NICPB activity report, May 2019

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1 Introduction

The document contains hyperlinks to other documents, CV-s of personnel and projects. Please follow these links to further details. The summary of the development of NICPB until 2016 is available in previous activity reports.

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. The main mission of NICPB is to do excellent research and to supervise PhD students. In 2017 NICPB performed very well in the regular state evaluation of sciences.

Coordinating Estonian research in CERN is our most important task on the national level. NICPB is organizing the Estonian summer students and high-school teachers' programmes at CERN. The high energy physics group of NICPB has been very active promoting the idea that the Republic of Estonia should become a member state of CERN. As a result, the Estonian government applied for CERN membership in 2018 and the positive decision of membership was made by the CERN council in 2019.

The funding of NICPB has increased in the last years (graphs is section 5.1 "Budget of NICPB"), accompanied by an increase of the number of researchers with PhD in NICPB (graphs in section 5.2,"Human resources of NICPB"). New topics have been started and the average NICPB researcher is getting younger, the number of graduate students is increasing.

At the same time the Estonian science funding system is changing. All institutional grants of NICPB end with 2019 except one, and several groups must compete for new grants to continue their research at current level. Although the financial situation is good today, it contains risks because the new grants are shorter in time and not necessarily larger in amount. The institute plans to allocate resources in next year's budget to be able to keep the positions of key scientists until they have secured enough grant funding. Establishing a tenure track system is under discussion in Estonia, but currently lacks non-grant-based funding.

1.1 NICPB institutional development programme IMPAKT

In 2016 NICPB got some funding from the Estonian development programme ASTRA[1] for the strategic development of R&D institutions and universities.

1.1.1 Strategic development of competences and capabilities

The strategic development part of IMPAKT (0.95 M€) targets NICPB's capability to better serve the society by increasing institute's competitiveness and its impact on Estonian economy. The main activities are:

- Enhancing our excellence in science and developing new competences,
- Increasing the efficiency in educating new generations of scientists,
- Creating new collaborations between different fields of research, and
- Promoting collaborations with industry.

To enhance the collaboration between NICPB and Estonian universities the Ministry of Education and Research in 2017 lead negotiations between NICPB and University of Tartu and in parallel between NICPB and Tallinn University of Technology (TalTech). During the negotiations all partners obtained a better understanding of each other and realised that possible opportunities of merging NICPB with one of the universities may be a disadvantage to the other; there are risks to the research groups of NICPB and most of all, the merger would require investments that none of the universities nor the ministry was willing to commit. On top of that, having a national institute creates additional opportunities. Thus, NICPB carries on with strengthening scientific collaborations with the universities and participating in the teaching of graduate and undergraduate students.

The institute has developed new competences within the framework of the program IMPAKT:

- Nuclear hyperpolarization in NMR by hiring Dr. Indrek Reile after his postdoctoral research in Radboud University, Nijmegen. His work focusses on parahydrogen hyperpolarization to allow the detection of molecules at very low concentration in solutions, section 3.2.2 (Applied Nuclear Magnetic Resonance);
- Novel bioassays for studying the efficiency of antimicrobial surfaces, 'green' ionic liquids and complex nanomaterials and the effects of microplastics (Dr. Alla Khosrovyan) on the environment. This work is done in collaboration with major Estonian universities, doctoral schools and Ministries, section 3.4 (Laboratory of Environmental Toxicology);
- Developing the study of cancer metabolomics, Dr. Shiva Kumar Gudlawar, section 3.3 (Laboratory of Chemical Biology);
- Search for new experimental techniques in CERN, including the CMS upgrade and future accelerator hardware. Planned collaboration with the electronics team of TalTech to include them in the CERN activities, Dr. Sandeep Bhowmik and Dr. Christian Veelken, section 3.1.1 (Experimental High Energy Physics).

The institute has also upgraded laboratory equipment from the program IMPAKT:

- Maintenance and upgrades to the liquid-He infrastructure, supporting both the NMR and low-temperature research and supplying liquid He to partner universities;
- Upgrading the GRID node (section 2.1.3 High Performance Computing) by increasing the storage capacity, number of servers and installing 100 Gbit/s networking;
- Some essential laboratory equipment for the Environmental Toxicology and Chemical Biology labs.

[1] ASTRA – a strategic development programme for Estonian R&D institutions and universities to increase the competitiveness of the institutions and the efficiency of the whole system, including structural changes

1.1.2 Renovation of the Akadeemia tee 23 building

The infrastructure development part of IMPAKT (2.2 M€) has the goal to increase the energy efficiency and enhance working conditions in the Akadeemia tee 23 building. The works include replacing windows, heating and ventilation systems, new roofs and better insulation of the outside walls. Modernization of the ventilation system is extremely important, because the original one from 1990-s has never really worked. The renovation is expected to be completed by the end of 2019. This is a mayor development for the institute.

2 Strategic research programmes

The topics of research are determined by the NICPB Act. These include research areas of national and European importance and as a rule, are bound to 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 and theoretically. In addition to this, the theoretical physics programme of the NICPB covers different topics in theoretical physics and in cosmology. As a new development, the NICPB has also established a group for gravity research to address modern developments in theories of gravity. To enable the research activities, the institute has established a 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. Presently the group has concentrated on the latter topic.

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.

The acceptance of Estonia to become a member state of CERN would likely not have happened without the excellent research of the high energy physics group.

2.1.2 Theoretical Particle Physics

The theoretical physics programme of NICPB contains three main directions. The *first* and the main research activity covers theoretical and phenomenological research topics in particle physics, astroparticle physics and cosmology. The *second* direction established most recently and somewhat related to the former one, covers different research topics of gravity theories beyond the General Relativity. Finally, the *third* research direction covers statistical mechanics, complex systems and 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. Motivated by the discovery of gravitational waves, the most recent research topics of the group include also primordial black holes and their role in cosmology.

The gravity group was established in 2018 and is still under development. The group studies extensions of gravity to identify the new renormalizable theory of gravity including teleparallel formulation of gravity, biometric gravity etc. The group is also addressing phenomenology of gravitational theories to explain Dark Matter as a gravitational relic and to study and to predict different aspects of gravity that can be tested using gravitational wave signals.

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 dynamics, and econophysics and kinetic wealth exchange models.

2.1.3 High Performance Computing

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 7600+ computing cores and 4.5 PB 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. Functionalities of new compounds are usually highly unpredictable due to strong electron correlations (magnetism, charge order etc.) and due to complicated structure (large unit cells of intermetals and oxides, composites). Our research topics are (i) novel quantum materials, (ii) materials related to energetics, and (iii) supramolecular and catalyst chemistry. We focus on the use of our high quality unique experimental capabilities.

Where 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 using external large-scale scientific equipment such as high magnetic field laboratories, neutron scattering and synchrotron facilities, etc.

2.2.1 Emerging Quantum Materials

This research program focuses on fundamental physical properties of complex novel materials that may have high-tech applications in the future. Strong correlations between spin and charge degrees of freedom as well as continuous miniaturization of circuits mean that their properties can only be fully understood in the framework of quantum mechanics. Such materials include multiferroics, high-Tc superconductors, quantum magnets of various dimensionality, 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 prospects of 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 the 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. To enhance quantum effects, present in those systems, low temperatures (down to 0.1K) are used.

2.2.2 Applied Nuclear Magnetic Resonance

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 surrounding nuclei. Different magnetic field strengths and variable 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 is the essence of the program.

In chemistry, structural analyses and control of syntheses of enantiomers, diastereoisomers and other complex molecules and mixtures are our core competencies that find daily use for both internal and external academic and industrial collaborators. In chemical biology and bioenergetics, we are working to compile a comprehensive qualitative and quantitative profile of collateral cancer energy production processes using ^{1}H-NMR, ^{31}P-NMR and ^{18}O assisted ^{31}P-NMR. In NMR methodology, we are developing applications of parahydrogen hyperpolarization techniques to increase the sensitivity of NMR in biofluid analysis. We foresee applications for this work in cancer metabolomics and diagnostics and are developing such applications in collaboration with the North Estonian Medical Center.

In solid state physics the programme is strongly coupled and quintessential to both the Emerging Quantum Materials programme (see above) and to the Energy Technology programme (see below). Towards that end super-fast rotation techniques at extreme temperatures are developed. High resolution and sensitive measurements at temperatures ranging from ca 10 °K (quantum materials) up to 1200 °K (energy materials) combined with static measurements between 2-400 °K in arbitrary applied field up to 14 T open qualitatively new possibilities for detailed study of the structure and dynamics of molecular interactions and facilitate the development of new technological materials.

2.2.3 Energy materials

Research of energy materials is of utmost importance to the energy production and storage in next generation fuel cells, Li-ion batteries and supercapacitors. The energy materials programme encompasses solid oxide fuel cells (SOFC) research, novel materials and catalysts for low-temperature fuel cells, Li-ion battery recycling technologies and assessment of environmental impact of national oil shale energy production with applications of its ash residue.

Used lithium-ion batteries contain chemicals and materials that can pollute water and soil. The research goals are (i) to develop cost-effective recycling methods to extract metal-oxides and carbon powders from used Li-ion batteries and (ii) to synthesize from these recycled materials highly active and novel catalyst materials for the metal-air batteries and low-temperature fuel cells.

NICPB is involved in the development of commercially produced SOFC elements through our commercial partner Elcogen Ltd. where the current top priority is the use of SOFC as electrolysers for hydrogen production from water; the process is reversible and solves the energy storage issue of wind and solar farms, thus very important aspect in the European flagship project H2FUTURE.

NICPB is also involved in studies of modern permanent magnets that are essential to efficient wind turbines. We make use of our capacity to do X-ray diffraction, optical, magnetic, electric and thermal transport, heat capacity, electrochemical impedance, and thermogravimetric measurements of those compounds as well as solid state NMR studies at extremely low (10 °K) and high (1200 °K) temperatures.

2.2.4 Nonlinear optics

The goal of this programme is to establish a world-class metrological facility for nonlinear multiphoton light absorption- and calibration measurements.

We continue the development of physical principles of local electric field sensing by two-photon spectroscopy and microscopy by (i) investigating two-photon absorption (2PA) properties of a broad range of different fluorescent as well as non-fluorescent biomolecular constructs and probes, (ii) creating and characterizing novel types of molecular multi-photon optical sensors that are specially designed to detect and quantify local electric fields. Improving the 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 need to be addressed.

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 researchers for a broad range of biomolecular investigations and to perform multiphoton calibrations for quantum information applications. The utmost purpose of this research is to develop new experimental methods that allow us 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 to understand physical principles of life itself better.

2.3 Macromolecular interactions: Functional studies of mitochondrial metabolism in health and disease

Beyond the fundamental role in energy metabolism, mitochondria perform a great variety of other important cellular functions like synthesis of metabolites, thermogenesis, maintenance of cellular redox potential, apoptosis etc. 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 interactions in the regulation of energy metabolism in healthy cells as well as cells in pathology.

The main research topics in the laboratory of Chemical Biology are the biophysics and biochemistry of the energy transport through phosphotransfer networks, which are mostly presented by the creatine kinase and adenylate kinase systems, also by glycolysis. The metabolic feedback regulation of mitochondrial respiration and energy fluxes will be analysed in detail in skeletal muscle, heart and cancer cells from the point of view of molecular system bioenergetics. During the last years understanding of the tumour energy metabolism has been evolving very quickly and this underlines the importance of examining tumour cell behaviour in their natural environment. The high complexity and metabolic plasticity of cancer development provokes a need for a systematic approach that is now emerging as central to all areas of biology and medicine. 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 bioenergetics medicine.

In the case of skeletal muscle 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 kinases, VDAC 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.

