National Institute of Chemical Physics and Biophysics

Keemilise ja Bioloogilise Füüsika Instituut

Activity Report 2016

NICPB activity report, September 2016

Contents

1 Introduction

The document contains hyperlinks to some documents, CV-s of personnel and projects. Please follow these links to see more details.

NICPB is a legal person under public law and operates under the "National Institute of Chemical Physics and Biophysics Act" approved by the Parliament of Estonia in 1998. Unfortunately nothing is said in the law about funding of the institute. Today, about 85% of our funding is project based and our research groups are competing with all other groups. The remaining 15% comes from the Ministry of Education and Research as baseline funding and it is calculated based on previous performance (number of publications, amount of grants, etc.).

Currently the Ministry of Education and Research is carrying out a reform of universities and research institutes in Estonia with the general aim of integrating research institutes into few large universities, University of Tartu and Tallinn University of Technology. Since NICPB is situated right next to the campus of Tallinn Technical University all PhD students in the Laboratory of Chemical Physics are enrolled there; in other laboratories we have PhD students also from other Estonian universities. We in NICPB see ourselves more valuable when we can collaborate with all Estonian universities equally well. Right now we have had an advantage in getting the PhD students because of our relatively large amount of research grants as compared to universities.

From the discussions with the Ministry it has become obvious that we need to define clearly and very well the purpose of having an independent research institute in a small country like Estonia. We have made a list of our key competences that we consider important. It is much more complicated to come out with a good working model for an institute like ours, especially if virtually all of them contain some kind of funding commitment.

The summary of the development of NICPB from 2011 to the end of 2014 can be found in the activity report. The main change since then has been closing of the Laboratory of Bioorganic Chemistry, because of no successful grant applications over several years. Most of the institutional grants end in 2019 creating a critical situation for new grant applications in the coming years. Only the centres of excellence have a longer time span.

The funding of NICPB has increased from 2.9 M€ in 2011 to 5.0 M€ in 2014 and decreased to 4.4 M€ in 2015. In 2016 the budget stayed the same, but in addition to that we got about 2 M€ funding for the renovation of the institute main building. Although the financial situation is not bad today, it contains risks when the projects get shorter in time and not necessarily larger in amount.

2 Strategic research programmes

The topics of research are determined by the NICPB Act. They include research areas of national and European importance and as a rule, are integrated in international and national cooperation.

The scientific research in NICPB is realised via scientific programmes integrating different areas of science from quantum physics to experimental biology. NICPB`s programmes are accomplished by scientific infrastructure, which is available for universal usage by all programmes. In comparison to the research institutions based on universities, NICPB`s programmes are more extensive and interdisciplinary.

2.1 High Energy Physics, Theoretical Physics, Computing

The most important question in modern fundamental physics and in cosmology is the origin of different mass components of the Universe, including the Dark Matter and Dark Energy. The research strategy of the Institute includes a programme to address this question both experimentally as well as theoretically. In addition to this, the theoretical physics programme of the NICPB covers different topics in theoretical physics and in cosmology. To enable this research activity, the institute has established Datacentre for high performance computing that provides the physics groups with computing resources and develops grid and cloud platforms for scientific computing.

2.1.1 Experimental High Energy Physics

One of the key activities of the NICPB is to represent the Republic of Estonia at CERN and to coordinate research activities of Estonian universities at CERN. The institute is a member of the CMS Collaboration of the Large Hadron Collider and a group of experimental physicists is participating in the data analyses of the CMS results. Our researchers have been involved in two CMS working groups, in the top quark physics group studying single top production and in the Higgs physics group studying tau and top Yukawa couplings. In the nearest future the group will concentrate on the latter.

In order to contribute to the upgrade of the CMS experiment, the group is expanding also to include hardware aspects of high energy particle physics with initial plans for CMS upgrade contributions in the L1 trigger for better tracking decisions at high luminosity.

In addition to the participation in the CMS experiment, the NICPB is also organizing the Estonian summer student and high-school teachers' programmes at CERN.

2.1.2 Theoretical Particle Physics

The theoretical physics programme of the NICPB contains two main directions. The first one covers theoretical and phenomenological research topics in particle physics, astroparticle physics and in cosmology. This is the main theoretical research activity of the institute. The second covers statistical mechanics, complex systems/interdisciplinary physics.

The particle physics theory group studies several topics including the properties of the Higgs boson, naturalness of its mass and its implications for the vacuum stability of the Universe, the origin and properties of Dark Matter and Dark Energy, solutions to the hierarchy problem such as supersymmetry and relaxion, different ideas of cosmological inflation, the phenomenology of particle physics processes at the LHC and their connection to Dark Matter, neutrino mass models and leptogenesis, modifications of gravity in order to explain Dark Matter as a gravitational relic etc.

The statistical physics group studies a diversity of topics including diffusion and stochastic processes, classical and quantum Brownian motion, ecological competition models with population dispersal, culture and language dynamic, and econophysics and kinetic wealth exchange models.

2.1.3 High Performance Computing

In order to participate in the CMS experiment, the institute has created a Tier-2 computing centre which is one of the biggest computing centres for the CMS experiment in Europe. Today it consists of 6000 computing cores and 2.5PB of disk space plus dedicated machines for cosmological simulations. In addition to providing CPU power and disk space for the CMS experiment and for theorists, the Datacentre has also participated in early adoption and development of Grid computing in Estonia and Baltics and has since then moved to more modular and adaptive platforms mostly known as cloud computing. The NICPB Datacentre, together with the ones of University of Tartu and Tallinn University of Technology, is part of Estonian Scientific Computing Infrastructure. The Datacentre group is active in multiple EU and local level grants on architecture development and operations.

2.2 Physics of Condensed Matter and Material Science

The understanding of magnetic, optical and thermal properties of condensed phases of new materials and their applicability in novel technologies are key questions in contemporary condensed matter physics and material science. The functionality of new compounds is usually highly unpredictable due to strong electron correlations (magnetism, ferroelectricity, charge order etc.) and due to complicated structure (large unit cells of intermetals and oxides, composites). Our focus points are (i) on novel quantum materials, (ii) materials related to energetics and (iii) in high quality unique experimental capabilities.

Where ample in-house spectroscopic tools (nuclear magnetic resonance, THz spectroscopy in high magnetic fields, IR and optical spectroscopy) or experimental conditions are insufficient, experiments are performed at external facilities such as high magnetic field laboratories, neutron scattering and synchrotron facilities. For sample characterization we employ X-ray powder diffractometer, Physical Property Measurement System (PPMS) equipped with 14T magnet and multiple sample characterization probes including recently commissioned atomic force microscope insert for surface studies.

2.2.1 Emerging Quantum Materials

This research program focuses on fundamental physical properties of complex novel materials that may have high-tech applications. Strong correlations between spin and charge degrees of freedom as well as miniaturization mean that their properties can only be fully understood in the framework of quantum mechanics. Such materials include multiferroics, high-Tc superconductors, quantum magnets, nanomaterials, etc. Multiferroic materials can exhibit magneto-electric interaction that makes the magnetization and electric polarization mutually inter-dependent, offering new concepts for broad range of applications. High-Tc superconductors where the complex interplay between spin, charge and lattice remains elusive also have high applicability. Realizations of multiple model systems among quantum magnets allows to verify and improve theoretical models, study quantum phase transitions in pure systems and address the influence of disorder inherent in all realistic systems. Nanosized single molecule endofullerenes provide means to study quantum confinement, gain spectroscopic information on a particular trapped molecule as well as it's interaction with the confining carbon surface. Among strongly correlated electron materials the heavy fermion systems have been the source of unconventional superconductivity, novel magnetism and hidden order. For enhancement of quantum effects studies are performed at low temperatures.

2.2.2 Static and Dynamic Correlations in Matter

Our experimental capabilities allow to investigate material response functions over very wide spectral range covering 16 orders of magnitude in frequency starting from static susceptibility probes, nuclear magnetic resonance, THz, infrared up to UV optical spectroscopy, all contributing to the understanding of structure and structure-function relationship in matter. Perpetual development of these techniques towards higher detection sensitivity, increasing stability, variety and range of experimental control parameters allows us to tackle wide range of problems in physics, chemistry and biology.

For sample characterization we employ X-ray powder diffractometer, Physical Property Measurement System (PPMS) equipped with 14T magnet and multiple sample characterization probes including recently commissioned atomic force microscope insert for surface studies and home-built NMR probe for variable field values.

NMR spectroscopy is based on high-precision radio frequency measurement of nuclear spin energy levels in a magnetic field. Fine structure of the spectra depends on local interactions, generated by chemical bond and other nuclei. Different magnetic field strength and various temperatures allow for increased sensitivity and/or to alter the states and functionality of the sample at hand. Using NMR as an analytical tool in chemistry, biology and solid state physics forms an essential part of the program. Structural analyses and control of syntheses of enantiomers, diastereoisomers and other sophisticated molecules is addressed as an issue of basic chemistry. The goal of the molecular biology part is to determine protein mobility and interactions, regarding also quantum- and tunnelling effects, and also to develop studies on membrane and transport proteins (Cf also Bioenergetics). In solid state physics the programme is strongly coupled and quintessential to both the spin materials programme (see above) and to the energy materials' programme (see below). Towards that end super-fast rotation techniques at extreme temperatures are be developed. High resolution and sensitive measurements at temperatures ranging from 10°K (quantum materials) up to 1200°K (energy materials) combined with static measurements between 2-400°K in arbitrary applied field up to 14T open qualitatively new possibilities for detailed study of the structure and dynamics of molecular interactions and facilitate the development of new technological materials.

