PhD topics, starting on Februray 1st, 2024

1. **AI-Driven Human Exome Analysis in Clinical Data**

Exome analysis has become a cornerstone of clinical genomics, enabling the identification of rare and common genetic variants linked to diseases. Despite advances in sequencing technologies, the challenge lies in integrating computational methodologies to interpret exome data with precision. This includes leveraging heuristic algorithms and artificial intelligence (AI) to analyze data efficiently and improve variant annotation. One promising application is the calculation of the PSI (Percent Spliced-In) coefficient, critical for understanding alternative splicing in disease-related genes. This work focuses on developing an AI-based pipeline for analyzing human exomes in clinical datasets. The research will involve the design of heuristic algorithms optimized for calculating PSI coefficients, which quantify alternative splicing patterns in genes of clinical interest. The project's main objectives are: 1. To develop and validate a heuristic-algorithm-based method for PSI computation. 2. To integrate AI for enhanced variant interpretation, focusing on alternative splicing. 3. To identify clinically actionable splicing variants linked to complex diseases. 4. To deploy the pipeline within clinical genomics settings, enabling personalized therapeutic strategies. The project will be solved mainly at the Department of Biomedical Engineering. However, cooperation with our national partner University Hospital Ostrava is expected. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend.

Tutor: Provazník Valentine, prof. Ing., Ph.D.

2. **Bioreactor optimization for cultivation of thermophiles**

White biotechnology, i.e. a technology that uses living cells to produce value added chemicals, usually loses the competition with standard petrochemical production due to higher financial costs. The reason can be found in the need to protect these processes against contamination. This inefficiency could be reduced by using naturally robust organisms, so called extremophiles. However, these organisms are not so well studied, partly also because of the lack of instrumentation for extremophilic cultivation on a small scale in laboratory bioreactors. The topic is focused on developing a small laboratory bioreactor especially suited for thermophilic cultivations. Large industrial processes usually generate waste heat that is unfavourable for mesophiles and needs to be reduced for them to proliferate. On the other hand, this environment is naturally suitable for extremophiles, particularly thermophiles. Unlike large scale processes, small scale lab cultivation does not produce waste heat, therefore, the heat has to be added for successful cultivation and research of thermophiles. Such experiments are needed to develop novel concepts as the Next-Generation Industrial Biotechnology concept that relies on the use of naturally robust organisms. Unfortunately, small bioreactors designed for thermophilic cultivations are currently missing. The aim of the research is to develop novel hardware for cultivations of bacterial thermophiles and its software control for various cultivation modes. A wide range of currently available parts will be used rather than building the reactor up from scratch. Platforms like Chi.Bio can be used as a base for it presents an open system orchestrated through Arduino and programmable in Python. Thus, it offers almost unlimited possibilities for bioreactor augmentation. The project will be solved mainly at the Department of Biomedical Engineering. However, cooperation with our national (University Hospital Brno, the Faculty of Chemistry BUT, and Czech Collection of Microorganisms) and foreign partners (Ludwig-Maximilians-Universität München in Germany and HES-SO Valais-Wallis in Switzerland) is expected. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend when joining a grant project or engaging in teaching.

Tutor: Sedlář Karel, doc. Mgr. Ing., Ph.D.

3. **Computational Polygenic Risk Score Models for Sudden Cardiac Arrest in Central European Populations**

Sudden cardiac arrest (SCA) is a leading cause of mortality, with a complex interplay of genetic and environmental factors contributing to its risk. Polygenic Risk Scores (PRS) are emerging as vital tools for assessing genetic susceptibility to SCA. However, existing PRS models often fail to account for the unique genetic makeup of geographically and ethnically homogeneous populations, such as the Central European population. This work aims to design and validate a PRS model tailored to the Central European population, utilizing large-scale genomic datasets from collaboration with University Hospital Ostrava. The research will integrate genomic data with AI-based statistical modeling techniques to identify genetic variants most predictive of SCA. Key objectives include: 1. Development of a computational pipeline for PRS calculation incorporating population-specific allele frequencies. 2. Application of machine learning techniques to optimize variant weighting within the PRS framework. 3. Validation of the PRS model on Central European cohorts to ensure predictive accuracy. 4. Exploration of gene-environment interactions and their influence on SCA risk. The project will be solved mainly at the Department of Biomedical Engineering. However, cooperation with our national partner University Hospital Ostrava is expected. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend.

Tutor: Provazník Valentine, prof. Ing., Ph.D.

4. **Modern image processing methods in cardiac MRI applications**

Nuclear magnetic resonance imaging is one of the most advanced imaging systems in medicine. The development of these methods and the improved availability of these systems brings additional areas in which these methods can be used for diagnosis. This brings with it much larger volumes of data acquired by this modality and the resulting need for new methods that will allow for the processing of these data while providing more advanced and accurate diagnostics. One of these areas is cardiac MRI, which is the topic of this dissertation. The very first step is the correct orientation of the heart, i.e. finding the radiological planes that are important for the correct imaging of the heart using nuclear magnetic resonance. Here it is shown that the use of machine learning based methods (deep learning) could enable automatic detection from the survey data and thus can both speed up the scanning process and make it more accurate. The next step is to design appropriate methods to support the diagnosis of heart disease. These include both segmentation methods that can lead to a more detailed analysis of the heart (cardiac volumes, myocardial thickness, etc.) and other advanced methods based on deep learning to support diagnosis (detection of tissue changes, lesions, anatomical differences, etc.). However, cooperation with external partners - national clinical centres (FN Brno, VFN Prague, FNUSA/ICRC Brno) and foreign institutions (IRST IRCCS Meldola Italy, Philips Healthcare Netherlands, DKFZ Heidelberg Germany) is envisaged, enabling clinical evaluation of results and their discussion with expert physicians. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend when joining a grant project or engaging in teaching.

