

Colloquium: Computational Medicine

10. - 14. February 2025

BMTEG138 (HS BMT) | Stremayrgasse 16, Erdgeschoß

It is a pleasure to invite you to the colloquium for our Professorship in Computational Medicine at Graz University of Technology. The public part will be a short educational presentation Bachelor's level in Biomedical Engineering, 4th semester in "Introduction to Computational Modelling", a scientific talk (titles below), and a discussion with the audience.

Gruber Andreas

10. February 2025 | 09:30 | BMTEG138 (HS BMT)

Title: "Computational Medicine for a Healthy Future"

Abstract: Understanding, preventing and curing complex human disease, such as cancers, belong to the most urgent medical needs of our time in terms of both societal life quality and health care costs. Importantly, prevention is the most effective way to fight cancer. The World Health Organization (WHO) estimates that between 30-50% of cancer cases are preventable based on already known risk factors. Consequently, identifying all of the factors that contribute to cancer development is key to further empower cancer prevention. Cancer-causing mutations can be introduced by a multitude of mutational processes, such as UV light exposure. Importantly, not all mutagenic sources are known to date. Thus, we are working on the characterization of mutational processes that contribute to cancer development. Knowing all mutation-causing sources will allow deliberate avoidance, and will thus ultimately empower systematic cancer prevention. However, as some known mutational processes are endogenous, understanding the molecular foundations of cancer development and progression is undoubtedly highly relevant for the development of efficient treatment strategies. Currently available therapies are mostly designed for the average patient. However, 'one-size-fits-all' treatment approaches are not very well suited for heterogeneous diseases, such as cancers, as they often neglect tumor-specific properties. Thus, to unravel the molecular mechanisms underlying individual tumors another important area of our research is to detect unknown cancer driver mutations and characterize associated molecular cancer subtypes. Further, we are developing computational tools that are able to identify and annotate tumor-specific RNA molecules as well as computational models that enable to pinpoint regulators that are key to the oncogenic properties of individual tumors. These precision analytics tools seek to make an important step towards improved clinical diagnostics, ultimately aiming to support personalized treatment strategies in the future, thereby delivering the vision of precision oncology.

Nordsletten David

10. February 2025 | 14:00 | BMTEG138 (HS BMT)

Title: "Image-Based Computational Modeling in the Heart"

Abstract: Cardiovascular Diseases remain one of the most significant medical challenges worldwide. Addressing these challenges requires a concerted effort from clinicians, to medical technologists, to biomedical engineers. Image-based computational modeling presents the opportunity to integrate medical imaging and biophysics to truly personalize medicine, providing opportunities for improved

diagnostics and therapy planning. In this talk, we explore how computational modeling across patients with genetic cardiomyopathy can be used across scales to understand pathophysiology and disease progression. We also explore how image-based computational modeling can help to provide insights into left ventricular assist device therapy - and the impact of heart repair. repair.

Lenk Kerstin

11. February 2025 | 09:30 | BMTEG138 (HS BMT)

Title: “The role of astrocytes in the brain's function”

Abstract: Astrocytes, a crucial type of glial cells in the brain, are actively involved in neuronal information processing and synaptic plasticity. Computational models can guide experimentalists toward the most relevant experiments by forming a theoretical framework to characterize and predict the system functions. In my presentation, I will briefly introduce astrocytes and explain the rationale behind my research focus. Then, I will present our developed computational models, with which we investigate the tight interaction of neurons and astrocytes at both single-cell and network levels. These models are particularly relevant in understanding neurological disorders such as epilepsy and schizophrenia, where alterations in neurotransmitter uptake and release, ion exchange, and astrocyte morphology are observed. With the aid of our computational models, we investigate these aspects on several temporal and spatial levels. I will conclude by outlining future research directions, including developing digital twins of astrocytes for translational medicine and new therapeutic strategies.

Leichtle Alexander

11. February 2025 | 14:00 | BMTEG138 (HS BMT)

Title: “From Code to Clinics: How Computational Medicine Drives Research and Routine Care”

Abstract: Computational Medicine is revolutionizing laboratory medicine by enabling the secondary use of clinical data for innovative applications. I will demonstrate key advancements in predictive modeling, personalized reference intervals, and the integration of multimodal data using artificial intelligence (AI) and machine learning (ML). I will also address Challenges related to data governance, anonymization, and the implementation of FAIR (Findable, Accessible, Interoperable, and Reusable) data principles.

Case studies illustrate the potential of advanced algorithms in mortality risk prediction, glycemic control, and diagnostic decision-making. These examples underscore the importance of high-quality, privacy-preserving data frameworks in supporting medical practice and improving patient outcomes. The findings provide a roadmap for leveraging data-driven approaches to enhance both research and clinical care.

Kulakovskiy Ivan

12. February 2025 | 09:30 | BMTEG138 (HS BMT)

Title: “Bioinformatics of eukaryotic gene regulatory regions: from DNA text patterns to better RNA” therapeutic

Abstract: Insights yielded by molecular genetics, genomics, and bioinformatics are shaping the present and the future of personalized biomedicine and human healthcare. While the priority is

traditionally given to protein-coding genes, recent research advances highlight the less explored non-coding genome as no less important. Particularly, for many pathological phenotypes, the majority of associated individual genome variants do not alter protein sequence and function directly but disturb the cellular state by altering gene expression and protein abundance. The non-coding variants are often located in the gene regulatory regions and may affect transcription or post-transcription regulation e.g. by changing protein-DNA or protein-RNA interactions.