The modifications of intracellular metabolism accompanied by adaptation of energy fluxes, metabolic control and feedback regulation depending on the cell type, degree of differentiation and health/pathology state are topics of strategic importance. 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 mitochondrial myopathies, changes in the energy metabolism for Wolfram syndrome, and mechanisms of bioenergetics of cancer. This program allows explaining the perturbations in biological system that bring to pathology (e.g. heart disease, tumours) and thereby help to predict new outcomes of medical diagnostics and drug treatments. The results of this program enable the development of rapid and cost-effective diagnostic tests for mitochondrial and muscle diseases and cancer aggressiveness.

2.4 Environmental Toxicology and In Vitro Toxicology

2.4.1 Environmental Hazard Evaluation of Nanomaterials and Emerging Contaminants

Evaluation of the potential hazard of contaminants that are released by human activity and may be harmful to ecosystems as well as to people – is an interdisciplinary research field that involves biology, medicine, physics, chemistry, and material science. An interdisciplinary institution such as the NICPB is therefore highly suitable for the successful development of this field and environmental studies continue to be one of the central research strategies of NICPB.

The main strategic goal of the environmental toxicology & *in vitro* toxicology research direction in NICPB is to elucidate the hazard of (industrial) chemicals, including novel man-made nanoparticles[2] (NP) and nanomaterials, that either already are in the environment or have the potential to end up there. The evaluation of the environmental hazard of synthetic NPs that are already produced in large scale in a variety of compositions, shapes and sizes is especially challenging. Due to their small size, NPs 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 humans and the environment.

To approach the strategic goal of elucidating the hazard of existing and emerging toxic chemicals we address the following: (i) is it (the given chemical/NP/nanomaterial) toxic? (ii) to whom and how toxic? (iii) why is it

[2] Nanoparticles are particles with at least one dimension less than 100 nm

toxic? and (iv) how to assess the toxicity comprehensively and cost-effectively? According to the chemicals regulation in the European Union (REACH), all new chemical substances produced more than 1 tonne per year (estimated number exceeds 100 000) must be characterized in terms of toxicity. It is a considerable burden for the European industry (including Estonian industry), since the responsibility of assessments lies on the manufacturer or importer. 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 among others include QSAR approaches. Quantitative Structure-Activity Relationships (QSARs) are widely used for the prediction of toxicity of conventional organic chemicals relying on 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, NPs are considerably more difficult for QSAR modelling and need relevant (eco)toxicity data, to feed the model. The NICPB Laboratory of Environmental Toxicology (LET) has the 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 NPs using rapid and cost-efficient assays that allow high-throughput. In NICPB LET we have the facilities and competence for the 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 have analogous sensor bacteria also 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 NPs. For all the bioassays' test 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 is embedded throughout the world 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 the products must be safe on all the stages of their life-cycle (from 'cradle to grave' principle). The latter approach (toxic-by-design) can be applied for design of novel surface coating 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, NPs, surfactants) using unicellular test organisms (bacteria, fungi, algae) allows to shortlist new efficient antimicrobials, antifungals and algaecides.

In addition to ecotoxicological studies, knowledge on the fate of the pollutants (sorption, desorption, solubility, complexation etc.) in different environmental compartments (water, soils and sediments) is needed for environmental hazard evaluation. Environmental hazard evaluation involving the fate as well as ecotoxicity analysis of pollutants has been carried out for soils polluted with heavy metals, oils, phenolic compounds and PAHs but also oil-shale industry and energy production related by-products such as fly ash and semicoke. The current strategic program also aims to explore the possibilities of large-scale reuse of oil-shale industry (fly)ashes.

2.4.2 Efficiency and Toxicity of Antimicrobial (Nano)materials

The knowledge obtained from mechanistic studies of various types of nanomaterials is being used for the design of efficient antimicrobials as the prevention and cure of the bacterial infections is a major current healthcare concern. In NICPB LET the antimicrobial effects of different types of chemicals (ionic liquids, silver, copper and zinc-based NPs) are studied. One special direction is the design of efficient antimicrobial surface coatings based on TiO_2 NPs that are 'activated' by UV-light. The other aim of this research topic is to design new methods, including (i) metal-inducible bioluminescent sensor bacteria; (ii) mutants of yeast *Saccharomyces cerevisiae* defective of cell wall, ROS-neutralising mechanisms, endocytosis; (iii) different models for clinically relevant microbes such as *Staphylococcus aureus*, *E. coli*, *Pseudomonas aeruginosa* and *Candida albicans* for comparative evaluation of antimicrobial effects of different types of chemicals. An important part of our work is the development of new test formats for the study of antimicrobial efficacy. In the case of metal-based antimicrobials the test environment plays a crucial role (e.g. by complexation of metal ions that reduces their bioavailability) and its effects must be minimised. We have also started to explore the effects of antimicrobial surface coatings on microbial biofilms using various microscopy techniques.

2.4.3 *In Vitro* Toxicology for Nanomedicine

We are exploring new directions to use NPs (NPs) in medicine as antibacterials and drug carriers. For antibacterials, we use metal-based nanomaterials (NMs) (with the focus on Ag and CuO NMs) and study their toxicity to bacteria and human cells *in vitro* including human immune cells (macrophages and microglia), intestinal cells and keratinocytes. More specifically, Ag and CuO NMs are promising antibacterials that can be used in wound-healing products or implants, where they come into the contact with human immune and skin cells and exert toxicity. Given the functionalization of metal-based NMs may help to overcome their toxicity to human cells and improve their therapeutic potential as antimicrobials, we study the impact of surface functionalization on the antibacterial activity of NPs vs their safety to the human cells. For example, we showed that the safety profile of antibacterial CuO NMs can be significantly improved with the surface functionalization, whereby carboxyl group and polyethylene glycol-functionalized NMs proved to be the most biocompatible for human cells while retaining antibacterial activity.

For the drug carriers, we explore inherently non-toxic NMs such as silica and poly(lactic-co-glycolic acid) (PLGA) NMs. In collaboration with Prof. Mart Saarma's group (University of Helsinki), we have just started the research utilizing these NMs to increase the stability and improve the targeted delivery of potential therapeutics in Parkinson's disease.

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 M. Raidal.

The Laboratory has been growing rapidly. Currently the Laboratory employs 28 researchers and postdocs with PhD, including two top researchers. They supervise 6 doctoral students, 6 master students and 4 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
- 5 Personal Research Grants
  - PRG434 "Multimessenger astronomy as a probe of new physics (2019 – 2023)", K. Kannike
  - PRG445 "Study of Higgs boson production in the decay channel to tau leptons (2019 – 2023)", C. Veelken
  - PRG356 "Gauge gravity: unification, extensions and phenomenology (2019 – 2023)", T. Koivisto
  - MOBJD323 "Cosmological impacts of the electroweak vacuum instability (2018 – 2020)", T. Markkanen
  - MOBJD381 "Dynamically induced Planck, dark matter, neutrino and electroweak mass scales (2018 – 2020)", A. Karam
  - PUT1026 "Phenomenology of the Dark Sector of the Universe (2016 – 2019)", A. Racioppi
- 2 Top Researchers Grants
  - MOBTT5 " Beyond the Standard Model of Particle Physics (2017 – 2022)" J. Ellis.
  - MOBTT86 " Probing the Higgs sector at the LHC and beyond (2018 – 2022)" A. Djouadi.

The successful hiring of two international top researchers, Abdelhak Djouadi and John Ellis is of utmost importance for our lab, contributing to the teaching of PhD students and postdoctoral fellows.

The Laboratory's plans follow from the recommendations given by the evaluation committee of Estonian research evaluation in 2017 and from the recommendations put forward by the ISAB of the NICPB. The future of the Laboratory relies on the Laboratory's status in Estonian research landscape – it is the internationally most visible lab in theoretical physics and high-energy physics in Estonia. The Laboratory hosts one of the two Centres of Excellence in physics in Estonia. Several members of the Laboratory are among the most cited researchers of Estonia. However, 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. Most of the recommendations of international evaluators concern the sustainability of the Lab.

The Laboratory plans to grow from the current personnel, 28 researchers and 16 students, to 35 researchers and 20 students in next three years. The Laboratory plans to open new research directions in gravity, in cosmology and in engineering in addition to the present research directions in theoretical physics, high-energy physics and in computing. The first two new topics must be opened to address the new physics potential provided by the discovery of gravitational waves. The latter is related to Estonia becoming a member state of the CERN.

To achieve these goals, the Laboratory must open 10 permanent positions to cover all the Lab's research directions with permanent staff responsible for the research carried out in the Lab. The reforms of research financing in Estonia and the financing of the NICPB must enable the financing of those permanent research positions. This follows directly from the evaluators' advice.

Researchers of the Laboratory have worked hard to enhance our collaboration with Estonian universities and to promote doctoral studies at the NICPB and in those universities. For that purpose, we actively searched for international PhD student candidates who could be accepted for doctoral studies in Estonian universities. The need for this action comes from the lack of Estonian PhD students in physics and engineering. We successfully found three international PhD student candidates who all are enrolled in Estonian universities as PhD students by now (Nico Benincax from Belgium, Ruiwen Quyang from China, Maksim Budnitsky from Ukraine) and who carry out their research in our laboratory.

The Laboratory plans to play the central role at CERN to enable Estonian researchers, engineers, students and teachers to profit most from the Estonian membership at CERN.

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 two experienced researchers Mario Kadastik, Christian Veelken as well as three post-docs (Ram Krishna Dewanjee, Sandeep Bhowmik and Alexandra Carvalho) and graduate students Karl Ehatäht, Diana Rand, Marten Pärg and Gleb Bogomol.

Past, present and future

The experimental group was originally part of the particle physics group at NICPB and split away in the last decade during the LHC operational phase after a recommendation from ISAB to give more active roles to younger researcher. The experimental group has been growing ever since, mostly through partnerships with experienced researchers coming to Estonia through Mobilitas grants as well as via the training of students of whom some are now completing their PhD or post-doc at various universities abroad (including for example ETH-Zurich, Caltech etc). We also have several 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 early topics of interest was in phenomenology, where in cooperation with the theory group we have performed various simulations on dark matter theories including several 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 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 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 results of this search are in the process of being finalized for the LHC Run I and Run II.

The group plans 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 currently ongoing accelerator 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 to the actual R&D of the experimental apparatus as well. We find the current CMS upgrade to be an ideal time to allocate resources to bringing in competency in this field as well as cooperate with local universities to further enhance our competency and to expand the local knowledge on working such specialized projects. We have already developed initial excellent contacts with local electronics groups at the universities as well as some of the major R&D companies and are anticipating several post-doctoral 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.

Collaborations

- CERN
- CMS collaboration
- Estonian Universities

Key publications in 2016 – 2018

1) CMS Collaboration. Measurement of top quark polarisation in t-channel single top quark production. *Journal of High Energy Physics*, (4):073, APR 13 2016.
2) CMS Collaboration. Observation of (tt)over-barH Production. *Phys. Rev. Lett.,* 120(23): 231801, JUN 4 2018.
3) Lorenzo Bianchini, Betty Calpas, John Conway, Andrew Fowlie, Luca Marzola, Lucia Perrini, and Christian Veelken. Reconstruction of the Higgs mass in events with Higgs bosons decaying into a pair of tau leptons using matrix element techniques. *Nuclear Instruments & Methods in Physics Research Section A Accelerators Spectrometers Detectors and Associated Equipment*, 862:54–84, AUG 1 2017.
4) CMS Collaboration. Reconstruction and identification of tau lepton decays to hadrons and nu(tau) at CMS. *Journal of Instrumentation*, 11:P01019, JAN 2016.
5) CMS Collaboration. Measurement of the top quark mass using proton-proton data at root(s)=7. *Phys. Rev. D*, 93(7):072004, APR 7 2016.