Tutor: Harabiš Vratislav, Ing., Ph.D.

5. **New approaches for multimodal retinal image processing and analysis**

This topic is focuses on advancing ophthalmology through the development of novel image processing and analysis methods for multimodal retinal imaging. By leveraging state-of-the-art techniques such as adaptive optics, spectral imaging, and machine learning, the study aims to enhance the detection and diagnosis of specific eye diseases. The work also explores the integration of multimodal imaging data to provide a holistic view for clinical decision-making, thereby improving diagnostic accuracy, treatment planning, and monitoring of disease progression. The dissertation topic based on collaboration with Lappeenranta University of Technology and the PhD student will be under double supervision during the PhD studies.

Tutor: Kolář Radim, doc. Ing., Ph.D.

6. **New approaches in computational analyses of bacterial communities for biotechnology**

Thanks to their diversity, non-model bacteria represent an inexhaustible resource for microbial biotechnology. While tools, including the computational ones, to study pure bacterial cultures are developed to at least a certain point, their counterparts for analysis of mixed cultures are underdeveloped or completely missing. This prevents us to further study biotechnological capacity of bacterial consortia to produce value added chemicals. The topic is focused on computational methods for a comprehensive analysis of microbial consortia in order to reveal their functional capacity for industrial biotechnology and production of value-added chemicals, primarily bioplastics. While particular tools for taxonomic profiling based on amplicon sequencing and metagenome analysis based on shotgun sequencing exist, they are oriented to perform descriptive rather than functional analysis. This provides only limited use for biotechnology research where the emphasis is put on function. This is partly caused also by the lack of tools oriented on processing of bacterial metatranscriptomes. Finally, there is an absolute lack of tools to connect potential functional capacity inferred from a metagenome with running biological processes measured with metatranscriptomics and metabonomics approaches. The aim of the research is to set up comprehensive computational pipeline to analyse diversity of a selected mixed bacterial culture, to set up a metagenome of this community, and to match its observed behaviour through analyses of other omics data revealing running biological and metabolic processes. The pipeline will include specific steps to process short NGS as well as long TGS reads to cover all currently used sequencing technologies. The project will be solved mainly at the Department of Biomedical Engineering. However, cooperation with our national (University Hospital Brno, the Faculty of Chemistry BUT, and Czech Collection of Microorganisms) and foreign partners (Ludwig-Maximilians-Universität München in Germany and HES-SO Valais-Wallis in Switzerland) is expected. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend when joining a grant project or engaging in teaching.

Tutor: Sedlář Karel, doc. Mgr. Ing., Ph.D.

7. **New approaches in recruiting bacterial genomes from metagenomes**

Recent advances in DNA sequencing allowed routine sequencing of environmental samples. However, current computational tools hardly keep up with constantly changing lab techniques and the growing output of sequencing devices. Therefore, novel computationally efficient techniques are needed to recruit particular genomes from metagenomes. The topic is focused on methods for recruiting particular bacterial genomes from environmental samples, i.e., metagenomes. While in the past all newly described bacteria had to be isolated and their culture had to be made publicly available, a recent initiative SeqCode brought a nomenclatural code for prokaryotes described directly from sequence data as many microbial species are uncultivable with current techniques.

Moreover, even for newly published cultured bacteria, environmental evidence based on searching in publicly available metagenomes is nowadays required by scientific journals. Although tools to produce metagenome-assembled genomes exist, searching metagenomes for particular analysed genomes is done exclusively with BLAST and is not rigorously described. Unfortunately, due to the repetitive segments of bacterial genomes, false hits are always found and quantification of data, i.e., assuming an abundance of a genome in a metagenome, is therefore biased. The aim of the research is to find a method for quantification as precise as possible. The applied method will include specific steps to process short NGS as well as long TGS reads to cover all currently used sequencing technologies. The project will be solved mainly at the Department of Biomedical Engineering. However, cooperation with our national (University Hospital Brno, the Faculty of Chemistry BUT, and Czech Collection of Microorganisms) and foreign partners (Ludwig-Maximilians-Universität München in Germany and HES-SO Valais-Wallis in Switzerland) is expected. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend when joining a grant project or engaging in teaching. PhD students will complete a six-month internship at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or a part-time contract beyond the state stipend when joining a grant project or engaging in teaching.

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8. **3D Bio Printing of Cancer-Model Structures with Controlled Polymerization Using PET-RAFT Technique and Variable Light Intensity for Drug Testing Applications**

This dissertation thesis focuses on the innovative application of 3D bioprinting technology for creating cancer-model structures with precise control over polymerization using the PET-RAFT technique and variable light intensity. The research aims to develop a sophisticated platform for simulating cancer tissues in a controlled in vitro environment, allowing for the testing of various medications and treatment modalities. By leveraging advanced biofabrication techniques and tailored polymerization processes, this study contributes to the advancement of personalized medicine and drug efficacy assessment in oncology research. Responsibilities include research, experimental design, data analysis, collaboration, publication, innovation, regulatory compliance, and continuous professional development in the field of 3D bioprinting for cancer modelling and drug testing applications. As part of their studies, doctoral students complete six-month internships at attractive partner universities abroad. UBMI provides doctoral students with a stipend and/or part-time in addition to the state stipend when participating in a grant project or participating in teaching.

Tutor: Fohlerová Zdenka, doc. Mgr., Ph.D.