INCF Lithuanian Workshop on Neuroscience and Information Technology

February 3, 2012 – Kaunas, Lithuania

incf

Opening: Lithuanian folk song and dance ensemble "Žilvitis", from Vytautas Magnus University.

Workshop audience. In the foreground: Dr. Sean Hill, INCF Executive Director, and Prof. Jeanette Hellgren-Kotaleski, Coordinator of the INCF National Node of Sweden.

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Location
February 3, 2012 – Vytautas Magnus University, Kaunas, Lithuania

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Supported by INCF and Vytautas Magnus University, Kaunas, Lithuania

Introduction

The aim of this workshop was to discuss the strategies for forming the Lithuanian Neuroinformatics Node and becoming a member of INCF. The workshop was organized by Dr. Aušra Saudargiene (Department of Informatics, Vytautas Magnus University, Kaunas, and Faculty of Natural Sciences, Vilnius University, Lithuania) and INCF.

The workshop was attended by 15 invited speakers, among them 4 guests and 11 Lithuanian neuroscientists, and over 20 participants. The workshop was organized into three main sessions: overview of the INCF activities including the Swedish and UK nodes of INCF; presentations on Neuroscience research carried out in Lithuania; discussion about the strategies for forming an INCF national node, and the benefits of having such a node in Lithuania (Appendix A: Program).

Session 1

The meeting was opened with an address from Prof. Rūta Marcinkevičienė of the Research Council of Lithuania. Prof. Rūta Marcinkevičienė welcomed the participants of the workshop emphasizing its interdisciplinarity and attempts to contribute to the global research infrastructure. She pointed out that both trends have high priority in European research area as well as in the Research Council of Lithuania.

In the first session, Dr. Sean Hill described the aim of INCF, its structure, activities and strategy. Prof. Jeanette Hellgren-Kotaleski presented the activities of the Swedish INCF node and continued with her research on computational modeling of molecular mechanism underlying synaptic plasticity in basal ganglia. Prof. Leslie Smith introduced the UK INCF node and pointed out the benefits of being a member of INCF. Dr. Bruce Graham presented a computational modeling study on associative learning in hippocampal CA1 microcircuit as a case of neuroinformatics application in science (Appendix B: Abstracts).

Session 2

The second session consisted of presentations given by the Lithuanian neuroscientists from Neuroscience Institute (Kaunas), Lithuanian University of Health Sciences (Kaunas), Vilnius University (Vilnius), Vytautas Magnus University (Kaunas), Institute of Psychophysiology and Rehabilitation (Palanga), the Republican Vilnius Psychiatric Hospital (Vilnius) (Appendix B: Abstracts).

Guest speaker Prof. Leslie Smith, from the Institute of Computing Science and Mathematics, University of Stirling, UK.

Discussion

The presentations were followed by a discussion on benefits of having a Lithuanian INCF node and conditions of joining INCF. It was noted by the Lithuanian scientists that the membership fee is relatively high for Lithuania ($10 000 per annum) considering its economical status and the small neuroscience community. On the other hand, the Research council of Lithuania shows interest in developing the infrastructure for science and Lithuania taking active part in international scientific organizations, therefore its support for forming the Lithuanian INCF node might be expected. The representatives of INCF pointed out the advantages of being a member of INCF that include data and computing resource sharing, international collaboration, training in Neuroinformatics, direct impact on defining the future activities of INCF, travel grants, increased visibility of Lithuanian neurosciences.

Outcome & Next steps

It was agreed both by the INCF representatives and Lithuanian scientists that joining INCF would be beneficial for Lithuania.

The next step to be taken is the preparation of the proposal to the Research Council of Lithuania to ensure Lithuania annual contribution as a member country of INCF.

Appendix A: Program

INCF Lithuanian Workshop on Neuroscience and Information Technology

Vytautas Magnus University, S. Daukanto 28, Kaunas, 3 February 2012

9.00 Lithuanian folk song and dance ensemble "Žilvitis", Vytautas Magnus University

Opening

9.15 **Prof. Rūta Marcinkevičienė,** Research Council of Lithuania

Introduction and welcome

Session 1: International Neuroinformatics Coordinating Facility INCF

9.20 **Dr. Sean Hill**, INCF Executive Director, INCF Secretariat, Karolinska Institute, Stockholm, Sweden

