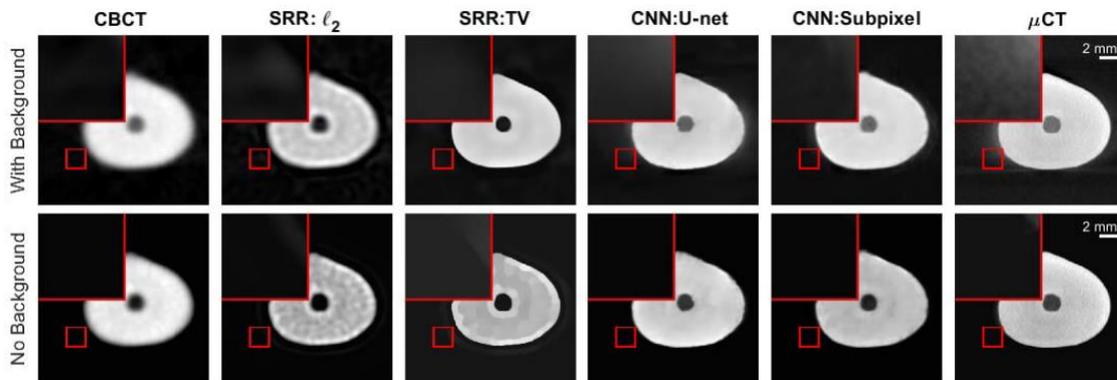

Fig. 4 *A comparison of classical image resolution enhancement approaches with deep learning approaches to enhance the resolution of CT teeth images. From left to right: original cone-beam CT image, two classical deconvolution approaches, two CNN approaches, ground truth micro-CT image. Top: with original background. Bottom: with background removal. With the aid of background removal, CNN methods are superior to classical deconvolution methods. Image source: [4].*

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14. SPINTRONIC AND NANOCOMPUTING LABORATORY

GYÖRGY CSABA, Associate Professor; ÁDÁM PAPP, Postdoc

LABORATORY OVERVIEW

The magnetics group uses optical methods to probe magnetic phenomena on submicrometer spatial resolution and with subnanosecond temporal resolution – these measurements help in the characterization of spin-based computing devices.

OPTICS, NANOMAGNETICS

Our group is working on nanomagnet and spin-wave-based computing devices – these emerging computing architectures replace electrical signals by magnetic (spin-based) signals and may allow ultra low energy and fast electronic circuitry. One promising direction of spintronic research is to use spin waves and spin wave interference patterns for microwave signal processing. This requires understanding magnetization processes with high spatial and temporal resolution.

In our lab we are currently building a one of a kind Time-Resolved Magneto-Optical Kerr Effect (TR-MOKE) setup. This uses subnanosecond laser pulses to excite magnetization dynamics in magnetic nanostructures and uses the light reflected from the sample to map magnetization dynamics.

A primary goal of the research is to characterize the spectrum analyzer device that our group has recently proposed and patented. The samples will be fabricated by our collaborators at the University of Notre Dame, USA and at the Technical University of Munich, Germany. Measuring, characterizing the samples is perhaps the most challenging aspect of the work and lion share of this work will be done in this lab.
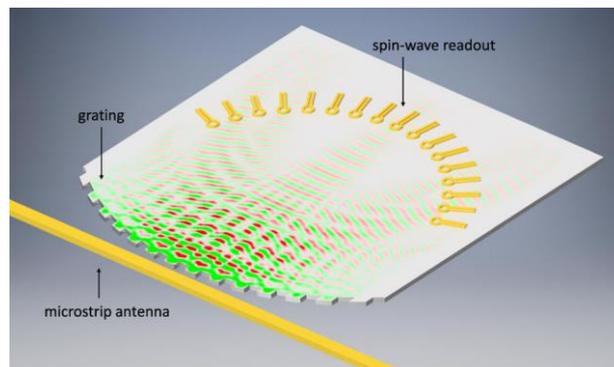
Fig. 1 *A schematic drawing of a spin-wave-based spectrum analyzer as described in [1].*

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15. BIOMICROFLUIDICS RESEARCH GROUP

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Research assistant: MÁRIA LAKI

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

- Hydrophoresis

- Acoustophoresis

The main aim of the Biomicrofluidics Laboratory is to develop devices for medical, veterinary and industrial purposes. We are focusing on miniaturization of analytical processes into microfluidic devices. Fundamental and applied research is carried out in strong collaboration with large science institutes and industrial partners. The scope of our laboratory contains the fields of food safety, human healthcare and chip integrated separation techniques.

FOOD SAFETY

Food safety is an extensive scientific discipline that describes handling, preparation and storage of food in ways that prevent foodborne illnesses. This includes a number of routines that should be followed to avoid potentially severe health hazards. Food is able to transmit diseases from person to person, or it can serve as a growth medium of bacteria that might cause food poisoning. In developed countries, there are complex standards for food

preparation, whereas in less developed countries the availability of safe water is the main issue. In theory, food poisoning is 100% preventable; according to the WHO, there are five key principles of food hygiene:

- Stave off contaminating food with pathogens spreading from people, pets and plants
- Separate raw and cooked foods in order to prevent contaminating the cooked foods
- Cook foods for the appropriate length of time and at the appropriate temperature
- Store foods at the proper temperature
- Use safe water and raw materials

The main goals of the Biomicrofluidics laboratory related to the field of food safety are the development of novel methods to detect foodborne pathogens and to provide help medical doctors, veterinarians and laboratory attendants. The consumption of food is evolving thanks to the growing population and needs. In order to protect the health of the consumers all actors involved in food processing are responsible for the quality of their product from farms to the cook. Foodborne pathogen testing and detection is a major concern for food industries. The process of pathogen detection generally takes place in two steps: the sample preparation (enrichment from high volume), and genotyping (the usage of new generation gene sequencing). Our highlighted ongoing research project is to combine the traditional sample preparation techniques with the genotype sequencing within one microfluidic device. Our lab is dealing with the most spread foodborne parasites and pathogens. One of the most widely known foodborne illness is listeriosis which is a bacterial infection caused by *Listeria monocytogenes*. The infection of food with the *Listeria* bacterium could be detected by traditional microbiological methods, but these methods require very long analysis time and adequate sample preparation methods. Lab-on-a-Chip systems are new opportunities to decrease the sampling and examination time in clinical applications using isotherm amplification method with high specificity, low detection limit and lower volume of the samples. In our laboratory we develop a fully automatized microfluidic device that can make lysis, DNA purification and amplification and the validation on a chip.
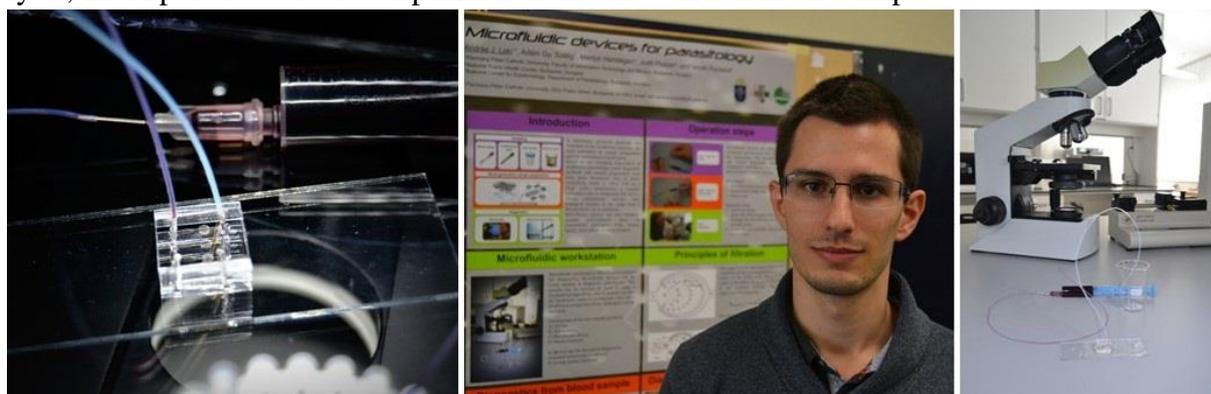
HUMAN HEALTHCARE

The human blood should be considered as a diagnostic tool that carries information about the condition of the human body. We are also able to monitor the state of each organ, moreover the functionality of the cells without any biopsy only from the analysis of the bloodstream. The variance with the normal state can imply the presence of different diseases.
The scope of the Biomicrofluidics Laboratory related to the human healthcare is focusing on

the analysis of serological samples. The potential coming from the analysis of the extracellular microvesicles/exosomes highlights the opportunity the better understanding of the cell-to-cell communication, the seeds for subsequent growth of additional tumors (metastasis) and the behavior of circulating tumor cells (CTCs).

In the last two decades, the increasing number of medical researchers on the field of cancer diagnostics are turning their interest onto the CTCs. The idea is getting to be accepted that these CTCs are responsible for the cancer transfer between different organs and for the majority of cancer-related deaths.

The enumeration of circulating tumor cells (CTC) using microfluidic devices is a challenging research field nowadays. The main aim of our project is to construct a robust, throughway, reliable microfluidic device, which could filter out the CTCs from human blood efficiently. The number of CTCs could be counted easily and their viability could be estimated.

Tumor cells will be filtered out in so-called chalices. The process can also be monitored by the fluorescence staining of the cells. However, the tumor cells circulating in the blood stream are very rare: approximately one circulating tumor cell can be found among a few millions of white blood cells and billions of red blood cells. Even in patients who have tumors in a highly metastatic state, the number of CTC's just a few pieces in one milliliter of blood. Therefore it is essential to design a more efficient filtering device for the isolation of the cells.
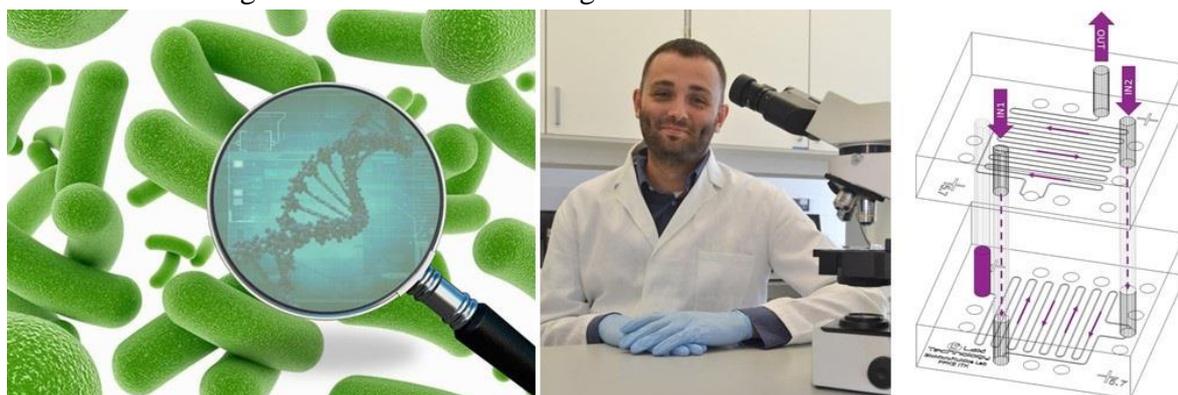

PARTICLE SEPARATION

The separation of sub-micron and micron-sized particles is the most highlighted research area in microfluidics regarding the increasing number of the research groups, scientific results and publications. 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. Separation and sorting of microparticles in a continuous manner could be managed by using external forces (acoustophoresis, electrophoresis, magnetophoresis, applying mechanical forces and optophoresis) and varying the shape of the channel (hydrophoresis). The Biomicrofluidics Laboratory is focusing on hydrophoresis and acoustophoresis because these techniques are label-free, continuous and significantly effective.

