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Fraunhofer-Institut für
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High-Speed Microscopy

Automated Cell laboratory

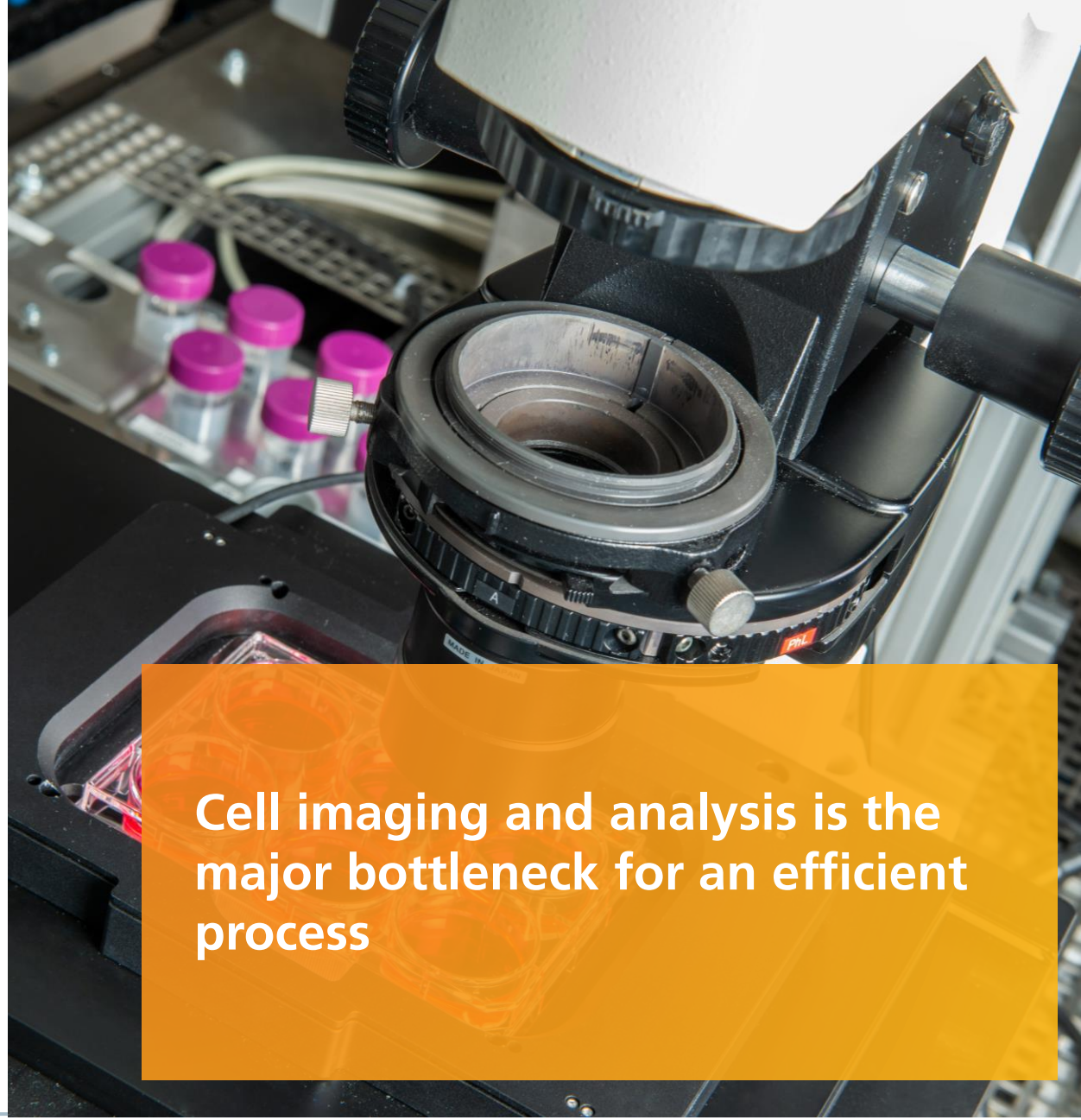
High throughput stem cell cultivation

StemCell Factory

Initial situation

Implementation of a fully automated stem cell cultivation plant

Cells must be screened daily to monitor growth and vitality



Cell imaging and analysis is the major bottleneck for an efficient process

Microscopy in Motion

Continuous scanning process

Challenges

- Full automation necessary for integration into cultivation process
- Cell culture screening needs resolution in low micrometer range
- Higher magnification → smaller field of view
- Large-area samples: Thousands of individual exposures necessary

