Lendület Laboratory of Microscopic Image Analysis and Machine Learning

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Group website: http://sysbiol.brc.hu/horvath-peter-lab-index.html

Group members

Name	Title	Publications	CV
Péter HORVÁTH	Senior Research Associate	publications	CV
Krisztina BUZÁS	Research Associate	publications	
Krisztián KOÓS	Research Associate	publications	
Ede MIGH	Research Associate	publications	
József MOLNÁR	Research Associate	publications	
Tamás BALASSA	Junior Research Associate	publications	
Edina GYUKITY-SEBESTYÉN	Junior Research Associate	publications	
Mária HARMATI	Junior Research Associate	publications	
Dávid BAUER	Scientific Administrator		
Attila BELEON	Scientific Administrator		
Gabriella GRESKOVICS-DOBRA	Scientific Administrator	publications	
Réka HOLLANDI	Scientific Administrator	publications	
Ákos DIÓSDI	PhD Student	publications	
István GREXA	PhD Student	publications	
Dominik HIRLING	PhD Student	publications	
Nikita MOSHKOV	PhD Student	publications	
Ervin TASNÁDI	PhD Student	publications	
Tímea TÓTH	PhD Student	publications	
Tímea BÖRÖCZKY	Undergraduate Student		
Filippo PICCININI	Research Associate	publications	
András KRISTON	Scientific Administrator	publications	
Ferenc KOVÁCS	Scientific Administrator	publications	

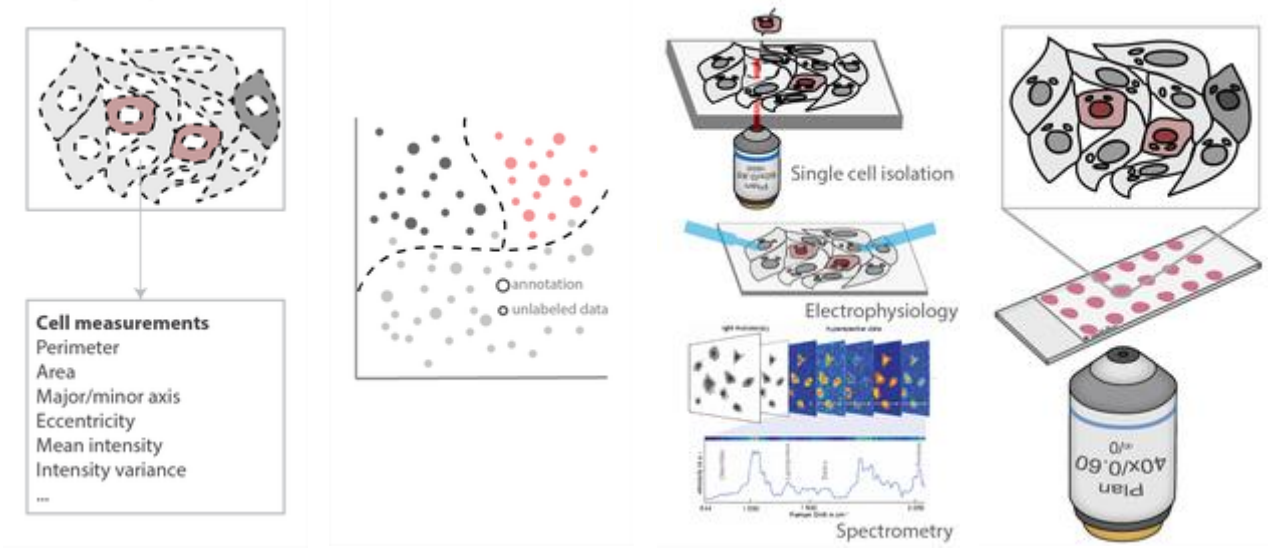
Research

Overview

Recent technological advancements in systems biology, lab automation, and high-throughput microscopy have opened the door to systematic discovery of complex biological systems using high-throughput light microscopy. Modern equipments produce massive amounts of data which cannot be analyzed manually.