Role of INCF: Toward a global collaborative infrastructure for neuroscience

10.10 **Prof. Jeanette Hellgren-Kotaleski**, Coordinator, INCF National Node of Sweden, Royal Institute of Technology, Stockholm, Sweden

Multiscale modeling in neuroscience, and a brief update on the Swedish INCF node activities

10.40 **Prof. Leslie Smith**, Institute of Computing Science and Mathematics, University of Stirling, UK

INCF activities in UK

11.10 **Dr. Bruce P. Graham**, Institute of Computing Science and Mathematics, University of Stirling, UK

Modelling the hippocampal CA1 microcircuit

11.40 Lunch

Prof. Rūta Marcinkevičienė, from the Research Council of Lithuania, welcomed the workshop participants.

Session 2: Neuroscience in Lithuania

13.00 **Prof. Osvaldas Rukšėnas**, President of Lithuanian Association for Neurosciences, Faculty of Natural Sciences, Vilnius University, Vilnius, Lithuania

Dynamics of receptive fields

13.20 **Prof. Vilma Borutaitė**, Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

Beta amyloid and neuronal death

13.40 **Dr. Kastytis Dapšys**, Republican Vilnius Psychiatric Hospital, Vilnius, Lithuania

Effect of electroconvulsive therapy on the auditory event-related potential P300

14.00 **Dr. Saulius Šatkauskas**, Faculty of Natural Sciences, Vytautas Magnus University, Kaunas, Lithuania

Sema3A signaling in the growth of dorsal root ganglia

14.20 **Dr. Aidas Alaburda**, Faculty of Natural Sciences, Vilnius University, Vilnius, Lithuania

Activation of spinal motoneurons during locomotor network activity

14.40 **Dr. Gytis Baranauskas**, Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania and Dept. of Physiology, Ben Gurion University of Negev, Beer Sheba, Israel

Simulating the brain: from channels to neuronal assembles

15.00 Coffee break

15.30 **Prof. Robertas Bunevičius**, Director, Institute of Psychophysiology and Rehabilitation, Lithuanian University of Health Sciences, Palanga, Lithuania

Well-being of patients

15.50 **Dr. Aleksandr Bulatov**, Institute of Biological Systems and Genetics, Lithuanian University of Health Sciences, Kaunas, Lithuania

Misperception of positional relations

16.10 **Dr. Gytis Svirskis**, Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

Collision detection in frog optic tectum

16.30 **Dr. Gailius Raškinis**, Department of Informatics, Vytautas Magnus University, Kaunas, Lithuania

Learning world model in simulated environment

16.50 Coffee break

Discussion

17.20 Discussion about the strategies for forming an INCF national node, and the benefits of having such a node in Lithuania

19.00 Conference Dinner

Neuroscience and Information Technology

3 February 2012

Vytautas Magnus University
S.Daukanto 28, Kaunas, Lithuania

International workshop

Modern Neuroscience relies heavily on Information science – computational tools, mathematical models, databases. Neuroinformatics stands at the intersection of neuroscience and information science.

The aim of this workshop is to discuss the strategies for forming the Lithuanian Neuroinformatics Node and becoming a member of the International Neuroinformatics Coordinating Facility INCF.

Special Guests

Jeanette Hellgren-Kotaleski, INCF, Sweden
Sean Hill, INCF Executive Director, Sweden
Leslie Smith, INCF,UK
Bruce P. Graham, UK

Invited Speakers

Osvaldas Rukšėnas, Vilnius University
Vilma Borutaitė, Neuroscience Institute, Kaunas
Gytis Svirskis, Neuroscience Institute, Kaunas
Aidas Alaburda, Vilnius University
Saulius Šatkauskas, Vytautas Magnus University, Kaunas
Robertas Bunevičius, LSMU, Palanga
Gytis Baranauskas, Neuroscience Institute, Kaunas, and Israel
Kastytis Dapšys, Vilnius University
Aleksandr Bulatov, LSMU, Kaunas
Gailius Raškinis, Vytautas Magnus University, Kaunas