Overall process very time-consuming

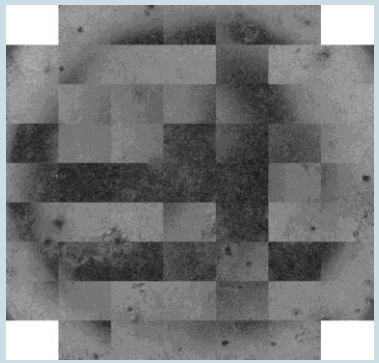
Solution

- Continuous scanning microscopy
- Stitching of individual shots to high-resolution overall images
- AI-based automated image analysis
- Smart software to control and connect all processes

Accelerating Microscopic Imaging

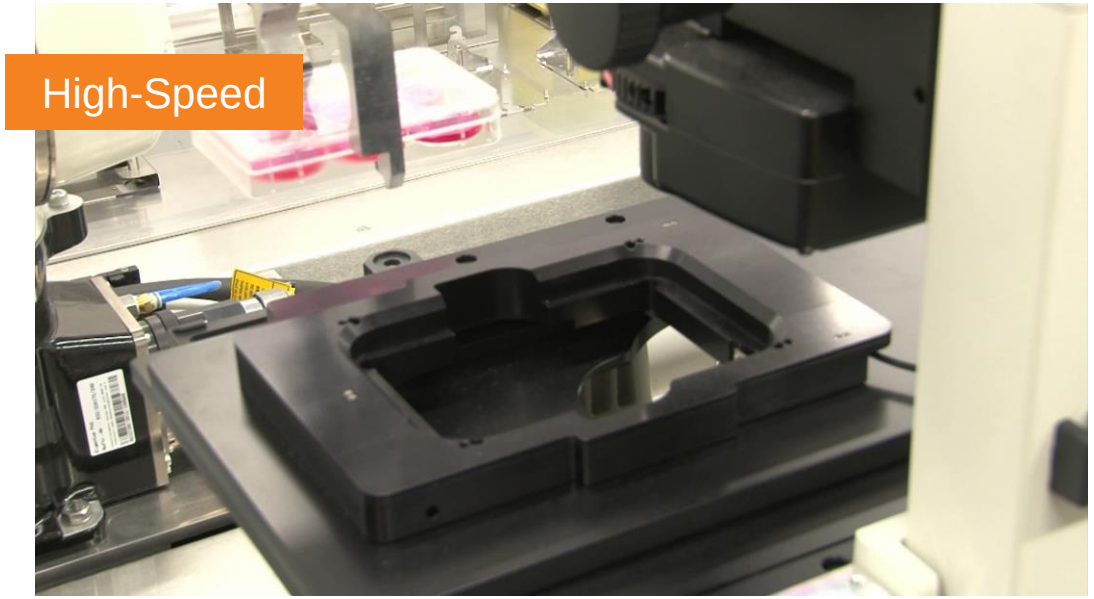
Stop and go and high-speed microscopy in comparison

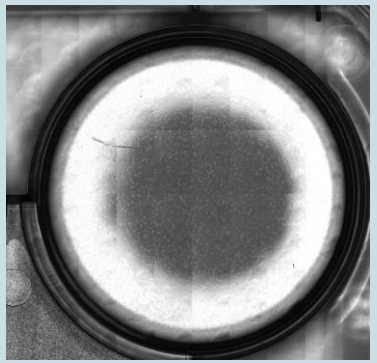
Stop and go



Fluid sloshing due to constant acceleration and deceleration prevents image acquisition