3.1.2 Theoretical Physics

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

Group members: Abdelhak Djouadi, John Ellis, Emidio Gabrielli, Els Heinsalu, Andi Hektor, Gert Hütsi, Kristjan Kannike, Alexandros Karam, Tomi Koivisto, Gionni Marchetti, Tommi Markkanen, Carlo Marzo, Luca Marzola, Marco Patriarca, Antonio Racioppi, Martti Raidal, Glenn Robins, Hardi Veermäe and a number of PhD, MSc and BSc students as follows. BSc: Kaius Loos, Jass Kaarama, Sven Põder, Tõnu-Priit Tammepuu; MSc: Aleksei Kubarski, Kristjan Müürsepp, Venno Vipp; PhD: Nico A. Benincasa, Taavi Tuvi, Ruiwen Ouyang, David Navidad Maeso, Maksim Budnitski.

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 and the ultraviolet completion of gravity, 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.

Collaborations

- CERN, Geneva, Switzerland
- LLR/Ecole Polytechnique, Paris, France
- Cornell University, Ithaca, US
- Universidad de Oviedo, Oviedo, Spain
- Chinese Academy of Sciences, Beijing, China
- Institut de Physique Nucléaire de Lyon, Lyon, France
- Tata Institute of Fundamental Research, Mumbai, India
- National Institute of Science Education and Research, Bhubaneswar, India

Key publications in 2016 - 2018

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) L. Järv, K. Kannike, L. Marzola, A. Racioppi, M. Raidal, M. Rünkla, M. Saal and H. Veermäe, "Frame-Independent Classification of Single-Field Inflationary Models," [arXiv:1612.06863 [hep-ph]], doi:10.1103/PhysRevLett.118.151302, Phys. Rev. Lett. 118 (2017) no.15, 151302.
6) B. Carr, M. Raidal, T. Tenkanen, V. Vaskonen and H. Veermäe, "Primordial black hole constraints for extended mass functions," Phys.Rev.D 96, (2017) no.2, 023514, [arXiv:1705.05567 [astro-ph.CO]]. doi:10.1103/PhysRevD.96.023514,
7) J. Ellis, A. Hektor, G. Hütsi, K. Kannike, L. Marzola, M. Raidal and V. Vaskonen, "Search for Dark Matter Effects on Gravitational Signals from Neutron Star Mergers," Phys. Lett. B781 (2018) 607, doi:10.1016/j.physletb.2018.04.048, [arXiv:1710.05540 [astro-ph.CO]].
8) S. Fraser et al., "The EDGES 21 cm Anomaly and Properties of Dark Matter," Phys. Lett. B785 (2018) 159, doi:10.1016/j.physletb.2018.08.035, [arXiv:1803.03245 [hep-ph]].
9) S. Fraser, C. Marzo, L. Marzola, M. Raidal and C. Spethmann, "Towards a viable scalar interpretation of RD," Phys. Rev. D98 (2018) no.3, 035016, doi:10.1103/PhysRevD.98.035016, [arXiv:1805.08189 [hep-ph]].

10) T. Złośnik, F. Urban, L. Marzola and T. Koivisto, "Spacetime and dark matter from spontaneous breaking of Lorentz symmetry," Class. Quant. Grav. 35 (2018) no.23, 235003, doi:10.1088/1361-6382/aaea96, [arXiv:1807.01100 [gr-qc]].

3.1.3 High Performance Computing

Group members: Mario Kadastik, Lauri Liibert, Ilja Livenson, Andres Toomsalu.

Past, present and future

The computing centre has been built up in stages of various intermittent funding rounds over the past fifteen 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 centre 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 7600+ core cluster that also hosts a distributed storage of 4.5 PB (raw). The whole system has an interconnect on standard 100 GbE and 10 GbE networking mesh 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 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 regular upgrade periods assuming funds are available for such upgrades.

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 15y and 13y, respectively. In addition, we have a very capable admin/developer Lauri Liibert, who's been with us for many years and is overseeing daily operations. Beyond that we also have occasional help from students.

Collaborations

- Estonian Scientific Computing Infrastructure
- CMS collaboration, CERN

Key publications in 2016 – 2018

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

3.2 Laboratory of Chemical Physics

The head of laboratory during the reporting period was Dr. D. Hüvonen; Starting from March 16th, 2019 the laboratory is led by Dr. R. Stern, as Dr. Hüvonen left the institute to continue his career in industry[3]. The laboratory employs full time 24 researchers with PhD who supervise 9 graduate and 2 master students. Three persons out of the technical staff of 9 work at the cryogenic facility and take care of the superconducting magnets.

[3] https://roofit.solar/ , producing cost-effective photovoltaic steel roof panels.

The laboratory runs the largest infrastructure of the institute, the Tallinn branch of the Estonian Magnet Laboratory that has several nuclear magnetic resonance (NMR) instruments, THz spectroscopy and low temperature physics setups, all backed by the in-house helium liquefier. NICPB joined the Estonian Center of Analytical Chemistry in 2019, making laboratory's instruments available within a broader scientific infrastructure network. The Estonian Center of Analytical Chemistry is a distributed interdisciplinary scientific research infrastructure for the development and application of modern analytical methods as well as the quality assurance of chemical measurements in research, surveillance and industry laboratories.

Laboratory's experimental capabilities allow the investigation of material response functions over very wide spectral range covering 16 orders of magnitude in frequency starting from static susceptibility probes, NMR, THz, infrared, and 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, increased stability, variety and range of experimental control parameters allows to address wide range of problems in physics, chemistry and biology. For sample characterization there are an X-ray powder diffractometer, the Physical Property Measurement System (PPMS) equipped with a 14 T magnet and multiple sample characterization probes including an atomic force microscope insert for surface studies and home-built probe for variable field NMR. THz and optical laboratory facilitate spectrometers to measure transmission and reflection in wavelength range from 3 mm up to 200 nm (3 - 50000 cm^{-1}) in various sample environments.

National collaborations include thin film sample preparation at University of Tartu (UT) and NP preparation at the Estonian University of Life Sciences. In addition, UT, TalTech 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 the collaborations are with leading crystal growers and theoreticians in the world. Joint experiments are performed 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), low-T fuel cell and catalyst development with PowerUp Fuel Cells OÜ (I. Kruusenberg), synthesis of nanocarbon materials from pulp and paper industry waste in collaboration with Stora Enso (I. Kruusenberg), and environmental toxicology assessments and investigation of oil shale ash residue recycling opportunities (J. Reinik) with Environmental Investment Centre and the Estonian energy company Eesti Energia.

In 2019 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
- 6 Personal Research Grants (Team/Start-up/Postdoc grants: PRG/PSG/PUTJD)
  - PUT1046 "Synthesis and functionalization of Fe based NPs for high-sensitivity Magnetic Resonance Imaging (2016 – 2019)", L. Seinberg
  - PRG4 "Emerging Novel Phases in Strongly Frustrated Quantum Magnets (2018 – 2022)", R. Stern (NICPB)/A. Tamm (UT)
  - PRG399 "Adaptable supramolecular chirality sensors (2019 – 2023)", R. Aav (TalTech)/J. Adamson (NICPB)

- PSG11 "Quantitative detection of cancer biomarkers in urine by hyperpolarized NMR (2018 – 2021)", I. Reile
- PSG312 "Metal Oxide-based Catalyst Materials from Recycled Li-ion Batteries for Metal-air Battery and Fuel Cell Applications (2019 – 2022)", I. Kruusenberg
- PSG317 "Quantitative sensing of intramolecular electric fields by DNA-intercalating organometallic two-photon probes (2019 – 2022)", C. Stark

- 5 Mobilitas Returning Researcher or Postdoc Grants (MOBTP or MOBJD)
  - MOBTP51 "Profiling phosphometabolomic pathways in colorectal cancer by 18O isotope effect assisted 31P NMR spectroscopy (2017 – 2019)", I. Reile
  - MOBTP128 "Nonlinear-optical metrology (2018 – 2020)", M. Sildoja
  - MOBJD69 "Femtosecond multi-photon spectroscopy of transition metal complexes (2017 – 2019)", C. Stark
  - MOBJD295 "Novel electronic states of low-dimensional and magnetically frustrated systems (2017 – 2019)", T. Chakrabarty
  - MOBJD449 "Unconventional superconductivity in the $Mo_nGa_{(5n+1)}$ intermetallics (2018 – 2020)", V. Verchenko
- 1 ERA-Net Grant
  - ERA.Net RUS Plus MOBERA6 "Novel Heteroatom-doped Nanocarbon Catalysts for Fuel Cell and Metal-air Battery Applications (2018-2021)", I. Kruusenberg

3.2.1 Emerging Quantum Materials

There are 8 researchers with PhD in the Emerging Quantum Materials programme: Dan Hüvonen (until 16.03.2019), Enno Joon, Urmas Nagel, Toomas Rõõm, Raivo Stern, Anna Šugai, Valery Verchenko, Tanmoy Chakrabarty. PhD students Laur Peedu, Johan Viirok, Joosep Link, Kirill Amelin, Tanzeeha Jafari are all from TalTech.

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.

The main mode of operation for this programme is on-site experimental work on samples provided by worldwide network of collaborators. Although high quality single crystal growth infrastructure is absent at NICPB, some sample synthesis and growth efforts have been started, most recently by T. Chakrabarty, from 2017. Late 2018 the programme welcomed postdoc V. Verchenko who is synthesizing samples either at site or at partner institutions. Subsequent sample characterization is made in house using X-ray diffractometer and PPMS with multiple probes including a low temperature AFM/MFM.

Particularly useful for studying emergent quantum materials is the THz spectral range that encompasses paramagnetic electron spin and collective magnon resonances. Several dedicated spectrometers are in use: TeslaFIR (equipped with 17T magnet, covers 100 GHz - 6 THz, has static electric field capability and light polarization control, provides sample temperature down to 2.5 K and has high sensitivity bolometric detection at 0.3 K), TLE200 (a modified dilution refrigerator with 12 T magnet, sample temperature below 1 K, covers 100 GHz - 2 THz) and Toptica continuous wave phase sensitive THz spectrometer (photomixing of two IR lasers, frequency from 50 GHz to 2 THz, currently usable sample temperature down to 5 K). Conventional IR to UV spectroscopy can be performed down to 5 K temperature using Bruker Vertex 80v.