THz and optical laboratory facilitates spectrometers to measure transmission and reflection in wavelength range from 3mm up to 200nm (3 - 50000 cm^{-1}) at various sample environments. Particularly useful for studying emergent quantum materials is the THz spectral range that encompasses electron spin and magnon resonances. To that end several dedicated spectrometers are used: TeslaFIR (equipped with 17T magnet, covers 100 GHz - 6 THz, has static electric field capability and light polarization control, provides sample temperature down to 2.5K and has high sensitivity bolometric detection at 0.3K), TLE200 (a modified dilution refrigerator with 12T magnet, sample temperature below 1K, covers 100 GHz - 2 THz) and Toptica continuous wave phase sensitive THz spectrometer (photomixing of two IR lasers, frequency from 50 GHz to 2THz, currently usable sample temperature down to 5K). Conventional IR to UV spectroscopy can be performed down to 5K temperature using Bruker Vertex 80v.

An additional optical tool is two-photon absorption that enables accurate measurement of local electrostatic field and associated key molecular parameters in a variety of configurations and environments, including bulk solutions, amorphous solids, surfaces, solid-liquid interfaces, membranes, biopolymers etc. The same hardware is suitable for second harmonic generation to characterize ME materials.

2.2.3 Energy materials

Research of energy materials is of utmost importance to the energy production and storing in the next generation fuel cells, Li-ion batteries and supercapacitors. In one end the programme focuses on solid oxide fuel cells (SOFC), on the other it encompasses assessment of environmental impact of national oil shale energy production and applications of it ash residue. We make use of our capacity to do X-ray diffraction, optical, magnetic, electric and thermal transport, heat capacity, electrochemical impedance, thermogravimetric measurements of those compounds as well as solid state NMR studies at extremely low (10°K) and high (1200°K) temperatures. We are also active in the development of commercially usable SOFC elements with our commercial partner Elcogen Ltd. where the main challenge is long term stability of SOFC systems. There are three aspects to it: Firstly, long term phase stability of stack components, mainly cell electrodes at cell working conditions. Secondly, interdiffusion of stack component materials in long term operation. And thirdly, influence of impurities in both air and fuel mixture to electrode and interconnect structure and electrochemical behaviour. These interrelated issues could be efficiently addressed only by close cooperation of a production unit with a research facility with multiple analytical options and competences. We are also involved in studies of modern permanent magnets that are essential to efficient wind turbines.

2.3 Macromolecular interactions

2.3.1 Molecular System Bioenergetics

Beyond the fundamental role in energy metabolism, mitochondria perform a great variety of other important cellular functions like signalling and control of apoptosis. The interplay among these several roles of mitochondria is still not clear and the growing body of evidence indicates that underlying mechanisms can be related to system level properties. System Biology paradigm assumes the description of complicated biological systems through the study of relatively independent subsystems describing their structure, function and interactions between them. The Molecular System Bioenergetics approach is aimed to study intracellular structural interactions in the regulation of energy metabolism in healthy cells as well as in pathology.

The main research topics in the laboratory of Bioenergetics are the biophysics and biochemistry of the energy transport through phosphotransfer networks, which are mostly presented by the creatine kinase and adenylate kinase systems. The metabolic feedback regulation of mitochondrial respiration and energy fluxes will be analysed in detail in some neural, muscle and cancer cells from the point of view of molecular system bioenergetics.

In the case of cardiac and skeletal muscle cell bioenergetics this approach requires a description of the kinetics of co-functioning of the multicomponent system comprising of respiratory chain, ATP sythasome in the mitochondrial inner membrane (including ATP synthase, adenosine-nucleotide translocase and phosphate transporters), mitochondrial creatine kinase and adenylate kinase, porine channel in the mitochondrial outer membrane (through which the metabolites are exchanged to cytosol) and protein factors modulating this channel, one of which is assumed to be tubulin heterodimer and plectin.

Alterations in the intracellular structural interactions of the oxidative muscle cell and the formation of a mature energy metabolism during postnatal development and impairment these interactions during ageing is an ideal model to study highly organised intracellular systems, where the regulation of cellular bioenergetics varies according to their structure. Changes in the cell bioenergetics are one of the first signs of the cell pathology; therefore the studies of the bioenergetics of the malignant clinical material and cell cultures are of great importance. Recent advances in basic science have allowed the development of anti-cancer bioenergetic medicine. The modifications of intracellular structure-function interactions accompanied by adaptation of energy fluxes, metabolic control and feedback regulation depending on the cell type, degree of differentiation and health/pathology state will be studied. The heterogeneity of mitochondrial function among different tissues and states demonstrates an additional level of mitochondrial complexity. This is a new, challenging area in mitochondrial research that potentially leads to integration of mitochondrial bioenergetics and cellular physiology with various physiological and pathophysiological implications.

The program gives us the theoretical background to understand the bioenergetics of healthy muscle cells, as well as cellular pathologies like ischemia, heart failure, myocardial infarction, neurodegenerative diseases, bioenergetic mechanisms of cancer, and mechanisms of ageing. This program allows explaining the perturbations in biological system that bring to pathology (e.g. heart disease, tumors) and thereby help to predict new outcomes of medical diagnostics and drug treatments.

2.3.2 Two-photon Absorption (2PA) in Biomolecules

Two-photon fluorescence microscopy is becoming one of the standard and most informative methods in biological research because it facilitates increased spatial resolution and increased depth of tissue penetration. These useful attributes occur due to special physical properties of two-photon absorption (2PA) phenomena, which include quadratic dependence of the excitation probability on instantaneous photon flux density, and which also allow using near-infrared wavelengths to excite visible fluorescence.

There is however at least one more unique physical property of 2PA that can and should be exploited to obtain important novel information, especially in order to address numerous critical questions regarding structure and function of biopolymers. Namely, because 2PA constitutes a higher-order interaction between light and molecular chromophore, the probability of this process depends not only on transition dipole moments between different molecular energy levels, but also depends on the value of permanent electric dipole moments of the same chromophore, which itself varies as a function of local electric field. Recently it was shown that quantitative measurement of 2PA cross section in biological chromophores such as fluorescent proteins can be used to determine accurate value of the corresponding dipole moment difference parameter, and thus determine the strength and direction of the local electric field acting inside 3-nm diameter barrel protein. This type of novel physical measurement is uniquely valuable because it allows beginning shedding light on the very fundamental, but still largely unknown properties of local electrostatic interactions in- and between biopolymers on nanometre scale.

The purpose of the research work in this area is two-fold. The first goal is to continue developing physical principles of local electric field sensing by two-photon spectroscopy and microscopy. This is addressed by investigating 2PA properties in broad range of different fluorescent as well as non-fluorescent biomolecular constructs and probes, in order to create and characterize novel type of molecular multi-photon optical sensors that are specially designed to detect and quantify local electric fields. Improving accuracy and reliability of 2PA data, as well as improving acquisition speed, optimizing wavelength range, integration with existing microscope systems etc. are examples of numerous critical technical issues that also need to be addressed. The second and at this time a more distant goal is to initiate R&D level work on specialized hardware and software that, in combination with the specialized 2PA-optimized molecular probes can be used by other researches' for a broad range of biomolecular investigations.

The utmost purpose of this strategic research direction is to develop new experimental methods and physical instruments or tools that will allow us and other researchers worldwide to understand how biopolymers perform their most amazing complex functions, and perhaps how man-made technology could augment or mimic these functions. All this will ultimately allow us better understand physical principles of life itself.

2.4 Environmental Toxicology and Chemistry

Research of environmentally hazardous materials – toxic substances that are released by human activity and are harmful to ecosystems as well as to people – is a field that involves biology, physics, chemistry, material science and healthcare. An interdisciplinary institution such as NICPB is therefore highly suitable for the successful development of this field of research and environmental studies continue to be one of the central research strategies of NICPB.

The main strategic goal of the environmental toxicology & chemistry research direction in NICPB is to elucidate the hazard of (industrial) chemicals, including novel man-made nanoparticles and nanomaterials, that either already are in the environment or have the potential to end up there.

Especially challenging is evaluation of the environmental hazard of **synthetic nanoparticles** (particles with at least one dimension less than 100 nm) that are already produced in large scale in a variety of compositions, shapes and sizes. Due to their small size nanoparticles have novel properties, exploitation of which may lead to breakthroughs in many technologies starting from energy production and ending with medicine, but also may lead to adverse effects for man and the environment.

In order to approach the strategic goal on elucidating the **hazard of existing and emerging toxic chemicals** we address following: (i) is it (the given chemical/nanoparticle/nanomaterial) toxic? (ii) to whom and how toxic? (iii) why toxic? and (iv) how to assess the toxicity comprehensively and cost-effectively? According to the chemicals regulation in the **European Union (REACH)** all chemical substances produced in excess of 1 tonne per year (estimated number exceeds 100 000) have to be characterized in terms of toxicity by the year 2018. It is a considerable burden for the European chemical industry (including Estonian chemical industry), since the responsibility of assessments lies on the manufacturer. Moreover, this task is especially challenging in case of nanomaterials that exist in countless varieties and thus due to economic reasons cannot be tested one-by-one. Therefore, novel intelligent test strategies are needed that include also **QSAR approaches**. Quantitative Structure-Activity Relationships (QSARs) are widely used for the prediction of toxicity of conventional organic chemicals that explores the concept of basal toxicity, i.e. as a rule, the toxicity of chemicals is related to **adverse effects on cell membranes** and processes of basal metabolism, which can be predicted reliably using *in vitro* assays (including tests with e.g., bacteria, protozoa and invertebrates). However, nanoparticles as considerably more difficult for **QSAR modelling** and need also relevant (eco)toxicity data, to feed the model. The NICPB exotoxicology team has know-how and facilities to conduct several **regulatory assays** for ecotoxicological evaluation of chemicals/materials important for REACH: *Daphnia magna* acute immobilisation assay (OECD202), *Daphnia magna* reproduction test (OECD211) and algal 72 h growth inhibition assay (OECD201). In addition, we have the know-how and facilities for ISO 21338:2010 assay (Water quality -- Kinetic determination of the inhibitory effects of sediment, other solids and coloured samples on the light emission of *Vibrio fischeri* (kinetic luminescent bacteria test) and water plant *Lemna sp*. growth inhibition test (OECD 221).