High-Speed



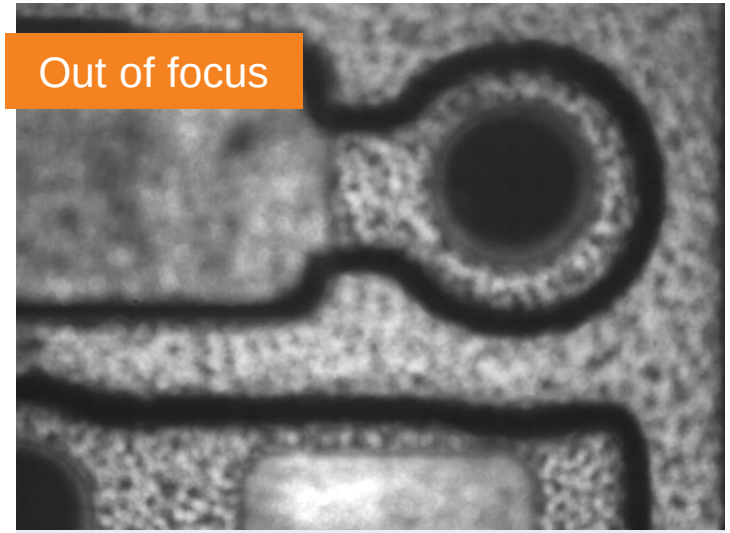


Still liquid surface due to constant velocity

Up to 32 times faster

Always in focus

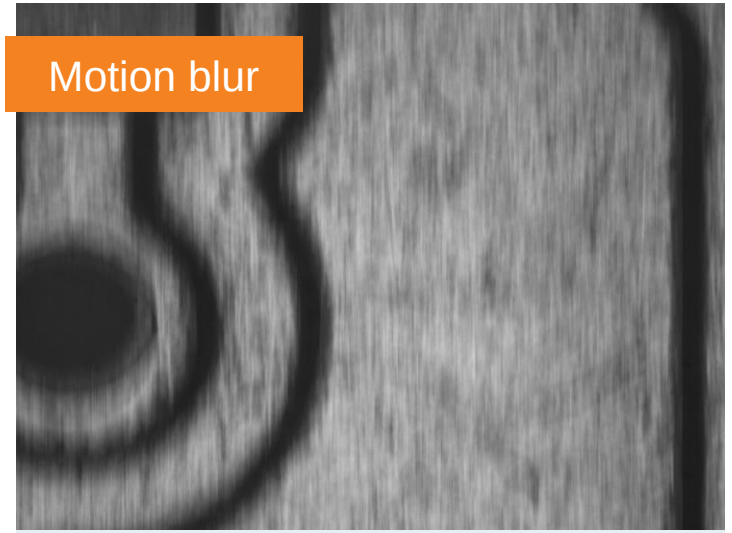
Challenges for high-resolution images



Autofocus

Sensor acquires height map prior image acquisition

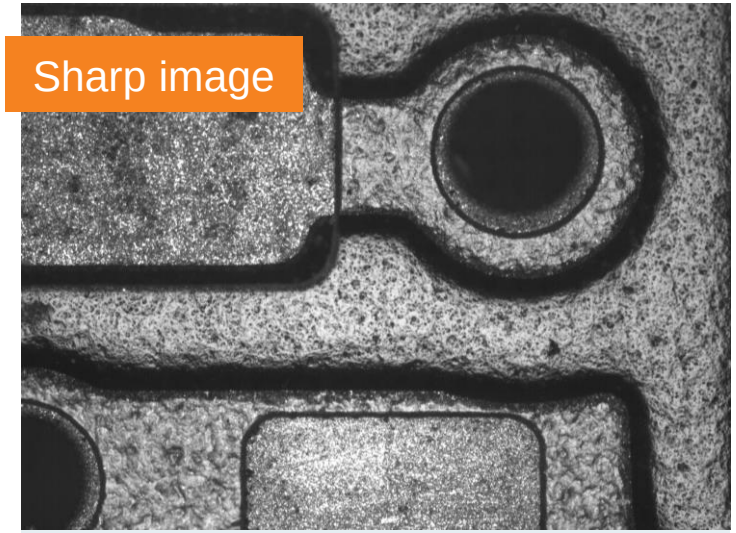
Piezo quickly adjusts focal plane during the main process