Collaborations

1. A. Tamm, Institute of Physics, Tartu University – Atomic layer deposition of thin films
2. K. Kukli, Institute of Chemistry, Helsinki University – Atomic layer deposition of thin films
3. V. Kocsis from prof. Y. Tokura's group at RIKEN, Japan – Single crystal preparation
4. R. S. Fishman, Oakridge National Laboratory, USA – Spin wave theory
5. R. J. Whitby group, Southampton University, UK - Preparation of endofullerene samples
6. M. H. Levitt group, Southampton University, UK – NMR of endofullerene samples
7. K. Penc, P. Balla, J. Romhanyi, MTA-BME, Budapest, Hungary – Theory of spin excitations
8. IR group in HFML, Nijmegen, Netherlands – High magnetic field experiments
9. I. Kezsmarki's, University of Augsburg, Germany – Spectroscopy of multiferroics
10. S. Bordacs, Budapest University of Technology and Economics, Hungary – Spectroscopy of multiferroics
11. T. Kimura, Tokyo – single crystal growth of quantum materials
12. J. Pyrhonen's group, Lappeenranta Univ Technol, Finland – Permanent magnets and PMSM design
13. M. Horvatic, NMR group at G-LNCMI/EMFL – High magnetic field NMR experiments
14. A. Reyes NMR group at NHMFL, USA – High magnetic field NMR experiments
15. J. Wosnitza, Dresden HML/EMFL – Experiments in pulsed high magnetic fields

Key publications in 2016 - 2018

1) Andrea Krachmalnicoff, Richard Bounds, Salvatore Mamone, Shamim Alom, Maria Concistre, Benno Meier, Karel Kouril, Mark E. Light, Mark R. Johnson, Stephane Rols, Anthony J. Horsewill, Anna Shugai, Urmas Nagel, Toomas Room, Marina Carravetta, Malcolm H. Levitt, and Richard J. Whitby. The dipolar endofullerene HF@C60. Nat. Chem., 8(10):953–957, OCT 2016.
2) A. Mannig, J. S. Moller, M. Thede, D. Huvonen, T. Lancaster, F. Xiao, R. C. Williams, Z. Guguchia, R. Khasanov, E. Morenzoni, and A. Zheludev. Effect of disorder on a pressure-induced z=1 magnetic quantum phase transition. Phys. Rev. B, 94(14):144418, OCT 14 2016.
3) Aleksander Trummal, Lauri Lipping, Ivari Kaljurand, Ilmar A. Koppel, and Ivo Leito. Acidity of Strong Acids in Water and Dimethyl Sulfoxide. J. Phys. Chem. A, 120(20):3663–3669, MAY 26 2016.
4) F. Weickert, N. Harrison, B. L. Scott, M. Jaime, A. Leitmae, I. Heinmaa, R. Stern, O. Janson, H. Berger, H. Rosner, and A. A. Tsirlin. Magnetic anisotropy in the frustrated spin-chain compound betaTeVO4. Phys. Rev. B, 94(6):064403, AUG 1 2016.
5) R. S. Fishman, S. Bordács, V. Kocsis, I. Kézsmárki, J. Viirok, U. Nagel, T. Rõõm, A. Puri, U. Zeitler, Y. Tokunaga, Y. Taguchi, and Y. Tokura. Competing exchange interactions in multiferroic and ferrimagnetic CaBaCo4O7. Phys. Rev. B, 95(2):024423, JAN 23 2017.
6) Ilya Petrov, Dmitry Egorov, Joosep Link, Raivo Stern, Sami Ruoho, and Juha Pyrhonen, Hysteresis Losses in Different Types of Permanent Magnets Used in PMSMs. IEEE Trans. Ind. Electr., 64(3): 2502-2510, MAR 2017
7) Zhe Wang, S. Reschke, D. Hüvonen, S. H. Do, K. Y. Choi, M. Gensch, U. Nagel, T. Rõõm, and A. Loidl. Magnetic Excitations and Continuum of a Possibly Field-Induced Quantum Spin Liquid in alpha-RuCl3. Phys. Rev. Lett., 119(22):227202, NOV 28 2017.
8) Vilmos Kocsis, Karlo Penc, Toomas Room, Urmas Nagel, Jakub Vit, Judit Romhanyi, Yusuke Tokunaga, Yasujiro Taguchi, Yoshinori Tokura, Istvan Kezsmarki, and Sandor Bordacs. Identification of Antiferromagnetic Domains Via the Optical Magnetoelectric Effect. Phys. Rev. Lett., 121(5):057601, AUG 1 2018.

9) Harlyn J. Silverstein, Ryan Sinclair, Arzoo Sharma, Yiming Qiu, Ivo Heinmaa, Alexander Leitmae, Christopher R. Wiebe, Raivo Stern, and Haidong Zhou. Naturally tuned quantum critical point in the S=1 kagome YCa3(VO)(3)(BO3)(4). Phys. Rev. Mat., 2(4):044006, APR 26 2018.
10) C. M. Pasco, B. A. Trump, Thao T. Tran, Z. A. Kelly, C. Hoffmann, I. Heinmaa, R. Stern, and T. M. McQueen, Single-crystal growth of $Cu_4(OH)_6BrF$ and universal behavior in quantum spin liquid candidates synthetic barlowite and herbertsmithite. Phys. Rev. Mat. 2(4), 044406 – APR 27 2018

3.2.2 Applied Nuclear Magnetic Resonance

There are 7 researchers with PhD who are active in the Applied Nuclear Magnetic Resonance (NMR) programme: Jasper Adamson, Kerti Ausmees, Ivo Heinmaa, Tõnis Pehk, Indrek Reile, Liis Seinberg, Raivo Stern with PhD students Joosep Link. Anna Peterson, Riho Rästa and Maria Volokhova, undergraduate students Karl-Kristian Kaup, Mar-Liis Ludvig.

NICPB was founded around the experimental method of NMR. 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. The availability of liquid He from the in-house liquefier has allowed running multiple NMR systems for solution and for solid state probes.

Today, for most complex and complicated studies local universities and companies are benefiting from the 800 MHz NMR spectrometer and expertise in the data interpretation (T. Pehk, J. Adamson, I. Reile, K. Ausmees). Solid state NMR on powder samples has a unique capability to spin the sample at 10 kHz down to the low temperature of 5 K. (I. Heinmaa, R. Stern).

The Lab endorsed several new research ideas by young researchers until they obtained their own research grants for self-sufficient funding:

- early cancer diagnostic methods (I. Reile),
- supramolecular chemistry (J. Adamson) and
- development of MRI contrast agents (L. Seinberg).

Several cancers are detectable before any pathological symptoms appear by the concentrations of certain modified nucleosides in urine. One of the reasons why such promising biomarkers are not in clinical use is the difficulty of detecting and resolving isomeric nucleosides with identical molar masses in low-μM concentrations. Recent developments in parahydrogen hyperpolarization NMR methodology address these issues and resolve sub-μM analytes in urine by fast NMR experiments. The research of Dr. I. Reile aims to provide a new tool for cancer- and metabolomics research by optimizing sample preparation methods, hyperpolarization catalysts and hyperpolarized NMR method itself. The new diagnostics technology allows early detection of cancers, potentially offering the society large savings in healthcare costs.

The supramolecular chemistry group of J. Adamson focuses on the synthesis and structure elucidation of large and functional oxacalixarene macrocycles and their interaction studies with functional molecules that can bind into the cavity of the macrocycles. The group is currently focused on the synthesis of water-soluble macrocycles with interest in utilising mechanochemistry in the synthesis of these cavitands. The potential applications of such host compounds range from drug design and delivery to catalysis and sensor materials. As an example, over the recent years, we have synthesised an oxacalix[4]arene carboxylate that can bind a known herbicide paraquat with strong affinity and could thereby lead to treatment methods for paraquat poisoning by wrapping the toxicant in a stable host-guest complex. The work is performed in collaboration with Prof. Riina Aav at TalTech.

Superparamagnetic metal NPs (diameter ≤50 mm) synthesis and application as MRI contrast agents continues to suffer from several drawbacks, such as long-term magnetic stability, aggregation and coagulation and lack of crystallinity. Dr. L. Seinberg focuses on the synthesis and functionalisation of doped iron, iron carbide (Fe3C), and pure iron (Fe(0)) NPs with stable magnetic properties and with functionalised nontoxic and corrosion-resistant biocompatible organic shells. Such NPs could overcome aggregation and coagulation and would be applicable as improved MRI contrast agents with magnetic properties that take a leap forward in early disease diagnosis by MRI.

In the future the need for high quality NMR data will persist and a change of generations is underway in the NMR group as outlined above. Problem of aging NMR infrastructure needs to be addressed aggressively soon to sustain the scientific output.

Collaborations

1. Riina Aav, TalTech – Supramolecular chemistry, NMR, synthesis and X-ray.
2. Tõnis Kanger, TalTech – NMR of halogen bonding of compounds
3. Dzmitry Kananovich, TalTech – NMR measurements of organogatalysts
4. Dmitry Murzin, Abo Akademi Turkku, Finland   Zeolites chemistry, NMR analysis
5. Marina Carravetta, University of Southampton, UK – NMR of superconductors, fullerides
6. Denis Arcon, Uni Josef Stefan, Ljubljana, Slovenia – NMR in organic- and superconductors
7. M. Jebrane, Swedish University of Agricultural Sciences, Uppsala, Sweden – Wood chemistry
8. R. K. Kremer, MPI für festkörperphysik, Stuttgart, Germany – NMR study of magnetic materials
9. A. Gräslund, University of Stockholm, Sweden – Biochemistry
10. S. Haravifard, Duke University, USA – NMR study of doped $SrCu_2(BO_3)_2$
11. Lauri Vares, Dr U. Mäeorg, Tartu University – Materials chemistry
12. M. Lopp, Prof. R. Aav, Dr O. Parve, TalTech – Materials chemistry
13. R. Tuvikene, Dr K. Truus, University of Tallinn – Chemistry of seaweeds
14. D. Meissner, TalTech – NMR of solar cell materials
15. K. Kirsimäe, Tartu University – Study of oil shale ashes
16. VKG Oil AS – NMR of novolac and resol resins
17. University of Tartu, Institute of technology – NMR of new bio-based polymers
18. TalTech, Department of Chemistry and Biotechnology – NMR in enzymatic catalysis; NMR of asymmetric organocatalytic synthesis products
19. Biofire OÜ – Developing of lighting gel
20. Marco Tessari, Radboud University, Nijmegen, NL – NMR methodology development for hyperpolarization

Key publications in 2016 - 2018

1) Sandra Kaabel, Jasper Adamson, Filip Topic, Anniina Kiesila, Elina Kalenius, Mario Oeren, Mart Reimund, Elena Prigorchenko, Aivar Lookene, Hans J. Reich, Kari Rissanen, and Riina Aav. Chiral hemicucurbit[8]uril as an anion receptor: selectivity to size, shape and charge distribution. Chemical Science, 8(3):2184–2190, MAR 1 2017.
2) Jasper Adamson, Ryszard B. Nazarski, Juri Jarvet, Tonis Pehk, and Riina Aav. Shortfall of B3LYP in Reproducing NMR J(CH) Couplings in Some Isomeric Epoxy Structures with Strong Stereoelectronic Effects: A Benchmark Study on DFT Functionals. ChmePhysChem, 19(5):631–642, MAR 5 2018.
3) Mohamed Jebrane, Nasko Terziev, and Ivo Heinmaa. Biobased and Sustainable Alternative Route to Long-Chain Cellulose Esters. Biomacromolecules, 18(2):498–504, FEB 2017.

4) C. M. Pasco, B. A. Trump, Thao T. Tran, Z. A. Kelly, C. Hoffmann, I. Heinmaa, R. Stern, and T. M. McQueen. Single-crystal growth of Cu-4(OH)(6)BrF and universal behavior in quantum spin liquid candidates synthetic barlowite and herbertsmithite. Phys. Rev. Mat., 2(4):044406, APR 27 2018.
5) Livia Matt, Jaan Parve, Omar Parve, Tonis Pehk, Thanh Huong Pham, Ilme Liblikas, Lauri Vares, and Patric Jannasch. Enzymatic Synthesis and Polymerization of Isosorbide-Based Monomethacrylates for High-T-g Plastics. ACS Sustainable Chemistry & Engineering, 6(12):17382–17390, DEC 2018.
6) Dmitri Trubitson, Sergei Zari, Sandra Kaabel, Marina Kudrjashova, Kadri Kriis, Ivar Jarving, Tonis Pehk, and Tonis Kanger. Asymmetric Organocatalytic Cascade Synthesis of Tetrahydrofuranyl Spirooxindoles. Synthesis-Stuttgart, 50(2):314–322, JAN 2018.
7) A. Yu. Sidorenko, A. V. Kravtsova, A. Aho, I. Heinmaa, T. F. Kuznetsova, D. Yu. Murzin, and V. E. Agabekov. Catalytic isomerization of α-pinene oxide in the presence of acid-modified clays. Molecular Catalysis, 448: 18-29, APR 2018.