VYTAUTAS MAGNUS UNIVERSITY MCMXXII

incf International Neuroinformatics Coordinating Facility

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Appendix B: Abstracts

Toward an international infrastructure for collaborative neuroscience

Sean Hill
INCF Secretariat, Karolinska Institute, Stockholm, Sweden

The International Neuroinformatics Coordinating Facility (INCF) was launched in 2005, following the proposal by the Global Science Forum of the Organization for Economic Cooperation and Development (OECD) to create an organization to coordinate an open international infrastructure and integrate heterogeneous neuroscience data and knowledge bases and enable new insights from analysis, modeling and simulation. Here we present the INCF multi-phase strategy to deploy such an infrastructure with specific capabilities and milestones. The first phase would establish a globally federated dataspace with searchable metadata. The second phase would develop an object-based data integration layer employing web services to ensure the unique identification of all data through ontologies and spatial coordinates, while using data models to access diverse data formats through standard interfaces. The third phase would establish standard workflow management for analysis, visualization, modeling and simulation can then be built on top of the data integration layer. The development of portal interfaces will be critical to provide interactive user access to data, analyses and simulation results. This infrastructure should facilitate international sharing, publication and integration of neuroscience data across multiple levels and scales.

Multiscale modeling in neuroscience, and a brief update on the Swedish INCF node activities

Jeanette Hellgren Kotaleski
School of Computer Science and Communication, KTH Royal Institute of Technology, Stockholm, Sweden

To understand the inner workings of the brain it is necessary to integrate data from the molecular level to systems level function. Here computational modeling provides an important tool. Insights gained through modeling and simulations will be exemplified through the research going on in Stockholm with regard to the control of goal-directed motor behaviour and decision making.

The lamprey is one of the few vertebrates in which the cellular and synaptic level mechanisms for motor behaviour, including locomotion, steering and control of body orientation, are well described. The insights gained from combining large-scale computational modeling with detailed experiments are reviewed. We are today able to model the motor system with biophysically detailed compartmental Hodgkin-Huxley neurons and with the approximate number of neurons that are responsible in the behaving animal. It will further be demonstrated how modeling may help when extrapolating from rodent experiments to in vivo like conditions in the search for the mechanisms involved in basal ganglia dependent learning and decision making.

Finally the Swedish INCF National Node activities will be summarized. The Node is located at The Royal Institute of Technology (KTH) in Stockholm and was established in August 2006. The Chair and Coordinator is Professor Jeanette Hellgren Kotaleski at the Department of Computational Biology, School of Computer Science and Communication, KTH. The Node functions as a network of research groups, which in most cases are tightly tied to the Stockholm Brain Institute. The research activities are covering large-scale computing and software tools for modeling and simulations, and databases for brain imaging. Also neurorobotics is represented. Sweden has representatives in the taskforces for two of the INCF programs: 'Multi Scale Modeling', and 'Standards for Datasharing'.The Swedish node is also coordinating an Erasmus Mundus PhD training network in neuroinformtics (see www.kth.se/eurospin) involving partners from four of the INCF member countries.

INCF activities in UK

Leslie Smith
Institute of Computing Science and Mathematics, University of Stirling, UK

The UK Neuroinformatics Node is an organisation funded by the UK research councils, whose aim is to promote dialogue between researchers in the broad area of Neuroinformatics in the UK and those elsewhere in the world. It acts as the UK link with the International Neuroinformatics Coordinating forum (INCF). The Node was set up in 2005, and is run by a committee headed up by Prof David Willshaw, of Edinburgh University.

The Node aims to develop the UK agenda in Neuroinformatics, stimulating this, and supporting training, and ensuring active UK presence in this area worldwide. It has five special interest groups, in electrophysiology, in image-based neuroinformatics, in neurally-inspired engineering, in computational modelling and simulation environments, and in artificial intelligence, cognition and behaviour. The Node holds regular meetings, as well as contributing to the international activities of the INCF.

Modelling the hippocampal CA1 microcircuit

Bruce P. Graham
Institute of Computing Science and Mathematics, University of Stirling, UK

For historical reasons related to behavioural evidence for the role of the hippocampus in declarative memory, and due to the technical facility with which the neurobiology of the hippocampus can be studied in experiments, we have the most detailed data on the hippocampus, compared to any cortical brain region. This data alone does not tell us how the hippocampus works as an information processing device, but it does provide a rich resource with which we can build plausible mathematical models of the hippocampal circuitry.