One direction of this strategic program is development of **novel test systems** and strategies that enable cost-efficient assessment of biological effects of chemicals and nanomaterials. In this research we mostly focus on *in vitro* tests that allow the assessment of adverse effects and toxicity mechanisms of chemicals and nanoparticles using **rapid and cost-efficient assays** allowing high-throughput. In NICPB KTL we have facilities and knowledge on evaluation of biological effects of chemicals and nanomaterials using various types of **animal cells *in vitro*** (e.g., Caco2, A549, balb/c3T3, K562, TPH1, Hep2). We also design and use **novel bioassays** based on mechanism-based modification of bacteria such as luminescent recombinant bacteria that 'sense' very low concentrations of bioavailable heavy metals (metal sensing bacteria), for example Cu and Ag-sensing E. coli MC1061 (pSLcueR/pDNPcopAlux). We also have analogous sensor bacteria for bioavailable Zn, As, Cr and Pb. We possess know-how in working with **single-gene knock-out** *Saccharomyces cerevisiae* strains (from EUROSCARF) that we use for **profiling of toxicity mechanisms** of synthetic nanoparticles. For all the bioassay organisms deposited in NICPB, see https://kbfi.ee/e-tox-collection/. Our strategy on widening *in vitro* research and use of non-vertebrate animal models in toxicology research is coherent with the **3R's strategy** (Replacement, Reduction and Refinement) – a research principle that throughout the world is embedded in legislation which governs the use of animals in science.

The scientific **knowledge on mechanisms of toxic action** of chemicals/nanomaterials allows to design more safe chemicals/nanomaterials (**safe-by-design**), or, contrarily, to design more toxic chemicals/nanomaterials (**toxic-by-design**). The former approach is crucial to support the sustainable development of nanotechnologies as its products must be safe on all stages of their life-cycle (from 'cradle to grave' principle). The latter approach (toxic-by-design) can be applied for design of novel surface cover materials for food industry and hospitals, for example, where the spread of harmful microorganisms should be avoided or minimized. The toxicological analysis of the **chemical libraries of novel chemicals** (ionic liquids, nanoparticles, surfactants) using unicellular test organisms (bacteria, fungi, algae) allows to shortlist new efficient antimicrobials, antifungals and algaecides.

In addition to ecotoxicological studies also the **fate of the pollutants** in different environmental compartments (water, soils and sediments) is needed for environmental hazard evaluation. The NICPB researchers have studied the **mobility of pollutants** in the environment (sorption, desorption, solubility, complexation etc.). The evaluation of the mobility of environmental pollutants coupled to ecotoxicological studies has been used for the environmental hazard assessment of pollution originating from the oil-shale industry and energy production (such as fly ash and semicoke) but also in soils polluted with **heavy metals, oils, phenolic compounds and PAHs**. The earlier research initiated by NICPB scientists led to the reclassification of one of the most important pollution flows of the oil-shale industry – fresh semi coke – as hazardous waste in 2003, resulting in the change of its deposition according to the rules of the European Union. The current strategic program also aims to explore the possibilities of large scale reuse of oil-shale industry (fly)ashes.

3 Laboratories

3.1 Laboratory of High Energy Physics and Computational Physics

The research activities of the NICPB covering the high-energy physics, theoretical and computational physics are confined to the Laboratory of High Energy and Computational Physics, head of the laboratory Prof. M. Raidal. The Laboratory has been growing rapidly. Currently the Laboratory employs 21 researchers and postdocs with PhD, all of them are young and active. They supervise 4 doctoral students and a number of master and bachelor students in different Estonian universities. The Datacentre employs 3 technicians. Those researchers have been successful in grant applications. Today the Laboratory hosts

- 1 Centre of Excellence
  - TK133 "Dark Side of the Universe (1.01.2016−31.08.2023)" M. Raidal
- 3 Institutional Research Grants of the Estonian Research Council
  - IUT23-4 "Experimental high energy physics at the CMS experiment at LHC (2014 − 2019)" M. Kadastik
  - IUT23-6 "Origin of Mass (2014 − 2019)" M. Raidal
  - IUT39-1 "The role of diversity in complex systems (2015 − 2020)" E. Heinsalu
- 4 Personal Research Grants
  - PUT716 "LHC Phenomenology at 13-14 TeV and Physics beyond the Standard Model (2015 − 2016)" C. Spethmann
  - PUT808 "Indirect Probes of New Physical Phenomena in Space (2015 − 2018)" A. Hektor
  - PUT799 "Rethinking Naturalness – Electroweak Symmetry Breaking, Dark Matter, Inflation, and Planck Scale (2015 − 2018)", K. Kannike
  - PUT1026 "Phenomenology of the Dark Sector of the Universe (2016 − 2019)" A. Racioppi
- 1 Marie Curie Reintegration Grant
  - MSCA-IF "Indirect Probes of New Physical Phenomena in Space (2015 − 2016)" A. Hektor.

The laboratory is divided into three research groups responsible for experimental high energy physics, theoretical physics and for computing, details are presented below.

3.1.1 Experimental High Energy Physics

The group consists currently of three experienced researchers Mario Kadastik, Christian Veelken and Andrea Giammanco as well as two post-docs (Ram Krishna Dewanjee and Lucia Perrini) and a number of PhD, MSc and BSc students.

Past, present and future

The experimental group was originally part of the particle physics group at NICPB as it was established only in the last decade with majority of the development happening in the past 3-5 years since the LHC turned on. It was recommended during the last ISAB meeting, that more active roles be given to younger researchers and as one such example the HEP group split into a theory group led by the previous HEP group leader Martti Raidal and to an experimental group led by Mario Kadastik. The experimental group has been growing ever since, mostly through partnerships with experienced researchers coming to Estonia through Mobilitas grants as well as the training of students of whom some are now completing their PhD degrees at various universities abroad (including for example ETH, Zurich). We also have a number of prior students as post-docs abroad, whom we expect to see back in Estonia in the next 3-4 years.

One of the group's topics of interest has been in phenomenology, where in cooperation with the theory group we have performed various simulations on dark matter theories including a number of model independent studies that have been well received by the community. But the main emphasis is on the LHC data analysis and major focus has been in Higgs physics (doubly charged Higgs, ttH, H->2tau etc) as well as top quark physics (single top cross section and polarization measurements).

The group's main focus these days is on combining the prior expertise of top and Higgs and especially a lot of experience in tau reconstruction into one consistent analysis of Higgs production in association to a top quark pair and the subsequent decay of said Higgs to tau leptons. It is a very tough final state to observe, yet provides various essential measurements like top-Higgs coupling and that in a Higgs decay channel that is second to only bb-bar. The work is still ongoing with initial results for 8TeV known, but full dataset of 13TeV is needed to reach sensitivity.

The groups future plans include continued work on most interesting fields in Higgs physics, especially in the ttH channels as well as Higgs self-interactions once enough luminosity is available, i.e. after the upgrade. But we also anticipate a major new field to be development and operation of new HEP related hardware. The group has previously been only related to analysis efforts, but most healthy groups in the world contribute both to the final analysis as well as the actual R&D of the experimental apparatus as well. We find the upcoming CMS upgrade to be an ideal time to allocate resources also to bring in competency in this field as well as cooperate with local universities to further enhance our competency and to expand also the local knowledge on working such specialized projects. We have already developed initial excellent contacts with local electronics groups in the universities as well as some of the major R&D companies and are anticipating a number of post-doc and possibly PhD positions for hardware development and testing. In cooperation with a Tallinn University of Technology electronics group we have already supplied CMS with muon channel testing hardware in the previous years and hope to be able to contribute into L1 trigger developments in the future.

Key publications in 2015 – 2016

1) CMS Collaboration, "Observation of a new boson at a mass of 125 GeV with the CMS experiment at the LHC", Phys.Lett. B716 (2012) 30-61
2) CMS Collaboration, "Evidence for the direct decay of the 125 GeV Higgs boson to fermions", Nature Phys. 10 (2014)

3) CMS Collaboration, “Evidence for the 125 GeV Higgs boson decaying to a pair of tau leptons”, JHEP 1405 (2014) 104
4) CMS Collaboration, “A search for a doubly-charged Higgs boson in pp collisions at sqrt(s)=7TeV”, Eur.Phys.J. C72 (2012) 2189
5) CMS Collaboration, “Measurement of top quark polarisation in t-channel single top quark production”, JHEP 1604 (2016) 073
6) CMS Collaboration, “Measurement of the t-channel single-top-quark production cross section and of the |Vtb| CKM matrix element in pp collisions at sqrt(s)=8TeV”,JHEP 1406 (2014) 090
7) CMS Collaboration, “Reconstruction and identification of tau lepton decays to hadrons and nutau at CMS”, JINST 11 (2016) no.01, P01019
8) CMS Collaboration, “Search for additional neutral MSSM Higgs bosons decaying to a pair of tau leptons in pp collisions at sqrt(s) = 7 and 8 TeV”, CMS PAS HIG-14-029
9) CMS Collaboration, “Model independent search for Higgs boson pair production in the bbtautau final state”, CMS PAS HIG-15-013, journal publication in preparation

3.1.2 Theoretical Physics

The theory programme of the NICPB addresses several hot topics in particle physics, statistical physics and in cosmology.