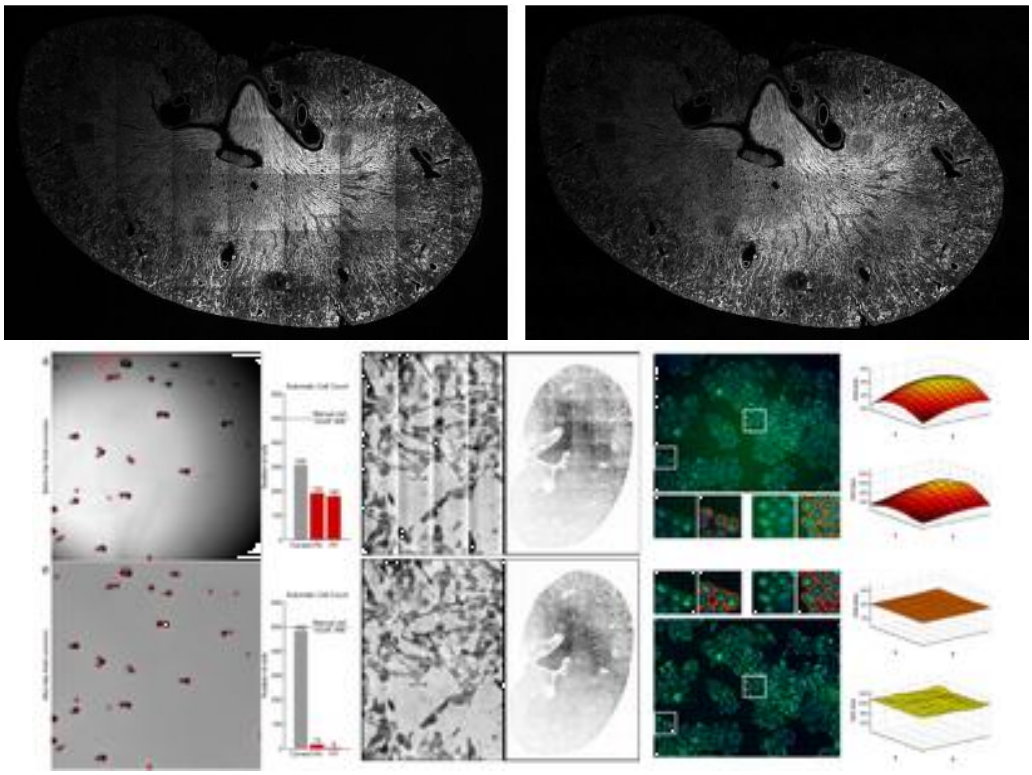
Automating the analysis process poses several challenges related to computational cell biology. Our group dedicated to finding computational solutions to biological problems. Our research focuses on the intersection of biology and computer science, and combine wet-lab and light microscopy with image analysis and machine learning methods.

Image analysis **Machine learning** **Single cell analysis** **Imaging**



I. Image analysis

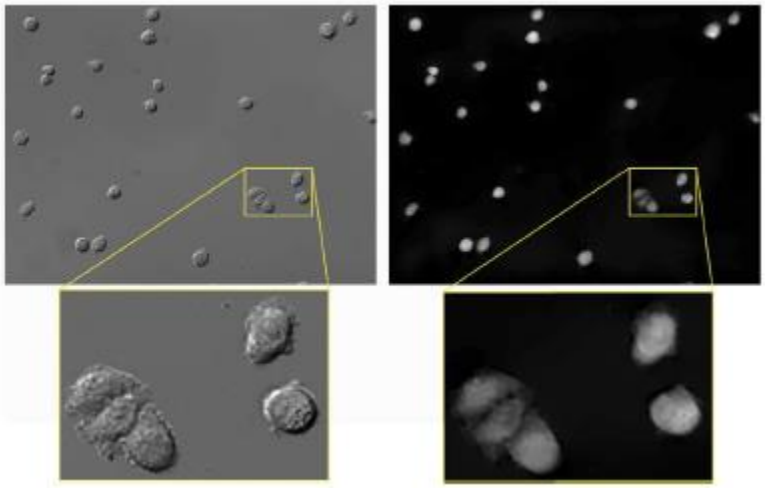
Illumination Correction
For quantitative measurements based on light microscopy and especially fluorescent intensities, it is essential to normalize the image data to correct for aberrations inherent in the acquisition process. One common source of error is the result of a non-ideal illumination field produced by the objective. Our novel algorithms addresses these issues using energy minimization. The corrected field resulting from our approach is extremely flat, and we can achieve this level of quality without requiring a calibrated reference sample.