In this talk I describe a neural network model of the CA1 subregion of the hippocampus that is a tool for studying the roles of individual classes of local inhibitory interneurons in controlling pyramidal cell activity and synaptic plasticity. In accord with various experiments, the model demonstrates that different half cycles of the 4Hz theta rhythm, that is prominent in rats exploring an environment, may correspond to a period of storage of new information followed by recall of previously stored information. The storage half cycle corresponds to strong perisomatic inhibition that inhibits pyramidal cell output while allowing strong depolarisation in the dendrites that results in increases in the strengths of active synapses and so the storage of new patterns of information. During the recall half cycle, dendritic inhibition is strong, inhibiting synaptic plasticity but still allowing synaptic input to be integrated and generate cell spiking in the axon.

This research sits firmly within the sphere of neuroinformatics, as it combines data from experiments that has been suitably digitised, such as cell morphologies, with cutting-edge computational tools, such as the NEURON simulation package, to enable the building and simulation of the network model. Simulations are run on a parallel compute cluster.

Guest speaker Dr. Bruce P. Graham presented modeling research from University of Stirling, UK.

Dynamics of receptive fields

Osvaldas Rukšėnas
Faculty of Natural Sciences, Vilnius University, Vilnius, Lithuania

Sharpness of vision depends on the resolution of details conveyed by individual neurons in the visual pathway. In the dorsal lateral geniculate nucleus (LGN) the neurons have receptive fields with center-surround organization, and spatial resolution may be measured as the inverse of center size.

We studied dynamics of receptive field center size of single LGN neurons during the response to briefly (400-500 ms) presented static light or dark spots. Center size was estimated from a series of spatial summation curves made for successive 5 ms intervals during the stimulation period. The center was wide at the start of the response, but shrank rapidly over 50-100 ms after stimulus onset, whereupon it widened slightly. Thereby, the spatial resolution changed from coarse-to-fine with average peak resolution occurring about 70 ms after stimulus onset. The changes in spatial resolution did not follow changes of firing rate; peak firing appeared earlier than the maximal spatial resolution.

We suggest that the response initially conveys a strong but spatially coarse message that might have a detection and tune-in function, followed by transient transmission of spatially precise information about the stimulus. Experiments with spots presented inside the maximum but outside the minimum center width suggested a dynamic reduction in number of responding neurons during the stimulation; from many responding neurons initially when the field centers are large to fewer responding neurons as the centers shrink. Thereby, there is a change from coarse-to-fine also in the recruitment of responding neurons during brief static stimulation.

Prof. Osvaldas Rukšėnas, President of Lithuanian Association for Neurosciences and Dean of the Faculty of Natural Sciences at Vilnius University, presented vision research.

Beta amyloid and neuronal death

Vilma Borutaitė
Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

Alzheimer's disease is the most common neurodegenerative disease and the most prevalent form of dementia and affects over 35 million people worldwide according to WHO.

Neuropathological features of Alzheimer's disease are progressive memory and cognitive impairment, formation of neuritic plaques that contain dead and dying neurons, inflammatory-activated microglia, β-amyloid peptides Aβ1–40 and Aβ1–42.

Our results show that small oligomers of Aβ1-42 (dimers – pentamers) at submicromolar concentrations induce rapid neuronal necrosis most likely due to the direct effect on neuronal membranes, causing depolarization and Ca2+ influx into neuronal cells; Aβ1-42-oligomer-induced neuronal death can be prevented by MK801, EGTA and estrogens suggesting that toxicity of Aβ1-42 may be mediated by accumulation of intracellular Ca2+. This may lead to opening of mitochondrial permeability transition pore leading to necrosis.

Prof. Vilma Borutaitė presented Alzheimers research from the Neuroscience Institute at the Lithuanian University of Health Sciences in Kaunas.

Dr. Kastytis Dapšys, from the Republican Vilnius Psychiatryc Hospital and Vilnius University, presented ERP studies of electroconvulsive therapy outcomes.

Effect of electroconvulsive therapy on the auditory event-related potential P300

Kastytis Dapšys
Republican Vilnius Psychiatric Hospital; Vilnius University, Vilnius, Lithuania

Electroconvulsive therapy (ECT) may have a negative impact on patient's cognitive functions, especially on memory. However, the study of non-memory cognitive functions after ECT has been relatively neglected. Event-related potentials (ERP) are thought to reflect some cognitive processes, mainly related to attention and working memory. Aim of the study was to examine the effect of ECT on auditory ERP P300.