Group members: Stefano DiChiara, Sean Fraser, Emidio Gabrielli, Els Heinsalu, Gert Hütsi, Andi Hektor, Kristjan Kannike, Luca Marzola, Marco Patriarca, Martti Raidal, Antonio Racioppi, Christian Spethmann, Alessandro Strumia, Federico Urban and a number of PhD, MSc and BSc students.

Past, present and future

The theoretical physics group was established in 2004 and has grown steadily to the largest research group in theoretical physics in Estonia. Initially the group consisted of Martti Raidal and couple of his students, and the research topic was particle physics. Being successful in grant applications and in supervising students allowed the group to hire new researches as well as to extend the research topics to include statistical physics, experimental high-energy physics, topics of cosmology etc. Today the group is the main force in the Estonian Centre of Excellence "Dark Side of the Universe” and collaborates with the gravity group of the University of Tartu and the cosmology group of the Tartu Observatory.

Today the group members attempt to address acute research topics in particle physics, astrophysics, cosmology, gravity and in statistical physics. Despite of the experimental efforts in all those fields, the unfortunate outcome is that we still do not know the origin of the standard model, the nature of dark matter and the dark energy etc. Those are the topics we address.

The existence of the group is guaranteed until the end of the present grants. No realistic plans can be made beyond 2020 because grant based financing does not allow long term planning.

Key publications in 2015 - 2016

1) Eugeny Babichev, Luca Marzola, Martti Raidal, Angnis Schmidt-May, Federico Urban, Hardi Veermäe, Mikael von Strauss. ”Gravitational Origin of Dark Matter”, arXiv:1604.08564 [hep-ph] (accepted for publication by Phys Rev).
2) Andrew Fowlie, Csaba Balazs, Graham White, Luca Marzola, Martti Raidal. “Naturalness

of the relaxion mechanism", arXiv:1602.03889 [hep-ph].10.1007/JHEP08(2016)100. JHEP 1608 (2016) 100.

3) Stefano Di Chiara, Luca Marzola, Martti Raidal. "First interpretation of the 750 GeV diphoton resonance at the LHC", arXiv:1512.04939 [hep-ph], 10.1103/PhysRevD.93.095018. Phys.Rev. D93 (2016) no.9, 095018.
4) Stefano Di Chiara, Kristjan Kannike, Luca Marzola, Antonio Racioppi, Martti Raidal, Christian Spethmann. "Relaxion Cosmology and the Price of Fine-Tuning", arXiv:1511.02858 [hep-ph], 10.1103/PhysRevD.93.103527. Phys.Rev. D93 (2016) no.10, 103527.
5) Matti Heikinheimo, Martti Raidal, Christian Spethmann, Hardi Veermäe, "Dark matter self-interactions via collisionless shocks in cluster mergers", arXiv:1504.04371 [hep-ph]. 10.1016/j.physletb.2015.08.012. Phys.Lett. B749 (2015) 236-241.
6) Kristjan Kannike, Gert Hütsi, Liberato Pizza, Antonio Racioppi, Martti Raidal, Alberto Salvio, Alessandro Strumia. "Dynamically Induced Planck Scale and Inflation", arXiv:1502.01334 [astro-ph.CO]. 10.1007/JHEP05(2015)065. JHEP 1505 (2015) 065.
7) Patriarca, M.; Hernandez-Garcia, E.; Toral, R., "Constructive effects of diversity in a multi-neuron model of the homeostatic regulation of the sleep–wake cycle", Chaos, Solitons and Fractals, 81, (2015). 567−574.

3.1.3 High Performance Computing

Group members: Mario Kadastik, Lauri Liibert, Ilja Livenson

Past, present and future

The computing center has been built up in stages of various intermittent funding rounds over the past ten years. The architecture has always been chosen to be off the shelf hardware that is then distributed with a scheduling system. Recently it has been virtualized to remove any dependence on the actual varying hardware. Competence to build such a large scale center has come from prior experience in the industry by the people involved as well as various local and EU projects (i.e. BalticGrid, EGI, and various cloud projects).

The current architecture uses commodity hardware to build a uniform 6000+ core cluster that also hosts a distributed storage of 2.5PB (raw). The whole system has an interconnect on standard 10GbE networking and can sift through a large amount of data in parallel. The software architecture is custom built, but uses industry standard schedulers as well as Grid endpoints for distributed computing. We also partake in local cloud initiatives to open up the platform to allow custom images to be submitted.

As leaders in HPC in the region we represent also Estonia in the European Grid Infrastructure (EGI) council and are one of the founding and core members of the Estonian Science Infrastructure as well as the new Estonian Research Cloud initiative. As the path of EGI is to create the EU wide cloud architecture we feel to be perfectly positioned to help evolve it towards such a future goal. Expansion wise we expect to use the same physical capacity of the server room and expand in resources that we can fit there over the next few funding rounds in 2018 and later.

The people involved have varied depending on projects, but the core competency has remained strong with both Mario Kadastik (chief architect) and Ilja Livenson (foremost cloud expert) having been with the institute already 12y and 10y respectively. In addition we have a very capable admin/developer Lauri Liibert, who's been with us for over a year and is overseeing daily operations. Beyond that we also have occasional help from students.

Key publications in 2015 - 2016

No publications. The staff provides technical support for physicists to run their physics jobs.

3.1.4 General comments on the future of the Laboratory

The most important concern for the future of the Laboratory is its sustainability. The Laboratory exists today because (i) its members have been able to obtain many research grants and (ii) they were smart to use the grants to develop science consistently. This has been a miracle rather than a result of long term planning. Because NICPB is practically 100% on grant based financing, and because the financing of research in Estonia has steadily decreased since 2007 (and is expected to decrease further in the future), negative drawbacks after 2020 seem inevitable.

3.2 Laboratory of Chemical Physics

The acting head of laboratory, starting from May 2016 is Dr. D. Hüvonen. The laboratory employs full time 18 researchers with PhD who supervise 4 doctoral and 2 master students. Three persons out of the technical staff of 9 work at the cryogenic facility and also take care of the superconducting magnets.

The main topic of research in the laboratory is physics of condensed matter and material science. This covers the work of all groups, except the group of A. Rebane, who is studying two-photon absorption in biomolecules. The laboratory runs the largest infrastructure of the institute, the Estonian Magnet Laboratory that has several NMR instruments, THz spectroscopy and low temperature physics setups, all backed by the in-house helium liquefier. Although we have not been able to secure national funding to enlarge operations and join the European Magnet Laboratory we have been able to run advanced experiments and publish papers in high impact journals. Annual publication rate in journals indexed by Web of Science has been 49 ± 4 for last 3 years and totals 232 since 2010.

National collaborations include thin film sample preparation at University of Tartu and nanoparticle preparation at Tartu College of Tallinn University of Technology. In addition UT, TUT and NICPB collaborate in designing and building European Spallation Source (ESS) neutron scattering facility in Lund. The international collaboration network is broad. For example, in the field of multiferroics, quantum magnets and correlated electron systems we are collaborating with leading crystal growers and theoreticians in the world. We perform joint experiments in Tallinn and at high magnetic field and neutron scattering facilities in Europe and USA. Industrial collaborations include high-T fuel cell development with Elcogen (J. Subbi) and environmental toxicology assessments and investigation of coal ash residue recycling opportunities (J. Reinik) with Environmental Investment Centre and the Estonian energy company Eesti Energia.

In 2016 the laboratory hosts:

- 1 Centre of Excellence
    - TK134 "Emerging orders in quantum and nanomaterials (2015 – 2023)", U.Nagel
- 3 Institutional Research Grants
    - IUT23-3 "Interaction of THz radiation with magnetic excitations (2014 – 2019)", T. Rõõm
    - IUT23-7 "NMR investigations of the local structure and dynamics in solids and solutions (2014 – 2019)", I. Heinmaa

    - IUT23-9 "Multi-photon functional optical sensing materials (2014 – 2019)", A. Rebane
- 3 Personal Research Grants
    - PUT210 "Emerging Quantum Frustrated Magnets (2013 – 2016)", R. Stern)
    - PUT451 "Disorder in Quantum Magnets: Dynamics and Criticality (2014 – 2017)", D. Hüvonen
    - PUT1046 "Synthesis and functionalization of Fe based nanoparticles for high-sensitivity Magnetic Resonance Imaging (2016 – 2019)", L. Seinberg

3.2.1 Emerging Quantum Materials

There are 6 researchers with PhD in the Emerging Quantum Materials programme: Dan Hüvonen, Enno Joon, Urmas Nagel, Toomas Rõõm, Raivo Stern, Anna Šugai.

The history of the programme extends back to about 2000 when first publications on low dimensional quantum magnets were published using the newly commissioned THz spectrometer by T. Rõõm, U. Nagel and in parallel by R. Stern using the solid state NMR technique.

Today the scope of the programme has widened notably to include topics such as multiferroics, quantum phase transitions, disorder, frustration, superconductivity, single molecule endofullerenes, etc. Only recently the programme hosted a Mobilitas top researcher grant holder A. Tsirlin and his postdoc O. Janson doing DFT calculations. Currently they have new positions in Augsburg and Vienna, but remain active contributors to some local grants. In 2014 D. Hüvonen returned from PSI/ETH postdoc extending the programme by neutron scattering technique and disorder in quantum magnets. Currently T. Rõõm and U. Nagel supervise 2 PhD students and R. Stern one PhD student.

