**Use of non-traditional microorganisms in the production of beer**

*Supervisor: Doc. Ing. Tomáš Brányik, Ph.D.*  
*Spec. Supervisor: Ing. Marcel Karabin, Ph.D.*

Increasing market competition leads breweries to expand their product range. One possibility of new product development is the use of non-traditional microorganisms throughout the fermentation process. One such group of non-traditional microorganisms are probiotics, beneficial to human health, typically in improving immunity and maintaining the balance of intestinal microflora. The aim of the project will be to obtain a set of microorganisms with probiotic properties with the ability to ferment brewery wort and/or tolerate the environment of traditional and alcohol-free beers without reducing viability. In addition will be studied the fermentation capacity of selected microorganisms, the formation of flavor active compounds and the effect of the presence of non-traditional microorganisms on taste and colloidal stability of the products.

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**Influence of metal nanoparticles and their oxides on the microorganisms populations**

*Supervisor: prof. Ing. Alena Čejková, CSc.*

Study of interactions of nanoparticles with biological systems is a promising strategy to enable obtaining new knowledge that can be applied in various fields of science. Due to its small size and large reaction area, nanoparticles of metals and their oxides have considerable chemical and biological activity. Subject of the dissertation will monitoring of the impact of nanoparticles on selected prokaryotic and eukaryotic cells under various environmental conditions.

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**Optimizing the operating conditions of the bioreactor for the treatment of hot waste gases**

*Supervisor: doc. Ing. Martin Halecký, Ph.D.*

Biofilters working under high operating temperatures (above 60 °C) represent a suitable solution for cleaning waste air from sources such as roasting plants, production of dry feed or plastics industry. Thermophilic biofiltration has many specifics over commonly used mesophilic one and currently there are only a limited number of studies on this topic. The object of the dissertation is to optimize process parameters thermophilic pilot plant bioreactor including evaluation of the impact of fluctuations of input parameters on qualitative and quantitative composition of the microbial population and on the reactor operational parameters. The results will be used for final optimization of biofiltration equipment intended for industrial use.
Characterization and use of thermophilic microorganisms for cleaning of hot waste gases  
Supervisor: doc. Ing. Martin Halecký, Ph.D.

Use of thermophilic microorganisms in technologies of environment protection is rare, although it is suitable option for hot waste media treatment. The goal of the dissertation is isolation and subsequent selection of suitable microorganisms with ability to degrade volatile organic compounds from exhaust air at high temperatures (above 60 ° C) in the bioreactor. Evaluation of selected microorganisms will include morphological and basic biochemical description, habitat requirements, and a description of the biochemical conversion of selected pollutants, intermediates and products, and the mechanism of those reactions. The findings will be directed towards the application of thermophilic microorganisms in a pilot thermophilic bioreactor.

Interaction of microorganisms in multi-species biofilms  

Microorganisms usually prefer living in biofilm, in which the cells creates an entirely different phenotype compared to cells in a planktonic population. Phenotype change is controlled by the wide variety of control mechanisms using signaling molecules produced by the microorganisms. The specificity or universality of signaling molecules produced by individual taxa significantly influence the final appearance and properties of multi-species biofilms. Subject of the dissertation is a deeper understanding of above mentioned relationships and their use as a tool to control colonization of biotic or abiotic surfaces by pathogenic microorganisms.

Modulation of quorum sensing systems in relation to biofilm formation  

The system quorum sensing (QS) is considered one of the key regulatory mechanisms involved in the formation of microbial biofilms. Actual concentration signaling molecules participating in this system is directly dependent on the environmental conditions in which the population is growing. Interference of the signaling molecules with structurally similar compounds is another factor that can modulate QS. Subject of the dissertation is to find tools which effectively influence activity of QS in a way that leads to suppression or eradication of biofilm especially in microorganisms causing infectious diseases.

Microbial production of succinic acid  
Supervisor: doc. Dr. Ing. Petra Patáková

At present, succinic acid is the required feedstock for production of plastic materials, solvents, surfactants or pharmaceuticals, which can be produced by the bacterial fermentation with simultaneous consumption of carbon dioxide in addition to usual chemical way of production. The thesis will be focused on optimization of production conditions (medium composition, temperature, pH, presence of CO2, process arrangement) for selected strains, e.g. Actinobacillus succinogenes, using statistic methods like RSM- response surface methodology. Further, different methods for isolation of the acid from the fermentation broth will be tested.
Complex treatment of agricultural wastes for production of organic acids

*Supervisor: doc. Dr. Ing. Petra Patáková*

The thesis will be focused on processing different kinds of agricultural wastes originating in both plant and animal production on fermentable substrate. Main goal of the formulation of this type of substrate is to combine different types of wastes which can become sources of not only carbon but also nitrogen and phosphorus and to minimize addition of pure chemicals. The substrate will be utilized for production of organic acids, especially lactic and succinic, using convenient bacterial producers (lactic acid or rumen bacteria). Development of the sustainable and profitable process using problematic wastes with minimum ecological impact will be stressed.

*Study program: P1417 Chemistry*
*Study subprogram: 1406V002 Biochemistry*
*Department of Biochemistry and Microbiology*

Testing of biological activities of transgenic and non-transgenic plant extracts

*Supervisor: Prof. Ing. Tomáš Macek, CSc.*
*Spec. Supervisor: Ing. Jitka Viktorová, Ph.D.*

Concerns about the use and consumption of genetically modified foods are, even after 32 years of preparation the first transgenic plants, still exist. This work will therefore be focused on comparison of biological activities of extracts from various kinds of transgenic and non-transgenic plants. In particular, their toxicity will be tested to human tissue cells as well as their possible positive impacts, e.g. anti-tumor effects and antimicrobial activity.

The role of phospholipid signalling in response of *Arabidopsis thaliana* to salt stress

*Supervisor: doc. Dr. Ing. Zuzana Novotná*
*Spec. Supervisor: RNDr. Jan Martinec, CSc.*

Phospholipases are phospholipid hydrolyzing enzymes that generate lipid second messengers: phosphatic acid or diacylglycerol and free head group. Phospholipases are activated during responses to biotic and abiotic stress and these enzymes play important roles in the regulation of a variety of cellular functions such as membrane remodeling and membrane lipid degradation, vesicular trafficking and cytoskeletal rearrangements. Phospholipases family in higher plant is composed of multiple members and each of the phospholipase displayes distinguishable properties in activity regulation and/or lipid preferences. Cold, salinity and drought are one of the most common environmental abiotic stress factors in modern agriculture, having negative effects on plant growth and development and productivity of plants. The aim of the work will be study of molecular mechanism of salt stress in connection with the signal pathway of phosphatidic acid and diacylglycerol.
Study of the expression of genes involved in biofilm formation of *Staphylococcus aureus*

*Supervisor:* prof. Ing. Kateřina Demnerová, CSc.
*Spec. Supervisor:* Ing. Kamila Zdeňková, Ph.D.

Staphylococcal enterotoxins (SEs) are members of the extracellular mature toxin family, secreted by a variety of *Staphylococcus aureus* strains that are responsible for human disease called Staphylococcal Food Poisoning (SFP). Many representatives of the genus *Staphylococcus* form biofilms, i.e. community of microbial cells on the surface of different objects. The dissertation thesis will focus on the study of the expression of genes involved in biofilm formation and survival. The rate and affect expression will be studied at the mRNA level using the method of reverse transcription real-time quantitative PCR (RT-qPCR). Basic phenotypic and genotypic characterization of *S. aureus* strains will be monitored in addition. Standard and modern microbiological and molecular-biological methods will be used (culture assay, spectrophotometric techniques, electrophoretic techniques, different variants of the PCR method, MALDI-TOF MS et al.).