P300 potential was elicited using auditory "oddball" paradigm in 38 patients. 22 patients had schizophrenia spectrum disorders and 16 patients had various mood disorders. Mean age of patients was 40±13 years (from 22 to 72 years). ERPs were recorded before the first ECT procedure and the next day after the last ECT. Recordings were made at Fz, Cz and Pz electrode sites. Latency of N2 and P300 waves, peak-to-peak amplitude of P300 wave and target stimulus recognition time was measured. Correlation between P300 parameters, clinical symptoms (measured using PANSS, MADRS, HAM-D scales) and parameters of ECT procedure - delivered energy, seizure energy index (SEI) and duration of seizure - was evaluated.

After course of ECT clinical symptoms of both schizophrenia and depression has improved. There was also a statistically significant increase in P300 amplitude. Increase was greater in the schizophrenia spectrum disorders group than in group of mood disorders. Decrease in P300 latency was insignificant. Correlation between P300 latency and SEI, and between P300 amplitude and delivered energy was more reliable in the mood disorders group.

1. Abnormal P300 potential was found in both groups of patients at baseline, but in the group of schizophrenia spectrum disorders it was more considerable.

2. There was significant improvement of clinical symptoms after ECT.

3. After ECT course the amplitude of P300 potential had increased in both groups.

4. ECT may improve information processing in patients with treatment-resistant schizophrenia spectrum disorders and mood disorders as assessed by event-related potential P300.

Sema3A signaling in the growth of dorsal root ganglia

Saulius Šatkauskas
Faculty of Natural Sciences, Vytautas Magnus University, Kaunas, Lithuania

During nervous system development the growth of axons and dendrites of neuronal cells depends on various signaling molecules. One of them is a protein semaphorin 3A (Sema3A). The binding of Sema3A to the growth cones of dorsal root ganglion (DRG) initiates depolymerization of cytoskeletal protein actin and induces growth cone collapse. Recently it became evident that calcium is an important factor in the responses of DRG axons to various signaling molecules.

In our study we examined the changes of the responses of DRG axons to Sema3A as a consequence of blocked and modified various calcium channel activity and calcium ion chelation in the growth medium. The results showed that inhibition or modification of calcium channels slows down growth of DRG axons as well as increase collapse rate in concentration dependent manner. In addition to that experimental results revealed that the changes in activity of plasma membrane calcium channels can modify the DRG axon responses to the Sema3A. The study also revealed that Sema 3A slightly decreases the expression of cation channel TRP.

Dr. Saulius Šatkauskas from the Faculty of Natural Sciences at Vytautas Magnus University in Kaunas.

Dr. Aidas Alaburda from the Faculty of Natural Sciences at Vilnius University in Vilnius.

Activation of spinal motoneurons during locomotor network activity

Aidas Alaburda
Faculty of Natural Sciences, Vilnius University, Vilnius, Lithuania

The characteristic scratch network activity can be elicited by both mechanical stimulation and electric nerve stimulation in the isolated carapace-spinal cord preparation of the adult turtle. Induction of scratching can be controlled by varying the frequency and intensity of the electrical nerve stimulus. The isolated low intensity stimuli do not evoke activity in the motor nerve while repeated stimulation (≥0.2Hz) leads to temporal integration of sensory inputs and onset of a scratch episode.

We investigated the mechanisms of temporal integration by intracellular recordings from motoneurons. At threshold intensity the first nerve stimulus evoked a brief synaptic barrage (≈100 ms) but it did not lead to changes in motoneuron membrane potential, excitability or membrane conductance before second stimuli.

However, increased background synaptic activity was observed in motoneurons before second stimuli. Moreover, the synaptic response winds-up when more than one stimulus was applied before the onset of scratching. The time course of the temporal integration, sustained synaptic activity and wind-up of synaptic responses that leads to scratching is compatible with wind-up of L-type Ca2+ channels in spinal neurons. Indeed, perfusion of the spinal canal with medium containing nimodipine (L-type Ca2+ channel blocker) increases the threshold stimulus frequency for evoking scratching.

The cutaneous silent period (CSP) like suppression of nerve activity was noticed after cutaneous nerve stimulation. Postsynaptic potentials in motoneurons during CSP suppress firing and reverse below threshold for action potential generation.

In conclusion, we found no evidence for sustained changes in intrinsic properties of motoneurons during the gradual onset of a scratch. Our results show that L-type Ca2+ channels in pre-motor interneurons contribute to gradual induction of the scratch network activity. The direct postsynaptic inhibition of motoneurons contributes to CSP. However we do not exclude inhibition of excitatory drive to motoneurons as a mechanism of CSP.