The future is to develop further the in-house capabilities and attract new competences. A joint proposal has been submitted by V. K. Thorsmølle for establishing a group of ultrafast nonlinear optics at NICPB.

The scientific output of the programme has been 20 papers to date in 2016, 30 papers in 2015 and 81 papers from 2010 to 2014.

Key publications in 2015 - 2016

1) Andrea Krachmalnicoff, Richard Bounds, Salvatore Mamone, Shamim Alom, Maria Concistrè, Benno Meier, Karel Kouřil, Mark E. Light, Mark R. Johnson, Stéphane Rols, Anthony J. Horsewill, Anna Shugai, Urmas Nagel, Toomas Rõõm, Marina Carravetta, Malcolm H. Levitt, Richard J. Whitby, The dipolar endofullerene HF@C60, Nature Chemistry 2563 (2016), DOI: 10.1038/nchem.2563
2) Pascal Puphal, Denis Sheptyakov, Natalija van Well, Lars Postulka, Ivo Heinmaa, Franz Ritter, Wolf Assmus, Bernd Wolf, Michael Lang, Harald O. Jeschke, Roser Valentí, Raivo Stern, Christian Rüegg, and Cornelius Krellner, Stabilization of the tetragonal structure in (Ba1-xSrx)CuSi2O6, Phys.Rev.B 93, 174121 (2016), DOI: 10.1103/PhysRevB.93.174121
3) M. Majumder, M. Schmidt, H. Rosner, A. A. Tsirlin, H. Yasuoka, and M. Baenitz, Anisotropic Ru3+ 4d(5) magnetism in the alpha-RuCl3 honeycomb system: Susceptibility, specific heat, and zero-field NMR, Phys.Rev.B 91, 180401(R) (2015), DOI: 10.1103/PhysRevB.91.180401

4) Kézsmárki, U. Nagel, S. Bordács, R. S. Fishman, J. H. Lee, Hee Taek Yi, S.-W. Cheong, and T. Rõõm, Optical Diode Effect at Spin-Wave Excitations of the Room-Temperature Multiferroic $BiFeO_3$, Phys.Rev.Lett. 115, 127203 (2015), DOI: 10.1103/PhysRevLett.115.127203
5) M. Hälg, D. Hüvonen, T. Guidi, D. L. Quintero-Castro, M. Boehm, L. P. Regnault, M. Hagiwara, and A. Zheludev, Finite-temperature scaling of spin correlations in an experimental realization of the one-dimensional Ising quantum critical point, Phys.Rev.B 92, 014412 (2015), DOI: 10.1103/PhysRevB.92.014412

3.2.2 Static and Dynamic Correlations in Matter

There are 7 researchers with PhD who are active in the Static and Dynamic Correlations in Matter programme: Jasper Adamson, Ivo Heinmaa, Jüri Jarvet, Tõnis Pehk, Liis Seinberg, Raivo Stern, Aleksander Trummal.

NMR as a cornerstone of this programme was also the basis NICPB was founded on. In the past the NMR group has been the leading group in the institute, but also worldwide due to developing and using ultrafast magic angle sample spinners for solid state NMR and low temperature experimental capabilities. NICPB has been in a unique position due to availability of liquid He from in-house liquefier that has allowed running multiple NMR systems for solution as well as for solid state samples. Additionally, about 8 years ago a 14T PPMS system was installed with the ^3He.

Currently, due to widespread commercialization of NMR technique the need for our capabilities has dropped both nationally and internationally. Still for more complicated studies local universities and companies are benefiting from our 800MHz NMR spectrometer as well as expertize in the data interpretation (T. Pehk, J. Adamson, J. Jarvet). Solid state NMR on powder samples allows measurements down to 5 K at 10 kHz rotation speed (I. Heinmaa, R. Stern). During past two years an X-ray diffractometer was commissioned (L. Seinberg) and a low temperature AFM/MFM probe acquired for PPMS (R. Stern). Currently there are 1 PhD students and 2 master's students in the research programme from Tallinn University of Technology.

In the future the need for high quality NMR data will persist and a change of generations is underway in the NMR group. In addition to young NMR students and specialists present currently, there have been negotiations with former NICPB postdoc I. Reile for returning from Radboud University, Netherlands. We see potential for establishing accredited XRD and NMR analysis methods to attract more applied research. The development of the tuneable field solid state NMR option for the PPMS will be completed soon and put into use.

Scientific output of the programme has been 8 papers to date in 2016, 11 papers in 2015 and 80 papers from 2010 to2014.

Key publications in 2015 - 2016

1) Axel Abelein, Jüri Jarvet, Andreas Barth, Astrid Gräslund, and Jens Danielsson, Ionic Strength Modulation of the Free Energy Landscape of Aβ40 Peptide Fibril Formation, Journal of the American Chemical Society 138 (21), 6893-6902 (2016), DOI: 10.1021/jacs.6b04511
2) Aile Tamm, Liis Seinberg, Jekaterina Kozlova, Joosep Link, Piret Pikma, Raivo Stern, Kaupo Kukli, Quasicubic alpha-Fe2O3 nanoparticles embedded in TiO2 thin films grown by

atomic layer deposition, Thin Solid Films, Volume 612, Pages 445-449 (2016) , DOI: 10.1016/j.tsf.2016.06.036

3) Haies IM, Jarvis JA, Bentley H, Heinmaa I, Kuprov I, Williamson PT, Carravetta M, N-14 overtone NMR under MAS: signal enhancement using symmetry-based sequences and novel simulation strategies,.Phys Chem Chem Phys. 17(9):6577-87 (2015), DOI: 10.1039/c4cp03994g
4) Carolina Vieira Viêgas, Imane Hachemi, Suely Pereira Freitas, Päivi Mäki-Arvela, Atte Aho, Jarl Hemming, Annika Smeds, Ivo Heinmaa, Filipe Batista Fontes, Débora Cristina da Silva Pereira, Narendra Kumar, Donato Alexandre Gomes Aranda, Dmitry Yu. Murzin, A route to produce renewable diesel from algae: Synthesis and characterization of biodiesel via in situ transesterification of Chlorella alga and its catalytic deoxygenation to renewable diesel, Fuel 155, 144-154 (2015), DOI: 10.1016/j.fuel.2015.03.064
5) Adamson, J.; Lucas, T. C.; Cairns, A. B.; et al., Competing hydrostatic compression mechanisms in nickel cyanide, Physica B-Condensed Matter 479, 35-40 (2015), DOI: 10.1016/j.physb.2015.09.027

3.2.3 Energy materials

There are 4 researchers with PhD who are active in the topic of energy materials: Natalja Irha, Reio Põder, Janek Reinik, and Juhan Subbi.

The environmental chemistry group dates back 25 years and was established by U. Kirso to study impact of oil shale ash aerosols from the Estonian power plants. From 2013 the environmental chemistry group (J. Reinik, N. Irha) is working on oil shale environmental studies, co-financed by oil shale companies and the Environmental Investment Centre. In the near future the environmental chemistry group aims to continue oil shale related applied research. Expansion of the group depends on the health of local oil shale industry which in turn depends on global oil prices.

Fuel cell research dates back over 10 years and was started by J. Subbi. Fuel cell research is in the development phase of commercially usable SOFC elements with our commercial partner Elcogen Ltd. where the main challenge is long term stability of SOFC systems (J. Subbi, R. Põder).

Scientific output of the programme has been 1 paper to date in 2016, 3 papers in 2015 and 23 papers from 2010 to 2014.

Key publications in 2015 - 2016

1) Uibu, Mai; Somelar, Peeter; Raado, Lembi-Merike; Irha, Natalja; Hain, Tiina; Koroljova, Arina; Kuusik, Rein, Oil shale ash based backfilling concrete – Strength development, mineral transformations and leachability, Construction and Building Materials 102:620-630 (2016), DOI: 10.1016/j.conbuildmat.2015.10.197
2) Reinik, Janek; Irha, Natalya; Steinnes, Eiliv; Piirisalu, Eero; Aruoja, Villem; Schultz, Eija; Leppanen, Matti, Characterization of water extracts of oil shale retorting residues form gaseous and solid heat carrier processes, Fuel Processing Technology 131, 443 (2015), DOI: 10.1016/j.fuproc.2014.12.024
3) Irha, Natalya; Reinik, Janek; Jefimova, Jekaterina; Koroljova, Arina; Raado, Lembi-Merike; Hain, Tiina; Uibu, Mai; Kuusik, Rein, PAHs in leachates from thermal power plant wastes and ash-based construction materials, DOI: 10.1007/s11356-015-4459-x, Environmental

Science And Pollution Research 22 (15), 11877 (2015), DOI: 10.1007/s11356-015-4459-x

3.2.4 Two-photon Absorption (2PA) in Biomolecules

The two-photon absorption group is led by Aleksander Rebane while Merle Uudsemaa and Aleksander Trummal are involved in quantum chemical calculations to support the experiments.

The main research is experiments and theory on ultrafast nonlinear optics, in particular, femtosecond multi-photon absorption spectroscopy of organic fluorophores for applications in molecular sensing and imaging. The programme was initiated by acquisition of Ti:sapphire laser by G. Liidja for two-photon fluorescence microscopy for biological applications. However, insufficient funding resulted in an incomplete system without confocal microscope and the original project was halted. Possible use of the system for two-photon 2PA spectroscopy was realized by close collaborator and part time researcher in NICPB, A. Rebane (professor at Montana State University) who started to use the laser system with the help of J. Pahapill. In 2012 group was joined by a PhD student (Tallinn University of Technology) S. de Reguardati, initially funded by a Marie Curie TOPBIO grant (2012-2014).

