CEITEC | Central European Institute of Technology
BRNO | CZECH REPUBLIC

RESEARCH OVERVIEW

EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
INVESTING IN YOUR FUTURE

2007–13
OP Research and
Development for Innovation

FOREWORD BY CEITEC EXECUTIVE DIRECTOR

Markus Dettenhofer

The objective of CEITEC is to create an environment where high level scientific discovery can be fostered, so as to be competitive on the world stage.

Welcome to the Central European Institute of Technology (CEITEC) in the city of Brno, Czech Republic. Our Institute was founded in June 2011 with generous financing from European Structural Funds and the Czech Ministry of Education, Youth and Sports. The objective of CEITEC is to create an environment where high level scientific discovery can be fostered, so as to be competitive on the world stage. To accomplish our goals, we are constructing two new research building complexes to house our newly purchased state-of-the-art equipment for life and material sciences research. Additionally, CEITEC has more than 60 research group leaders, with several recently recruited international scientists. We actively promote researcher mobility so that a culture of the continuous exchange of ideas is the norm.

As a testament to achieving our goal of excellence in science, we have been successful in publishing our discoveries in top journals and being awarded prestigious European grants. We see this as a good start, and CEITEC will continue to provide the environment for scientists who are positioned to achieve these goals. As education and research are within the core competencies of CEITEC, we are committed to positively impacting society through training the next generation of highly qualified scientists.

In this brochure you will learn more about our research groups and core facilities. Science at CEITEC covers the range of biological topics from gene discovery, through structural and functional analysis of molecules, to cell biology and animal models. On the materials and technology side, our work ranges from applications on the nano-scale to large engineering projects; and technologies covering micro-fluidics, plasma physics, photonics and robotics. Additionally, our scientists are experimenting at the interface of biology and material sciences.

CEITEC has established several strategic partnerships with some of the best research centres in Europe and we will continue to be committed to working with our current and new collaborators in the future.

CONTENT

CENTRAL EUROPEAN INSTITUTE OF TECHNOLOGY

CEITEC is a scientific centre in the fields of life sciences, advanced materials and technologies whose aim is to establish itself as a recognized centre for basic as well as applied research. CEITEC offers a state-of-the-art infrastructure and excellent conditions for the employment of outstanding researchers. We are a consortium whose partners include the most prominent universities and research institutes in Brno, Czech Republic: Masaryk University, Brno University of Technology, Mendel University in Brno, Institute of Physics of Materials of the Academy of Sciences of the Czech Republic, University of Veterinary and Pharmaceutical Sciences Brno and the Veterinary Research Institute. We work closely with the Region of South Moravia and the City of Brno to help increase the local innovative capacity.

01 VISION

CEITEC will lead on the path to global scientific recognition through science based on synergy and collaboration in order to achieve a regional knowledge-based economy.

02 MISSION

CEITEC has been created to advance existing basic and applied research in South Moravia to reach new levels. Its purpose is not only to provide its researchers with the best equipment and new laboratory facilities, but also to engage in scientific discovery at a globally competitive level. To achieve this, CEITEC aims to retain and recruit talented people who can address important research questions. The training of PhD students and post-doctoral fellows for future careers in science or technologically demanding fields is important for the development of the region. By conducting research that bridges technological disciplines, CEITEC will see its greatest advances in enhancing the innovative environment of the region.

BASIC OVERVIEW

- 6 **partners**
- 7 **research programmes**
- 61 **research groups**
- 557 **researchers (2015)**
- 25 000 m^2 **of new laboratories**
- 9 **core facilities**
- **Total budget of** € 208 mil.
- **Approval by the European Commission on** 6th June 2011
- **Start of research activities:** Q1 2011

INTERDISCIPLINARY COOPERATION

The combined knowledge and resources of the six participating institutions will ensure a more efficient attainment of quality results and higher levels of involvement from the application sphere.

INTERNATIONAL MANAGEMENT

International mobility and a system of management are gained from experience of the best research institutes worldwide.

COORDINATION BOARD

Composed of representatives from prominent Czech firms in R&D fields and representatives from the best international research institutes

EVALUATION

Evaluations of the quality of research results are conducted by independent teams of prominent global experts in their respective fields

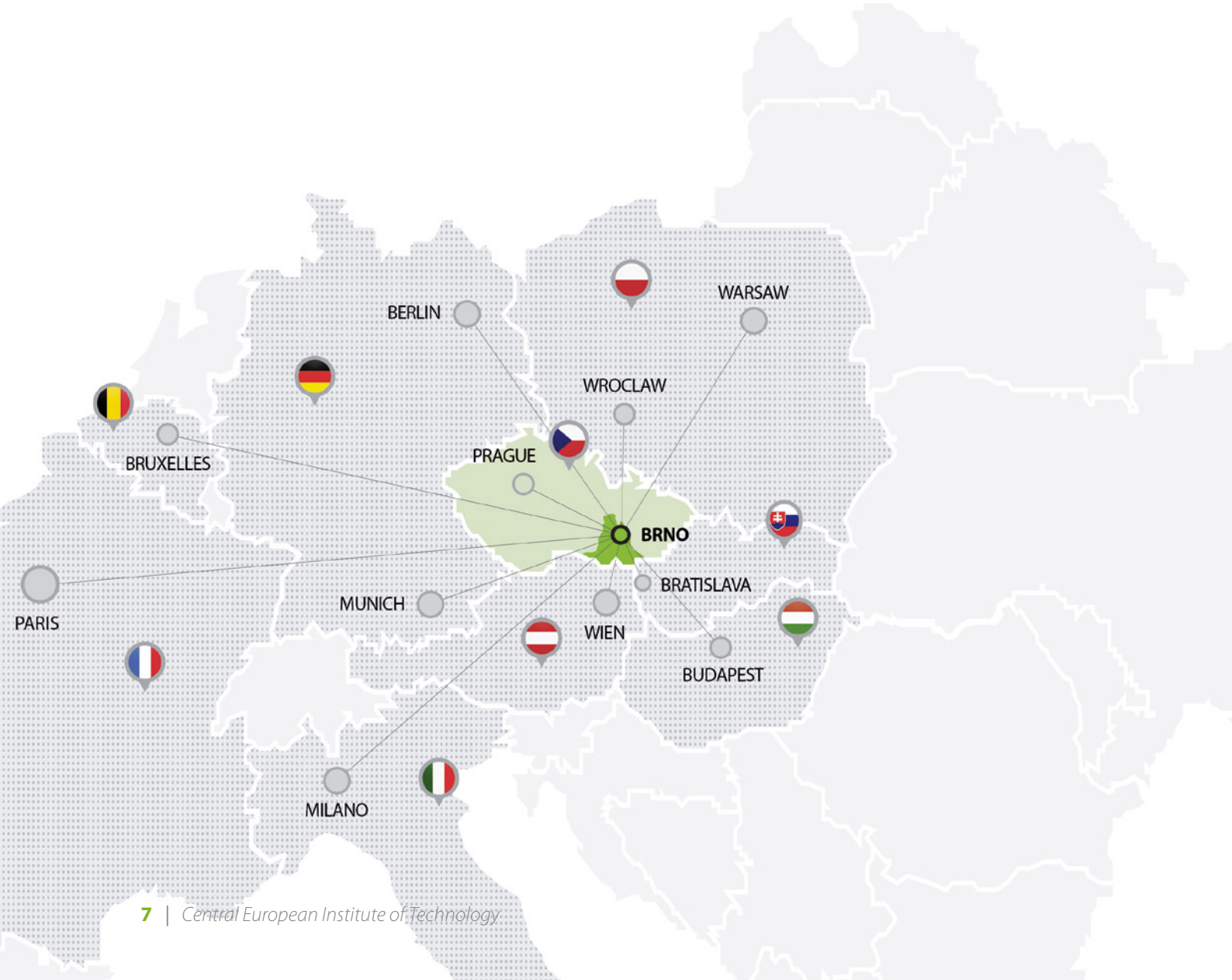
INTERNATIONAL SCIENTIFIC ADVISORY BOARD

Members of ISAB are exclusively representatives of important international research institutes

BENEFITS TO THE REGION

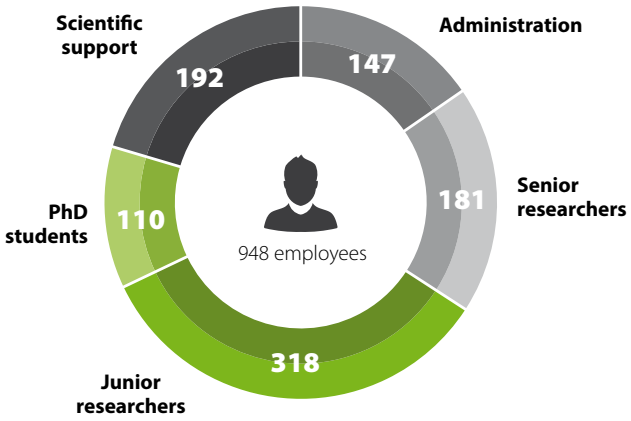
- Improvement in student education – predominantly in graduate studies
- Research laboratories for nearly 600 scientists and more than 1200 students
- Creation of new innovative firms and attraction of domestic and international investors
- Creation of new jobs in the respective fields of research
- Attraction of foreign experts and respected Czech scientists to the area

CEITEC will significantly contribute to a long-term increase in the competitiveness of Brno, the Region of South Moravia and the Czech Republic as a whole.

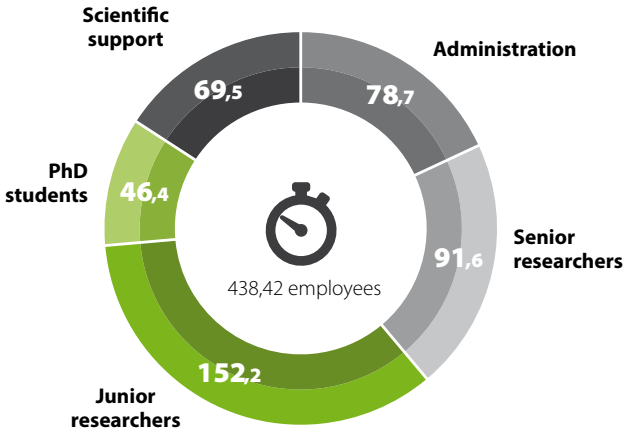


CEITEC EMPLOYEES

01 NUMBER OF EMPLOYEES (HEADCOUNT)

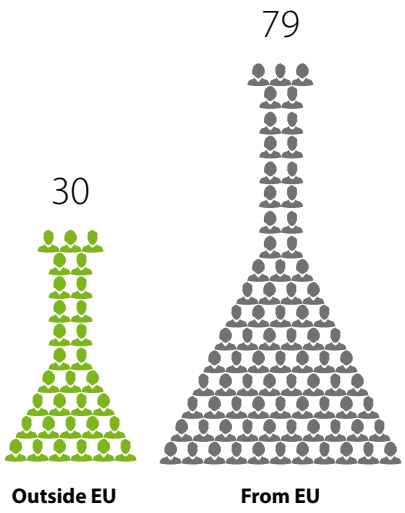


02 NUMBER OF EMPLOYEES (FTE)



Full-time equivalent (FTE) is a unit that indicates the workload of an employed person (or student) in a way that makes workloads comparable across various contexts. An FTE of 1.0 means that the person is equivalent to a full-time worker, while an FTE of 0.5 signals that the worker is only half-time.

03 FOREIGN EMPLOYEES



EU (79): Austria (2), Belgium (1), Estonia (1), France (4), Germany (4), Greece (4), Hungary (4), Italy (4), Poland (5), Romania (2), Slovakia (39), Spain (6), United Kingdom (3)

Outside EU (30): Belarus (3), Canada (1), Egypt (2), India (11), Iran (2), Palestine (1), Russia (5), Taiwan (1), Ukraine (1), USA (3)

PARTNERING INSTITUTIONS

MASARYK UNIVERSITY
www.muni.cz

BRNO UNIVERSITY OF TECHNOLOGY
www.vutbr.cz

MENDEL UNIVERSITY IN BRNO
www.mendelu.cz

INSTITUTE OF PHYSICS OF MATERIALS AS CR
www.ipm.cz

UNIVERSITY OF VETERINARY AND PHARMACEUTICAL SCIENCES BRNO
www.vfu.cz

VETERINARY RESEARCH INSTITUTE
www.vri.cz

FINANCING

Total budget of € 208 mil.

Source of funding: The European Regional Development Fund to be financed through the Operational Programme Research and Development for Innovations, priority axis 1 – European Centres of Excellence, which is managed by the Ministry of Education, Youth and Sports of the Czech Republic.

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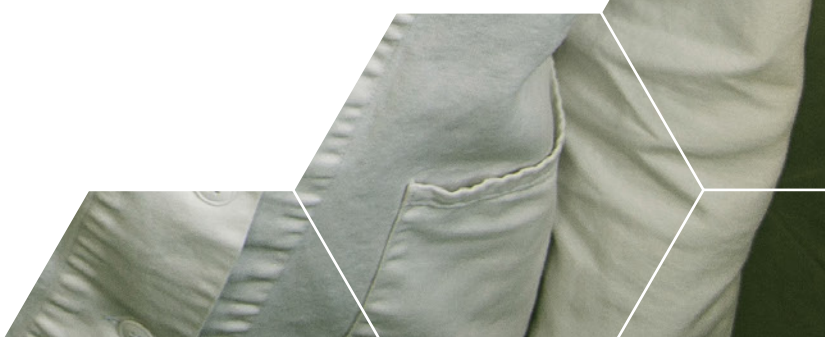
RESEARCH PROGRAMMES

The multi-departmental nature of CEITEC and the extent to which the fields of life sciences and advanced materials and technologies are integrated make it the first research centre of its kind in the Czech Republic. The high-tech technologies at its disposal will facilitate synergistic study in the subjects of life and material sciences on all currently available levels of complexity, starting with individual atoms, through molecules, molecule groups and cells to whole organisms.



ADVANCED NANOTECHNOLOGIES AND MICROTECHNOLOGIES

The research is aimed at nanotechnologies covering materials and structures to be used in nanoelectronic and nanophotonic applications. The research comprises the preparation, characterisation and analysis of the properties of nanostructures enabling an active application of principles that determine the unique and specific properties of nanostructures. Attention will be focused on research of 2D-0D nanostructures produced by lithographic (top-down) methods and self-organizing (bottom-up) methods. The research will consider semiconductor nanostructures, magnetic and metallic nanostructures, nanotubes and nanofibres, etc. The interconnection of nanostructures with peripheries and special micro-circuits will also be researched.

Research Programme Coordinator:
Tomáš Šikola | tomas.sikola@ceitec.vutbr.cz

OVERALL GOAL

The principal goal of this programme is to develop methods for the fabrication of nanostructures, to learn their unique properties and to utilise them in nanoelectronics and nanophotonics with respect to various relevant application outputs, including bio- and medical sensing and diagnostic methods and tools. The programme relies on the links and mutual cooperation among research groups within the programme and beyond it, both in material/communication areas and life sciences. To meet this goal the shared clean-room laboratories equipped with complex planar technologies and state-of-the-art diagnostic techniques will be developed. Such facilities will be made available not only to research groups from CEITEC but also to external groups from academic institutions and industry. This will contribute to widening the cooperation on application subjects in the Czech Republic and the Central European region. The laboratory will seek associate membership in ESFRI (PRINS) and collaborate with other centres at home and worldwide.

RESEARCH DIRECTIONS

- Fabrication of nanostructures by bottom-up methods
- Fabrication of nanostructures by top-down methods (nanolithography)
- Investigation of functional properties of nanostructures
- Development of submicron devices and nanostructures
- Development of analytical and measurement methods

RESEARCH GROUPS | LEADERS

Functional Properties of Nanostructures | *Josef Humlíček*

Smart Nanodevices | *Jaromír Hubálek*

Experimental Biophotonics | *Radim Chmelík*

Fabrication and Characterisation of Nanostructures | *Tomáš Šikola*

Development of Methods for Analysis and Measuring | *Petr Klapetek*

X-ray Micro CT and Nano CT | *Jozef Kaiser*

Optoelectronic Characterisation of Nanostructures | *Lubomír Grmela*

Micro and Nanotribology | *Ivan Křupka*

Plasma Technologies | *Lenka Zajíčková*

Synthesis and Analysis of Nanostructures | *Jiří Pinkas*

Transport and Magnetic Properties | *Bohumil David*

Functional Properties of Nanostructures

Prof. RNDr. Josef Humlíček, CSc.
Research Group Leader
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RESEARCH AREAS

- Electronic and vibronic structure of materials and metamaterials
- Optical spectroscopy and polarimetry of micro- and nanostructures
- X-ray analysis of micro- and nanostructures

MAIN OBJECTIVES

Investigation of the functional properties of nanostructures

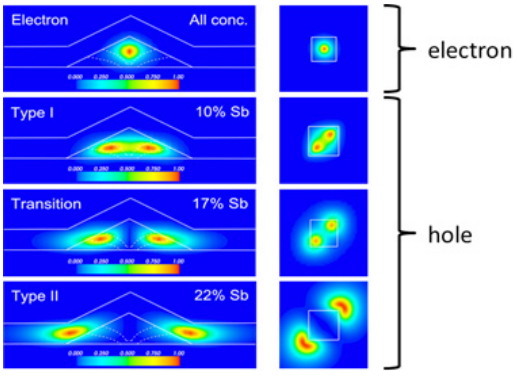
- Specification and optimization of the functional properties of nanostructures for nanoelectronics, nanophotonics and (bio)sensing, and their correlation with the geometrical/structural parameters of nanostructures and operational parameters
- Novel and unique properties of nanostructures not observable in conventional materials and microstructures which open the way to qualitatively new applications
- Physical properties of bulk materials, mainly those involved in the studied nanostructures

Selected Publications

CHALOUPKA J., JACKELI G., KHALIULLIN G. 2013. Zigzag Magnetic Order in the Iridium Oxide Na2IrO3. *Physical Review Letters* 110 (9), 097204.

KLENOVSKY P., BREHM M., KRAPEK V., LAUSECKER E., MUNZAR D., HACKL F., STEINER H., FROMHERZ T., BAUER G., HUMLICEK J. 2012. Excitation intensity dependence of photoluminescence spectra of SiGe quantum dots grown on prepatterned Si substrates: Evidence for biexcitonic transition. *Physical Review B* 86 (11), 115305.

VASATKO J., MUNZAR D. 2012. Quantum mechanical picture of the coupling between interlayer electronic excitations and infrared active phonons in bilayer cuprate superconductors. *Physical Review B* 86 (1), 014512.



Electron and hole states in InAs quantum dots on GaAs, covered with GaAsSb capping layer.

CONTENT OF RESEARCH

Nanostructuring leads usually to essential changes in the properties of matter. Theoretical and experimental investigations of nanostructures reveal a wealth of unexpected and useful properties.

Investigation of the functional properties of nanostructures

The main goal is to find a correlation between the properties and the geometrical and structural parameters of nanostructures and to use this knowledge for feedback in the technology of their preparation and for various applications.

Self-assembled semiconductor nanostructures, fundamental electronic properties

Self-assembling processes in nanostructures of III-V semiconductors (e.g. self-assembled rings of InAs in the matrix of GaAs). A study of electronic structures aimed at optimizing their properties with respect to optoelectronic and transport applications, and analysis of the influence of capping layers.

Oxide superconductors and magnetics, transport at optical frequencies

Deposition of layered systems, nanostructures in systems of superconductors/magnetics.

An experimental and theoretical study of electronic and vibrational structures. Optimizing them with respect to sensor applications. Experimental determination of the electrical, thermal and magnetic properties of high-temperature superconductors and superlattices with respect to their structural characterization and chemical composition.

Smart Nanodevices

Assoc. Prof. Ing. Jaromír Hubálek, Ph.D.
Research Group Leader
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RESEARCH AREAS

- Integrated systems for sensing (MEMS/NEMS)
- Integration of analytical methods on a chip (Lab on a chip)
- Bottom-up synthesis of nanostructures and nanoparticles
- Cell electrophysiology tools (MEA chips)

MAIN OBJECTIVES

- Development of novel electrochemical methods employing nanoelectrodes and nanopotenciostats, and other systems on a chip based on a physical transducer such as MEMS
- Synthesis of biocompatible colloidal nanoparticles and nanostructured surfaces for medical and environmental applications (biosensing, diagnostics, drug delivery, in vivo imaging techniques and targeted therapy of serious diseases, photocatalytic water/air treatment, chemosensing)
- Development of microelectrode arrays for the extracellular field potential recording of excitable cells, e.g. neuronal cells. Patch clamp - based recording from cells
- Construction of nanodevices with special properties for nanoelectronics

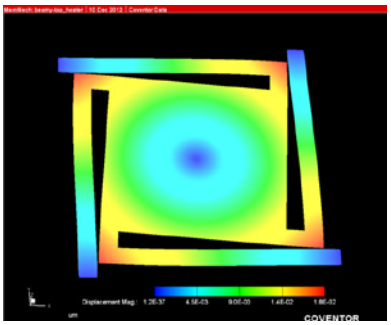
Selected Publications

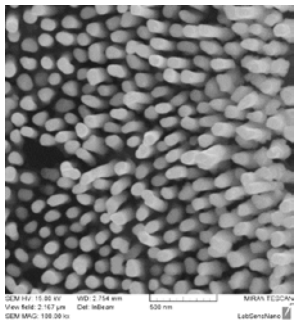
DRBOHLAVOVA J., CHOMOUCKA J., ADAM V., RYVOLOVA M., ECKSCHLAGER T., HUBALEK J., KIZEK R. 2013. Nanocarriers for Anticancer Drugs - New Trends in Nanomedicine. *Current Drug Metabolism* 14 (5), p. 547-564.

NEUZIL P., GISELBRECHT S., LANGE K., HUANG T.J., MANZ A. 2012. Revisiting lab-on-a-chip technology for drug discovery. *Nature Reviews Drug Discovery* 11 (8), p. 620-632.

PRASEK J., DRBOHLAVOVA J., CHOMOUCKA J., HUBALEK J., JASEK O., ADAM V., KIZEK R. 2011. Methods for carbon nanotubes synthesis-review. *Journal of Materials Chemistry* 21 (40), p. 15872-15884.

JUSKOVA P., NEUZIL P., MANZ A., FORET F. 2013. Detection of electrochemiluminescence from floating metal platelets in suspension. *Lab on a Chip* 13 (5), p. 781-784.





Thermo-mechanical simulation of a heating membrane for a bolometer (left)

SEM image of vertically aligned gold nanorods (right).

CONTENT OF RESEARCH

Research of methods and technology for creation of advanced nanodevices and nanoprobes for electronics, sensing, and nanomedicine is the main goal.

The research is focused on more complex systems, both electrical and electromechanical (MEMS/NEMS). The research looks at the mechanical, thermal and electrical effects on different parts or on complex MEMS structures. Currently, the realization of a microbolometer with carbon nanotubes and a mechanical filter bank used as a cochlear implant is under development.

The research also covers the manufacture of electrochemical and optical bio-detection systems based on nanostructured surfaces covered with self-ordered arrays of nanowires, nanopillars, nanodots, and quantum dots. Nanostructures from various noble metals, metal oxides or their composites are being created via an advanced non-lithographic template based technique. The nanostructured surfaces are utilized for the construction of a new type of gas sensors, photocatalytically active surfaces, photovoltaic applications, electronics and electrochemical devices. Aside from fixed nanostructures, colloidal fluorescent carbon dots (F-CDs) and Cd-based semiconductor quantum dots (QDs) functionalized with various thiol-linking molecules are prepared via direct synthesis.

Experimental Biophotonics

Prof. RNDr. Radim Chmelík, Ph.D.
Research Group Leader
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RESEARCH AREAS

- Advanced light (holographic, multimodal, correlative) microscopy (ALM) – theory & innovation
- ALM in experimental biophotonics – new approach to live cell behaviour evaluation
- Analysis of micro- and nanostructures using ALM

MAIN OBJECTIVES

- ALM theoretical research into imaging
- ALM techniques and methodologies development
- Study and measurement of living cells' behaviour and characteristics using ALM
- ALM contribution to assessment of cancer cell malignancy
- ALM based rapid appraisal of cytotoxicity
- ALM examination of nano- and microstructure of materials
- ALM investigation of cell reactions to these materials

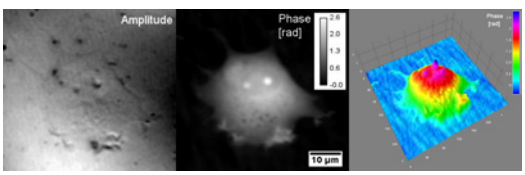
Selected Publications

SLABY T., KOLMAN P., DOSTAL Z., ANTOS M., LOSTAK M., CHMELIK R. 2013. Off-axis setup taking full advantage of incoherent illumination in coherence-controlled holographic microscope. *Optics Express* 21 (12), p. 14747-14762.

NIZAR K., UHLIROVA H., TIAN P., SAISAN P., CHENG Q., REZNICHENKO L., WELDY K., STEED T., SRIDHAR V., MACDONALD C., CUI J., GRATIY S., SAKADZIC S., BOAS D., BEKA T., EINEVOLL G., CHEN J., MASLIAH E., DALE A., SILVA G., DEVOR A. 2013. In vivo Stimulus-Induced Vasodilation Occurs without IP3 Receptor Activation and May Precede Astrocytic Calcium Increase. *The Journal of Neuroscience* 33 (19), p. 8411-8422.

BOUCHAL P., BOUCHAL Z. 2013. Wide-field common-path incoherent correlation microscopy with a perfect overlapping of interfering beams. *Journal of the European Optical Society – rapid publications* 8, 13011.

BOUCHAL P., BOUCHAL Z. 2012. Selective edge enhancement in three-dimensional vortex imaging with incoherent light. *Optics Letters* 37 (14), p. 2949-2951.



Imaging of a live cell – amplitude, quantitative phase in greyscale and in 3D representation. The coherence-controlled holographic microscope enables imaging of phase objects and can thus be useful for the imaging of transparent objects (for example live cells).

CONTENT OF RESEARCH

The group concerns particularly with innovations and applications of holographic and confocal light microscopies. Experimental biophysical research enabled by these techniques is focused mainly on living cell biology and interactions among cells and with different structures and/or microenvironment including culture media.

Advanced light microscopy – innovative technologies

The theoretical study of advanced light microscopy is concerned especially with the field of holographic and confocal light microscopy, with simulations and the experimental verification of results. We investigate the influence of coherence effects, optical and coherence vortices in holographic imaging and explore imaging in turbid media by coherence gating. Our main objectives are the development of coherence controlled and SLM optical systems for holographic and multimodal (correlative) microscopy, and advanced image processing methods for holographic reconstruction, quantitative phase evaluation, dynamic phase differences observation, and pattern and process recognition.

Evaluation of live cell behaviour & analysis of micro- and nanostructures

Coherence-controlled holographic microscopy (CCHM) and advanced image processing methods are used for the quantitative evaluation of live cells behaviour. CCHM measurements of intracellular dry mass translocation are used for assessment of subtoxic impact or toxicity of nanomaterials. CCHM by these measurements enables novel classification of patterns of cell behaviour and thus investigation of the *in vitro* qualification of cancer cell malignancy. Nanostructure properties and their interactions are observed and also studied by advanced light microscopy.

Fabrication and Characterisation of Nanostructures

Prof. RNDr. Tomáš Šikola, CSc.
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RESEARCH AREAS

- Surface science and thin film physics
- Nano-micro lithography (EBL, FIB, SPM, ...), selective growth, nanowire growth, 2D materials (graphene, ...) and their application
- Plasmonics, spintronics
- Development of complex UHV technological and analytical systems

MAIN OBJECTIVES

- Fabrication of nanostructures using bottom-up methods
- Fabrication of nanostructures using top-down methods (nanolithography)
- Investigation of the functional properties of nanostructures
- The development of analytical and measurement methods

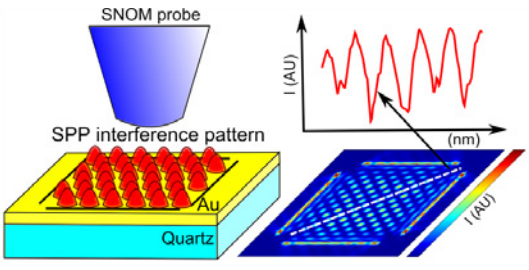
Selected Publications

UHLIR V., URBANEK M., HLADIK L., SPOUSTA J., IM M., FISCHER P., EIBAGI N., KAN J., FULLERTON E., SIKOLA T. 2013. Dynamic switching of the spin circulation in tapered magnetic nanodisks. *Nature Nanotechnology* 8 (5), p. 341-346.

DVORAK P., NEUMAN T., BRINEK L., SAMORIL T., KALOUSEK R., DUB P., VARGA P., SIKOLA T. 2013. Control and Near-Field Detection of Surface Plasmon Interference Patterns. *NANO LETTERS* 13 (6), p. 2558-2563.

KOLIBAL M., KONECNY M., LIGMAJER F., SKODA D., VYSTAVEL T., ZLAMAL J., VARGA P., SIKOLA T. 2012. Guided Assembly of Gold Colloidal Nanoparticles on Silicon Substrates Prepatterned by Charged Particle Beams. *ACS Nano* 6 (11), p. 10098-10106.

KOLIBAL M., VYSTAVEL T., NOVAK L., MACH J., SIKOLA T. 2011. In-situ observation of <110> oriented Ge nanowire growth and associated collector droplet behavior. *Applied Physics Letters* 99 (14), 143113.



Near-field Interference patterns measured by scanning near-field optical microscopy (SNOM).

CONTENT OF RESEARCH

Investigation of correlation between novel functional properties and geometrical, structural and compositional parameters of nanostructures. Utilization of this knowledge in feedback for improvement of their fabrication and properties, and to increase application potential.

Research is primarily focused on the fabrication and characterisation of nanostructures and understanding the relationship between the material/structural parameters of these nanoobjects and their functional properties. It covers investigation of the phenomena essential for the growth of thin films and the self-assembly of nanostructures (e.g. ultrathin films, nanowires, nanodots) of specific properties, the development of nanolithographic methods and their application (electron beam lithography, focused ion beam lithography, AFM lithography,…), and hybrid top-down/bottom-up approaches (e.g. selective growth of nanostructures on substrates pre-patterned by lithographic methods).

Further, the functional properties of the fabricated nanostructures are studied. This includes measurement of the properties of metallic nano/microstructures suitable for plasmonics, namely experimental and theoretical research on the generation, detection and application of surface plasmon polaritons and localised surface plasmons in the field of nanoelectronics, nanophotonics, energy conversion (incl. photovoltaics) and (bio)sensing. The experimental and theoretical study of transport properties (e.g. giant- and tunnelling magnetoresistance) and the dynamics of domain walls and vortexes for applications in magnetic recording, sensing and spintronics is a subject of interest as well.

The development and application of instruments and complex systems for technological and analytical methods related to surfaces, (ultra)thin films and nanostructures is also part of the activities.

Development of Methods for Analysis and Measuring

Mgr. Petr Klapetek, Ph.D.
Research Group Leader

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RESEARCH AREAS

- Quantitative scanning probe microscopy for the measurement of dimensional, electrical, thermal and optical properties with resolution in order of nanometres
- Metrology support for microstructured and nanostructured materials analysis and for functional nanostructures characterization
- Numerical methods in nanoscale metrology

MAIN OBJECTIVES

Research and development of analytical and measurement methods

- Development of the techniques and methodologies for microscopy, analysis and metrology of nanomaterials/nanostructures, and for diagnostics of their properties – new techniques in nanometrology with SPM, optical methods, and combinations of other techniques (SEM, AFM, etc.)
- Development of numerical tools for quantitative interpretation of measurement results
- Metrological traceability for other research groups

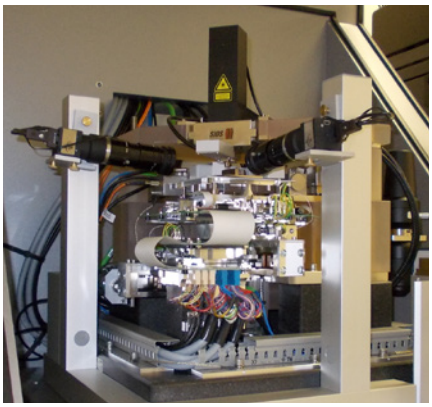
Selected Publications

KLAPETEK P. et al. 2012. *Quantitative Data Processing in Scanning Probe Microscopy*. Elsevier. 368 p., ISBN: 9781455730582.

KLAPETEK P., PICCO L., PAYTON O., YACOOT A., MILES M. 2013. Error mapping of high speed AFM systems. *Measurement Science & Technology* 24 (2), 025006.

NECAS D., KLAPETEK P. 2013. One-dimensional autocorrelation and power spectrum density functions of irregular regions. *Ultramicroscopy* 124, p. 13-19.

NECAS D., KLAPETEK P. 2012. Gwyddion: an open-source software for SPM data analysis. *Central European Journal of Physics* 10 (1), p. 181-188.



Nano-positioning and Nanomeasuring machine (SIOS) that is used as a basis for specialized metrology SPM, offering very low positioning uncertainties over a large area.

CONTENT OF RESEARCH

The group focuses on the development of methods and methodologies for the measurement of properties of nanomaterials and nanostructures with high spatial resolution, also including testing the manufacturing results of other CEITEC research groups and providing metrological traceability to their measurement techniques. The main tool for these measurements is a specialised metrology scanning probe microscope being built by the group, consisting of both commercial and custom-made sensors (like fibre interferometer head) and a very precise 3D optical interferometer (part of a Nanopositioning and Nanomeasuring Machine from the SIOS company). In combination with the use of high performance computing on graphics cards this serves as a basis for the development of quantitative scanning probe microscopy techniques and finally for the quantitative analysis of different physical properties with nanometre resolution.

