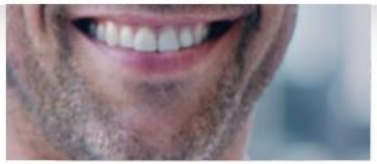
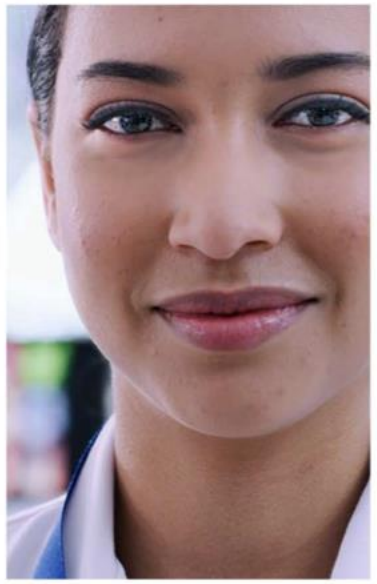
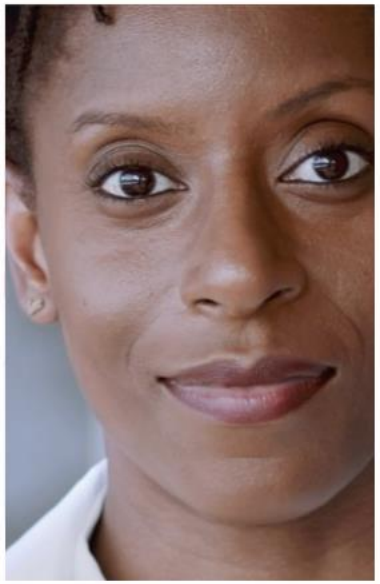
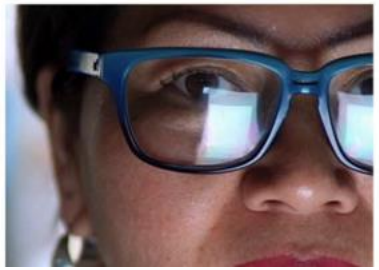
Step into the Microhub era.

Leica




What if every scientist could access spatial Information?

Meet Mica
The world's first Microhub

- Access for all
- No constraints
- Radically simplified workflows

Step into the era of **Access for all**

Everyone can now leverage microscopy to make more discoveries

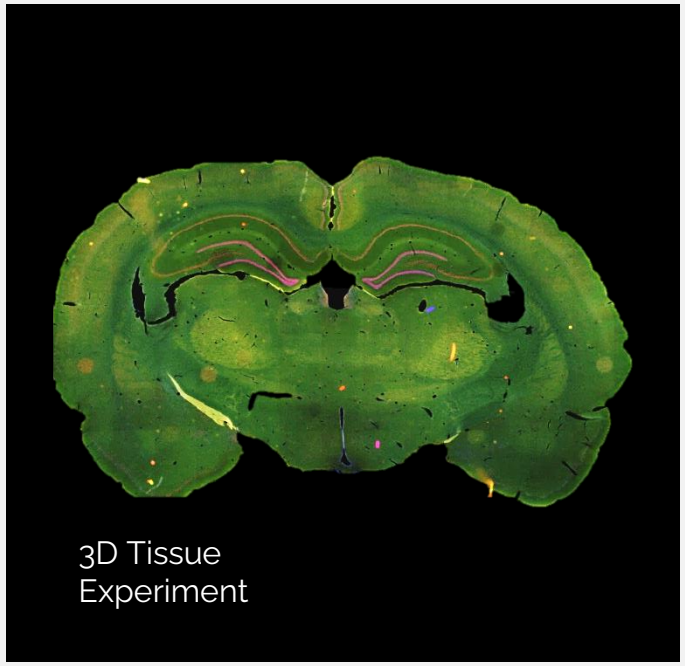
Eliminate over

85%

of tedious setup steps that require special expertise

Everyone can now leverage microscopy to make more discoveries

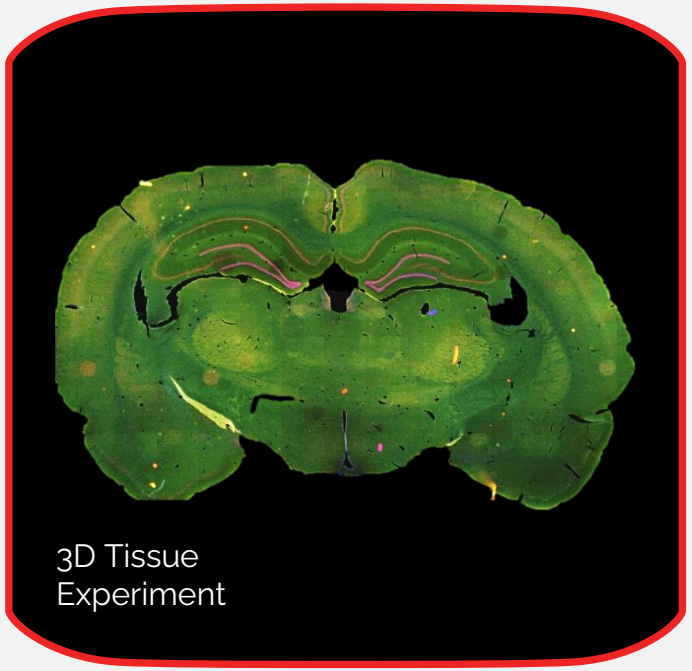
Conventional Microscope



VS

Steps	**85%** fewer steps to the first image
Minutes	**1/3** Less time to the imaging result
Hours	**1/2** of the training time

Mica



Powered by:

- Intelligent automation
- Intelligent Imaging

Tissue slice form the rat brain. Nuclei are stained with DAPI (blue), STL with FITC (green), astrocytes (GFAP) with Cy3 (yellow), and newborn neurons (NeuN) with Cy5 (red). 10x widefield tile scan, all 4 labels acquired simultaneously.

