Ph.D. projects in progress

1.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Doctoral School of Interdisciplinary Medicine

Ph.D. student: István Grexa

Title of the research topic: Developing intelligent microscopy systems

Description of the research topic: Multicellular three-dimensional (3D) "-oids" (e.g. spher-oids, organ-oids) are predicted to become the next generation drug discovery models of diseases such as cancer, because they model the physiology of the disease better than classical 2D cell cultures. The aim of this project is to develop intelligent microscope systems that are able to monitor and interact with the samples. For example, detect, manipulate or treat spheroids which have a certain size and other morphological properties. To this end, we will combine microscopy with high-end computational methods including deep learning and phenotypic cellular analysis.

2.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Faculty of Science and Informatics, Doctoral School of Computer Science

Ph.D. student: Dominik Hirling

Title of the research topic: 3D image analysis and machine learning methods using deep learning for understanding neuron cell communication

Description of the research topic: Understanding cellular complexity is a key element of better disease treatment and answering fundamental questions of biology (Horvath, 2016, Nature Drug Disc., 15, 751). Recent advancements in systems microscopy and computational cell biology made possible to automatically and objectively analyse images even in scales as large as millions of images and billions of cells (Badertscher, 2016, Cell Reports, 13, 12, 2879). One of the most demanding of these tasks is to analyse label-free 3D microscopy images at the single-cell level. The aim of this project is to develop a system that first corrects imaging problems caused by imperfections of the microscope's optical system (Smith, 2015, Nature Methods, 12, 404). On the corrected images, we perform a reconstruction step that reverts the imaging model of the microscope and the result is suitable for image segmentation. Cellular phenotypes are identified using deep machine learning algorithms. We presented an automated patch clamp control method, that calibrates the needle (Koos, SCIA, 2017, accepted) and

navigates it to an arbitrary position. The aim will be that using this system automatically target a single neuron cells and measure their communication.

3.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Faculty of Science and Informatics, Doctoral School of Computer Science

Ph.D. student: Ervin Tasnádi

Title of the research topic: Image segmentation methods for single cell analysis of 3D biological samples

Description of the research topic: During my PhD, I am working on methods and algorithms to segment 3D microscopy images containing lots of nuclei. Processing such images are challenging because nucleus instances usually touch each other, and it is hard to identify the boundary, furthermore the signal can be weak at the top or the bottom of the image producing a blurry image. We have extended the selective active contour model to 3D, developed a regularization method for active contours, included everything to a real software based, and now we are working on a method that uses the output of strong 2D segmentation pipelines to reconstruct the dense segmentation in 3D.

4.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

Ph.D. student: Ákos Diósdi

Title of the research topic: Development of a 3 dimension (3D) high-throughput system for single cell analysis in cancer research

Description of the research topic: Two-dimensional (2D) cell cultures have been used as model systems for decades, however, they have their limitations and they can alter the morphology and proliferation of the cells. Moreover, the structure of the culture does not represent the structure of the tissues properly. In recent years, three-dimensional (3D) cell culture systems have been gaining popularity because these systems resemble in vivo conditions better. 3D systems have the possibility to increase the clinical success rate in drug discovery. Unfortunately, the lack of unified methodology guidelines for spheroid generation to single-cell detection is a huge problem. In our work, we generate spheroids from human carcinoma cell lines, treat them with optical clearing protocols, and create single-cell resolution imaging with light-sheet microscope. Our aim is to establish a high-throughput pipeline, which can speed up and make the spheroid analysis easier on a single-cell level.

5.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Doctoral School of Interdisciplinary Medicine

Ph.D. student: Nikita Moshkov

Title of the research topic: Improving efficiency of deep learning algorithms for single-cell segmentation and phenotyping

Description of the research topic: The goal of the Ph.D. thesis research is to propose techniques for enhancing deep learning image segmentation in biological (cell) images and propose deep learning techniques for single cell phenotyping.

To achieve those goals, the following objectives will be done, experimentally assess the test-time augmentation approach, experimentally assess usefulness of image style transfer for dataset augmentation, design a novel active learning framework for instance segmentation, which will reduce the number of needed annotations and develop software for single-cell phenotyping with means of deep learning.

6.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

Ph.D. student: Tímea Tóth

Title of the research topic: Single-cell image analysis and machine learning methods using the cellular microenvironment

Description of the research topic: To treat diseases better and to answer major questions of cell biology we need to understand cellular complexity. Based on recent advances in microscopy and computational cell biology, it is now possible to automatically analyse millions of images containing often billions of cells. Regardless that these images are acquired on tissue sections or cell-based assays, based on our results, we could increase the performace of the characterization by taking the cellular microenvironment into account. Microenvironmental effects get even more evident in case of 3D in vitro studies. 3D cell cultures have the advantages over 2D flat biology, that there's physiologic cell-cell contact in them, the cells interact with extracellular matrix, and a co-culture of multiple cells mimics an in vivo microenvironment. In drug discovery in vitro 3D cultures have the potential to fill the gap between conventional 2D in vitro testing and animal models.

High-content screening is a method that is used widely with 2D cell cultures to identify substances such as small molecules, peptides, or RNAi that alter the phenotype of a cell in a desired manner. However, there is no such platform for 3D cell cultures. There are several technologies available that promote solutions to create spheroids (a type of 3D cultures). In our laboratory, we use two kind of plates with gravity-based approach for the generation. One of them is the InSphero GravityPLUS and the other is the SphericalPlate 5D. We work with many optical clearing methods to be able to acquire good-quality images with a light-sheet microscope. We develop an automated platform (named Sheroid Picker) to plate the spheroids and the drugs. We created a software tool (3D-Cell-Annotator) that is able to segment the single cells of the spheroids. With that we can collect training data for machine learning to test the effect of microenvironmental features in 3D.

7.

Mentor: Péter Horváth

Doctoral school: University of Szeged, Faculty of Science and Informatics, Doctoral School of Computer Science

Ph.D. student: Krisztián Koós

Title of the research topic: Image Analysis and Machine Learning Methods for Personalized Medicine Applied in Anti-Cancer Drug Discovery and Brain Research

Description of the research topic: Development of image processing methods for the differential interference contrast (DIC) label-free microscopy technique. Development of a differential geometry based reconstruction algorithm that transforms the images to a format similar to fluorescence ones to make analysis easier. Development of pipette tip detection algorithms for DIC microscopy. The models should optimize a few parameters that describe a pipette model and fit them either on projection images in 2D, or dark image regions in 3D. Development of an automatic patch clamp system, including hardware and software development. The software should handle all hardware components, including stage, manipulator, camera, electrophysiological amplifier, and air pressure controller. The neurons should be detected automatically and tracking algorithms should follow the selected one during the patch clamping process.