Knowing the gene regulatory grammar is essential to perform functional annotation of non-coding variants and reveal the involved molecular mechanisms that link nucleotide substitutions with particular pathologies. The traditional "bottom-up" approach aims to decipher the structure of regulatory regions by analyzing individual protein binding sites, particularly, by cataloguing the sequence patterns, "motifs", recognized by different regulatory proteins. The synergy of machine learning and high-throughput experimental techniques enabled the "top-down" approach to study the activity of a regulatory region as a whole. Combining both strategies with direct omics data allows for interpreting non-coding sequence variation and rational design of regulatory DNA and RNA regions, and, in the end, opens the way to optimized gene and RNA therapy.

Satagopam Venkata

12. February 2025 | 14:00 | BMTEG138 (HS BMT)

Title: Clinical and translational medicine multi-modal data approaches to investigate complex diseases

Abstract: Neurodegenerative (e.g. PD - Parkinson's disease), immunological (e.g. IBD - Inflammatory Bowel Disease, MS - Multiple Sclerosis, RA - Rheumatoid Arthritis) and recent COVID19 diseases are quite complex in their etiology. In order to stratify and discover the signatures, biomarkers for early diagnosis, we need high quality clinical cohort studies. This talk will focus on the clinical and translational medicine informatics approaches developed to build up cohorts and to capture the clinical data using state-of-the-art electronic Case Report Forms (eCRFs) encoded with standard ontologies and controlled terminologies. Secure management and efficient integration of clinical, associated molecular data (multi omics - genomics, transcriptomics, proteomics, metabolomics, lipidomics, microbiome data), imaging and sensor/mobile data. Interoperability of this heterogeneous data in content and format is another challenge. It involves, mammoth task of data curation, harmonisation and FAIRification (making data Findable, Accessible, Interoperable and Reusable) to facilitate the cross study analysis. Application of statistical and Machine Learning (ML) methods to analyse multi-layered data to stratify the patients into different subgroups based on disease severity and progression and identification of biomarkers representing each subgroup. In addition, application of knowledge management methods, disease maps, to discover the mechanistic models and co-morbidities of these complex diseases.

Schmid Franca

13. February 2025 | 09:30 | BMTEG138 (HS BMT)

Title: Why Microvascular Perfusion and Topology are Key Players to Understand, Diagnose, and Treat Neurological Disorders

Abstract: Despite consuming 20% of the body's energy, the brain only has limited capabilities to store energy. Consequently, a robust supply of oxygen and nutrients via the brain vasculature is indispensable for healthy brain function. The bulk of oxygen and nutrient discharge occurs in the microcirculation. At the same time, evidence increases that microcirculatory disturbances are

common during neurological disorders such as stroke and Alzheimer's disease and might even precede neurological deficits. By blood flow simulations in realistic microvascular geometries, we provide evidence for the crucial role of microvascular alterations and topological variability on overall brain perfusion. These insights and the strong connection to in vivo experiments ensure that our work is directly relevant for understanding disease progression and suggesting novel strategies for early diagnosis and treatment.

Hausser Jean

13. February 2025 | 14:00 | BMTEG138 (HS BMT)

Title: Machine-learning of novel cancer-immune interactions to target in therapy

Abstract: Cancer therapy is shifting toward targeting the tumor microenvironment.

For example, immune checkpoint inhibitors (ICI) can restore anti-tumor immunity by blocking PD1 and CTLA4 receptors. Yet, they fail to provide long-term tumor control for most patients. This suggests additional immune evasion mechanisms requiring new immunotherapy targets.

Single-cell and spatial transcriptomics enable detailed tumor characterization, offering potential for unbiased target discovery. Yet, current computational methods produce extensive but hard-to-interpret gene lists.

To address this, I will outline our efforts towards machine-learning approaches to identify actionable immunotherapy targets, by developing

(1) Tissue Dynamics Inference (TIDYI) to infer tumor dynamics from transcriptomics data, (2) Growth-driving cell Interaction identification

(GRINT) to identify tumor-modulating interactions using machine learning, and by (3) validating GRINT targets in vivo and using patient datasets.

Preliminary validation confirm that GRINT re-discovers known tumor-promoting and suppressing interactions and correlate with genetic perturbations. This research will maximize the power of single-cell and spatial transcriptomics in identifying new genes to target for effective cancer immunotherapy therapy and accelerate innovation in this area.

Ulz Peter

14. February 2025 | 09:30 | BMTEG138 (HS BMT)

Title: Precision medicine in cancer: a liquid biopsy approach

Abstract: Advancements in sequencing technology have led to tremendous steps forward in the analysis of cancer genomes. Particularly, the analysis of cell-free DNA (cfDNA) has shown great potential in non-invasive diagnostics and monitoring throughout the cancer disease course as it allows repetitive sampling of the cancer genome. While analysis of somatic mutations are slowly making their way into the clinic, there is a wealth of additional information provided in cfDNA that can be used to get a glimpse of the underlying biological changes that lead to the development of cancer. In this talk I will give a short overview of precision medicine and how liquid biopsies help get a complete picture over the course of a cancer disease. In particular, I will talk about the use of cell-free DNA fragment attributes that can be used differentiate cancer subtypes, lead to early detection and even expand the use of cell-free DNA analyses to other diseases in which specific cell-death can be used for disease detection.