Metagenomic analysis of new bacterial genes and pathways with bioremediation potential for polycyclic and monoaromatic hydrocarbons

*Supervisor:* prof. Kateřina Demnerová
*Spec. Supervisor:* Maria Brennerova, Ph.D.

Metagenomics uses genomic libraries to retrieve genes and pathways catalysing a desired function from natural bacterial communities without cultivation. Our group is working on projects directly related to the biological diagnostics of sites in the Czech Republic, contaminated with aliphatic hydrocarbons, BTEX and PAHs. We are using the alternative metagenomic approach allowing the discovery of new genes for degradation of xenobiotics. The doctoral work will include molecular biological and biochemical methods for characterization of newly isolated biodegradation pathways for biodegradation of mono- and polycyclic aromatic pollutants. The required candidate will work on bacterial clones encoding catechol extradiol dioxygenase activity for catecholic substrates: 1,2-dihydroxynaphthalene, 2,3-dihydroxybiphenyl, 3-methylcatechol and catechol.
Phenotypic and genotypic diversity of Cronobacter spp. isolated from foods, environment and clinical samples

Supervisor: Doc. Ing. Igor Hochel, CSc.

Cronobacter species have been recognized as opportunistic pathogens and as etiological agents in life-threatening diseases mostly in neonatal and premature infants. The most frequent mode of an infection is meningitis often complicated by ventricle compartmentalization due to necrosis of brain tissue, brain abscess, hemorrhagic and non-hemorrhagic infarction, cyst formation and late development of hydrocephalus. Elder patients, immunocompromised individuals or those with chronic, acute or serious illnesses are considered as another risk group. All Cronobacter species are pervaded in environment. However, neither a source nor the modes of penetration into a human food chain are known. This project is focused on i) identification and detailed characterization of cronobacters in different food, environmental clinical samples, ii) the study of some virulence factors including biofilm formation and factors affecting formation and development of the bacterial biofilm, iii) development and optimization of genetical instrumental or immunochemical methods for the reliable and rapid identification of Cronobacter spp. and testing of their traits. Results gained by the biochemical and genomic characterization of the Cronobacter isolates collected during a project solving will serve to the formation of criteria enabling categorization of the individual isolates into corresponding category (biofilm formation, resistance to antibiotics, serotype, habitat, etc.). These criteria will be a basis for building of standard operative procedure for the isolation and identification of cronobacters.

Isolation and characterisation of biological active compounds from natural material

Supervisor: Ing. Petra Lovecká, Ph.D.

Pathogens responsible for infections are usually resistant and multiresistant strains to conventional antibiotics. Such pathogens are for example members of genera Staphylococcus (S. aureus, S. epidermis) resistant to methicillin (MRSA) and vankomycin (VRSA). The goal of work is isolation, characterisation, modification and synthesis or production of the active compounds, differing in primary structure and fulfilling high antimicrobial activity, high stability to proteolytic digestion, low toxicity. These materials could be substituted for the now almost nonfunctional antibiotics.

Study of interactions leading to assembly of retroviral particles – a tool for inhibition of their formation

Supervisor: Dr. Ing. Michaela Rumlová
Spec. Supervisor: Doc. Ing. Richard Hrabal, CSc

An extensive network of interactions among structural domains of the Gag polyprotein precursor is necessary for formation of hexameric lattice of immature retroviral particles. Detailed understanding of these interactions is a key step on the way toward inhibition of the retroviral assembly. The study will be focused on characterization of selected regions and amino acids within capsid and nucleocapsid proteins of HIV and M-PMV (Mason-Pfizer monkey virus) that are critical for mediating interactions within and between hexamers. The results obtained by alanine scanning mutagenesis complemented with data from biochemical, virological and molecular biology methods together with structural techniques as NMR spectroscopy and cryo-EM will lead to selection of small compounds with potential inhibitory activity. The most promising candidates will be tested using in vitro assembly assay.
Diversity and function of biodegradative genes in the environment
Supervisor: Assoc. Prof. Ondřej Uhlík, Ph.D.

Metagenomics is currently a very fast developing field especially due to advances in high-throughput sequencing and improved bioinformatic tools. Metagenomics primarily aims to reconstruct metabolic pathways of microbes within a community and identify the role of populations in the ecosystem. At the same time, metagenomics is useful when analyzing the diversity of functional genes, e.g. biodegradative ones.

Biodegradative genes are often studied in relation with pollutant removal. However, their role in pristine environments remains unknown. This project is aimed to analyze the diversity of biodegradative genes, especially aromatic ring hydroxylating dioxygenases, in both contaminated and pristine environments.

The major methods employed are going to be gene-targeted metagenomics, gene-mining, stable isotope probing, qPCR, cloning and expression of selected enzymes while determining their substrate specificity.

Functional genomic analysis of bacterial communities with bioremediation capabilities
Supervisor: Assoc. Prof. Ondřej Uhlík, Ph.D.
Spec. Supervisor: Hynek Strnad, Ph.D.

Metagenomics has experienced rapid development, mainly thanks to the development of methods for parallel sequencing (NGS). The basic idea behind metagenomics is based on the observation that different types of microorganisms metabolically interact with the rest of community. The main goal of metagenomics studies is to determine representation of individual species in the microbial community, identify key differences between different communities and also determine the metabolic potential of the whole community. This can be estimated based on the presence of individual functional genes. To obtain complete genetic information, it would be necessary to sequence the genomes of all species that form a community. For capacity reasons this is only possible in part because the average size of metagenome is in the tens of billions of base pairs. Biologically serious problem is that the presence of some gene does not imply presence of coded protein in cells. The ideal would therefore be to determine the representation of all proteins (metaproteome). It is yet technologically impossible, and therefore it is used determination of mRNA profiles also called meta-transcriptome. In case of meta-transcriptomes we do not have information about quantitative representation of proteins, we only know about their presence in the community.

The student will study biodegradation diversity of expressed genes in microbial communities that were isolated from the environments contaminated with chlorinated aromatics compounds. Reference communities will come from similar environments that were not affected by contamination.

The main experimental step will be to determine meta-transcriptional profiles of all studied communities using methods of next-generation sequencing. Sequenced profiles will be further processed by conventional bioinformatics methods. Individual transcripts will be annotated and expression profiles will be compared with each other in order to clarify the role of biodegradation genes. Knowledge of bioinformatics is not necessary at the beginning of project. The work will be largely held in the Laboratory of Genomics and Bioinformatics at the Institute of Molecular Genetics, Academy of Sciences.
**Study program:** P2906  **Food chemistry and technology**  
**Study subprogram:** 2901V013  **Food technology**  
**Department of Saccharides and Cereals**

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**Design and simulation of a separation process for removal of colour substances from sugar solutions**  
**Supervisor:** Prof. Ing. Zdeněk Bubník, CSc.  
**Spec. Supervisor:** Ing. Svatopluk Henke, Ph.D.

This work is focused on testing of new membrane and chromatographic techniques to reduce the concentration of colour substances in sugar solutions and compare them with traditional filtrations using activated carbon and filtration aids. The main target is to design an optimised producing scheme to reduce the colour of the final product after the sucrose inversion, including processing of intermediate and waste products. A mathematical model of the whole process should be an integral part of the results. This model will serve for the design of the control system.

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**Monitoring of chocolate quality**  
**Supervisor:** prof. Ing. Jana Čopíková, CSc.  
**Spec. Supervisor:** doc. Mgr. Andriy Synytsya, PhD.

The thesis is focused on a development of a set of methods that can explain the reason of technological problems in chocolate technology and products with different fillings and chocolate coating. Fundamental analytical data (e.g. chromatographic methods) in connection with data of physical methods (e.g. microscopy and thermal analysis) will serve as a scientific basis for prediction of technological failures like fat bloom, and verify the authenticity.