Hydrophoresis is a technique whereby the velocity profile is defined by varying the geometry of the microfluidic channels, which is responsible for the manipulation (transport, separation and sorting) of the particles.

Acoustophoresis is ultrasound-based manipulation of microparticles in microfluidics, which has a huge advantage, such as, label-free separation based on purely mechanical properties

(size, shape, density, and compressibility).

Particle recognition and classification is crucial for the verification of separation techniques. The real-time recognition, classification and counting of different objects (particles, cells or debris) require the usage of high-fps camera systems (Cellular Nonlinear Network based machines).
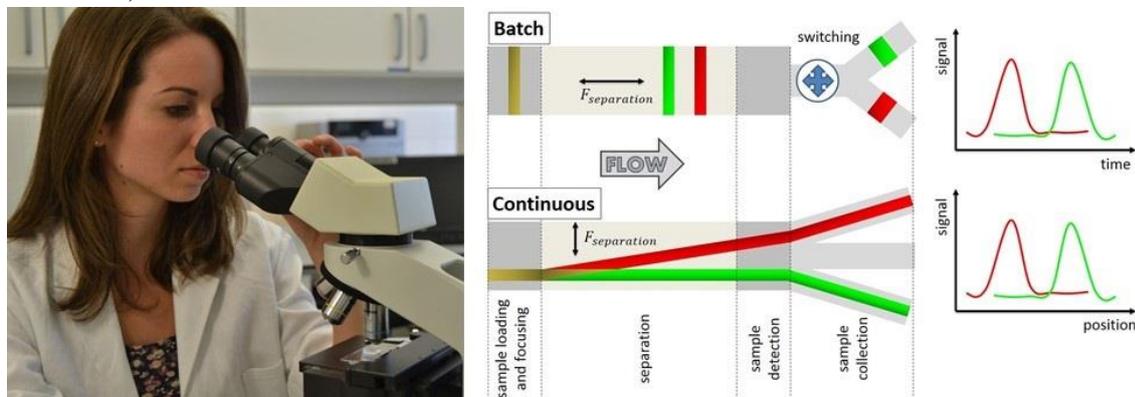
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16. EXPERIMENTAL MATHEMATICS

BARNABÁS GARAY, 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], [10], [11].
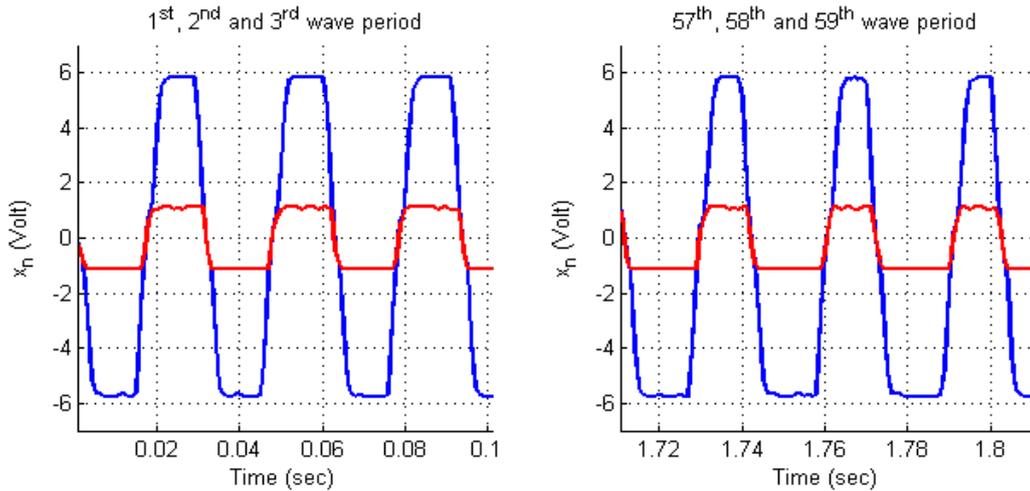

Fig. 1 *Case N=16. The metastable periodic rotating wave as shown on the oscilloscope. (Inner state in blue, output in red.) The oscillation collapses after 74 wave periods and settles down suddenly to an asymptotically stable equilibrium.*

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 system of equations above [11]) have an important role in Kelso's coordination dynamics modeling cognitive and decisional tasks performed by neurons and neural networks. Barnabás Garay and *Balázs Indig* coauthored a computer-assisted proof for chaos in Vallis' conceptual model for El Niño [7], 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 and those on neural networks [8], [9] were motivated by recent results of brain research.

One of the hot topics using methods from discrete mathematics is coding theory. The contributions in [2] and in the related papers coauthored by Miklós Ruszinkó have improved several bounds on parameters of certain codes frequently used as well as 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. Even more applied research is going on FPGAs [3], [4], [5]. The attempt is to accelerate unstructured finite volume computations on FPGAs. The novelty in the latter investigations, with a larger group around *Péter Szolgay*, is the combination of algebraic non-elementary clustering methods to achieve a better computational performance.

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17. SOFTWARE DEFINED ELECTRONICS AND VIRTUAL INSTRUMENTATION

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Students: PÉTER KUN, ÁKOS MÓROCZ
Research assistant: ATTILA TIHANYI

In the advanced ICT systems, the HW and SW components are completely separated, the different applications are implemented entirely in SW, and only one universal HW device is used to perform the transformation between the data streams processed and generated in SW and the physical signals measured in the real world. The most important feature of SW implementation is that both the *functionality* and *parameters* of the application can be changed easily in SW. This approach is referred to as Software Defined Electronics (SDE) and Virtual Instrumentation (VI) in ICT applications and measurement engineering, respectively.

USRP- and PXIe-based SDE-VI platforms have been elaborated in the SDE-VI Lab. These platforms have been successfully used in both education and research. This paper will discuss the basic idea of SDE-VI concept and will introduce the way how these platforms are used in education and research.

CONCEPT OF UNIVERSAL SDE-VI PLATFORM

In general, band-pass signals are used in ICT systems to carry the information. In SDE, every application is implemented entirely in SW and universal RF HW transformers are used to establish the connection between the analog band-pass signals measured in the real world and the data sequences processed and generated in baseband [1]. To implement an application in SW, the real-world analog signals have to be digitized or reconstructed from their samples. The crucial issue is the sampling rate, it has to be minimized without corrupting or loosing the information carried by the original real-world analog band-pass signals. The lowest sampling rate, attainable theoretically, can be achieved by using the theory of complex envelopes [2] and equivalent BaseBand (BB) transformation [3].

To get the minimum sampling rate, the RF band-pass signal is decomposed into a product of a complex envelope and a center frequency. When a modulated signal is considered then the center frequency is referred to as the carrier. Except the center frequency, the complex envelope preserves all information carried by the original RF band-pass signal, therefore, every RF band-pass signal processing can be substituted by its BB equivalent relying on the complex envelopes. Note, the complex envelope is a complex-valued waveform, its real and imaginary parts are referred to as in-phase (*I*) and quadrature (*Q*) components. Because the center frequency has been removed, the complex envelope is a low-pass signal and its bandwidth is equal to the half of the bandwidth of original RF band-pass signal. Consequently, the required sampling rate in BB does not depend on the center frequency, it is determined exclusively by the half of RF bandwidth.

BB equivalents are available for (i) deterministic signals, (ii) LTI blocks and (iii) random processes, that is, for all constituting elements of a linear system.

Block diagram of SDE concept is shown in Fig. 1 where the real-world RF band-pass analog signals and the BB data sequences are plotted in red and blue, respectively. Note, the RF band-pass signals are represented by the *I* and *Q* components of their complex envelopes in BB.
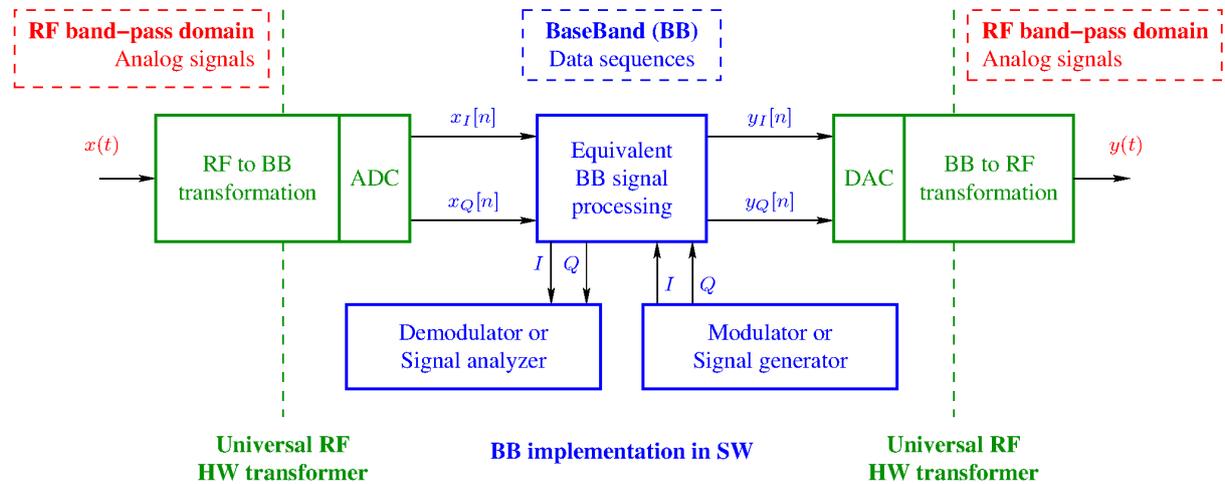

Fig. 1 *General block diagram of equivalent BB implementation.*

The SDE theory is a generalization of Software Defined Radio (SDR) concept [4] where the SDE concept can be used to implement any kind of band-pass applications. In SDE, the transformations between the RF band-pass and BB low-pass domains are performed by the *universal RF HW transformers* shown in green in Fig. 1. The SDE concept relies on BB equivalents, that is, on the equivalent BB representations of original RF band-pass problems. In SDE, each RF analog band-pass signal processing task is fully substituted by an equivalent low-pass digital one defined in BB. Distortion does not occour, information is neither lost nor distorted.

