BIOPHYSICS

A study of biophysical properties of spider silk proteins from Araneus diadematus
supervisor: doc. RNDr. Erik Sedlák, PhD., / Centrum interdisciplinárnych biovied TIP-UPJŠ
consultant: RNDr. Gabriel Žoldák, PhD., / Centrum interdisciplinárnych biovied TIP-UPJŠ
study form: full time
Annotation: This Ph.D. thesis focuses on the detailed analysis of the properties of spider silk proteins, specifically, the ADF4 sequence of dragline fibroin 4 from European spider *Araneus diadematus*. Spider silk filaments display unique properties; they are biocompatible materials having an extraordinary tenacity of 1400 MPa – which is about threefold higher in comparison to stainless steel. Unique properties of spider silks are determined by the complexity of the internal structure of microfilaments, which are further built from the pairwise interacting cross □-fibres. Recently, such cross □-fibres are in the focus of the scientists in material nanotechnology in that they are promising building blocks for bottom-up engineering of new biocompatible modular mesoscopic structures. Ph.D. thesis will further focus on scrutinizing processes leading to fibril formation including thermodynamic analysis of the underlying structural processes.

Mechanism of cell responses to oxidative stress: time-resolved imaging of cell
supervisor: prof. RNDr. Pavol Miškovský, DrSc.
consultants: RNDr. Veronika Huntošová, PhD., / Centrum interdisciplinárnych biovied TIP-UPJŠ, RNDr. Zuzana Naďová, PhD.
study form: full time
Annotation: The main aim of the Thesis is to apply time-resolved fluorescence microscopy for monitoring of cellular responses to oxidative stress. Classical fluorescence microscopy is intensity-based technique. The interaction between molecule-molecule, molecule-biomolecule and molecule-cell structures required to apply fluorescence/phosphorescence lifetime measurements (FLIM/PLIM). From the fluorescence lifetime values of fluorescence probes, we will be able to estimate the localization and the environment of the used fluorescence probe. FLIM/PLIM will be used mostly to monitor important signaling pathways agents. These agents will be fluorescence immune-stained. Their involvement to cell survival will be assumed according to the changes in fluorescence lifetimes of immune-probe.

Mechanism of cell resistance and apoptosis in 3D spheroids: cross-correlation of protein kinase C and ABC transporters functions
supervisor: prof. RNDr. Pavol Miškovský, DrSc.
consultants: RNDr. Veronika Huntošová, PhD., / Centrum interdisciplinárnych biovied TIP-UPJŠ, RNDr. Zuzana Naďová, PhD.
study form: full time
Annotation: The main aim of the Thesis is to investigate cross-correlation of protein kinase C and ABC transporters during apoptosis and generally, during cell response after stimulation with different drugs. Preferentially, we will pay attention to cancer. Tumors are spherical systems. For this reason the study will be performed in 3D spheroids. The results will be compared with cell monolayers approach. Protein kinase C (PKC) phosphorylates different proteins and enzymes in cells that are active in apoptotic signaling pathways. Drug resistance is one of the main problem in cancer treatment. We will focus our study to investigate mechanism of PKC interactions with ABC transporters and other multi-drug resistance proteins. Mechanisms will be studied by the techniques available at Center for

Interdisciplinary Biosciences and Department of Biophysics: steady-state and time-resolved microscopy, spectroscopy, western blotting, different isolation technique for protein expression determination in cells.

Nanoparticles in relation to protein amyloid aggregation
supervisor: RNDr., Ing. Katarína Šipošová, PhD., /ÚEF SAV
consultant: doc. RNDr. Peter Kopčanský, CSc., /ÚEF SAV
study form: full time
Annotation: The self-assembly of proteins resulting in the formation of amyloid fibrillar aggregates has emerged as a subject of fundamental importance in biomedical research as well as in protein chemistry due to its involvement in a number of neurodegenerative disorders. The PhD thesis covers three key research tasks:(i) designing of nanoparticles with an appropriate coating and their screening in regard to effectiveness to inhibit amyloid formation and/or disassemble pre-formed fibrils (ii) studying of the mechanism of interaction of selected nanoparticles with amyloidogenic proteins; (iii) enhancing the effect of nanoparticles on protein amyloid formation using various types of irradiation such as thermal, photon, and others.