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**Modern separation techniques for isolation of valuable substances from food materials**  
**Supervisor:** Andrea Hinková, PhD.  
**Spec. Supervisor:** Ing. Svatopluk Henke, PhD.

In last decades, we can see a rapid development of new technologies, which enable more gentle treatment of raw materials, further use and exploitation of by-products and material which used to be considered as wastes. Membrane separation techniques (e.g. nanofiltration and ultrafiltration) together with continuous chromatographic separation process of simulated moving bed (SMB) represent a very effective tool for isolation of valuable substances and improvement of process economy. The thesis will be aimed at study of conditions affecting the velocity and efficiency of membrane separation, on modelling and simulation of SMB process as well as acquisition and evaluation of data from the separation of various extracts and mixtures originating from food industry.
Testing of non-traditional materials in pasta

Supervisor: Assoc. Prof. Marie Hrušková, Ph.D.
Spec. Supervisor: Ivan Švec, Ph.D.

Pasta products form an important part of human nutrition and their asset is increased by the resistant starch content and positive GI value. Non-traditional raw materials (pseudocereals, pulses, small seeds - hemp, teff, chia, nopal, fonio etc.) can be characterized by specific nutritional value and ensure innovation of pasta including sorts for special diet. In spite of many benefits they have often negative influence on a traditional technology in pasta factory. The study will be focused on utilization of non-traditional raw materials with aim to predict on base of the laboratory tests the changes of technology regime. Sensory evaluation and nutrition composition of enriched products (content of protein, food fiber, resistant starch, beta-glukans) allow choosing of non-traditional raw materials of new industrial pasta products including special diet.

Using of non-traditional raw materials in cereal products

Supervisor: Assoc. Prof. Marie Hrušková, Ph.D.
Spec. Supervisor: Ivan Švec, Ph.D.

Non-traditional raw materials (pseudocereals, pulses, small seeds - hemp, teff, chia, nopal, fonio, bio cereals etc.) can be characterized by specific nutritional value and ensure innovation of cereal products. In spite of many benefits they have often negative influence on traditional technology in baking industry. The study will be focused on utilization of non-traditional raw materials with aim to predict on base of the analytical and rheological methods the changes of technology regime and suggest a modified recipe with addition of active components. Sensory evaluation and nutritional composition of enriched products (content of protein, food fiber, resistant starch, beta-glukans) allow choosing a non-traditional raw material for industrial scale.

Nutritional importance of resistant and slowly digestible starch

Supervisor: doc. Ing. Evžen Šárka, CSc.

Digestibility of starches has been attributed to the interplay of many factors, such as starch source, granule size, amylose to amyllopectin ratio, the type and degree of crystallinity etc. Resistant and slowly digestible starch starches are nutritionally very worth. The thesis is focused on the properties of starch modified by changing of amylose/amyllopectin ratio, by chemical modification or by extrusion cooking.

Analysis of bioactive compounds in fresh water algae

Supervisor: doc. Mgr. Andriy Synytsya, PhD.

With the help of a combination of chemolytic, separation and spectroscopic methods, the constitution and structure of polysaccharides and biological active compounds from marine and cultivated algae will be studied. Initially, attention will be paid to the isolation and purification of these compounds from the specified materials. Isolated fractions will be analysed by a combination of the afore-mentioned methods, mainly GC/GC gas chromatography (multidimensional gas chromatography), GC/MS (gas chromatography coupled with mass spectrometry), FTIR, Raman and NMR spectroscopy.
Deep desalting of whey

**Supervisor:** Doc. Ladislav Čurda, CSc.
**Spec. Supervisor:** Ing. Jiří Ečer (MemBrain s.r.o.)

Cheese whey can be desalted by different technologies like nanofiltration, electrodialysis or ion exchange chromatography. Relatively new process is electrodeionization, which is not sufficiently described for complex matrices like whey. Deep desalting of whey significantly increases the value of whey and enlarges its application possibilities. The thesis will focus on the proposal and validation of whey desalting by combination of electrodialysis and electrodeionization to ash content in dry matter 0.8 %. Whey treated by evaporation, reverse osmosis or by nanofiltration will be used as raw material. The technological configuration of both basic apparatuses (electrodialysis and electrodeionization) will be proposed in cooperation with MemBrain s.r.o. including accessory devices, technology of desalting and cleaning. Performance parameters of both partial apparatuses will be proposed and process conditions and processing of concentrate will be determined. Technology will be optimized from the point of view of lowest capital and operating costs.

Application of preparative chromatography for isolation of minor milk and whey constituents

**Supervisor:** Doc. Ladislav Čurda, CSc.

Milk and whey contain many minor components like oligosaccharides, nucleotides, some proteins and peptides, enzymes, cytokines etc. Chromatography techniques are used in dairy industry only in limited extent. Isolation of minor constituents can bring interesting economic evaluation of raw material. The aim of thesis is to select compounds suitable for chromatographic separation and utilizable as food supplements or for fortification of food for specific groups of the population. The objective of the next step is to test different stationary phases and separation conditions. Pressure membrane processes or electrodialysis can be involved in the separation procedure if needed. If possible the resulting technology should be verified in pilot scale.

Encapsulation of probiotics

**Supervisor:** doc.Ing. Milada Plocková, CSc.
**Spec.Supervisor:** Ing. Šárka Horáčková, CSc.

The interest in the use of probiotic bacteria in food and non-food applications has been constantly growing. Simultaneously requirements to ensure their viability during the production and storage of functional probiotic products are tightened. A certain possibility to increase bacterial resistance to adverse external and internal environmental conditions is encapsulation. The goal of thesis will be the selection of a suitable material and encapsulation techniques and the comparison of the stability, activity and functional properties of free and encapsulated cells in an environment of dairy and non-dairy foods and in model conditions of human gastrointestinal tract. The co-encapsulation of probiotics with suitable prebiotics will be also tested.
Antioxidative and microbistatic effect of phenolic acid derivatives

**Supervisor:** Prof. Ing. Jan Šmidrkal, CSc.
**Spec. Supervisor:** Ing. Iveta Hrádková, Ph.D.

Shelf life of food and cosmetic products is increased by additives – antioxidants and preservatives. These compounds act against oxidation by oxygen and can increase microbiological stability of these products. Some already known derivatives of phenolic acids show both antioxidative and microbistatic, respectively microbicidal, effect.
The aim of this study is propose of structures of new phenolic acid derivatives, their synthesis and determination of their antioxidative and microbistatic effect.

Effect of phosphates on the colloidal stability of the liquid dairy products

**Supervisor:** Doc. Ing. Jiří Štětina, CSc.

Milk is a polydisperse system of protein and fat whose good colloidal stability is an essential requirement for heat treatment and storage of liquid dairy products. The addition of various kinds of phosphates is one possibility to modify these properties. The aim of the work will be the characterisation of the influence of chosen phosphates on colloidal stability and rheological properties of liquid dairy products during their heat treatment and storage.

Preparation and properties of multiple emulsions in dairy products

**Supervisor:** Doc. Ing. Jiří Štětina, CSc.

The use of multiple emulsions of type w/o/w is one of the possibilities for encapsulating of biologically active substances in functional dairy food. Their implementation requires good efficiency of preparation and also good stability during storage. The aim of work will be to develop the preparation process of multiple emulsions in dairy products, to evaluate their properties and optimize formulations to increase of colloidal stability.