- Related publications: Piccinini et. al. ISBI 2013, Smith et. al. Nat. Meth. 2015
- Contributors: F. Piccinini, P. Horvath, K. Smith
- GitHub code: CIDRE

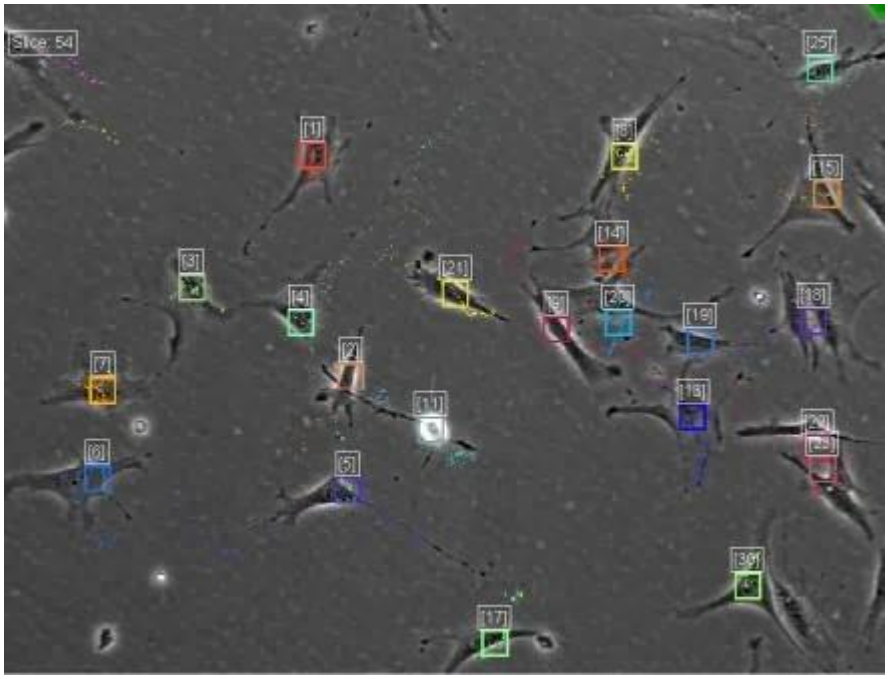
Reconstruction

We developed an algorithm based on energy minimization to convert differential interference contrast (DIC) images to phase images to make them easier to analyze.



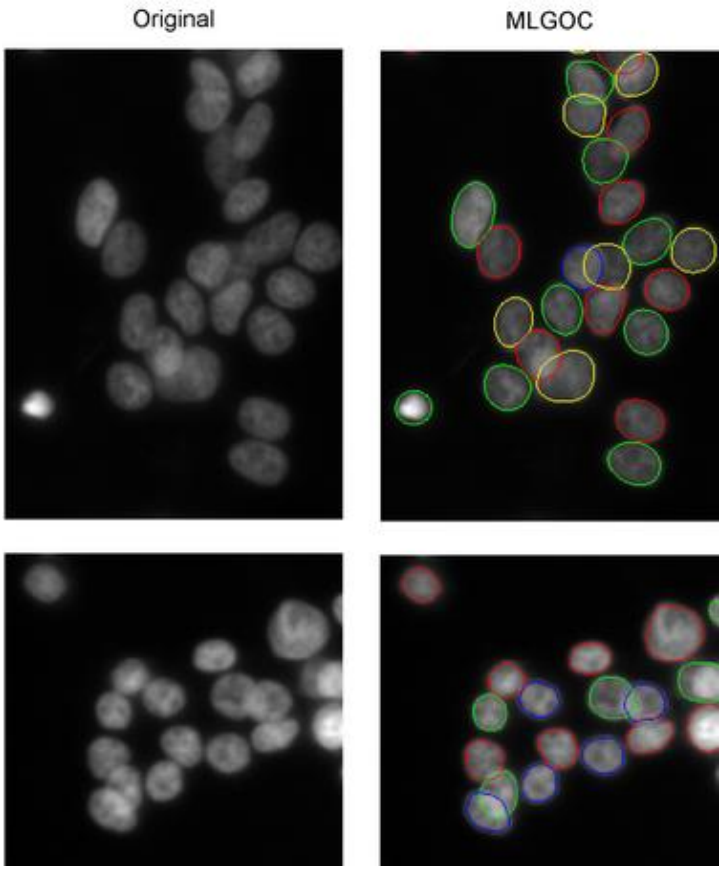
- Related publications: Koos et. al. Scientific Reports 2016
- Contributors: K. Koos, J. Molnar, P. Horvath