3.2.3 Energy Technology and materials

Energy technology research topic encompasses 3 research groups, summing up to 6 researchers with PhDs. These groups are (i) environmental chemistry group: Janek Reinik, Natalja Irha,(ii) solid oxide fuel cell development group: Juhan Subbi, Reio Põder and (iii) energy technology group of Ivar Kruusenberg, Kerli Liivand with PhD students, Kätlin Kaare and Ehsan Zarmehri.

The environmental chemistry group dates back 25 years. From 2013 on Dr. J. Reinik and Dr. N. Irha are working on oil shale environmental studies, co-financed by oil shale companies and the Environmental Investment Centre. For the last two years the group has been involved in oil shale ash implementation studies. This includes (i) use of granulated oil shale ash in remediation of post-harvested peatlands - field study, (ii) use of granulated oil shale ash in purification of phenolic wastewater from shale oil production industry, (iii) use of oil shale ash in road construction - follow-up environmental monitoring. There are also several smaller projects such as granulation of algae waste and waste compliance tests. Now the focus of the group is on use of granulated oil shale ash in organic farming and the group plans to give consultation service for a company wishing to establish an oil shale granulation plant in Maardu, Estonia. The group is also involved in a cluster together with the University of Earth Studies for making fertilizer from oil-shale ash and bio char. The 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 15 years and was started by J. Subbi together with our commercial partner Elcogen AS. Now the research is in the development phase of commercially usable Solid Oxide Fuel Cell (SOFC). The main challenge is the long-term stability of SOFC systems under operating conditions. NICPB has a contract with Elcogen AS, where J. Subbi is the PI. Currently the industrial scale experiments and tests are carried out by Elcogen and the group of J. Subbi provides their expert knowledge to address the upcoming issues and carries out electrochemical testing and whatever further studies are needed. There are three aspects to address: *Firstly,* long term phase stability of stack components, mainly of cell electrodes at cell working conditions. *Secondly,* interdiffusion of stack component materials in long term operation. *Thirdly*, the influence of impurities in both air and fuel mixture to electrode and interconnect structure and electrochemical behaviour.

In 2018 Dr. I. Kruusenberg returned from postdoc stay at UC Berkeley, USA, to start an Energy Technology group at NICPB that focuses in recycling of Li-ion batteries, synthesis of nanocarbon materials for different applications and development of novel materials for the low-temperature fuel cells. He has been successful in securing national funding (PSG312) as well as from EU by establishing M-era.NET consortium (ERA-Net RUS Plus, MOBERA6). Several applications have been submitted in early 2019 (H2020, EEA Baltic Research Programme, Nutikas, etc.) to expand the group (currently 5 people) and ensure long term viability. Strong collaboration has been established with the fuel cell-based electric generator developer PowerUp Fuel Cells OÜ and with one of the biggest pulp and paper producers in Scandinavia - Stora Enso. Used Li-ion batteries are environmental hazards which contain chemicals and materials that can pollute water and soil. Such pollutants are: organic solvents, nano-carbon powders, and harmful heavy metals, like Co, Ni, Mn, Cu, etc. The main limitations for the effective recycling of Li-ion battery materials have been technical difficulties to separate and treat different materials so that they could be re-used, along with the high cost of that process. Project goals are (i) to develop cost-effective recycling methods to re-use metal-oxides and carbon powders from spent lithium-ion batteries and (ii) to synthesize highly active and novel catalyst materials from these recycled materials for the metal-air batteries and low-temperature fuel cells.

Collaborations

1. Elcogen – Solid oxide fuel cell element and stack development
2. Nanomaterials Laboratory, Institute of Systems, Information Technologies and Nanotechnologies, Fukuoka 819-0388, Japan – Physical characterization of the nanomaterials including EDX, TEM, SEM.
3. A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of Russ. Ac. Sci., 1 Favorsky Street, Russian Federation – DFT calculations
4. Research Laboratory of Functional Materials Technologies, Faculty of Materials Science and Applied Chemistry, Riga Technical University – Synthesis of different nanomaterials and physical characterization including XPS, SEM, TEM.
5. Latvian State Institute of Wood Chemistry – Synthesis of bio-based nanocarbon materials
6. DLR Institute of Networked Energy Systems, Urban and Residential Technologies, Germany – Fuel cell tests and catalyst characterization with various electrochemical methods including rotating disc electrode method and impedance spectroscopy
7. State research institute Centre for Physical Sciences and Technology, Lithuania – Physical characterization of the catalysts, including Raman spectroscopy and testing of the fuel cell anode materials.
8. Ira A. Fulton Schools of Engineering, Arizona State University, AZ, United States of America - Fuel cell tests
9. Digby Macdonald, University of California at Berkeley, USA – Catalyst synthesis and characterization with various electrochemical methods including cyclic voltammetry and impedance spectroscopy
10. Fuel cell group, University College London, United Kingdom – Metal-air battery and fuel cell tests
11. TalTech – Polymer-based material preparations and 3D printing

Key publications in 2016 - 2018

1) Jekaterina Jefimova, Jasper Adamson, Janek Reinik, and Natalya Irha. Leaching of PAHs from agricultural soils treated with oil shale combustion ash: an experimental study. Environmental Science and Pollution Research, 23(20):20862–20870, OCT 2016.
2) Janek Reinik, Natalya Irha, Arina Koroljova, and Tonis Meriste. Use of oil shale ash in road construction: results of follow-up environmental monitoring. Environmental Monitoring And Assessment, 190(2):59, FEB 2018.
3) Janek Reinik, Natalya Irha, Eiliv Steinnes, and Ivo Heinmaa. Granulation Of Oil Shale Ash With Sodium Alginate For The Removal Of Phenols From Shale Oil Wastewater. Oil Shale, 35(3):265–278, 2018.
4) Kätlin Kaare, Aleksandrs Volperts, Galina Dobele, Aivars Zurins, Alexander Dyck, Loreta Tamasauskaite-Tamasiunaite, Eugenijus Norkus, Ivar Kruusenberg, Highly Active Wood-Derived

Nitrogen-Doped Carbon Nanomaterial for Low Temperature Fuel Cells and Metal-Air Batteries, Applied Catalysis B: Environmental, Article in press

3.2.4 Nonlinear optics

Nonlinear optics lab is led by Aleksander Rebane, staffed by researchers Charlie Stark, Mait-Meelis Sildoja, Jüri Pahapill and supported by quantum chemical calculations done by Merle Uudsemaa and Aleksander Trummal. The group has a PhD student Matt Rammo and a master's student Katrin Petritsenko. In 2017 Sophie Marinucci de Reguardati defended her PhD thesis in TalTech, supervised by Dr. Rebane.

The main research is experiments and theory on ultrafast nonlinear optics: femtosecond multi-photon absorption spectroscopy of organic fluorophores for applications in molecular sensing and imaging. The programme was initiated by Dr. Rebane (also professor at Montana State University) who started to use an existing femtosecond laser system with the help of J. Pahapill. The programme has been funded by the institutional IUT23-9 grant (2014-2019) with Dr. Rebane as PI. The group was reinforced in 2017 with postdoc (MOBJD69) Charlie Stark who secured a personal starting grant (PSG317) in 2019. In 2018 Dr. Sildoja joined the group, funded by the Mobilitas Returning Researcher programme (MOBTP128, 2018-2020).

In recent years the group has developed a high-accuracy quantitative measurement technique for determining two-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. In 2018 the group has received a large positive impact thanks to a new state of the art laser system from Light Conversion Inc. The new laser system consists of a mode-locked pumped amplified laser Pharos and optical parametric amplifier Orpheus allowing to tune the wavelength of femtosecond pulses from 400 - 2000nm, which is over 6 times increase in the range compared to previous system. Using this advanced laser source, the group is constructing and characterizing a measurement system that determines absolute two-photon and three-photon absorption cross section spectra of organic fluorophores in a broad range of wavelengths with unprecedented accuracy of better than 5%. An additional long-term goal is to perform multiphoton calibrations for quantum information applications. The same experimental setup is applied to deoxyribonucleic acid (DNA) fine structure sensing. These experiments aim at developing new tool for probing of electric field strength inside- and in close vicinity to DNA structures. Femtosecond light pulses of the ultrafast laser are used to measure two-photon absorption spectra of organometallic ruthenium complexes that spontaneously insert themselves (intercalate) between DNA strands. Because two-photon spectra are exclusively sensitive to electrostatic interactions, these luminescent species act as tiny nanometer-scale "molecular voltmeters" to probe forces responsible for important properties of DNA.

The future scope of the programme depends whether Dr. Rebane can secure enough funding either nationally or through European programmes. Short term viability is assured through running grants of Dr. Stark and Dr. Sildoja.

Collaborations

1. Materials and Manufacturing Directorate, Air Force Research Laboratory, Wright-Patterson Air Force Base, Ohio 45433, USA – Quantum chemistry calculations
2. Centro de Investigación en Quimica Aplicada (CIQA), 25294 Saltillo, Coahuila, Mexico – Sample synthesis
3. Institute of Organic Chemistry, Polish Academy of Sciences – Sample synthesis and characterization
4. School of Physical, Environmental and Mathematical Sciences, The University of New South Wales, Canberra ACT 2600, Australia – Experiments

5. Department of Chemistry, Oxford University, Oxford, OX1 3TA, United Kingdom – Sample synthesis and characterization

Key publications in 2016 - 2018

1) S. De Reguardati, J. Pahapill, M. Rammo, and A. Rebane. Improving the fidelity of two-photon absorption reference standards. In Heisterkamp, A and Herman, PR and Meunier, M and Osellame, R, editor, FRONTIERS IN ULTRAFAST OPTICS: BIOMEDICAL, SCIENTIFIC, AND INDUSTRIAL APPLICATIONS XVII, volume 10094 of Proceedings of SPIE, page UNSP 100941Q. SPIE; Amplitude Syst; APE GmbH; TRUMPF Inc, 2017. Conference on Frontiers in Ultrafast Optics - Biomedical, Scientific, and Industrial Applications XVII, San Francisco, CA, JAN 29-FEB 02, 2017.
2) Lukasz G. Lukasiewicz, Hye Gun Ryu, Alexander Mikhaylov, Cloe Azarias, Marzena Banasiewicz, Boleslaw Kozankiewicz, Kyo Han Ahn, Denis Jacquemin, Aleksander Rebane, and Daniel T. Gryko. Symmetry Breaking in Pyrrolo[3,2-b]pyrroles: Synthesis, Solvatofluorochromism and Two-photon Absorption. Chemistry – an Asian Journal, 12(14):1736–1748, JUL 18 2017.
3) Alexander Mikhaylov, Merle Uudsemaa, Aleksander Trummal, Eduardo Arias, Ivana Moggio, Ronald Ziolo, Thomas M. Cooper, and Aleksander Rebane. Spontaneous Symmetry Breaking
4) Facilitates Metal-to-Ligand Charge Transfer: A Quantitative Two-Photon Absorption Study of Ferrocene-phenyleneethynylene Oligomers. Journal of Physical Chemistry Letters, 9(8):1893– 1899, APR 19 2018.

3.3 Laboratory of Chemical Biology

The Laboratory of Chemical Biology is the smallest laboratory of the NICPB, employing 8 PhD researchers: V. Chekulayev, S. Gudlawar, A. Klepinin, A. Koit, 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 Dr. T. Käämbre.

In 2018 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, I. Ševtšuk), Horizon 2020
  - COST Action EU CARDIOPROTECTION, Horizon 2020 (T. Käämbre)

The keywords of expertise are mitochondria, energy transfer networks, adenylate kinase, creatine kinase, cytoskeleton, development, cancer, regulation of mitochondrial respiration, 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 and applied aspects of energy metabolism, biochemistry and biophysics.