Study program: P2906  Food chemistry and technology
**Study subprogram:** 2901V013  Food technology
**Department of Food Preservation**

Development of methodologies and databases for detecting the causes of quality defects in food

**Supervisor:** doc. Ing. Helena Čížková, Ph.D.
**Spec. Supervisor:** Ing. Iveta Horsáková, Ph.D.

Detection of causes of technological defects in complaints disputes requires a systematic approach. The purpose of the project is to develop methodologies and procedures to detect these common defects in various food commodities, such as off-flavours and taints, turbidity, colour and consistency change. The aim of the project is to summarize and validate common methods and to summarize and develop databases for the diagnosis of defects and suggestions for corrective measures for selected commodities. The methodology of the project will, in addition to the basic analytical an microbiological methods, also involve the use of modern instrumental analysis techniques such as mass spectroscopy in real time, GC/MS, LC/MS etc.
Advances in analysis of profiles of volatile substances for assessing the quality and authenticity of food

Supervisor: doc. Ing. Helena Čížková, Ph.D.

Gas chromatography with mass spectrometric detection in various configurations (chiral, multidimensional, with olfactometry) will be used for the analysis of volatile compounds profiles and their use for the evaluation of quality, freshness and authenticity of the food (including assessment of the declared technology, date of production, harvesting, etc.). The results of standard laboratory methods will be compared with metabolic profiles and content of target analytes measured by GC. For the interpretation of analytical results reflecting the impact of raw materials, recipes, and storage technology, the advanced chemometric methods will be employed.

Influence of technological processes on functional parameters of food packages

Spec. Supervisor: Ing. Lenka Votavová, PhD.

Food package design is based on functional parameters of package, e.g. barrier and mechanical properties, thermal stability, irradiation transmission, etc. During processing of packaged product these characteristics could be changed. The extent of such parameter modification is mostly unknown. The aim of this thesis will be to test methodically the effect of basic technological processes (sterilization, freezing, high pressure treatment, irradiation, microwave heating, etc.) on main functional parameters of basic types of polymer food packaging materials.

Methods for testing of safety of food packages


Safety of food packages is one of the crucial problems of food packaging. The thesis will be aimed on study of application of modern analytical procedures (GC-MS, LC-MS, DART-TOF-MS, electroseparation techniques, atomic force microscopy, field-flow fractionation, etc.) for evaluation of suitability of packaging materials (including materials with nanoparticles) for food contact.

Application of capillary electrophoresis for evaluation of food authenticity


Capillary electrophoresis is a powerful tool in food authentication especially within specific areas such as peptide or protein analysis. However the identification of plant or animal species based on protein patterns becomes more difficult once food has been processed and morphological characteristics are no longer visible. CE is not as reliable when used on highly processed food products as the proteins become denatured. DNA based methods have therefore become the most appropriate approach to species identification as DNA remains detectable in all but the most heavily processed samples. The combination of PCR with CE analysis is very promising technique in the field of food authentication. The aim of this study is to summarize applications of capillary electrophoresis in food authentication and develop new electrophoretic methods in this field.
The use of modern analytical methods for evaluating the quality of food raw materials  
*Spec. Supervisor: Ing. Aleš Rajchl, Ph.D.*

Quality of raw materials is a key parameter in food production. The quality of plant origin raw materials can be very variable and depends on a variety, growing conditions, harvesting method, etc. For these reasons, it is necessary to develop new analytical methods for comprehensive assessment of selected parameters of raw materials. A goal of this study will be development of new analytical procedures, using modern analytical methods for evaluating the quality of selected food raw materials of plant origin.

Shelf life and properties of meat products as influenced by natural antioxidants and preservatives  
*Supervisor: Prof. Ing. Petr Pipek, CSc.*

The tendency to replacement of chemical additives in food production obliges the producers to search natural substances (mainly plant extracts) that are suitable to assure shelf-life and other technological properties of meat products and theirs raw materials. The goal of the thesis is to choose suitable natural preservatives and bioactive substances for meat products and evaluate their influence on shelf-life and quality of meat products. It should be focused mainly on the products of fermentation, extracted antioxidants and by products in the wine production and spices.

Composition and technology of meat product and their impact on quality and legislation.  
*Supervisor: Prof. Ing. Petr Pipek, CSc.*

The changes in technology of meat products, their composition and application of new natural additive substances and raw materials bring about a confrontation with the actual and future legislation. This is often no offence against the hygienic or technological principles, but a new situation that was not expected or could not be expected in the moment of forming of the corresponding legislation. The goal of the thesis is to evaluate the technology development under extreme condition (extreme product composition), assess the influence on the product quality and suggest possible solution of future legislation changes. Special attention will be given to problematic of shelf-stable products.

The effectiveness of sterilization process for the microorganisms elimination in the pet food cans  
*Supervisor: Prof. Ing. Petr Pipek, CSc.*

The growing interest in the manufacture of pet food, their innovation and diversity in the used raw materials requires a detailed assessment of the entire production process with regard to preservation, quality and safety. The aim of the thesis is to assess the microbiological situation in raw materials used for the manufacture of preserves for pets and to assess the resistance of undesirable micro-organisms to the sterilization in connection with the other hurdles during the production and storage. It will be assessed the relationship between the value of the sterilization effect and the possibility of the survival of the individual thermophiles and the possible multiplication during the storage under different conditions.
Non-enzymatic browning reactions’ products of physiological and sensory significance

Supervisor: doc. Dr. Ing. Karel Cejpek

The topic is a set of reactions which represent complex changes during food processing known as non-enzymatic browning reactions. The work will be focused on the formation and characterization of low-molecular products responsible in significant way for the changes of flavour development, redox status and other attributes. The study of formation and characteristics of melanoidins, incl. Advanced Glycation End-products (AGEs), will be also among the subjects of the thesis. The experiments will be carried out in both selected foods and model reaction mixtures. An emphasis will be put on the reaction systems containing phenolic compounds and secondary lipoxidation products in addition to reducing saccharides, amino compounds and Maillard intermediates. Application and optimization of proper techniques and methods for the quantitative and qualitative analyses of target compounds will be required.

Ion mobility: additional separation dimension for applications based on high resolution liquid chromatography coupled with tandem mass spectrometry

Supervisor: Prof. Ing. Jana Hajšlová, CSc.

Natural products, foods or food supplements represent complex matrices thus for analysis of their composition, especially when isomeric or isobaric compounds are of concern, multidimensional techniques are needed. Within this doctoral thesis, the application potential of a unique instrumental platform will be investigated. The ion mobility (IM) represents here an additional dimension of system consisting from high resolution liquid chromatography coupled to tandem high resolution mass spectrometry with time of flight mass analyser (Q-TOF HRMS). Using this system, various pilot studies will be performed including non-target screening for the authentication purpose or toxicity testing.

Metabolomics as a tool for a comprehensive study of bioactive molecules


Metabolomics represents a modern analytical strategy applicable for a comprehensive study of biological effects induced by some compounds isolated from plant matrices on living organisms or cell cultures. “Fingerprints” of a set of small molecules (metabolome components) will be obtained by non-target screening using various chromatographic techniques coupled with tandem high resolution mass spectrometry. The interpretation of generated data, i.e. assessment of health promoting properties or toxicity of isolates, will be performed on interdisciplinary basis, jointly with medical experts.
Forensic monitoring of psychotropic and other biologically active substances in food supplements


The research will be focused on the development of rapid and effective analytical methods (mainly mass spectrometric coupled with liquid or gas chromatography) applicable for monitoring of various groups psychotropic substances, compounds with hormonal activity etc. that have been in a growing extent used for adulteration of food supplements. For the purpose of forensic investigation, specifically for obtaining an evidence of the earlier use of these compounds, implemented analytical methods will enable also detection of their metabolites and/or degradation products. Within the pilot experiments, the transfer of illegally used adulterants across the chain raw material – processing intermediates – final product will be investigated.

A comprehensive study of quality and safety of thermally processed foods

Supervisor: Prof. Ing. Jana Hajšlová, CSc.