Simulating the brain: from channels to neuronal assembles

Gytis Baranauskas
Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania and Dept. of Physiology, Ben Gurion University of Negev, Beer Sheba, Israel

To understand how genetic makeup shapes brain function we need to know investigate the brain at different levels: from how single proteins that make ionic channels contribute to the biophysical properties of neurons to how neuronal networks generate spike patterns and, ultimately, behavior. I was lucky enough to be able to contribute to several different levels of our understanding about brain function.

Sodium channels drive the action potential generation, the elementary units of information in the brain. The biophysical properties of sodium channels largely determine the shape of action potentials that can be important for information transfer between neurons. It has been long believed that for all sodium channel subtypes in all species the activation time-course can be described by the famous Hodgkin and Huxley model [1], which assumes the presence of 3 independent gates responsible for a delay in the activation time-course. In this model it is assumed that sodium currents can be fit with a cube of an exponential function. However, Hodgkin and Huxley performed their studies on the axon of a squid, an animal species very distant from mammals. High temporal resolution recordings of sodium currents in central mammalian neurons revealed that a first order exponent fits better the time course of sodium currents in these cells [2]. Thus, there is a single, rate-limiting transition ('gate') that accounts for the shape of the sodium current activation time-course. Computer simulations show that such channels result in steeper onset of spikes, a property that is known to be necessary for faster information transfer between neurons [3].

Such information transfer in the brain is usually accomplished by neuronal assemblies and their properties can be investigated by recording local field potential (LFP) because LFP is generated by a large number of neurons representing their population response. Because of that, LFP signals are more robust than single neuron recordings that covey information about single neuron activity. However, the exact nature of LFP is still debated. We employed multichannel recordings and compared the power spectra of single spikes and LFP. We demonstrate that these spectra are dramatically different even if recorded in the same location. The difference is due to the fact that LFP reflect more changes in the neuronal membrane potential than spiking activity [4]. We show that the observed 1/f2 scaling of local field potential power spectrum is due to sharp transitions between UP and DOWN states of cortical neurons and this scaling has little to do with the patterns of spiking activity in these neurons [4]. Thus the low frequency LFP can be used to detect synchronized changes in membrane potential while the higher frequency LFP can be used to detect synaptic activity in neurons.

1. Hodgkin, A.L. and A.F. Huxley, A quantitative description of membrane currents and its application to conductance and excitation in nerve. J Physiol (Lond), 1952. 117: p. 500-544.

2. Baranauskas, G. and M. Martina, Sodium currents activate without a Hodgkin-and-Huxley-type delay in central mammalian neurons. J Neurosci, 2006. 26: p. 671-84.

3. Fourcaud-Trocme, N., et al., How spike generation mechanisms determine the neuronal response to fluctuating inputs. J Neurosci, 2003. 23: p. 11628-40.

4. Baranauskas, G., et al., The origins of 1/f2 scaling in the power spectrum of intra-cortical local field potential. J Neurophysiol, 2012. 107: p. 984-994.

Dr. Gytis Baranauskas from the Neuroscience Institute at the Lithuanian University of Health Sciences in Kaunas, and the Department of Physiology at the Ben Gurion University of Negev in Beer Sheba, Israel.

Patients' wellbeing in PONTE

Robertas Bunevičius
Institute of Psychophysiology and Rehabilitation, Lithuanian University of Health Sciences, Palanga, Lithuania

PONTE, "Efficient Patient Recruitment for Innovative Clinical Trials of Existing Drugs to other Indications", is 7F project that aims providing a platform following a Service Oriented Architecture (SOA) and Semantic approach that will offer automatic intelligent identification of patients eligible to participate within well-specified clinical trials for drug repositioning with specific focus on mitigating patient safety risks, reducing clinical trial costs and improving clinical trial efficacy. Work towards this direction involves decision support mechanisms fed with information retrieved from a semantic search engine; the latter operating on top of a data representation linking data within drug and disease knowledge databases, clinical care and clinical research information systems.