Tracking
We are interested in developing methods for identifying and tracking cells or sub-cellular structures on live cell images. We have been developed a software the CellTracker, which corrects illumination problems, finds alignments, as well as automatically and manually tracks cells, mainly on phase contrast images. The program is available with MatLab GUI.
[Download CellTracker]



- Related publications: Piccinini et. al. Bioinformatics 2015
- Contributors: F. Piccinini, P. Horvath, A. Kiss
- Webpage: CellTracker

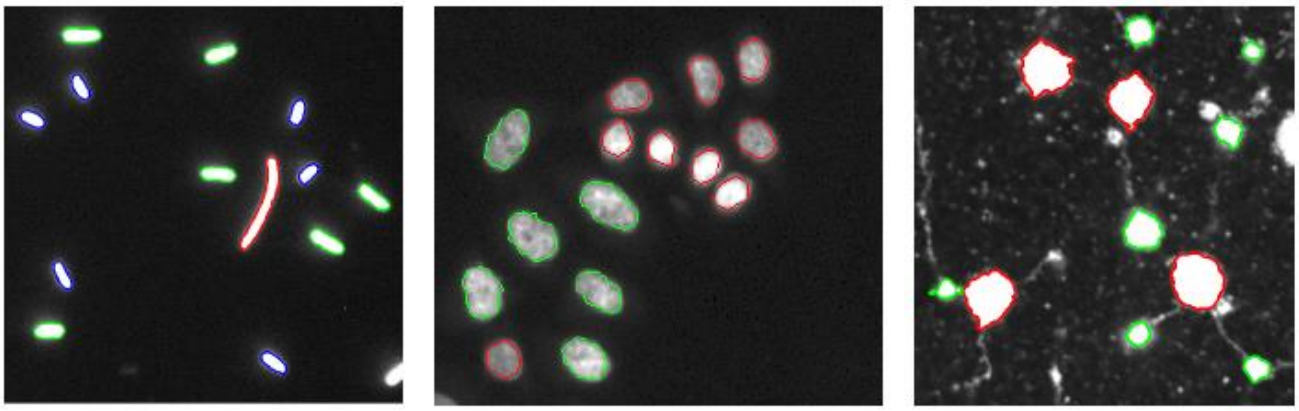
Segmentation of overlapping cells (the 'gas of circles' model)
Variational methods for shape modeling to extract near-circular objects (e.g. nuclei).
The multi-layered 'gas of near-circles' model is capable of segmenting touching or even overlapping cells on high confluency images.



- Related publications: Molnar et. al., Scientific Reports 2016
- Contributors: C. Molnar, P. Horvath

Selective Active Contours

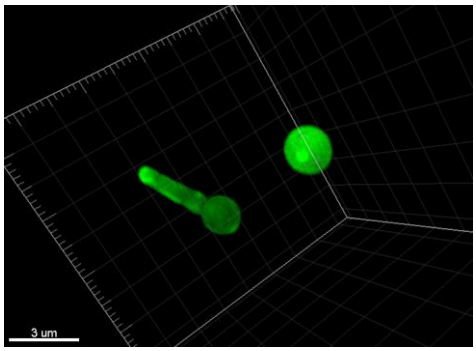
The selective active contours utilize simple shape characteristics such as area and perimeter, to describe objects that can provide computationally efficient shape selective segmentation.