Thermal processing induces in raw materials a range of reactions that may result not only in changes of nutritional quality and sensorial properties but may also impact chemical food safety. The research within this doctoral study will mainly focus on cereal-based products obtained by using novel technologies and new types of recipes. Advanced chromatographic techniques coupled with mass spectrometry will be employed for the assessment of quality and safety parameters. Special attention will be paid to investigation of mechanisms responsible for observed changes and possibilities of their modulation.

Novel instrumental techniques in modern food analysis


The doctoral thesis will be concerned with performing case studies employing various instrumental platforms for analysis of volatile and semivolatile components of natural products, foodstuffs and food supplements. For this purpose the application of (i) gas chromatography (GC) coupled with several types of high resolution mass spectrometry (HRMS) and (ii) ambient mass spectrometry (AMS) employing DART (Direct Analysis in Real Time) ion source is planned. Using non-target screening, markers of food quality, authenticity and chemical safety will be identified.

A study of sensory characteristics of astringency taste

Supervisor: doc. Dr. Ing. Zdeňka Panovská

The astringent taste is typical for beverages, fruits and vegetables. Research about astringency taste is mainly focused on tannin - protein interactions, because tannins bind the salivary proteins. Current research shows that astringency is elicited by a wide range of phenolic compounds as well as some non-phenolic compounds in various foods. The study will focus on astringent compounds themselves but also on sensory characteristics, such as bitter or sour properties, or their possibilities to enhance or suppress other sensory properties.
Chemical changes of flavour and their impact on the organoleptic properties of foodstuffs  
*Supervisor: doc. Dr. Ing. Zdeňka Panovská*

Sensory perception of food flavourings are related to the compositions and structures of individual odoriferous substances. Effect of different factors may lead to changes in their organoleptic properties.  
Study will be monitoring the impact of physical and chemical factors on the stability of natural and synthetic flavourings in model systems and in food products consequently. Changes of sensory properties in flavourings will be studied by sensory analysis and by using mass spectrometric techniques and will be correlated reciprocally.

Tocopherol losses during culinary processing of foods  
*Supervisor: doc. Ing. Zuzana Réblová, Ph.D.*  
*Spec. Supervisor: doc. Dr. Ing. Marek Doležal*

During culinary processing of foods, considerable tocopherol losses take place. These losses can attain up to 90% of the initial content and can result in the insufficient vitamin E intake observed in some studies. However, tocopherol losses during culinary procedures (other than repeated frying) have not been studied in a sufficient range yet. Therefore, the purpose of the planned study will be to enlarge knowledge in tocopherol losses during culinary processing of foods as well as in content of vitamin E in heat-treated dishes.

New strategies for the analysis of pesticide residues and their metabolites in food  
*Supervisor: doc. Ing. Jana Pulkrabová, Ph.D.*  

This thesis will study the current trends and requirements for the analysis of pesticide residues together with their metabolites, and will be mainly focused on the development of new, rapid procedures for their determination. One part will be devoted to the implementation methods employing liquid chromatography coupled with various types of mass spectrometry. The new approaches for both target and non-target analysis of pesticide residues will be optimized and critically reviewed the procedures are.

Application of mass spectrometry in the comprehensive evaluation of biological samples  
*Supervisor: doc. Ing. Jana Pulkrabová, Ph.D.*  

The main aim of this topic will be the implementation of the new instrumental techniques for the rapid analysis of different groups of contaminants in human biological samples. The new multi-analyte strategies employing mass spectrometry coupled with gas or liquid chromatography will be developed. For the detection of target analytes high resolution mass spectrometry (HRMS) will be mainly applied. Within the comprehensive assessment of samples also the metabolomics strategy profiling will be used.
Biologically active compounds of plant material
Supervisor: doc. Dr. Ing. Věra Schulzová

Plants are an important source of biologically active compounds, products of primary and secondary metabolism, and can be used as dietary supplements and functional foods. The levels of these compounds in plants depend on the plant species, climate conditions, influence of stress factors, cultivation (organic vs. conventional) etc. and may also be influenced by the conditions of storage and processing. For monitoring of biologically active compounds the modern analytical techniques based especially on ultra-performance liquid chromatography with mass spectrometry detection.

Application of ambient mass spectrometry for food quality evaluation
Supervisor: Doc. Dr. Ing. Věra Schulzová

One of the novel analytical method allowing evaluation of food quality and authenticity is ambient mass spectrometry employing direct analysis in real time ion source. This technique enables a comprehensive quality assessment of food and food ingredients, nutritional and hygienic-toxicological quality assessment, and evaluate the effect of storage and processing of raw materials to final product quality.

Modern strategies for authenticity evaluation of food raw materials and foodstuffs
Supervisor: doc. Ing. Milena Zachariášová, Ph.D.
Supervisor spec.: prof. Ing. Jana Hajšlová, CSc., Ing. Monika Tomaniová, Ph.D.

For control of authenticity of raw materials, as well as the final foods, modern types of hybrid mass spectrometric techniques, enabling the non-target screening (fingerprinting) and profiling of small molecules, will be exploited. Utilization of sophisticated chemometric tools enabling identification of specific markers exploitable for construction of particular models will be accentuated. The normalized data will be used for establishment of databases, which will be continuously actualized, and the models will be validated in order to implement them easily in real practice.

Study program: P1417 Chemistry
Study subprogram: 1402V001 Organic chemistry
Department of Chemistry of Natural Compounds

Synthesis and study of sesquiterpene lactones derivatives
Supervisor: Prof. RNDr. Pavel Drašar, DSc.

Sesquiterpene lactones are important for their interesting biological properties, e.g. for their influence on SERCA system, or for their cytostatic and immunomodulation properties. Synthesis and study of spectrum of derivatives of this kind of compounds may not only unveil and prove the respective pharmacophores, but also help to change the properties of compounds under study, as e.g. bioavailability. Derivatives synthesized may also help to localize these biologically active compounds directly in the cell.
Synthesis of metabolites and their deuterium labelled analogues of selected new psychoactive substances.

*Supervisor:* Prof. Dr. RNDr. Oldřich Lapčík

*Spec. Supervisor:* Ing. Martin Kuchař, Ph.D.

New psychoactive substances (NPS) are highlighted for their toxicology and psychopharmacology study in the last few years. Relatively frequent intoxication by NPS except fatal cases is caused by lack of information and additionally quite difficult identification in biological matrixes. Only a small part of hundreds of known NPS was submitted for pharmacology study and even less metabolites of NPS are known. The gradual recognition of NPS metabolism may help to create precondition for a progress in their diagnostics of intoxication and further treatment. First of all, the study will be focused on the synthesis of metabolites as analytical standards. The main metabolites will be labelled by deuterium as internal standards for pharmacokinetics study.

Sugar-based conjugates for multivalent recognition of pathogens

*Supervisor:* Prof. Ing. Jitka Moravcová, CSc.

Primary step of many vital processes involves selective interactions between membrane proteins called lectins on the surface of a one cell and peripheral oligosaccharides in the glycocalyx of the second cell. Such interaction mediates among other proteins trafficking and function, cell-cell recognition and adhesion, and many aspects of the immune response. Moreover, the importance of carbohydrate-carbohydrate interactions in cell recognition was also declared recently. The aim of this PhD study is the synthesis of multivalent presentations of saccharides on properly substituted calixarene derivatives or nanodiamonds surrounding with different moieties. Their interaction with other saccharides, proteins and pathogen lectin receptors in water will be assessed with FTIR, UV, confocal fluorescence microscopy, NMR and surface plasmon resonance, and other techniques.

New synthetic approaches to the preparation of glycomimetics for intervention of recognition of pathogens

*Supervisor:* Prof. Ing. Jitka Moravcová, CSc.

*Spec. Supervisor:* Ing. Kamil Parkan, Ph.D.