The group is involved in research into and development of instruments and methods for the investigation of nanomaterials and nanostructures, including different variants of scanning probe microscopy and related numerical modelling techniques. We are working on the development of a specialized metrology scanning probe microscope offering high speed, a large scanning area and smallest uncertainty in both dimensional and other physical properties determination. To fulfil these requirements, scanning probe microscopy techniques are being developed to serve as a quantitative tool instead of merely a qualitative one (as is typically done in practice).

X-ray Micro CT and Nano CT

Prof. Ing. Jozef Kaiser, Ph.D.
Research Group Leader

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RESEARCH AREAS

- Development and application of micro- and nano-radiography and computed tomography (μCT, nanoCT) techniques in different fields
- High-resolution 3D metrology
- Combination of micro- and nano-radiography and μCT, nanoCT techniques with other analytical approaches, e.g. with Laser-Induced Breakdown Spectroscopy (LIBS)

MAIN OBJECTIVES

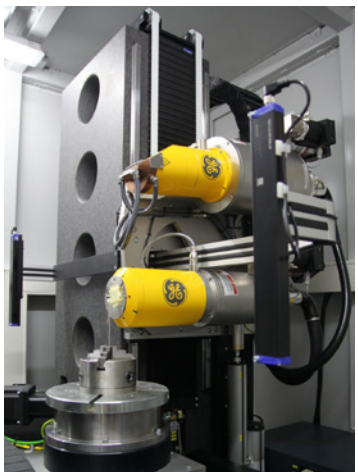
- Research and development of analytical and measurement methods
- Research and development of advanced X-ray based imaging techniques
- Research and development of techniques and methodologies for LIBS and its modification for laboratory and on-site analysis

Selected Publications

KAISER J., NOVOTNY K., MARTIN M., HRDLICKA A., MALINA R., HARTL M., ADAM V., KIZEK R. 2012. Trace element analysis by laser-induced breakdown spectroscopy - Biological applications. *Surface Science Reports* 67 (11), p. 233-243.

KAISER J., STEPANKOVA K., KORISTKOVA T., SEDO O., MELNYK G., HARTL M., PALOUSEK D., KUCERA J. 2012. Determination of the cause of selected canine urolith formation by advanced analytical methods. *Journal of Small Animal Practice* 53 (11), p. 646-651.

VITKOVA G., NOVOTNY K., PROKES L., HRDLICKA A., KAISER J., NOVOTNY J., MALINA R., PROCHAZKA D. 2012. Fast identification of biominerals by means of stand-off laser induced breakdown spectroscopy using linear discriminant analysis and artificial neural networks. *Spectrochimica Acta Part B* 73 (7), p. 1-6.

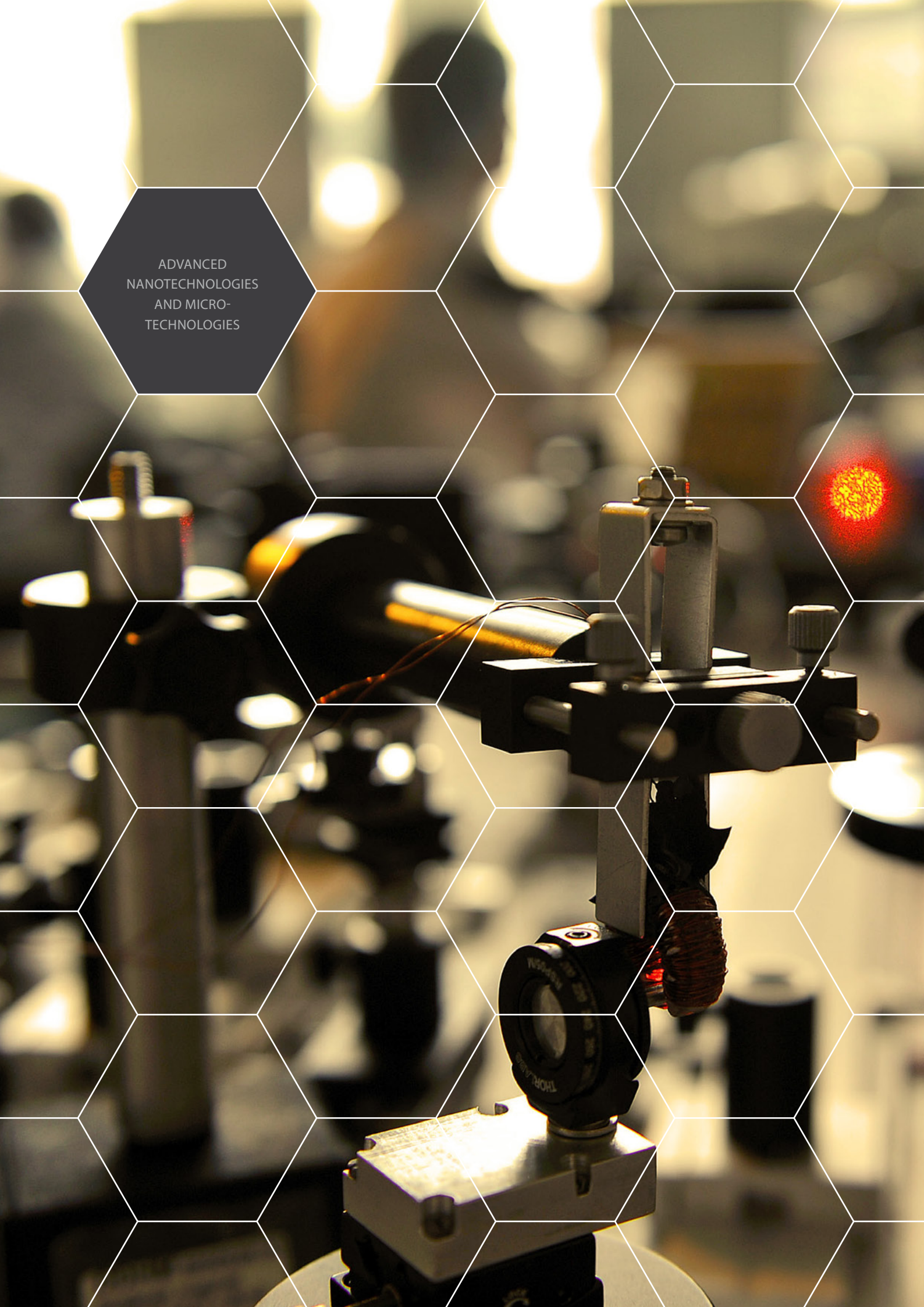


The microfocus and nanofocus X-ray tubes in CEITEC´s state of the art GE v|tome|x L 240 μCT station.

CONTENT OF RESEARCH

Research into and development of instruments and methods for the investigation of a wide variety of different samples (including micro and nano structures). The development of μCT methodology for non-invasive inspection and visualization of advanced materials and structures. The development and application of laser-ablation based analytical techniques such as LIBS and their modification for the investigation of micro- and nanosystems.

The basic impulse to investigate and apply μCT and related techniques came from the need to identify non-destructively a proper cross-section for elemental mapping in various samples, preferably by LIBS. The Laboratory of Laser Spectroscopy (http://libs.fme.vutbr.cz/) has more than 15 years of experience with the development of LIBS methods and disposes of all the necessary devices for the implementation of general single-pulse LIBS and also its variations: double-pulse LIBS (with increased detection limits), LIBS + LIFS (Laser Induced Fluorescence Spectroscopy), LIBS of liquids and remote techniques: remote LIBS (by optical fibre) and stand-off LIBS (via air). Going back to X-rays, the development of μCT techniques in the research group started with cooperation with synchrotron Elettra, Trieste, Italy. Based on this continuing cooperation and also research projects realized at other synchrotrons in Europe, the founding of the new laboratory was decided within the framework of CEITEC's structure. The μCT lab, equipped with a state-of-the-art GE v|tome|x L 240 μCT station, has been in full operation since September 2012.



ADVANCED NANOTECHNOLOGIES AND MICRO-TECHNOLOGIES

Optoelectronic Characterisation of Nanostructures

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RESEARCH AREAS

- Application of novel diagnostic methods
- Experimental and theoretical research into stochastic processes and charge carrier transport as a basis for new advanced technologies
- Methods for non-destructive diagnostics of electronic components and structures
- Investigation of material surfaces, characterization of local structure inhomogeneities
- Electromagnetic emission in dielectrics for the monitoring of the generation and growth of cracks under mechanical load

MAIN OBJECTIVE

- Investigation of functional properties of nanostructures

Selected Publications

SEDLAK P., SIKULA J., MAJZNER J., VRNATA M., FITL P., KOPECKY D., VYSLOUZIL F., HANDEL P. 2012. Adsorption–desorption noise in QCM gas sensors. *Sensors and Actuators B-Chemical* 166, p. 264–268.

GRMELA L., SKARVADA P., TOMANEK P., MACKU R., SMITH S. 2012. Local investigation of thermal dependence of light emission from reverse-biased monocrystalline silicon solar cells. *Solar Energy Materials and Solar Cells* 96 (1), p. 108-111.

SEDLAKOVA V., SIKULA J., CHVATAL M., PAVELKA J., TACANO M., TOITA M. 2012. Noise in Submicron Metal-Oxide-Semiconductor Field Effect Transistors: Lateral Electron Density Distribution and Active Trap Position. *Japanese Journal of Applied Physics* 51 (1), 024105.

SIK O., GRMELA L., ELHADIDY H., DEDIC V., SIKULA J., GRMELA P., FRANC J., SKARVADA P., HOLCMAN V. 2013. Study of electric field distribution and low frequency noise of CdZnTe radiation detectors. *Journal of Instrumentation* 8, C06005.

CONTENT OF RESEARCH

The recent progress of emerging nanostructured materials and devices calls for their profound local electrical and optical characterisation.

The research group deals with diagnostic methods based on noise and dielectric spectroscopy and local optical and electrical measurements. The physical foundation lies in the fact that charge transport and irradiation or absorption of light are of a stochastic nature and they can be monitored and analysed using methods developed in reliability theory and mathematical statistics.

It includes a study of effects related to the nanometric interaction of a probe and the surface of a sample, such as topography, local photoluminescence and spatial super-resolution spectroscopy, using scanning tunnelling microscopes with a local probe (SNOM, SFM, STM).

The main goal is to find a correlation between the properties and the geometrical and structural parameters of nanostructures, and to use this knowledge for feedback in the technology of their preparation.

Computing procedures, using up-to-date software, will be developed. Dielectric and conductance characteristics of materials under test at varying stages of their life cycle (at different manufacturing stages, upon delivery from the assembly line, after stabilization and during ageing) will be compared. Also, variations of other characteristics and their mutual correlations will be examined and analysed, such as noise, acoustic emissions and IR spectra.

An optical nanometrology laboratory will be established, which will allow the measurement of local electrical and optical properties of microelectronic and photonic structures. The physical quantities scanned at the sample surface or at the structure interface will be visualized with spatial super-resolution, which supersedes the diffraction limit of classical optical instruments. In-depth information about material composition will be obtained. Visible and near IR spectra measurement and analysis will be utilized for the optical diagnostics of plasmochemical processes.

Micro and Nanotribology

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RESEARCH AREAS

- Experimental study of molecular degradation of lubricants
- Real roughness behaviour within lubricated contacts
- Thin-film-lubrication studies under non-steady-state conditions
- Lubricant film formation in biotribology applications
- Lubrication, friction and wear of textured surfaces

MAIN OBJECTIVES

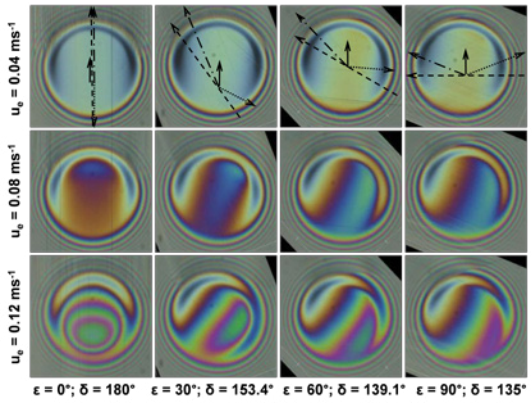
- Experimental verification of surface roughness behaviour within lubricated contacts
- Experimental evidence of the effects of proteins on the tribological performance of hip joint replacements
- Friction and wear reduction using surface texturing within lubricated contacts
- Understanding of the effects of high pressure rheology on lubrication film formation

Selected Publications

VRBKA M., NAVRAT T., KRUPKA I., HARTL M., SPERKA P., GALLO J. 2013. Study of film formation in bovine serum lubricated contacts under rolling/sliding conditions. *Proceedings of the Institution of Mechanical Engineers Part J – Journal of Engineering Tribology* 227 (5), p. 459-475.

SPERKA P., KRUPKA I., HARTL M. 2012. The Behavior of Surface Roughness in EHL Contacts under Small Slide to Roll Ratios. *Tribology Letters* 47 (3), p. 357-366.

KUMAR P., BAIR S., KRUPKA I., HARTL M. 2010. Newtonian quantitative elastohydrodynamic film thickness with linear piezoviscosity. *Tribology International* 43 (11), p. 2159-2165.



Chromatic interferograms depicting the effect of entrainment velocity orientation on lubricant film formation between steel ball and glass disc.

CONTENT OF RESEARCH

Experimental study of lubricated conformal and non-conformal contact behaviour under steady state and transient operational conditions considering the effect of pressure, temperature and surface topography between rubbing surfaces.

Tribological and mechanical properties of lubricant films, rubbing surfaces and protective coatings

The experimental study of the tribological properties (lubrication, friction and wear) of rubbing surfaces and protective coatings is focused on the evaluation of the effects of operational conditions (materials, load, speed, temperature, etc.) on performance and reliability. Lubricant films play an important role in diminishing friction and wear on contacting surfaces in relative motion both at micro and nanoscales. Hence there is a need to understand lubrication mechanisms of large machine parts as well as MEMS/NEMS. Optical measurement techniques (colorimetric interferometry, spectroscopic reflectometry, infrared radiometry, etc.) are used to better understand tribological phenomena in these applications. Research activities are focused on the effects of surface topography and lubricant rheology on lubricant film formation between rubbing surfaces used in mechanical engineering and biomechanical applications. Surface topography effects involve both real and artificial asperities that make it possible to consider beneficial and adverse effects of surface topography on the tribological behaviour of lubricated contacts between components in relative motion. Lubricant rheology study makes it possible to take high pressure changes in lubricants into consideration, including the effects of additives, proteins, etc.

Plasma Technologies

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RESEARCH AREAS

- Plasma processing of materials, plasma diagnostics and simulations
- Functional coatings, materials for sensors, biomaterials
- Methods for characterization of optical and mechanical properties
- Algorithms and software for scanning probe microscopy (SPM) data analysis

MAIN OBJECTIVES

- Development of low and atmospheric pressure plasma processes for the deposition of thin films, the modification of metal and polymer surfaces and the preparation of nanostructured materials
- Understanding the interaction of plasma with surfaces
- Development of physical methods for characterization of surfaces and thin films

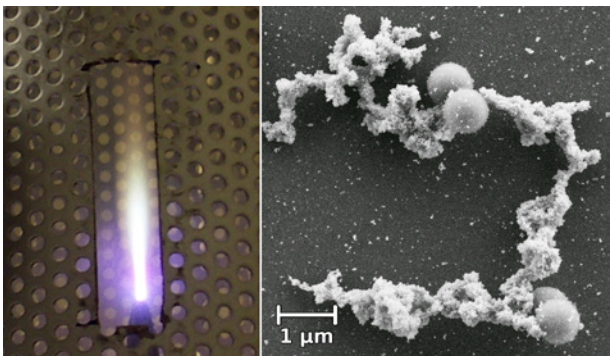
Selected Publications

ZAJICKOVA L., ELIAS M., BURSIKOVA V., STUDYNKOVA Z., MAZANKOVA V., MICHLICEK M., HOUDKOVA J. 2013. Low Pressure Plasmachemical Processing of Multi-Walled Carbon Nanotubes for the Production of Polyurethane Composite Films with Improved Mechanical Properties. *Thin Solid Films* 538, p. 7-15.

FRANTA D., NECAS D., ZAJICKOVA L. 2013. Application of Thomas–Reiche–Kuhn sum rule to construction of advanced dispersion models. *Thin Solid Films* 534, p. 432-441.

NECAS D., KLAPETEK P. 2013. One-dimensional autocorrelation and power spectrum density functions of irregular regions. *Ultramicroscopy* 124, p. 13-19.

SYNEK P., JASEK O., ZAJICKOVA L., DAVID B. , KUDRLE V. , PIZUROVA N. 2011. Plasmachemical synthesis of maghemite nanoparticles in atmospheric pressure microwave torch. *Materials Letters* 65 (6), p. 982-984.



Microwave plasma torch (left) used for the synthesis of nanomaterials, here carbon nanoballs with superparamagnetic iron oxide nanoparticles (right).

CONTENT OF RESEARCH

Plasma is highly tuneable environment of electrons, ions and reactive species combining chemical and physical phenomena and eliminating aggressive chemicals. Therefore, it can be more effective and less harmful to the environment than pure chemical processing.

The plasma processing of materials covers a wide range of advanced technological issues as it is applied e.g. for etching and thin film deposition in microelectronics, the deposition of optical or protective coatings, the improvement of adhesion to metals or polymers, the functionalization of surfaces and the synthesis of nanomaterials. We study the plasma enhanced chemical vapour deposition (PE-CVD) of organosilicon plasma polymers, diamond-like carbon (DLC) films and organic plasma (co)polymers containing carboxyl, carbonyl or amine functional groups. Part of our research is devoted to the synthesis and functionalization of carbon nanotubes (CNTs), carbon nanowalls (CNWs) and graphene. Plasmachemical processes are also used for the synthesis of iron oxide nanoparticles with desired magnetic or photocatalytic properties. Materials technologists have to collaborate closely with scientists developing analytical methods. Therefore, we also work on the development of our approach to the understanding of the dielectric response of materials. It is based on dispersion models valid in a wide spectral range from VUV to IR and utilizing parameters that are directly related to the material's structure. We perform complex analyses of relations between nanoindentation response and microstructure of multilayered and nanocomposite materials. Our activities cover also the development of the scanning probe microscopy (SPM) data analysis software, Gwyddion.

Synthesis and Analysis of Nanostructures

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RESEARCH AREAS

- Syntheses of porous metal oxides, phosphates, silicates, metallo-organic coordination polymers and nanoparticles of oxides, metals and alloys
- Theoretical studies of structural, magnetic and thermodynamic properties of intermetallic phases, magnetism of grain boundaries and phase equilibria modelling
- Macrocyclic ligands, physico-chemical properties of complexes and applications in medicine, radiotherapy, and diagnostics (MRI, PET, SPECT, luminescence probes)
- Development of sensors and sensor arrays – environmental/in vivo analysis
- Laser ablation-ICP-MS applications to elemental mapping and microanalysis of geological, archaeological, and biological samples
- Laser Induced Breakdown Spectroscopy (LIBS) for elemental mapping and microanalyses
- Application of nanomaterials in biological analysis (SALDI MS)

MAIN OBJECTIVES

- **Fabrication of nanostructures by bottom-up methods**: Synthesis of inorganic-organic nanomaterials such as coordination polymers, xerogels, nanopowders, nanoalloys, and supramolecular systems with the aim of developing new methods for their preparation based on a bottom-up approach
- **Investigation of the functional properties of nanostructures:** Application of theoretical calculations in the search for correlations between the properties and the structural parameters of nanostructures, and application of this knowledge as feedback in their preparation
- **Research and development of instruments and methods for the investigation of nanomaterials and nanostructures:** The development of methods and methodologies for the analysis of nanomaterials and nanostructures, and the development of new analytical and diagnostic equipment and components

Selected Publications

SOBOTNIK J., BOURGUIGNON T., HANUS R., DEMIANOVA Z., PYTELKOVA J., MARES M., FOLTYNOVA P., PREISLER J., CVACKA J., KRASULOVA J., ROISIN Y. 2012. Explosive Backpacks in Old Termite Workers. *Science* 337 (6093), p. 436.

VSIANSKA M., SOB M. 2011. The effect of segregated sp-impurities on grain-boundary and surface structure, magnetism and embrittlement in nickel. *Progress in Materials Science* 56 (6), p. 817-840.

SPICHAL Z., JANCARIK A., MAZAL C., PINKAS J., PEKARKOVA P., NECAS M. 2013. Lanthanide coordination polymers with bis(diphenylphosphoryl)bicyclo[1.1.1]pentane. *Polyhedron* 62, p. 83-88.

TOMALOVA I., LEE C.H., CHEN W.T., CHIANG C.K., CHANG H.T., PREISLER J. 2013. Analysis of the Formation Process of Gold Nanoparticles by Surface-Assisted Laser Desorption/Ionization Mass Spectrometry. *Journal of the American Society for Mass Spectrometry* 24 (2), p. 305-308.

CONTENT OF RESEARCH

Development of new synthetic procedures for the controlled fabrication of nanostructured materials. Design and development of analytical techniques for investigation of nanostructures and biological samples.

The fabrication of nanostructures by bottom-up methods, the development of new synthetic techniques, such as nonhydrolytic sol-gel syntheses, sonochemical methods, the synthesis of nanoporous, inorganic-organic and complex materials, and surface-mounted functional molecules.

The characterization and optimization of the functional properties of nanostructures for catalysis, nanoelectronics, nanophotonics, and (bio)sensing; their correlation with compositional, morphological, and structural parameters. Theoretical ab initio calculations of structural, magnetic, and thermodynamic properties of materials.

Research and development of analytical and measurement methods and methodologies for analysis of nanomaterials/nanostructures, new techniques of elemental mapping, microanalysis, surface imaging, medical diagnostics, and biosensing.

Transport and Magnetic Properties

Ing. Bohumil David, Ph.D.
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RESEARCH AREAS

- Measurements of magnetic behaviour and electronic/thermal transport properties of materials
- Multiscale modelling of extended defects in materials

MAIN OBJECTIVES

- Experimental investigations into relationships between structure and magnetic and transport properties in metallic materials
- Theoretical studies of electronic and magnetic properties of disordered alloys, epitaxial multilayers, surfaces and interfaces as well as quantum-mechanical studies of extended defects in metallic materials

Selected Publications

GROGER R., VITEK V. 2012. Constrained nudged elastic band calculation of the Peierls barrier with atomic relaxations. *Modelling and Simulation in Materials Science and Engineering* 20 (3), 035019.

DAVID B., PIZUROVA N., SCHNEEWEISS O., SANTAVA E., KUDRLE V., JASEK O. 2012. γ-Fe_2O_3 nanopowders synthesized in microwave plasma and extraordinarily strong temperature influence on their Mössbauer spectra. *Journal of Nanoscience and Nanotechnology* 12 (12), p. 9277-9285.

ZIVOTSKY O., TITOV A., JIRASKOVA Y., BURSIK J., KALBACOVA J., JANICKOVIC D., SVEC P. 2013. Full scale magnetic, microstructural, and physical properties of bilayered CoSiB/FeSiB ribbons. *Journal of Alloys and Compounds* 581, p. 685-692.

DAVID B., PIZUROVA N., SCHNEEWEISS O., KUDRLE V., JASEK O., SYNEK P. 2011. Iron -based nanopowders containing α-Fe, Fe_3C and γ-Fe particles synthesized in microwave torch plasma and investigated with Mössbauer spectroscopy. *Japanese Journal of Applied Physics* 50 (8), 08JF11.

CONTENT OF RESEARCH

The specification and optimization of the functional properties of nanostructures for nanoelectronics, nanophotonics and (bio)sensing, and their correlation with the geometrical/structural parameters of nanostructures and operational parameters.

The main goal is to find a correlation between the properties and the geometrical and structural parameters of nanostructures and to use this knowledge for feedback in the technology of their preparation and for diverse applications.

Magnetic properties and electrical/thermal transport properties of nanostructures, thin layered structures, and high-temperature superconductors can be determined experimentally in the temperature range of 2–300 K on a Physical Property Measuring System (PPMS), which enables measurements in applied magnetic fields up to 9 T. A vibrating sample magnetometer (VSM) is used to investigate magnetic properties at high temperatures (293–1093 K). Structural and magnetic properties of Fe-based nanostructures are studied using Mössbauer spectroscopy at low (5–293 K) and high (293–1093 K) temperatures.

We also focus on atomistic modelling of extended defects in materials crystallizing in BCC and HCP structures and develop thermodynamic models of plastic flow incorporating atomic-level details of the dislocation glide. The length and time scales in modelling plasticity are bridged by employing mean-field models.

ADVANCED MATERIALS

The research of advanced materials covers the synthesis of materials and the analysis of the structure and properties of advanced materials. The aim of the research is to develop novel materials with complex properties and propose novel application areas for these materials. The research is focused on advanced ceramic materials; advanced polymeric materials and composites; and advanced metallic materials.

Research Programme Coordinator:
Jaroslav Cihlář | jaroslav.cihlar@ceitec.vutbr.cz

OVERALL GOAL

The overall goal is to establish an equipment and personnel infrastructure further enhancing excellence in the research of advanced (polymeric, ceramic, metallic and composite) materials and their applications in various industrial sectors, medicine and services. The main effort will be devoted to investigating advanced methods of preparing multifunctional homogeneous and heterogeneous advanced materials, characterising their structure on various dimensional scales; quantifying structure-property-function relationships on the various structural levels and developing procedures for engineering properties of this class of materials in the process of their preparation.

RESEARCH DIRECTIONS

- Advanced ceramic materials
- Research and diagnostics of electrical properties of advanced materials
- Advanced polymers and composites
- Advanced metallic materials and metal-based composites
- Structure and phase analysis

RESEARCH GROUPS | LEADERS

Advanced Ceramic Materials | *Jaroslav Cihlář*

Cybernetics in Material Science | *Pavel Václavek*

Advanced Polymers and Composites | *Josef Jančář*

Advanced Metallic Materials and Metal Based Composites | *Jan Klusák*

Advanced Coatings | *Jiří Švejcar*

Advanced Ceramic Materials

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RESEARCH AREAS

- Ceramic biomaterials for dental and surgical applications
- Ceramics for energy and electrochemical applications
- Transparent ceramics for ballistic and high-temperature applications
- Structural nanoceramics and composites with high strength and toughness

MAIN OBJECTIVES

- Research and development of ceramics processing methods (synthesis, consolidation, shaping, and densification of ceramic particles)
- Research into properties of advanced ceramics
- Correlation between properties of advanced ceramics and their processing

Selected Publications

BERA O., TRUNEC M. 2012. Optimization of Fine Alumina Gelcasting Using In Situ Dynamic Rheology. *Journal of the American Ceramic Society* 95 (9), p. 2849-2856.

CIHLAR J., DRDLIK D., CIHLAROVA Z., HADRABA H. 2013. Effect of acids and bases on electrophoretic deposition of alumina and zirconia particles in 2- propanol. *Journal of the European Ceramic Society* 33 (10), p. 1885-1892.

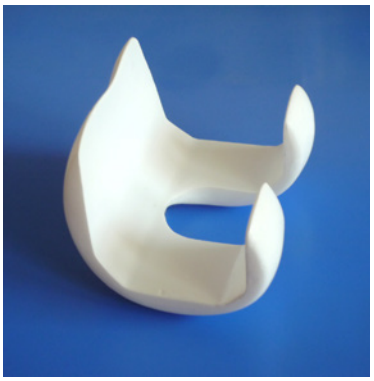
CIHLAR J. Jr., BARTONICKOVA E., CIHLAR J. 2013. Low-temperature sol-gel synthesis of anatase nanoparticles modified by Au, Pd and Pt and activity of TiO2/Au, Pd, Pt photocatalysts in water splitting. *Journal of Sol-Gel Science and Technology* 65 (3), p. 430-442.

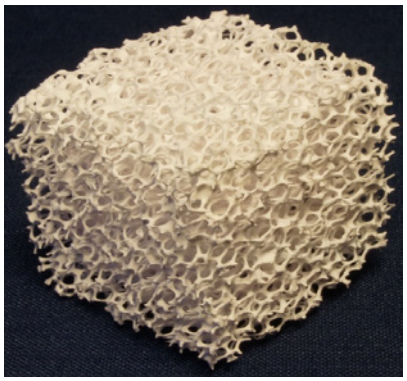
POUCHLY V., MACA K., SHEN Z. 2013. Two-stage master sintering curve applied to two- step sintering of oxide ceramics. *Journal of the European Ceramic Society* 33 (12), p. 2275-2283.

CONTENT OF RESEARCH

The considerable progress in ceramics processing in recent decades has enabled the wide utilization of advanced ceramic materials in most areas of everyday life and this process is accelerating.

The research into the processing and properties of advanced ceramics is focused on the preparation of precursors of advanced ceramic materials and composites using modern advanced methods of inorganic ceramic powder synthesis and surface or bulk modifications of ceramic nanoparticles. By means of the application of novel ceramic shaping and sintering methods and using advanced ceramic precursors, new heterogeneous, functionally graded and nanostructural ceramic materials are being developed. Characterisation of composition structure and properties of advanced ceramic materials, modelling of the structure-property-function relationships and testing of ceramic materials from the view of potential applications is being carried out. The particular research areas include bioinert ceramic orthopaedic implants and bioactive porous scaffolds for bone restoration, ceramic dental structures, ceramic membranes and electrolytes with mixed electrical conductivity for oxygen transport, piezosensors, transparent armour and high-temperature windows.





Ceramic bicondylar knee implant prepared by gelcastig process (left).

Bioactive scaffold on a base of calcium phosphate ceramics for bone therapy (right).

Cybernetics in Material Science

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RESEARCH AREAS

- Smart sensors and signal processing, sensor design using new materials
- Advanced control technologies, control of electrical actuators
- Mobile robotic systems, reconnaissance robotics, telepresence
- Embedded systems and communications technologies

MAIN OBJECTIVES

- Development of novel sensors, control and communications technologies
- Development of an advanced reconnaissance mobile robotic system equipped with novel chemical, biological and nuclear sensors
- Application of new materials and technologies in sensors, actuators and robotic systems
- Development of control systems and instrumentation for research into, and the production of, new materials

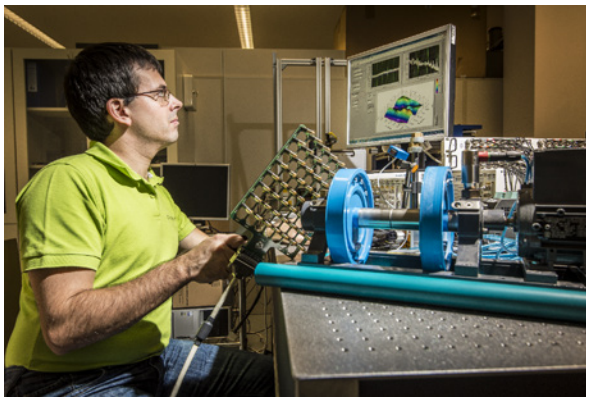
Selected Publications

VACLAVEK P., BLAHA P., HERMAN I. 2013. AC Drive Observability Analysis. *IEEE Transactions on Industrial Electronics* 60 (8), p. 3047-3059.

FIALKA J., BENES P. 2013. Comparison of Methods for the Measurement of Piezoelectric Coefficients. *IEEE Transactions on Instrumentation and Measurement* 62 (5), p. 1047-1057.

REBENDA J., SMARDA Z. 2013. Stability and asymptotic properties of a system of functional differential equations with non-constant delays. *Applied Mathematics and Computation* 219 (12), p. 6622-6632.

REBENDA J., SMARDA Z. 2013. Stability of a Functional Differential System with a Finite Number of Delays. *Abstract and Applied Analysis*, 85313.



Acoustics holography

CONTENT OF RESEARCH

Advanced control, sensors and communications technologies are key components of many industrial systems. Current progress in the development of these technologies is enabling new possibilities of practical applications of new results of other research fields including advanced materials.

Research into advanced control technologies is aimed at the energy-optimal, safe and reliable control of robotics systems and technological processes. Special attention is paid to the advanced control of electrical drives with applications in precise servo-drives in robotics, technological processes, actuators and ecological transportation systems. In the sensors field the research deals with the development of special smart sensors and power harvesting devices. The main goal is the application of advanced materials and new methods of signal processing, especially for data fusion, signal processing of sensor arrays, autocalibration and autodiagnostics. Special attention is paid to acoustic and vibration sensors and acoustic emission transducers. Interests in embedded systems include the development of communication interfaces for special instrumentation including smart sensors and actuators, the design of new solutions for distributed data acquisition and data fusion, and the development of special electronics for technological processes. Mobile robotic reconnaissance systems for special environments are being developed. The systems are to work in hazardous environments, such as areas with chemical, nuclear and biological contamination. Due to the nature of these environmental conditions the systems use special materials to be able to withstand massive contamination, decontamination processes, and to decrease their detectability. Smart sensors are used on-board the robots to enhance their functionality.

ADVANCED
MATERIALS

Advanced Polymers and Composites

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Research Group Leader

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RESEARCH AREAS

- ATRP, ROMP and other advanced syntheses of defined nano-scale building blocks (NSBBs)
- Bottom-up hierarchical assembly of NSBBs
- Molecular dynamics and segment scale models of viscoelasticity and the non-linear deformation response of hierarchical polymers and composites
- Multi length- and time- scale structure-property-function relationships in hierarchical polymer systems

MAIN OBJECTIVES

- Syntheses of precisely defined polymers and hybrid organic-inorganic polyphilles
- External field accelerated bottom-up assembly of multiscale structures from hybrid block copolymers and polyphilles
- The development of algorithms bridging the theoretical models of structure-property relationships in polymers and composites between different length and time scales
- Development of physico-chemical processes controlling the formation of bioinspired, responsive, hierarchical composites for medicine, advanced mechanical engineering and electronics

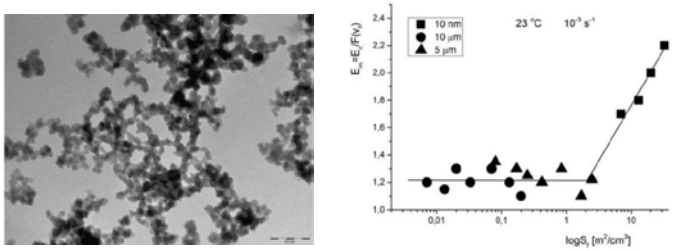
Selected Publications

POLACEK P., SALAJKOVA M., JANCAR J. 2013. The shear adhesion strength between the FRC substructure and denture base resin: Effects of FRC architecture, adhesive composition and hydrolytic degradation. *Composites Science and Technology* 77, p. 22–28.

