Projektvorschlag für Projekt 2 / Bachelor Thesis, Steven Cardini

Biological Background

The Pertz research group at the University of Bern studies cell-signaling processes that regulate cell morphogenesis and cell fate decisions. The study of those processes could be a crucial step in the R&D pipeline for future cancer therapies.

The response of genetically identical cells to an external stimulus such as a growth factor or an inhibitor of a specific protein component of cell-signaling processes generally varies among the individual cells in a given population. For example, when a cell culture of neuroblastoma cells is treated with NGF, part of the cells form neurites while others do not. Thus, there is a cell-to-cell heterogeneity in the cellular response to external stimuli.

Some tumor types are associated with a modified MAPK / ERK1/2 signaling pathway. Modern medicine uses inhibitors of some effectors in this pathway to stop the growth of those tumors. However, tumors often acquire resistance to these inhibitors after an initial shrinking phase. A cell-to-cell heterogeneity in the resistance to these inhibitors was found in cell culture experiments. The current theory is that the inhibitors introduce a selective pressure to the tumor cells such that resistant cells survive and propagate to rebuild the tumor tissue.

The quantification of cell-to-cell heterogeneity is greatly facilitated by computer vision approaches. Other quantification methods such as Western blotting are not suitable to evaluate variance among individual cells, as these techniques average all the cells.

The Project

The main goal of the project is to evaluate different machine-learning approaches for feature analysis of individual cells.

The Pertz research group uses CellProfiler, a Python-based open-source image analysis software, for image segmentation and feature extraction of time-lapse microscopy images. The output of this software is a set of feature vectors of the individual cells.

In order to determine whether drug-resistant cells are associated with specific traits, these features need to be analyzed and cross-correlated. The project topic is to do a benchmarking of a few machine-learning techniques with the aim to determine the important cell features, i.e. the features that correlate with drug resistance.

R will be the main programming language of this project.

The anticipated project phases will be:

- Choose approaches
- Review them theoretically
- Apply to data sets