The transformation between the RF analog band-pass and digital low-pass BB domains is performed in both directions by universal HW transformers shown in green in Fig. 1. These devices are universal because the *same transformers* are required in each application and the implementation of a new application needs to change only the SW used in BB.

A universal HW transformer performs two tasks: (i) the transformation between the RF band-pass and BB low-pass domains and (ii) ADC or DAC conversion.

PORTABLE SDE PLATFORM

Our goal was to develop a portable SDE platform which can be used everywhere, even in classrooms and not only in labs, to implement any kind of ICT systems. The SDE concept has been used because it offers that level of flexibility which we need in education. In SDE, every application is implemented entirely in SW, therefore, the students can change each parameter of the ICT system under study, including even its configuration and block diagram. Even more, the students can implement and test their own solutions.

The universal portable SDE platform developed needs only one laptop and two RF HW transformers. The photo of our SDE platform is shown in Fig. 2 where a 4-FSK radio link is tested. The constituting parts of the SDE platform are as follows:

- the SW which is run on the laptop in baseband;

- one universal RF HW transformer for the transmitter (Tx) and another one for the receiver (Rx);

- the transmit (Tx) and receive (Rx) antennas;

- USB cables which connects the universal RF HW transformers to the laptop, that is, to the computing platform.

The SDE platform uses two Universal Software Radio Peripheral (USRP) devices as RF HW transformers. The real-world analog RF band-pass signals are fed into and are available from the front-panel SMA connectors (see Tx USRP on the left) while the digitized complex envelope is available at the rear-panel USB connector (see Rx USRP on the right). These USRP devices can be used from 70 MHz up to 6 GHz.

The two applications, that is, the 4-FSK transmitter (Tx) and 4-FSK receiver (Rx), are implemented in BB and entirely in SW run on the laptop. The two Front Panels shown on the laptop screen provide graphical interfaces to the SW. All data and waveforms are controlled and/or visualized on the Front Panels. The 4-FSK signal is radiated into the air by the Tx transmit antenna and picked up by the Rx receive antenna.
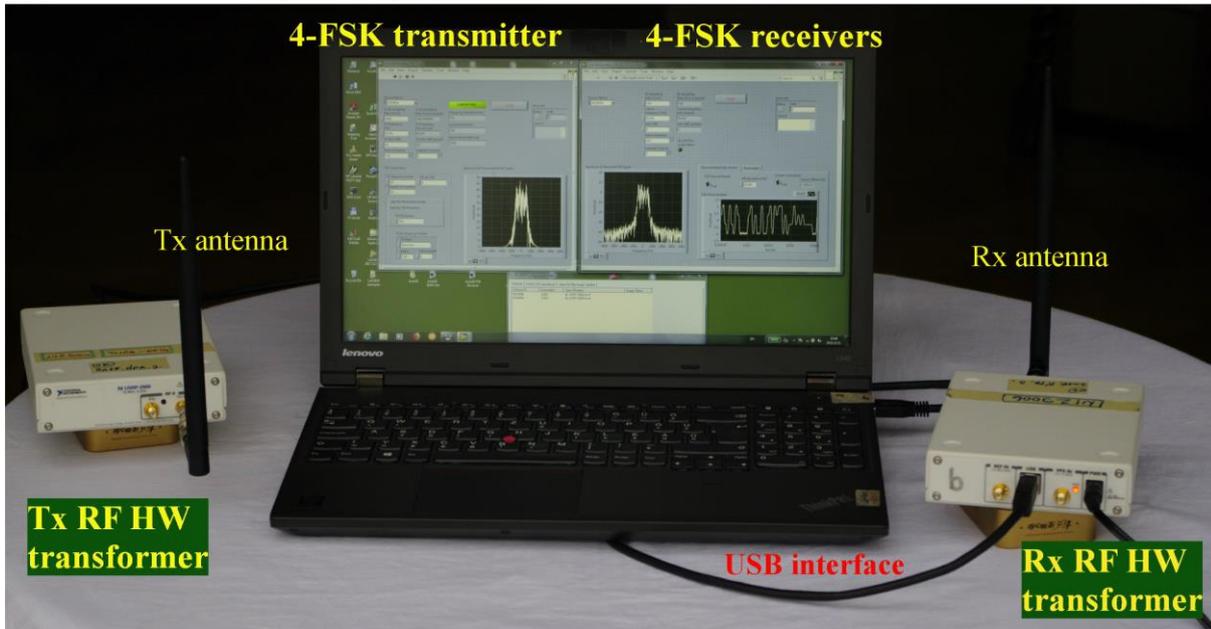

Fig. 2 *Universal portable SDE platform testing a 4-FSK radio link.*

TEACHING ICT SYSTEMS VIA HANDS-ON EXAPLES

A three-level step-by-step approach has been developed

- simulations at system level;

- SDE implementations of stand-alone applications;

- SDE implementations and testing of complete radio links where real antennas and radio channels are used.

This approach leads the students from the theory to the implementation, and helps them to understand the operation principle, design rules and practice of ICT systems. Students have

access to the computer programs written in an easy-to-understand graphical programming language. Each SW from the system level simulators to the SDE implementation of complete radio links relies on the complex envelopes. The only difference is that the transformation between BB and RF domains is not performed in the simulators, consequently, USRP transformers are not used at the system level simulation.

USE OF SDE CONCEPT IN SCIENTIFIC RESEARCH

Results achieved in scientific research are verified by computer simulation, mostly on a MATLAB platform. The universal HW transformer relies the *I/Q* components of complex envelopes, consequently, any software capable of generating and processing the *I/Q* sequences can be integrated directly into the SDE platform. The complex envelopes provide the generic interface among the different SW platforms. To illustrate the efficiency of SDE concept in scientific research, a MATLAB BB simulator is turned into a real radio system in this section.

Frequency Modulated-Differential Chaos Shift Keying (FM-DCSK) modulation [5] offers an alternative solution to the spread spectrum systems where the digital sequence to be transmitted is mapped directly into an inherently wideband chaotic carrier. The BB equivalent of an FM-DCSK radio link was derived in [6] and is depicted in Fig. 3. Based on the BB equivalent a MATLAB BB simulator was developed.
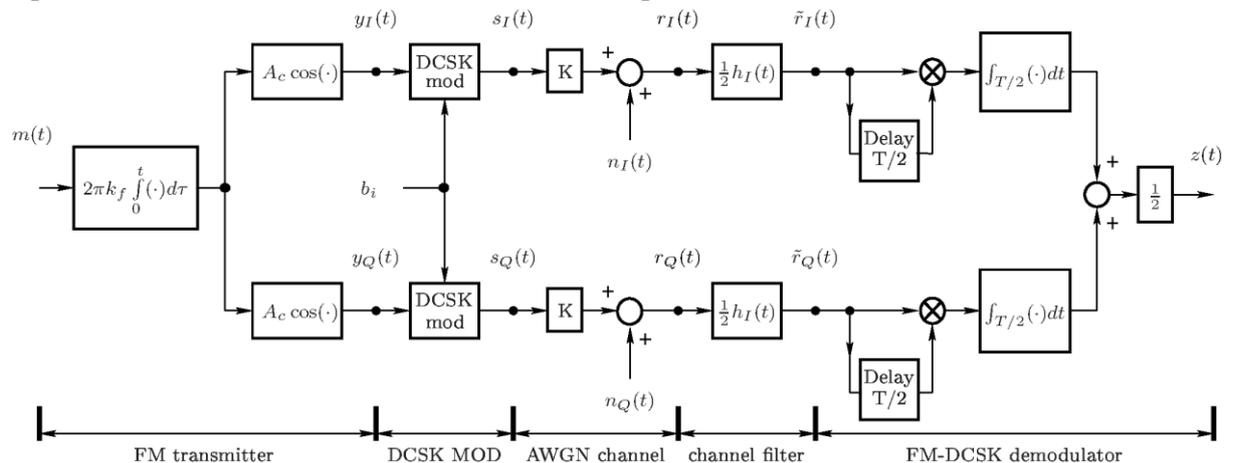

Fig. 3 *Baseband equivalent of the FM-DCSK radio link. The BB equivalent of radio channel is also included.*

This MATLAB BB simulator was integrated into a LabVIEW SW environment as shown in Fig. 4. The MATLAB program can be seen on the top of the figure in the box called "MATLAB script." The interface between MATLAB and LabVIEW platforms was done via the complex envelopes. The implemented PXIe-based testbed was used to very the feasibility of FM-DCSK modulation scheme and evalute its performance in a noise multipath radio channel.