Carbohydrate can be considered as highly important class of biomolecules. It is becoming increasingly clear that oligosaccharides are example of chemically complex biological markers that act critically in important extracellular and organismal processes such as microbial infection, immune response, cellular adhesion, cancer metastasis and inflammation. Their remarkable structural diversity means that they can often mediate highly specific and therefore complex processes. Particular problem for the application of carbohydrates as drugs is the lability of the glycosidic bond. To address the issue that oligosaccharides are prone to enzymatic degradation in the organism, stable glycomimetics have to be prepared. The goal of this project is the development of original and novel modular synthesis of various biologically perspective glycomimetics using lithiation-borylation methodologies and cross-coupling reactions from simple building blocks. The conformational behaviour of the tittle compounds will be studied by NMR and their affinity towards lectin receptors of selected pathogens will be assessed, as well.
Synthesis and study of new glycocojugates
Supervisor: Prof. Ing. Jitka Moravcová, CSc.
Spec. Supervisor: Ing. Kamil Parkan, Ph.D.
Chemistry of calix[n]arenes and porphyrins represents one of the main cornerstones of contemporary supramolecular chemistry. In contrast to other frequently used macrocycles, they are very interesting because of easy derivatization and low toxicity. This project is mainly aimed at the preparation of non-hydrolyzable glycoclusters, using the original synthetic procedures based on cross-coupling reactions and different ligation techniques to study their biological and physical properties.

Selective enzymic acylation and deacylation of saccharides: combined computational and experimental study
Supervisor: Doc. Dr. Ing. Ivan Raich
In carbohydrate chemistry acylation and deacylation are the most frequent reactions. In many cases they can be carried out using enzymes which often simplify the procedure and bring also an interesting but difficult to predict selectivity. Molecular modeling helps to clarify this selectivity through a detailed study of enzyme active site interactions with a carbohydrate substrate.

Interaction of model synthetic drugs with receptors: computational study
Supervisor: Doc. Dr. Ing. Ivan Raich
Receptors interacting with drugs and other psychoactive compounds, their classification and binding mode play an important role in revealing their effect. Molecular modeling techniques help to clarify structural and stereochemical aspects of these interactions which might be of therapeutic significance.

Peptidomimetic derivatives of triterpenoid acids and lactones
Supervisor: Prof. Ing. Zdeněk Wimmer, DrSc.
Derivatives of triterpenoic acids and lactones from sustainable resources with non-natural aminoacids and oligopeptides able to act against different cancer types, and against different microbes will be investigated. The target structures will bear peptidomimetic systems with several amide bonds, through which feature this part of their molecules will mimic oligopeptides. A combination of non-polar and polar part of the target molecules may be advantageous for application and transportation of these potentially pharmacologically active compounds in organism. The objective of the investigation will be focused on designing and synthesizing synthons for modifications of the above molecules, and, based on them, on synthesizing novel compounds capable of displaying required biological activity.
Topics of Ph.D. Theses available at Contractual Institutes for the Academic Year of 2015/2016

Study program: P1417 Chemistry
Study subprogram: 1406V002 Biochemistry
Institute of Physiology of the ASCR, v.v.i.

Molecular Regulations of the mitochondrial ATP Synthase and their Impact on Cell Physiology
Supervisor: Ing. Andrea Dlasková, PhD.

The mitochondrial ATP synthase and its regulation is a critical element in mitochondrial and cellular physiology. Activity of mt ATP synthase influences ATP/ADP ratio, mt membrane potential, rate of ROS generation by mt respiratory chain, organization of mt cristae, ion homeostasis, and other essential processes. Aim of the study will be to examine mt ATP synthase supramolecular organization in cells under various physiological conditions as hypoxia, starvation, or oxidative stress. Molecular mechanisms involved in the regulation of oligomeric status and activity of mt ATP synthase will be searched. Moreover, mitochondrial morphology and ultrastucture will be examined and correlated with oligomeric status of mt ATP synthase.

Study of the mechanism of signal protein function regulation
Supervisor: RNDr. Veronika Obšilová, Ph.D.

Mechanistic understanding of molecular mechanisms by which signal protein functions are regulated requires the elucidation of the relationships between the structure and function of proteins. This project will be focused on studying the molecular mechanisms of regulation of selected proteins involved in signal transduction. The main attention will be given to the complexes with the 14-3-3 proteins, which play a key role in the regulation of many biological processes. The 14-3-3 proteins bind to and regulate the function of other proteins usually in a phosphorylation-dependent manner. Despite the great importance of these proteins, many structural details of their function remain elusive. This project involves both biochemical and biophysical approaches including recombinant protein expression, site-directed mutagenesis, fluorescence spectroscopy, analytical ultracentrifugation and dynamic light scattering to understand the details of how the activity and function of protein-protein complexes are regulated. Good knowledge of molecular biology techniques and recombinant protein production is an advantage. More information: http://www.biomed.cas.cz/d312/.
The role of heavy metals and alimentary selenium on antioxidative stress factors in selected patients and experimental model

Supervisor: Václav Zídek
Spec. Supervisor: Jarmila Zídková

Heavy metals (Cd, Pb, Hg, As) are common environmental pollutants. Any amount of them is known to have a negative impact on health of animals, including human beings. In contrast, selenium (Se) is a trace mineral that is essential to good human and animal health mostly because of its antioxidant activity and the role in the balance of several hormones. Se is incorporated into proteins and various organoselenium compounds differing in their biological activity. Its lack is accompanied by various defects (neurological malfunctions, cognitive decline, reproduction disorders, and Keshan and Kashin-Beck syndromes). In excess, however, selenium is toxic. The aim of the thesis will be to monitor possible alterations of biochemical parameters, mainly of selected antioxidant enzymes and also levels of vitamin E, metallothioneins and reduced glutathione in accordance with applied diets.

Regulation components of immune system and adipose tissue

Supervisor: Václav Zídek
Spec. Supervisor: Jarmila Zídková

Immune system is the one of most complex regulated parts of organism. Complexity lie mostly in connection with other tissue as for example neural tissue. Relatively recently was find out that, wide variety of formerly immunospecific factors as IL 18, PBEF1 or C3, is produced also in adipose tissue. It was proved that also obesity is followed by inflammatory processes in adipose tissue. Work will be focused on in vitro studies of selected factors, stimulation of their production and secretion. Mechanism of selected immunospecific factors’ impact will be studied on adipocyted and immune cells- monocytes. Work will be focused on in vitro study of selected adipokine/immunospecific factors impact on molecular level an their possible participation on the insuline resistance development.
**Study program: P1417 Chemistry**

**Study subprogram: 1406V002 Biochemistry**

**Institute of Microbiology of the ASCR, v.v.i.**

Biotransformation of minor silymarin flavonolignans

*Supervisor: Prof. Ing. Vladimír Křen, DrSc.*

*Supervisor Specialist: Doc. Ing. Kateřina Valentová, Ph.D.*

Silymarin, an extract from the milk thistle (Silybum marianum L. Gaertn), is used as effective hepatoprotectant with various pharmacological activities. Present in nutraceutics, produced and marketed in Czech Rep, it contain flavonolignans [1] and their 2,3-dehydro-derivatives. To elucidate their metabolism authentic standards of the metabolites are needed.

This interdisciplinary study will touch biochemistry, chemistry of natural compounds, pharmacology, microbiology etc. The work focus on mostly chemoenzymatic preparation of sulfates and glucuronides of flavonolignans [2-4]. The student will prepare recombinant enzymes using methods of molecular biology. Metabolites will be prepared by enzymatic synthesis and combined biochemical methods. The group expertise of enzymatic synthesis and biocatalysis together with advanced analytical methods and separation techniques will be used. Biological activities of new compounds will be studied including a robotic screening. Intensive international collaboration will be included.

The work will be financed from the project GAČR 15-03037S (2015-2017).