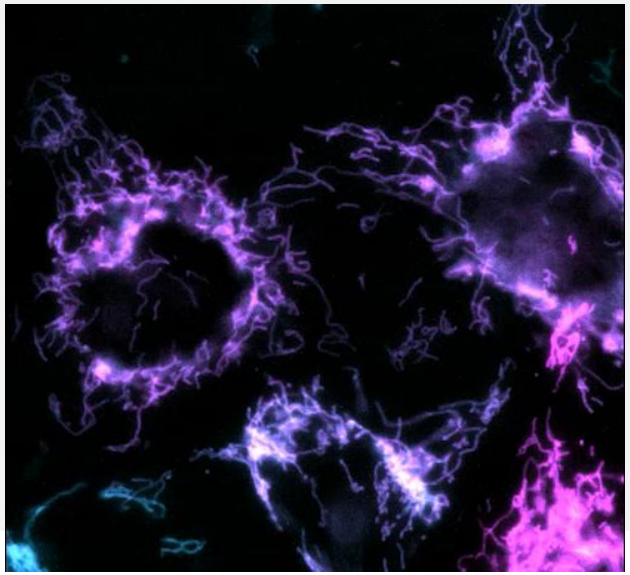
Step into the era of **No constraints**

Everything you need to enable discoveries, unified in one easy-to-use system

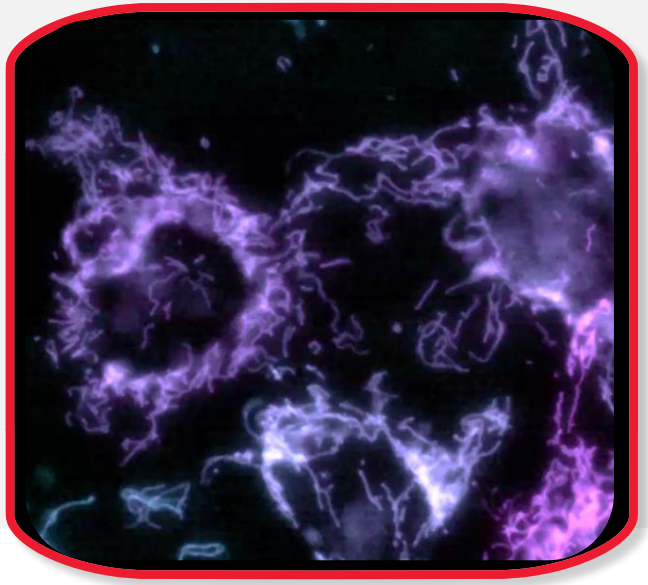
4x More data with **100%** correlation

Access key contextual information with absolute spatiotemporal correlation

Conventional Microscope
Sequential Acquisition



Mica
Simultaneous Acquisition



Mica delivers absolute correlated labels without spatiotemporal mismatch

U2OS cells stained with MitoTracker green (mitochondria structure, cyan) and TMRE (active mitochondria, magenta). **Sequential acquisition** (left side, conventional microscope) and **simultaneous acquisition** (right side, Mica) of the two channels over 2 minutes 100 frames using the 63x/1.20 CS2 Water MotCORR objective..

Powered by:

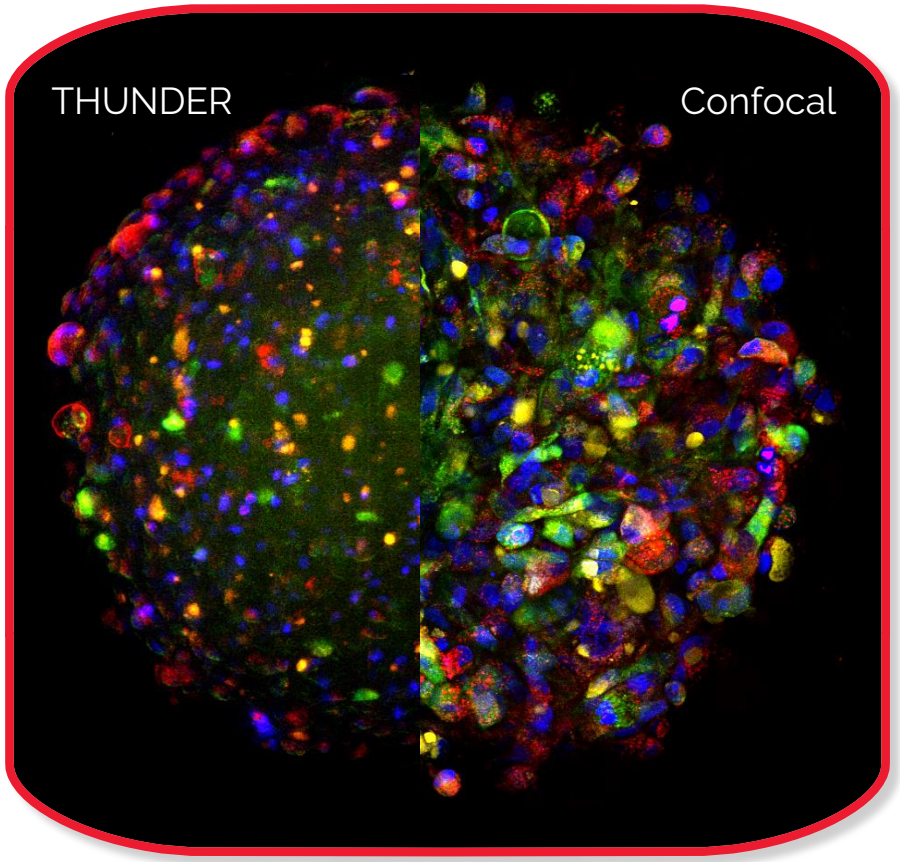
- 4 labels simultaneously
- 4 labels 100% correlated
- Patented FluoSync technology

Select the right modality in real-time

Seamlessly move from fast overview to high resolution when required by your experiment

Powered by:

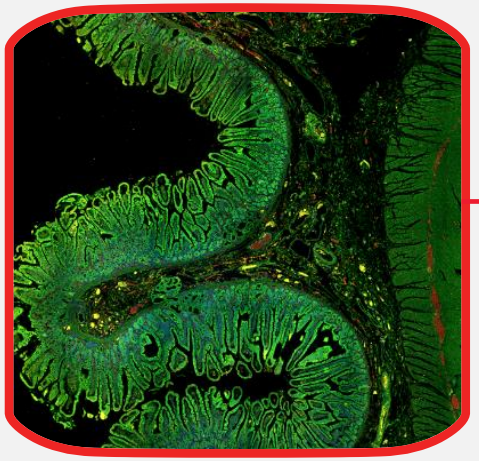
- Unified Imaging Modalities
- Point Scanning Confocal
- Mica is an incubator

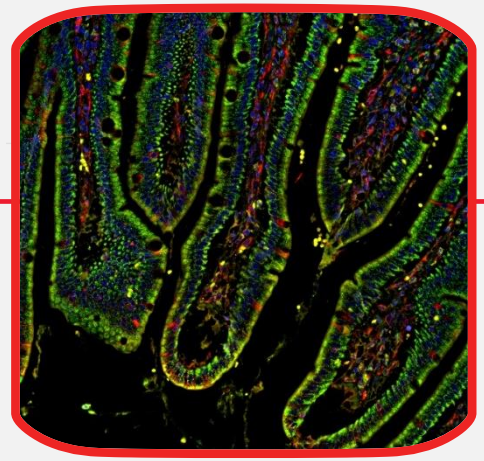


3D Cell Culture, 7d spheroid formation of U343 cells. tfLC3 EGFP and mRFP + DAPI + WGA Alexa 680. Objective: 20x/0.75 CS2 DRY

Seamlessly move from fast overview to high resolution

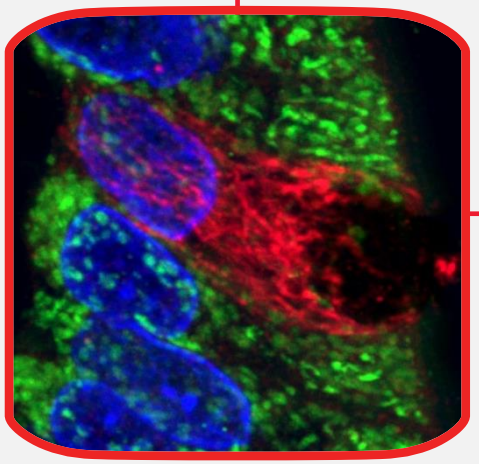
1.6x Widefield
Create Overview

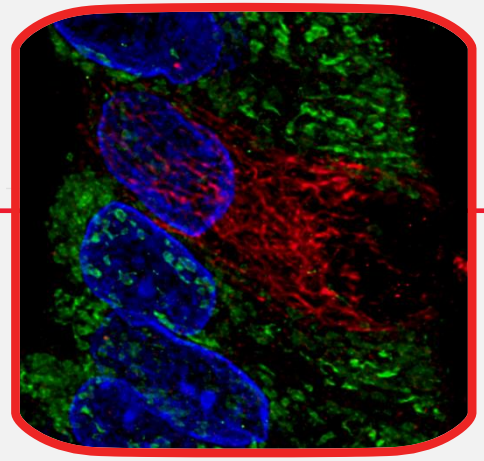




20x THUNDER
Select the cell of interest

63x Confocal
Get the subcellular information





63x LIGHTNING
Get even more of the subcellular information

Intestine tissue section acquired with different objectives ranging from low to high magnification (1.6x, 10x, 20x, 63x), using widefield and confocal imaging. 20x widefield images are processed with THUNDER and 63x confocal images with LIGHTNING. Nuclei are labeled in blue, mitochondria in green, and detyrosinated tubulin in red.

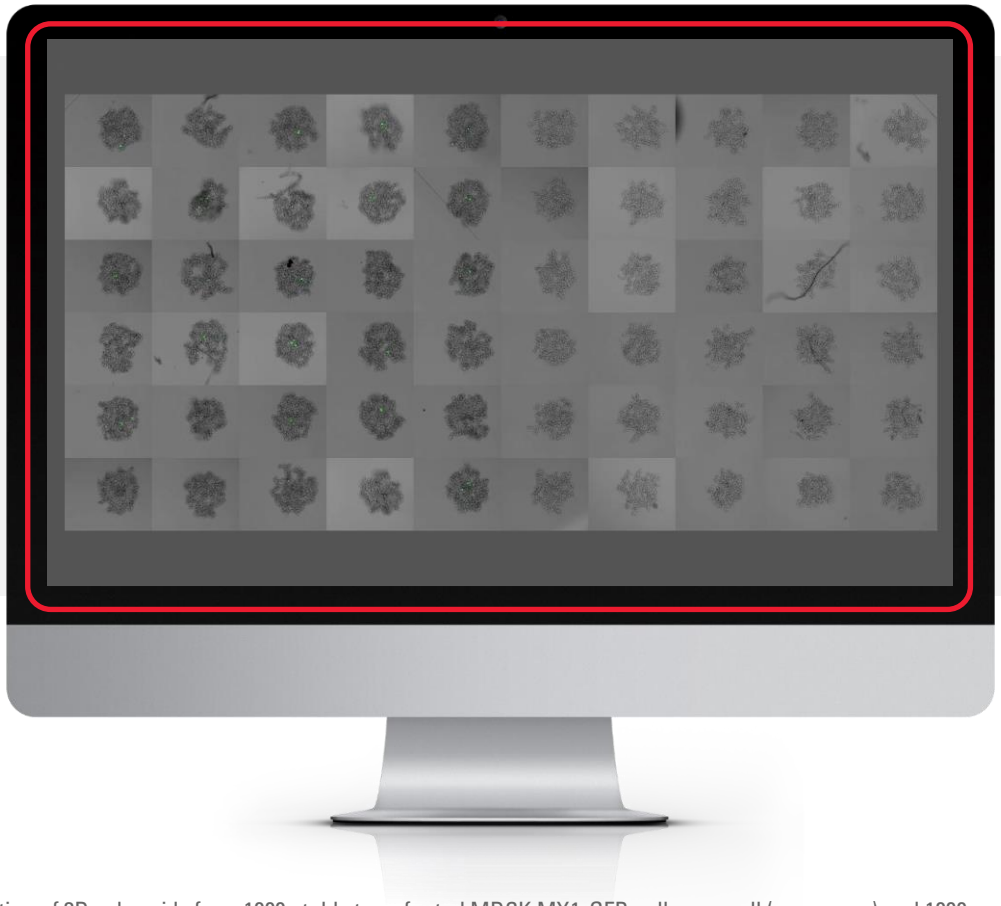
Powered by:

Unified Imaging Modalities

Point Scanning Confocal

Mica is an incubator

Achieve physiological-like conditions throughout your experiment



Multiple Spheroids Growing over 2.5 days

Powered by:

Mica is an incubator

Formation of 3D spheroids from 1000 stably transfected MDCK MX1-GFP cells per well (upper row) and 1000 U2OS cells per well (lower row) shown at 5 different timepoints. Time-lapse acquisition over 60 hrs with 30 minutes interval. Green, GFP. Gray, integrated modulation contrast.

Mica is an incubator to maintain your sample in optimal conditions and to minimize evaporation

Multiple Spheroids Growing over 2.5 days

Powered by:

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Formation of 3D spheroids from 1000 stably transfected MDCK MX1-GFP cells per well (upper row) and 1000 U2OS cells per well (lower row) shown at 5 different timepoints. Time-lapse acquisition over 60 hrs with 30 minutes interval. Green, GFP. Gray, integrated modulation contrast.

Step into the era of **Radically simplified workflows**

Bringing you faster from sample to discovery

Reduce over

60%

of process steps through system intelligence

Reduce time and effort from sample to insight by simplifying the entire workflow

Conventional Microscopes

Mount sample
Position sample
Define illumination 1
Define illumination 2
Define illumination 3
Define Illumination 4
Define detector gain
Define pinhole
Define scanning mode
Choose images
Process data
Acquire
Define averaging number
Define averaging method
Define averaging mode
Define Line Step
Define Offset
Define dwell time
Define thresholds
Define separators
Run segmen-tation
Run Analysis
Extract information
Create figures

24 STEPS

Mica

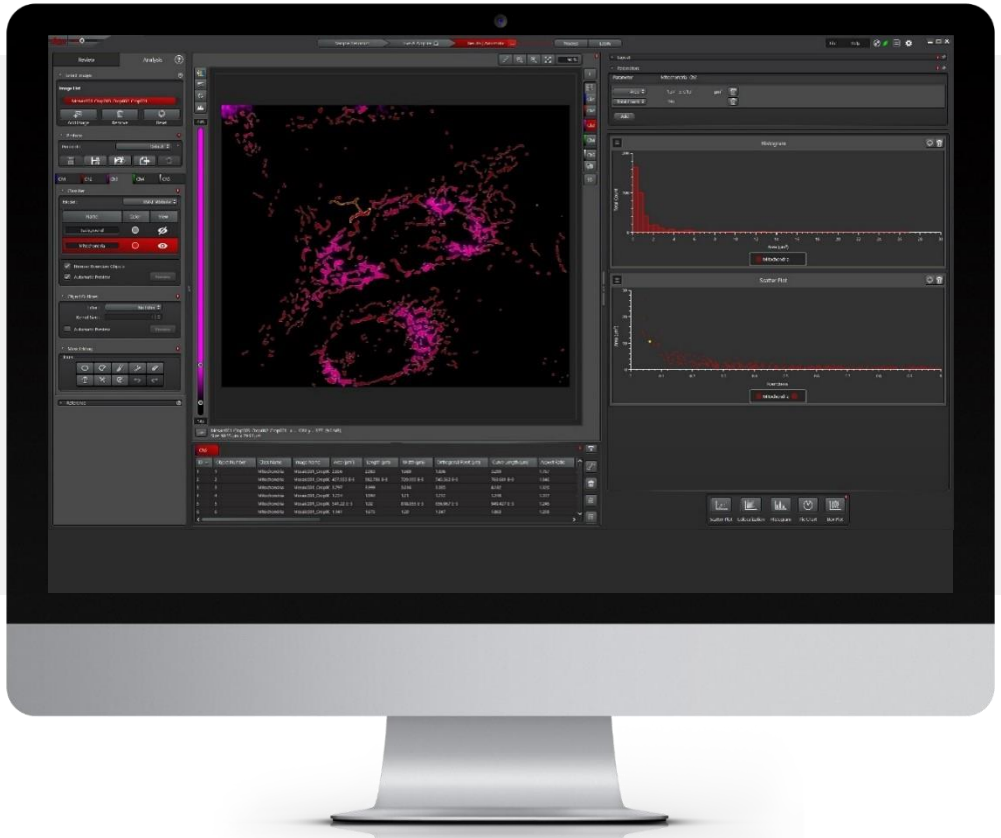
1. Mount sample
2. Position sample
3. Start Live Acquisition
4. Define positions
5. Acquire
6. Choose images
7. Run segmentation
8. Run analysis

8 STEPS

Powered by:

- Sample finder
- OneTouch-Auto Illumination
- AI-based Analysis

Reduce time and effort from sample to insight by simplifying your entire workflow



U2OS cells were labelled with SiR-Actin, TMRE (mitochondria activity), CellEvent (caspase activity), and DAPI (nuclei).
Apoptosis inducer staurosporine was added at time-point 0.
63x magnification, widefield mode. 13 hours time-lapse.