Figure 4 shows that the FM-DCSK receiver was implemented in MATLAB. The lower part of the figure shows the configuration of the PXIe platform and provides the interfaces to the RF HW transformers.
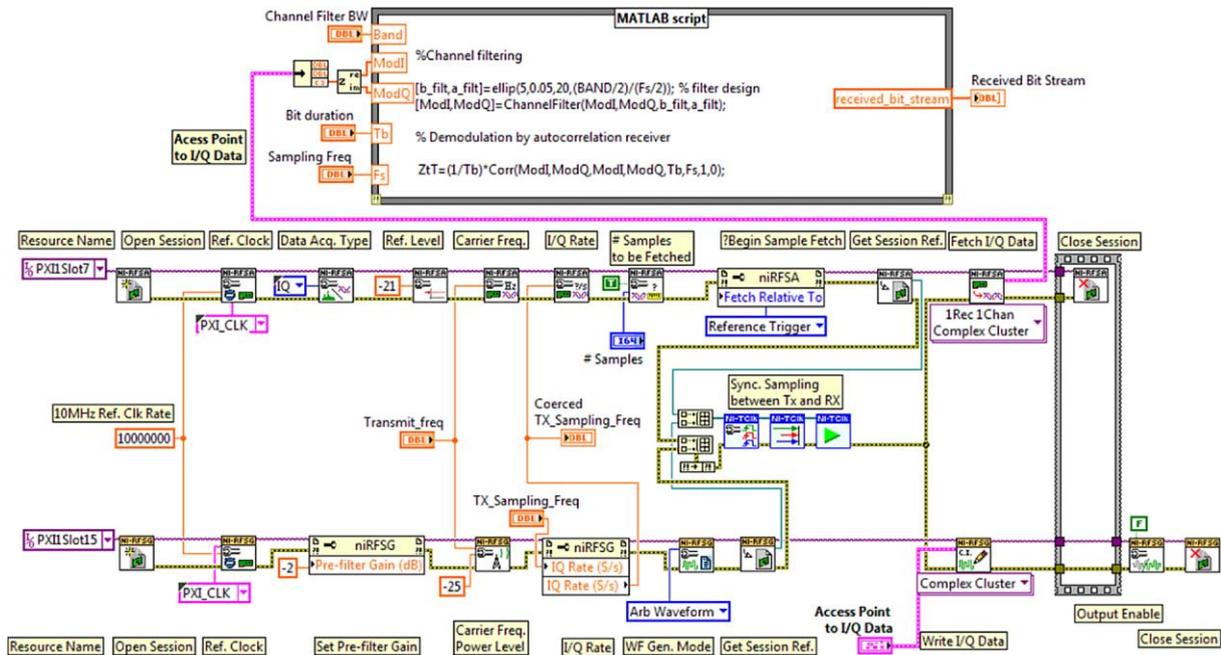
Fig. 4 *Block diagram of the FM-DCSK radio link implemented in SW. The MATLAB script which implements the FM-DCSK receiver is integrated into the LabVIEW environment.*

CONCLUSIONS

SDE concept integrates many already known solutions into one unified theory in order to get a universal SW defined platform for the implementation of RF telecommunications and measurement systems. The SDE approach offers a very high level of flexibility where either the functionality or the parameters of an application can be changed in SW, even dynamically. This feature

- is a must in many emerging applications such as cognitive radio, adaptive systems, etc.;

- makes the verification of scientific research results possible because the computer simulator used to verify the new theoretical result can be turned into a real working system;

- reduces the time-to-the-market considerably in industry because there is no need to re-design the HW during prototyping. Any change to be done needs only to modify the software;

- helps in education to fulfill the gap between the theory and practice because the students can design and implement any kind of real working telecommunications and test systems.

Another unique feature of SDE concept is that many parallel signal processing tasks can be implemented and run simultaneously on the same host computer. For example, the received signal can be used not only to recover the transmitted information but also can be considered as a test signal to determine the channel conditions.

The SDE concept makes the integration of different SW and HW platforms into one solution possible. Then a universal SDE testbed can be developed where every application can be

implemented on the same universal SDE platform by changing only the SW in the application layer.

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18. ARTIFICIAL INTELLIGENCE AND SPATIAL-TEMPORAL SEMANTICS

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Graduate students: MIHÁLY RADVÁNYI

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

I. 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.

II. 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.

III. 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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19. SENSING-ACTUATING ROBOTICS

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Students: MÁRIA LUJZA DAOUD, BENEDEK JÓZSEF TASI, ANNA IGNÁCZ, ATTILA RÉPAI, MIHÁLY GALAMBOS

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.
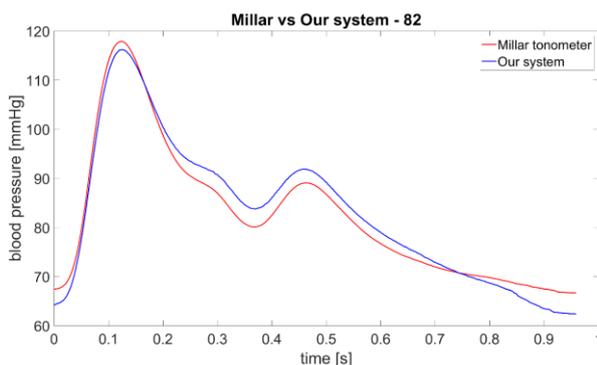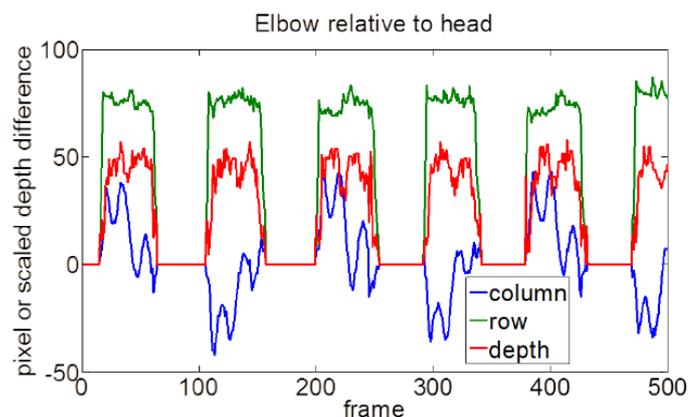
The accurate, non-invasive, measuring of the continuous arterial blood pressure waveform faces some difficulties and an innovative blood pressure measurement technology is urgently needed. The aim of this project is to introduce a novel non-invasive measuring system that can measure the arterial blood pressure waveform with high accuracy. A pilot study compared our system to an applanation tonometry system. Our system utilizes a new measurement strategy enabled by the OptoForce 3D force sensor, which is attached to the wrist at the radial artery. To validate the accuracy, 30 simultaneous measurements were taken with a Millar tonometer. For the simultaneously recorded non-invasive signals, the similarity was high (the average correlation was 0.9213±0.063). The average differences (±SD) for simultaneously recorded systolic, diastolic, mean arterial and incisura pressures were: 0.35±1.75 mmHg, 0.02±0.19 mmHg, 2.88±2.42 mmHg and 3.84±3.90 mmHg, respectively. These results satisfy the AAMI criteria. Further development and validation against invasive

arterial blood pressure monitoring is required in order to prove its in patient monitoring, emergency care, and pulse diagnosis.

In the field of visuo-servoing the lab has two preliminary results. The first one is a pure simulation of a robotic arm playing table tennis. In this case, the physical environment is realized with the help of Open Dynamics Engine and OpenAI Gym in Python. The machine learning part based on reinforcement learning and combined with the modified versions of DDPG and Prioritized Experience Replay algorithms. The neural network receives two camera-images (both the viewpoint of the player and the top view of the table) and tries to generate the linear and angular velocity-components in each spatial dimensions necessary to hit back properly the received ball. In the case of the second result, the main scope is at the reaching and grasping of objects with a robotic arm. The focus is at the modeling of reinforcement movement-learning and at the visuomotor control during movements in such an envinronment, where the system is built partially on simulational and partially on real physical environment.
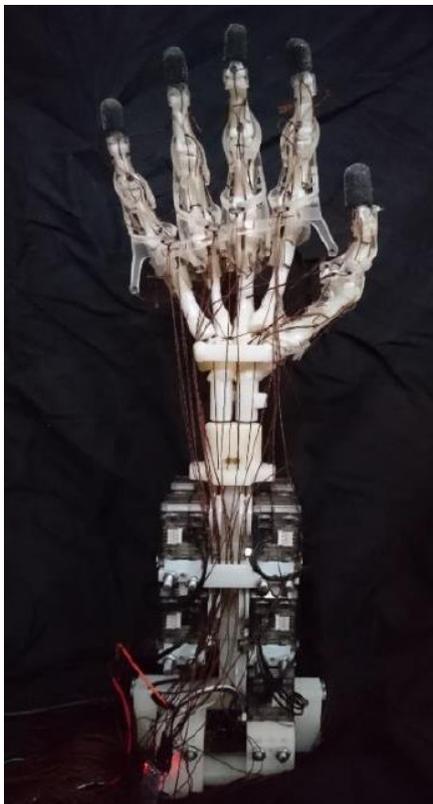
With the Anatomically Correct Biomechatronic Hand, our aim is to restore not just basic hand functionality (like the ability to produce simple grasps and gestures), but to mimic the delicate dexterity of the human hand, which would facilitate the development of a prosthetic device that can be reliably, comfortably and intuitively used in everyday situations. As opposed to the general approach of anthropomorphic hand design, which includes the employment of simple mechanized joints (hinges and gimbals) and usually aims to restore the generic properties of the hand like its most prominent degrees of freedom, our design is born of a biomimetic point of view. Based on a thorough understanding of functional anatomy, we attempt to accurately implement all salient features of the human hand like bones, ligaments, finger-actuating intrinsic and extrinsic muscles, along with their tendinous networks and pulley systems, as the dexterity of the human hand directly originates from the intricate structure and active-passive behaviour of these biomechanical components. The rigid bones were 3D printed, while the fibrous tissue of tendons and ligaments was mimicked by laser-cut silicone. The hand is actuated by high-quality Dynamixel servos, arranged in accordance with the anatomical location of the muscles in a custom-designed forearm-frame, which allow for reliable precision control beside position and torque feedback. While the model is still under development, the current version is already capable of performing movements in a natural and human-like manner, preserving the „feel" and behaviour of the human hand.

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20. MOBILE SENSOR PLATFORMS AND MULTIMODAL SENSING NETWORKS

ANDRÁS OLÁH, Associate Professor; KÁLMÁN TORNAI, Associate Professor
Graduate students: ANDRÁS HALÁSZ, MÁTÉ LŐRINCZ
Student: RICHÁRD BAGDI
Research assistants: ATTILA TIHANYI, ÁRON PAPP

INTRODUCTION

The laboratory was established by János Levendoszky in 2006, to research energy efficient communication protocols for wireless sensor networks. In the past years several PhD and MSc students were working on the related developmental and research tasks. The focus of the projects were the industrial application of wireless sensor networks (WSNs) wherein based on the processed sensor readings the distributed control of the actuator-network also has to be implemented. The main constraints are to maximize the lifetime of the battery-driven network as well as to minimize the latency of data processing and decision.

Since 2011, the application area of the research is transitioned to the smart grid networks. We created novel methods and algorithms not only for the information retrieval problems, but for user-demand driven scheduling for power devices as well. In case of smart grid system, the efficiency and reliability of the system is critically dependent on the balance of demand and supply.