**Study program: P1417 Chemistry**

**Study subprogram: 1406V002 Biochemistry**

**Institute of Organic Chemistry and Biochemistry of the ASCR, v.v.i.**

Isolation of DNA motifs that alter the properties of reverse transcriptase

*Supervisor: Edward Curtis, Ph.D.*

Since its development in the late 1970s, reverse transcription has played a key role in the development of a wide range of technologies, including RT-PCR, *in vitro* selection, and DNA microarrays. Although a powerful way to produce DNA from an RNA template, generating reaction products from low abundance RNA transcripts can be difficult using standard methods. To facilitate the analysis of low-abundance transcripts by reverse transcription, here we propose using *in vitro* selection to generate a DNA motif that, when fused to the 5' end of a conventional reverse transcription primer, will increase the efficiency of the reaction. If successful, this method should increase the detection limit of rare RNA transcripts in applications such as single-cell gene expression profiling. In principal, this general approach can be used to isolate motifs that alter other properties of reverse transcriptase, such as the ability to catalyze cDNA synthesis at elevated reaction temperatures.
Study of biomolecular interactions by capillary electromigration methods  
*Supervisor: RNDr. Václav Kašička, CSc. (PhD.)*

The thesis will be oriented to the development of new high-performance electromigration methods, affinity capillary electrophoresis and affinity open-tubular capillary electrochromatography, and on their application to the investigation of the non-covalent interactions of biologically active peptides, proteins, nucleosides, nucleotides and other biomolecules with low- and high-molecular-mass ligands or receptors. New procedures will be developed for quantitative characterization of both weak and strong interactions of biomolecules in a free solution and on the interface of the liquid and solid phases. Interactions of biomolecules, e.g. peptide hormones or drugs with receptors, enzymes with substrates and inhibitors, and ionophores with small ions in a free solution will be investigated by different modes of affinity capillary electrophoresis. Interactions of biomolecules on the interface of solid and liquid phases will be studied by affinity open tubular capillary electrochromatography with ligands or receptors immobilized on the inner surface of the fused silica capillary. Strength of the interactions of biomolecules will be quantified by the stability constants of their complexes.

Cathepsin proteases as therapeutic targets  
*Supervisor: RNDr. Michael Mareš, CSc.*

The project will be conducted at the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic (www.uochb.cz/web/structure/186.html). The thesis is focused on proteases of cathepsin type that are critically involved in the pathology and are target molecules for therapy. Cathepsins of human origin and those from blood-feeding parasites will be investigated. The aim of the project is to analyze their structure, function, and regulation. The research includes the following approaches: proteomics, recombinant expression, protein purification, enzymology, protein crystallography, and molecular modeling.

Structure-based design of human carbonic anhydrase inhibitors  
*Supervisor: Václav Veverka, PhD.*

The project will be conducted at the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic in the team of Pavlina Rezacova (www.uochb.cz/rezacova). Project focuses on structural studies of therapeutically relevant isoenzymes of human carbonic anhydrase. Structural information will be used for design of isoform specific inhibitors. The work on this project provides the opportunity to acquire an expertise in protein biochemistry, biophysics and structural biology, as well as to get an insight into the rational drug design process through a close collaboration with the medicinal and computational chemistry research teams.

Ion channels in health and disease  
*Supervisor: Dr. Norbert Weiss, Ph.D.*

Calcium (Ca2+) channels, which act as gated pathways for the movement of Ca2+ across the cell membranes, play a central part in the initiation of intracellular Ca2+ signals, and defects in Ca2+ channel function have dramatic consequences resulting in sever human diseases - so-called channelopathies – including neuropathic pain. The research project will elucidate the implication of one particular class of calcium channel, the T-type channel, in the development of peripheral painful diabetic neuropathy. The candidate will use a combination of cellular electrophysiological (patch-clamp), molecular biology (site directed mutagenesis, chimeras) techniques, protein biochemistry, and confocal imaging microscopy, to analyze the cellular trafficking and regulation of T-type Ca2+ channels in diabetic-like condition (hyperglycemia) using cell lines and primary nociceptors in culture.
The changes in activities of protein kinases and protein phosphatases essential for meiotic cell division, which are induced in the oocytes by aging.

*Supervisor: Ing. Michal Kubelka, CSc.*

It has been shown that mammalian meiosis is associated with high incidence of errors, leading to chromosomal aberrations, which are more prevalent in female gametes and seem to increase with maternal age. Oocyte aneuploidy has severe consequences including pregnancy loss or birth defects. Aneuploidy is supposed to occur in two steps; first is an error in early meiotic program during recombination, the second is a failure of mechanisms controlling the chromosome segregation during resumption of meiosis.

In our project we plan to focus on characterization and quantification of the age-related changes during oocyte meiosis. The aim of this project is to reveal the changes in timing and degree of activation of protein kinases and protein phosphatases, which are essential for meiotic cell division.

**Main methods:** biochemistry & molecular biology, kinase assays, immunocytochemistry, live cell imaging.

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**RNA metabolism related to the control of gene expression in the oocyte and embryo.**

*Supervisor: Ing. Michal Kubelka, CSc.*

*Spec. Supervisor: Ing. Andrej Susor, PhD.*

Fully grown oocyte utilizes only transcripts synthesized during earlier development. Mechanisms of mRNA metabolism in the mammalian oocyte are still far from being fully understood. In the first meiotic division, shortly after nuclear envelope breakdown, translational hotspots develop in the chromosomal area and in a region which previously surrounded the nucleus. This hotspot is controlled by the activity of the mTOR/4F axis. We suppose that the localization of specific mRNAs and their in situ translation is essential for the generation of developmentally competent oocyte. Thus, the objective of the current project is to investigate translation regulation and polysome profiling of the oocyte after NEBD. We will test our hypothesis that translation of specific mRNAs is essential for meiotic progression before first polar body extrusion. This represents a first attempt to unveil novel regulators of mTOR/4F axis and will add substantial information concerning translational control of specific transcripts after NEBD in order to understand molecular physiology of mammalian oocyte.

**High-throughput translation analysis after resumption of meiosis in the mammalian oocyte.**

Regulation of the mTOR/elf4E pathway after nuclear envelope breakdown.

Translation and genomic stability in the mammalian oocyte.

**Main methods:** Next Generation Sequencing, biochemistry, molecular biology, FISH.
Environmental drivers of the development of microbial communities during primary succession

Supervisor: RNDr. Petr Baldrian, Ph.D.

During primary succession, major changes in soil structure and chemistry are observed that are largely shaped by the developing vegetation and the role of soil biota. As a consequence of these macroorganism-mediated processes, successive development of microbial communities is typically observed. These are composed both of plant symbionts and decomposers with variable response to environmental traits. So far, the understanding of processes that underlie the development of the microbial community is incomplete, but it is presumed that the changes of soil physico-chemical properties and direct influence of plants are the most important determinants. This work aims to characterize the relative effect of these two factors on the development of soil bacterial and fungal communities on the models of selected primary succession chronosequences and model manipulative experiments, where the studied factors can be addressed both simultaneously and separately. The work will include environmental sampling, manipulative experiments as well as processing of the environmental samples in the laboratory using the modern methods of molecular biology such as high-throughput sequencing.

New metabolite labeling strategies for targeted and comparative metabolomics by high resolution mass spectrometry

Supervisor: RNDr. Petr Šimek, CSc.

The goal of the proposed PhD study is to participate on development of new strategies for labeling of protic metabolites with functional groups possessing stable isotopes and to examine them in the targeted and comparative mass spectrometry-based metabolomic analysis of important biological models (human tissues, body fluids, drosophila). The research will particularly be directed to improve bottlenecks of current metabolomics involving:

(i) Metabolite identifications in complex aqueous biological matrices
(ii) Metabolite labeling in comparative (differential) metabolomics enabling direct comparison of control and targeted samples;
(iii) Finding new ways of the metabolite quantitation in complex biological material.
(iv) Isotopromeric analysis of labeled metabolites for investigation of metabolic pathways and metabolites fluxes.