ZIDEK J., MILCHEV A., VILGIS T.A. 2012. Dynamic behavior of acrylic acid clusters as quasi-mobile nodes in a model of hydrogel network. *The Journal of Chemical Physics* 137 (24), 244908.

JANCAR J., FIORE K. 2011. Molecular weight scaling of the spherulite growth rate in isothermally melt crystallized polyethylene nanocomposites. *Polymer* 52 (10), p. 5851-5857.

JANCAR J., TOCHACEK J. 2011. Effect of thermal history on the mechanical properties of three polypropylene impact-copolymers. *Polymer Degradation and Stability* 96 (9), p. 1546-1556.



▲ Experimental proof of the segment scale reinforcing mechanism in polymer nanocomposites resulting in a novelmolecular model of the "non-classical" polymer stiffening induced by nanoparticles.

CONTENT OF RESEARCH

Obtaining quantitative relationships governing the synthesis of NSBBs, their multi length scale assembly and principles of how structure of the NSBB is translated into the physico-chemical response of their assembled superstructures at much larger length and time scales is the basis for a new materials design paradigm.

We investigate various types of ATRP and ROMP syntheses well suited for preparing nano-scale structure-defined NSBBs using novel metal-free catalysts. The use of multiple thermo-mechanical and simultaneous mechanical/structural characterization techniques and a combination of unique experiments with the development of theoretical models is the basis for investigating laws relating the mechanism and kinetics of NSBB synthesis to the hierarchical assembly of multifunctional polymeric systems, characterizing these systems from nano to macro length scale over a timescale from nanoseconds to years, quantifying structure-property-function relationships on various structural levels and to develop procedures for engineering the properties of this class of materials in the process of their synthesis and preparation. The development of novel molecular scale computer models and simulation algorithms for the computer modelling of structure-property-function relationships (viscoelasticity, non-linear deformation response, rheology, non-affine network deformation, etc.) in bottom-up assembled hierarchical systems is also targeted.

Advanced Metallic Materials and Metal Based Composites

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Research Group Leader

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RESEARCH AREAS

- Basic mechanisms of creep, fatigue, brittle fracture and their combination in relation to the microstructure of metallic materials and metal-based composites
- Theoretical studies of crack behaviour in metallic materials, metal-based composites and components
- Multi-scale simulation of deformation and fracture processes, quantitative fractography and prediction of fatigue life under multiaxial loading
- Solutions to problems related to fatigue, creep and brittle fracture of both currently applied and developed materials in industrial applications

MAIN OBJECTIVES

- The study of the relationship between material structure and properties
- The investigation of fatigue, creep, their interaction, and fracture properties of advanced materials and metal based composites used or currently being developed for application in power engineering, transport and medicine
- The generation of material data necessary for the safe and reliable application of engineering structures and components in service, and the extension of basic knowledge in material damage mechanisms

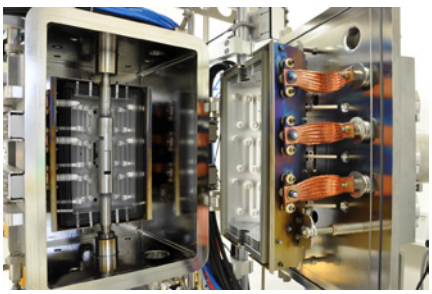
Selected Publications

CERMAK J., KRAL L. 2012. Improvement of hydrogen storage characteristics of Mg/Mg2Ni by alloying: Beneficial effect of In. *Journal of Power Sources* 214, p. 208-215.

SEVCIK M., HUTAR P., ZOUHAR M., NAHLIK L. 2012. Numerical estimation of the fatigue crack front shape for a specimen with finite thickness. *International Journal of Fatigue* 39, p. 75-80.

CERNY M., SESTAK P., POKLUDA J., SOB M. 2013. Shear Instabilities in Perfect bcc Crystals during Simulated Tensile Tests. *Physical Review B* 87 (1), 014117.

HALASOVA M., CHLUP Z., STRACHOTA A., CERNY M., DLOUHY I. 2012. Mechanical response of novel SiOC glasses to high temperature exposition. *Journal of the European Ceramic Society* 32(16), p. 4489–4495.



New MAYTEC high temperature furnace (up to 1400 °C) installed on Zwick creep machine KAPPA 50 LA.

CONTENT OF RESEARCH

The properties of engineering materials have to be continuously improved in order to achieve heightened performance, safety and reliability in engineering systems.

Research concerning the mechanical properties of materials currently focuses on basic mechanisms operating in materials during creep, fatigue, combined creep/fatigue and brittle fracture, and on their relation to microstructures. The testing facilities allow tests in a broad range of temperatures, strain rates and other external parameters. An integral part of the group's research activity is in theoretical studies of crack behaviour.

Research in the area of multiaxial fatigue primarily focuses on the elevated temperature behaviour of materials used preferably in aeronautics. The computer controlled tensile-torsion testing system facilitating high temperature cyclic multiaxial straining allows the study of damage mechanisms and the resistance parameters of advanced metallic materials. The testing system for thermo-mechanical tests enables for example testing to identify the temperature and strain parameters of shape-memory actuators, stents and other components of advanced medical devices based on the shape-memory effect.

Investigation of the structures of materials in relation to their thermodynamic and diffusion properties is performed in the group. Structure is understood over a wide range of length scales starting with atomic bonds, through the crystallographic lattice and its imperfections, to the size and morphology of crystallites (grains) in material.

Advanced Coatings

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RESEARCH AREAS

- Electron microscopy, microanalysis and X-ray diffraction
- Surface engineering and technology
- Metal matrix composites
- Ultra-fine grain materials
- Powder metallurgy

MAIN OBJECTIVES

- Research and development of novel diffusion or environmental/thermal barrier coating systems for aerospace, wear resistant and hydrophobic coatings for power engineering, and extremely hard coatings for vacuum systems and technologies
- Research and development of materials and their production technologies using bulk surface cooling conditions to create directional microstructure and/or advanced powder sintering techniques to produce lightweight non-ferrous (especially magnesium, aluminium, zinc, etc. alloys) bulk materials/composites
- Research and development of unconventional technologies for magnetically conductive or magnetically non-conductive ultrafine/nanopowder production

Selected Publications

CELKO L., DIAZ DE LA TORRE S., KLAKURKOVA L., KAISER J., SMETANA B., SLAMECKA K., ZALUDOVA M., SVEJCAR J. 2013. The Effect of Temperature Height on Microstructural Evolution in Al-Ni Binary Couples Produced by Unconventional Method. *Journal of Alloys and Compound.* (under review)

CELKO L., KLAKURKOVA L., SMETANA B., SLAMECKA K., ZALUDOVA M., HUI D., SVEJCAR J. 2013. Application of Sacrificial Coatings and Effect of Composition on Al-Al3Ni Ultrafine Eutectic Formation. *Journal of Mining and Metallurgy*, *Section B: Metallurgy.* (accepted to publish)

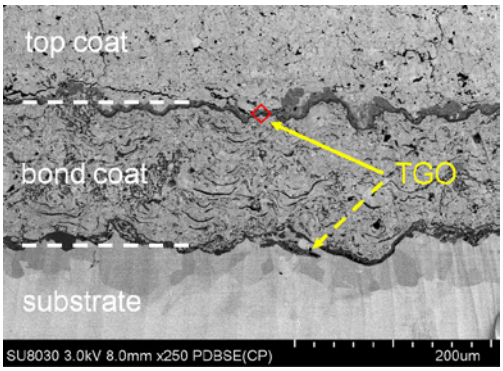
DOLEZAL P., ZAPLETAL J., HORYNOVA M., GEJDOS P., CELKO L. 2011. Cyclic Deformation Response of AZ31 Magnesium Alloy after Corrosion Degradation. *Chemicke listy* 105 (S), p. 787-789.

CELKO L., RICANKOVA V., KLAKURKOVA L., PODRABSKY T., DVORACEK E., SVEJCAR J. 2011. Changes in Microstructure of Air Plasma Sprayed MCrAlY Coatings after Short Thermal Exposure in Argon Atmosphere. *Acta Physica Polonica* A120 (2), p. 336-339.

CONTENT OF RESEARCH

The research group Advanced Coatings is predominantly focused on research into, and the development of, novel materials and coatings for aerospace (diffusion coatings, overlay coatings and environmental/thermal barrier coatings), functional and decorative electroplating, and coatings for the power generation industries.

Part of the research activities are focused also on unconventional routes for powder processing (hydrodynamic and chemical), new aluminium, zinc and magnesium alloy development (eutectic, hypereutectic alloys, bulk intermetallics and directional solidification of alloys) and on the design of new apparatuses and technologies (machining of hard thermally sprayed coatings, cyclic oxidation testing, burner rig testing, etc.). The research group is highly experienced in solving problems for industry and also well strongly cooperate in the field of applied science directly with globally known industrial partners (Honeywell, Edwards Vacuum, ZKL, etc.).



▲ Structure of thermal barrier coating (SEM).

STRUCTURAL BIOLOGY

The research programme will integrate structural knowledge at different resolution levels into contexts of large macromolecular assemblies in order to gain understanding of vital processes at the cellular level. It aims to achieve European competitiveness, stimulate regional development, and facilitate biomedical research and biotechnologies.

Research Programme Coordinator:
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OVERALL GOAL

The research programme will integrate the three dimensional structural information describing large macromolecular assemblies – proteins, nucleic acids and their complexes – into functional contexts in order to gain an understanding of the vital processes at the cellular level. A variety of experimental techniques with a wide range of spatial resolutions; including single crystal X-ray diffraction; nuclear magnetic resonance; cryo-electron microscopy and tomography; and atomic force microscopy will be applied together with the methods providing an insight into the intermolecular interactions. Systematic in vitro studies using a wide range of biophysical tools will be important for understanding the fundamental principles of molecular recognition. The experimental approach will be complemented by theoretical studies using tools of computational chemistry and bioinformatics. Time variations of three-dimensional structures, supplying essential information indispensable for painting a dynamic picture of key cellular functions, will be investigated in detail. A new integrated infrastructure built within CEITEC will be used to develop modern methods of structural biology and to extract molecular data crucial for biochemical and biomedical applications. The research programme is aimed at achieving European competitiveness, stimulation regional development, and facilitating biomedical research and biotechnologies. At the application level, its results will facilitate developments of next-generation diagnostic and therapeutic strategies for the treatment of human diseases and solutions of health problems.

RESEARCH DIRECTIONS

- Investigation of the role of RNA in development and human diseases
- Therapeutic aspects of recognition and adhesion phenomena in host-pathogen interactions
- Visualisation and modification of biological objects including tissues, cells, cellular structures, and biomolecules
- Development of new methodologies for investigating the structure, interactions and dynamics of biomolecules
- High throughput structural characterisation of macromolecular assemblies by single crystal diffraction
- Establishing a high-end cryo-electron microscopy laboratory for highly sophisticated 3D imaging studies for structural biology at the cellular level

RESEARCH GROUPS | LEADERS

Bioinformatics | *Hedi Hegyi*

CD Spectroscopy of Nucleic Acids and Proteins | *Michaela Vorlíčková*

CryoEM | *Jürgen Plitzko*

Glycobiochemistry | *Michaela Wimmerová*

RNA Quality Control | *Štěpánka Vaňáčová*

Nanobiotechnology | *Petr Skládal*

Biomolecular NMR Spectroscopy | *Vladimír Sklenář*

RNA-based Regulation of Gene Expression | *Peter Lukavsky*

Structural Biology of Gene Regulation | *Richard Štefl*

Structural Virology | *Pavel Plevka*

Structure and Dynamics of Nucleic Acids | *Jiří Šponer*

Structure and Interaction of Biomolecules at Surfaces | *Miroslav Fojta*

Computational Chemistry | *Jaroslav Koča*

Bioinformatics

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RESEARCH AREAS

- Computational analysis and prediction of the viability of alternatively spliced proteins with truncated globular domains
- Sequence analysis and census of alternatively spliced proteins in the human genome and various human tissues, including different brain compartments
- Repetitive elements in the human genome and their role in regulatory functions and disease
- Next-generation sequence (NGS) analysis in healthy and diseased tissues
- Intrinsic structural disorder of orphan proteins

MAIN OBJECTIVES

- The investigation of normal (tissue-specific) and aberrant (cancer-related) alternative splicing and chromosomal translocation, with special respect to the viability of spliced variants on the protein level
- Delineating Pfam domain use in healthy and diseased tissues, with special respect to alternative splicing and chromosomal translocations
- Sequence analysis of schizophrenia-related genes and genomic regions; possible implications with respect to the cause of the disease
- Showing the origin of orphan proteins (de novo creation from noncoding genomic sequences) and resolving the inherent contradiction between the de novo creation of proteins and the long evolutionary time necessary for the evolution of protein folds

Selected Publications

HEGYI H. 2013. GABBR1 has a HERV-W LTR in its regulatory region – a possible implication for schizophrenia. *Biology Direct* 8, 5.

SCHAD E., TOMPA P., HEGYI H. 2011. The relationship between proteome size, structural disorder and organism complexity. *Genome Biology* 12 (12), R120.

HEGYI H., TOMPA P. 2012. Increased structural disorder of proteins encoded on human sex chromosomes. *Molecular Biosystems* 8 (1), p. 229-236.

HEGYI H., KALMAR L., HORVATH T., TOMPA P. 2011. Verification of alternative splicing variants based on domain integrity, truncation length and intrinsic protein disorder. *Nucleic Acids Research* 39 (4), p. 1208-1219.

CONTENT OF RESEARCH

Bioinformatics has transformed itself from child's play into a major player in the biomedical field over the last three decades. We cover several different subjects in this data-rich field, investigating different aspects of both the world of proteins/proteomics and the complete human genome, with special respect to disease-related phenomena.

The main focus of the group is researching the structural aspects of the integrity and stability of globular domains truncated by alternative splicing. We are developing a web server that uses the principles of protein disorder and exposed hydrophobic surfaces to predict the chances of survival for such domains and, by proxy, alternatively spliced proteins containing such domains.

The group is also interested in various aspects of intrinsic protein disorder and the role it might have played in the evolution of new proteins. As it is difficult for globular proteins to spring into existence from scratch, it is highly probable that most proteins were entirely disordered in the beginning. The gradual evolution of globular folds is a fascinating process that we are also studying in the group.

A third project is the analysis of regulatory elements in the human genome as recent developments in experimental techniques have uncovered the enhancer/silencer regions for each protein-coding human gene. Analysis of this data has the potential to lead to new conclusions about complex diseases such as schizophrenia and cancer.

CD Spectroscopy of Nucleic Acids and Proteins

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RESEARCH AREAS

- Conformational properties of genomic DNA fragments important from biological and medical points of view
- Structures and interactions of biomacromolecules and their relation to living systems functions, diseases and therapies

MAIN OBJECTIVES

- To map the conformational properties of DNA sequence motifs occurring in important regions of the human genome
- To characterize the physico-chemical properties of non-B DNA structures, chemical alterations in DNA, and other external factors affecting their stability, dynamics and recognition by proteins

Selected Publications

PALACKY J., VORLICKOVA M., KEJNOVSKA I., MOJZES P. 2013. Polymorphism of human telomeric quadruplex structure controlled by DNA concentration: A Raman study. *Nucleic Acids Research* 41 (2), p. 1005-1016.

VORLICKOVA M., TOMASKO M., SAGI A.J., BEDNAROVA K., SAGI J. 2012. 8-Oxoguanine in a quadruplex of the human telomere DNA sequence. *FEBS Journal* 279 (1), p. 29-39.

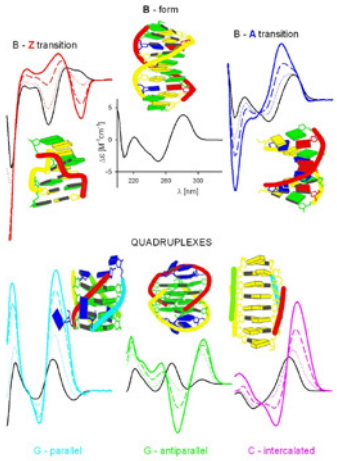
DE RACHE A., KEJNOVSKA I., VORLICKOVA M., BUESS-HERMAN C. 2012. Elongated Thrombin Binding Aptamer: A G-Quadruplex Cation-Sensitive Conformational Switch. *Chemistry – A European Journal* 18 (14), p. 4392-4400.

VORLICKOVA M., KEJNOVSKA I., SAGI J., RENCIUK D., BEDNAROVA K., MOTLOVA J., KYPR J. 2012. Circular dichroism and guanine quadruplexes. *Methods* 57 (1), p. 64-75.

CONTENT OF RESEARCH

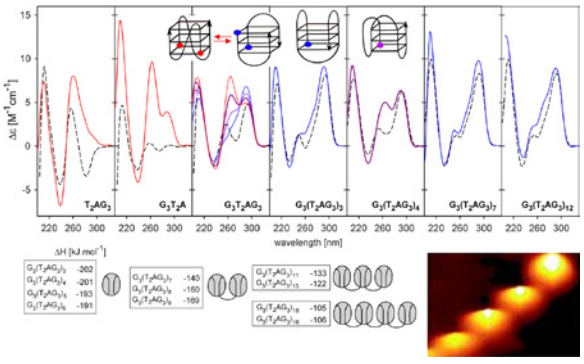
Depending on sequence, DNA can adopt various secondary structures distinct from Watson and Crick's classic double helix. These unusual secondary structures are frequently implicated in various biological functions or diseases. At present, the most frequently studied unusual secondary structures are quadruplexes.

There are numerous regions in the human genome prone to forming quadruplexes. They frequently occur in gene promoters and control their expression. We focus on the quadruplexes formed by telomeric DNA and DNA of selected oncogenes. The quadruplexes formed in telomeres influence ageing and cancer, and thus have become targets for the design of anticancer agents.



The main method used by the group is electronic circular dichroism (CD) spectroscopy. It is extremely sensitive to changes in the mutual orientation of DNA constituents and, therefore, it is uniquely suited to DNA conformational studies. Particular DNA arrangements (classical B- and A-forms, left-handed Z-form, parallel and antiparallel guanine quadruplexes or intercalated cytosine tetraplexes) provide characteristic CD spectra.

CD spectra, and thus the structure of the human telomere DNA quadruplex depend on the DNA length. Based on the observed jumps in ΔH values for 8, 12 and 16 G3 blocks we suggested that long telomere molecules adopt a beads on a string like arrangement. The structure was later visualized by Xu et al.



CryoEM

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RESEARCH AREAS

- The structure and function of macromolecular complexes and cellular assemblies
- The molecular mechanisms of virus replication and host--pathogen interactions
- Time-resolved electron microscopy of biological processes at millisecond timescales

MAIN OBJECTIVES

- To investigate the structure, interactions and conformational dynamics of macromolecular complexes and assemblies in order to understand the structural basis of their function and regulation
- To elucidate the structural and conformational features of viral capsids so as to understand the molecular mechanisms of virus assembly, maturation and interaction with the host cell
- To develop and apply new methods of time resolved cryo--electron microscopy to study assembly and conformational dynamics of transient macromolecular complexes

Selected Publications

RIGORT A., BAUERLEIN F., VILLA E., EIBAUER M., LAUGKS T., BAUMEISTER W., PLITZKO J.M. 2012. Focused ion beam micromachining of eukaryotic cells for cryoelectron tomography. *Proceedings of the National Academy of Sciences of the United States of America* 109 (12), p. 4449-4454.

NEMECEK D., BOURA E., WU W., CHENG N., PLEVKA P., QIAO J., MINDICH L., HEYMANN J.B., HURLEY J., STEVEN A.C. 2013. Subunit folds and maturation pathway of a dsRNA virus capsid. *Structure* 21 (8), p. 1374–1383.

YOKOYAMA T., SHAIKH T.R., IWAKURA N., KAJI H., KAIJ A., AGRAWAL R.K. 2012. Structural insights into initial and intermediate steps of the ribosome-recycling process. *The EMBO Journal* 31 (7), p. 1836-1846.

CONTENT OF RESEARCH

Cryo-electron microscopy (cryo-EM) has established itself as a key technique for studying the structure of large and flexible macromolecular complexes at subnanometer resolution. However, the overall challenge today is to bring the molecular resolution made possible by cryo-electron microscopy to cellular studies and thus bridge the gap between molecular and cellular structural studies.

The trend in structural biology is towards studying macromolecular complexes and supramolecular assemblies of ever--increasing size and complexity, ideally in their native environment. Cryo-electron microscopy (cryo-EM) is a powerful tool for studying isolated and purified molecular structures and assemblies. On the other hand, cryo-electron tomography (cryo-ET) has matured to a point when macromolecular complexes can be studied in the context of the intricate network and crowded environment of the cell in which they naturally function. However, there is still a discrepancy between the level of ultra-structural characterization of the cell interior and the structural analysis of its molecular inhabitants. In particular, the study of structure and motion *in situ* has remained a real challenge for such high--resolution imaging methods.

Many supramolecular structures of great interest are present only in low copy numbers or are so deeply rooted in their cellular environments that it is not possible to isolate them without violating their structural integrity. With the advent of cryo-FIB micromachining, these structures can be captured in intact cells, not only revealing their structure but also their location and interactions within the cell. By comparing and classifying different populations of molecular assemblies one can address and reveal structures at different times of the cell cycle, at different locations within the cell, or in different functional states. The cryo-EM group will utilize cryo-electron microscopy and tomography together with novel sample preparations and advanced computational methods of image classification and 3D reconstruction to reveal the structural basis for the functioning of important macromolecular complexes both in vitro and inside the cell. Further, the results will be combined with other existing techniques of structural analysis (e.g. NMR, crystallography), biological imaging and biochemical analysis. Taken together, these integrative approaches could revolutionize the way we understand the complex inner and outer workings of molecular key players within their unaltered cellular context.

Glycobiochemistry

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RESEARCH AREAS

- Carbohydrate-binding proteins involved in host-pathogen interactions
- Human glycosyltransferases and their role in cancerogenesis
- Glycosyltransferases participating in mycobacterial cell wall synthesis
- *In silico* and *in vitro* protein engineering of lectins
- Biomolecular interactions

MAIN OBJECTIVES

- To study the therapeutic aspects of recognition and adhesion phenomena in host-pathogen interactions
- Investigations of the structures and interactions of biomacromolecules and their relationship to the functions of living systems, disease and therapy
- Designing new lectins with modified specificity and/or affinity for bioanalytical and biochemical purposes

Selected Publications

MARCHETTI R.*, MALINOVSKA L.*, LAMEIGNERE E., ADAMOVA L., DE CASTRO C., CIOCI G., STANETTY C., KOSMA P., MOLINARO A., WIMMEROVA M., IMBERTY A., SILIPO A. 2012. Burkholderia cenocepacia lectin A binding to heptoses from the bacterial lipopolysaccharide. *Glycobiology* 22 (10), p. 1387-1398.

WIMMEROVA M., KOZMON S., NECASOVA I., MISHRA S.K., KOMAREK J., KOCA J. 2012. Stacking Interactions between Carbohydrate and Protein Quantified by Combination of Theoretical and Experimental Methods. *PloS One* 7 (10), e46032.

SULAK O., CIOCI G., LAMEIGNERE E., BALLOY V., ROUND A., GUTSCHE I., MALINOVSKA L., CHIGNARD M., KOSMA P., AUBERT D.F., MAROLDA C.L., VALVANO M.A., WIMMEROVA M., IMBERTY A. 2011. Burkholderia cenocepacia BC2L-C Is a Super Lectin with Dual Specificity and Proinflammatory Activity. *PLoS Pathogens* 7 (9), e1002238.

SULAK O., CIOCI G., DELIA M., LAHMANN M., VARROT A., IMBERTY A., WIMMEROVA M. 2010. A TNF-like trimericlectin domain from Burkholderia cenocepacia with specificity for fucosylated human histo-blood group antigens. *Structure* 18 (1), p. 59-72.

CONTENT OF RESEARCH

The cell surfaces of all living cells are covered by diverse glycoconjugates (glycolipids and glycoproteins), which modulate or mediate a wide variety of processes and are crucial to the development and functioning of complex multicellular organisms. An understanding of the proteins and enzymes involved in their recognition and synthesis is a key to revealing the biological rules of living systems.

Carbohydrates play essential roles in many recognition events. Specific recognition of glycoconjugates is an important event in biological systems and plays a role in numerous physiological and pathophysiological processes including cell signalling, differentiation, fertilization and inflammatory response, as well as in cancerogenesis or pathogen-cell adhesion and recognition.

For example, the life cycles of pathogenic bacteria, fungi and viruses require the specific recognition of host tissue for adhesion and subsequent invasion. A common strategy, often used by pathogens, involves recognition and adhesion to the host glycoconjugates, which is essential for initiating an infection. Their sugar-binding proteins can display exceptional specificity for the target tissue. Subsequent chronic colonization and biofilm formation make pathogen eradication difficult because of the mechanical barrier creation and the increase in their resistance to antibiotics. Inhibitors blocking protein-carbohydrate interactions can serve as new anti-adhesive drugs in therapeutic applications.

We use a multidisciplinary approach to the study of proteins connected with the synthesis, recognition and hydrolysis of glycoconjugates. Proteins are identified using bioinformatics tools, and produced in recombinant form. The complementary techniques of binding experiments such as isothermal titration microcalorimetry, surface plasmon resonance and high resolution X-ray crystallography are used to decipher connections between structure and function.

RNA Quality Control

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RESEARCH AREAS

- RNA processing and quality control in the yeast nucleus
- RNA processing, modification and degradation in mammalian cells
- RNA processing and disease

MAIN OBJECTIVES

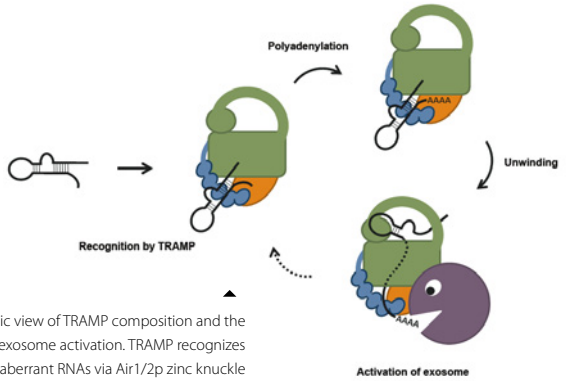
- Mechanisms of nuclear and cytoplasmic RNA surveillance in yeast and mammals
- Mechanisms and function of noncanonical polyadenylation
- The regulation of small RNAs by 3'-terminal uridylation
- Identification of RNA targets by CLIP-Seq methodologies

Selected Publications

USTIANENKO D., HROSSOVA D., POTESIL D., CHALUPNIKOVA K., HRAZDILOVA K., PACHERNIK J., CETKOVSKA K., ULDRIJAN S., ZDRAHAL Z., VANACOVA S. 2013. Mammalian DIS3L2 exoribonuclease targets the uridylated precursors of let-7 miRNAs. *RNA* 12 (19), p. 1-7.

KUBICEK K., CERNA H., HOLUB P., PASULKA J., HROSSOVA D., LOEHR F., HOFR C., VANACOVA S., STEFL R. 2012. Serine phosphorylation and proline isomerization in RNAP II CTD control recruitment of Nrd1. *Genes & Development* 26 (17), p. 1891-1896.

HOLUB P., LALAKOVA J., CERNA H., PASULKA J., SARAZOVA M., HRAZDILOVA K., SANUDO M.A., STEFL R., VANACOVA S. 2012. Air2p is critical for the assembly and RNA-binding of the TRAMP complex and the KOW domain of Mtr4p is crucial for exosome activation. *Nucleic Acids Research* 40 (12), p. 5679-5693.



Schematic view of TRAMP composition and the mechanism of exosome activation. TRAMP recognizes and binds aberrant RNAs via Air1/2p zinc knuckle domains (in blue), Trf4/5p (in orange) add short poly(A) tails, secondary structures are resolved by Mtr4p helicase (in green) and the tailed RNAs are targeted to exosome (in purple) for degradation. Modified from Holub and Vanacova, The Enzymes, Vol.31, 2012.

CONTENT OF RESEARCH

Recent advances in high-throughput technologies have allowed the identification of a vast range of new types of RNAs and RNA modifications. The next step is to understand if there are any functional consequences of their production.

RNA is essential for cell survival. It is not only a messenger between the genomes and proteomes but also carries out or participates in many functions such as RNA processing and protein translation, acting as structural scaffolds, transporters, gene regulators and biocatalysts. Eukaryotic cells produce diverse types of RNAs. Most, if not all, are synthesized in a form of a precursor that needs to be post-transcriptionally processed and/or modified in order to form mature functional molecules. In yeast, nuclear RNA maturation and stability is under the strict control of RNA surveillance by the nuclear exosome and its cofactors the TRAMP4 and TRAMP5 noncanonical polyadenylation complexes and the Nrd1 RNA binding complex.

We aim to clarify the molecular mechanisms underlying RNA quality control and degradation in eukaryotic cells through investigation of the detailed biochemical principles of RNA recognition, processing and degradation. These include (1) in-depth characterization of the biochemistry of the yeast TRAMP4 and similar complexes in mammalian cells; (2) identification of new RNA substrates by combination of in vivo crosslinking, immunoprecipitation and high-throughput sequencing and study of the functional consequences of their targeting; (3) structural and biochemical characterization of proteins involved in the recognition of aberrant RNAs in eukaryotic cells.

Nanobiotechnology

Assoc. Prof. RNDr. Petr Skládal, CSc.

Research Group Leader

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RESEARCH AREAS

- Imaging of biomolecules, cells and biosensor interfaces using scanning probe microscopies (AFM, SNOM, STM, SECM)
- Biointeractions studied at the molecular level (AFM force robot) and in real time (piezosensors, surface plasmon resonance)
- Bio-electronic systems – behaviour of natural and chemically modified biomacromolecules at electrical surfaces linked to electrochemical biosensors and bioassays
- Immobilization, modification, conjugation and separation of biomolecules and fluorescent nanoparticles

MAIN OBJECTIVES

- Multidisciplinary research in the field of bioanalytical chemistry, advanced biosensor technologies and nanobiotechnologies, and the application of the obtained know-how to real problems in healthcare, food production and environmental control
- Visualization and modification of biological objects – the structure and interactions of biomacromolecules in relation to the functions of living systems, disease and therapy

Selected Publications

SKLADAL P., KOVAR D., KRAJICEK V., SISKOVA P., PRIBYL J., SVABENSKA E. 2013. Electrochemical immunosensors for detection of microorganisms. *International Journal of Electrochemical Science* 8 (2), p. 1635-1649.

FOHLEROVA Z., TURANEK J., SKLADAL P. 2012. The cell adhesion and cytotoxicity effects of the derivate of vitamin E compared for two cell lines using a piezoelectric biosensor. *Sensors and Actuators B-chemical* 174, p. 153-157.

LACINA K., VONDAL J., SKLADAL P. 2012. A novel approach to the uniform distribution of liquid in multi-channel (electrochemical) flow-through cells. *Analytica Chimica Acta* 727, p. 41-46.

HLAVACEK A., SKLADAL P. 2012. Isotachophoretic purification of nanoparticles: Tuning optical properties of quantum dots. *Electrophoresis* 33 (9-10), p. 1427-1430.

CONTENT OF RESEARCH

The characterisation of biomolecules and affinity interactions using scanning probe microscopies and advanced biosensors, and the development of bioanalytical devices.

The Nanobiotechnology research group utilises advanced scanning probe microscopic techniques, nanolithographic manipulation and various artificial nanostructures applied for either visualization or modification of biological objects including tissues, cells, cellular structures and biomolecules. The unique opportunity to touch a single individual molecule of the protein or nucleic acid with the scanning tip provides high-resolution sub-nanometre and 3-dimensional images providing details in the native state. These approaches are currently revolutionizing many fields of biology, biophysics and biochemistry and provide innovative results and methodologies for application in healthcare - nanobiosensing systems, nanoparticles for visualisation and the smart distribution of drugs (nanomedicine).

Imaging of biosurfaces and biomolecules using scanning probe microscopies

Atomic force microscopy (AFM) scanning in both dry state and in liquids in non-contact (tapping) mode. Modified tips allow characterisation of surface hydrophobicity and specific target molecules and cellular surfaces (tips modified with antibodies) to be imaged while conductive tips with applied potential serve for bioelectrochemical studies. Repeated scans provide movement and morphological changes of cells. Supplementary information on cells and cellular elements results from scanning near optical field microscopy (SNOM, overcoming the diffraction limit) and scanning tunnelling microscopy (STM) is chosen when atomic resolution of bio-electronic interfaces is required.

Biosensors and advanced bioanalytical systems

Development of advanced bioelectronic systems closely linked to information technologies and smart processing algorithms. Electrochemical, piezoelectric and optical biosensors for health care, military and food analysis. Nanobiosensors – cantilever as nanomechanical transducer bending due to the affinity interaction or biomechanical events. Nanoarrays – biochips consisting of sets of specific recognition proteins (antibodies, engineered receptors and enzymes, artificial recognition molecules). Microfluidics for biosensing and separations, ink-jet based spotting technologies.