Also, in 2011 a new laboratory for Mobile Application Development has been set up. In the laboratory the current devices are available in the most widespread platforms. We are working on timeseries processing related problems such as efficient and accurate signal processing algorithms for IMU (inertial measurement unit) of the smartphones. Furthermore the other objective of the laboratory to provide cutting-edge technologies and knowledge for other research groups and projects as well.

CURRENT ACTIVITIES

The current research fields of the laboratory are related to mobile sensor platforms, including wireless ubiquitous sensor networks, intelligent and automated home systems, and smart mobile devices, and some other current areas of Internet of Things. The research group is focusing on the algorithmic improvements to balance between the accuracy of data processing methods and the energy consumption of the devices.

In case of smart phones, we are researching methods for IMU sensor reading based user authentication. The existing methods that identify physical characteristics of users by fingerprint and face recognition are to be combined or augmented methods using soft biometric identification such as behavioral patterns or short gestures. In this way, the reliability and precision can be improved and in the absence of one of the biometric factors, the identification still can be performed.

PROJECTS

The research group has a thirteen-year experience in research and development. The

corresponding projects, education activities are as follows:

- Development and Implementation of Wireless Indoor Climate Monitoring System (a completed project with EnerG Kft. sponsored by Hungarian Scientific Research Fund)

- Signal processing and wireless device design and prototyping for analog sensors (completed project for Research Institute for Technical Physics and Materials Science (MFA) of the Hungarian Academy of Sciences)

- Signal processing for mobile phone assisted cardiopulmonary resuscitation (completed report for Alerant Zrt. (with the assistance of the OMSz –National Ambulance Service)

- Development and research for failure forecasting of industrial automated factories based on vibrational and audible information. (Ongoing project with a consortial partner: Hungarian Suzuki.)

- Open-set recognition based user authentication methods for smartphones using inertial measurements. Ongoing research collaboration with College of Engineering, University of Notre Dame, IN, USA.

- In recent years, we have published book chapters, journal papers, and conference papers in the field.

- In this area, 4 Ph.D. were awarded and more than 70 BSc and MSc students were working on the field.

SELECTED PUBLICATIONS

[1] K. Tornai, A. Oláh, J. Levendovszky, Monitoring Scheme for Event and Danger Detection in Wireless Sensor Networks, *Ad Hoc & Sensor Wireless Networks*, 30(1-2): 145-161, 2016

[2] K. Tornai, L. Kovács, A. Oláh, R. Drenyovszki, I. Pintér, D. Tisza, J. Levendovszky, Classification for consumption data in smart grid based on forecasting time series, *Electric Power Systems Research*, 141: 191-201, 2016

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21. MICROELECTRONIC SYSTEMS AND INTEGRATED CIRCUITS

FERENC KOVÁCS, Professor; PÉTER FÖLDESY, Associate Professor
Graduate students: MÁRTON ÁRON GODA, BÁLINT ÁRON ÜVEGES

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.
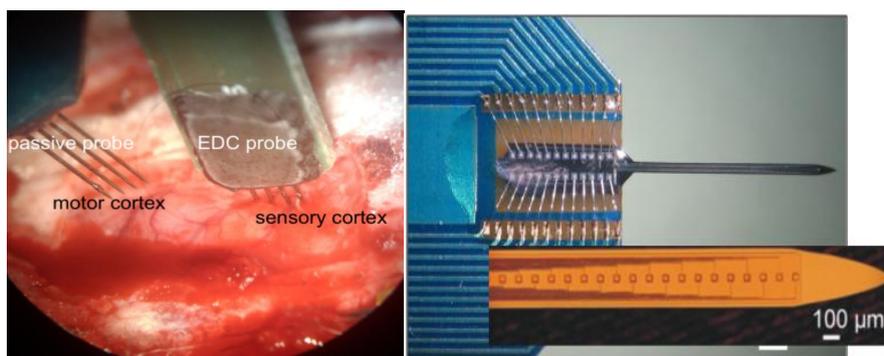

Fig. 1 *Brain electrodes with multiple contacts.*

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.
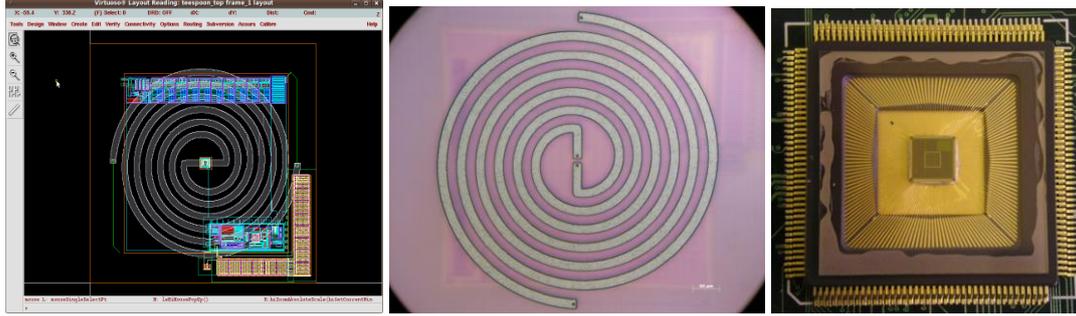

Fig. 2 *Different stages of development of a sub-THz imager: design, microphoto, and complete IC.*

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.
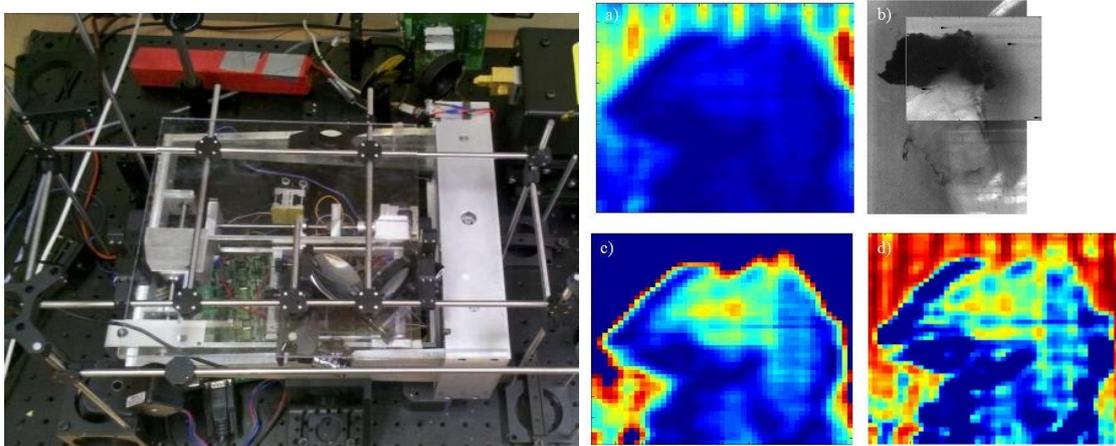

Fig. 3 *Experimental skin scanner and in vitro sample images captured at 460 GHz.*

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[1] P. Földesy, Terahertz single-shot quadrature phase-shifting interferometry, *Optics Letters*, 37 (19): 4044-4046, 2012

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[3] P. Földesy, A. Zarandy, Integrated CMOS sub-THz imager array, in Proceedings of the 13th International Workshop on Cellular Nanoscale Networks and their Applications (CNNA), Turin, Italy, 2012

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22. DATA.MEDIA.COMMUNITY

GERGELY LUKÁCS, Associate Professor
Students: KHORANI MAIKEY, BETTINA HEGEDŰS

The technical focus of the laboratory is on scalable data mamagement. Beside core technologies, such as index structures, join execution algorithms and cost based query optimization, introduced in relational database management systems, we work with and evaluate horizontally scaling systems, as well as systems for data mining/machine learning and scientific data management (e.g. Apache Spark and Hadoop, Python Dask, SAP HANA, Paradigm4 SciDB). One sidegoal of this work is to support the research work on bioinformatics at the faculty.

The major application area of the group is – with external cooperations – social and community media, as well as how human relationships are effected and could be positively influenced by IT solutions. The area is interdisciplinary, touching sociology, psychology and media, in addition to a number of technical areas. Concerning technical areas, graph data management, audio media analysis and Web analytics are just a few among many relevant topics. Media richness and naturalness are major arguments underlining the importance of audio media. For this reason, we collected and analyzed a dataset of ca. 20 000 hours of radio recordings, covering 20 radio stations in 4 countries. In a cooperation, we also collected and evaluated social network data on Hungarian clinical pastorals.
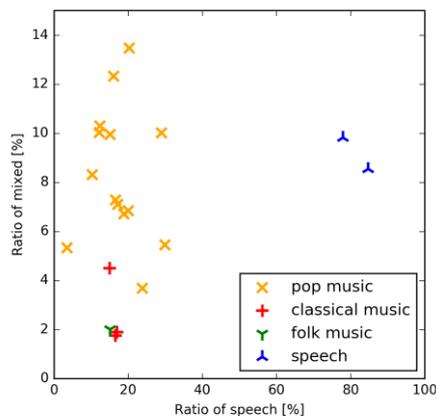

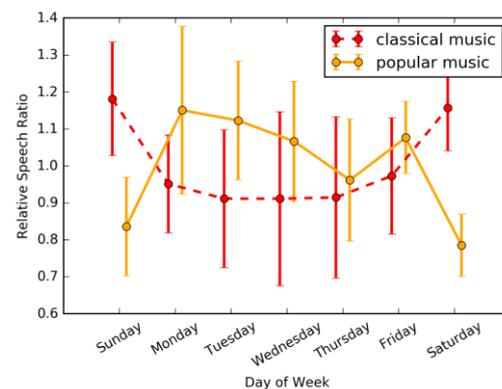**Fig. 1** *Ratio of speech and mixed blocks to total time for radio channels in four categories*

Fig. 2 *Weekly pattern of relative speech ratio for popular and classical music radio channels*
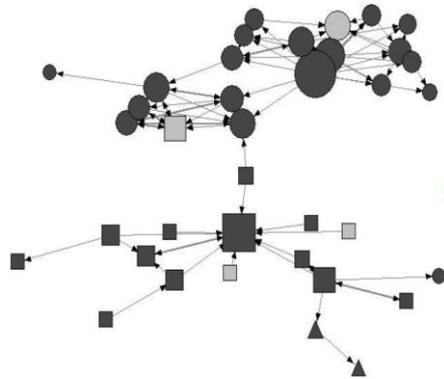
Fig. 3 *Social network ("Asks for support") of Hungarian clinical pastorals, by Christian denominations*