Dr. Petr Šimek, Biology Centre, Czech Academy of Sciences, v.v.i., Laboratory of Analytical Biochemistry&Metabolomics, simek@bcab.eu, +420723648892.
**Study program:** P1417 Chemistry  
**Study subprogram:** 1402V001 Organic chemistry  
**Institute of Organic Chemistry and Biochemistry of the ASCR, v. v. i.**

**Modifications of DNA by reactive groups for bioconjugations**  
*Supervisor: Prof. Ing. Michal Hocek, PhD. DSc.*

DNA bearing reactive functional groups in major groove will be prepared by polymerase incorporations of modified nucleoside triphosphates. Bioorthogonal reactions of these groups will be studied, e.g. cross-linking with proteins, attachment of other useful functional groups and applications in chemical biology and diagnostics.

Leading references:


**Synthesis of novel hetero-fused 7-deazapurine nucleosides and nucleotides with potential biological activity or for modifications of DNA and RNA**  
*Supervisor: Prof. Ing. Michal Hocek, PhD. DSc.*

Novel hetero-fused analogues of 7-deazapurine nucleosides and nucleotides will be designed and prepared for studying of their cytostatic and antiviral activity. Most of them will be based on new or scarcely studied heterocyclic systems, e.g. diverse isomers of thieno-, furo-, pyrido- or pyrimido-pyrrolo[2,3-d]pyrimidinů etc. In addition to testing of biological activity, selected nucleosides will be converted to NTPs and studied as potential inhibitors or substrates for polymerases in enzymatic synthesis of modified nucleic acids.

Leading references:

Approaches to the total synthesis of bioactive epidithiodiketopiperazine alkaloids.

*Supervisor: Dr. habil. Ullrich Jahn*

Epidithiodiketopiperazine alkaloids are fungal metabolites, which display wide ranging biological activity. Aim of the project is the development of short and high-yielding total syntheses of natural products, exemplified by gliotoxin and of analogs.

![Chemical structure of epidithiodiketopiperazine alkaloid](image)

Selective Oxidative Amino Acid and Peptide Modification.

*Supervisor: Dr. habil. Ullrich Jahn*

Oxidative transformations of amino acids and proteins are normally unselective and lead to degradation. In this project selective oxygenation reactions of amino acids will be developed. The resulting products should have an excellent potential in C-C bond formation reactions with the aim to synthesize new non-natural amino acids. These results will be subsequently applied to the selective oxidative modification of oligopeptides. This may lead to metabolically stable biologically active products.

![Chemical structure of oxidized amino acids](image)

Synthesis of compounds with a potential epigenetic activity

*Supervisor: RNDr. Marcela Krečmerová, CSc.*

The theme comprises a synthesis of analogues of natural compounds, e.g. nucleosides bearing a triazine, thiazole or thiadiazole heterocycle (free or condensed with another heterocycle). Under certain circumstances, these pharmacophores can inhibit methyltrasferases (DNA-MT, histone-MT) through their specific interaction with the cysteine –SH group at the enzyme active site and thus reactivate gene expression (e.g. the genes silenced by aberrant methylation in tumor cells). The mentioned types of compounds also inhibit other enzymes with the cysteine thiol on an exposed place (e.g. cathepsin B), which extends their therapeutic potential. The target compounds will be tested for antitumor, antiviral and antibacterial activity, for their influence on the cell cycle and gene expression. A structure - activity study is also supposed as a part of the Ph. D. thesis. The conception of the project is flexible enough to pursue other attractive targets, if they emerge. Polar structures with biological activity will be further transformed to appropriate prodrug forms to improve their bioavailability.

The focus of the work lies in organic synthesis especially in the chemistry of heterocyclic compounds, nucleosides and peptides, and in the basic knowledge of biochemistry.
Novel heterocyclic derivatives as lipid and protein kinase inhibitors

Supervisor: Mgr. Radim Nencka, Ph.D.

Lipid and protein kinases represent important molecular targets for advanced therapeutics with a wide range of indications. The project will be focused on rational design and synthesis of novel inhibitors of phosphatidylinositol 4-kinase, which may serve as potential therapeutics against various types of solid tumors, viral infections or neurodegenerative diseases.

Preparation of isosteric 3´-phosphono nucleoside derivatives and oligonucleotides

Supervisor: Ing. Ivan Rosenberg, CSc.
Spec. Supervisor: Ing. Ondřej Šimák, Ph.D.

Our studies on synthetic modified oligonucleotides containing phosphonate nucleotide units have showed the interesting biological effects, e.g., (i) increased stimulation of RNase H activity, the key enzyme for successful application of antisense oligonucleotides as therapeutic agents, (ii) a short RNA-RNA duplexes (siRNA) are capable of gene silencing, and (iii) some phosphonate oligonucleotides form thermally very stable duplexes with a complementary counterpart. The search for new nucleotide and oligonucleotide modification and investigation of their biological properties and thus therapeutic potential is highly desirable. PhD thesis is focused on the synthesis of branched furanosylphosphonates as starting synthons for nucleosidation reaction. The obtained new types of nucleoside phosphonates will be chemically introduced into short oligonucleotides whose physico-chemical and biological properties will be examined. Modified oligonucleotides whose phosphodiester internucleotide linkages are partially replaced by nuclease stable phosphonate function are not studied in highly recognized worldwide laboratories.

Synthesis of phosphonate monomers derived from 3´-amino-3´-deoxy and 5´-amino-5´-deoxyadenosine and the preparation of modified oligoribonucleotides.

Supervisor: Ing. Ivan Rosenberg, CSc.
Spec. Supervisor: Ing. Ondřej Páv, Ph.D.

Project is focused on the synthesis of phosphonate monomers derived from 3´-amino-3´-deoxy and 5´-amino-5´-deoxyadenosine. These compounds will be introduced into the oligoribonucleotide strand and their influence on the hybridization properties and enzymatic stability will be studied. The ability of these oligoribonucleotides to activate RNase L or RNA interference will be examined.

Synthesis and theoretical studies of exotic fullerene molecules

Supervisor: Ing. Jaroslav Šebestík, Ph.D.
Spec. Supervisor: Ing. Jaroslav Šebestík, Ph.D.

Exotic fullerene derivatives, for example with actinides, exhibit potential as components to nanomemory and nanomagnets. Other compounds can serve as dendrimer cores used for a drug transport, intelligent self-healing materials for medical applications, etc. Many such compounds were prepared experimentally, but their properties are rather unexplored. The project will consist in synthesis of model compounds and theoretical and spectroscopical studies of fullerenes. (Collaboration with laboratories in Finland, Norway, Japan, a research within GACR grant).
Development of Chemical Tools for Selective Protein Activation

Supervisor: Dmytro Yushchenko, PhD

Tools which permit the control of protein-protein interactions in living cells provide us with the ability to modulate cellular behavior and to study the factors that determine their fate. Chemical inducers of protein dimerization (CIDs) are one of the best examples of such tools. However, quantification, regulation of level of dimerization as well as localization of sites of interaction are often difficult tasks when “classical” CIDs are used. The goal of this research project is synthesis of a new generation of CIDs based on fluorogenic dyes. These tools will be design not only to induce but also to visualize protein-protein interaction or protein activation and to follow them in real time by light microscopy. They will permit spatial and temporal control of the protein interaction in living cells. These chemical tools will be initially tested in vitro and then will be applied in live cell studies to address the questions of cell biology related to neurodegenerations and diabetes type 2.