Biomolecular NMR Spectroscopy

Prof. RNDr. Vladimír Sklenář, DrSc.
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RESEARCH AREAS

- NMR methodology (fast acquisition, non-linear sampling, *ab initio* calculations of NMR parameters)
- *In vivo/in vitro* 3D structure determination of proteins and nucleic acids
- Relaxation studies of biomolecular dynamics in complex systems
- Structural characterization of small, biologically interesting molecules

MAIN OBJECTIVES

- Development of new methodologies for investigating the structures, interactions, and dynamics of biomolecules
- Investigation into the structure and interactions of biomacromolecules and how they relate to the functions of living systems, diseases and therapies

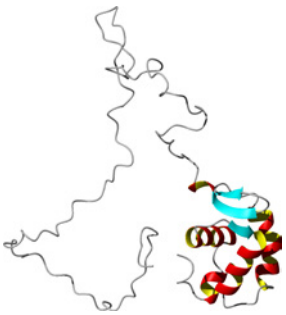
Selected Publications

NOVACEK J., JANDA L., DOPITOVA R., ZIDEK L., SKLENAR V. 2013. Efficient protocol for backbone and side-chain assignments of large intrinsically disordered proteins: transient secondary structure analysis of 49.2 kDa microtubule associated protein 2c. *Journal of Biomolecular NMR* 56 (4), p. 291-301.

PRECECHTELOVA J., MUNZAROVA M., VAARA J., NOVOTNY J., DRACINSKY M., SKLENAR, V. 2013. Toward Reproducing Sequence Trends in Phosphorus Chemical Shifts for Nucleic Acids by MD/DFT Calculations. *Journal of Chemical Theory and Computation* 9 (3), p. 1641-1656.

NOVOTNY J., KULHANEK P., MAREK R. 2012. Biocompatible Xanthine-Quadruplex Scaffold for Ion-Transporting DNA Channels. *Journal of Physical Chemistry Letters* 3 (13), p. 1788-1792.

NOVACEK J., ZAWADSKA-KAZIMIERCZUK A., PAPOUSKOVA V., ZIDEK L., KOZMINSKI W., SKLENAR, V. 2011. 5D ^{13}C-detected NMR experiments for backbone assignment of unstructured proteins with a very low signal dispersion. *Journal of Biomolecular NMR* 50 (1) p. 1-11.



3D structure of the delta subunit of RNA polymerase from *Bacillus subtilis* including a disordered C-terminal tail determined by NMR spectroscopy.

CONTENT OF RESEARCH

The progress of structural biology over the past decade has been closely linked to the development of new methods providing detailed information about spatial structure and temporal phenomena in biomolecular systems.

Nuclear Magnetic Resonance (NMR) is one of the prominent methods for the study of the structure and dynamics of complex biomacromolecular systems at atomic resolution. NMR can be used to rapidly assess the conformational properties of proteins and nucleic acids, both *in vitro* and *in vivo*, and to identify their functional states. Contemporary NMR methodology supplies information providing an insight into the delicate interplay of interatomic forces governing the formation of biomolecular complexes involved in essential cellular processes. Methodological developments will improve the efficiency and throughput of NMR data collection routines and will optimise computational protocols for data processing, structural calculations of proteins and protein-nucleic acid complexes, and interpretation of NMR relaxation data in terms of molecular motions. The newly introduced NMR tools will meet the requirements for experimentally addressing biological samples with limited stability, for studying biological processes that occur on very fast time scales (protein folding, RNA folding in regulation, enzyme kinetics) and for investigating large, multimeric complexes between proteins, nucleic acids and various ligands. The new developments will be applied to study proteins, nucleic acids and their assemblies as well as small molecules including potential drugs of particular interest for projects embedded in work packages of the Structural Biology research programme and other CEITEC life science programmes.

STRUCTURAL BIOLOGY

RNA-based Regulation of Gene Expression

Mgr. PharmDr. Peter Lukavsky
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RESEARCH AREAS

- The molecular principles of post-transcriptional regulation of gene expression through alternative splicing, RNA transport and translational control
- 3D structure determination of large RNAs and RNA-protein complexes by solution NMR spectroscopy
- Biochemical and biophysical studies of RNA-protein interactions
- Development of novel purification methods and isotope labelling schemes for NMR studies of large RNAs and their assemblies

MAIN OBJECTIVES

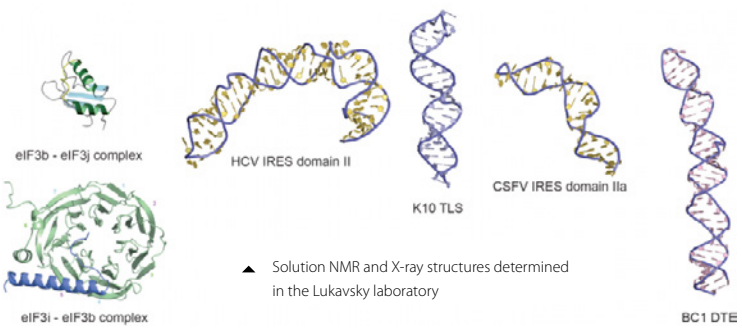
- The molecular basis of spatial and temporal control of gene expression through directed RNA transport in dendrites and during development
- Investigation of molecular principles of RNA-protein interaction networks regulating alternative mRNA splicing of disease-related genes
- Advancing the size of RNAs and their assemblies amenable to solution NMR studies

Selected Publications

LIU Y., SALTER H.K., HOLDING A.N., JOHNSON C.M., STEPHENS E., LUKAVSKY P.J., WALSHAW J., BULLOCK S.L. 2013. Bicaudal-D uses a parallel, homodimeric coiled coil with heterotypic registry to coordinate recruitment of cargos to dynein. *Genes & Development* 27 (11), p. 1233-1246.

HERRMANNOVA A., DAUJOTYTE D., YANG J.C., CUCHALOVA L., GORREC F., WAGNER S., DANYI I., LUKAVSKY P.J., VALASEK L.S. 2012. Structural analysis of an eIF3 subcomplex reveals conserved interactions required for a stable and proper translation pre-initiation complex assembly. *Nucleic Acids Research* 40 (5), p. 2294-2311.

BULLOCK S.L., RINGEL I., ISH-HOROWICZ D., LUKAVSKY P.J. 2010. A'-form RNA helices are required for cytoplasmic mRNA transport in Drosophila. *Nature Structural & Molecular Biology* 17 (6), p. 703-709.



▲ Solution NMR and X-ray structures determined in the Lukavsky laboratory

CONTENT OF RESEARCH

Complex RNA-protein networks regulate post-transcriptional gene expression and any imbalance can lead to disease. Deepening our molecular understanding of these regulatory networks is therefore essential for opening novel approaches to curing diseases.

Regulatory RNA elements determine the protein sequence through alternative pre-mRNA splicing and control temporal and spatial patterns of protein synthesis. These mechanisms ensure the protein diversity of complex organisms and their expression at the right time and in the right place within the cell. This compositional, spatial and temporal control of gene expression is tightly regulated and deregulation often leads to human disease.

We aim to unravel the molecular principles governing the post-transcriptional regulation of gene expression. Using NMR spectroscopy, we study RNA-protein (RNP) interaction networks regulating alternative splicing of disease-related genes and RNA elements and their protein assemblies crucial for the control of protein synthesis in the cytoplasm. With the excellent high-field NMR equipment in place at CEITEC, we are in a good position to tackle these large biological RNP systems. Our NMR structural work is always complemented with biochemistry, x-ray crystallography, other biophysical methods and cell biology to create a comprehensive molecular description of RNP function. Failure to properly splice mRNAs or to transport them into the right cellular compartment can lead to impairment of memory formation and severe human diseases. Molecular insights into mechanisms governing RNA-based regulation of gene expression are therefore fundamentally important for understanding neurobiology, neurological disorders and human disease, and are crucial for the development of successful therapies in the future.

Structural Biology of Gene Regulation

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RESEARCH AREAS

- Protein-RNA and protein-protein interactions and their roles in the regulation of gene expression
- 3'-end processing, transcription termination, cross-talk between chromatin and Pol II machinery

MAIN OBJECTIVES

- Investigation of the role of RNA in gene expression, development and human diseases
- Establishing an isotope laboratory for NMR studies and the development of new strategies for the preparation of isotopically-labelled proteins in eukaryotic cells

Selected Publications

KUBICEK K., CERNA H., HOLUB P., PASULKA J., HROSSOVA D., LOEHR F., HOFR C., VANACOVA S., STEFL R. 2012. Serine phosphorylation and proline isomerization in RNAP II CTD control recruitment of Nrd1. *Genes & Development* 26 (17), p. 1891-1896.

PORRUA O., HOBOR F., BOULAY J., KUBICEK K., D'AUBENTON-CARAFA Y., GUDIPATI R.K., STEFL R., LIBRI D. 2012. In vivo SELEX reveals novel sequence and structural determinants of Nrd-1-Nab3-Sen1-dependent transcription termination. *EMBO Journal* 31 (19), p. 3935-3948.

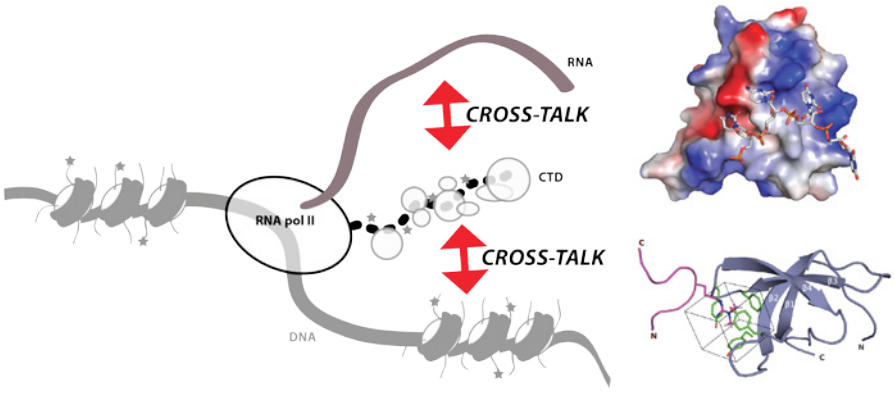
SIKORSKY T., HOBOR F., KRIZANOVA E., PASULKA J., KUBICEK K., STEFL R. 2012. Recognition of asymmetrically dimethylated arginine by TDRD3. *Nucleic Acids Research* 40 (22), p. 11748-11755.

STEFL R., OBERSTRASS F.C., HOOD J.L., JOURDAN M., ZIMMERMANN M., SKRISOVSKA L., MARIS C., PENG L., HOFR C., EMESON R.B., ALLAIN F.H. 2010. The solution structure of the ADAR2 dsRBM-RNA complex reveals a sequence-specific readout of the minor groove. *Cell* 143 (2), p. 225-237.

CONTENT OF RESEARCH

Integrated structural biology seeks to provide a complete and coherent picture of how RNA polymerase II cross-talks to chromatin and RNA processing machinery at the atomic level.

RNA is essential for cell survival. Not only is it a messenger between the genomes and proteomes but it also carries out, or participates in, many functions such as RNA processing and protein translation, acting as structural scaffolds, transporters, gene regulators and biocatalysts. We will help to clarify molecular mechanisms underlying RNA quality control in eukaryotic cells through the investigation of the detailed biochemical principles of RNA recognition, processing and degradation. We will use a combination of biochemical, genetic, and structural methods to unravel the molecular mechanism of eukaryotic RNA surveillance.



Example of structural biology investigation of RNA polymerase II cross-talks with chromatin and RNA processing machinery at the atomic level.

Structural Virology

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RESEARCH AREAS

- X-ray crystallography of proteins, macromolecular complexes, and icosahedral viruses
- Cryo-electron microscopy and single particle reconstruction of viruses in complexes with antibodies or cellular receptors
- Cryo-electron tomography of virus cell entry, replication, and assembly intermediates

MAIN OBJECTIVE

- To obtain a structural understanding of virus life-cycles and use it to develop anti-viral therapies

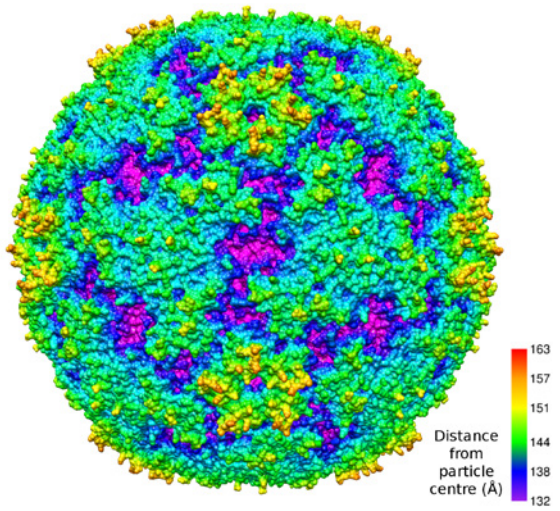
Selected Publications

PLEVKA P.*, PERERRA R.*, YAP M.L., CARDOSA J., KUHN R.J., ROSSMANN M.G. 2013. Structure of human enterovirus 71 in complex with a capsid binding inhibitor. *Proceedings of the National Academy of Sciences of the United States of America* 110 (14), p. 5463-5467.

PLEVKA P., PERERA R., CARDOSA J., KUHN R.J. 2012. Crystal Structure of the Hand, Foot, and Mouth Disease Virus, Enterovirus 71. *Science* 336 (6086), p. 1274.

PLEVKA P., BATTISTI A.J., JUNJHON J., WINKLER D.C., HOLDAWAY H.A., KEELAPANG P., SITTISOMBUT N., KUHN R.J., STEVEN A.C., ROSSMANN M.G. 2011. Maturation of flavi viruses starts from one or more icosahedrally independent nucleation centers. *EMBO Reports* 12 (6), p. 602-606.

* these authors contributed equally



Molecular surface rendering of human enterovirus 71 (EV71). The picture is based on an all atom model of the EV71 capsid. The surface is coloured according to the distance from the virus centre (valleys are purple, mountains are red).

CONTENT OF RESEARCH

Viruses are the smallest self-replicating organisms. Even though individually viruses are rather simple, as a group they are exceptionally diverse in both replication strategies and structures. Many viruses are important human pathogens.

We use X-ray crystallography, cryo-electron microscopy, and molecular biology to study the life cycle of human viruses. We investigate macromolecular interactions associated with virus cell entry, genome replication, assembly, and maturation. Viruses are simple enough that we can aspire to understand their biology at a molecular level. Our efforts are directed towards using structural information for the development of anti-viral drugs and vaccines.

Our research is focused on three projects:

01 Rhinoviruses and Enteroviruses that usually cause the common colds, but may induce more serious symptoms such as foot, hand, and mouth disease or life-threatening encephalitis.

02 Viruses from the iflaviridae and dicistroviridae families that infect honeybees and contribute to the collapse of honeybee colonies.

03 Leishmania RNA Virus 1 that infects Leishmania and enables the parasite to evade the human immune system. This results in a more serious form of the human disease leishmaniasis.

Structure and Dynamics of Nucleic Acids

Prof. RNDr. Jiří Šponer, DrSc.
Research Group Leader

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RESEARCH AREAS

- Studies of structure, dynamics and molecular interactions of RNA molecules using explicit solvent molecular dynamics simulations and quantum chemistry
- Studies of canonical and noncanonical DNA molecules
- Quantum chemical modelling of processes relevant to the prebiotic synthesis of nucleic acid components
- Testing and refinement of force fields for atomistic simulations of nucleic acids
- Application of large-scale quantum chemical calculations to nucleic acids

MAIN OBJECTIVES

- Investigation of the role of RNA and DNA in development and human diseases
- Development of new methodologies for investigating the structure, interactions, and dynamics of biomolecules
- Providing an interdisciplinary bridge between modern physical chemistry and structural biology of nucleic acids

Selected Publications

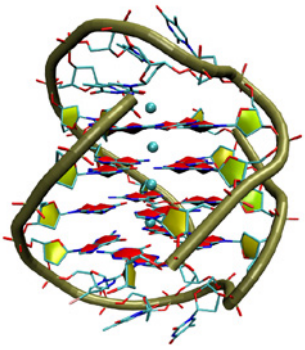
STADLBAUER P., KREPL M., CHEATHAM T.E., KOCA J., SPONER J. 2013. Structural dynamics of possible late-stage intermediates in folding of quadruplex DNA studied by molecular simulations. *Nucleic Acids Research* 41 (14), p. 7128-7143.

SPONER J., MLADEK A., SPACKOVA N., CANG X., CHEATHAM T.E., GRIMME S. 2013. Relative stability of different DNA guanine quadruplex stem topologies derived using large-scale quantum-chemical computations. *Journal of the American Chemical Society* 135 (26), p. 9785-9796.

FERUS M., CIVIS S., MLADEK A., SPONER J., JUHA L., SPONER J.E. 2012. On the Road from Formamide Ices to Nucleobases: IR-Spectroscopic Observation of a Direct Reaction between Cyano Radicals and Formamide in a High-Energy Impact Event. *Journal of the American Chemical Society* 134 (51), p. 20788-20796.

SPONER J., CANG X., CHEATHAM T.E. 2012. Molecular dynamics simulations of G-DNA and perspectives on the simulation of nucleic acid structures. *Methods* 57 (1), p. 25-39.

Example of a cation-stabilized structure of quanine quadruplex (G-DNA) molecule.



CONTENT OF RESEARCH

Due to fast development of hardware and software, computational methods are becoming an established tool that efficiently complements experimental studies of nucleic acids.

Computational studies, combining a full range of leading computational methods (explicit solvent molecular dynamics simulations, quantum-chemical calculations, hybrid quantum-classical calculations and bioinformatics), are used to study nucleic acids. The work deals with ribosomal RNAs, ribozymes and some other classes of RNAs, and is gradually extended to protein-RNA complexes. We analyse chemical reactions to capture atomistic picture of catalytic strategies of ribozymes and to model prebiotic chemical reactions using modern electronic structure methods. Extended studies are carried out on selected DNA systems, mainly to understand the role of sequence-dependency of B-DNA structure and the principles of folding of quadruplex DNA. Modern computational techniques fill specific gaps in the present knowledge of the DNA and RNA function. We classify DNA and RNA building blocks and their molecular interactions, to unravel the link between their physical-chemical properties and evolutionary patterns. Much effort is devoted to the development and verification of computational methods, including parameterisation of simulation force fields.

Structure and Interaction of Biomolecules at Surfaces

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Research Group Leader

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RESEARCH AREAS

- The interactions of natural and chemically modified biopolymers with electrodes, and the relationships between biopolymer structure and its electrochemical, interfacial and electrocatalytic properties
- Novel techniques in biopolymer labelling
- Effects of DNA and/or protein chemical modification on biopolymer molecular recognition features
- Development of novel bioanalytical/bioelectroanalytical and diagnostic tools

MAIN OBJECTIVES

- Investigations into the behaviour of natural and chemically modified biomacromolecules at electrically charged surfaces linked to the development of novel electrochemical biosensors and bioassays
- The development of new techniques of biopolymer labelling
- Studies of the relations between nucleic acids structure, their chemical modifications and biorecognition properties
- The development of novel electrochemical biosensors, bioassays and diagnostic approaches

Selected Publications

HOCEK M., FOJTA M. 2011. Nucleobase modification as redox DNA labelling for electrochemical detection. *Chemical Society Reviews* 40 (12), p. 5802-5814.

BRAZDOVA M., NAVRATILOVA L., TICHY V., NEMCOVA K., LEXA M., HRSTKA R., PECINKA P., ADAMIK M., VOJTESEK B., PALECEK E., DEPPERT W., FOJTA M. 2013. Preferential Binding of Hot Spot Mutant p53 Proteins to Supercoiled DNA In Vitro and in Cells. *PLoS ONE* 8 (3), e59567.

MENOVA P., CAHOVA H., PLUCNARA M., HAVRAN L., FOJTA M., HOCEK M. 2013. Polymerase synthesis of oligonucleotides containing a single chemically modified nucleobase for site-specific redox labelling. *Chemical Communications* 49 (41), p. 4652-4654.

DADOVA J., ORSAG P., POHL R., BRAZDOVA M., FOJTA M., HOCEK M. 2013. Vinylsulfonamide and Acrylamide Modification of DNA for Cross-linking with Proteins. *Angewandte Chemie International Edition* 52 (40), p. 10515-10518.

CONTENT OF RESEARCH

Electrochemical detection has recently been utilized for various analytical applications, including the detection of DNA damage, sequence-specific DNA sensing, probing DNA interactions with drugs, etc. The recent literature reflects a remarkable boom in the development of electrochemical biosensors and bioassays, with a considerable contribution by the group.

Interactions of nucleic acids, proteins and their components with/at electrically charged surfaces is studied by the group in detail with respect to nucleotide/aminoacid composition/sequence and secondary, tertiary or higher-order structures. Novel techniques of biopolymer labelling are being developed to design new bioanalytical and diagnostic tools. Various techniques are used, including the enzymatic incorporation of labelled nucleotides into nucleic acids using enzymes and the direct chemical modification of natural nucleic acids and their synthetic analogues using oxoosmium complexes. Modified nucleic acids are studied in detail with regard to the effects of site-specific, terminal or global modification on their molecular recognition features (such as DNA hybridization, mismatch sensitivity and protein-DNA recognition). Sensitive electrochemical or other detection techniques are being developed using label-specific analytical signals. The strong interdisciplinary expertise of the group is being exploited to efficiently link biochemical, biophysical and electrochemical studies of model biomolecules with practical applications in real biological systems.

Computational Chemistry

Prof. RNDr. Jaroslav Koča, DrSc.
Research Group Leader

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RESEARCH AREAS

- The structure and dynamics of proteins, nucleic acids, saccharides, and their complexes in relationship to their biological function
- Mechanistic studies on enzymatic reactions
- Chemoinformatics and structural bioinformatics
- The structure and dynamics of supramolecular complexes

MAIN OBJECTIVES

- To study the therapeutic and bioanalytical aspects of recognition and adhesion phenomena in host-pathogen interactions
- To develop new methodologies for investigating the structure, interactions, and dynamics of biomolecules
- New tools for structural bioinformatics and chemoinformatics
- The development of soft matter models and the understanding of self--assembled bimolecular systems

Selected Publications

VACHA R., MARTINEZ-VERACOECHEA F.J., FRENKEL D. 2012. Intracellular Release of Endocytosed Nanoparticles upon a Change of Ligand-Receptor Interaction. *ACS Nano* 6 (12), p.10598-10605.

TVAROSKA I., KOZMON S., WIMMEROVA M., KOCA J. 2012. Substrate-Assisted Catalytic Mechanism of O-GlcNAc Transferase Discovered by Quantum Mechanics/Molecular Mechanics Investigation. *Journal of the American Chemical Society* 134 (37), p. 15563-15571.

BERKA K., HANAK O., SEHNAL D., BANAS P., NAVRATILOVA V., JAISWAL D., IONESCU C.-M., SVOBODOVA VAREKOVA R., KOCA J., OTYEPKA M. 2012. MOLEonline 2.0: Interactive Web-based Analysis of Biomacromolecular Channels. *Nucleic Acids Research* 40 (W1), p. W222–W227.

MISHRA S.K., ADAM J., WIMMEROVA M., KOCA J. 2012. In Silico Mutagenesis and Docking Study of Ralstonia solanacearum RSL Lectin: Performance of Docking Software to Predict Saccharide Binding. *Journal of Chemical Information and Modeling* 52 (5), p. 1250-1261.

CONTENT OF RESEARCH

Computational chemistry helps to interpret experimental observations or to get new information about systems where experimental approaches are not applicable or difficult to apply. It is widely employed in, for example, design and studies on new molecules with a possible biological impact.

Protein/carbohydrate interactions play an important role in the recognition of host cells by several pathogenic bacteria; thus their understanding can be helpful in the development of new glycomimetics (antibiotics) against these pathogens. We employ molecular dynamics, docking, virtual screening and free energy calculation methods to study the mechanism of these interactions, complemented by high level QM methods to evaluate, for example, CH-π interactions between proteins and carbohydrates.

To understand the behaviour of biomolecular systems on significantly larger time scales than is possible with the full atom description we develop **coarse-grained methods** that can help to understand the self-assembly of rod-like molecules (peptides, carbon nanotubes) and their interaction with lipid membranes.

We are also developing **methods for free energy calculations** and use them to identify reaction pathways in enzymatic reactions where glycosyltransferases or endonucleases are involved, and to calculate free energies of supramolecular complexes that are then compared with experimental (e.g. NMR) data.

In the field of **structural bioinformatics and chemoinformatics** we focus on the development of software tools for searching for tunnels and cavities in biomacromolecules and calculation of their physico-chemical properties. Such spots are often responsible for the biological activity of the biomacromolecules and recognizing them may uncover important candidates for targeting drugs.

GENOMICS AND PROTEOMICS OF PLANT SYSTEMS

The research programme is focussed on understanding of evolution-based developmental strategies of plant systems to promote their applications in next-generation technologies and medicine.

Research Programme Coordinator:
Jiří Fajkus | jiri.fajkus@ceitec.muni.cz

OVERALL GOAL

Plants present a unique experimental system due to their enormous genome plasticity and the naturally totipotent character of their cells which makes it possible to regenerate the whole organism from a single cell easily and without ethical problems. The developmental outcomes of molecular manipulations can thus be studied at the level of whole organisms.

RESEARCH DIRECTIONS

- Genome, karyotype and chromosome evolution; the role of repetitive DNA in genome dynamics; the structure, evolution and maintenance of telomeres and their role in chromosome stability and plant speciation; epigenetic regulations
- Molecular mechanisms governing hormonal regulations and their role in plant development and stress response; developmental outputs of subcellular protein trafficking and cell polarity will be established
- Metabolic profiling approaches for understanding and exploitation of plant secondary metabolites; using bacterial metabolomics as a model for systems biology; metabolite biomarkers for diagnostics; the development of a miniaturised drug metabolism system based on capillary electrophoresis (CE)
- To provide access to state-of-the-art technologies based on shared resources and highly trained staff in proteomics; the development of novel techniques for the separation and analysis of nucleic acids, proteins, small bioactive molecules & drugs and their complexes based on electrophoretic and microfluidic systems, electrochemical and optical methods and nanotechnologies

RESEARCH GROUPS | LEADERS

Bioanalytical Instrumentation | *František Foret*

Plant Cytogenomics | *Martin A. Lysák*

Functional Genomics and Proteomics of Plants | *Jan Hejátko*

Hormonal Crosstalk in Plant Development | *Eva Benková*

Metabolomics | *Zdeněk Glatz*

Proteomics | *Zbyněk Zdráhal*

Developmental and Cell Biology of Plants | *Jiří Friml*

Chromatin Molecular Complexes | *Jiří Fajkus*

Developmental and Production Biology - Omics Approaches | *Břetislav Brzobohatý*

Plant Stress Signalling and Adaptation | *Vanesa Tognetti*

Plant Molecular Biology | *Karel Říha*

Bioanalytical Instrumentation

Ing. František Foret, CSc.
Research Group Leader
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RESEARCH AREAS

- Capillary separations
- Mass spectrometry coupling
- Miniaturisation
- Breath analysis

MAIN OBJECTIVES

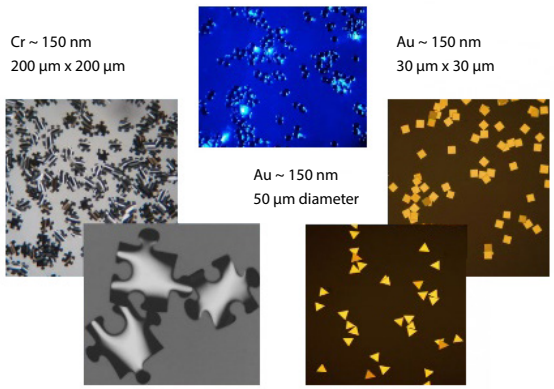
- The development of new techniques for the separation and analysis of biomolecules & drugs
- System miniaturization using microfluidics and nanotechnologies

Selected Publications

KUBAN P., FORET F. 2013. Exhaled breath condensate: Determination of non-volatile compounds and their potential for clinical diagnosis and monitoring. *Analytica Chimica Acta.* (in press)

KUBAN P., FORET F., BOCEK R. 2013. Capillary electrophoresis with contactless conductometric detection for rapid screening of formate in blood serum after methanol intoxication. *Journal of Chromatography A* 1281, p. 142-147.

JUSKOVA P., NEUZIL P., MANZ A., FORET F. 2013. Detection of electrochemiluminescence from floating metal platelets in suspension. *Lab on a Chip* 13 (5), p. 781-784.



Structured metal nanosheets under development for sample preconcentration and detection.

CONTENT OF RESEARCH

Faster, cheaper, more sensitive – exploration of new ways for achieving enhancements in resolution, sensitivity and selectivity of analyses is the key part of current developments in (bio)analytical chemistry.

With advances in biology, medicine and related fields there is also a growing need for new analytical techniques and protocols. This is clearly seen especially in the –omics areas where a large number of components have to be separated and detected, often in miniscule samples down to single cell level. The utilization of theoretical and instrumental approaches for the development and applications of microfluidics, nanotechnologies and novel chemistries is the key to success. The research of this group is focused on novel techniques for the separation and analysis of nucleic acids, proteins, small bioactive molecules, drugs and their complexes using separation (electrophoretic, chromatographic) and microfluidic systems coupled with electrochemical, optical and mass spectrometric methods. Besides microseparation, new combinations of microfluidic chips with structured nanoparticles are also in development. In addition computer simulations are also performed for optimization of the microfluidic structures.

Plant Cytogenomics

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Research Group Leader
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RESEARCH AREAS

- Karyotype and genome evolution in plants
- Chromosome rearrangements in speciation
- Whole-genome duplications (polyploidy)
- Chromosome structure
- Evolution of repetitive DNA
- Comparative and evolutionary phylogenomics
- Molecular phylogenetics

MAIN OBJECTIVES

- Analysis of chromosome and genome collinearity using comparative molecular cytogenetics and sequence genomics methods
- Investigations into the evolution of chromosome complements (karyotypes) in land plants
- Understanding the role of chromosome repatterning and whole-genome duplication events in genome evolution and speciation

Selected Publications

MANDAKOVA T., KOVARIK A., ZOZOMOVA-LIHOVA J., SHIMIZU-INATSUGI R., SHIMIZU K.K., MUMMENHOFF K., MARHOLD K., LYSAK M.A. 2013. The more the merrier: recent hybridization and polyploidy in *Cardamine*. *Plant Cell* 25 (9), p. 3280-3295.

CHENG F., MANDAKOVA T., WU J., XIE Q., LYSAK M.A., WANG X. 2013. Deciphering the diploid ancestral genome of the mesohexaploid *Brassica rapa*. *Plant Cell* 25 (5), p. 1541-1554.

LONG Q., RABANAL F.A., MENG D., HUBER C.D., FARLOW A., PLATZER A., ZHANG Q., VILHJALMSSON B.J., KORTE A., NIZHYNSKA V., VORONIN V., KORTE P., SEDMAN L., MANDAKOVA T., LYSAK M.A., SEREN U., HELLMANN I., NORDBORG M. 2013. Massive genomic variation and strong selection in *Arabidopsis thaliana* lines from Sweden. *Nature Genetics* 45 (8), p. 884-890.

SCHUBERT I., LYSAK M. A. 2011. Interpretation of karyotype evolution should consider chromosome structural constraints. *Trends in Genetics* 27 (6), p. 207-216.

SLOTTE T., HAZZOURI K. M., ÅGREN J. A., KOENIG D., MAUMUS F., GUO Y., STEIGE K., PLATTS A. E., ESCOBAR J. S., NEWMAN L. K., WANG W., MANDAKOVA T., VELLO E., SMITH L. M., STEFFEN J., TAKUNO S., BRANDVAIN Y., COOP G., ANDOLFATTO P., HU T. T., BLANCHETTE M., CLARK R. M., QUESNEVILLE H., NORDBORG M., GAUT B. S., LYSAK M. A., JENKINS J., GRIMWOOD J., CHAPMAN J., PROCHNICK S., SHU S., ROKHSAR D., SCHMUTZ J., WEIGE D., WRIGHT S. I. 2013. The *Capsella rubella* genome and the genomic consequences of rapid mating system evolution. *Nature Genetics* 45 (7), p. 831–835.

CONTENT OF RESEARCH

Evolutionary plant genomics is an expanding research field quickly implementing newly available methodologies and resources. Combining whole-genome sequencing, genetic mapping, cytogenetics and phylogenetics has made possible a quantum leap in the study of plant genomes.

The overarching objective of the Plant Cytogenomics group is to document, analyse and compare genome structure across the plant kingdom at different levels of complexity: (i) DNA level (genome size, repetitive elements), (ii) chromosomal level (chromosome collinearity, karyotype evolution), (iii) whole-genome level (genome collinearity, polyploidy), (iv) species level (molecular phylogenetic frameworks, paleobiogeography). We focus on comparative cytogenomics in species and plant groups with contrasting genome features, sequenced genomes and robust phylogenetic frameworks. The prime focus of our research is the comparative and evolutionary genomics of the mustard family (crucifers, Brassicaceae). Our research concentrates on understanding (i) the extent of chromosome and genome collinearity between species, (ii) the role of chromosome rearrangements in diversification and speciation, (iii) the impact of whole-genome duplication events on genome structure and cladogenesis, and (iv) the chromosome organization and dynamics of repetitive elements. Several collaborative projects in the laboratory are concentrating on the construction of comparative cytomolecular maps to assist whole-genome assembly efforts in sequenced crucifer genomes.