Pulsed light source

Ultra low exposure time prevents motion blur

Sample moves less than half a pixel during acquisition



High-resolution image

Synchronized components ensure always sharp images

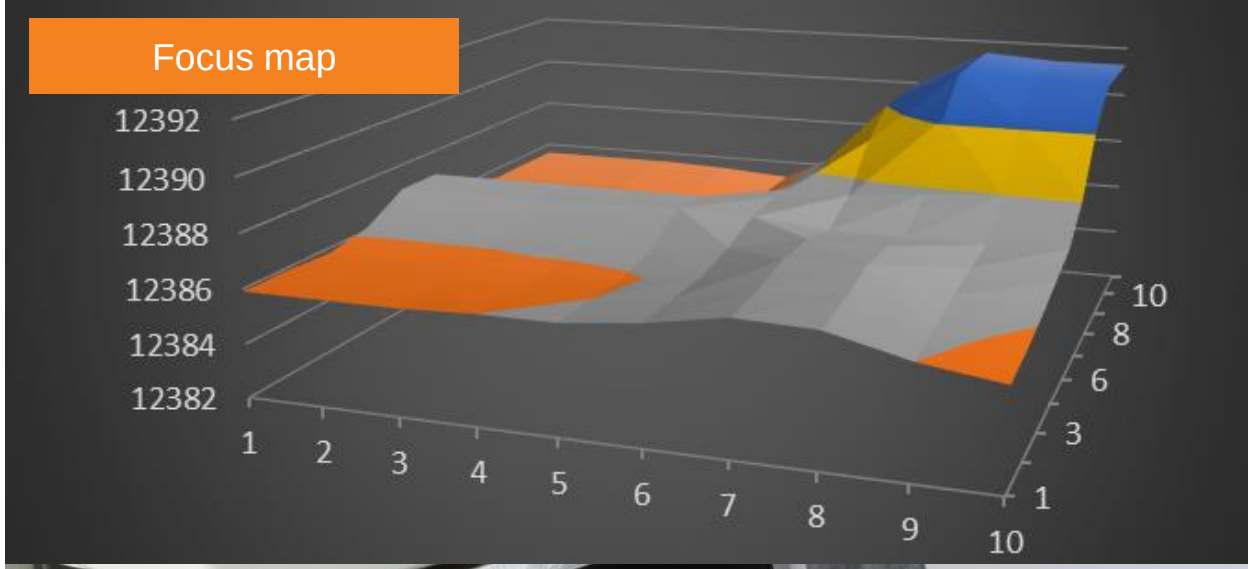
Resolution down to 300nm/pixel

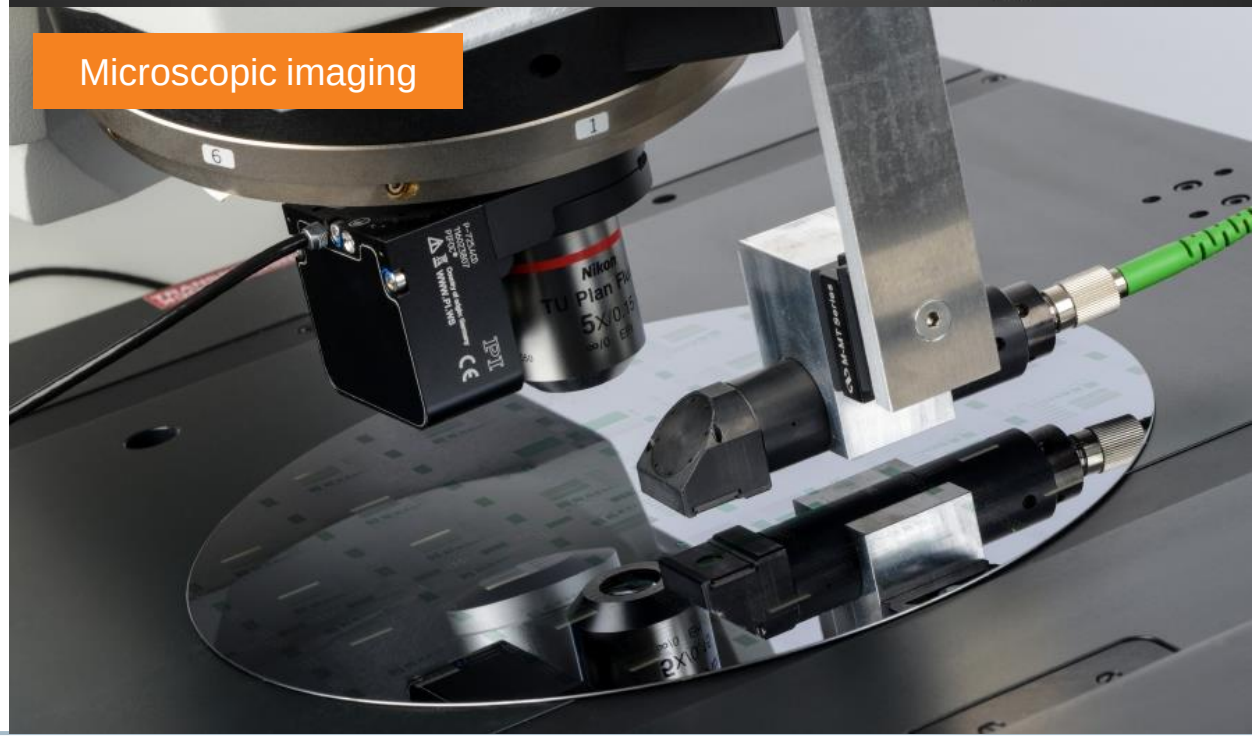
100 images per second

Always in focus

Technical implementation in detail

1. Height scan with confocal chromatic sensor
2. Calculation of focal plane
3. Meandering scan over region of interest
4. Rapidly adjusting height with piezo z-stage
5. Microscope stage triggers camera and ligh source
6. Short light pulses for low exposure time





