Project Proposals for Doctoral Researcher Positions 2025

ID01: Robust knowledge discovery of cell interactions in multichannel imaging flow cytometry and live cell imaging (Ralf Mikut, Daniel Hübschmann)
Karlsruhe, KIT, Automated Image and Data Analysis

The analysis of cellular interactions is important for understanding organismal development, tissue homeostasis and immunity. This includes in particular the understanding of disease and therapeutic effects in comparison to healthy organisms. Quantifying and understanding these interactions can contribute to a deeper understanding of basic mechanisms, earlier diagnosis of diseases, personalized selection of the most appropriate therapy options, and improved monitoring of therapy progress.

However, current single-cell genomic technologies for the analysis of physically interacting cells suffer from low cellular throughput, long processing times, high costs, and are typically limited to predefined cell types. In addition, they do not provide full insight into the morphology of involved cells, attached antibodies and dynamics of cellular interactions. Multichannel imaging flow cytometry combines flow cytometry and imaging to analyze cells. It is a high-throughput method for counting and characterizing cells. Traditionally, flow cytometry has focused on characterization of single cells. However, flow cytometry and in particular multi-channel imaging flow cytometry can be leveraged to count and characterize physical interactions between cells in great detail. Artificial Intelligence (AI) has successfully been applied for event detection and classification in the context of imaging flow cytometry. The potential of applying AI to study cellular interactions, however, has not been fully exploited.

The goal of the proposed project is to study, characterize and analyze the distributions, kinetics, and alterations under pathological conditions of cellular interactions by developing and applying an AI-based generic and standardized pipeline capable of handling data from different modalities.

ID02: Close proximity human-robot interaction in medical interventions - combining robot control and data science approaches (Katja Mombaur, Jan Stallkamp)
Karlsruhe, KIT, Institute for Anthropomatics and Robotics

Global healthcare systems are under immense pressure due to aging populations and persistent staff shortages, a situation amplified by events like pandemics. While existing hospital robots primarily handle surgery, cleaning, and logistics, there's a growing need for intelligent robots to assist with more routine tasks like patient admission, medical testing, and general hospital operations. This shift would free up human caregivers to focus on more complex, patient-centered care.

However, enabling robots to perform such tasks requires a significantly higher level of machine intelligence and advanced skills. These robots must be able to autonomously navigate complex environments, perceive individuals, understand situational requirements, and perform dexterous fine manipulation with human tools, all while interacting safely and efficiently in close proximity to people.

This PhD project will contribute crucial initial steps towards integrating humanoid robots for medical testing in hospitals. It will define a suitable benchmark for these actions, develop novel concepts and computational methods for robot control in such dynamic situations, and conduct human-robot interaction experiments in both laboratory and clinical settings. The project will utilize a TiagoPro humanoid robot to implement and test these skills. The innovative methods will combine efficient robot control algorithms that account for the robot's physical embodiment with data science approaches based on foundation models, allowing robots to manage real-world variability and interact safely and efficiently. This thesis is designed to initiate a larger collaboration aimed at bringing humanoid robots into hospitals for broader medical testing and interventions, with a specific focus on supporting the unique demands of intensive care.

ID03: Fragments filtration for helium radiography and computed tomography (Francesca Spadea, Oliver Jäkel)
Karlsruhe, KIT, Institute for Biomedical Technology

Helium radiography and computed tomography are experimental imaging techniques capable of providing high-resolution, low-dose images for various applications in ion beam therapy, including treatment planning, patient positioning verification, and motion management. Owing to their fundamental properties, helium ions exhibit low scattering and can produce metal artifact–free images. Recently, the concept of simultaneous helium imaging during carbon ion radiotherapy (CIRT) has been proposed, offering new possibilities for real-time adaptive CIRT.

However, this approach presents significant challenges due to the presence of high energy fragments generated in helium and especially in mixed carbon-helium beams. These fragments are detected by the imaging system and degrade image quality, limiting the benefits of helium-based imaging. Because these fragments can have energies comparable to primary ions but follow unpredictable trajectories, standard filtering techniques are often ineffective. In this context, deep learning (DL) approaches offer a promising solution. DL-based methods have already demonstrated success in various radiotherapy imaging applications, such as synthetic CT generation from MRI and CBCT, which are crucial for adaptive radiotherapy workflows. The application of DL techniques could enable effective filtration of high energy fragments, allowing only primary helium ions to be used for image reconstruction.

This project lies at the intersection of data science, particle physics, and life sciences, offering advancements that could benefit all three domains.

ID04: Knowledge Graph Reasoning for Generalized Surgical (Lena Maier-Hein, Karl-Friedrich Kowalewski)
Heidelberg, DKFZ, Intelligent Medical Systems

Death within 30 days after surgery has recently been found to be the third-leading cause of death worldwide, with research suggesting that a large proportion of these deaths are due to surgical error. The newly established domain of Surgical Data Science [Mai22] aims to address this issue, yet, clinical translation of data science methods remains limited due to challenges in generalization and adaptability across diverse surgical environments. To bridge this gap, this project proposes a novel approach that integrates knowledge graphs (KGs) with Vision-Language Models (VLMs) to achieve a generalized understanding of unannotated surgical procedures. KGs serve as structured representations of surgical instruments, anatomical structures, and procedural steps, enabling AI models to infer contextual relationships during real-time surgical scenes. Through multi-modal learning, we aim to extend the zero-shot capabilities of VLMs to interpret complex, unseen surgical actions by leveraging hierarchical reasoning and contextual awareness embedded in the KG.