PUBLICATIONS

[1] G. Lukács, M. Jani, Analyzing speech and music blocks in radio channels: Lessons learned for playlist generation, in *Proceedings of 2016 Eleventh International Conference on Digital Information Management (ICDIM)*, Porto, Portugal, pp. 179-184, 2016

[2] M. Jani, G. Lukács, and Gy. Takács, Experimental Investigation of Transitions for Mixed Speech and Music Playlist Generation, in *Proceedings of ACM International Conference on Multimedia Retrieval*, Glasgow, United Kingdom, pp. 392–398, 2014

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23. MICRODIALYSIS AND PHARMACOLOGY

FRANCISKA ERDŐ, Assistant Professor; ÁGNES BAJZA, Postdoc
Graduate students: LUCA BORS, ZSÓFIA VARGA-MEDVECZKY
Students: DOROTTYA KOCSIS, ORSOLYA BEREZVAI, RÓZSA MOLNÁR, CSABA VINCZE, AMRO AHMADAL, FRIEDREICH LILLA
Collaboration partners: BÁLINT PÉTERFIA (PPCU FITB); ISTVÁN ANTAL, GELLÉRT KARVALY, ISTVÁN GYERTYÁN and KATALIN DÖME (Semmelweis University); ATTILA CSORBA (University of Szeged); PÉTER KRAJCSI and JUDIT MOLNÁR (Solvo Biotechnology); KINGA TÓTH (Institute of Cognitive Neuroscience and Psychology); DOMOKOS MÁTHÉ (CROMed); IMOLA WILHELM (BRC, Szeged)

RESEARCH TOPICS

- Age-associated changes in the blood-brain barrier (BBB) permeability – functional and morphological evaluation in rats – a multidirectional approach

- Testing drug-transporter inetractions at the blood-brain barrier

- Investigation of the benefits of intranasal drug administration for CNS indication

- Functional investigation of the role of drug transporters at the dermal barrier by transdermal microdialysis

- In vivo - in vitro correlation study for evaluation of transdermal delivery of P-glycoprotein (P-gp) substrates across the dermal barrier

- Comparison of various drug formulations and routes of drug administration by in vivo microdialysis in rodents

- Introduction of soil microdialysis and its application for the analysis of the ionic composition of different healing muds.

The in vivo consequences of aging on the BBB integrity was tested by dual- and triple-probe microdialysis in young adult and middle aged Wistar rats. The function of P-gp at the BBB was also investigated by single photon emission computed tomography (SPECT) by administration of a P-gp substrate radiotracer. The morphological changes at the BBB were analysed by electronmicroscopy, and magnetic resonance imaging (MRI). The impact of aging on learning and memory was tested in three behavioral assays (Morris Water maze test, New Object Recognition test and Pot Jumping test). The age-dependent changes at RNA and protein levels were investigated by qPCR, immunohistochemistry and Western Blot.
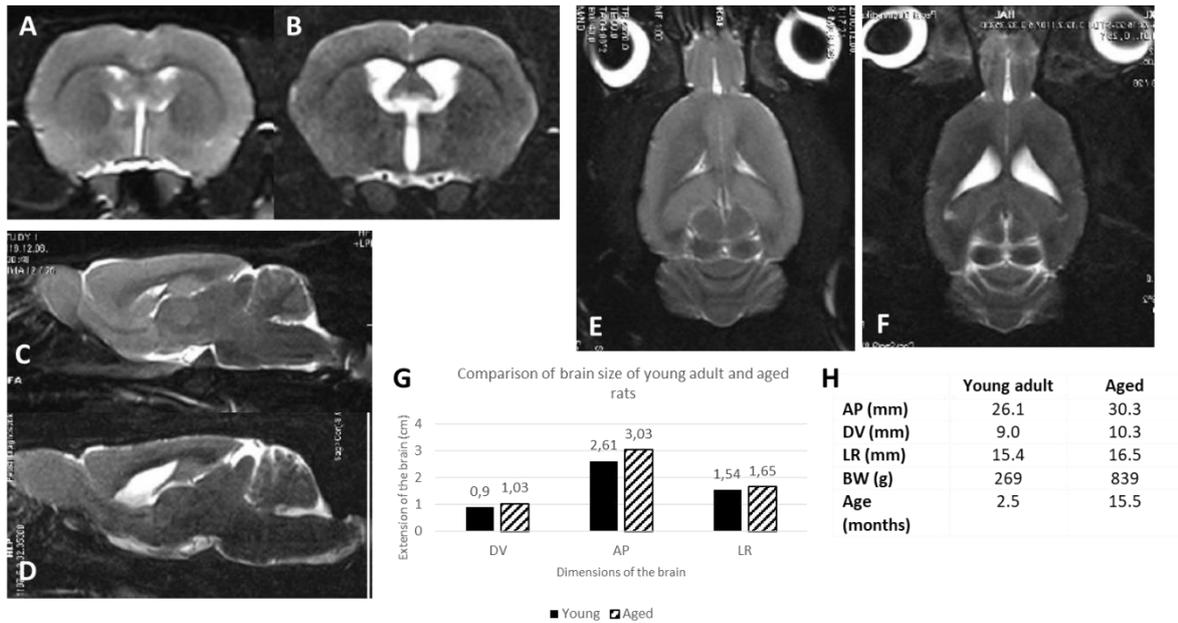
Fig. 1 *MR imaging of the brain of a representative young adult and a middle aged Wistar rats. Coronal (A,B), sagittal (C, D) and also axial images (E, F) show a significant difference in the extension of the cerebral ventricles between the young (A, C, E) and middle aged (B, D, F) rats. The difference between the maximum dorso-ventral (DV), anterior-posterior (AP) and lateral (LR) dimensions of the young and old brains are shown in panel G. The comparison of brain size, age and bodyweight of the two observed animals are displayed in panel H.*

For intranasal delivery of CNS acting drugs we started a new collaboration with the University of Reykjavik. We are working on a joint review artcile and also a laboratory visit is scheduled for this summer.

For in vivo-in vitro correlation studies we have a close collaboration with Semmelweis University in Franz diffusion cell experiments to evaluate the skin penetration of caffeine and erythromycin in vivo, in vitro and ex vivo.
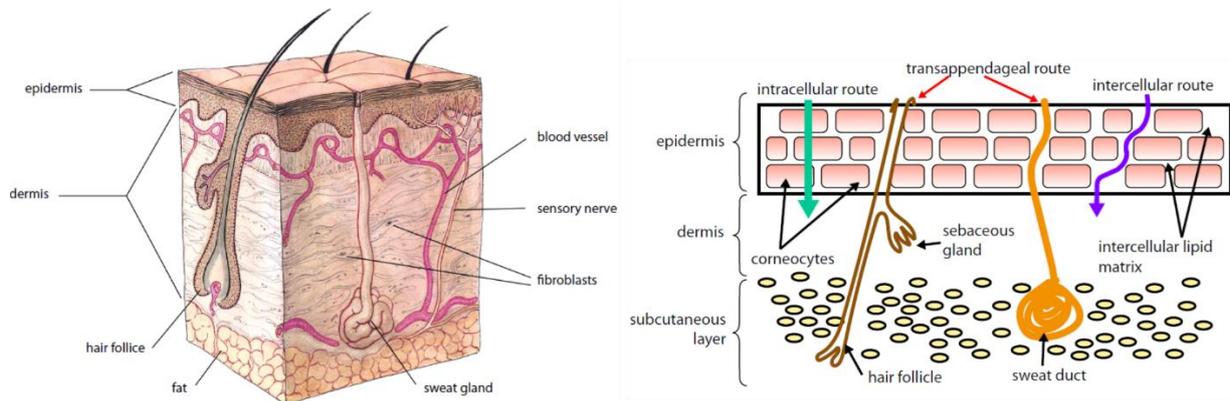
Fig. 2 *Schematic representation of anatomical structure of human skin (Left panel). Routes of percutaneous absorption (Right panel).*

A new application possibility of microdialysis technique was described recently by an Australian research group. They applied this technique for the firts time to analyse the composition of soil for agricultural purposes. On the basis of their results our group started to use the method for the evaluation of the ionic composition of different healing muds (Libád,

Hévíz, Dead Sea).

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24. SYSTEMS BIOLOGY OF MOLECULAR AND CELLULAR NETWORKS

ATTILA CSIKÁSZ-NAGY, Professor; CSABA ISTVÁN PONGOR, Postdoc; JÁNOS JUHÁSZ, Postdoc
Graduate students: TÜNDE GAIZER, SUCHANA CHAKRAVARTY, BENCE KEÖMLEY-HORVÁTH, MARCELL MISKI
Students: PÉTER ANGI, ZSÓFIA BUJTÁR, BENCE MAKOVE, NÓRA MOLNÁR, BÍBORKA PILLÉR

The lab combines computational systems biology modelling techniques with experiments to investigate the dynamics of molecular and cellular interaction networks.

We translate the wiring diagrams of molecular interaction networks into mathematical forms and analyse the equations to understand the physiological responses the system might give. We investigate various biological regulatory networks by deterministic and/or stochastic simulations and study the systems properties with different tools of dynamical systems theory. The main research line focuses on the regulation of cell growth and proliferation, especially dealing with cell cycle regulation and its connection to the circadian clock and spatial control of cell growth. We also work on theoretical ideas related to simulation methods and game-like interactions and their role in network dynamics. We collaborate with several experimental labs that provide data and platform for testing the predictions of our models, but recently we have established our own laboratory where we investigate how spatially localised cell-cell interactions affect the colony developed by various yeast strains. These results are compared with computational models, where cell to cell interactions are considered from a "games on a cell network" perspective.