Currently the program is funded by the institutional IUT23-9 grant with A. Rebane as PI. In recent years the group has developed a high-accuracy quantitative measurement technique for determining 2-photon absorption cross sections of organic fluorophores in solution using a mode-locked Ti:sapphire laser (Coherent Mira 900 with 10W Coherent Verdi pump laser) in 690 -950 nm excitation wavelength range. Future scope of the programme depends whether A. Rebane can secure sufficient funding from Europe. An ERC grant has been submitted to facilitate growth of the group and reintegration of PI to Estonia.

Scientific output of the programme has been 5 papers to date in 2016, 10 papers in 2015 and 44 papers from 2010 to 2014.

Key publications in 2015 - 2016

1) Korzycka, Karolina A.; Bennett, Philip M.; Cueto-Diaz, Eduardo Jose; Wicks, Geoffrey; Drobizhev, Mikhail; Blanchard-Desce, Mireille; Rebane, Aleksander; Anderson, Harry L., Two-photon sensitive protecting groups operating via intramolecular electron transfer: uncaging of GABA and tryptophan, Chemical Science 6 (4), 2419 (2015), DOI: 10.1039/c4sc03775h
2) Friese, Daniel H.; Mikhaylov, Alexander; Krzeszewski, Maciej; Poronik, Yevgen M.; Rebane, Aleksander; Ruud, Kenneth; Gryko, Daniel T., Pyrrolo[3,2-b]pyrroles-From Unprecedented Solvatofluorochromism to Two-Photon Absorption, Chemistry-A European Journal 21 (50), 18364 (2015), DOI: 10.1002/chem.201502762
3) Rebane, Aleksander; Wicks, Geoffrey; Drobizhev, Mikhail; Cooper, Thomas; Trummal, Aleksander; Uudsemaa, Merle, Two-Photon Voltmeter for Measuring a Molecular Electric Field, Angewandte Chemie-International Edition 54 (26), 7582 (2015), DOI: 10.1002/anie.201502157
4) Mikhaylov, Alexander; Kondratuk, Dmitry V.; Cnossen, Arjen; Anderson, Harry L.; Drobizhev, Mikhail; Rebane, Aleksander, Cooperative Enhancement of Two-Photon Absorption in Self-Assembled Zinc-Porphyrin Nanostructures, Journal Of Physical Chemistry C 120 (21), 11663 (2016) DOI:10.1021/acs.jpcc.6b01394

5) de Reguardati, Sophie; Pahapill, Juri; Mikhailov, Alexander; Stepanenko, Yuriy; Rebane, Aleksander, High-accuracy reference standards for two-photon absorption in the 680-1050 nm wavelength range, Optics Express 24 (8), 9053 (2016), DOI: 10.1364/OE.24.009053

3.3 Laboratory of bioenergetics

The Laboratory of the Bioenergetics is the smallest laboratory of the NICPB, employing 6 PhD researchers: V. Chekulayev, T. Käämbre, M. Puurand, I. Shevchuk, K. Tepp, N. Timohhina.They have various backgrounds in chemistry, physics, biochemistry and systems biology and they supervise 6 PhD students and 2 master students. The head of the Laboratory is senior researcher T. Käämbre.

In 2016 the laboratory hosts

- 1 Institutional Research Grant
    - IUT23-1 "Mechanisms of regulation of integrated energy metabolism in tumour and muscle cells (2014 – 2019)", T. Käämbre,
- Other projects
    - COST Action CA15203 MITOEAGLE (T. Käämbre, K. Tepp, N. Timohhina), Horizon 2020
    - The biological significance of mitochondrial adenylate kinase AK2 isoform (A. Klepinin, PhD studies at Division of Cardiovascular Diseases, Metabolomics NMRS Core, Mayo Clinic, Rochester, USA).

The keywords of expertise are mitochondria, energy transfer networks, adenylate kinase, creatine kinase, cytoskeleton, development, ageing, colon cancer, breast cancer, regulation of mitochondrial respiration, heart and skeletal muscles.

The laboratory combines multidisciplinary expertise and state-of-art methodologies into research related to energy metabolism of muscle and cancer cells and aims to integrate and extend the knowledge on basic aspects of energy metabolism, biochemistry and biophysics.

Historically, the topic of cellular bioenergetics has been in NICPB for 23 years. Since molecular system bioenergetics (MSB) is an interdisciplinary field, it will impact with other NICPB strategic research programs. The first group leader of NICPB bioenergetics laboratory was Prof. Valdur Saks, member of the Estonian Academy of Sciences. Since 2012 the laboratory was headed by senior researcher Tuuli Käämbre. The results of our previous studies are related with normal adult cardiomyocytes. The main topic was intracellular local restrictions of diffusion of adenine nucleotides and metabolic feedback regulation of respiration via phosphotransfer networks. This topic is related to the complex structural organization of these cells and was analysed from the point of view of molecular system bioenergetics, including the description of development of mathematical modelling of these processes. The concepts of Intracellular Energetic Units (ICEUs) and Mitochondrial Interactosome (MI) was developed on the basis of information of cardiac cell structure and experimental data obtained in the studies of permeabilized cardiomyocytes and fibers.5 doctoral students defended their doctoral thesis in the Laboratory of Bioenergetics; three of them are currently working as researchers in the laboratory.

Currently, one of our main topics is the changes in the ICEU and MI structures during development and ageing. The second topic -cancer cell bioenergetics-forms the basis for developing the fundamental and applied bioenergetics aspects of cancer bioenergetics at NICPB as well as in Estonia.The Laboratory of Bioenergetics is concentrated on the investigation of the fundamental aspects of cell energetics to find possible applications for medicine. Research of the team is multifaceted:

- compartmentation of adenine nucleotides,
- functional coupling and direct transfer of metabolite substrates from enzyme to enzyme in multienzyme complexes (in the network of mitochondrial kinases),
- compartmentalized systems of oxidative phosphorylation and intracellular energy transfer in cardiac and cancer cells *in vivo,*
- functional and molecular characterization of the proteins responsible for a control over intracellular localization of mitochondria *in vivo,*
- determination of energy fluxes via different phosphotransfer pathways (6)mechanisms of injury of energy metabolism in mitochondria of tumor cells,
- metabolic control analysis.

This very wide scale of competence gives us the possibility to study cancer bioenergetics with the methods of system biology.

Future plans include continued work on most interesting fields of bioenergetics: muscle bioenergetics, cancer bioenergetics and stem cells bioenergetics. The continuity of the theme is assured, in addition to the good scientific results, by the institutional support to bring in young master and doctoral students, which is the prerequisite for the sustainability of a topic. The very wide scale of competence of Laboratory of Bioenergetics gives possibility to study cancer bioenergetics with the methods of system biology. We continue bioenergetic profiling of human malignant tumors by the application of methods and approaches of MSB: the area of cellular bioenergetics in transition from molecular to the system level properties and to study in malignancies of different histological types (such as colorectal cancer, breast cancer and the blood cancers). The second future perspective of our work is to perform the metabolic profiling of some normal and cancerous tissues by 18O-assisted 31P NMR and 1H NMR. In collaboration with NMR group we also continue already started studies of metabolomics of aged heart. By comparing the metabolic profiles and fluxes in normal and cancerous tissues from the patients we should be able to distinguish healthy and diseased samples and make a map of the most important bioenergetics abnormalities that cause the pathological state. We also plan to strengthen the direction of applied bioenergetics in collaboration with hospitals and the small enterprise "Mitogro". The cooperation with universities enhances our competency and allows us to find new young talented PhD students, post-docs and group members.

Collaborations of the laboratory:

- Two groups from our institute: Nuclear Magnetic Resonance spectroscopy (J. Adamson) and the Stochastic Processes Group (E. Heinsalu, M. Patriarca)
- Two groups from University of Tartu (prof. S. Kõks and prof. T. Maimets)
- Tallinn University (prof. R. Shimmo)
- Tallinn University of Technology (prof. L. Järvekülg, senior scientist V. Tõugu)

- Division of Cardiovascular Diseases, Metabolomics NMRS Core, Mayo Clinic, Rochester, USA (Dr. Petras Dzeja)
- Grenoble Alpes University (Dr. R. Guzun, Dr. U. Schlattner)
- Department of Membrane Transport Biophysics, No. 75, Institute of Physiology, Academy of Sciences of the Czech Republic (Dr. K. Smolkova)
- Department of General and Transplant Surgery, D. Swarovski Research Laboratory, Medical University of Innsbruck, Austria (Dr.E. Gnaiger)
- North Estonia Medical Centre (Dr. V. Valvere)
- Small enterprise “Mitogro”
- The laboratory is the member of the MitoGlobalNetwork.