AI based training of mitochondrial segmentation using your scientific expertise

Enable 100% reproducibility and repeatability throughout your experiment

Powered by:

- Pixel classifier
- GUI operated annotations
- Reusable AI models and projects parameters

Meet Mica

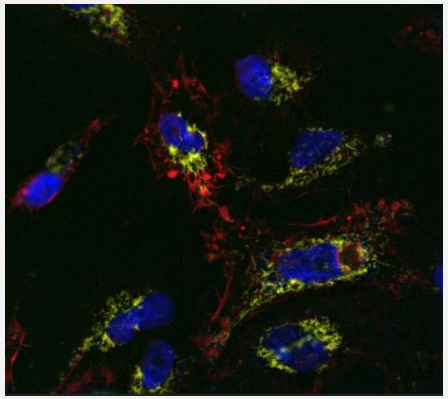
Experience the future in key applications

- Fluorescence Assay
- 3D Tissue Imaging
- Long-term Time-lapse

Meet Mica in key applications

Fluorescence Multi-well Plate Assay

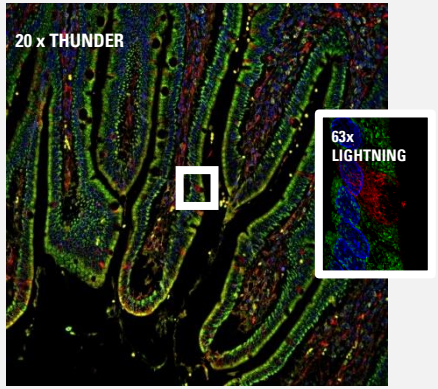
Mica allows you to image 4 labels simultaneously, with 100% spatiotemporal correlation. This key application shows how Mica is used with fluorescent multi-well plate assays around Caspase 3/7 activations in apoptosis.



U2OS cells were labelled with SiR-Actin, TMRE (mitochondria activity), CellEvent™ (caspase activity), and DAPI (nuclei). Apoptosis inducer staurosporine (3µM) was added at time-point 0. 63x magnification, widefield mode. 13 hours time-lapse.

3D Tissue Imaging

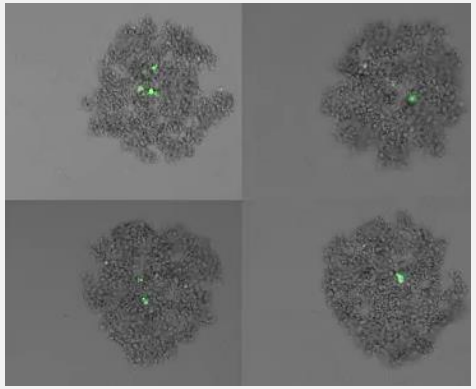
Mica enables you to seamlessly move from fast overview to high resolution when required by your experiment. See how Mica allows you identify a detyrosinated tubulin positive cell and progress from overview to the segmentation of the tubulin network.



Intestine tissue section acquired with 20x and 63x magnification, using widefield and confocal imaging. 20x widefield images are processed with THUNDER and 63x confocal images with LIGHTNING. Nuclei are labeled in blue, mitochondria in green, and detyrosinated tubulin in red.

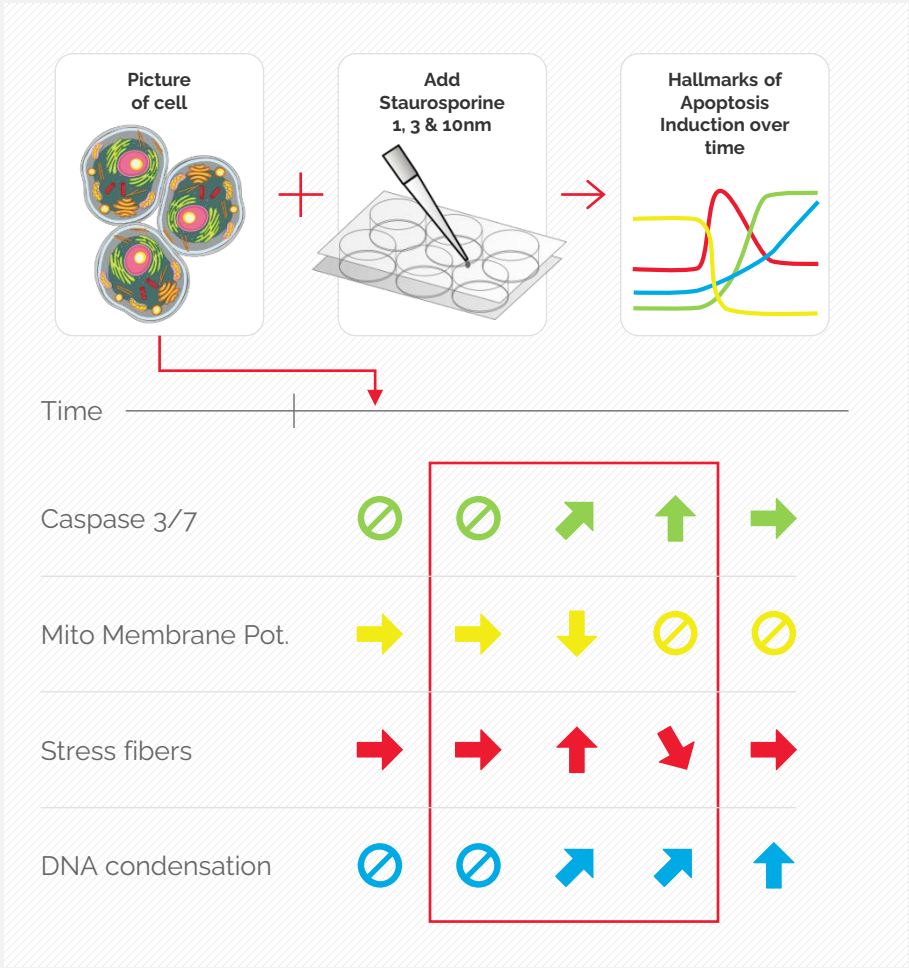
Long-term Time-lapse

Mica is an incubator to maintain your sample in physiological-like conditions and to minimize evaporation. Discover how Mica allows you to measure spheroids growth and to analyze protein expression levels.