- Related publications: Molnar et. al., IEEE WACV 2016
- Contributors: E. Tasnadi, C. Molnar, I. Grexa, P. Horvath

Selective Active Contours in 3D
3D extension of the selective 2D active contours.

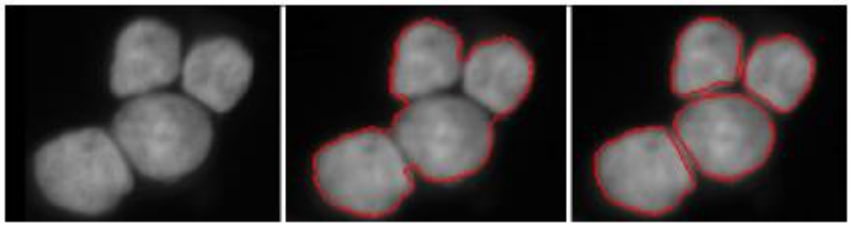
- Computationally expensive
- Utilizing GPU-s to achieve high enough performance for practical use



Cells in pseudohyphae and in normal form. ***Finding the pseudohyphae form.***

- Related publications: Molnar et. al., DICTA, IEEE 2017
- Contributors: E. Tasnadi, T. Danka, J. Molnar, P. Horvath

Spliting touching cells
Segment individual cell nuclei by splitting touching ones. The two-step approach merely based on energy minimization principles using a higher-order active contour framework.

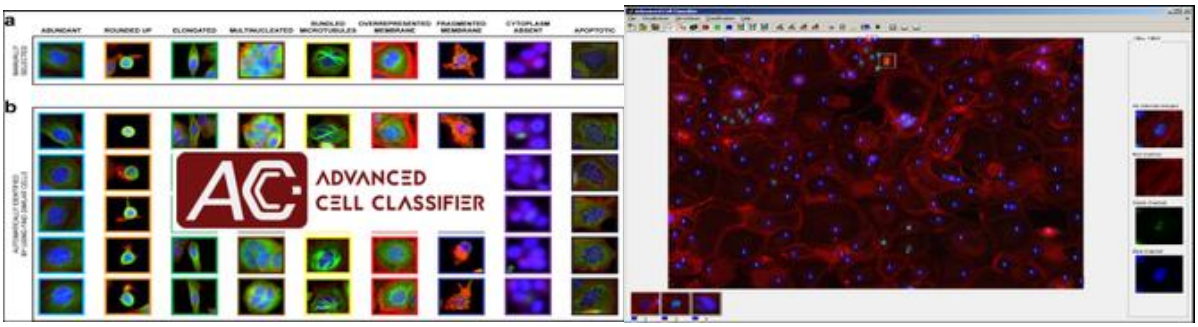


- Related publications: Molnar et. al., ISVC, IEEE 2016
- Contributors: C. Molnar, J. Molnar, P. Horvath

II. Machine learning

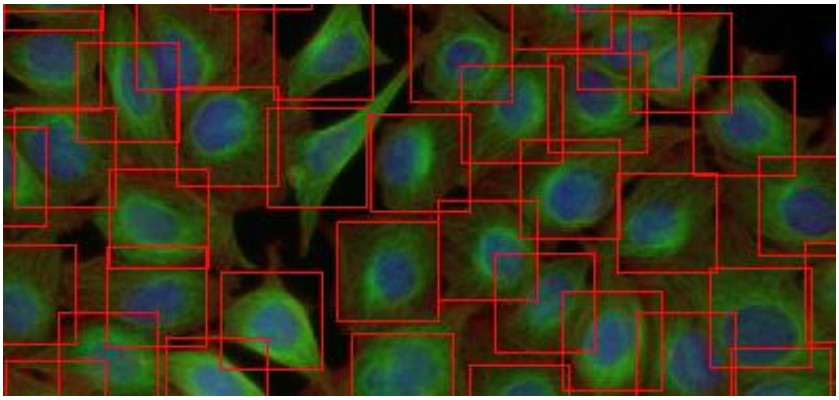
Phenotyping - Advanced Cell Classifier
Advanced Cell Classifier is a data analyzer program to evaluate cell-based high-content screens and tissue section images developed at the Biological Research Centre, Szeged and FIMM, Helsinki (formerly at ETH Zurich). The basic aim is to provide a very accurate analysis with minimal user interaction using advanced machine learning methods. ACC was used to analyze some of the first large whole genome scale RNAi screens and all together for more than 300.000.000 images and several billion single cell-based machine learning decisions.