Key publications in 2015 – 2016

1) K. Tepp, N. Timohhina, M. Puurand, A. Klepinin, V. Chekulayev, I. Shevchuk, T. Kaambre, “Bioenergetics of the aging heart and skeletal muscles: Modern concepts and controversies”, Ageing research reviews, 28 (2016) 1-14.
2) R. Bagur, S. Tanguy, S. Foriel, A. Grichine, C. Sanchez, K. Pernet-Gallay, T. Kaambre, A.V. Kuznetsov, Y. Usson, F. Boucher, R. Guzun, “The impact of cardiac ischemia/reperfusion on the mitochondria-cytoskeleton interactions”, Biochim Biophys Acta, (2016).
3) V. Chekulayev, K. Mado, I. Shevchuk, A. Koit, A. Kaldma, A. Klepinin, N. Timohhina, K. Tepp, M. Kandashvili, L. Ounpuu, K. Heck, L. Truu, A. Planken, V. Valvere, T. Kaambre, “Metabolic remodeling in human colorectal cancer and surrounding tissues: alterations in regulation of mitochondrial respiration and metabolic fluxes”, Biochemistry and Biophysics Reports, 4 (2015) 111-125.
4) R. Guzun, T. Kaambre, R. Bagur, A. Grichine, Y. Usson, M. Varikmaa, T. Anmann, K. Tepp, N. Timohhina, I. Shevchuk, V. Chekulayev, F. Boucher, P. Dos Santos, U. Schlattner, T. Wallimann, A.V. Kuznetsov, P. Dzeja, M. Aliev, V. Saks, “Modular organization of cardiac energy metabolism: energy conversion, transfer and feedback regulation”, Acta physiologica, 213 (2015) 84-106.
5) K. Tepp, K. Mado, M. Varikmaa, A. Klepinin, N. Timohhina, I. Shevchuk, V. Chekulayev, A.V. Kuznetsov, R. Guzun, T. Kaambre, “The role of tubulin in the mitochondrial metabolism and arrangement in muscle cells”, J Bioenerg Biomembr, 46 (2014) 421-434.
6) T. Anmann, M. Varikmaa, N. Timohhina, K. Tepp, I. Shevchuk, V. Chekulayev, V. Saks, T. Kaambre, “Formation of highly organized intracellular structure and energy metabolism in cardiac muscle cells during postnatal development of rat heart”, Biochim Biophys Acta, 1837 (2014) 1350-1361.

General comments

The workgroup is too small and in the conditions of only project based project-based funding it is very difficult to enlarge the group. The second difficulty is related to the very high cost of biological experiments that makes hiring new people even more difficult.

3.4 Laboratory of environmental toxicology

The research in environmental toxicology and related chemistry is mostly conducted in the Laboratory of Environmental Toxicology (head Academy Professor Dr. Anne Kahru) with contribution from the Laboratory of Chemical Physics (J. Reinik and N. Irha).

The laboratory employs 9 PhD researchers (V. Aruoja, I. Blinova, O. Bondarenko, M. Heinlaan, A. Ivask, A. Kahru, A. Lukjanova, M. Sihtmäe, J. Siigur) who supervise 8 PhD students. The PhD students are mostly enrolled to Tallinn University of Technology (6), but also to University of Tartu (1) and Tallinn University (1). The team is young, enthusiastic and has received recent post-doc training in top-level environmental and nanotoxicology laboratories in Switzerland, US, Italy and Australia. Age-wise, half of the group is younger than 35. Gender wise, 19% of the group are male researchers. K. Kasemets, A. Käkinen and M. Mortimer are currently in post-doc.

In 2016 the Laboratory hosts

- 1 Institutional Research Grant
    - IUT23-5 "Nano(eco)toxicology and beyond (ToxBe) (2014 – 2019)", A. Kahru,
- 3 Personal Research Grants
    - PUT748 "In vitro toxicological tool-box for targeted design of antimicrobial nanomaterials (2015 – 2018)" A. Ivask
    - PUT1015 "Nanoparticle-macrophage interactions in vitro: focus on nanosafety (2016 – 2020)" O. Bondarenko
    - ETF9347 "Adverse effects of nanosized Ag, Au and CuO to particle-ingesting crustaceans: an integrated approach (2012–2017)", M. Heinlaan
- Academy Professor Grant (A. Kahru)
- partnership in the NICPB Centre of Excellence TK134 (A. Ivask)
- partnership in the Estonian Scientific Infrastructure Roadmap Object NAMUR+ (A. Kahru)
- research contract grant from Ministry of Environment to review the current limit values of non-prioritized but hazardous air pollutants (M. Sihtmäe).

Past, present and future

PAST: The Lab of Environmental Toxicology of NICPB has evolved from the group created by A. Kahru about 20 years ago within the Laboratory of Molecular Genetics of NICPB. Her group started the novel research directions for Estonia – in vitro- and ecotoxicology. Since then, their research of the team has remarkably contributed to new scientific knowledge on chemical safety, heavy metals adverse environmental effects and bioavailability as well as evaluation of environmental hazard of the waste waters and polluted soils and Estonian oil-shale chemicals and solid waste. For that we used a combined approach, applying a suite of bioassays, environmental chemistry and molecular biology techniques (recombinant sensor bacteria). An important activity initiated by the team led to the reclassification of one of the most important pollution flows of the oil-shale industry – fresh semi coke – as hazardous waste in 2003, resulting in the change of its deposition according to the rules of the European Union. Currently, the know-how on evaluation of the toxicity of polluted soils, solid waste and wastewaters using various bioassays, including also ISO and OECD assays (algae, duckweeds, daphnids, bacteria) is our unique competence in Estonia. The group has been involved in developing of QSARs for substituted anilines and phenols. We have generated several web-based databases, incl. on toxicological information on REACH-relevant chemicals published in the Russian language (E-SovTox).

The laboratory was among the first ones in nanoecotoxicological studies of metal oxide nanoparticles (since 2004). The team publishes in high IF journals indexed by Web of Science (Nanotoxicology, Accounts of Chem Res, ACS Nano, PLOS One, Arch. Toxicol., Water Res, Aquatic Toxicology, Env Pollution). In past 10 years the team has published more than 100 papers, mostly on nanotoxicology, that have been cited >2000 times (>30 cites/paper). As a result, the team has currently 8 highly-cited papers in ISI-ESI concerning environmental and antimicrobial effects of synthetic nanoparticles. A. Kahru and A. Ivask belong to 1% worldwide top cited authors in area of Environment/Ecology and A. Kahru in addition in the area of Pharmacology/Toxicology. In 2011, A. Kahru received the Estonian State Science Award for her research "Ecotoxicology of synthetic nanoparticles and their toxicity mechanisms".

Currently, the team is focused on developing of (i) in vitro/ecotoxicological test methods for analysis of hazard of synthetic nanoparticles to non-vertebrate organisms on different levels of biological organization; (ii) medium-to-high throughput analysis tools for ecotoxicity/bioavailability studies (involving multitrophic test batteries of microbiotests comprising bacteria, crustaceans, algae, protozoa) and (iii) analysis tools for mechanistic profiling of chemicals, e.g; using specific luminescent recombinant bacterial whole-cell sensors and mutants of prokaryotic and eukaryotic microorganisms defective on certain stress targets.

Keywords of expertise: (eco)toxicity, bioavailability, in vitro, 3R's, bioluminescence, microbial physiology; algae, bacteria, protozoa, crustaceans as in vitro and ecotoxicity models, food-chain transfer, recombinant microbial biosensors, environmental pollution, nanoparticles, heavy metals, metal speciation, oil-shale, pesticides, polluted soils.

Future: At 2016, we have started in cooperation with Norwegian Company CerPoTech (synthesizes rare earth oxides of very different compositions and dopings) the ecotoxicology research of lanthanides (La, Ce, Pr, Nd, Gd), as soluble salts but also in the form of particles of (doped) metal oxides. These materials are increasingly used in modern electronics, fuel cells, as fuel additives but also in medicine (Gd). The information on ecotoxicological effects of these elements is still very limited, however.

We will expand our *in vitro* toxicology research by new competence of A. Ivask who returns in October 2016 from University of South Australia, Adelaide and K. Kasemets who returns in October 2016 from Milano University Bicocca. We will introduce *in vitro* immunotoxicity models (O. Bondarenko's PUT1015), will expand the know-how using various bacterial and in vitro animal cell models for toxicological profiling of ionic liquids and surfactants (cooperation with ERA Chair on Green Chemistry, Tallinn University of Technology, a joint PhD student with Prof. Gathergood). Analogous joint work is planned with a University of Tartu young chemist (application submitted in Sept 2016), who has planned her Marie-Curie secondment to our Lab, to learn in vitro toxicological work of certain chemical libraries. In cooperation with University of Tartu experts in algal physiology and ecology (K. Olli – supervisor of the joint PhD student E. Joonas) we have started to introduce ecotoxicological work with different types of algae.

Partnership in the Estonian Scientific Infrastructure Roadmap Object NAMUR+ will yield us in next 5 years new laboratory equipment (microscopes, incubators etc.) that will improve the facilities for successful research. However, we still need renovation of some rooms in order to install this new equipment.

Funding: The big grant (IUT 23-5) that provides the salaries for majority of the researchers will end at 2019. The PUT-based funding is even more hectic and as these grants are smaller, they fund basically just the applicant + 1-2 students. The H2020 funding is getting more and more complicated to obtain but we keep on trying. Our salaries relay totally on projects and therefore the future of this research field in Estonia is uncertain. As my Lab has the 'monopoly' in Estonia in know-how on ecotoxicology and in vitro toxicology, this uncertain funding scheme is not providing sustainable development of this important knowledge needed for developing novel materials, drugs and chemicals but also for educating Estonian people on chemical safety issues.

Other issues: in the team there are young people, mostly female researchers, who have been, are and are going to maternity leave. That makes planning of the work a bit hectic. As most of the PhD students are female in the areas we are recruiting students (biology, gene technology, chemistry), it is difficult to find male students interested in the topic. This gender pattern (majority of female researchers) is analogous also in other European toxicity labs.