Past, present and future

Historically, the field of cellular bioenergetics has been in NICPB for 26 years. Molecular system bioenergetics (MSB) is an interdisciplinary field and it impacts well with other NICPB strategic research programs. Since 2012 the laboratory is headed by research professor Tuuli Käämbre. The laboratory (previously Lab. of Bioenergetics) was renamed as the Laboratory of Chemical Biology what is more compatible with the topics of the laboratory.

The results of our previous studies are related with normal adult cardiomyocytes. The main topics are 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 based on information about cardiac cell structure and on experimental data obtained in the studies of permeabilized cardiomyocytes and fibres. Three doctoral students defended their doctoral thesis in the lab during the reporting period; two of them are currently working as researchers in the laboratory.

Currently we focus on the understanding of the bioenergetics in malignant cells and study how the energy transfer pathways in healthy tissues are linked or changed by a disease. We test our discoveries on clinical samples to get real world validity, but also control whether the research outcome has any direct value to cancer patients, and hence, medical applicability. The research of the team is multifaceted with the following topics being covered:

- in vivo fluxomics in cancer and muscle tissues
- Functional and molecular characterization of systems involved in cellular respiromics that control mitochondrial function in vivo
- Cancer metabolomics.

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

Future includes continued work on most interesting but still underestimated fields of bioenergetics: muscle and cancer energy metabolism. The very wide scale of competence of the Lab gives a possibility to study the cancer bioenergetics with the methods of system biology. *Secondly,* we have started to perform the metabolic profiling of some normal and cancerous cells and tissues by ^{18}O-assisted ^{31}P NMR and ^{1}H NMR, in collaboration with I. Reile form our own institute. We continue the studies of metabolomics of breast and colorectal cancer clinical material. 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 functional abnormalities of the cellular energy conversion that cause the pathological state. We also plan to strengthen the direction of applied bioenergetics in collaboration with hospitals and the small enterprise "Mitogro" for the development of quick and cheap diagnostic tests of rare mitochondrial and muscle diseases and tumors. The cooperation with universities enhances our competences and allows us to find new young talented PhD students, post-docs and group members.

Collaborations

1. The Nuclear Magnetic Resonance spectroscopy from our institute
2. University of Tartu (Institute of Biomedicine and Translational Medicine, Institute of Molecular and Cell Biology)
3. Tallinn University
4. Tallinn University of Technology
5. Division of Cardiovascular Diseases, Metabolomics NMRS Core, Mayo Clinic, Rochester, USA
6. Grenoble Alpes University
7. Department of General and Transplant Surgery, D. Swarovski Research Laboratory, Medical University of Innsbruck, Austria

8. Barcelona University, Department of Physiological Sciences
9. Latvian Institute of Organic Synthesis, Laboratory of Pharmaceutical Pharmacology
10. Charles University in Prague, Department of Physiology (Hradec Králové)
11. Department of Life Sciences, Ben-Gurion University of the Negev
12. Stockholm University
13. COST network EU CARDIOPROTECTION CA15203
14. COST network MIOEAGLE CA-16225
15. Small enterprise "Mitogro"
16. The laboratory is the member of the worldwide MitoGlobalNetwork.
17. The laboratory is the member of O2k-Network as a reference laboratory for High-Resolution FluoRespirometry
18. North Estonia Medical Centre
19. East-Tallinn Central Hospital
20. West Tallinn Central Hospital

Key publications in 2016 – 2018

1) Aleksandr Klepinin, Lyudmila Ounpuu, Kati Mado, Laura Truu, Vladimir Chekulayev, Marju Puurand, Igor Shevchuk, Kersti Tepp, Anu Planken, and Tuuli Kaambre. The complexity of mitochondrial outer membrane permeability and VDAC regulation by associated proteins. Journal Of Bioenergetics And Biomembranes, 50(5):339–354, OCT 2018.
2) Andre Koit, Igor Shevchuk, Lyudmila Ounpuu, Aleksandr Klepinin, Vladimir Chekulayev, Natalja Timohhina, Kersti Tepp, Marju Puurand, Laura Truu, Karoliina Heck, Vahur Valvere, Rita Guzun, and Tuuli Kaambre. Mitochondrial Respiration in Human Colorectal and Breast Cancer Clinical Material Is Regulated Differently. Oxidative Medicine And Cellular Longevity, pages 1–16, 2017.
3) Lyudmila Ounpuu, Aleksandr Klepinin, Martin Pook, Indrek Teino, Nadezda Peet, Kalju Paju, Kersti Tepp, Vladimir Chekulayev, Igor Shevchuk, Sulev Koks, Toivo Maimets, and Tuuli Kaambre. 2102Ep embryonal carcinoma cells have compromised respiration and shifted bioenergetic profile distinct from H9 human embryonic stem cells. Biochimica Et Biophysica Acta-General Subjects, 1861(8):2146–2154, AUG 2017.
4) Lyudmila Ounpuu, Laura Truu, Igor Shevchuk, Vladimir Chekulayev, Aleksandr Klepinin, Andre Koit, Kersti Tepp, Marju Puurand, Egle Rebane-Klemm, and Tuuli Kaambre. Comparative analysis of the bioenergetics of human adenocarcinoma Caco-2 cell line and postoperative tissue samples from colorectal cancer patients. Biochemistry And Cell Biology, 96(6):808–817, DEC 2018.
5) Kersti Tepp, Natalja Timohhina, Marju Puurand, Aleksandr Klepinin, Vladimir Chekulayev, Igor Shevchuk, and Tuuli Kaambre. Bioenergetics of the aging heart and skeletal muscles: Modern concepts and controversies. Ageing Research Reviews, 28:1–14, JUL 2016.
6) MitoEAGLE Collaboration: Gnaiger, E. et al. Mitochondrial respiratory states and rates: Building blocks of mitochondrial physiology Part 1. In: COST Action CA15203 MitoEAGLE preprint Version: 2018-10-25(45). MitoFit Preprint Arch (2019) doi:10.26124/mitofit:190001.

3.4 Laboratory of Environmental Toxicology

The research of the Laboratory is led by academician Dr. Anne Kahru and employs 9 PhD researchers (V. Aruoja, I. Blinova, O. Bondarenko, M. Heinlaan, A. Kahru, K. Kasemets, A. Lukjanova, M. Sihtmäe, J. Siigur and a guest researcher Dr. A. Khosrovyan) who supervise 8 PhD students. The PhD students are mostly enrolled in the Tallinn University of Technology (5), but also in the University of Tartu (2) and in the Estonian University of Life Sciences. The team is young, enthusiastic and has received recent post-doc training in top-level environmental and nanotoxicology laboratories in Switzerland, US, Italy, Sweden and Australia.

The research focuses on three directions:

(i) ecotoxicology of nanomaterials and emerging toxicants (e.g., micro- and nanoplastics and lanthanides). The research in this direction is conducted under the leadership of Drs. Anne Kahru, Irina Blinova, Margit Heinlaan and Villem Aruoja with contribution from the Laboratory of Chemical Physics (Drs J. Reinik and N. Irha);
(ii) evaluation of the efficiency and safety of various antimicrobial compounds (e. g., metal-based nanomaterials, ionic liquids) is conducted under the leadership of Drs. Anne Kahru, Kaja Kasemets and Mariliis Sihtmäe;
(iii) *in vitro* toxicology of nanomaterials for nanomedicine – a research direction led by Dr. Olesja Bondarenko and contributed to by Dr. Kaja Kasemets.

In 2019 the Laboratory hosts

- 1 Institutional Research Grant
    - IUT23-5 "Nano(eco)toxicology and beyond (ToxBe) (2014 – 2019)", A. Kahru,
- 3 Personal Research Grants
    - PUT1015 "Nanoparticle-macrophage interactions in vitro: focus on nanosafety (2016 – 2020)" O. Bondarenko
    - PUT1512 "Evaluation of the potential hazardous effects of microplastic to marine and freshwater zooplankton (2017 – 2021)", M. Heinlaan
    - PSG311 Response of algal communities to toxicants with different modes of action (2019 – 2022). V. Aruoja
- RITA1/02-10-09 research grant from the Ministry of Agriculture 'Opportunities for mitigation of bee losses' (ForBee), 2019 – 2021. A. Kahru, M. Sihtmäe, I. Blinova. Coordinator Dr Marika Mänd (Estonian University of Life Sciences)
- Marie Skłodowska-Curie Individual Fellowship grant from the European Commission "Novel blood-brain barrier permeable CDNF-derived therapeutic peptides for the protection and regeneration of dopamine neurons" (THERAPE), 2019 – 2021, O. Bondarenko
- partnership in the Centre of Excellence; TK134 "Emerging orders in quantum and nanomaterials (1.08.2015 – 31.08.2023)", Leader: Dr Urmas Nagel, NICPB. Participants A. Kahru, K. Kasemets, O. Bondarenko
- partnership in the Estonian Scientific Infrastructure Roadmap Object NAMUR+ (2017 – 2021 (A. Kahru, K. Kasemets). Coordinator of the project: Dr. Vambola Kisand (Tartu University)
- Other projects
    - COST Action CA15114 Anti-Microbial Coating Innovations to prevent infectious diseases (AMICI; A. Kahru, K. Kasemets, M. Rosenberg)
    - COST Action CA16231 European Network of Vaccine Adjuvants (O. Bondarenko)
    - COST Action CA17140 Cancer nanomedicine - from the bench to the bedside (O. Bondarenko)
    - COST Action TD1407 Network on technology-critical elements – from environmental processes to human health threats (NOTICE; A. Kahru, I. Blinova)

Past, present and future

PAST: The Laboratory of Environmental Toxicology (LET) 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 novel research directions for Estonia – *in vitro*- and ecotoxicology. Since then, their research has remarkably contributed to new scientific knowledge on chemical safety, adverse environmental effects and bioavailability of heavy metals as well as evaluation of environmental hazard of wastewaters and polluted soils and Estonian oil-shale chemicals and solid waste. For that a combined approach has been used, 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 QSARs for substituted anilines and phenols. We have generated several web-based databases, including on toxicological information of REACH-relevant chemicals published in the Russian language (E-SovTox). In 2016, LET started cooperation with the Norwegian Company CerPoTech (the company synthesizes rare earth oxides of very different compositions and doings) on 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.

The laboratory was among the pioneers of nanoecotoxicological studies of metal oxide NPs (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, Scientific Reports). In the past 10 years the team has published >110 papers, mostly on nanotoxicology, that have been cited >5000 times (>45 cites/paper; the Estonian average (2008-2018) is 37 cites/paper). As a result, the team has currently 9 highly-cited papers in ISI-ESI concerning environmental and antimicrobial effects of synthetic NPs. Six researchers of the team belong to 1% of the most cited researchers in Estonia and two team members, A. Kahru and K. Kasemets belong to top 1% most cited scientists worldwide in Environment/Ecology and Pharmacology & Toxicology (A. Kahru) and cross-field (K. Kasemets) (Clarivate Analytics, 2018).

In 2011, A. Kahru received the Estonian State Science Award for her research "Ecotoxicology of synthetic NPs and their toxicity mechanisms" and she is the awardee of the State Order of the White Star (Class IV) (2017). In 2018, A. Kahru was elected the academician of Estonian Academy of Sciences in ecotoxicology.

Currently, the team is focused on developing of (i) in vitro/ecotoxicological test methods for analysis of hazard of synthetic NPs 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; (iv) evaluation of the potential environmental hazard of emerging pollutants such as metal-based antimicrobial nanomaterials, ionic liquids, lanthanides and microplastics; (v) evaluation of potential toxicity of nanomaterials to human cells in vitro and (vi) new directions for the application of nanomaterials in medicine as antimicrobials and drug carriers.