Functional Genomics and Proteomics of Plants

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RESEARCH AREAS

- Role of cytokinins in vascular tissue and root apical meristem formation and development
- Interaction of cytokinin and other hormones, particularly auxin and ethylene
- Interaction of cytokinins with light
- Structural basis of multistep phosphorelay signalling in plants

MAIN OBJECTIVES

- Determination of molecular mechanisms governing hormonal regulations and their functions in plant development
- Elucidating principles of hormonal and environmental signal integration
- Employing knowledge of the molecular mechanisms of multistep phosphorelay-based hormonal signalling in "green" biotechnologies and molecular breeding

Selected Publications

BENITEZ M., HEJATKO J. 2013. Dynamics of cell-fate determination and patterning in the vascular bundles of Arabidopsis thaliana. *PloS ONE* 8 (5), e63108.

ZDARSKA M., ZATLOUKALOVA P., BENITEZ M., SEDO O., POTESIL D., NOVAK O., SVACINOVA J., PESEK B., MALBECK J., VASICKOVA J., ZDRAHAL Z., HEJATKO J. 2013. Proteome analysis in Arabidopsis reveals shoot- and root-specific targets of cytokinin action and differential regulation of hormonal homeostasis. *Plant Physiology* 161 (2), p. 918-930.

PEKAROVA B., KLUMPLER T., TRISKOVA O., HORAK J., BORKOVCOVA P., JANSEN S., DOPITOVA R., PAPOUSKOVA V., NEJEDLA E., ZIDEK L., SKLENAR V., MAREK J., HEJATKO J., JANDA L. 2011. Dynamic structure and binding specificity of the receiver domain of sensor histidine kinase CKI1 from Arabidopsis thaliana. *Plant Journal* 67 (5), p. 827-839.

PERNISOVA M., KLIMA P., HORAK J., VALKOVA M., MALBECK J., SOUCEK P., REICHMAN P., HOYEROVA K., DUBOVA J., FRIML J., ZAZIMALOVA E., HEJATKO J. 2009. Cytokinins modulate auxin-induced organogenesis in plants via regulation of the auxin efflux. *Proceedings of the National Academy of Sciences of the United States of America* 106 (9), p. 3609-3614.

CONTENT OF RESEARCH

Plants have evolved a unique developmental and adaptation strategy based on postembryonic de novo organogenesis that is largely under hormonal control. Elucidating the molecular mechanisms of the hormone-driven regulation of the developmental plasticity of plant cells promises to uncover the fundamental mechanisms equilibrating cell division and differentiation.

The research group is interested in the hormonal regulation of plant development with an emphasis on the understanding of cytokinin (CK) signalling, action and interaction with other plant growth regulators.

Plant cells are well known for their tremendous developmental plasticity. Plant hormones, particularly auxins and CKs, were found to be major regulators of intrinsic developmental programmes associated with changes of differentiation status of plant cells and tissues. That allows *de novo* formation of an entire plant from virtually all types of specialised plant tissue. Identification of basic molecular principles involved in the regulation of plant cell division and differentiation will provide a developmental model useful in the identification of the corresponding regulatory and developmental events in other, including human, cell systems via comparative biology approaches.

We are particularly interested in the study of the following problems:

01 Interaction of auxin, cytokinins and ethylene in the processes of *de novo* organogenesis, regulation of root meristem patterning and vascular tissue development.

02 Elucidating the molecular determinants of specificity in multistep phosphorelay (MSP), with special emphasis on the role of MSP in CK signalling and CK/ethylene crosstalk.

03 Identification of molecular targets acting downstream from the CK signalling pathway and the role of gene regulatory networks constituting CK-dependent developmental circuits.

Hormonal Crosstalk in Plant Development

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RESEARCH AREAS

- The growth and development of plants are regulated by signalling substances such as plant hormones. In plants, interactions between hormonal pathways represent crucial factors that govern their actions. The molecular basis for hormonal crosstalk is largely unknown.
- The research group aims to identify the molecular and cellular mechanism(s) underlying the crosstalk of hormonal pathways in organogenesis and other plant developmental processes.
- The research group uses lateral root formation in Arabidopsis as an ideal experimental model to study the mechanisms of plant hormone action, the molecular basis of their interactions, and the role of these interactions in organogenesis.

MAIN OBJECTIVES

- **The convergence of hormonal pathways on transport-dependent auxin distribution upstream of lateral root formation:** Identification of key points in which auxin and other signalling pathways converge during lateral root formation and the molecular components involved in the process
- **The role of auxin-cytokinin interaction in lateral root formation:** Cell type-specific transcriptome analysis to investigate molecular events involved in auxin-cytokinin-regulated lateral root organogenesis
- **The identification of components of hormonal crosstalk by genetic approaches:** Mutant screens that will specifically target interactions between selected hormonal pathways
- **The formulation of general models for hormonal regulation of organogenesis:** The knowledge acquired on molecular networks and their mutual interactions in lateral root organogenesis will be used to mathematically model these processes and to extrapolate them onto other developmental situations

Selected Publications

MARHAVY P., VANSTRAELEN M., DE RYBEL B., ZHAOJUN D., BENNETT M.J., BEECKMAN T., BENKOVA E. 2013. Auxin reflux between the endodermis and pericycle promotes lateral root initiation. *EMBO Journal* 32 (1), p. 149-158.

BIELACH A., PODLESAKOVA K., MARHAVY P., DUCLERCQ J., CUESTA C., MÜLLER B., GRUNEWALD W., TARKOWSKI P., BENKOVA E. 2012. Spatiotemporal regulation of lateral root organogenesis in Arabidopsis by cytokinin. *Plant Cell* 24 (10), p. 3967-3981.

BIELACH A., DUCLERCQ J., MARHAVY P., BENKOVA E. 2012. Genetic approach towards the identification of auxin-cytokinin crosstalk components involved in root development. *Philosophical Transactions of the Royal Society B-Biological Sciences* 367 (1595), p. 1469-1478.

VANSTRAELEN M., BENKOVA E. 2012. Hormonal Interactions in the Regulation of Plant Development. *Annual Review of Cell and Developmental Biology* 28, p. 463-487.

CONTENT OF RESEARCH

The main focus of our research is on the understanding of molecular mechanisms and the principles underlying hormonal interactions in plants and the identification of key points in which hormonal signalling pathways converge to control plant growth and development.

Plants exhibit a unique developmental flexibility to ever changing environmental conditions. Post-embryonic initiation and the formation of new organs, a major determinant of the plant body architecture, are responsive to different environmental inputs such as light, temperature, and nutrition. Plant hormones are the important endogenous mediators that allow plants to rapidly adjust their development and growth to these external cues. Physiological and genetic studies have dissected the molecular components of signal perception and transduction of the individual hormonal pathways. However, over recent years it has become evident that hormones do not only act in an inert linear pathway. Hormonal pathways are interconnected by a complex network of interactions and feedback circuits, which determine the final outcome of the individual hormone actions. Thus, hormonal interactions generate an important additional level of complexity in the regulation of developmental processes and provide a network for feedback mechanisms balancing two key attributes of developmental systems: their robustness and stability on one side, and their dynamicity and flexibility on the other side. Understanding the molecular mechanisms underlying hormonal crosstalk and how these hormonal networks are established, maintained, and modulated throughout plant development represents a major challenge in the coming years for plant biology research.

Metabolomics

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RESEARCH AREAS

- Metabolomics
- Systems biology
- Biomarkers
- Drug metabolism
- Mass spectrometry
- Liquid chromatography
- Gas chromatography
- Capillary electrophoresis

MAIN OBJECTIVES

- Using bacterial, plant and stem cell metabolomics as models for systems biology
- Establishing metabolite biomarkers for disease diagnostics
- Development of a miniaturised drug metabolism system based on capillary electrophoresis

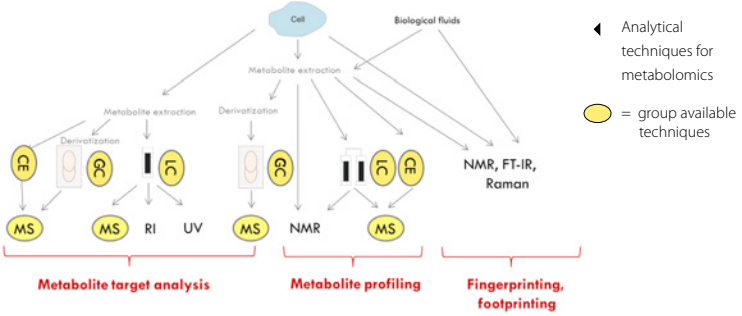
Selected Publications

MUSILOVA J., GLATZ Z. 2011. Metabolomics - Basic Concepts, Strategies and Methodologies. *Chemicke listy* 105 (10), p. 745-751. Awarded Hanus Prize for best publication of the year.

REMINEK R., PAUWELS J., WANG X., HOOGMARTENS J., GLATZ Z., VAN SCHEPDAEL A. 2013. Application of capillary electrophoresis for high-throughput screening of drug metabolism. In Carlos D. García, Karin Y. Chumbimuni-Torres, Emanuel Carrilho. *Capillary Electrophoresis and Microchip Capillary Electrophoresis: Principles, Applications, and Limitations.* p. 309-317.

REMINEK R., ZEISBERGEROVA M., LANGMAJEROVA M., GLATZ Z. 2013. A New Capillary Electrophoretic Method for On-line Screenings of Drug Metabolism Mediated by Cytochrome P450 Enzymes. *Electrophoresis* 34 (18), p. 2705-2711.

SALYKIN A., KUZMIC P., KYRYLENKO O., MUSILOVA J., GLATZ Z., DVORAK P., KYRYLENKO S. 2013. Nonlinear Regression Models for Determination of Nicotinamide Adenine Dinucleotide Content in Human Embryonic Stem Cells. *Stem Cell Reviews and Reports.* (in press)



CONTENT OF RESEARCH

Metabolomics is one of the newest "omics" in the field of systems biology. The subject of its study – the metabolome – is the complete set of metabolites that are present in cells under particular physiological or developmental circumstances.

Since the metabolites are downstream of all genome and proteome regulatory structures, they provide valuable information about the regulatory and catalytic properties of a gene product. In this consequence there is a growing interest in the application of metabolomics in functional genomics studies, for the detection of metabolic dysfunctions and diseases and for the study of drug metabolism.

The main analytical techniques employed for metabolomic studies are based on NMR spectroscopy and mass spectrometry (MS). Besides direct injection MS, this technique usually requires pre-separation of the metabolic components using either gas (GC) or liquid chromatography (LC). In addition to these well-established methodologies capillary electrophoresis (CE), even in combination with MS, is gaining a position in this field.

As a result the metabolomic research will be focused on three key outcomes:

01 Comprehensive development of metabolomic analytical tools for purpose of systems biology

02 New diagnostic tools based on metabolomic biomarker discovery for the detection of metabolic dysfunctions and diseases

03 High throughput analytical tools for drug development processes, especially for drug metabolism studies

All the above-mentioned analytical techniques should be applied for these research tasks.

Proteomics

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RESEARCH AREAS

- MS-based proteomics methodology
- Separation of complex protein mixtures
- Characterization of proteins and their modifications by mass spectrometry

MAIN OBJECTIVES

- Development of new methods for characterization of proteomes
- Application of MS-based proteomics in biomedical research

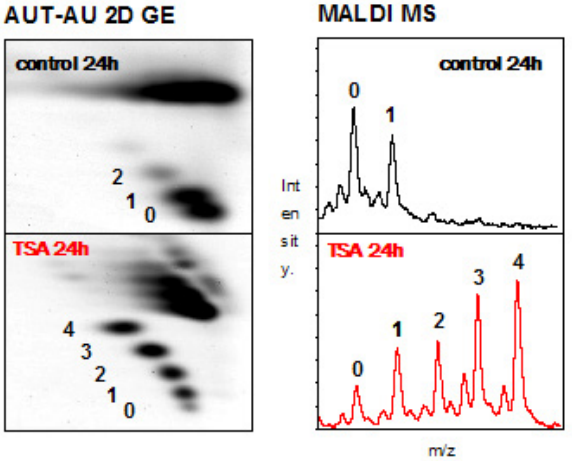
Selected Publications

STEJSKAL K., POTESIL D., ZDRAHAL Z. 2013. Suppression of Peptide Sample Losses in Autosampler Vials. *Journal of Proteome Research* 12 (6), p. 3057-3062.

KONECNA H., FRIDRICHOVA D., LOCHMANOVA G., BARTA J., ZDRAHAL Z. 2013. Preventing the mixed-detergent-micelle effect in two-dimensional electrophoresis on Tris-Tricine gels. *Electrophoresis* 34 (13), p. 1969-1971.

CINCAROVA L., LOCHMANOVA G., NOVAKOVA K., SULTESOVA P., KONECNA H., FAJKUSOVA L., FAJKUS J., ZDRAHAL Z. 2012. A combined approach for the study of histone deacetylase inhibitors. *Molecular BioSystems* 8 (11), p. 2937-2945.

SEDO O., VORAC A., ZDRAHAL Z. 2011. Optimization of mass spectral features in MALDI-TOF MS profiling of Acinetobacter species. *Systematic and Applied Microbiology* 34 (1), p. 30-34.



Separation of acetylated forms of intact histone H4 by 2D gel electrophoresis (AUT-AU) and MALDI MS spectra of N-terminal H4 fragments prior to and after histone deacetylase inhibitor treatment (Trichostatin A, 1 μM, 24 hrs.). Numbers in picture correspond to the acetylation number present in particular histone forms.

CONTENT OF RESEARCH

The uncovering of the molecular basis of cellular processes is intimately related to advances in proteomics methodology.

Proteomics is a dynamically evolving discipline enabling to enlarge our understanding of basic molecular mechanisms via the detailed characterization of proteomes. Our increasing knowledge in this field is strongly dependent on technological and methodological advances.

Our research interests are focused on MS-based proteomics including the development and optimization of techniques for protein isolation from various matrices, fractionation and separation of complex protein mixtures by chromatographic or electrophoretic methods, the qualitative and quantitative characterization of complex protein mixtures and protein modifications by mass spectrometry.

At present, we are participating in several research projects with diverse topics in areas of molecular biology, biomedicine and agriculture. Our roles within these projects include activities in the development and application of MALDI-MS profiling for taxonomic studies of selected bacterial genera and fungi, the characterization of differentially expressed proteins (e.g. plant proteins after hormonal treatment), the characterization of protein complexes, the characterization of posttranslational modifications such as phosphorylation, ubiquitination or histone acetylation (evaluation of changes in the histone acetylation state induced by selected histone deacetylase inhibitors), the characterization of groups of patatin proteins in different potato cultivars, and the search for potential disease biomarkers in blood plasma.

Developmental and Cell Biology of Plants

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RESEARCH AREAS

- Plants as sessile organisms must adapt to ever changing environmental conditions.
- The adaptation processes rely on the sensing and transduction of environmental signals, integration with endogenous signalling pathways and determination of the final response.
- The plant hormone auxin and its transport-mediated distribution are crucial for these adaptive developmental responses.

MAIN OBJECTIVES

- **Plant hormonal signalling for the regulation of cell polarity and subcellular dynamics:** The identification of key entry points by which auxin and other signalling pathways modulate subcellular dynamics and polar trafficking of PIN auxin transporters
- **Cell polarity and subcellular dynamics in plant cells:** Elucidation of the molecular and cellular mechanisms underlying cell polarity and trafficking processes by a combination of genetics and high resolution microscopy
- **Perception of external signals and their integration into subcellular dynamics and cell polarity:** Using a combination of reverse genetic, chemical genomics, live cell and high-resolution imaging approaches; we are gaining new insights into how the perception of gravity and light is integrated into the regulation of subcellular dynamics
- **Integration of hormonal signalling and subcellular dynamics for multicellular tissue development by mathematical modelling:** The acquisition of knowledge of hormonal networks; processes of subcellular dynamics and integration of different signals will be used to mathematically model these processes and to extrapolate them onto multicellular developmental situations

Selected Publications

NODZYNSKI T., FERARU E., HIRSCH S., DE RYCKE R., NICULAES C., BOERJAN W., VAN LEENE J., DE JAEGER G., VANNESTE S., FRIML J. 2013. Retromer subunits VPS35A and VPS29 mediate prevacuolar compartment (PVC) function in Arabidopsis. *Molecular Plant.* (in press)

BARBEZ E., KUBES M., ROLCIK J., BEZIAT C., PENCIK A., WANG B., ROSQUETE M.R., ZHU J., DOBREV P.I., LEE Y., ZAZIMALOVA E., PETRASEK J., GEISLER M., FRIML J., KLEINE-VEHN J. 2012. A novel putative auxin carrier family regulates intracellular auxin homeostasis in plants. *Nature* 485 (7396), p. 119-122.

LOFKE C., ZWIEWKA M., HEILMANN I., VAN MONTAGU M.C., TEICHMANN T., FRIML J. 2013. Asymmetric gibberellin signaling regulates vacuolar trafficking of PIN auxin transporters during root gravitropism. *Proceedings of the National Academy of Sciences of the United States of America* 110 (9), p. 3627-3632.

ZWIEWKA M., FERARU E., MOLLER B., HWANG I., FERARU M.I., KLEINE-VEHN J., WEIJERS D., FRIML J. 2011. The AP-3 adaptor complex is required for vacuolar function in Arabidopsis. *Cell Research* 21 (12), p. 1711-1722.

CONTENT OF RESEARCH

We focus on how plants can adapt their physiology and development to different environmental conditions using endogenous signalling pathways. In particular how these signals are integrated into the subcellular dynamics and polar localisation of PIN transporters for the plant hormone auxin.

Plant development is characterised by a remarkable adaptability to different environmental conditions and exceptional flexibility in terms of growth and survival. Differential distribution (gradients) of the plant signalling molecule auxin underlies many plant-specific developmental events, including embryogenesis, organogenesis, tissue regeneration and tropisms. These gradients are established and maintained by directional, intercellular auxin transport. Our goal is to elucidate the molecular and cellular mechanism of auxin transport and to understand how auxin transport provides positional and directional information for plant adaptive development.

The key feature of auxin transport – its controlled directionality – results from the polar subcellular localisation of the auxin efflux carriers from the PIN family. PIN polar targeting is related to their continuous subcellular movement between endosomes and the plasma membrane. This constitutive cycling provides an entry point for internal and external signals, which in this manner can rapidly modulate PIN polarity and divert auxin flow during different developmental events. Thus polar auxin transport represents a unique model system for studying the functional link between basic cellular processes, such as endocytosis or cell polarity establishment, and their developmental outcome at the level of the multicellular plant organism.

GENOMICS AND PROTEOMICS OF PLANT SYSTEMS

Chromatin Molecular Complexes

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RESEARCH AREAS

- Structure, evolution and maintenance of telomeres and their roles in chromosome stability and plant speciation; this includes the characterization of the nucleoprotein composition of telomeres and telomerases, biophysical analysis of interactions between telomere components by quantitative methods, analysis of structure-function relationships of telomerase subdomains and analysis of alternative (telomerase independent) strategies of telomere maintenance
- Epigenetic mechanisms in the regulation of gene expression, chromosome stability and telomere homeostasis
- Structure, evolution and functions of SMC complexes; the characterization of SMC5-6 complex subunits and MAGE proteins in vitro and in vivo; their roles in DNA repair and chromosome dynamics

MAIN OBJECTIVES

- To investigate epigenetic processes involved in the regulation of telomere maintenance
- To clarify connections between dynamics of telomere composition and DNA damage response
- To explore the evolution of telomeres, telomerase and alternative mechanisms of telomere maintenance
- To decipher the functional links between chromatin (nucleosome) assembly and genome stability
- To examine the interactions and functions of SMC5-6 complex subunits and MAGE proteins

Selected Publications

FULNECKOVA J., HASIKOVA T., FAJKUS J., LUKESOVA A., ELIAS M., SYKOROVA E. 2012. Dynamic Evolution of Telomeric Sequences in the Green Algal Order Chlamydomonadales. *Genome Biology and Evolution* 4 (3), p. 248-264.

OGROCKA A., SYKOROVA E., FAJKUS J., FOJTOVA M. 2012. Developmental silencing of the AtTERT gene is associated with increased H3K27me3 loading and maintenance of its euchromatic environment. *Journal of Experimental Botany* 63 (11), p. 4233-4241.

ZIMMERMANN M., LOTTERSBERGER F., BUONOMO S.B., SFEIR A., DE LANGE T. 2013. 53BP1 Regulates DSB Repair Using Rif1 to Control 5′ End Resection. *Science* 339 (6120), p. 700-704.

PONTVIANNE F., BLEVINS T., CHANDRASEKHARA C., MOZGOVA I., HASSEL C., PONTES O.M., TUCKER S., MOKROS P., MUCHOVA V., FAJKUS J., PIKAARD C.S. 2013. Subnuclear partitioning of rRNA genes between the nucleolus and nucleoplasm reflects alternative epiallelic states. *Genes & Development* 27 (14), p. 1545-1550.

CONTENT OF RESEARCH

Since eukaryotic genomes are folded into nucleoprotein assemblies called chromatin, all genome functions occur in the context of this highly dynamic structure. Understanding processes such as DNA replication and repair, transcription or cell differentiation thus requires an understanding of the structure and function of chromatin, and its specific domains such as centromeres, telomeres or nucleoli.

Chromatin is a supramolecular complex of DNA, proteins and other associated molecules (e.g. RNA species). It is the building material of chromosomes, which can be observed during cell division in their most condensed state. Chromatin was first discovered in plant cells – as were the cells themselves, or genes.

While the nucleotide sequence of the DNA component of chromatin constitutes the genetic material of the cell, the other chromatin components (and also modifications of bases in DNA itself) participate in so-called epigenetic functions. These include spatiotemporal regulation of gene activity and DNA replication, correct and precise segregation of genetic material to daughter cells, maintenance of chromosome stability, and protection of genetic material against damage. Importantly, the chromatin structure compacts several metres of genomic DNA to fit the size of a cell nucleus (several microns in diameter) while keeping it functional despite the high degree of compaction (10^5-10^6 fold).

Our research group integrates studies in the field of telomere biology, chromatin structure and epigenetics. Using unique features of plant systems (namely their high developmental plasticity), and their comparison to yeast or animal models, we aim to characterise pathways involved in the control of chromosome stability and to distinguish between the specific and general mechanisms involved. Outcomes of our studies (e.g. understanding mechanisms contributing to genome stability, aging or adaptation to changing environmental conditions) can be applied in agriculture, biotechnologies or medicine.

Developmental and Production Biology – Omics Approaches

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RESEARCH AREAS

- Characterization of plant responses to environmental cues by omics approaches
- Interactions of environmental and hormonal signalling
- Control of plant growth and development by intertwined environmental and hormonal signals
- Structure-function relationships in proteins involved in cytokinin metabolism and signalling
- Engineering novel properties in proteins involved in cytokinin metabolism and signalling

MAIN OBJECTIVES

- Deciphering the molecular mechanisms involved in plant-environment interactions
- Unravelling the interactions of environmental and hormonal signals and their projection into the regulation of plant growth and development
- The development of novel molecular tools for the modulation of metabolism and signalling of plant hormones

Selected Publications

CERNY M., KUKLOVA A., HOEHENWARTER W., FRAGNER L., NOVAK O., ROTKOVA G., JEDELSKY P.L., ZAKOVA K., SMEHILOVA M., STRNAD M., WECKWERTH W., BRZOBOHATY B. 2013. Proteome and metabolome profiling of cytokinin action in Arabidopsis identifying both distinct and similar responses to cytokinin down- and up-regulation. *Journal of Experimental Botany* 64 (14), p. 4193-4206.

CERNY M., SKALAK J., CERNA H., BRZOBOHATY B. 2013. Advances in purification and separation of posttranslationally modified proteins. *Journal of Proteomics* 92, p. 2-27.

NOVAK J., PAVLU J., NOVAK O., NOZKOVA-HLAVACKOVA V., SPUNDOVA M., HLAVINKA J., KOUKALOVA S., SKALAK J., CERNY M., BRZOBOHATY B. 2013. High cytokinin levels induce a hypersensitive-like response in tobacco. *Annals of Botany* 112 (1), p. 41-55.

FILIPI T., MAZURA P., JANDA L., KIRAN N.S., BRZOBOHATY B. 2012. Engineering the cytokinin-glucoside specificity of the maize β-D-glucosidase Zm-p60.1 using site-directed random mutagenesis. *Phytochemistry* 74, p. 40-48.

CONTENT OF RESEARCH

Sustaining agricultural production in a rapidly changing climate requires a detailed knowledge of the molecular basis of plant--environment interactions. As hormones play a crucial role in modulating plant responses to environmental cues, hormonal control of plant responses to environmental stimuli is receiving ever growing attention.

Hormonal control of plant responses to environmental cues

As sessile organisms plants must continually sense environmental conditions and adjust their growth and development processes accordingly, through adaptive responses regulated by various internal factors including hormones such as cytokinin. Genome-wide microarray studies reveal overlapping transcriptional responses between cytokinin and various environmental inputs. The components of the cytokinin biosynthetic and signalling pathway are, in turn, transcriptionally altered by environmental stimuli. Because of the wide range of outputs of the cytokinin signalling pathway, dissecting the role of cytokinin in the response to a particular stress remains challenging. We are employing a number of tools now available to alter cytokinin levels and responsiveness in combination with non-targeted transcriptomic, proteomic and metabolomic analyses to deepen our knowledge of this subject. The investigation of structure-function relationships in proteins involved in these interactions will provide us with knowledge of their mechanisms of action at the molecular level. We will focus on the interactions of cytokinin and the light, temperature and drought response pathways. As we deepen our understanding of the circuitry underlying the input of cytokinin into the response of the environmental signals, we expect to be able to engineer these pathways to produce plants with increased tolerance to abiotic stresses.

Plant Stress Signalling and Adaptation

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RESEARCH AREAS

- ROS-auxin crosstalk regulatory network underlying plant adaptation to environmental challenges
- Plastid ROS-redox signalling on the response of plants to stress and on hormone homeostasis
- Stress-perturbed auxin signalling on photosynthesis modulation

MAIN OBJECTIVES

- To decipher how environmental and developmental signals are integrated by ROS-auxin crosstalk
- To unravel how the interaction between ROS and hormones synchronizes stress-induced growth reorientation and photosynthetic performance, which are vital for plant survival
- To shed light on mechanisms by which the interplay between chloroplast and auxin signalling pathways modulate plant growth and development
- Discovery of stress avoidance genes and new stress tolerance strategies to improve crop performance under changing global conditions

Selected Publications

SKIRYCZ A., VANDENBROUCKE K., CLAUW P., MALEUX K., DE MEYER B., DHONDT S., PUCCI A., GONZALEZ N., HOEBERICHTS F., TOGNETTI V.B., VAN BREUSEGEM F., VUYLSTEKE M., INZED. 2011. Survival and growth of Arabidopsis plants given limited water are not equal. *Nature Biotechnology* 29 (3), p. 212-214.

TOGNETTI V.B., MUHLENBOCK P., VAN BREUSEGEM F. 2012. Stress homeostasis - the redox and auxin perspective. *Plant, Cell & Environment* 35 (2), p. 321-333.

MITTLER R., VANDERAUWERA S., SUZUKI N., MILLER G.,TOGNETTI V.B., SHULAEV V., GOLLERY M., VAN BREUSEGEM F. 2011. ROS signaling: the new wave? *Trends in Plant Science* 16 (6), p. 300-309.

TOGNETTI V.B., VAN AKEN O., MORREEL K., VANDENBROUCKE K., VAN DE COTTE B., DECLERCQ I., CHIWOCHA S., FENSKE R., PRINSEN E., GENTY B., INZE D., VAN BREUSEGEM F. 2010. Perturbation of indole-3-butyric acid homeostasis by the UDP-glucosyltransferase UGT74E2 modulates Arabidopsis architecture and water stress tolerance. *Plant Cell* 22 (8), p. 2660-2679.

CONTENT OF RESEARCH

Besides evolutionary adaptations that have shaped the development of plants and led to the diversity of forms in existence today in all kind of habitats, plants can also respond to rapid and often very substantial fluctuations in their environments.

In contrast to animals, plants cannot move away from negative stimuli. To deal with this lack of mobility, plants have developed adaptation strategies by which they adjust their patterns of growth and development in response to the environment.

Environmental cues represent major hardships for crop productivity worldwide. Therefore, elucidation of plant stress adaptation networks has become a major biotechnology research objective. The main players in plant adaptation responses are reactive oxygen species (ROS) and the phytohormone auxin. However, knowledge of the regulatory events governing ROS and auxin interplay is at this point still superficial. On the other hand, environmental factors primarily affect photosynthesis, compromising plant growth and yield. Basically, photosynthesis acts as a global stress sensor activating stress responses, which directly affect ROS and auxin homeostasis. We use several approaches, including phenotypic and genetic screenings for in-depth identification and characterization of the components of the ROS-auxin crosstalk regulatory network. We are also interested in the role of chloroplast signalling on auxin-driven development and stress responses.

The long-term objective is to unravel the ROS--auxin molecular network controlling photosynthesis and plant morphology, which are the most relevant traits in plant breeding programmes, for better engineering of crops with superior biomass production.

Plant Molecular Biology

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RESEARCH AREAS

- Telomeres and genome stability
- Regulation of meiosis
- Role of RNA decay in genome regulation

MAIN OBJECTIVES

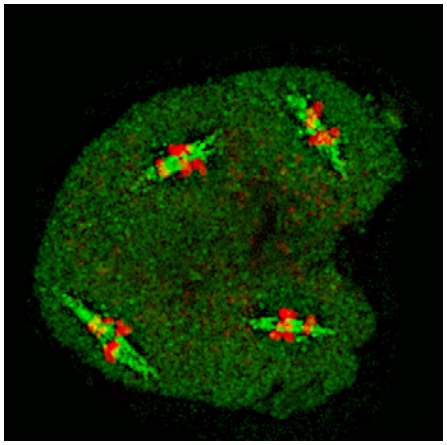
- Deciphering mechanisms of chromosome end protection
- Understanding regulatory pathways that define the meiotic mode of chromosome segregation and application of this knowledge in plant breeding
- Investigating non-canonical functions of the proteins involved in nonsense mediated RNA decay

Selected Publications

BULANKOVA P., AKIMCHEVA S., FELLNER N., RIHA K. 2013. Identification of Arabidopsis meiotic cyclins reveals functional diversification among plant cyclin genes. *PLoS Genetics* 9 (5), e1003508.

KAZDA A., ZELLINGER B., ROSSLER M., DERBOVEN E., KUSENDA B., RIHA K. 2012. Chromosome end protection by blunt-ended telomeres. *Genes & Development* 26 (15), p. 1703-1713.

BULANKOVA P., RIEHS N., NOWACK M.K., SCHITTGER A., RIHA K. 2010. Meiotic progression in Arabidopsis is governed by complex regulatory interactions between SMG7, TDM1 and meiosis I specific cyclin TAM. *Plant Cell* 22 (11), p. 3791-3803.



Third meiotic division in Arabidopsis tdm1mutants that fail to exit meiosis (green – spindle, red – chromosomes).

CONTENT OF RESEARCH

We study processes governing genome stability and chromosome segregation. Our research aims to decipher the molecular mechanisms that stabilize and protect chromosome ends, called telomeres, from being perceived by the cell as DNA damage. We also investigate the regulatory pathways that define meiosis, the cell division necessary for sexual reproduction and the generation of haploid gametes.

Telomeres form the ends of eukaryotic chromosomes and are important for the complete replication of linear genomes and for chromosome stability. We found that the opposite ends of a chromosome adopt different end protective structures, the formation of which is dictated by the mode of DNA replication. Furthermore, we discovered a fundamentally novel mechanism of chromosome end protection that relies on the evolutionary conserved DNA repair complex Ku. In our current research we aim to understand how Ku mediates protection of these telomeres without triggering a DNA repair reaction. In our meiotic research we aim to delineate pathways involved in remodelling of the cell cycle machinery to enable the meiotic mode of chromosome segregation. We have identified Arabidopsis meiotic cyclins and revealed their contributon to diverse meiotic processes. Furthermore, we have discovered a genetic module, consisting of SMG7 and TDM1 that inhibits meiotic CDKs and facilitates the transition from meiosis to mitosis. Our current work is directed towards a molecular understanding of the SMG7/TDM1 function and characterization of additional genes involved in meiotic progression.

MOLECULAR MEDICINE

The research programme plans to study the genetic background of important human diseases and to improve their diagnostics and therapy using application of modern genomic and molecular biological technologies. The project also aims to bring novel findings into the pathogenesis of studied diseases and produce experimental strategies for their treatment and prevention. The main diseases studied will be cancer (both haematological malignancies and solid tumours); inherited diseases – mainly neuromuscular, neurodegenerative, metabolic and skin; infectious diseases and immune defects.

Research Programme Coordinator:
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OVERALL GOAL

The main goals of this research programme are: (1) introduction of modern approaches of genome analysis; (2) the characterisation of cell behaviour on a molecular level, with the emphasis on malignant transformation, and resistance to modern anti-cancer treatment; (3) the analysis of the mechanisms leading to disturbances in immune response. New approaches for genome-wide analysis including comparative and functional genomics and proteomics will enable the development of specific molecular diagnostics, predictive and personalised medicine, and perhaps also gene therapy.