Automation and robotization of biophysical experiments
supervisor: assoc. prof. Zoltán Tomori, PhD., /ÚEF SAV
consultant: doc. Mgr. Gregor Bánó, PhD.
study form: full time / external
Annotation: „Light robotics" is a new trend of optical micromanipulation which integrates biophotonics, robotics and artificial intelligence. The robot having the size of several microns is created by the 3D nanoprinting technology. The optical tweezers drives the robots by multiple laser traps giving them the autonomous functionality in the surrounding environment. The proposed theme aims to study the possibilities of robotization of biophysical experiments in measuring the mechanical properties of particles, temperature, SERS, fusion of cells, drugs transport, sorting etc.

Role of membrane contact sites between ER and mitochondria in neurodegenerative diseases and photobiomodulation effect on their function
supervisor: doc. RNDr. Katarína Štroffeková, PhD.
study form: full time
Anotation: Membranous organelle presence (endoplasmic reticulum, ER, Golgi apparatus, GA, mitochondria, etc.) in eukaryotic cells enabled compartmentalization and diversification of biochemical and metabolic functions. In the same time, it also underlined need to coordinate organelle function and communication between them. Interorganelle communication is accomplished by several means such as signalization pathways, vesicular transport and at the membrane contact sites (MCSs). Contact sites between ER and mitochondria (mitochondria associated membranes, MAMs) play important role in lipid synthesis, regulation of Ca^{2+} homeostasis, and mitochondria dynamic and biogenesis. MAMs functions are severely compromised in neurodegenerative diseases (AD,PD, ALS). Research in this project will focus on MAMs communication mechanisms in damaged neuronal cells. In addition, we will study a possible therapeutic effect of photobiomodulation in MAMs function. We will use interdisciplinary approach of metabolic fluxes measurements, confocal fluorescent microscopy, molecular biology and spectroscopy.

3D reconstruction of biological objects from limited number of hard X-ray projections.
supervisor: doc. RNDr. Jozef Uličný, CSc.
consultant: dr. Patrik Vagovič, PhD., / CFEL a XFEL Hamburg
study form: full time
Annotation: obtaining 3D structure of submicroscopic biomedicinal objects using extremely high brilliance X-ray femtosecond pulses requires single-shot multiple imaging projections before the significant radiational damages occur [TDR13]. In our group, we devised, constructed and succesfully tested experimental setup allowing such measurements[DIA17]. The main task of this PhD will be to create the reconstruction procedures for CDI and holographic imaging modalities for selected model objects [HRI16]. Compared to known CT reconstruction algorithms, the procedures must take into account apriori information about the objects, including information from fiducial particles (gold nanocrystals and/or other nanoparticles with high electron density) by using artificial intelligence techniques [PAG06,LOH09]. The work involves participation on experimental design and imaging experiments (under dr. Patrik Vagovič, Single Particles and Biomolecules workstation, European XFEL, Hamburg).

Spectroscopic studies on organic matter from the bone tissue and eggshells of extinct organisms
supervisor: doc. Mgr. Daniel Jancura, PhD.
consultants: RNDr. Zuzana Jurašeková, PhD., doc. RNDr. Martin Kundrát, PhD., /CIB TIP-UPJŠ
study form: full time
Annotation: A long-standing paradigm referring to degradation of organic substance excluded a possibility for preservation of soft tissues of organisms that lived during the Mesozoic Era. Recently, such claims were revised by discovery of the Cretaceous Jehol Biota in China. Fossilized organic remains of the Jehol animals had preserved under taphonomic processes that are linked with volcanic activity. Other factors involved in mummification of soft tissues are arid climatic conditions. These are more typical for the Mesozoic fossils discovered in the Gobi Desert. The present PhD project aims to understand taphonomic selectivity in the preservation of fossil biomolecules as well as in the mineral replication of soft tissues due to different climatic and ecological factors. The principal analytical technique to be used is Raman spectroscopy. The method itself and its potential applications in molecular paleobiology is the object of investigation as well. We shall study a wide range of fossil tissue samples of the Mesozoic and Cenozoic animals discovered in Europe, Asia, Madagascar, Australia and New Zealand.

Drug tansport in biological systems
supervisor: doc. Mgr. Gregor Bánó, PhD.
consultant: prof. RNDr. Pavol Miškovský, DrSc.
study form: full time
Annotation: Drug treatment optimization requires the knowledge of the pharmacokinetic properties of the used drug molecules. The concentration time course of active substances in the organism is greatly influenced by their transport in the blood stream, in tissue, and inside cells. The passage of substances across biological membranes plays an important role here. Membrane transport can be monitored using model systems (vesicles or various artificial lipid bilayers) or directly on live cell cultures. The project is focused on experimental study of drug

transport in solutions and membranes using a modular micro-Raman apparatus in combination with optical tweezers. The project comprises development of new experimental techniques for monitoring drug movement dynamics in biological systems.