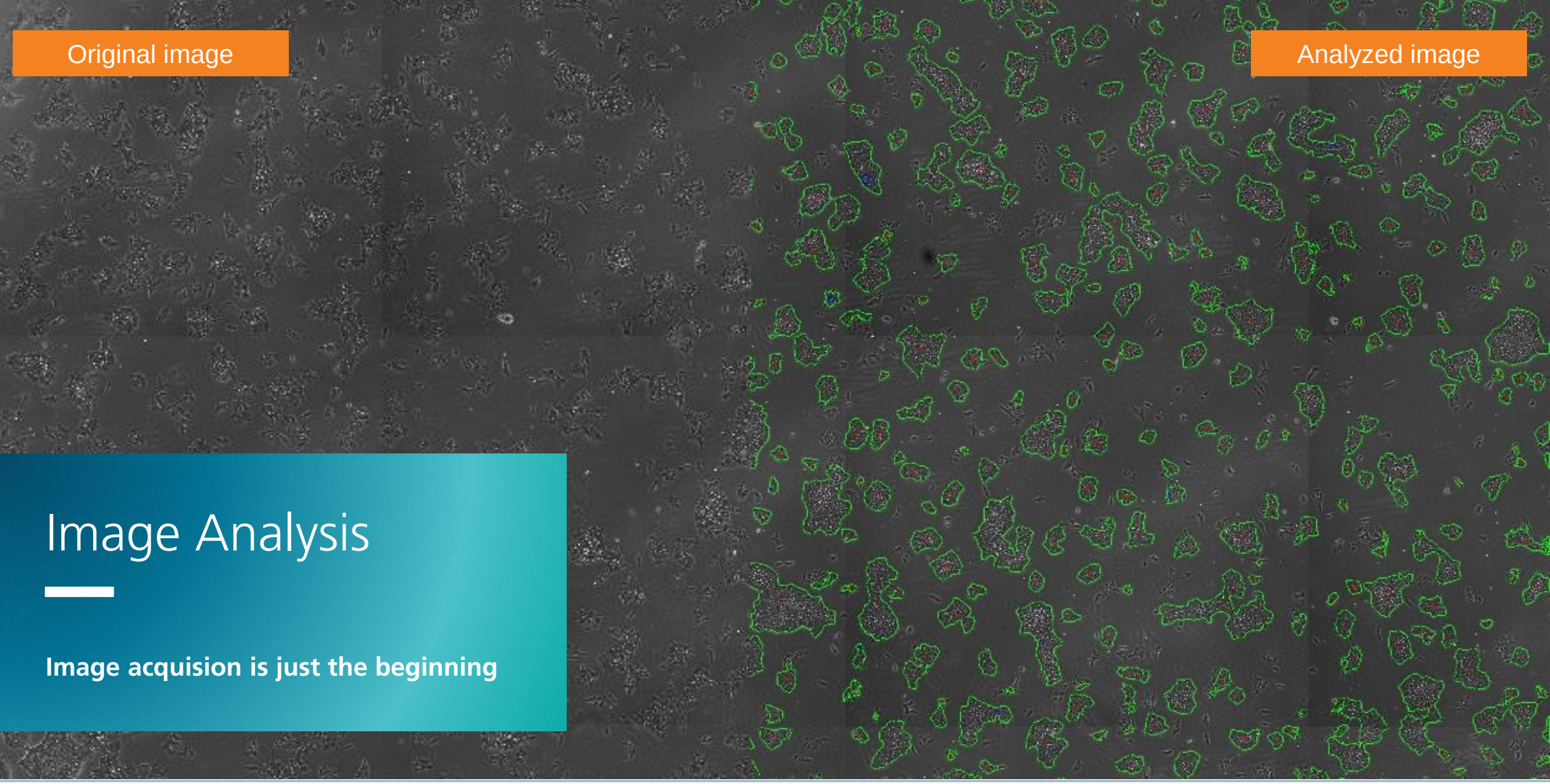


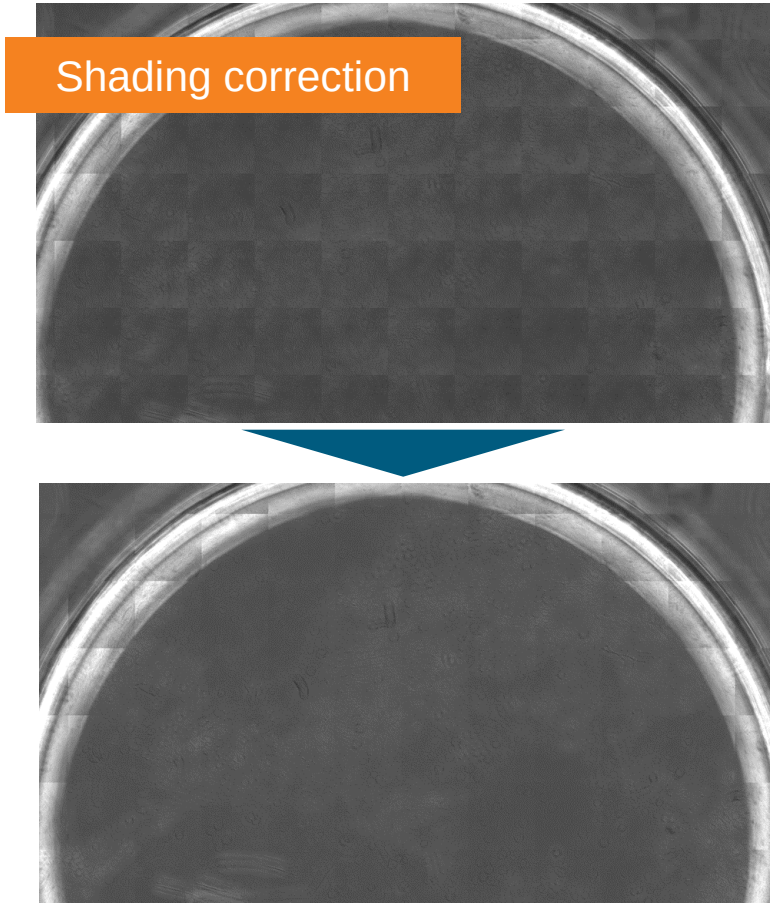
Image Analysis

Image acquision is just the beginning

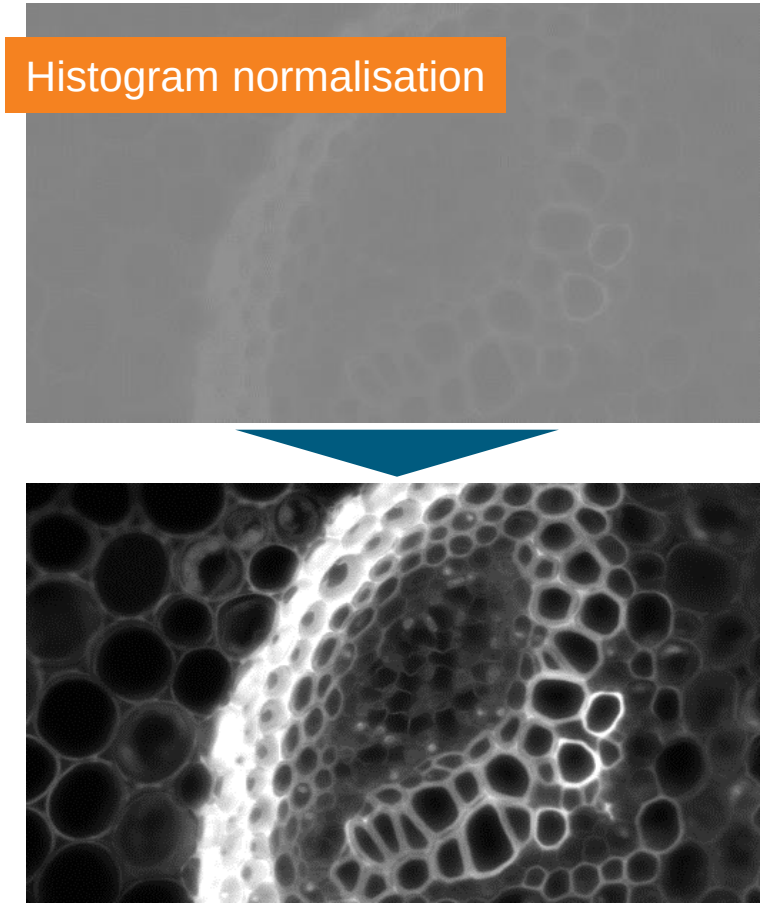
Image Preprocessing

Large high-contrast images with smooth transitions from frame to frame

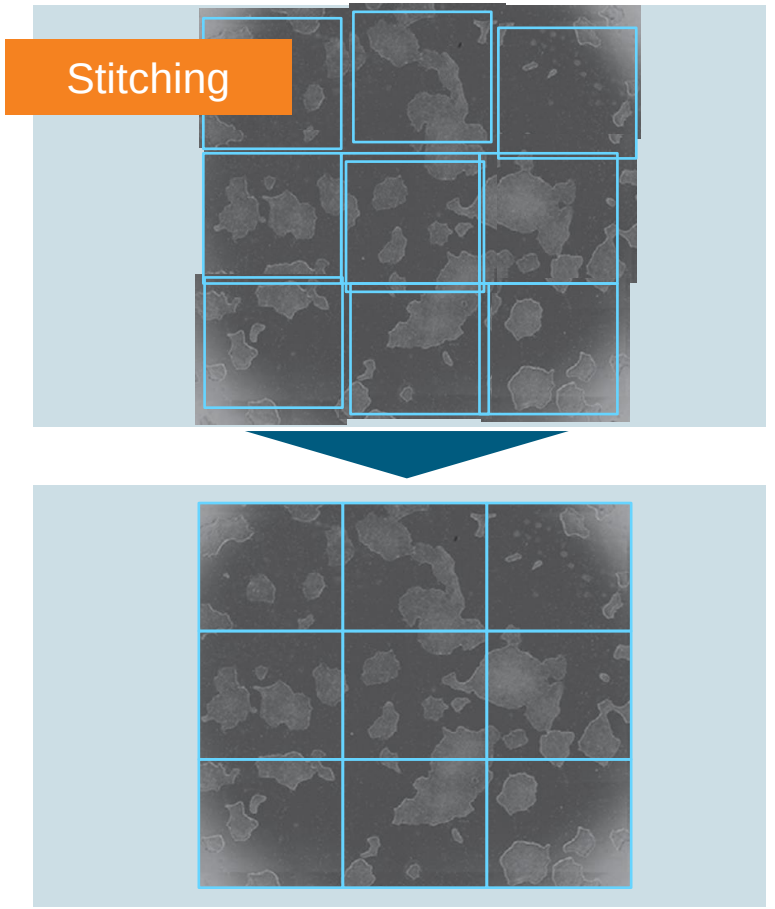
Shading correction



Histogram normalisation



Stitching



Deep-Learning-Based Image Analysis

Automated cell image classification