Key publications in 2015 – 2016

1) Aruoja, V., Pokhrel, S., Sihtmäe, M., Mortimer, M., Mädler, L., and Kahru, A. (2015) Toxicity of 12 metal based nanoparticles to algae, bacteria and protozoa, Environmental Science: Nano 2, 630-644. 4 citations. IF 5.90
2) Bondarenko. O.M., Heinlaan, M., Sihtmäe, M., Ivask, A., Kurvet, I., Joonas, E., Jemec, A., Mannerström, M., Heinonen, T., Rekulapelly, R., Singh, S., Zou, J., Pyykkö, I., Drobne, D, Kahru, A. (2016) Multilaboratory evaluation of 15 bioassays for (eco)toxicity screening and hazard ranking of engineered nanomaterials: FP7 project NANOVALID. Nanotoxicology. 2016 Nov; 10(9):1229-1242. IF 7.91
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5) Käkinen, A., Kahru, A., Nurmsoo, H., Kubo, A.-L., and Bondarenko, O.M. (2016) Solubility-driven toxicity of CuO nanoparticles to Caco2 cells and Escherichia coli: effect of sonication energy and test environment, Toxicology in vitro 36, 172-179. IF 3.34
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7) Aruoja, V., Pokhrel, S., Sihtmäe, M., Mortimer, M., Mädler, L., and Kahru, A. (2015) Toxicity of 12 metal based nanoparticles to algae, bacteria and protozoa, Environmental Science: Nano 2, 630-644. IF 5.90
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nanoparticles to three mammalian cell types in vitro, Current Topics in Medicinal Chemistry 15, 1914-1929. IF 2.9

9) Joost, U., Juganson, K., Visnapuu, M., Mortimer, M., Kahru, A., Nõmmiste, E., Joost, U., Kisand, V., and Ivask, A. (2015) Photocatalytic antibacterial activity of nano-TiO2 (anatase)-based thin films: Effects on Escherichia coli cells and fatty acids, Journal of Photochemistry and Photobiology B-Biology 142, 178-185. IF 3.0
10) Juganson, K., Ivask, A., Blinova, I., Mortimer, M., and Kahru A. (2015) NanoE-Tox: New and in-depth database concerning ecotoxicity of nanomaterials, Beilstein Journal of Nanotechnology 6, 1788-1804. IF 2.78
11) Kaweeteerawat, C., Chang, C. H., Roy, K. R., Liu, R., Li, R., Toso, D., Fischer, H., Ivask, A., Ji, Z., Zink, J. I., Zhou, Z. H., Chanfreau, G. F., Telesca, D., Cohen, Y., Holden, P. A., Nel, A. E., and Godwin, H. A. (2015) Cu Nanoparticles Have Different Impacts in Escherichia coli and Lactobacillus brevis than Their Microsized and Ionic Analogues, ACS Nano 9, 7215-7225. IF 13.33
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4 Key competences of NICPB

4.1 High level research

4.2 Coordination of Estonian activities in CERN

According to the Cooperation Agreement between the Republic of Estonia and CERN, the NICPB is representing the Republic of Estonia and coordinates the research activities of Estonian universities at CERN. As a part of this collaboration, the institute is a member of the CMS Collaboration of the Large Hadron Collider. In addition to the participation in the CMS experiment, the NICPB is also organizing Estonian summer student as well as Estonian high-school teachers' programmes at CERN.

As a by-product of Estonian participation at CERN, the NICPB has established a Tier-2 level CMS experiment Datacentre which is currently one of the biggest scientific computing centres in Estonia. It is part of the Estonian Scientific Computing Infrastructure that is supported by the Ministry of Education and Research. The NICPB Datacentre is the leading developer of grid and cloud computing in Estonia.

4.3 Neutron scattering for research and participation in European Spallation Source

NICPB collaborates with University of Tartu and Tallinn University of Technology in designing and building the European Spallation Source (ESS) neutron scattering facility in Lund.

4.4 Estonian magnet laboratory and the helium liquefier

We need to work with developing the Estonian Magnet Laboratory and establish better collaborations with groups in the universities who are using NMR and other spectroscopies that require high magnetic fields. We are running the only helium liquefier in the Baltic countries.

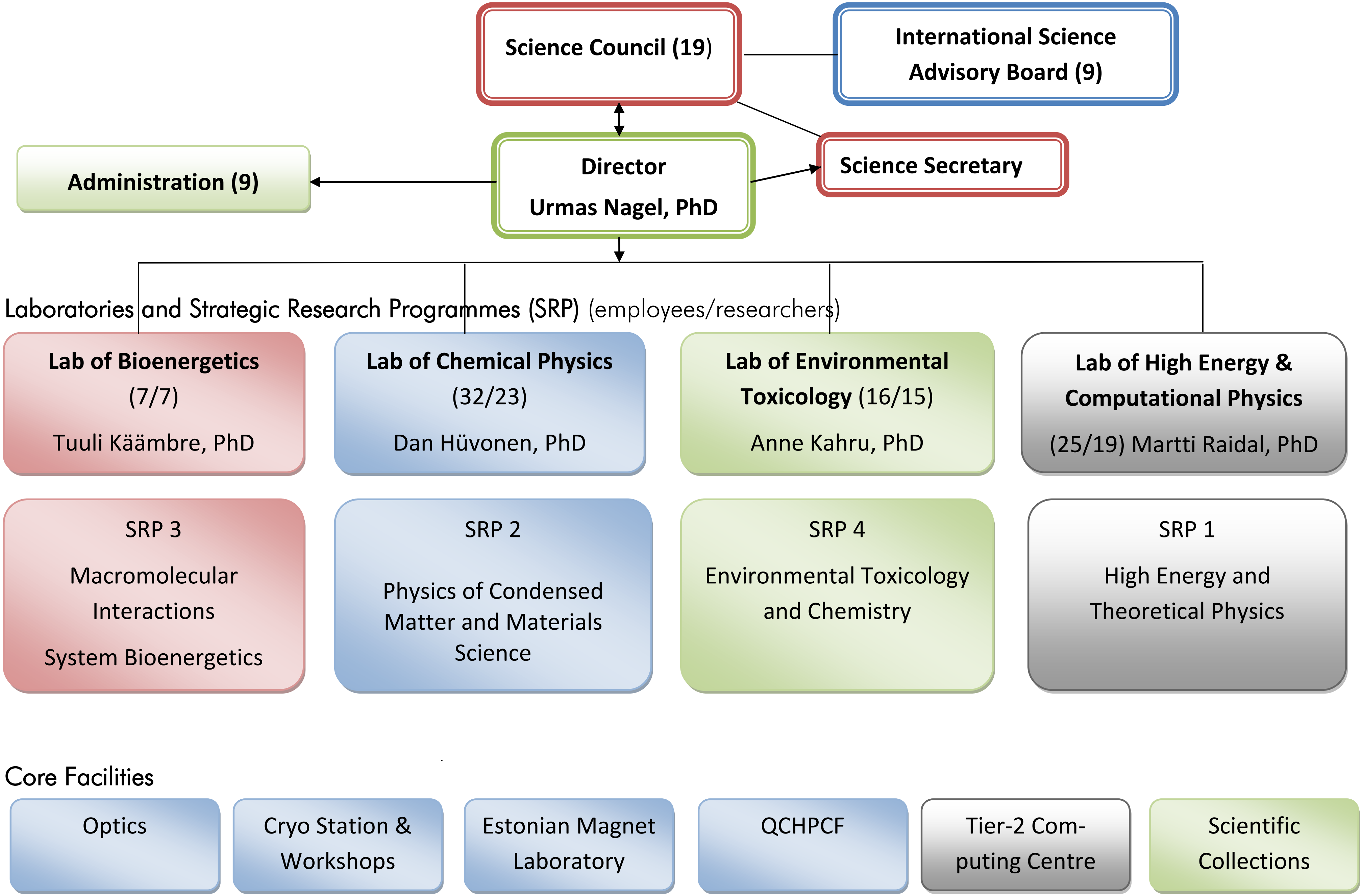
4.5 Environmental and nanotoxicology

The research into ecotoxicology and especially nanoecotoxicology in Estonia was introduced by NICPB researchers 20 and 10 years ago, respectively. These are the key competences of Laboratory of Environmental Toxicology lead by A. Kahru. This competence is unique for Estonia and is based on know-how, facilities and international cooperation on evaluation of hazard of existing and emerging environmental pollutants, industrial chemicals and man-made nanomaterials. This is a competence crucial for EU new chemical regulation REACH. Our competence in this field has been incorporated into EU FP6, FP7 and Interreg projects (OSIRIS, MODERN, NanoValid, RIMA) and has yielded currently 8 highly cited papers in ISI-ESI, mostly concerning environmental and antimicrobial effects of synthetic nanoparticles.

5 Appendix

NICPB organization chart and administration chart are appended on separate pages.

NICPB Organization Chart, 01 Sept. 2016



NICPB: Administration & Ancillary services

Director

General strategic leadership, personnel policy, scientific projects & programmes, co-operation, governmental & inter-national relations

MAS Systems Ltd

Production of Scientific Instrumentsation

Librarian

Purchase of scientific and reference literature, library work

Deputy Director

General Department

General management, Accountancy and budgeting, Personnel and health Archives, ICT-services, Asset accounting and control, Planning

Employees:

Chief Accountant
Accountant-budget estimator
Personnel Officer - Archivist
IT-specialist

Administrative Department

House Manager (Head of Dep)

Maintenance of real estate, Utilities,

Maintenance and cleaning services, Purveyance, Fire and work safety

Employees:

Technicians, specialists, keepers

Deputy Director

Co-ordination of R&D activities and development of contacts with industry

Co-ordination of international R&D contracts

Development of contacts and co-operation with other R&D institutions and universities

Science Secretary

Managing the work of the Science Council

EU structural funds & programmes, R&D projects, grants:

compilation, co-ordination, management, accounting and monitoring

Procurement
Media relations

Board of Directors (3):

Director

Deputy Directors (2)

Management(5):

Directors (3)

Science Secretary

Area managers (2):

Chief Accountant

Personnel Officer

Administration (10):

Directors (3), Science Secretary Area Managers (2), Heads of Laboratories (4)