- most accurate analysis
- minimal user interaction
- intelligent modules
- performance feedback
- advanced machine learning



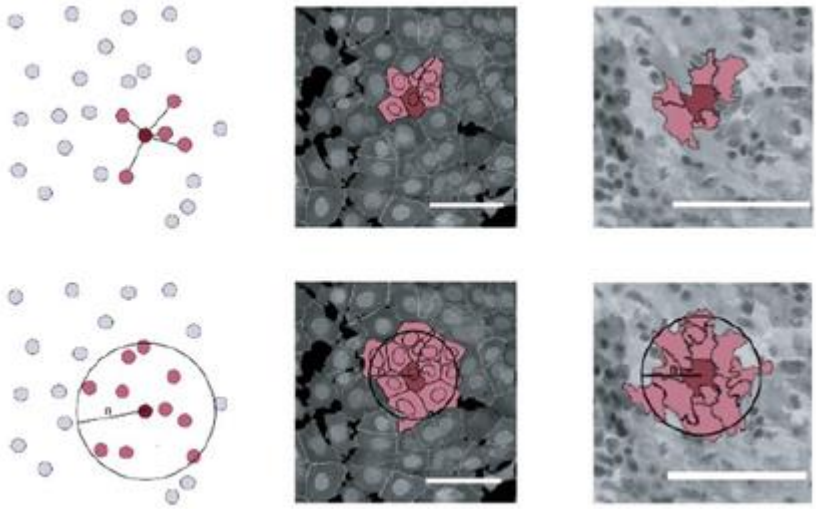
- Related publications: Piccinini et. al., Cell Systems 2017
- Contributors: F. Piccinini, T. Balassa, C. Molnar, A. Szkalisity, P. Horvath
- Webpage: Advanced Cell Classifier

Deep Learning
We developed a fast and fully automated tools that assesses the number and location of cells using Deep Convolutional Neural Networks (DCNN). Our methods highly outperforms state-of-the-art machine learning models and provides comparable detection accuracy to human field experts.



- Related publications: Balassa et. al., preprint 2017
- Contributors: T. Balassa, J. Gulyas, P. Horvath
- Webpage: FindMyCells

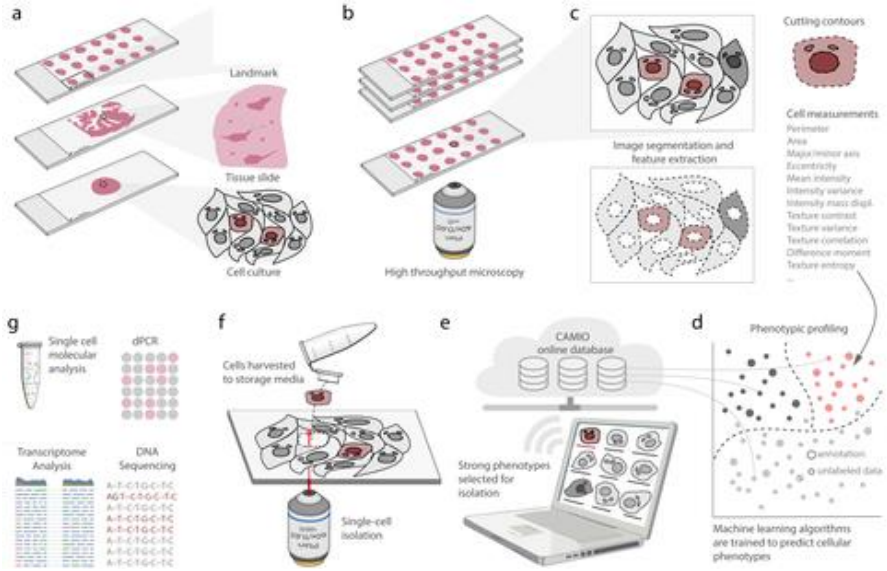
Microenvironment-based phenotyping
We research how various microenvironmental features contribute to identifying a cell and how such additional information can improve single-cell-level phenotypic image analysis.