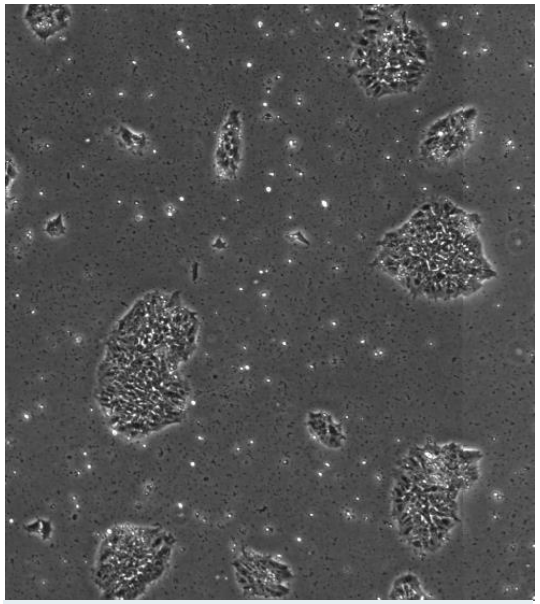
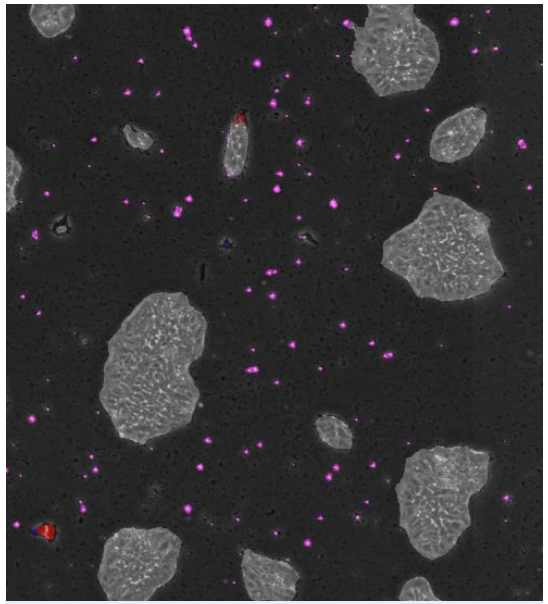
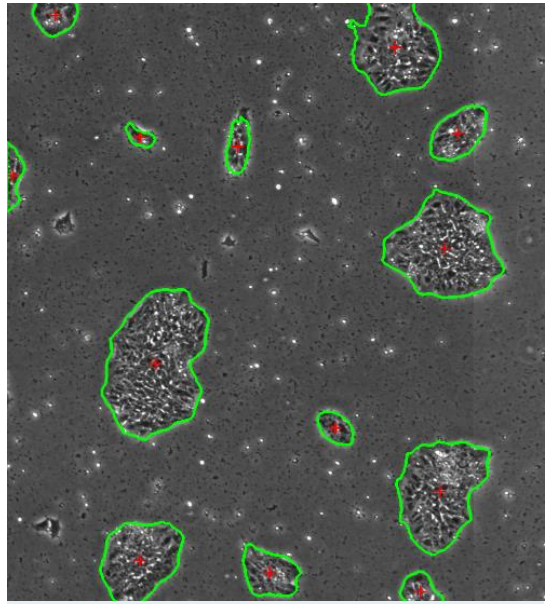


Image Acquisition
High resolution cell image



Segmentation
Recognizing and categorize different regions within the image



Parameter detection
Interpret the segmented image

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<cell number="219">
    <position>
        <X>942.5</X>
        <Y>611.8</Y>
    </position>
    <size>9072</size>
    <roundness>
    0.73
    </roundness>
    ...

</cell>
```

Data Output
Extract the most relevant information and store it in an output file

Key Facts

The High-Speed Microscope in Numbers

Speed
Up to 300cm²/min (4x magnification)

Automation
Completely automated process

Microscopy modes
Brightfield, darkfield, phase contrast, fluorescence

Modular
Add-On for existing microscopes

100% inspection
Complete scan of a whole MTP in less than a minute

Artificial intelligence
Costumized deep Learning based image analysis

High resolution
0.3µm per pixel possible

Autofocus
Allways sharp image due to fast hardware or software autofocus

Scan area
Up to 500mm x 500mm

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Thank you for your attention

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