In cooperation with experts in algal physiology and ecology from the University of Tartu (Dr. K. Olli) we have started ecotoxicological studies of different types of toxicants on algal communities (V. Aruoja). In cooperation with the University of Life Sciences (M. Mänd) and the University of Tartu we have started to evaluate the adverse effects of pesticide use on pollinators (M. Sihtmäe). The most recent direction in the Lab is the evaluation of potential hazard of microplastics on aquatic invertebrates (M. Heinlaan) and other types of organisms. This field is being developed in cooperation with the Estonian University of Life Sciences (K. Orupõld) with a co-supervised PhD student M. Pullerits. The environmental risk assessment of lanthanides led by I. Blinova has resulted in remarkable amount of papers as well as the PhD Thesis of M. Muna, defended on April 11, 2019. This work has been supported by COST TD1407 action 'Network on technology-critical elements – from environmental processes to human health threats' (NOTICE), 2015 – 2019. Currently the research on lanthanides is continuing in the direction of chronic toxicity evaluation that is especially valuable for meaningful environmental risk assessment. Another new direction in LET on pros and cons of antimicrobial coatings (A. Kahru, K. Kasemets) supported by COST CA15114 action 'Anti-Microbial Coating Innovations to prevent infectious diseases' (AMICI), 2016 – 2020 has yielded several joint publications with COST participants and two PhD students will involve this work in their PhD theses (A.-L. Kubo, M. Rosenberg).

Keywords of expertise: (eco)toxicity, bioavailability, *in vitro*, 3R's, bioluminescence, microbial physiology; algae and algal communities, bacteria, protozoa, crustaceans as in vitro and ecotoxicity models, food-chain transfer, recombinant microbial biosensors, environmental pollution, NPs, antimicrobials, heavy metals, rare-earth elements, metal speciation, ionic liquids, microplastics, pesticides.

Future: We will expand our *in vitro* toxicology research by new competence of O. Bondarenko, K. Kasemets, M. Heinlaan and V. Aruoja who recently returned from post-doc from Karolinska Insitute, Milano University Bicocca, Univ. of Geneva, Switzerland and Univ. of South Australia, Adelaide, respectively. We will further develop the research into environmental safety of microplastics (M. Heinlaan), will introduce in vitro immunotoxicity models (O. Bondarenko), novel antimicrobial materials (K. Kasemets), will expand the know-how using various bacterial and *in vitro* mammalian cell models for toxicological profiling of ionic liquids and surfactants (in cooperation with ERA Chair on Green Chemistry, Prof. N. Gathergood, TalTech; M. Sihtmäe, A. Kahru). In addition, we are exploring new directions aiming to use NPs in medicine. In collaboration with the Prof. Mart Saarma (University of Helsinki, Finland), we will use our expertise on the interactions of NPs with human cells to develop new nanomaterial-based drug carriers for delivery of therapeutics (neurotrophic factors restoring neurons in the Parkinson's disease) to the brain.

Partnership in the Estonian Scientific Infrastructure Roadmap Object NAMUR+ has provided and will provide us in the next few years with new laboratory equipment (microscopes, AAS, incubators etc.) that will further increase the potential for successful research. Currently (2019) the NICPB laboratories undergo massive renovation (ventilation, heat insulation) that will enable us to continue our work in more modern conditions from 2020.

Funding: The big grant (IUT 23-5) that provides the salaries for the majority of the researchers will end in 2019. The personal research grant (PUT)-based funding is even more hectic and as these grants are smaller, they basically fund just the applicant him/herself + 1-2 students. The H2020 funding is getting more and more competitive but we keep on trying. Our salaries fully depend on project funding and therefore the future of this research field in Estonia is uncertain. As the Laboratory of Environmental Toxicology (LET) is the only eco- and toxicology unit in Estonia, the unreliable funding does not enable sustainable development of this important competence needed for developing novel materials, drugs and chemicals but also for educating Estonian people on chemical safety issues.

Collaborations

1. Kalle Olli – Estonian Univ Life Sciences. Effects of toxicants on algal communities. V. Aruoja, A. Kahru, PhD student E. Joonas
2. Marika Mänd - Estonian Univ Life Sciences. Hazard of pesticides on pollinators. M. Sihtmäe, A. Kahru
3. Kaja Orupõld – Estonian Univ Life Sciences. Evaluation of adverse effects of microplastics for freshwater biota. M. Heinlaan, PhD student M. Pullerits.
4. Vambola Kisand – Univ. Tartu. Synthesis of TiO_2 and ZnO based antimicrobial surface coatings. A. Kahru, K. Kasemets, PhD students M. Rosenberg, M. Visnapuu
5. Tiina Alamäe – Univ. Tartu. Application of bacterial polysaccharides as surface functionalization of nanomaterials for nutraceutical use.
6. N. Gathergood, TalTech, Estonia. 'Green' ionic liquids. A. Kahru, M. Sihtmäe. PhD student D. Kusumahastuti.
7. Paride Mantecca - Milano University Bicocca, Italy. Microscopic analysis of cellular damage upon exposure to toxicants. K. Kasemets
8. Pu-Chun Ke — Monash University, Australia. Nanomaterials in nanomedicine. O. Bondarenko.
9. Ivana Vinkovic Vrček - Institute for Medical Research and Occupational Health, Zagreb, Croatia. Studies on antimicrobial metal-based nanomaterials. A. Kahru, K. Kasemets, PhD student A.-L. Kubo
10. Rimantas Daugelavičius – Univ. Kaunas, Lithuania. Effects of toxicants on bacterial membranes. O. Bondarenko.
11. C. William Keevil - University of Southampton, Southampton, UK. Antimicrobial copper surfaces. A. Kahru, PhD student M. Rosenberg
12. B. Fadeel - Institute of Environmental Medicine, Karolinska Institutet. Immunotoxicity of nanomaterials. O. Bondarenko. PhD student A.-L. Kubo
13. Vera Slaveykova – Univ. Geneva, Switzerland. Aquatic ecotoxicology and food-chain transfer of metallic pollutants. M. Heinlaan, A. Kahru, PhD student M. Muna

Key publications in 2016 – 2018

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2) Joonas, E., Aruoja, V., Olli, K., Kahru, A. Environmental safety data on CuO and TiO2 nanoparticles for multiple algal species in natural water: Filling the data gaps for risk assessment. Science of the Total Environment, 674, 973−980, 2019.
3) Muna, M., Blinova, I., Kahru, A., Vinkovi Vrek, I., Pem, B., Orupõld, K., Heinlaan, M. Combined effects of test media and dietary algae on the toxicity of CuO and ZnO nanoparticles to freshwater microcrustaceans Daphnia magna and Heterocypris incongruens: food for thought. Nanomaterials, 9 (1), 23, 2019.
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9) Katre Juganson, Monika Mortimer, Angela Ivask, Sandra Pucciarelli, Cristina Miceli, Kaja Orupold, and Anne Kahru. Mechanisms of toxic action of silver nanoparticles in the protozoan Tetrahymena thermophila: From gene expression to phenotypic events. Environmental Pollution, 225:481– 489, JUN 2017.
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11) Anita Jemec, Anne Kahru, Annegret Potthoff, Damjana Drobne, Margit Heinlaan, Steffi Boehme, Mark Geppert, Sara Novak, Kristin Schirmer, Rohit Rekulapally, Shashi Singh, Villem Aruoja, Mariliis Sihtmaee, Katre Juganson, Aleksandr Kaekinen, and Dana Kuehnel. An interlaboratory comparison of nanosilver characterisation and hazard identification: Harmonising techniques for high quality data. Environment International, 87:20–32, FEB 2016.
12) Olesja M. Bondarenko, Margit Heinlaan, Mariliis Sihtmae, Angela Ivask, Imbi Kurvet, Elise Joonas, Anita Jemec, Marika Mannerstrom, Tuula Heinonen, Rohit Rekulapelly, Shashi Singh, Jing Zou, Ilmari Pyykkoe, Damjana Drobne, and Anne Kahru. Multilaboratory evaluation of 15 bioassays for (eco)toxicity screening and hazard ranking of engineered nanomaterials: FP7 project NANOVALID. Nanotoxicology, 10(9):1229–1242, NOV 2016.
13) Olesja M. Bondarenko, Angela Ivask, Anne Kahru, Heiki Vija, Tiina Titma, Meeri Visnapuu, Urmas Joost, Ksenia Pudova, Signe Adamberg, Triinu Visnapuu, and Tiina Alamaee. Bacterial polysaccharide levan as stabilizing, non-toxic and functional coating material for microelementnanoparticles. Carbohydrate Polymers, 136:710–720, JAN 20 2016.

4 Key competences of NICPB

4.1 High level research

The high level of research is the trademark of NICPB.

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 organizing Estonian summer students' and Estonian high-school teachers' programmes at CERN.

4.3 Grid and cloud computing in Estonia

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.

4.4 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. Unfortunately, in 2019, one of the key persons in this field at NICPB, left the institute for industry. Still, building up the competences to participate in closest and most modern neutron facility is of valuable strategic asset for NICPB.

4.5 Estonian magnet laboratory and the helium liquefier

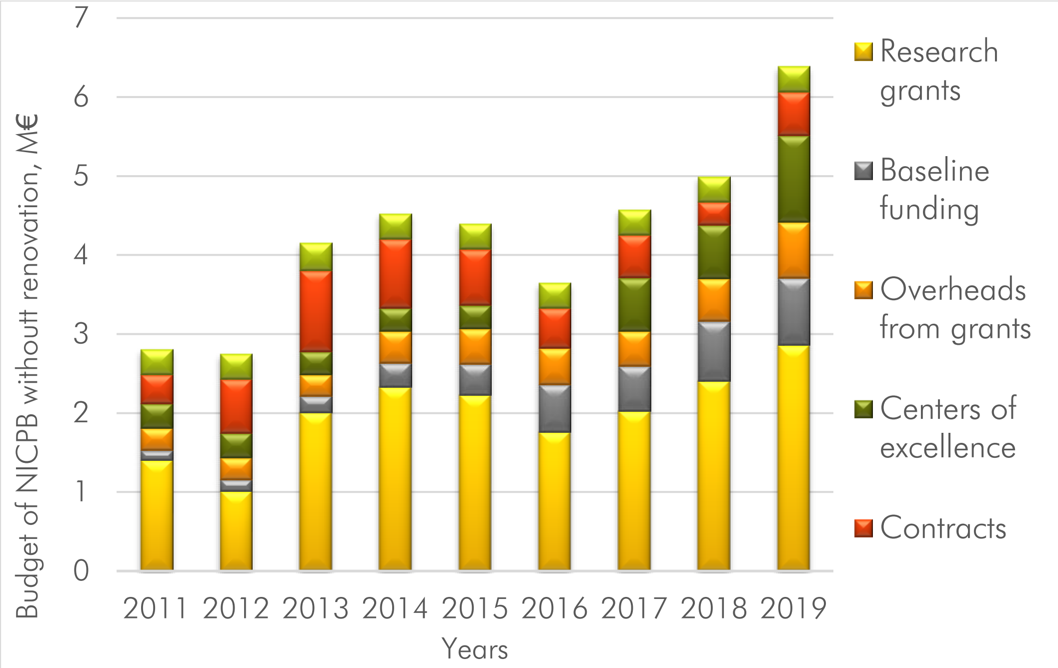
We need to work with developing the Estonian Magnet Laboratory and establish better collaborations with groups in the universities who are using NMR and other spectroscopies that require high magnetic fields. We are running the only helium liquefier in the Baltic countries. Using our research infrastructure and expertise NICPB became a member in the Estonian Center of Analytical Chemistry in 2019. The Estonian Center of Analytical Chemistry is a distributed interdisciplinary scientific research infrastructure for the development and application of modern analytical methods as well as the quality assurance of chemical measurements in research, surveillance and industry laboratories. We have been invited to become a member of the European High Field Laboratory (EMFL) which would require a national dedicated block grant towards further internationalisation of Estonian research.