Formation of 3D spheroids from 1000 stably transfected MX1-GFP cells per well. Time-lapse acquisition over 60 hours with 30 minutes interval. Green, GFP. Gray, integrated modulation contrast.

Fluorescence Caspase Assay



Experiment description:

This experiment combines multiple readouts, all connected to the early phases of apoptosis.

We are seeing a dose dependent activation of Caspase 3/7, preceeded by stress fiber formation and the depletion of the mitochondrial membrane potential.

Experiment Challenges:

- Collecting all 4 labels fastly to achieve a short time interval over whole sample carrier
- Separate 4 labels, avoiding crosstalk which leads to misinterpretation
- Correlation of data is difficult if not acquired simultaneously
- Context and morphological data are missed / not correlatable.

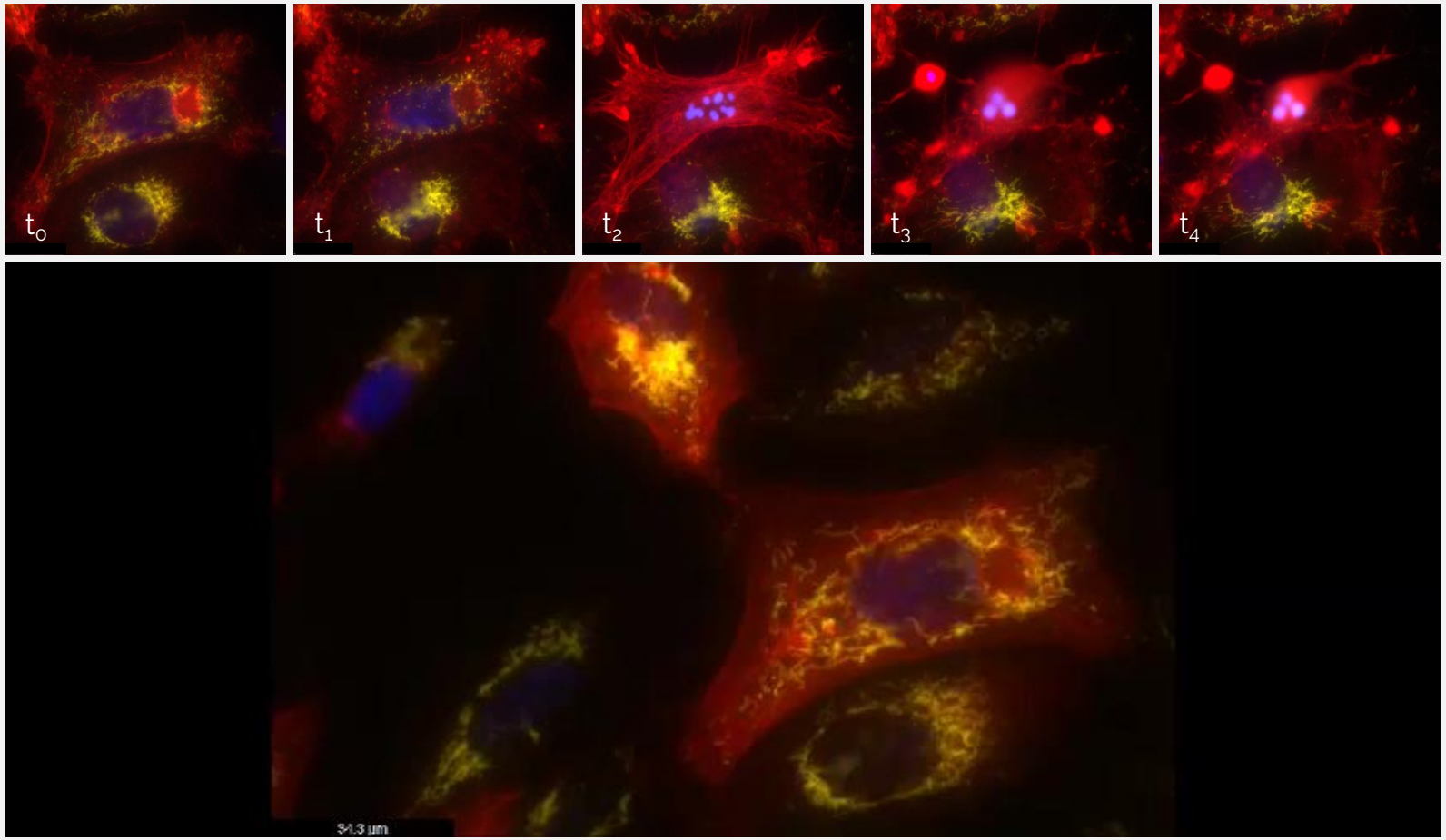
Mica's benefits:

Access for all : Mica allows the setup of complex assay readouts even for inexperienced users.

No constraints : Mica allows to image 4 labels simultaneously, with 100% spatiotemporal correlation.

Radically simplified workflows : Mica combines the collection of 4 markers and the subsequent analysis with significantly less steps.