RESEARCH DIRECTIONS

- Mapping of key genetic defects in cancer cells; genomic and proteomic analyses of cancer cells in relation to therapy administration
- Development of user-oriented research focusing on improvement of current therapeutic protocols and experimental strategies to design novel therapeutic approaches
- Application of high-throughput analyses of the human genome in predictive oncology
- Molecular genetic diagnostics of selected neuromuscular, neurodegenerative, metabolic and skin disorders, application of high-throughput methods in analysis of the human genome
- Study of mechanisms leading to disturbances in immune response with an emphasis on primary immunodeficiencies; analysis of genes involved in immune response
- Characterisation of genetic determinants of host-pathogen interactions; development of novel diagnostic strategies in human infections
- Non-coding RNAs (microRNAs, LncRNA, T-UCR, pyknons, etc.) in the pathogenesis of solid cancer, their characterisation as diagnostic biomarkers and potential therapeutic targets leading to the higher level of therapy individualization in solid cancer patients
- Study of most dynamic components of genomes – transposable elements and microsatellites – in plants, animals and human, and its relation to diseases
- T-cell receptor (TCR) and B-cell receptor (BCR) profiling, analysis of their specificity and diversity

RESEARCH GROUPS | LEADERS

Medical Genomics | *Šárka Pospíšilová*

Molecular Oncology I – Hematooncology | *Martin Trbušek*

Molecular Oncology II – Solid Cancer | *Ondřej Slabý*

Inherited Diseases I – Genetic Research | *Lenka Fajkusová*

Inherited Diseases II – Transcriptional Regulation | *Dalibor Blažek*

Molecular Immunology and Microbiology | *Tomáš Freiberger*

Genome Dynamics | *Eduard Kejnovský*

Adaptive Immunity Group | *Dmitriy Chudakov*

Medical Genomics

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Research Group Leader

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RESEARCH AREAS

- Identification of novel diagnostic and prognostic markers and therapeutic targets in tumour cells with a focus on leukaemias (CLL, ALL, CML, AML) and lymphomas
- MicroRNA analysis in lymphoproliferative disorders
- Detection of inherited genetic defects related to cancer development
- B-lymphocyte biology and genomics (genomic analyses of patients with lymphoproliferative disorders)
- Bioinformatics research of antigen receptor sequences in B and T cell repertoires in lymphoid malignancies: http://bat.infspire.org/arrest/
- Development of novel molecular genetic approaches with potential applications in medical diagnostics

MAIN OBJECTIVES

- Molecular genetics and genomics of haematological, oncological and other diseases – analyses of cancer genomes, detection of tumour-associated genetic changes, identification of novel therapeutic targets and molecular mechanisms responsible for the pathogenesis of human diseases
- Introduction of high-throughput genomic approaches into oncological research and clinical diagnostics, development of novel methods for determination of diagnosis, prognosis and therapy response prediction; introduction of novel techniques into postnatal, prenatal and pre-implant genetic research and diagnostics

Selected Publications

POSPISILOVA S., GONZALEZ D., MALCIKOVA J., TRBUSEK M., ROSSI D., KATER A.P., CYMBALISTA F., EICHHORST B., HALLEK M., DOHNER H., HILLMEN P., VAN OERS M., GRIBBEN J., GHIA P., MONTSERRAT E., STILGENBAUER S., ZENZ T. 2012. European Research Initiative on CLL (ERIC). ERIC recommendations on TP53 mutation analysis in chronic lymphocytic leukemia. *Leukemia* 26 (7), p. 1458-1461.

MRAZ M., DOLEZALOVA D., PLEVOVA K., STANO KOZUBIK K., MAYEROVA V., CERNA K., MUSILOVA K., TICHY B., PAVLOVA S., BORSKY M., VERNER J., DOUBEK M., BRYCHTOVA Y., TRBUSEK M., HAMPL A., MAYER J., POSPISILOVA S. 2012. MicroRNA-650 expression is influenced by immunoglobulin gene rearrangement and affects the biology of chronic lymphocytic leukemia. *Blood* 119 (9), p. 2110-2113.

RACIL Z., RAZGA F., DRAPALOVA J., BURESOVA L., ZACKOVA D., PALACKOVA M., SEMERAD L., MALASKOVA L., HALUZIK M., MAYER J. 2013. Mechanism of impaired glucose metabolism during nilotinib therapy in patients with chronic myelogenous leukemia. *Haematologica – The Hematology Journal* 98 (10), p. 124-126.

PLEVOVA K., SKUHROVA FRANCOVA H., BURCKOVA K., BRYCHTOVA Y., DOUBEK M., PAVLOVA S., MALCIKOVA J., MAYER J., TICHY B., POSPISILOVA S. 2013. Multiple Productive Immunoglobulin Heavy Chain Gene Rearrangements in Chronic Lymphocytic Leukemia Are Mostly Derived from Independent Clones. *Haematologica - The Hematology Journal*. [E-pub Sept 13]

CONTENT OF RESEARCH

The transformation of normal to malignant cells may be caused by many different mechanisms that share a single common feature – the alteration of genetic information and subsequent disruption of cellular regulatory mechanisms, which thus lead to uncontrolled proliferation. Some of these genetic alterations have already been described and are routinely analysed in oncological diagnostics, e.g. *TP53, ATM* or *BRCA* gene mutations or specific translocations occurring in leukaemias, lymphomas and other tumours. The importance of many other genomic aberrations found in tumours and their influence on the malignant potential of transformed cells should be analysed as well as the impact of individual genetic variants on tumour behaviour. Novel technologies including high-resolution SNP microarrays and high-throughput genome sequencing provide fast and complex analyses of the human genome and enable a deep insight into genetic events during the malignant transformation and evolution of specific tumour clones. These methods are used to characterize the genetic information of the patient's malignant and non-malignant cells to reveal the mechanisms of cellular transformation.

The expected outputs of our work are identification of recurrent genomic alterations in haematological and other malignancies, which could be used in cancer diagnostics and as potential therapeutic targets, and characterization of the regulatory pathways disrupted in tumour cells. The analysis will also be focused on the antigen receptor sequences in B-lymphocytes and microRNA analyses in patients with lymphoproliferative disorders. The outcome of these studies is expected to be used as an initial point for focused research as well as for direct application in diagnostics, prognostics and personalized therapy monitoring in haematological and oncological malignancies.

Molecular Oncology I – Hematooncology

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RESEARCH AREAS

- The role of the tumour suppressors p53 and ATM in cancer
- Pathogenesis and therapy of chronic lymphocytic leukaemia
- Innovative drug testing on cancer cells

MAIN OBJECTIVES

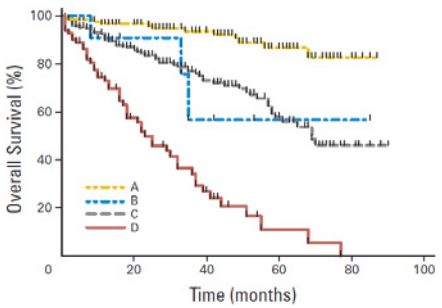
- Mapping of key genetic defects in cancer cells; genetic analyses of cancer cells in relation to therapy response prediction; stratification of cancer patients for DNA-damaging or other therapy
- Clonal selection of recurrent gene mutations in tumour cells populations
- Drug testing on selected high-risk cancer cells using the synthetic lethality concept in various models

Selected Publications

MALCIKOVA J., SMARDOVA J., ROCNOVA L., TICHY B., KUGLIK P., VRANOVA V., CEJKOVA S., SVITAKOVA M., SKUHROVA FRANCOVA H., BRYCHTOVA Y., DOUBEK M., BREJCHA M., KLABUSAY M., MAYER J., POSPISILOVA S., TRBUSEK M. 2009. Monoallelic and biallelic inactivation of TP53 gene in chronic lymphocytic leukemia: selection, impact on survival and response to DNA damage. *Blood* 114 (26), p. 5307-5314.

TRBUSEK M., SMARDOVA J., MALCIKOVA J., SEBEJOVA L., DOBES P., SVITAKOVA M., VRANOVA V., MRAZ M., FRANCOVA H.S., DOUBEK M., BRYCHTOVA Y., KUGLIK P., POSPISILOVA S., MAYER J. 2011. Missense mutations located in structural p53 DNA-binding motifs are associated with extremely poor survival in chronic lymphocytic leukemia. *Journal of Clinical Oncology* 29 (19), p. 2703-2708.

NAVRKALOVA V., SEBEJOVA L., ZEMANOVA J., KMINKOVA J., KUBESOVA B., MALCIKOVA J., MRAZ M., SMARDOVA J., PAVLOVA S., DOUBEK M., BRYCHTOVA Y., POTESIL D., NEMETHOVA V., MAYER J., POSPISILOVA S., TRBUSEK M. 2013. ATM mutations uniformly lead to ATM dysfunction in chronic lymphocytic leukemia: Application of functional test using doxorubicin. *Haematologica* 98 (7), p. 1124-1131.



Tumour cells genetic information impact on the survival of patients with leukaemia. The mutational status of just two critical genes determines completely distinct survival rates in chronic lymphocytic leukaemia patients, regardless of the therapy used (currently the most modern). Red curve: mutation in TP53 gene, no mutations in IGHV gene; Yellow curve: no mutation in TP53 gene, mutations in IGHV gene. The other curves: remaining combinations.

CONTENT OF RESEARCH

Effective anti-cancer therapy is inconceivable without a detailed knowledge of tumour cells' genetic background. Genetically characterized tumour cells can be used for the testing of innovative treatment approaches.

Development of novel therapeutic strategies for high-risk cancer patient

Genetic abnormalities in cancer cells conferring drug resistance have been attracting intensive research interest for several decades. Alterations in the key tumour-suppressor gene TP53 (coding for the p53 protein) represents the most common defect type, which substantially reduces therapeutic options. Also inactivation of the principal p53 regulator, ATM kinase, substantially changes conditions in a cell with respect to the DNA damage response. As a consequence, currently used therapies based on apoptosis induction after genotoxic stress are mostly ineffective in p53- or ATM-deficient patients. We intend to use chronic lymphocytic leukaemia and related B-cell lymphoproliferative disorders (e.g. mantle cell lymphoma, diffuse large B-cell lymphoma) as model systems and analyse (a) the most frequent genetic defects in tumour cells including their origin and selection (b) the applicability of the synthetic lethality concept for the elimination of aggressive cancer cells harbouring mutations connected with chemotherapy resistance. The work is methodological, using innovative functional tests and up-to-date modern methods for mutation screening, including next-generation sequencing. Primary leukemic and lymphoma cells, permanent cell lines and mouse models will be used.

Molecular Oncology II – Solid Cancer

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RESEARCH AREAS

- The biology of the non-coding RNAs (microRNA, sncRNAs, lncRNA etc.) and their involvement in carcinogenesis
- The significance of non-coding RNAs in solid cancer pathogenesis and the identification of new therapeutic targets
- The application of non-coding RNAs in solid cancer diagnostics and the individualization of therapy in cancer patients

MAIN OBJECTIVES

- The introduction of high-throughput analyses (whole genome sequencing and transcriptome profiling) of the human genome mainly focused on non-coding RNAs; utilization of these technologies in medicine and the development of diagnostic tests based on high-throughput methods
- Comprehensive analysis of non-coding RNAs (expression, SNPs, methylation profiles, according to Objective 1) in solid cancer (mainly colorectal cancer, renal cell carcinoma, oesophageal cancer, breast cancer, lung cancer and glioblastoma multiforme). The integration of experimental data with clinico-pathological characteristics of patients aiming at identification of potential susceptibility, diagnostic, prognostic, and predictive biomarkers, as well as new therapeutic targets in tumour tissue or the patient's body fluids; design and coordination of large multi-centric validation studies
- Detailed phenotypic characterization (e.g. validation of predicted targets of miRNAs and their integration into signalling pathways) and functional evaluation (proliferation, cell cycle, apoptosis, invasiveness, etc.) of non-coding RNAs suspected to be involved in carcinogenesis or cancer outcome (Objective 2) in vitro in relevant cell line models. Studies examining the oncogenic or tumour-suppressive function of particular non-coding RNA in vivo, with subsequent pharmacological analysis evaluating usage of this RNA as a therapeutic target
- The formulation and design of recommendations for potential implementation of novel biomarkers (according to Objectives 2 and 3) in the clinical management of solid cancer patients leading to a higher level of individualization and better therapeutic outcomes; the development and technological transfer of new targeted therapeutic strategies in solid cancer

Selected Publications

SLABY O., REDOVA M., POPRACH A., NEKVINDOVA J., ILIEV R., RADOVA L., LAKOMY R., SVOBODA M., VYZULA R. 2012. Identification of MicroRNAs associated with early relapse after nephrectomy in renal cell carcinoma patients. *Genes Chromosomes & Cancer* 51(7), p. 707-716.

FALTEJSKOVA P., SVOBODA M., SRUTOVA K., MLCOCHOVA J., BESSE A., NEKVINDOVA J., RADOVA L., FABIAN P., SLABA K., KISS I., VYZULA R., SLABY O. 2012. Identification and functional screening of microRNAs highly deregulated in colorectal cancer. *Journal of Cellular and Molecular Medicine* 16 (11), p. 2655-2666.

CONTENT OF RESEARCH

The discovery of microRNAs has created a paradigm shift in post-genomics biology. It is an extremely fast growing field, and microRNA knowledge is now believed to be also a pivotal element of cancer biology.

The non-coding RNAs (ncRNAs) play important biological roles in cellular development, physiology and pathologies. NcRNAs could be grouped into two major classes – small ncRNAs (i.e. microRNA, snoRNA) and long ncRNAs (i.e. lncRNA, lincRNA, T-UCR). The small number of characterized human lncRNAs have been associated with a spectrum of biological processes, for example, epigenetics, alternative splicing, nuclear import, as structural components, as precursors to small RNAs and even as regulators of mRNA decay. Furthermore, accumulating reports of deregulated lncRNA (HOTAIR, MALAT1, HULC, T-UCRs, etc.) expressions across numerous cancer types suggest that aberrant lncRNA expression may be an important contributor to tumorigenesis. Small ncRNAs are represented by a broad range of known and newly discovered RNA species, with many being associated with the 5′ or 3′ regions of coding genes. This class includes mainly the well-documented microRNAs, which significantly extended the concept of molecular carcinogenesis, and recently are the subject of intensive translational research in this field. Molecular Oncology II group focuses on the significance of ncRNAs in solid cancer pathogenesis, the identification of new therapeutic targets and the development of ncRNAs-based diagnostics leading to a higher level of therapy individualization in cancer patients.

Inherited Diseases I – Genetic Research

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RESEARCH AREAS

- Molecular issues of inherited neuromuscular, metabolic, and skin diseases
- *In silico* analysis of mutations using molecular dynamic methods and bioinformatic tools
- Functional analysis of mutations using site-direct mutagenesis, expression, and analysis of localisation and function of mutant proteins
- Introduction of next-generation sequencing into medical research and molecular diagnostics

MAIN OBJECTIVES

- Detection of mutation/mutations associated with a disease, analysis of correlation between patient's genotype and phenotype
- Molecular modelling and functional analysis of detected mutations
- Application of high-throughput analyses (sequence capture and targeted resequencing, whole genome sequencing, transcriptome profiling) of human genomes, utilisation of these technologies in diagnostics and the development of diagnostic tests

Selected Publications

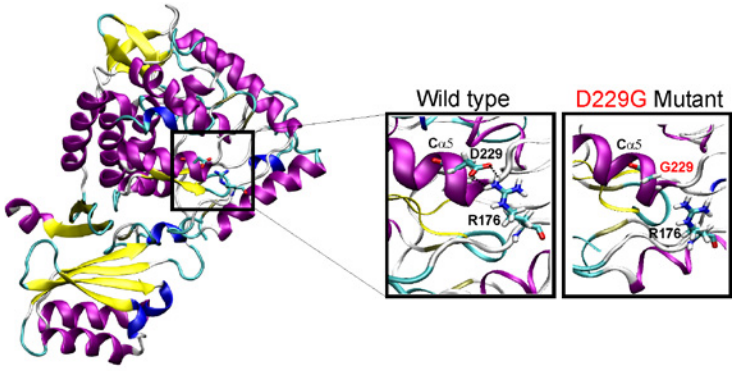
REBLOVA K., HRUBA Z., PROCHAZKOVA D., PAZDIRKOVA R., POUCHLA S., FAJKUSOVA L. 2013. Hyperphenylalaninemia in the Czech Republic: genotype-phenotype correlations and in silico analysis of novel missense mutations. *Clinica Chimica Acta* 419, p. 1-10.

TICHY L., FREIBERGER T., ZAPLETALOVA P., SOSKA V., RAVCUKOVA B., FAJKUSOVA L. 2012. The molecular basis of familial hypercholesterolemia in the Czech Republic: spectrum of LDLR mutations and genotype-phenotype correlations. *Atherosclerosis* 223 (2), p. 401-408.

DUSKOVA L., KOPECKOVA L., JANSOVA E., TICHY L., FREIBERGER T., ZAPLETALOVA P., SOSKA V., RAVCUKOVA B., FAJKUSOVA L. 2011. An APEX-based genotyping microarray for the screening of 168 mutations associated with familial hypercholesterolemia. *Atherosclerosis* 216 (1), p. 139-145.

CONTENT OF RESEARCH

Determination of mutation/mutations on the DNA level is the principal step in the molecular genetic diagnostics of inherited diseases. This step is essential for definitive confirmation of a diagnosis preliminary established on the basis of clinical symptoms and biochemical, histological, histochemical, and immunohistochemical findings. In a number of diseases, tens of genes can be associated with one specific phenotype or else an associated gene is not yet known. In these cases we perform high-throughput DNA sequencing to detect genetic defects. Detected mutations are evaluated on the basis of literature data and using molecular dynamics methods and bioinformatics tools. In selected types of disease functional analysis is used for determination of the impact of a mutation on protein structure and function. At the present time, functional analysis of mutations is applied for mutations determined in the low density lipoprotein receptor gene (LDLR) in patients with familial hypercholesterolemia. The expression, localization, and function of mutated LDLR are studied in vivo using confocal laser scanning microscopy.



3D structure of phenylalanine hydroxylase (PAH) and two detailed views showing wild type amino acid D229 forming salt bridge with R176 and newly discovered mutant amino acid G229 where the salt bridge is lost.

Inherited Diseases II – Transcriptional Regulation

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RESEARCH AREAS

- Regulation of eukaryotic transcription
- Role of Cdk9, Cdk12 and Cdk13 in regulation of gene expression
- Role of transcription cycle-related Cdks in maintenance of genome stability
- Transcription cycle-related Cdks in human disease

MAIN OBJECTIVES

- Role of Cdks in phosphorylation of the C-terminal domain of RNA polymerase II and in the regulation of gene expression
- Control of DNA damage response and genome stability via regulation of expression of DNA damage response genes

Selected Publications

KOHOUTEK J., BLAZEK D.* 2012. Cyclin K goes with Cdk12 and Cdk13. *Cell Division* 7 (12).

BLAZEK D.* 2012. The cyclin K/Cdk12 complex: An emerging new player in the maintenance of genome stability. *Cell Cycle* 11 (6), p. 1049-1050.

BLAZEK D.*, KOHOUTEK J., BARTHOLOMEEUSEN K., JOHANSEN E., HULINKOVA P., LUO Z., CIMERMANCIC P., ULE J., PETERLIN B.M. 2011. The Cyclin K/Cdk12 complex maintains genomic stability via regulation of expression of DNA damage response genes. *Genes & Development* 25 (20), p. 2158-2172.

* corresponding author

CONTENT OF RESEARCH

The major interest of our research group is the regulation of expression of protein-coding genes by RNA polymerase II and transcriptional cyclin-dependent kinanases. We are also interested in the deregulation of gene expression and its role in the onset of human diseases.

RNA polymerase II (RNAPII) directs transcription of protein coding genes and this process consists of several stages including preinitiation complex formation, productive elongation and termination. This transcription cycle is tightly linked to co-transcriptional maturation of nascent transcripts including pre-mRNA splicing and polyadenylation. RNAPII contains an unstructured C-terminal domain (CTD) with repeats of evolutionarily conserved heptapeptide YSPTSPS, where individual serines get phosphorylated. Several cyclin-dependent kinases (Cdks) regulate the phosphorylation status of the CTD and subsequent binding of transcription and pre-mRNA processing factors. Thus, the patterns of phosphorylation of the CTD direct actions of RNAPII during the transcription cycle and co-transcriptional processing of nascent transcripts. Moreover, CTD was also functionally linked to DNA damage response and maintenance of genome stability via regulation of transcription, mRNA processing and recombination. Thus, CTD and its posttranslational modifications, associated proteins and modifying enzymes are emerging as new players in cellular response to DNA damage. Our recent work led to the identification of the Cyclin K/Cdk12 complex that phosphorylates serine 2 in the CTD of RNAPII and directs expression of several crucial DNA damage response genes including BRCA1, ATR and FANCI. In my lab we apply a combination of biochemical, proteomics and genome-wide techniques to determine the molecular mechanism that regulates the expression of Cdk12-dependent genes with a focus on DNA damage response genes. The ultimate goal of our research is to uncover how the CycK/Cdk12 complex and the CTD of RNAPII contribute to the maintenance of genome stability, and how disruption of their functions leads to the onset of a malignant state.

Molecular Immunology and Microbiology

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RESEARCH AREAS

- Molecular diagnostics of primary immunodeficiencies
- Functional analysis of mutations in genes involved in immune response with particular focus on splicing affecting events
- Analysis of genotype-phenotype relationship in patients with primary immunodeficiencies
- Microarray based system of pathogen detection in blood
- Molecular detection of pathogens in polymicrobial clinical samples

MAIN OBJECTIVES

- Analysis of genes involved in disturbed immune response predominantly in patients with immunodeficiencies
- Mapping human mutations and polymorphisms associated with altered immune response and their functional analysis
- Development of new molecular diagnostic tools leading to improved early detection of etiological agents in patients with infectious complications

Selected Publications

FREIBERGER T., RAVCUKOVA B., GRODECKA L., PIKULOVA Z., STIKAROVSKA D., PESAK S., KUKLINEK P., JARKOVSKY J., SALZER U., LITZMAN J. 2012. Sequence variants of the TNFRSF13B gene in Czech CVID and IgAD patients in the context of other populations. *Human Immunology* 73 (11), p. 1147-1154.

MEJSTRIKOVA E., JANDA A., HRUSAK O., BUCKOVA H., VLCKOVA M., HANCAROVA M., FREIBERGER T., RAVCUKOVA B., VESELY K., FAJKUSOVA L., KOPECKOVA L., SUMERAUER D., KABICKOVA E., SEDIVA A., STARY J., SEDLACEK Z. 2012. Skin lesions in a boy with X-linked lymphoproliferative disorder: comparison of 5 SH2D1A deletion cases. *Pediatrics* 129 (2), p. E523-E528.

ZALOUDIKOVA B., NEMCOVA E., POL J., SORM Z., WURMOVA S., NOVOTNA K., VANERKOVA M., HOLA V., RUZICKA F., DUSEK L., NEMEC P., FREIBERGER T. 2012. Value of PCR in surgically treated patients with staphylococcal infective endocarditis: a 4-year retrospective study. *European Journal of Clinical Microbiology & Infectious Diseases* 31 (6), p. 1187-1194.

FREIBERGER T., GRODECKA L., RAVCUKOVA B., KURECOVA B., POSTRANECKA V., VLCEK J., JARKOVSKY J., THON V., LITZMAN J. 2010. Association of FcRn expression with lung abnormalities and IVIG catabolism in patients with common variable immunodeficiency. *Clinical Immunology* 136 (3), p. 419-425.

CONTENT OF RESEARCH

Primary immunodeficiencies make patients susceptible to infections. Using advanced molecular methods it is increasingly easy to detect DNA sequence changes in them, but further analyses are often required to assess the pathogenicity of mutations. The early detection of pathogens causing disease is important for the early initiation of targeted antimicrobial treatment and favourable outcomes in patients with infectious complications.

Immunodeficiencies are important in human medicine for their very significant consequences, including fatal infections, tumour development and autoimmune complications. Primary immunodeficiencies caused by mutations in different genes often have overlapping phenotypic features and the precise identification of responsible mutations is important for correct diagnosis, selection of the most appropriate treatment and genetic counselling. Advanced molecular technologies enable the detection of sequence changes in many genes promptly and it becomes increasingly important to determine if these variants cause disease or not. We use a number of methods to establish the functional significance of detected mutations with a particular focus on variants potentially affecting mRNA splicing. The results have implications not only in clinical settings but also contribute to a better understanding of disease pathogenesis.

Human infectious diseases cause about 25% of fatalities worldwide and arise from interactions between virulent microbes and the host's immune system. Early diagnostics of pathogens followed by targeted antimicrobial therapy is crucial for a favourable outcome. Currently we are interested in the development of novel molecular diagnostic tools for the fast, reliable and specific detection of pathogens in clinical samples. Our future concept includes the analysis of both the microbial and human genetic factors underlying the development of infections, and their mutual interplay.

Genome Dynamics

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RESEARCH AREAS

- The genomics of most dynamic genome components in human and model species
- The role of transposable elements activity and microsatellites expansion in human diseases
- The introduction of high-throughput analyses into medical research and diagnostics

MAIN OBJECTIVES

- The study of transposable elements, microsatellites and promiscuous DNA in plants and animals
- The characterization of transposable elements activity in relation to human diseases
- The identification of general mechanisms of microsatellites expansion in genomes
- The utilization of cytogenetic and functional genomic methods as well as next generation sequencing approaches combined with bioinformatics

Selected Publications

KEJNOVSKY E., MICHALOVOVA M., STEFLOVA P., KEJNOVSKA I., MANZANO S., HOBZA R., KUBAT Z., KOVARIK J., JAMILENA M.L., VYSKOT B. 2013. Expansion of Microsatellites on Evolutionary Young Y Chromosome. *PLoS One* 8 (1), e45519.

STEFLOVA P., TOKAN V., VOGEL I., LEXA M., MACAS J., NOVAK P., HOBZA R., VYSKOT B., KEJNOVSKY E. 2013. Contrasting Patterns of Transposable Element and Satellite Distribution on Sex Chromosomes (XY1Y2) in the Dioecious Plant Rumex acetosa. *Genome Biology and Evolution* 5 (4), p. 769-782.

STEFLOVA P., HOBZA R., VYSKOT B., KEJNOVSKY E. 2013. Strong accumulation of chloroplast DNA in the Y chromosomes of Rumex acetosa and Silene latifolia. *Cytogenetic and Genome Research*.

LEXA M., KEJNOVSKY E., STEFLOVA P., KONVALINOVA H., VORLICKOVA M., VYSKOT B. 2013. Quadruplex-forming sequences occupy discrete regions inside plant LTR retrotransposons. *Nucleic Acids Research*. [Epub Oct 7]

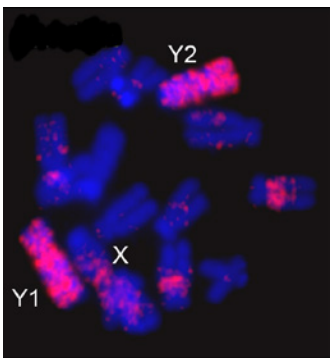


Figure: Fluorescence in situ hybridization showing the accumulation of (CAA)n microsatellite (red) on two Y chromosomes in sorrel (Rumex acetosa) [Kejnovsky et al. 2013, PLoS One]

CONTENT OF RESEARCH

The emerging paradigm represents a genome as a very dynamic system generating its own rearrangements where transposable elements are the key players. Recent studies have shown that transposable elements can also play a role in human diseases, including cancers.

Recently, we have been studying transposable elements, microsatellites and promiscuous DNA in model plant and animal species. We study structural features, genomic proportions, activity and silencing of transposable elements. In humans, we correlate the activity of transposable elements with types of cancer cells for example. The study of epigenetic changes can elucidate the role of DNA methylation and RNA interference in transposable element silencing. In humans, we will use this knowledge for prognoses for patients.

Microsatellites represent another dynamic component of genomes. We have shown that microsatellites have expanded on evolutionary young Y chromosomes in some plants and fishes. Expansion in specific human genes stands behind several neurodegenerative diseases. We are interested in the general mechanisms of microsatellite expansion. We also study the mechanisms of formation and turnover of promiscuous DNA - plastid and mitochondrial DNA transferred into the nucleus.

The utilization of massive parallel sequencing, which allows re-sequencing of individual human genomes or sequencing of transcriptomes, combined with bioinformatic analysis, will give an insight into the causes and development of human diseases and will open new space for medical applications.

Adaptive Immunity Group

Dmitriy Chudakov, Ph.D., DSc.
Research Group Leader
chudakovdm@gmail.com

RESEARCH AREAS

- T cell receptor (TCR) and immunoglobulin (IG) repertoires in health and disease
- Autoimmunity
- Hematopoietic stem cell transplantation

MAIN OBJECTIVES

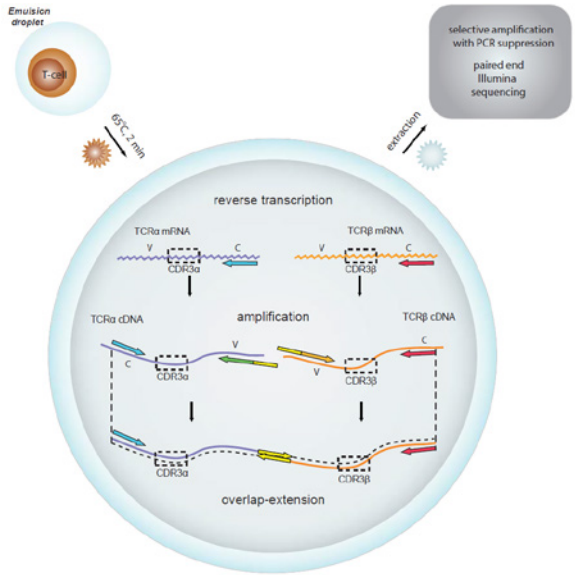
- To develop new technologies for the efficient deep profiling of immune repertoires
- To understand better the ensemble function of the adaptive immune system
- To rationally improve therapies that modulate immune function

Selected Publications

BOLOTIN D.A., SHUGAY M., MAMEDOV I.Z., PUTINTSEVA E.V., TURCHANINOVA M.A., ZVYAGIN I.V., BRITANOVA O.V., CHUDAKOV D.M. 2013. MiTCR: software for T-cell receptor sequencing data analysis. *Nature Methods* 10 (9), p. 813-814.

TURCHANINOVA M.A., BRITANOVA O.V., BOLOTIN D.A., SHUGAY M., PUTINTSEVA E.V., STAROVEROV D.B., SHARONOV G., SHCHERBO D., ZVYAGIN I.V., MAMEDOV I.Z., LINNEMANN C., SCHUMACHER T.N., CHUDAKOV D.M. 2013. Pairing of T-cell receptor chains via emulsion PCR. *European Journal of Immunology.* (in press)

BOLOTIN D.A., MAMEDOV I.Z., BRITANOVA O.V., ZVYAGIN I.V., SHAGIN D., USTYUGOVA S.V., TURCHANINOVA M.A., LUKYANOV S., LEBEDEV Y.B., CHUDAKOV D.M. 2012. Next generation sequencing for TCR repertoire profiling: platform-specific features and correction algorithms. *European Journal of Immunology* 42 (11), p. 3073-3083.



Emulsion PCR for the identification of paired TCR chains.
Each T cell is isolated in a separate emulsion droplet, in which reverse transcription, PCR amplification and overlap extension reactions are performed. This yields a library of linked native TCR chain pairs that can be analysed via deep paired-end Illumina sequencing.

CONTENT OF RESEARCH

Every individual's adaptive immune system is composed of tens of millions or more different T and B lymphocyte clones, each of which respectively expresses a distinct T cell receptor or antibody molecule. This tremendous diversity allows the immune system to generate receptors for a broad spectrum of antigens and to thereby ensure an efficient, targeted immune response. After the immune system has eliminated pathogens or diseased tissues, expanded pools of antigen-specific cells can subsequently persist for many years as memory cells, and these may therefore be used to track an individual's history of infections, vaccinations, and possibly even autoimmune and anti-tumour responses. Next generation sequencing (NGS) techniques are capable of reading millions of short DNA fragments, and thus allow deep analysis of the diversity of antibodies and T cell receptors within an individual repertoire. My team employs NGS to study adaptive immunity and, in parallel, also works on advanced molecular technologies and specialized software solutions that collectively allow us to minimize quantitative biases, eliminate input bottlenecks and efficiently correct PCR and sequencing errors to ensure accurate and quantitative analysis of T cell receptor and antibody repertoires.

BRAIN AND MIND RESEARCH

The research programme is dedicated to understanding how the nervous system works at different levels – from molecular and cellular to system; from basic structure and physiology to complex behaviour, including human emotional, cognitive, and social functions; from health to disease.

Research Programme Coordinator:
Ivan Rektor | ivan.rektor@ceitec.muni.cz

OVERALL GOAL

To promote a collaborative theoretical, experimental, and clinical study of the brain from the molecular to the behavioural and cognitive levels. In addition, extensive research will be performed on cellular, molecular, and clinical aspects of damage and reparation of neural tissue and selected brain disorders (e.g. schizophrenia, cerebellar disorders, etc.). Interdisciplinary research will be completed in the fields of neurobiology, neuropsychopharmacology, functional neuroanatomy, neurophysiology, neuroimaging, neuropsychology, neurology, psychiatry, and computational neuroscience. Advanced biomedical imaging methods currently start to cross the previously unreachable boundary of the microscopic and molecular level and their applications can substantially contribute to better understanding of the physiological and pathological changes in the nervous system, the multi-level study of animal and human behaviour, and translational research with a strong impact on the management of neuropsychiatric diseases.