RESEARCH TECHNIQUES WE USE

- Dynamical systems theory (analysis of ODE and PDE systems, bifurcations, multi-stability and oscillations)

- Data analysis

- Evolutionary game theory

- Network analysis

- Stochastic simulations

BIOLOGICAL TOPICS WE INVESTIGATE

- Cell cycle and cell growth regulation

- Establishment of cell polarity

- Cell size regulation

- Biological switches and their evolution

- Cell colony architecture changes as a result of local cell to cell interactions

- Protein complex composition and abundance predictions

- Protein aggregation and its effect on ageing

- Coupling between the circadian clock, cell cycle and DNA damage

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25. HIGH PERFORMANCE COMPUTING LAB

ISTVÁN ZOLTÁN REGULY, Assistant Professor
Graduate students: GÁBOR DÁNIEL BALOGH, BÁLINT SIKLÓSI

The goal of the HPC Lab is to carry out research in the field of scientific simulations, and accelerate them. The diversity of commonly available computational architectures (CPUs, GPUs, FPGAs) make it increasingly difficult to develop efficient code; we study the optimal mapping of algorithms to these hardware, and then making these more widely available. The lab is led by István Reguly, with one PhD student, and three MSc students.
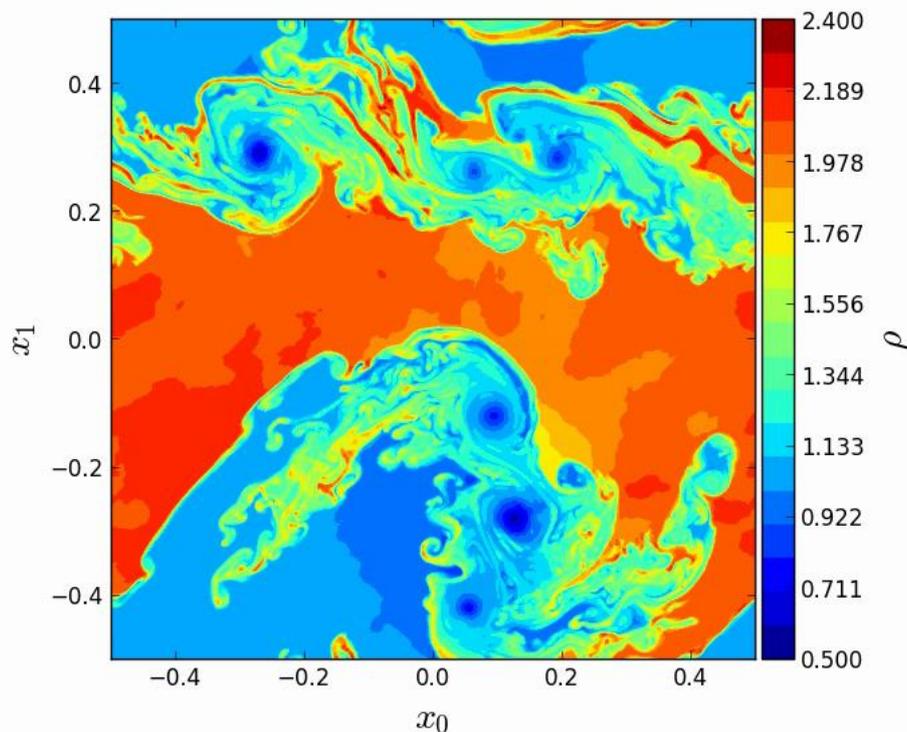

Fig. 1   *Kelvin-Helmholtz instability, simulated in OPS. Thanks to the researchers at the University of Southampton for the figure.*

After the end of frequency scaling of processors, the continued increase in performance is being delivered by increasing parallelism; computational units are being replicated. Traditional CPU architectures, various graphical processing units (GPUs) and field programmable gate arrays (FPGAs) use different architectural features and support different parallelization approaches − and new features are being introduced continuously. Efficiently programming these increasingly requires in-depth knowledge about them, which cannot be expected from domain scientists. Scientists want to be able to describe the problem they wish to solve in the simplest way possible, and get the solution fast on whatever computational resources they have at their disposal. Therefore, it is necessary to deliver the separation of concerns − separating what to compute from how to compute it. However, current programming tools do not allow this. The goal of our research is to develop programming abstractions that enable the simple description of computations, which is then automatically mapped to various computing architectures. This of course requires extensive experimentation

on our part on how to map certain algorithmic patterns to different hardware.

In our work, we explore the latest parallel programming techniques and hardware – such as the recently acquired NVIDIA Tesla P100 GPU, or the 64 core Intel Xeon Phi machine. Using simple hand-written algorithms, we explore the optimization space, and take these patterns and integrate them into domain specific frameworks that automate the process of code generation.

The primary field of study is the numerical solution of partial differential equations on structured and unstructured meshes. We develop the OP2 and OPS open source domain specific languages in cooperation with several companies and universities.

INTERNATIONAL COLLABORATIONS

In collaboration with Rolls-Royce and five universities in the UK, our 5-year goal is the comprehensive simulation of aircraft engines, coupling fluid flow, mechanical, chemical, and electrodynamics simulations. We work on the fluid dynamics component, which utilizes the OP2 library to run on modern architectures. Working with scientists at UCL and UCD, we have developed a tsunami simulation code that can model the entire life cycle of these events. Researchers an ETH Zurich use OP2 to simulate river morphodynamics, while a group at the University of Southampton studies acoustic phenomena due to turbulence around aircraft wings. We are also collaborating with the Numerical Algorithms Group who are developing a system on top of OPS for financial simulations. Finally, we study algorithms and data structures commonly occurring in nuclear simulations with AWE plc.

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26. SMART SENSORY COMPUTING LAB

ANDRÁS HORVÁTH, Associate Professor
Graduate students: DÓRA ESZTER BABICZ, ANDRÁS FÜLÖP, ÁKOS KOVÁCS, JALAL AL-AFANDI, FRANCISKA RAJKI
Students: GERGELY SZABÓ, MÁRK PETŐ

MACHINE LEARNING AND MACHINE VISION

In the Smart Sensory Computing Lab we have a special focus on machine vision and artificial intelligence. Many aspects of our comprehensive research are related to real-life applications, such as

- intelligent analysis of medical images (e.g. recognizing cancer cells on microscopic images, automatic eye diagnosis using fundus cameras)

- an internally-developed face recognition-based access control system,

- a cell phone app helping visually impaired people,

- vision systems for smart cities that identify vehicles and pedestrians as well as predict dangerous situations.

In our theoretical research we primarily focus on understanding the principles of learning and vision. A key challenge is improving the generalization ability of learning algorithms and more specifically neural networks. We can learn a great deal from the human nervous system in this regard, and our goal is to avoid huge datasets and to enable sensible inference based on just a few samples.
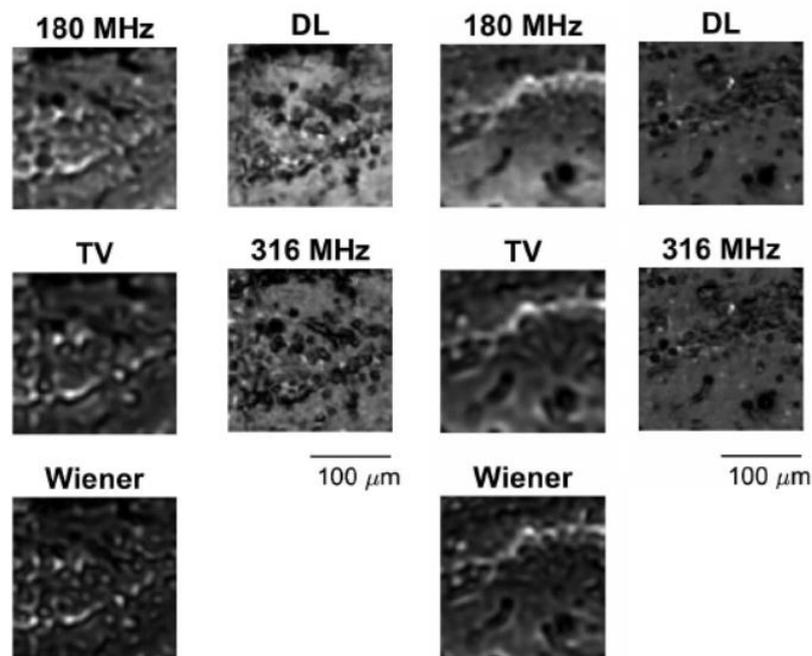

Fig. 1 *Comparison of different super-resolution algorithms on acoustic microscopy samples*

Our lab is focused on the theoretical aspects of machine learning and computer vision but also

investigates practical applications which ranges from image segmentation, prepossessing of surveillance videos, object detection, segmentation and super-resolution in the field of medical image processing.

PUBLICATIONS FROM THE PAST YEAR:

[1] Á. Makra, W. Bost, I. Kalló, A. Horváth, M. Fournelle, M. Gyöngy, Enhancement of Acoustic Microscopy Lateral Resolution: A Comparison Between Deep Learning and Two Deconvolution Methods, *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, 67(1): 136-145, 2019

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JOINT CENTERS WITH THE SEMMELWEIS UNIVERSITY

A. HUNGARIAN BIONIC VISION CENTER

B. CENTER OF NEUROMODULATION

A. HUNGARIAN BIONIC VISION CENTER

Director: KRISTÓF KARACS PhD, Associate Professor
Advisers: ÁKOS KUSNYERIK MD, PhD; JÁNOS NÉMETH MD, DSc, Professor; ILDIKÓ SÜVEGES MD, DSc, Professor; ÁKOS ZARÁNDY DSc, Professor
Postdoc: ATTILA STUBENDEK
Graduate student: ANDRÁS GELENCSÉR
Students: NAWAR SHEER, HUSAM BANNO

The goal of the Hungarian Bionic Vision Center is to improve the quality of life for visually impaired patients by medical and technological aids. We run a research program with the collaboration of physicians and engineers to study promising medical and engineering technologies. Interaction of expertise and multidisciplinary approach has utmost importance.

CURRENTLY ACTIVE PROGRAM

Our most important and currently active research and development program is the testing of universal electronic devices for visually impaired people. The focus of the program is the development and testing of a bionic eyeglass in cooperation with organizations representing visually impaired people.

The operation of the center is based on the cooperation between the Jedlik Laboratories and the Department of Ophthalmology of the Semmelweis University. The idea of the center was conceived by Tamás Roska, founding dean of the Faculty of Information Technology.
We put a strong emphasis on partnership with blind organizations. Our most important partner is the IT for Visually Impaired Foundation.