To implement the project, we have access to a multi-center world-wide unique video data set of unprecedented size comprising more than 10,000 videos annotated with procedural information and (partially) frame-based annotations related to procedure steps and adverse events. This unique resource combined with our domain expertise and innovative use of KGs, has the potential to set the stage for groundbreaking advancements in surgical scene understanding and generalization, enabling robust AI-driven decision-making across diverse surgical procedures and institutions.

ID05: Multimodal decision support for postoperative monitoring after brain tumor surgery (Klaus Maier-Hein, Jan-Oliver Neumann)
Heidelberg, DKFZ, Medical Image Computing

After brain tumor surgery, patients are typically admitted to an intensive care unit (ICU) in many healthcare settings. Economic pressures and concerns about unnecessary ICU admissions have led to a shift towards selectively admitting patients. While various decision aids have been proposed, the final decision often rests with the operating surgeon, who considers factors such as the patient's health status, surgery complexity, tumor characteristics, and any procedural complications. Surgeons tend to err on the side of caution, admitting even low-risk patients to the ICU or a step-down unit for close monitoring.

There is growing interest in developing automated approaches to support this decision-making process. Machine-learning models, trained on extensive patient data including surgical details and outcomes, have the potential to objectively predict postoperative complications. Leveraging data from Heidelberg University's Neurosurgical clinic, we propose a comprehensive decision support system using advanced techniques in joint image, language, and tabular data processing. By integrating preoperative imaging, clinical data, and patient records, this algorithm aims to predict ICU complications and provide a scoring system to guide clinicians in making informed decisions, minimizing patient risk and optimizing resource utilization.

ID06: Enhancing Biomarker Discovery through Covariate-Aware Multi-Omics Factorization Models (Oliver Stegle, Junyan Lu)
Heidelberg, DKFZ/EMBL, Computational Genomics and Systems Genetics

Multi-omics studies hold promise for enhancing our understanding of biological processes across multiple molecular layers, with significant implications for personalized medicine. However, analyzing high-dimensional multi-omic data remains challenging due to noise, incomplete sampling, and confounding sources of variation, limiting the ability to derive causal insights.

Matrix factorization methods, like multi-omics factors analysis pioneered by partnering PI groups, are promising for extracting biomedical insights from such data. Yet, current methods often overlook critical patient sample covariates such as genetic backgrounds, technical variations (e.g., batch effects), temporal/spatial structures, and experimental conditions (e.g., perturbations), hindering their applicability in clinical settings. Moreover, there's a lack of adaptable multi-omics models tailored to specific datasets, further impeding clinical adoption.

To address these gaps, this project proposes developing a flexible, programmable covariate-aware multi-omics factorization model. This model will be designed to analyze heterogeneous clinical samples with complex covariate structures, advancing multi-omics analysis by automating model definition and incorporating strategies to enhance causal representation learning using instrumental variables.

The project will apply these advancements to a comprehensive multi-omics cohort of lung cancer patients. The primary objective is to identify biomarkers predictive of tumor recurrence, a critical factor in treatment efficacy and patient outcomes in cancer care. This research aims to propel multi-omics analysis forward, facilitating its integration into clinical practice for improved patient stratification and personalized treatment strategies.

ID07: Data-based outlier detection and risk validation for multi-class prediction in newborn screening (Vincent Heuveline, Stefan Kölker)
Heidelberg, University Heidelberg, Engineering Mathematics and Computing Lab

Newborn screening plays a crucial role in early detection of rare, inherited metabolic diseases, facilitating timely interventions and improved outcomes for affected infants and families. However, the rarity of these diseases results in highly imbalanced datasets with few positive screening results, which are often perceived as outliers. This project seeks to address these challenges by developing advanced outlier detection algorithms capable of identifying positive screening results accurately.

Additionally, certain conditions like methylmalonic acidemia, propionic acidemia, homocystinurias, remethylation disorders, and infantile vitamin B12 deficiency face issues with false-positive screening results. The project aims to develop a multi-class machine learning approach to effectively classify newborns with these conditions, thereby reducing false positives and minimizing unnecessary treatments.

Integrating machine learning into clinical decision-making requires transparency and risk assessment. Hence, the project will focus on developing explainable AI methods to interpret algorithm decisions and uncover underlying metabolic patterns. Furthermore, a data-driven risk management model will be developed to provide clinicians with predictive risk values associated with disease likelihood.

In summary, this project aims to advance state-of-the-art methods for data-driven outlier detection and risk prediction in newborn screening, ultimately improving diagnostic accuracy and reducing the impact of false positives on newborns and their families.