RESEARCH DIRECTIONS

- Development of new biomedical imaging methods and their translation into clinical neuroscience
- Cellular and molecular neurobiology of nerve regeneration and neuropathic pain induction
- Studies dedicated to the neuropsychology-pharmacology-molecular biology interface
- Multimodal approach to the advanced study of cognitive and behavioural functions

RESEARCH GROUPS | LEADERS

Cellular and Molecular Neurobiology | *Petr Dubový*

Multi-modal and Functional Neuroimaging | *Ivan Rektor*

Experimental and Applied Neuropsychopharmacology | *Alexandra Šulcová*

Behavioural and Social Neuroscience | *Milan Brázdil*

Applied Neuroscience | *Irena Rektorová*

Cellular and Molecular Neurobiology

Prof. RNDr. Petr Dubový, CSc.
Research Group Leader
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RESEARCH AREAS

- Cellular and molecular interactions among neurons, glia and immune cells after lesion of nervous system
- Reprogramming of glial cells into neurons

MAIN OBJECTIVES

- The propagation of neuroinflammatory reactions from nerve lesion to remote structures of the nervous system, understanding of its signalling and control mechanisms for neuropathic pain induction and neuroprotection
- The role of extracellular matrix molecules as a substrate for binding of small molecules (neurotrophins, cytokines) for neuroprotection and correct navigation of regenerating axons
- Schwann cell differences alongside motor and sensory axons and their role in correct navigation of regenerating axons
- Cellular and molecular interactions among growing axons, glial and immune cells in nerve prostheses
- Reprogramming of astrocytes into neurons by gene manipulation

Selected Publications

DUBOVY P., RASKA O., KLUSAKOVA I., STEJSKAL L., CELAKOVSKY P., HANINEC P. 2011. Ciliary neurotrophic factor promotes motor reinnervation of the musculocutaneous nerve in an experimental model of end-to-side neurorrhaphy. *BMC Neuroscience* 12, 58.

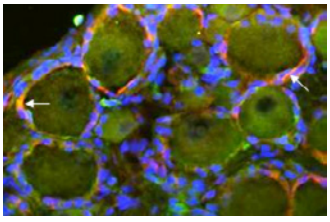
KUBEK T., GHALIB N., DUBOVY P. 2011. Endoneurial extracellular matrix influences regeneration and maturation of motor nerve axons-A model of acellular nerve graft. *Neuroscience Letters* 496 (2), p. 75-79.

BRAZDA V., KLUSAKOVA I., HRADILOVA-SVIZENSKA I., DUBOVY P. 2013. Dynamic response to peripheral nerve injury detected by in situ hybridization of IL-6 and its receptor mRNAs in the dorsal root ganglia is not strictly correlated with signs of neuropathic pain. *Molecular Pain* 9, 42.

DUBOVY P., BRAZDA V., KLUSAKOVA I., HRADILOVA-SVIZENSKA I. 2013. Bilateral elevation of interleukin-6 protein and mRNA in both lumbar and cervical dorsal root ganglia following unilateral chronic compression injury of the sciatic nerve. *Journal of Neuroinflammation* 10, 55.

HRADILOVA-SVIZENSKA I., BRAZDA V., KLUSAKOVA I., DUBOVY P. 2013. Bilateral changes of cannabinoid receptor type 2 protein and mRNA in the dorsal root ganglia of a rat neuropathic pain model. *Journal of Histochemistry and Cytochemistry* 61 (7), p. 529-547.

Double immunostaining of rat dorsal root ganglion section for tumour necrosis factor alpha (TNFa) and marker of satellite glial cells. Yellow-orange colour of fluorescence indicates expression of TNFa in the neuron envelope (arrows).



CONTENT OF RESEARCH

A balance of conditions for the regeneration process and neuropathic pain induction is a fundamental issue in the development of new approaches to repairing damaged connections of the nervous system.

The methods of cellular and molecular biology combined with in vivo and in vitro experimental models will be used to explore the machinery of the extracellular matrix and inflammatory molecules during both nerve regeneration and neuropathic pain induction. The experimental results will be used as the background for clinical improvement of the functional recovery of a damaged nervous system, the development of alternative or new approaches to reconnecting spinal cord neurons with the targeted structures as well as to treating neuropathic pain. Experimental models will also be correlated with findings in human diseases associated with neuropathic pain (such as diabetic neuropathy). Neuronal precursors delivered to the sites of neurodegeneration are able to stop or slow the progression of neurodegenerative diseases, e.g. Huntington's disease (HD). A lack of transplantable neuronal precursors is a bottleneck for clinical use and cellular reprogramming becomes more interesting for various cell replacement therapies. By means of delivering specific neurogenic transcription, we will induce reprogramming of astrocytes in HD animal models into neurons and we will test transdifferentiation efficiency cytologically as well as the functional recovery of motor coordination functions.

Multi-modal and Functional Neuroimaging

Prof. MUDr. Ivan Rektor, CSc.
Research Group Leader

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RESEARCH AREAS

- Support of the Molecular and Functional Imaging Core Facility
- Development and improvement of imaging methods
- Development and implementation of data analysis methods
- Research on functional brain organisation, plasticity and connectivity using imaging methods
- Development of new diagnostic methods

MAIN OBJECTIVES

- Development of new molecular and functional imaging methods and their translation into clinical neuroscience
- Usage of a multimodal approach to the advanced study of cognitive and behavioural functions
- Study of the complex interaction between cortical and subcortical structures when processing higher order brain activities

Selected Publications

BRAZDIL M., MARECEK R., URBANEK T., KASPAREK T., MIKL M., REKTOR I., ZEMAN A. 2012. Unveiling the mystery of deja vu: The structural anatomy of deja vu. *Cortex* 78 (9), p. 1240-1243.

REKTOROVA I., MIKL M., BARRETT J., MARECEK R., REKTOR I., PAUS T. 2012. Functional neuroanatomy of vocalization in patients with Parkinson's disease. *Journal of the Neurological Sciences* 313 (1-2), p. 7-12.

REKTOR I., TOMCIK J., MIKL M., MARECEK R., BRAZDIL M., REKTOROVA I. 2013. Association between the basal ganglia and large-scale brain networks in epilepsy. *Brain Topography* 26 (2), p. 355-362.

REKTOR I., KUBA R., BRAZDIL M., CHRASTINA J. 2012. Do the basal ganglia inhibit seizure activity in temporal lobe epilepsy? *Epilepsy & Behavior* 25 (1), p. 56-59.

REKTOR I., GOLDEMUND D., BEDNARIK P., SHEARDOVA K., MICHALKOVA Z., TELECKA S., DUFEK M., REKTOROVA I. 2012. Impairment of brain vessels may contribute to mortality in patients with Parkinson's disease. *Movement Disorders* 27 (9), p. 1168-1172.

CONTENT OF RESEARCH

Principles in neural connectivity underlying normal and pathological brain processing

The research group will be participating in the specific work package by providing expertise in data collection and their analyses, and by development and implementation of new neuroimaging techniques and data analysis. The research will be performed in the areas of multimodal imaging, computational neuroscience, and analysis of intracerebral EEG signals.

Mechanisms of CNS adaptation to pathological factors and therapy

The structural measures and functional properties of the brain will be studied using high field MR techniques (event related fMRI and spectroscopy, tractography and others), the high-frequency event-related electrophysiological methods handled by this research group. The influence of pharmacotherapy and neurostimulation methods on brain properties will be studied using pharmacoMR and measures of brain excitability (TMS).

MR technology for high-field MR imaging and spectroscopy

The work package is closely coupled with major instrumentation in the Multimodal and Functional Imaging Core Facility. Development will be oriented toward the maximum utilisation of the high spatial and spectral resolution available in the high field by addressing the specific challenges of high-field MR (RF field limitations, contrast mechanism alteration) and the needs of molecular and functional imaging of in vivo and ex vivo subjects. Special attention will be paid to the development of efficient experimental and data processing techniques for robust, fast MR spectroscopic imaging.

Experimental and Applied Neuropsychopharmacology

Prof. MUDr. Alexandra Šulcová, CSc.
Research Group Leader
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RESEARCH AREAS

Experimental pharmacology

- Behavioural pharmacology research is focused on neurobiology and the effects of drugs (including abused drugs: methamphetamine, ecstasy, cannabinoids) on motor functioning, emotionality, cognition, reward
- Pharmacokinetic research is focused on the biotransformation mostly of psychotropic drugs by cytochrome P450 isoenzymes, their interactions and sex differences

Applied pharmacology

- Analyses of the safety and efficacy of pharmacotherapy with psychotropics related to the patient´s metabolic activity of CYP2D6 and CYP1A2

MAIN OBJECTIVES

- Recognition of cellular and molecular mechanisms of selected neuropsychiatric disorders
- Development of new molecular and functional imaging methods and their translation into clinical neuroscience
- Usage of a multimodal approach to the advanced study of behavioural functions
- Analyses of peripheral and CNS metabolic pathways interactions

Selected Publications

KUCEROVA J., PISTOVCAKOVA J., VRSKOVA D., SULCOVA A. 2012. The effects of methamphetamine self-administration on behavioural sensitization in the olfactory bulbectomy rat model of depression. *International Journal of Neuropsychopharmacology* 15 (10), p. 1503-1511.

MACHALOVA A., SLAIS K., VRSKOVA D., SULCOVA A. 2012. Differential effects of modafinil, methamphetamine, and MDMA on agonistic behavior in male mice. *Pharmacology Biochemistry and Behavior* 102 (2), p. 215-223.

JURICA J., ZOURKOVA A. 2013. Dynamics and persistence of CYP2D6 inhibition by paroxetine. *Journal of Clinical Pharmacy and Therapeutics* 38 (4), p. 294-300.

MICALE V., DI MARZO V., SULCOVA A., WOTJAK C.T., DRAGO F. 2013. Endocannabinoid system and mood disorders: Priming a target for new therapies. *Pharmacology & Therapeutics* 138 (1), p. 18-37.

CONTENT OF RESEARCH

The impact of noxious factors on the anatomical, functional and behavioural properties of the CNS are studied. Namely the impact of neurodegenerative diseases, such as schizophrenia, depression and drug addiction.

In animal models of neuropsychiatric disorders (e.g. the MAM model of schizophrenia, bilateral olfactory bulbectomy in rodents for depression or agonistic behaviour for social behaviour) the specific neuronal receptor expression and in vivo neurotransmitter modulation by microdialysis in free moving animals will be contextualized with behavioural changes. The results of instrumental investigations will be compared with clinical, neuropsychological and behavioural data and therapy outcome. A search for new therapies will be based on a combination of basic research such as proteomics, animal experiments and disease modelling with clinical data and testing. In particular the endogenous cannabinoid system and its interactions with the limbic dopaminergic pathways will be studied to discover the basic mechanisms of schizophrenia, depression and addiction.


BRAIN AND
MIND RESEARCH
Exam
Viewing
Filming
3D
SIEMENS

Behavioural and Social Neuroscience

Prof. MUDr. Milan Brázdil, Ph.D.
Research Group Leader

milan.brazdil@ceitec.muni.cz

RESEARCH AREAS

- Large-scale neural network dynamics underlying human behaviour
- Multimodal study of structural and functional connectivity in the human brain in health and neuropsychiatric diseases
- Neural aspects linked to social cognition in healthy subjects and pathological conditions
- Motivational and decision-making mechanisms within the human brain as a background for neuroeconomics

MAIN OBJECTIVE

- Use of a multimodal approach to the advanced study of cognitive and behavioural functions

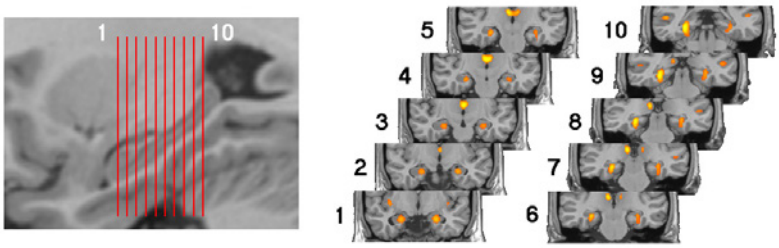
Selected Publications

BRAZDIL M., MARECEK R., URBANEK T., KASPAREK T., MIKL M., REKTOR I., ZEMAN A. 2012. Unveiling the mystery of deja vu: The structural anatomy of deja vu. *Cortex* 78 (9), p. 1240-1243.

KASPAREK T., PRIKRYL R., REHULOVA J., MARECEK R., MIKL M., PRIKRYLOVA H., VANICEK J., CESKOVA E. 2013. Brain functional connectivity of male patients in remission after the first episode of schizophrenia. *Human Brain Mapping* 34 (3), p. 726-737.

ZELINKOVA J., SHAW D.J., MARECEK R., MIKL M., URBANEK T., PETERKOVA L., ZAMECNIK P., BRAZDIL M. 2013. Superior temporal sulcus and social cognition in dangerous drivers. *Neuroimage.* [Epub ahead of print]

ROMAN R., BRAZDIL M., CHLADEK J., REKTOR I., JURAK P., SVETLAK M., DAMBORSKA A., SHAW D.J., KUKLETA M. 2013. Hippocampal negative event-related potential recorded in humans during a simple sensorimotor task occurs independently of motor execution. *Hippocampus.* [Epub ahead of print]



▲ Grey matter volume difference between déjà vu declarers and non-declarers (DV<nonDV) within hippocampus and parahippocampal gyrus.

CONTENT OF RESEARCH

The research group is principally participating in the work package "Principles in neural connectivity underlying normal and pathological brain processing" by comparing the network architecture of structural and functional connectivity and modelling their relationships. Special attention is also paid to studies of changes in neural connectivity in terms of developmental, physiological and pathological neuroplasticity. The principal aim will be to significantly contribute to our knowledge of "wiring" in healthy and diseased brains, as well as to identify the typically reorganised neural networks in some neuropsychiatric conditions that might be used by us in the future as extremely useful early biological markers of the disease. In a parallel way the research group is studying the impact of neurodegenerative diseases such as schizophrenia, and dystonia on the structural measures and functional properties of the brain using high field MR techniques (event-related fMR and spectroscopy, tractography and others), event-related electrophysiological methods (including invasive EEG), and neuromodulation techniques. The results of the instrumental investigations will be compared with clinical, neuropsychological and behavioural data and therapy outcome.

Applied Neuroscience

Prof. MUDr. Irena Rektorová, Ph.D.
Research Group Leader

irena.rektorova@ceitec.muni.cz

RESEARCH AREAS

- Multimodal brain and spinal cord imaging in patients with neurodegenerative brain diseases and in animal models of Parkinson's disease – translational research of early diagnostic biomarkers and markers for the disease's progression
- Pathophysiological mechanisms of peripheral and central neuropathic pain
- Neurological impairment in critical illness
- Repetitive transcranial magnetic stimulation (rTMS) – the development of new treatment stimulation paradigms and predictive markers of rTMS efficacy in neuropsychiatric disorders

MAIN OBJECTIVES

- The validation of early biomarkers of Parkinson's disease and Alzheimer's disease
- The development of new molecular and functional imaging methods and their translation into clinical neuroscience
- The use of a multimodal approach to the advanced study of neuropathic pain and cognitive and behavioural functions

Selected Publications

MITASOVA A., KOSTALOVA M., BEDNARIK J., MICHALCAKOVA R., KASPAREK T., BALABANOVA P., DUSEK L., VOHANKA S., ELY E.W. 2012. Poststroke delirium incidence and outcomes: Validation of the CAM-ICU. *Critical Care Medicine* 40 (2), p. 484-490.

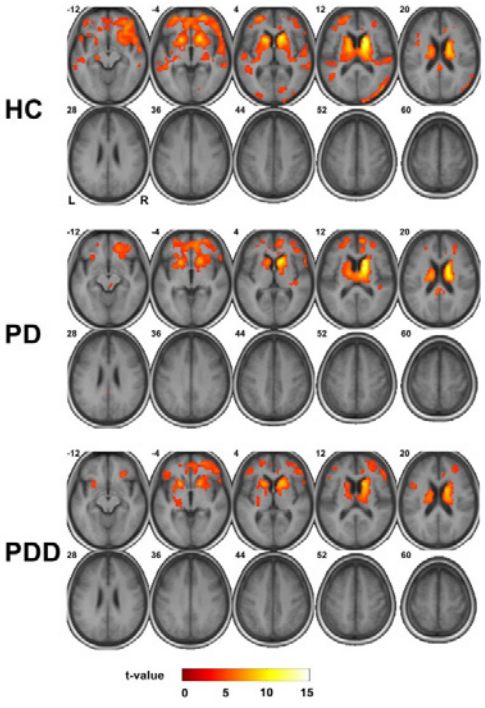
PRIKRYL R., USTOHAL L., PRIKRYLOVA KUCEROVA H., KASPAREK T., VENCLIKOVA S., VRZALOVA M., CESKOVA E. 2013. A detailed analysis of the effect of repetitive transcranial magnetic stimulation on negative symptoms of schizophrenia: a double-blind trial. *Schizophrenia Research* 149 (1-3), p. 167-173.

REKTOROVA I. 2013. Resting-State Networks in Alzheimer's disease and Parkinson's disease. *Neurodegenerative Diseases*.

SROVNALOVA H., MARECEK R., REKTOROVA I. 2011. The role of the inferior frontal gyri in cognitive processing of patients with Parkinson's disease: a pilot rTMS study. *Movement Disorders* 26 (8), p. 1545-1548.

CONTENT OF RESEARCH

The main research focus is on the study of early imaging, biochemical and genetic markers of neurodegenerative brain diseases, pathophysiological mechanisms for neuropathic pain, and cognitive and behavioural symptoms of Parkinson's disease, Alzheimer's disease and schizophrenia. We particularly use multimodal brain and spinal cord imaging and (in combination with) repetitive transcranial magnetic stimulation (rTMS). rTMS utilizes rapid magnetic pulses applied over the scalp with a small hand-held coil to induce precisely timed and localized electrical currents within the cortex of human subjects. It provides a non-invasive tool for studying pathophysiological mechanisms of various motor, cognitive and neuropsychiatric symptoms and may induce treatment effects. Other techniques have also been employed including quantitative sensory testing (QST), dynamic QST, and the immunohistochemistry of dermal nerve fibres using skin biopsy.



Mean brain connectivity maps by seeding the caudate nucleus in healthy controls (HC), patients with Parkinson's disease (PD) and PD dementia (PDD); resting state f-MRI data.

MOLECULAR VETERINARY MEDICINE

Important biological processes and diseases will be studied in selected animal models. Complex mechanisms of resistance to infectious diseases and of mammalian reproduction will be analysed by using various methodological approaches, including host and pathogen genomics and proteomics. Based on this knowledge, potential practical applications will be investigated, like prevention of circulation of important pathogens in the food chain and/or biotechnological potential of specific animal models of mammalian reproduction.

Research Programme Coordinator:
Petr Hořín | horinp@vfu.cz

OVERALL GOAL

Immunity and reproduction are the most important traits related to survival. Infectious diseases of animals have a significant economic impact and represent an environmental risk. This programme should promote the development of complex multidisciplinary approaches to study these basic biological processes and their potential applications in diagnostics, therapy, prevention and public health. Therefore, molecular and cellular mechanisms underlying host and pathogen interactions and mammalian reproduction will be studied. In the field of infectious diseases, pathogens causing important infections, including major foodborne pathogens and emerging pathogens at the human-domestic animal--wildlife interface will be studied in the context of host genetic mechanisms of disease. Possible applications, based on molecular techniques and on improvements in nanotechnologies and gene therapy, will be investigated. In the field of reproduction, chromosomes in somatic and germ-line cells, their evolution and role in reproduction will be analysed. Mechanisms controlling acquisition of meiotic competence during oocyte growth and ageing oocytes will be studied on animal models. Genomic, proteomic and bioinformatic approaches, cell culture, single cell techniques, live cell imaging, and biosensors will be used.

RESEARCH DIRECTIONS

- Analysis of causes, mechanisms and spread of infectious diseases in domestic animals
- Analysis and prevention of circulation of zoonotic pathogens in the food chain
- Host genomics and genetics in infections and reproduction
- Animal models of mammalian reproduction and their biotechnological potential

RESEARCH GROUPS | LEADERS

Molecular Virology | *Vladimír Celer*

Molecular Bacteriology | *Alois Čížek*

Parasitology | *Břetislav Koudela*

Food Safety | *Iva Steinhauserová*

Orthopaedics and Surgery | *Alois Nečas*

Animal Immunogenomics | *Petr Hořín*

Animal Cytogenomics | *Jiří Rubeš*

Mammalian Reproduction | *Martin Anger*

Molecular Virology

Prof. MVDr. Vladimír Celer, Ph.D.
Research Group Leader
celerv@vfu.cz

RESEARCH AREAS

- ssDNA viruses
- Porcine arteriviruses
- scFv antibodies
- Protein expression

MAIN OBJECTIVE

- To obtain novel information on the causes, mechanisms and spreading of infectious diseases in animals

Selected Publications

JAROSOVA V., CELER V., POGRANICHNIY R. 2011. Prevalence and age distribution of porcine torque teno sus virus (TTSuV) in the Czech Republic. *Folia Microbiologica* 56 (2), p. 90-94.

LOBOVA D., PRASEK J., CIZEK A., CELER V. 2011. Evaluation of the use of recombinant Bhlp29.7 in immunoblotting with pig serum as a means to identify herds infected with Brachyspira hyodysenteriae. *Letters in Applied Microbiology* 53 (4), p. 466-472.

LOBOVA D., KOHOUTOVA L., MOLINKOVA D., CELER V. 2012. Prevalence of etiological agents of selected respiratory infections in chicken and turkey farms in the Czech Republic. *Veterinarni medicina* 57 (3), p. 125-132.

JANKOVA J., CELER V. 2012. Expression and serological reactivity of Nsp7 protein of PRRS genotype I virus. *Research in Veterinary Science* 93 (3), p. 1537-1542.

JAROSOVA V., CELER V. 2013. Preliminary epitope mapping of Torque teno sus virus 1 and 2 putative capsid protein and serological detection of infection in pigs. *Journal of General Virology* 94, p. 1351-1356.

CONTENT OF RESEARCH

Current research into animal and human viruses is oriented to an understanding of virulence factors using genomic and proteomic tools.

The main objective of the research is to elucidate the pathogenesis of some single stranded DNA viruses and arteriviruses. Model viruses for this study are circoviruses and anelloviruses of different host species and porcine reproductive and respiratory syndrome virus. Sequencing of virus strains from different clinical conditions is used to define ORFs, which could have an impact on virus virulence. Virus genomes cloned into plasmid vectors to obtain infectious molecular clones as the conserved genetic material of these model viruses are an important tool for the analysis of the functional role of these genetic elements. Transcription of potential virulence factors could be subsequently modified by site-directed mutagenesis and by siRNA molecules in vitro and in vivo models. The in vitro model will be performed on tissue culture transfected with modified molecular clones and then analysed by quantitation of mRNA expression. For in vivo models infection of specific host animals will be used to analyse the virulence of molecular clones. Also the expression of recombinant structural and non-structural virus proteins will provide interesting research tools for the study of host immune response to virus infections.

Molecular Bacteriology

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Research Group Leader
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RESEARCH AREAS

- Molecular epidemiology and genetic background of antimicrobial-resistant bacteria
- Epidemiology of selected tick/vector-borne diseases
- The investigation of antimicrobial properties of potential chemotherapeutics

MAIN OBJECTIVES

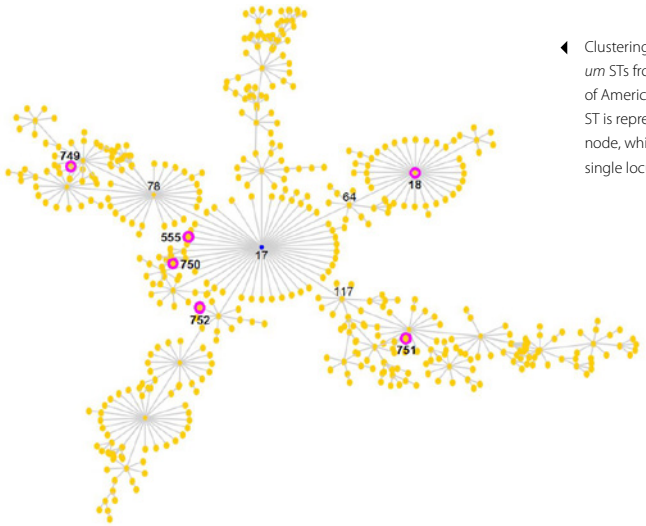
- Antimicrobial resistance in pathogenic and commensal bacteria
- Epidemiology of selected zoonotic bacterial pathogens

Selected Publications

ORAVCOVA V., GHOSH A., ZUREK L., BARDON J., GUENTHER S., CIZEK A., LITERAK I. 2013. Vancomycin-resistant enterococci in rooks (Corvus frugilegus) wintering throughout Europe. *Environmental Microbiology* 15 (2), p. 548-556.

DOLEJSKA M., BRHELOVA E., DOBIASOVA H., KRIVDOVA J., JURANKOVA J., SEVCIKOVA A., DUBSKA L., LITERAK I., CIZEK A., VAVRINA M., KUTNIKOVA L., STERBA J. 2012. Dissemination of IncFII(K)-type plasmids in multiresistant CTX-M-15-producing Enterobacteriaceae isolates from children in hospital paediatric oncology wards. *International Journal of Antimicrobial Agents* 40 (6), p. 510-515.

DOLEJSKA M., DUSKOVA E., RYBARIKOVA J., JANOSZOWSKA D., ROUBALOVA E., DIBDAKOVA K., MACECKOVA G., KOHOUTOVA L., LITERAK I., SMOLA J., CIZEK A. 2011. Plasmids carrying blaCTX-M-1 and *qnr* genes in *Escherichia coli* isolates from an equine clinic and a horseback riding centre. *Journal of Antimicrobial Chemotherapy* 66 (4), p. 757-764.



Clustering of six *E. faecium* STs from the faeces of American crows. Each ST is represented as a node, while lines connect single locus variants.

CONTENT OF RESEARCH

The application of molecular biology techniques in bacteriology is almost endless and clears the way for insight into the genetic background of the antimicrobial resistance and other properties of bacterial pathogens.

Most our research is based on understanding, at molecular, cellular and environmental levels, processes including selection, co-selection, the spread and maintenance of antimicrobial resistance and the flow of emerging resistance genes between commensals and pathogens (host and clone specificity, plasmid characterization, and association among plasmids and resistance genes). Other specific research goals include: (i) to identify the genetic background and epidemiology of resistant clones in food animals, companion animals and wild animals - especially migratory birds; (ii) to analyse the transfer of antibiotic resistant strains from animals to humans; (iii) to identify ways to eliminate resistant bacteria from animal populations and environments; (iv) to investigate the antimicrobial efficacy of new potential chemotherapeutics and natural products.

The biology of vectors and vector-borne diseases is another field of the research group. Since the distribution and spreading of numerous species of vectors acquired a new dynamic during last two decades, the discovery and exact defining of ecological and climatic variables influencing these current changeovers will help us formulate the most imperilled areas in respect to specific vector borne diseases. We concentrate on the study of the distribution, spread, and risk levels of selected tick/vector-borne diseases.

Parasitology

Prof. MVDr. Břetislav Koudela, CSc.
Research Group Leader
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RESEARCH AREAS

- Analysis of the aspects associated with diversity and host specificity of selected model groups of parasitic pathogens, their zoonotic potential and the risk of infectious diseases for human and domestic and wild animals emerging
- Development of specific and sensitive molecular tools for the diagnosis of toxoplasmosis
- Proteomic analysis of the excretory-secretory proteins of the *Trichinella* species and identification of key parasite proteins that are involved in the host-parasite interaction

MAIN OBJECTIVES

- To obtain novel information on the causes, mechanisms and spreading of infectious diseases in domestic animals
- The identification of mechanisms and prevention of the circulation of zoonotic pathogens and commensal antimicrobial-resistant bacteria in the food chain

Selected Publications

POMAJBIKOVA K., OBORNIK M., HORAK A., PETRZELKOVA K.J., GRIM J.N., LEVECKE B., TODD A., MULAMA M., KIYANG J., MODRY D. 2013. Novel insights into the genetic diversity of *Balantidium* and *Balantidium*-like cyst-forming ciliates. *Plos Neglected Tropical Diseases* 7 (3), e2140.

SAK B., PETRZELKOVA K.J., KVETONOVA D., MYNAROVA A., SHUTT K. A., POMAJBIKOVA B., KALOUSOVA B, MODRY D., BENAVIDES J., TODD A., KVAC M. 2013. Long-Term Monitoring of Microsporidia, *Cryptosporidium* and *Giardia* Infections in Western Lowland Gorillas (*Gorilla gorilla gorilla*) at Different Stages of Habituation in Dzanga Sangha Protected Areas, Central African Republic. *PloS ONE* 8 (8), e71840.

BASSO W., HARTNACK S., PARDIN L., MAKSIMOV P., KOUDELA B., VENTURINI M.C., SCHARES G., SIDLER X., LEWIS F.I., DEPLAZES P. 2013. Assessment of diagnostic accuracy of a commercial ELISA for the detection of *Toxoplasma gondii* infection in pigs compared with IFAT,TgSAG1-ELISA and Western blot, using a Bayesian latent class approach. *International Journal for Parasitology* 43 (7), p. 565-570.

JURANKOVA J., OPSTEEGH M., NEUMAYEROVA H., KOVARCIK K. FRENCOVA A., BALAZ V, VOLF J., KOUDELA B. 2013. Quantification of *Toxoplasma gondii* in tissue samples of experimentally infected goats by magnetic capture and real-time PCR. *Veterinary Parasitology* 193 (1-3), p. 95-99.

CONTENT OF RESEARCH

Analysis of the causes, mechanisms and spread of infectious diseases in domestic animals

Emerging diseases at the human-domestic animals-wildlife interface

The aim is to study the principles underlying epidemiology of selected parasitic pathogens transmissible between man and animals, including improving the methods of detection, understanding the links between molecular diversity and host specificity of selected model organisms, with emphasis on zoonotic potential.

Analysis and the prevention of the circulation of zoonotic pathogens in the food chain

Emerging food-borne parasites

This work package focuses mainly on nucleic acid-based and proteomic approaches for the diagnosis of a selected food-borne parasites and analysis of genetic variation among them. Among the major food-borne parasites are *Toxoplasma gondii* and *Trichinella* spp. Based on these two model parasites, the work package aims to contribute to understanding the principles underlying the epidemiology of selected food-borne parasites transmissible between man and animals, including improving methods of the detection.

Host genetics and comparative immunogenomics

Genetic diversity and host-pathogen interactions in specific populations of domestic dogs

Several hundred samples from Kenyan village dogs will be available for genetic diversity and association analysis of various populations and sub-populations of these dogs. For these purposes, selected infectious/parasitic diseases will be diagnosed by molecular and serological techniques: rabies, distemper and several parasite species and phenotypic classification will be made.

Food Safety

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RESEARCH AREAS

- The cultivation and identification of foodborne pathogens
- Molecular biology characterisation of foodborne pathogens
- The monitoring of zoonotic pathogens in the food chain
- Testing of the resistance and survival of selected foodborne pathogens under different processing conditions

MAIN OBJECTIVES

- To obtain novel information on the causes, mechanisms and spreading of infectious diseases in domestic animals
- The identification of mechanisms and prevention of the circulation of zoonotic pathogens and commensal antimicrobial-resistant bacteria in the food chain

Selected Publications

TOMANKOVA J., BORILOVA G., STEINHAUSEROVA I., GALLAS L. 2012. Volatile organic compounds as biomarkers of the freshness of poultry meat packaged in a modified atmosphere. *Czech Journal of Food Sciences* 30 (5), p. 395-403.

HULANKOVA R., BORILOVA G., STEINHAUSEROVA I. 2013. Combined antimicrobial effect of oregano essential oil and caprylic acid in minced beef. *Meat Science* 95 (2), p. 190-194.

HUTAROVA Z., VECEREK V., STEINHAUSEROVA I., MARSALEK P., BORILOVA G., FOREJTEK P. 2013. The effect of treating method of pithed pheasant on the content of biogenic amines in the meat during the course of storage. *Poultry Science* 92 (8), p. 2182-2187.

Campylobacter strains testing (Prof. MVDr. Iva Steinhauserova, CSc.).

CONTENT OF RESEARCH

In order to form effective strategies to prevent the circulation of food-borne pathogens in the food chain, it is necessary to elucidate the incidence, characteristics and behaviour of these bacteria in food.

Pathogenic and potentially pathogenic bacteria are nowadays of great interest from a food safety point of view. The contamination of food matrices will be studied by culture independent methods based on PCR and real time PCR in order to determine the impact of food processing on pathogens' presence and survival. The aims are the monitoring, typing/subtyping, quantification of selected microorganisms, and identification of genes responsible for the resistance and survival of selected food-borne pathogens under the stress conditions used in the food industry.

Selected food-borne pathogens (e.g. Campylobacter spp., Listeria sp., Salmonella spp.) will be monitored from farm to consumer. Isolated strains from various types of farm (conventional and organic), processing plants and from patients suffering from food-borne diseases will be characterised by phenotyping and genotyping methods. The resistance and survival of selected food-borne pathogens under different processing conditions will be studied directly in food samples.

Orthopaedics and Surgery

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Research Group Leader
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RESEARCH AREAS

- Small animal orthopaedics
- Bone and joint surgery
- Arthroscopy

MAIN OBJECTIVES

- The development and testing of new biomaterials for possible implantation into defects of musculoskeletal and soft tissues in model animals
- To obtain novel information on mechanisms of infections in animals
- Definition of the role of host genetics in infectious diseases

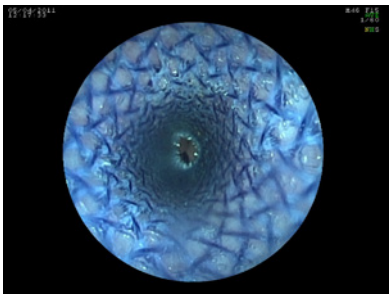
Selected Publications

URBANOVA L., BLAZEK-FIALOVA I., SRNEC R., PENCIK J., KRSEK P., NECAS A. 2012. Mathematical Model of Mechanical Testing of Bone-Implant (4.5 mm LCP) Construct. *Acta Veterinaria Brno*, 81 (2), p. 211-215.