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B. CENTER OF NEUROMODULATION

Director:
DR.LORÁND ERŐSS PHD., neurosurgeon, neurologist, fellow of interventional pain practice;
DR. ISTVÁN ULBERT DSC

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. ÁGNES STOGICZA, DR. BARTOS BALÁZS, DR. LASZLO HALÁSZ, DR. LORÁND ERŐSS
Deep Brain Stimulation Program for movement disorders: DR. ANNAMÁRIA TAKÁCS, PROF. ANITA KAMONDI, DR. MAGDOLNA BOKOR, DR. GERTRÚD TAMÁS, DR. LÁSZLÓ HALÁSZ, DR. LASZLÓ ENTZ, DR. DANIEL FABÓ, DR. LORÁND ERŐSS
Intrathecal Drug Delivery Program: DR. LORÁND ERŐSS, DR. LÁSZLÓ ENTZ
Psychologists: MÁRTA VIRÁG, NOÉMI CSÁSZÁR, CSABA BORBÉLY
Psychiatrist: DR. ÉVA CSIBRI
Neuromodulation nurse: KATALIN KIRÁLY

Senior researchers:
DR. ISTVÁN ULBERT, DR. LUCIA WITTNER, DR. MÁTÉ KISS

Graduate students:
DR. GYÖRGY PERCZEL, DR. LÁSZLÓ HALÁSZ, DR ÁGNES STOGICZA, DR LUCA BARNAFÖLDI

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 influance 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 bionical education at graduate level

- to promote animal research in neuromodulation and clinical investigations in the field of neuromodulation

- to develope 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 Lorand Erőss and founded by Professor Tamás Roska from the Pázmány Péter Catholic University and Professor Miklós Réthelyi Minister of National Resouces. 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 a foreign specialists in the field of neuromodulation. The director of the center is Lorand Erőss.

The center incorporate the Pázmány Péter Catholic University, Department 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 University Information Technology. The first research and development project is "Remote telemetrical programming of neuromodulation devices". The Neuromdulation 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 physican. It is important in cases of movement impaired, elderly, or very poor patients who can not 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 Neursurgical 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 throught 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 backround of bionical research and take part of the combined graduate and postgraduate medical and bionical education.
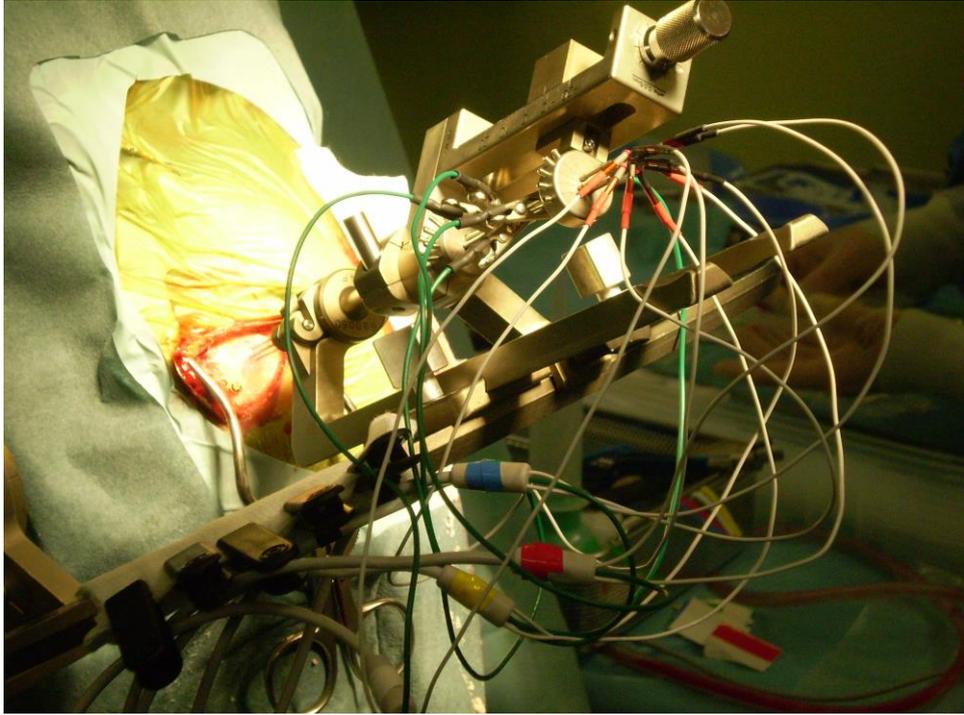
Fig. 1 *Intraoperative electrophysiological recording, during Deep Brain Stimulator implantation in a Parkinson's Desease patient (Institute of Clinical Neorosciences, Budapest)*
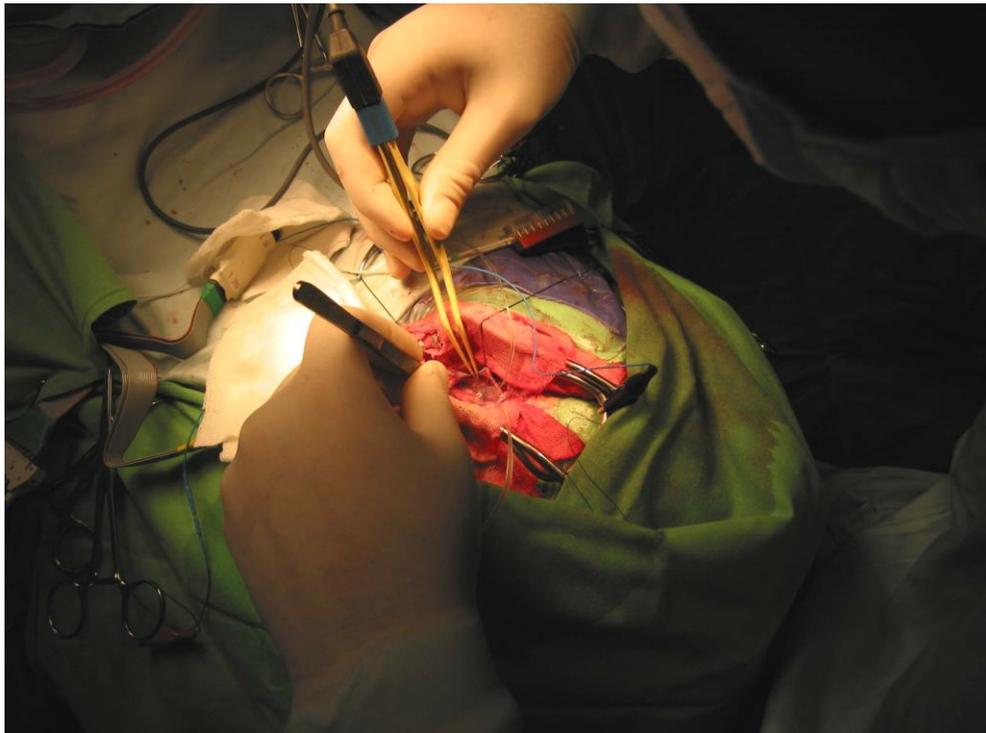

Fig. 2 *Strip electrode implantation in epilepsy surgery (National Institute of Clinical Neurosciences)*

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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, Balázs Ligeti, Postdoc

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

Dr. Ingrid Petrič, Centre for Systems and Information Technologies, University of Nova Gorica, Slovenia

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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

Arpad Karsai, Department of Neurobiology, Physiology, and Behavior, University of California-Davis, Davis, CA, USA

Maria J. Saraiva, Institute for Molecular and Cell Biology, University of Porto, Porto, Portugal, Instituto de Ciências Biomédicas de Abel Salazar, University of Porto, Porto, Portugal

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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 superresolution in optical, ultrasonic, and nanomagnetic devices (SOUND) laboratory *(see pp. 43)* 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 group has developed an early prototype of an ultrasound imaging platform and has research interests in segmentation (lesion detection), classification (early skin cancer detection), and the development of a scan conversion algorithm for a manually translated single element transducer. The results of this research have been disseminated via the publications below and are in the process of clinical translation through a spin-off Dermus Kft.
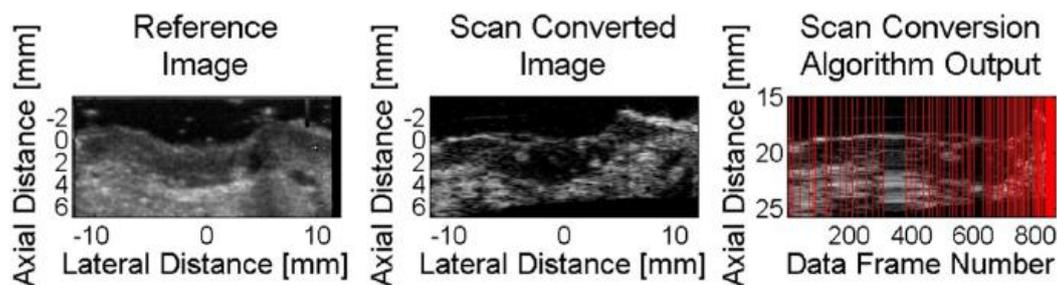

Fig. 1 *Demonstration of scan conversion using manual scanning of a single element transducer. Left: image from reference (commercially available) ultrasound scanner. Middle: demonstration of scan conversion method of same lesion. Right: raw data taken from manual scan, with red lines showing those lines that were selected for scan conversion. Source of image: [7].*

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IV. DIGICON (DIGITAL MEDICAL CONSULTATION)

GÁBOR PRÓSZÉKY, Professor, principal investigator; BORBÁLA NOVÁK, Assistant Professor; LÁSZLÓ LAKI, Postdoc, ATTILA NOVÁK, Postdoc

SHORT DESCRIPTION OF THE ACTIVITIES

Every day vast amount of clinical documents are gathered in hospitals 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 contain 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 is 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. As a side effect of exploring related concepts, a relational network is produced automatically based on the distributional behavior of terminological phrases in the clinical corpus.
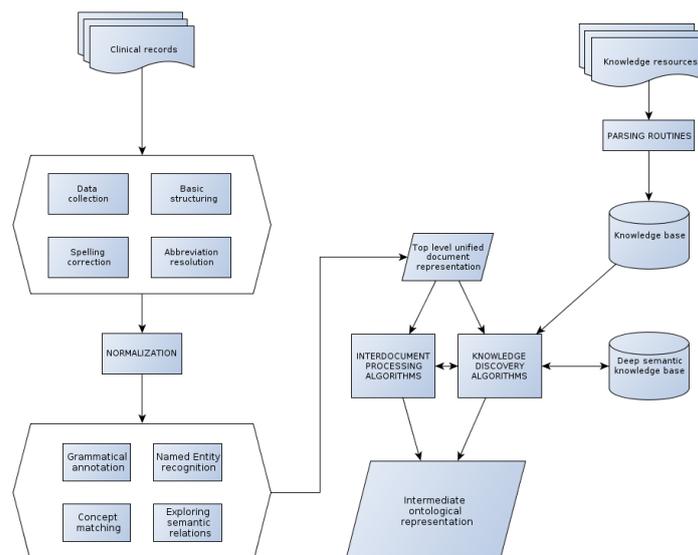
Fig. 1 *The preprocessing modules applied to the raw clinical documents in order to achieve a higher-level and normalized representation and ontological mappings*

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