Fluorescence Caspase Assay

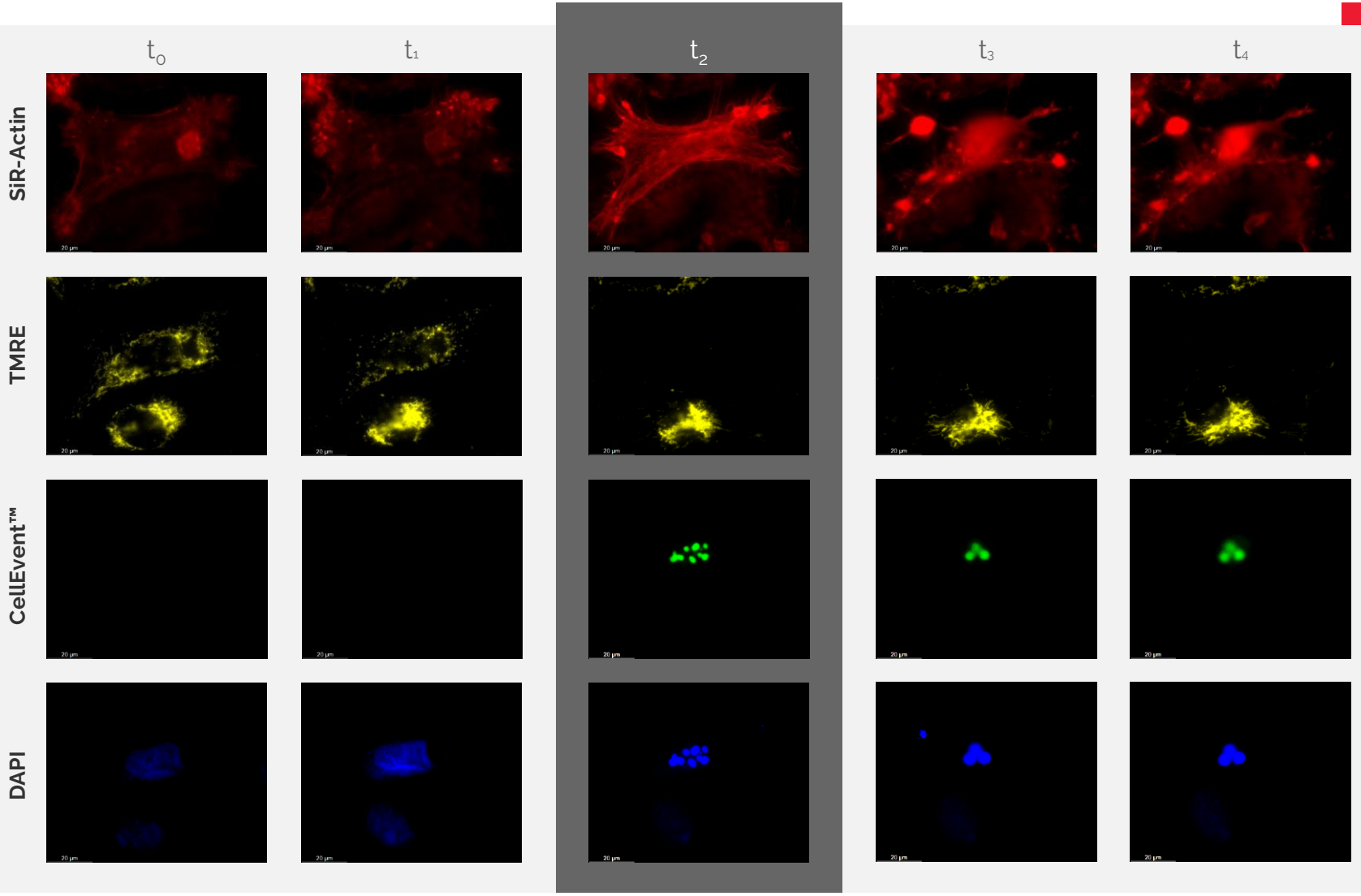


U2OS cells were labelled with SiR-Actin, TMRE (63x magnification, mitochondria activity), CellEvent™ (caspase activity), and DAPI (nuclei). Apoptosis inducer staurosporine was added at time-point 0. widefield mode. 13 hours time-lapse.

Absolute spatiotemporal correlation of 4 markers monitoring the hallmark of early apoptosis induction.

We can observe the formation of stress fibers coinciding with the loss of mitochondrial membrane potential at the beginning of Caspase 3/7 activation. DNA condensation is directly following the caspase activation.

Fluorescence Caspase Assay



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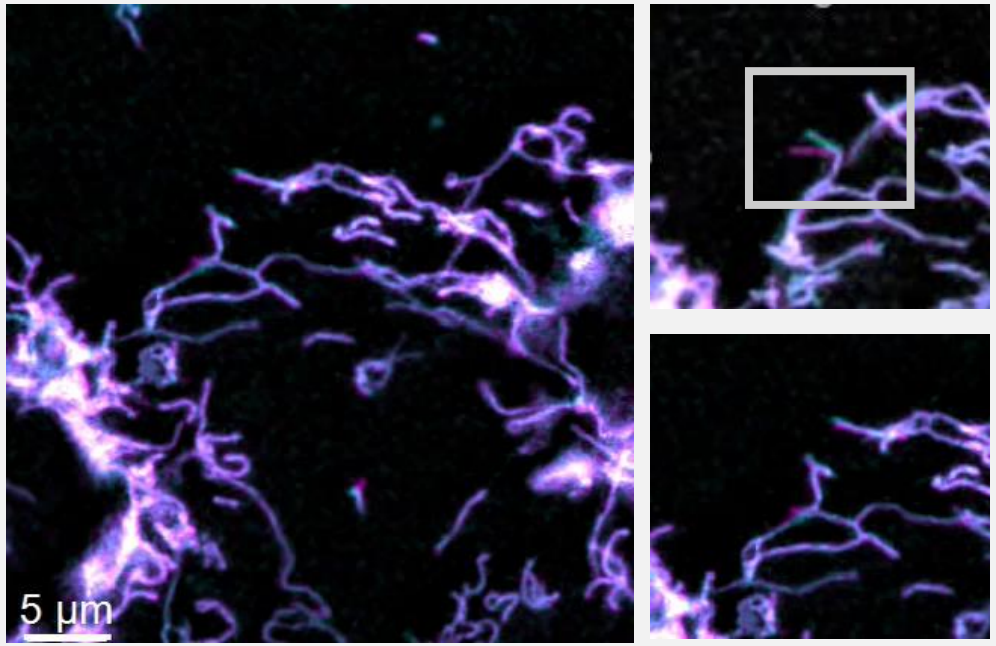
Challenge of spatiotemporal multicolor acquisition

