Berliner Colloquium für wissenschaftliche Visualisierung

Marc Alexa (TUB), Jürgen Döllner (HPI), Peter Eisert (HUB), Hans-Christian Hege (ZIB), Konrad Polthier (FUB), John Sullivan (TUB)

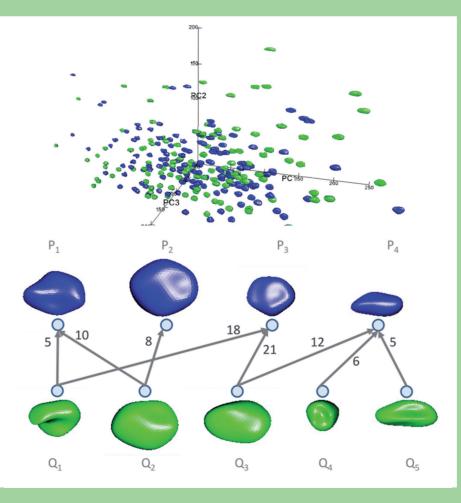## Quantitative Cellular Phenotyping in Tissue Microenvironments

Prof. Dr. Raghu Machiraju

The Ohio State University, Department of Computer Science and Engineering

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Zuse-Institut Berlin (ZIB), Takustraße 7, 14195 Berlin
Hörsaal (Rundbau, Erdgeschoss)

In the post-genomic era, there is a growing need for new experimental paradigms for investigating the links between genomics and biology. While entire genome sequences of many model systems are now available, the task of deciphering the genetic code requires characterizing the phenome of these systems in order to establish the genotype-phenotype links. This need has lead to the development of new quantitative phenotyping technologies across different levels of the biological hierarchy.

In this talk, I present new computational techniques to conduct image-driven in vivo phenotyping at the cellular level. The techniques have been developed in the context of investigating phenotypic variations of cells in cancer. Studies over the last decade have provided mounting evidence that the normal cells and molecules that surround tumor cells - collectively termed the tumor microenvironment - are involved in the initiation, growth, and spread of tumors. While examples of this phenomenon have been characterized in studies from a genetic standpoint, the lack of appropriate methodologies have precluded quantitative phenotyping studies at the cellular level.

The present work addresses this unmet need. Based on a novel method that uses local metric-learning to integrate different cellular features, I present a framework to identify major cell types in the microenvironment. I further propose a method to generate phenotypic profiles of cell populations and use the technique to detect the subtle global level changes that occur among certain cells in the microenvironment in gene knock-out experiments that seek to recapitulate human breast cancer. By proposing new computational and data analysis methods for cellular phenotyping, and using them to analyze the tumor microenvironment, I demonstrate that image-driven computational phenotyping provides a viable experimental paradigm to investigate the phenomic aspects of complex processes such as cancer.