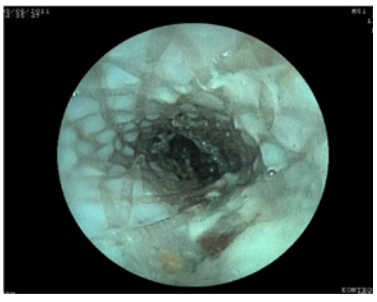
HLAVSA J., PROCHAZKA V., CRHA M., SVOBODOVA I., ANDRASINA T., RAUSER P., URBANOVA L., PAVLIK T., LORENZOVA J., NECAS A., KALA Z. 2012. Healing dynamics of porcine pancreatic parenchyma after radiofrequency ablation - in vivo experimental pilot study. *Acta Veterinaria Brno* 81 (4), p. 427-431.

CRHA M., HLAVSA J., GROLICH T., HEP A., NECAS A. 2013. An innovative covered biodegradable esophageal stent: experimental in vivo study in miniature pigs. Poster, The 1st World Congress on Controversies in Gastroenterology (CIGI), June 13-15, 2013, Berlin, Germany.

CRHA M., URBANOVA L., RAUSER P., NECAS A. 2013. Comparison of Harmonic scalpel® and Enseal® device utilization in preventive laparoscopic gonadectomy of bitches. Poster, World Veterinary Conference, September 17-20, 2013, Prague, Czech Republic.



Covered polydioxanon oesophageal stent (ELLA –CS, s.r.o., HK, CZ) immediately after implantation into oesophagus of miniature pig.



Covered polydioxanon oesophageal stent 4 weeks after implantation in a pig No.2.

CONTENT OF RESEARCH

Development and testing of biomaterials for possible implantation into defects of musculoskeletal and soft tissues in model animals. Analysis of the causes and mechanisms of infections in animals; host genetics and comparative immunogenomics.

The development and testing of new biomaterials for possible implantation into defects of musculoskeletal and soft tissues in model animals

The main objective is (in cooperation with research group Advanced Polymers and Composites from research programme Advanced Materials) to specify (in vitro, ex vivo) of newly developed biomaterials (with possible use in orthopaedics, neurosurgery and soft tissue surgery), their biomechanical properties and interactions of the biomaterials with specific cells.

Analysis of the causes and mechanisms of infections in animals

The objective is to evaluate the clinical manifestations and to make analyses of the causes of infections in surgically treated bone and joint diseases in model animals. Analysis of the causes of bone and joint infections in surgically treated model animals can contribute to the possible reduction of infection complications in veterinary surgery and human medicine.

Host genetics and comparative immunogenomics

The objective is to evaluate characteristics of clinical manifestations of bone and joint infections in relation to surgical procedures in animal models for the purposes of genetic analysis.

Animal Immunogenomics

Prof. RNDr. MVDr. Petr Hořín, CSc.
Research Group Leader

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RESEARCH AREAS

- Immunogenetics and immunogenomics
- Comparative and evolutionary genomics
- Genetic resistance to infectious disease, host and pathogen interactions

MAIN OBJECTIVES

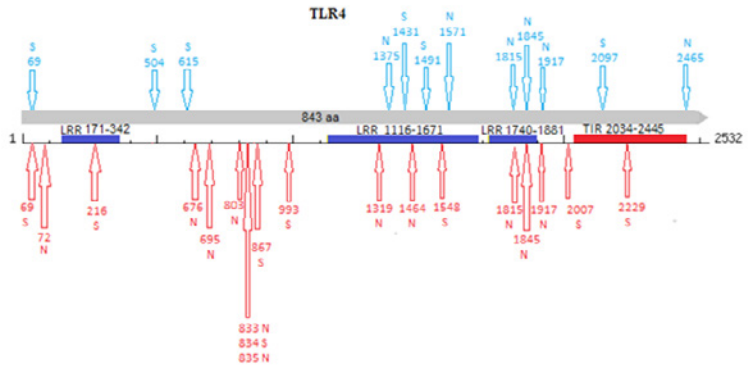
- To obtain novel information on the genetic mechanisms of infectious diseases in domestic animals
- Definition of the role of host genetics in infectious diseases
- Analysis of genetic diversity, evolution and selection in selected immunity-related genes based on comparative immunogenomic analysis
- Analysis of genetic mechanisms of host and pathogen interactions

Selected Publications

FUTAS J., HORIN P. 2013. Natural killer cell receptor genes in the Family Equidae: Not only Ly4. *PLoS One*, 8 (5), e64736.

KLUMPLEROVA M., VYCHODILOVA L., BOBROVA O., CVANOVA M., FUTAS J., JANOVA E., VYSKOCIL M., VRTKOVA I., PUTNOVA L., DUSEK L., MARTI E., HORIN P. 2013. Major histocompatibility complex and other allergy-related candidate genes associated with insect bite hypersensitivity in Icelandic horses. *Molecular Biology Reports* 40 (4), p. 3333-3340.

DURKIN K., COPPIETERS W., DROGEMULLER C., AHARIZ N., CAMBISANO N., DRUET T., FASQUELLE C., HAILE A., HORIN P., HUANG L., KAMATANI Y., KARIM L., LATHROP M., MOSER S., OLDENBROEK K., RIEDER S., SARTELET A., SOLKNER J., STALHAMMAR H., ZELENIKA D., ZHANG Z., LEEB T., GEORGES M., CHARLIER C. 2012. Serial translocation by means of circular intermediates underlies colour sidedness in cattle. *Nature* 482 (7383), p. 81-84.



Synonymous (S) and non-synonymous (N) interspecific differences (blue) and within-species polymorphisms (red) in the coding sequence of the toll-like receptor 4 (*TLR4*) gene in the family *Equidae*. S (by Petra Šplíchalová).

CONTENT OF RESEARCH

Infectious diseases are one of the most important causes of mortality and morbidity in man and animals. Novel genomic tools allow us to analyse the mechanisms of host and pathogen interactions and to identify important host genes contributing to susceptibility to disease.

The contribution of host genetic factors to infectious diseases is one of the fundamental issues in understanding their pathogenesis. The general objective of this research group is to identify candidate genes involved in host resistance to infectious disease and to analyse their diversity, evolution and selection. Two kinds of immunity-related candidate genes will be analysed: genes at the host and pathogen interface, involved in antigen presentation and recognition, and immunity-related genes involved in signalling, regulatory and effector immune pathways. Model populations of domestic, free-ranging and captive domestic animals will be studied for this purpose

The major histocompatibility complex and natural killer cell receptor genes represent complex genetic regions involved in evolutionary interactions between hosts and pathogens. Genomic structure, population diversity, evolution, selection and associations with disease of these regions will be studied in Equids, Camelids and other mammalian groups. For selected species, the role of the immunogenome in mechanisms of susceptibility to specific infections will be investigated.

Animal Cytogenomics

Prof. MVDr. Jiří Rubeš, CSc.
Research Group Leader
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RESEARCH AREAS

- Evolution of the mammalian karyotype
- Chromosomal abnormalities
- Male meiosis and errors of meiosis

MAIN OBJECTIVES

- To obtain novel information on chromosomal rearrangements that have taken place during the process of evolution in the family Bovidae and Equidae by using comparative FISH
- Determination of associations between the frequencies of chromosomally abnormal sperm, semen parameters and the reproductive outcome of the carriers of chromosomal translocations
- The meiotic process including homologous synapsis, and frequency and distribution of recombination events will be studied on pachytene spermatocytes in animal models to elucidate the progress of meiosis in individuals with normal and abnormal karyotypes
- The frequency of chromosomal rearrangements with breakpoints in T-cell receptor (TR) genes will be studied in selected species with respect to the proportion of γδ T-cells in the peripheral lymphocyte pool, karyotype evolution and TR genes structure

Selected Publications

MUSILOVA P., KUBICKOVA S., VAHALA J., RUBES J. 2013. Subchromosomal karyotype evolution in Equidae. *Chromosome Research* 21 (2), p. 175-187.

VOZDOVA M., HERACEK J., SOBOTKA V., RUBES J. 2012. Testicular sperm aneuploidy in non-obstructive azoospermic patients. *Human Reproduction* 27 (7), p. 2233-2239.

VOZDOVA M., KASIKOVA K., ORACOVA E., PRINOSILOVA P., RYBAR R., HORINOVA V., GAILLYOVA R., RUBES J. 2012. The effect of the swim-up and hyaluronan-binding methods on the frequency of abnormal spermatozoa detected by FISH and SCSA in carriers of balanced chromosomal translocations. *Human Reproduction* 27 (3), p. 930-937.

RUBES J., RYBAR R., PRINOSILOVA P., VEZNIK Z., CHVATALOVA I., SOLANSKY I., SRAM R.J. 2010. Genetic polymorphisms influence the susceptibility of men to sperm DNA damage associated with exposure to air pollution. *Mutation Research – Fundamental and Molecular Mechanisms of Mutagenesis* 683 (1-2), p. 9-15.

CONTENT OF RESEARCH

The use of comparative molecular cytogenetics for the study of genome reconstructions in animals, identification of highly conserved regions and study of genetic diversity. Study of chromosomal abnormalities in somatic and gamete cells.

Comparative cytogenomics and the genetics of reproduction

The conservation of selected chromosome regions in different species of Equidae and Bovidae is analysed. Changes in sizes and morphology are characteristic of the evolutionary process. The objectives are to obtain novel information on the chromosomal rearrangements that have taken place during the process of evolution in the Bovidae and Equidae families by using comparative FISH to provide further insights into the evolution of the karyotypes in these families. Meiotic cell division is a complex process including recombination and distribution of chromosomes into gametes. The objective of this work package is to obtain information on the meiotic behaviour of chromosomes separated in one and fused in other species of the Bovidae using immunofluorescence and FISH. Special attention is paid to the synapsis and recombination of sex chromosomes, especially in those species where sex-autosomal fusion occurred during karyotypic evolution. The primary cause of decreased reproductive potential in translocation carriers is incorrect meiotic segregation of chromosomal pairs included in translocation. Our aim is to draw a general conclusion on the associations between the frequencies of chromosomally abnormal sperm, semen parameters and the reproductive outcome. Chromosomal rearrangements with breakpoints in T-cell receptor genes are studied in selected species.

Mammalian Reproduction

MVDr. Martin Anger, Ph.D.
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RESEARCH AREAS

- Advanced confocal and widefield microscopy, live cell imaging, FRET and FRAP
- Image analysis revealing spatial and temporal interactions of molecules in cells
- Microinjection of oocytes and embryos, ICSI, in vitro fertilization and nuclear transfer
- Mouse transgenic technology for studying genes important for chromosome segregation

MAIN OBJECTIVES

- Characterization of mechanisms controlling chromosome segregation in mammalian oocytes and embryos
- Characterization of major changes in cell cycle regulation during transition from meiosis into mitosis after fertilization in mammals
- Characterization of mechanisms responsible for the creation of an euploidy in mammalian oocytes and embryos

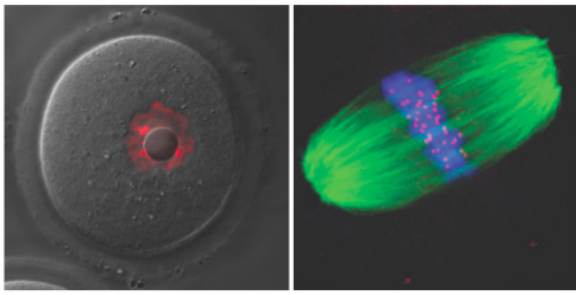
Selected Publications

BHATTACHARYYA T., GREGOROVA S., MIHOLA O., ANGER M., SEBESTOVA J., DENNY P., SIMECEK P., FOREJT J. 2013. Mechanistic basis of infertility of mouse intersubspecific hybrids. *Proceedings of the National Academy of Sciences of the United States of America* 110 (6), p. E468-E477.

SEBESTOVA J., DANYLEVSKA A., NOVAKOVA L., KUBELKA M., ANGER M. 2012. Lack of response to unaligned chromosomes in mammalian female gametes. *Cell Cycle* 11 (16), p. 3011-3018.

HORNAK M., JESETA M., MUSILOVA P., PAVLOK A., KUBELKA M., MOTLIK J., RUBES J., ANGER M. 2011. Frequency of aneuploidy related to age in porcine oocytes. *PLoS One* 6 (4), e18892.

XU Z., CETIN B., ANGER M., CHO U.S., HELMHART W., NASMYTH K., XU W. 2009. Structure and function of the PP2A-shugoshin interaction. *Molecular Cell* 35 (4), p. 426-441.



GV oocyte, DNA (red) labelled by microinjection of histone H2B fused to mCherry protein.

Mouse meiosis I spindle, chromosomes (blue) stained by DAPI, kinetochores (red) by CREST serum and tubulin (green) by monoclonal antibody.

CONTENT OF RESEARCH

Mammalian germ cells and embryos are known for their unique developmental potential and plasticity. They are however also known for a significantly high incidence of errors accompanying segregation of their chromosomes. The research interest of our group is focused on mechanisms controlling chromosome segregation in meiosis, during transition from meiosis into mitosis initiated by fertilization and during the first cleavage cycles of developing embryos. As it is known that the frequency of chromosome segregation errors responsible for aneuploidy increases with age, we are also interested in changes introduced into cell division by maternal ageing. Because mammalian oocytes and embryos are relatively rare cells, for our studies we are using methods that could be applied to a single cell, such as live cell imaging microscopy, FRET biosensors and kinase assays. Some of these methods were developed in our laboratory. An essential part of our research is accomplished by using mouse transgenic technology, which we employ to disrupt regulatory pathways or to address the role of a particular gene. We believe that our studies will have a clear impact on human IVF and also on animal biotechnology.

CORE FACILITIES

The CEITEC core facilities offer access to cutting-edge, and often expensive, equipment to the research community. Our goal is to be a central hub for shared resources that provide academic and industrial scientific investigators the use of instrumentation and also technology development and service.

CEITEC successfully networks with other research infrastructures across Europe. In June 2011, the Structural Biology core facilities were approved as a National Affiliated Centre of INSTRUCT. We also actively participate in other European infrastructure projects such as ELIXIR (bioinformatics).

All CEITEC core facilities are available to external users (academia or companies).

LOCATIONS OF CORE FACILITIES

The core facilities are being established in two locations in Brno:

- The campus of Masaryk University in Brno - Bohunice, the centre of life sciences and biomedicine, benefits from being near the Faculty Hospital in Brno and the INBIT Biotech incubator.

- The Brno University of Technology campus in Brno Pod Palackého vrchem, the centre for material science and advanced technologies, neighbours the Czech Technology Park and INMEC.

CORE FACILITIES | HEADS

Nanofabrication and Nanocharacterization | *David Škoda*

Structural Analysis Laboratory | *Ondřej Man*

Biomolecular Interaction | *Michaela Wimmerová*

Single Crystal X-ray Diffraction | *Jaromír Marek*

Josef Dadok National NMR Centre | *Radovan Fiala*

Cryo-electron Microscopy and Tomography | *Jürgen Plitzko*

Proteomics Core Facility | *Zbyněk Zdráhal*

Core Facility - Genomics | *Boris Tichý*

Multimodal and Functional Imaging Laboratory | *Ivan Rektor*

Nanofabrication and Nanocharacterization

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Head of Core Facility
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★ Unique Features

The core facility is equipped with a wide spectrum of instruments divided into three closely related parts: nano/micro-nanolithography processes, special nano/microfabrication processes and complex analysis of nano/microstructures (morphology, composition, structure and electrical, magnetic, and optical properties generally).

MAIN ACTIVITY

Core facility Nanofabrication and Nanocharacterization forms an essential part of the instrumental base for materials science and advanced technology research within CEITEC. To keep all related technologies and analysis methods close to each other, the equipment of the core facility is centralized into the one specially arranged laboratory. Depending on the fabrication and analysis process the laboratories are separated into isolated rooms with appropriate cleanness (100 –100 000).

KEY EQUIPMENT

Lithography infrastructure:

- Optical and electron beam lithography based systems (mask photolithography, UV direct laser writing – Heidelberg DWL66FS, e-beam lithography – Tescan MIRA3 + interferometric table)
- Lithographic digesters (spin coaters, hot plates, ultrasonic bath)
- Inspection instruments (profilometer, optical spectroscopy and microscopy)

Etching & Deposition:

- Deposition by sputtering and evaporation techniques (Atomic Layer Deposition – Cambridge NanoTech Fiji 200)
- Reactive Ion Etching techniques (Plasma stripper)

Packaging & Testing:

- Wire bonding machine (TPT HB 16)

Optical measurements:

- Optical spectroscopy and spectroscopic ellipsometry (J. A. Woollam)
- Raman spectroscopy (microRaman spectroscopy, Tip Enhanced Raman Spectroscopy - MDT NTegra Spectra), photoluminescence
- FT-IR Microscopy (Bruker Vertex 80 + Hyperion 3000)

Microscopy / Analysis:

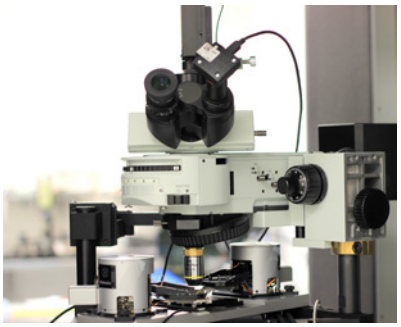
- Scanning Probe Microscopy (Atomic Force Microscopy, Scanning Tunnelling Microscopy, metrology SPM, …), Scanning Near-field Optical Microscopy (Nanonics MultiView 4000)
- Scanning Electron Microscopy (Tescan Mira3, Tescan Lyra3)

Nanolithography / Nanomanipulation:

- FIB/SEM system with nanomanipulators (Tescan Lyra3 XMH)

Electrical & Magnetic measurements:

- Low temperature electromagnetic properties measurement system



Wire bonding TPT 16 HB (left), SNOM MultiView 4000 02 (right)

Structural Analysis Laboratory

Ing. Ondřej Man, Ph.D.
Head of Core Facility
ondrej.man@ceitec.vutbr.cz

★ **Unique Features**

In its fully operational state, the core facility will provide high-level instruments such as HR TEM, HR SEM, FIB/SEM, X-ray diffractometer with high brightness source and an SAXS-enabled X-ray diffractometer. In the background, there will be fully equipped laboratories dedicated to sample preparation. The instruments will be handled by skilled operators ready to help with awkward samples. The operators will also participate in research projects.

MAIN ACTIVITY

The core facility will be - after completion - equipped with top-class instruments for transmission and scanning electron microscopy, microanalysis and X-ray diffraction. There will also be sufficient background for preparation of samples from various materials that can be described as "non-life science". The people within the core facility participate in various research activities which have a close relation to the activities of the Advanced Ceramic Materials, Advanced Polymers and Composites, and Cybernetics in Material Science research groups.

The priority is to focus on the study of the microstructure, submicrostructure and local chemical analysis of new advanced ceramic and polymer materials and composites based on those materials. Another research area is nanocrystalline thermal barrier coatings and materials with ultra-fine grains obtained via SPD (Severe Plastic Deformation), for instance by ECAP.

KEY EQUIPMENT

- X-Ray Powder diffractometer with attachments (high temperature chamber up to 1600 °C, low temperature chamber down to -190 °C and high temperature reactive chamber up to 900 °C) – fully operational in provisional space
- X-Ray diffractometer (with rotating Cu anode) for thin film measurements, Rigaku Smart Lab 9 kW with attachments (high temperature C-dome chamber up to 1100 °C, software for qualitative and quantitative analysis, crystallite size and lattice strain analysis, texture and stress analysis, etc.) – fully operational in provisional space
- High resolution transmission electron microscope (HR TEM) with an information limit better than 0.15 nm in TEM and 0.35 nm in STEM mode. Equipped with high resolution EELS and EDS spectrometers. To be brought into service during 2014.
- High resolution scanning electron microscope (HR SEM) with sub-nm resolution, capable of imaging at very low landing energies of primary electrons (of the order of tens of electronvolts), and in-lens detection of SE and BSE. Equipped with STEM detector and EDS + EBSD analysers. To be brought into service during 2014.
- Combined focussed ion beam/scanning electron microscope (FIB/SEM), with high resolution ion as well as electron columns. Equipped with a gas injection system, nanomanipulator, EDS and EBSD systems. To be brought into service during 2014.
- Various sample preparation tools for SEM and TEM samples, as well as samples for light microscopy (disc grinders and polishers, ion polishers, etc.). To be brought into service during 2014.

Biomolecular Interaction

Prof. RNDr. Michaela Wimmerová, Ph.D.
Head of Core Facility
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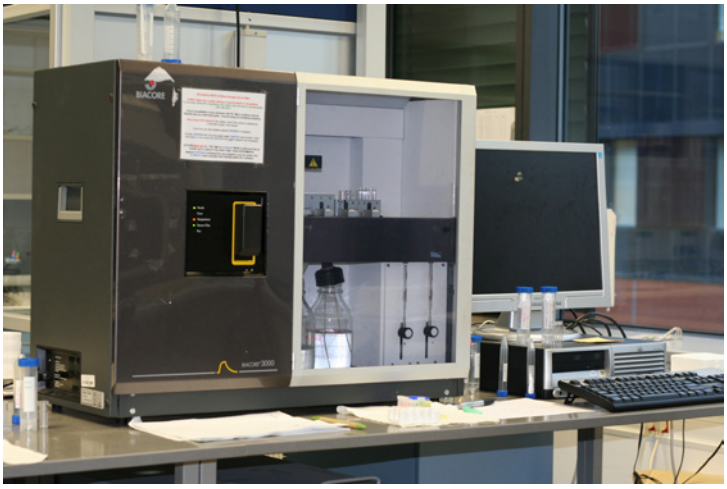
★ Unique Features

Centralised organisation of instrumentation and a team of experienced researchers will ensure expert services for untrained users and the cost-effective use of resources. The successful application of biosensor-related techniques in biology requires a multidisciplinary knowledge in biochemistry, biophysics, and bioorganic chemistry.

MAIN ACTIVITY

The core facility provides services to study (bio)molecular interactions in real time using biosensor and calorimetry-based methods.



KEY EQUIPMENT (CORE FACILITY FULLY OPERATIONAL FROM 2014)

- Semi-automated SPR biosensor
- Automated isothermal titration calorimeter (Auto ITC200 already installed and available to users)
- Multichannel SPR system

Before the core facility becomes completely operational, current instrumentation (consisting of SPR BiaCore 3000, calorimeters VP-ITC, VP-DSC, ITC200, analytical ultracentrifuge ProteomLab XLI, CD spectrometer Jasco 850) purchased within past projects at Masaryk University will be available for users upon request.

AutoITC (top picture),
Biacore (bottom picture)

Single Crystal X-ray Diffraction

Assoc. Prof. RNDr. Jaromír Marek, Ph.D.
Head of Core Facility
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★ **Unique Features**

The diffraction of X-rays in single crystal samples is the most important and – if an appropriate sample is available – also the fastest methodology currently available for the determination of the atomic structures of molecules and/or macromolecules and their complexes.

On the other hand, SAXS is a technique capable of determining structural characteristics such as mono dispersity or aggregation, oligomeric state, low resolution three-dimensional shape or even quaternary structure not from a crystal but from a solution of (bio) macromolecules.

The centralized organization of expensive instrumentation for SAXS and single crystal studies and highly trained staff allow the cost-effective use of resources and obtaining of experimental results in rapid responses to the demands of even untrained users.

MAIN ACTIVITY

The core facility of Single Crystal X-ray Diffraction is equipped with top-class instruments for diffraction experiments with single crystal samples focused on the determination of the 3-D structure of (macro) molecules down to atomic resolution and for small angle X-ray scattering (SAXS) experiments with isotropically scattering samples focused on determination of the shape and size of macromolecules or nanoparticles.

The range of applicable molecular mass for diffraction methods: from 10^2 up to 10^6, where the lower value covers molecules significant for nanotechnology, materials science or pharmacology and the upper limit covers biomacromolecules such as nucleic acids, proteins and their complexes.

Range of applicable particle sizes for SAXS: from 2 to 100 nm.

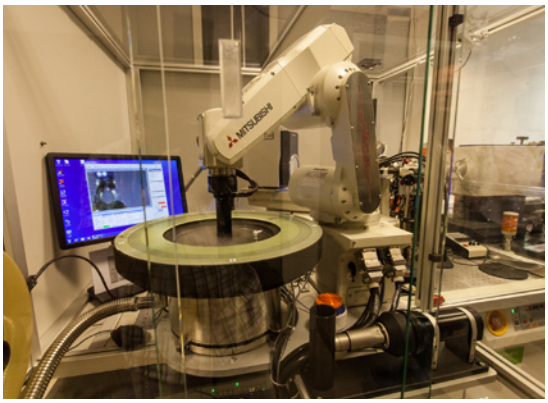
SERVICES PROVIDED

- Quality control of solution of biological macromolecules prior crystallization and/or SAXS
- Basic characterization of solutions of biological macromolecules by SAXS
- Determination of a low resolution 3-D shape of biological macromolecules by SAXS
- SAXS characterization of nanoparticles
- Robotized high throughput initial screening of crystallization conditions for biomacromolecules
- Optimization of selected crystallization conditions
- Screening and optimization of conditions for cryoprotection of protein crystals
- Testing of the diffraction quality of protein crystals, derivatives, etc. prior to data collection
- Collection of diffraction data from crystals of biological macromolecules at home source
- Data collection and solving of crystal structures from non-biological single crystals

More complex services, training courses, access to a wide list of crystallisation instrumentation purchased within the past projects at Masaryk University and/or help with diffraction data analysis are available on request.

KEY EQUIPMENT

- Rigaku HighFlux HomeLab™ robotized macromolecular diffraction system with ACTOR sample changer optimized for work at Cu-K_α wavelength
- Rigaku HighFlux HomeLab™ universal, dual wavelength (Mo-K_α and Cu-K_α) diffractometer
- Rigaku BioSAXS-1000 SAXS camera for small angle X-ray scattering from solutions of biological macromolecules
- Automated crystallisation laboratory – liquid handling, available from 2014
- Automated crystallisation laboratory – sample storage and inspection, available from 2014



▲ Rigaku BioSAXS-1000

Josef Dadok National NMR Centre

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★ **Unique Features**

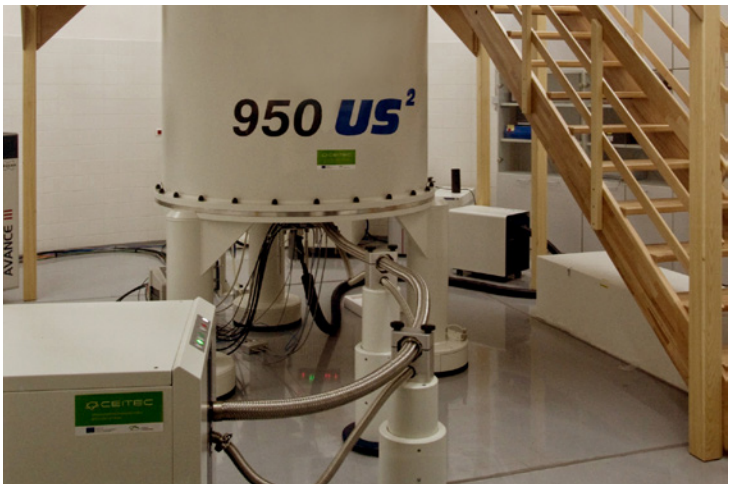
NMR (Nuclear Magnetic Resonance) spectroscopy is a key technology for research in the modern life sciences allowing detailed investigation of biomolecular structure and dynamics at the atomic level, both in solutions and in the solid state. The successful application of NMR in biology requires a multidisciplinary approach combining biochemistry, molecular biology, quantum physics, electronics, data analysis, and computational chemistry. The high-end instrumentation and the team of experienced researchers will ensure expert services, user training, and the cost-effective use of resources both for internal and external users. Benefits include access to state-of-the-art high-field NMR instrumentation and support in processing, analysis and interpretation of experimental data. External user projects will be selected by peer review on the basis of scientific merit, technical suitability and feasibility. The centre will also offer training enabling non-specialists to develop the necessary skills.

KEY EQUIPMENT

- 950 MHz NMR spectrometer for high-resolution spectroscopy in liquids
- 850 MHz NMR spectrometer for high-resolution spectroscopy in liquids
- 700 MHz NMR spectrometer for high-resolution spectroscopy in liquids
- 700 MHz NMR spectrometer for high-resolution spectroscopy in liquids and solids
- 600 MHz NMR spectrometer for high-resolution spectroscopy in liquids
- 500 MHz NMR spectrometer for high-resolution spectroscopy in liquids and solids

MAIN ACTIVITY

The core facility provides for investigation of biomolecular structure and dynamics by NMR spectroscopy, and the development of novel methodologies for biomolecular NMR spectroscopy (the development of new pulse sequences with improved sensitivity and resolution, the development of methods providing additional structural restraints, the improvement of strategies for three-dimensional structure calculations and analysis of relaxation data in terms of biomolecular dynamics).



Cryo-electron Microscopy and Tomography

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★ **Unique Features**

The main objective of the core facility is to establish a world--class facility for cryo-electron microscopy accessible also for external users. The centre will provide access to EM instrumentation set up for high-throughput image acquisition for single particle analysis as well as for the acquisition of cellular cryo-electron tomograms. Moreover, it will provide assistance to external users/collaborators in image processing (e.g. 3-D reconstruction, denoising, pattern recognition, segmentation and visualization). External user projects will be selected by peer review on the basis of scientific merit, technical suitability and feasibility. The centre will also offer training enabling non-specialists to develop the necessary skills. The high-end instrumentation and the team of experienced researchers will ensure expert services, user training and the cost-effective use of resources.

MAIN ACTIVITY

Modern electron microscopy in structural biology on a cellular and molecular level is performed by cryo-electron microscopy and cryo-electron tomography. Cryo-electron tomography (cryo-ET) is the only method to address pleiomorphic structures such as cells and organelles in a close-to-native state, while cryo--electron microscopy (cryo-EM) is applied to the study of single particles, primarily larger macromolecular complexes, which have been isolated and purified by biochemical methods. Both methodologies provide information on the cellular and molecular level and are therefore ideal for in-depth structural-functional analysis in combination with state-of-the-art biochemical characterisation. The main activities of the core facility will be centred on the application of cryo-EM and cryo-ET, implementation of the required image processing capabilities, and exploration of suitable cryo-preparation techniques.

KEY EQUIPMENT

- Transmission high-throughput cryo-electron microscope 300 kV
- Transmission cryo-electron microscope 200 kV
- Equipment for sample preparation
- Vitrification robot

FEI Titan Krios (300 kV) with FEI Eagle CCD (left)
FEI Tecnai F20 (200 kV) with FEI Falcon DDD (right)

Proteomics Core Facility

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★ **Unique Features**

The core facility provides the academic community and other subjects with access to advanced proteomic technologies, primarily state-of-the-art mass spectrometry instrumentation, based on shared resources and highly trained staff. The concentration of expensive technologies and know-how results in rapid responses to the demands of the research community and effective utilization of resources.

MAIN ACTIVITY

The core facility provides services in the field of mass spectrometry-based proteomics. The core facility activities cover all the steps of proteomic analysis – protein isolation, fractionation/separation of protein mixtures, and characterisation of proteins and protein modification by mass spectrometry including bioinformatic data processing. The core facility mainly cooperates with life science CEITEC research groups but also has close contacts with academic institutions and biotechnology companies outside CEITEC providing proteomic services within a wide range of projects covering the areas of molecular biology, human and animal medicine, food chemistry, ecology, agriculture, etc.

KEY EQUIPMENT

- LC-MS/MS with high-resolution mass spectrometer Orbitrap Elite (with ETD)
- LC-MS/MS with hybrid mass spectrometer Qtrap 6500
- LC-MS/MS with ion trap mass spectrometer HCT Ultra (with ETD)
- MALDI-TOF/TOF mass spectrometer

LC-MS/MS system with high resolution mass spectrometer Orbitrap Elite.

Core Facility – Genomics

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★ **Unique Features**

A combination of high-end equipment and expertise for the complete experimental workflow from advanced sample preparation to complex genome analysis. Precise sample preparation techniques (cell sorting, microdissection) followed by a combination of various complementary approaches in the analysis of the genome (massive parallel sequencing, microarrays, quantitative PCR) will make it possible to perform even very complex experimental designs, including single cell genomics or diseased vs. healthy cells genome and transcriptome analyses.

MAIN ACTIVITY

The core facility provides instrumentation and expertise for the application of new high-throughput methods in basic and applied research, and the development and optimisation of methods for genomic analyses.

KEY EQUIPMENT

- High-throughput massive parallel sequencers
- Illumina MiSeq
- Roche GS Junior
- FACS cell sorter
- Cell analysis system
- Olympus ScanR
- Digital PCR and real-time qPCR
- Microarray system
- Agilent

Multimodal and Functional Imaging Laboratory

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★ **Unique Features**

Basic as well as applied research in medicine including pharmacology, molecular and cell biology requires *in vivo* insight into live organs and tissues as a very important part of a multi-level and multidisciplinary approach. Modern MRI methods make it possible not only to visualize the anatomical structures of living things, but also to discover their functional organization and the chemical mechanisms underlying health and disease. Currently, effort is being put into tracking their dynamics, to multimodal imaging (such as by combining MR with electrophysiology or transcranial magnetic stimulation), and to visualizing biological processes at the cellular and molecular levels using molecular MRI by employing targeted contrast agents, spectroscopic imaging, diffusometry or relaxometry. The intended infrastructure will be also used for technological and methodological research aiming to improve existing imaging methods or to develop new methods and data processing strategies for the study of animate as well as inanimate matter, thus establishing a bridge between the life and material sciences.

MAIN ACTIVITY

The core facility provides for methodologies for *in vivo* magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) of humans and living tissues with spatial resolution down to 0.1 mm, with the main application in functional (fMRI), multimodal, and multiparametric imaging of the brain.

KEY EQUIPMENT

- Two whole-body human 3T MR scanners (with the possibility of simultaneous functional studies and multinuclear spectroscopy)
- MR compatible high-density EEG system
- MR compatible stimulation system

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