In the meanwhile, treatments with high efficacy may be limited by severe side effects or efficacy may be lost in translation. Translation into clinical therapy has to overcome substantial barriers at the preclinical and clinical levels. Thus, bridging basic science to clinical practice comprises a new scientific challenge which can result in successful clinical applications with low financial cost. However the outcome of such clinical research effort are closely dependent on the available data and the target population. In fact, clinical trials require the pursuit of a number of aspects that need to be addressed ranging from the aggregation of data from various heterogeneous distributed sources (such as electronic health records - EHRs) to the intelligent processing of this data based on the clinical trial-specific requirements for choosing the appropriate patients eligible for recruitment.

Clinical part of the PONTE runs THiRST study that is a prototype of the project. THiRST evaluates effects of known medication, triiodothyronine, on preventing heart failure in patients after acute myocardial infarction. This study is run by the Italian partners of the project in Pisa hospital. Clinic of the Institute in Palanga is a clinical partner of the PONTE consortium and is responsible for the evaluation of mood symptoms, fatigue and health related quality of life in association with thyroid hormone function in patients after myocardial infarction.

Misperception of positional relations

Aleksandr Bulatov
Institute of Biological Systems and Genetics, Lithuanian University of Health Sciences, Kaunas, Lithuania

The present communication addresses a possible role of the perceptual position shifts of the stimulus parts in geometric illusions of extent of the Müller–Lyer type. The results of the present psychophysical experiments with a single set of the Müller–Lyer wings are discussed in relation to the findings of some recent studies of full versions of illusory figures. It is shown that the effects obtained convincingly support the "centroid" explanation of illusions investigated.

Collision detection in frog optic tectum

Gytis Svirskis
Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

Collision detection is an important brain function in everyday life of diverse animals starting from invertebrates, e.g. locusts, and ending with humans. This function is employed for avoiding predators, and, thus, is necessary for survival; avoiding collision with surrounding objects during navigation in the environment, and catching prey. However algorithms employed for collision detection in the brain are not known. We created integrated eye-tectum preparation for investigation of synaptic integration of visual signals in the frog. Such preparation allows simultaneous visual stimulation and intracellular registration of synaptic currents or membrane potential changes in the frog optic tectum.

We showed that layer 6-7 neurons in the optic tectum received long-lasting strong excitation when stimulated with enlarging visual stimulus mimicking approaching object. The same neurons received only short-lasting excitation when they were stimulated with shrinking visual stimulus mimicking receding object. These properties suggest that layer 6-7 neurons projecting to the motor centers perform collision detection function. Voltage clamp recordings indicated that the neurons received mostly excitatory inputs suggesting their retinal origin.

Learning world model in simulated environment

Gailius Raškinis
Department of Informatics, Vytautas Magnus University, Kaunas, Lithuania

An intelligent (adaptive) agent needs to have a world model if it wants to be capable of addressing tasks that require action planning. A world model can be constructed by an agent itself on the basis of its experience accumulated during its interaction with the environment. Deterministic finite automaton (DFA) may serve as a support structure for a world model. DFA is a convenient choice for an agent operating in a partially observable, static and noise-free environment.

One particular way of learning a deterministic finite automaton (DFA) has been presented assuming that the agent starts the exploration of its environment without any a priori knowledge of the properties of the environment and the effects of its own actions.

The presented technique is based on the idea that names or descriptions of DFA states need not to be atomic labels. Instead, DFA states can be assigned compound names consisting of a set of values each characterizing some variable, where variables are shared across all states. Initially, DFA state description is based on the set of observed variables. DFA state description is further enriched by additional "hidden" variables when the agent faces the problem of non-determinism, i.e. the DFA state – action sequence fails to comply with the definition of the 1st order Markov decision process. Hidden variables are eliminated from the state description if their dependence on other variables is discovered. Separate predictor functions are learnt for every state variable and their consistency with the agent's experience is enforced and maintained. Supervised symbolic learning techniques are used for this purpose.

This procedure of repeatedly introducing and eliminating hidden variables effectively reduces observation-action sequence which is a higher order Markov decision process (because of the partial observability of the environment) to the DFA state – action sequence which is the 1st order Markov decision process. The algorithm was illustrated on a toy problem, where agent was navigating in partially observable 2x2 grid world. The algorithm succeeded in constructing a world model based on the minimal set of hidden variables but the overall number of model states was not minimal.

Prof. Robertas Bunevičius, Director of the Institute of Psychophysiology and Rehabilitation at the Lithuanian University of Health Sciences in Palanga.

Dr. Aleksandr Bulatov from the Institute of Biological Systems and Genetics at the Lithuanian University of Health Sciences in Kaunas.

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