- Related publications: Toth et. al., Scientific Reports 2017
- Contributors: T. Toth, P. Horvath

III. Single Cell Analysis Methods

CAMI - Computer Aided Microscopy Isolation system
We develop a high-throughput, non-disruptive, and cost-effective isolation methods that is capable of capturing individually targeted cells using widely available techniques. Using high-resolution microscopy, laser microcapture microscopy, image analysis, and machine learning, our technology enables scalable molecular genetic analysis of single cells, targetable by morphology or location within the sample. Cell data along with the location and contour ofeach cell is sent to our interactive online database CAMIO.



- Related publications: Brasko et. al., Nature Communications 2018
- Contributors: C. Molnar, T. Balassa, A. Szkalisity, P. Horvath

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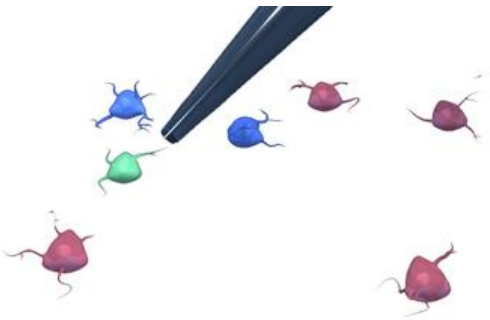
AutoPatcher
We are building an automated patch clamp system to analyze the electrophysiological properties of neurons in vitro. The system automatically selects a cell in label-free microscopy and performs patch clamping on it using image processing and deep learning.



- Related publications: unpublished
- Contributors: K. Koos, J. Molnar, P. Horvath

Microscopy

High content screening
The HCS technology employs different automated microscopes in a high throughput format to extract quantitative information from cells or tissue samples based on various parameters such as spatial distribution or the morphology changes of the target cells. To address these various cellular phenotypes, both widefield and confocal microscopes are used in the BIOMAG group:

PerkinElmer Operetta

Main features:

- laser-based autofocus system
- objectives ranging from low to high magnifications(2-100X)
- objectives with high numerical aperture
- live cell imaging

Analysis of cellular phenotypes:

- apoptosis and cell cycle studies
- cell differentiation and cell migration assays
- cell proliferation and cell shape changes
- cytoskeletal rearrangement and cytotoxicity
- protein expression and translocation experiments
- wound healing assays

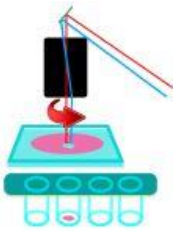
Leica SP8-digital light sheet

- DMi8 series with a motorized objective revolver
- automated image acquisition for mosaic or multiwell applications
- super-sensitive photon detection making it ideal for low light and live cell imaging
- the platform can be turned into a light sheet microscope

Laser microdissection systems

During LDM, a laser is focused on the tissue and it cuts the sample alongside a predefined trajectory. After the cutting process, the required elements can be extracted and collected for further analysis. The dissected material is then available for further downstream applications such as genomics, transcriptomics, next generation sequencing, proteomics or other analytical techniques. Based on the movement of the laser and sample collection, two main approaches have been used:

Leica LMD6



- the movement of the laser beam is achieved via optics
- the specimen is collected via gravity
- fully automated upright research microscope

Zeiss Palm Microbeam

- motorized microscope stage
- laser catapulting
- standard microscopic slides can also be used