Unsupervised Detection of Hematopoietic Stem Cell Subpopulations from Single Cell Time Lapse Movies

Interdisciplinary Project Description

Quantitative Single Cell Dynamics
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The vertebrate blood system consists of different cell types with common progenitors, referred to as hematopoietic stem cells (HSC). Due to their ability to differentiate into certain hematopoietic cell types, as well as their self renewability, HSCs are in the focus of research since they can be cultivated artificially [3]. Medicine is interested in these cells, as investigation of stem cells may improve the understanding of cell biology as well as the understanding and treatment of certain diseases like cancer [6]. To investigate the cells in a certain state, cell identification plays a major role in preparation of biological experiments and analytic methods. Stem cell identification shall be improved in scope of this project.

The data, on which this project is based, consists of three single cell time lapse movies (SCTLM) of sorted hematopoietic stem cells (HSC), further referred to as starting cells. These cells have been purified according to certain biological markers by fluorescence-activated cell sorting (FACS) [4] before they were cultivated. However, these cells and their descendants revealed, that the purification with respect to the biological markers only lead to purity of 60%. The movies were generated in the lab of Timm Schroeder. They have three different channels, each one showing either out of focus brightfield signals or fluorescence signals emitted from certain marked proteins.

The aim of this project is to develop an unsupervised detection method for HSCs based on features that can be extracted from the existing movies like cell size, cell shape and cell movement.

The project consists of two parts: first, the cells in the movie have to be segmented and tracked over time. This might be achieved automatically. For most of the cells it will be sufficient to track only the first or the first two generations, what will reduce the amount of work to a feasible degree. As there already exist various methods to perform segmentation [8] and tracking [5, 2], the major work will be to apply and validate promising methods, integrate the best ones into a pipeline and use this pipeline. The result of this first part will be a sufficiently segmented and tracked dataset of starting cells in the movies. Moreover, the students will assess how good auto tracking performs for starting cells. Additionally this task will allow the students to get a deeper understanding and sense for the data.

The second task is to implement, use and validate a number of different unsupervised machine learning approaches in order to differentiate between HSCs and non-HSCs in the starting cell

population. Some approaches already exist [1], which maybe have to be supplemented validated and integrated into a workflow. Deep tracked trees, which are available, can be taken into account for either learning or validation too. As, in order to certainly determine the type of one cell considerable effort in biological experiments is required, the validation will mainly be based on the general biological meaningfulness of the results e.g. certain cell symmetries, cell cycle lengths or tracking tree symmetries within clusters [7]. Additionally the results can be roughly compared against the assumed FACS purity according to previous investigations. The benefit of this method, if successful, is to optimize the subpopulation profiling and increase the HSC sorting purity, which may lead to an improvement of purifying methods and thereby to an improvement of subsequent methods and analyses.

References

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