4.6 Environmental and nanotoxicology

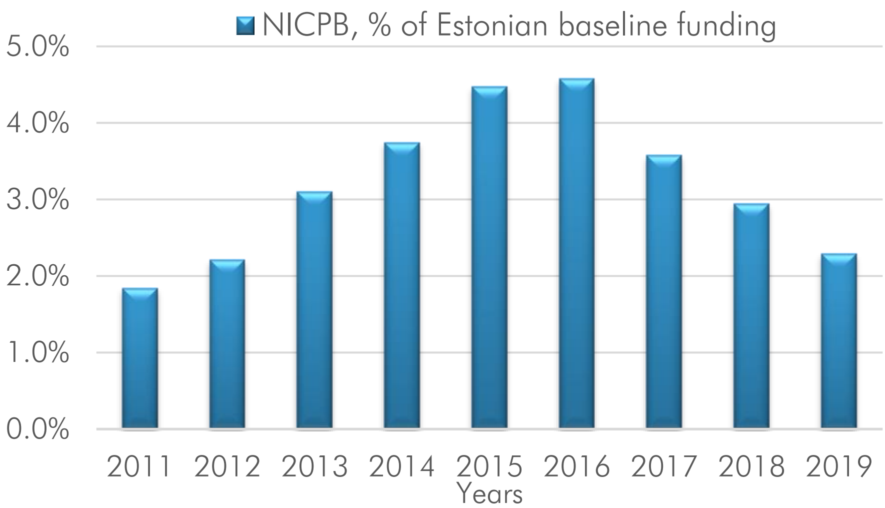
The research into ecotoxicology and especially nanoecotoxicology in Estonia was introduced by NICPB researchers 20 and 10 years ago, respectively, and is currently the key competence the of Laboratory of Environmental Toxicology, led by A. Kahru. This competence is unique for Estonia and is based on know-how, facilities and international cooperation for evaluation of hazard of existing and emerging environmental pollutants, industrial chemicals and man-made nanomaterials. This is a competence crucial for the EU 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 9 highly cited papers in ISI-ESI, mostly concerning environmental and antimicrobial effects of synthetic NPs.

5 Appendix

5.1 Budget of NICPB

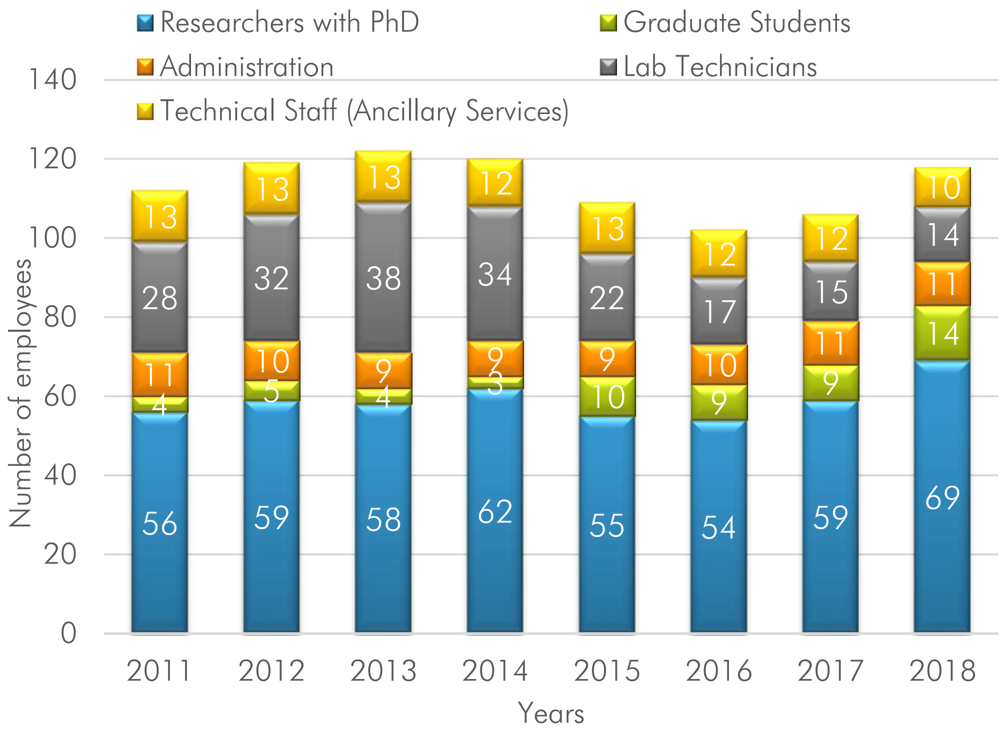


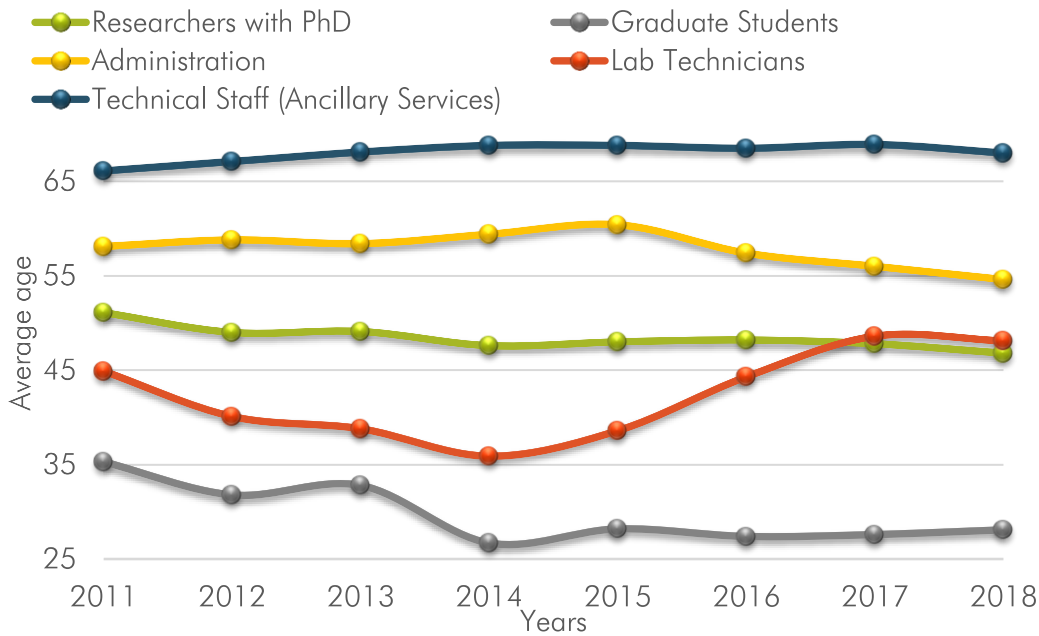
In addition to the budget shown on the graph, NICPB is renovating the Akadeemia tee 23 building. For that NICPB got about 2 M€ investment money from the ministry. NICPB is adding 1 M€ of our savings from previous years to complete the renovation. On top of that NICPB must renovate several laboratories as well in the coming years. In 2019 NICPB spends 0.44 M€ on salaries of the administration and 0.45 M€ on maintaining the buildings (heating, electricity, etc.).



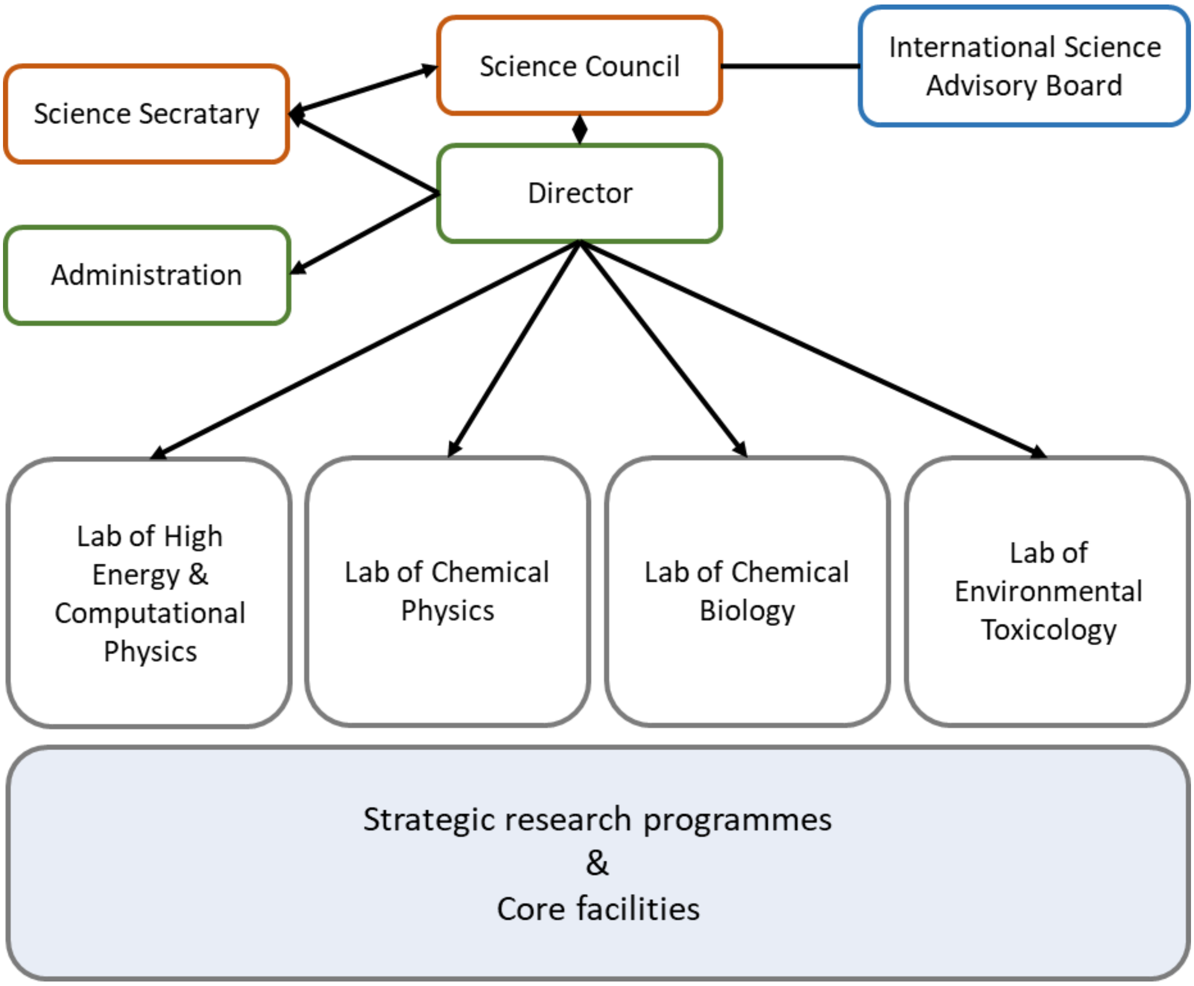
The decline in the share of NICPB's baseline funding after 2016 reflects the Estonian science policy. In 2016 the rules of calculating the baseline funding changed: R&D contracts gained weight while papers with more than 1000 authors, published by large international collaborations like the CMS collaboration, lost weight.

5.2 Human resources of NICPB





5.3 NICPB organization chart



5.4 NICPB administration chart