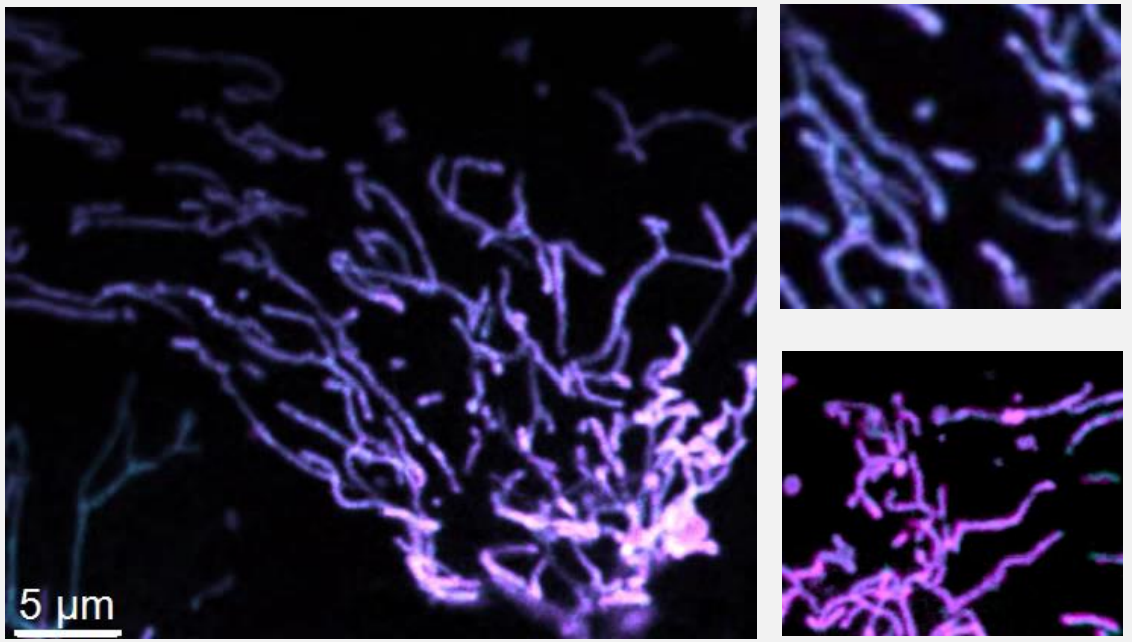
Mitochondrial dynamics
U2OS cells were stained with MitoTracker green (green) and TMRE (red). Short time-lapse sequences of 1 min have been acquired in widefield mode. The traditional widefield labels (left) were acquired sequentially, with Mica (right) the acquisition is done simultaneously.

Simultaneous detection eliminates spatiotemporal artifacts when visualizing mitochondrial structure and membrane potential.
When using traditional widefield imaging spatiotemporal artifacts – as a result of sequential acquisition – falsify measurements and prohibit correlation of structure and function. With FluoSync, the simultaneous acquisition ensures spatiotemporal correlation, no artifacts are acquired, and the membrane potential is correctly correlated with the mitochondrial structure.

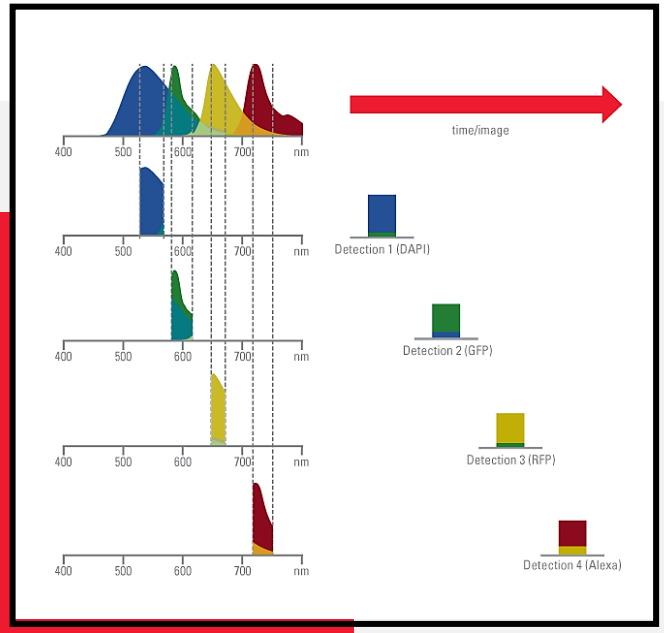
Traditional Widefield



Mica

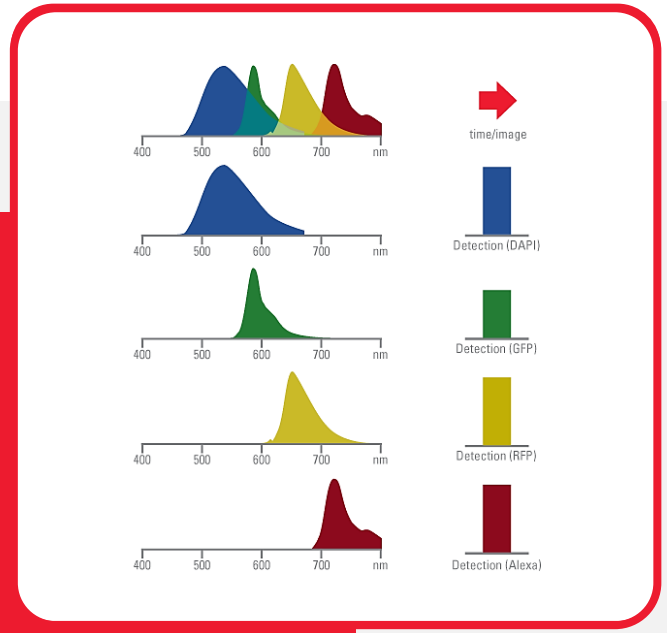


Simultaneous 4 Label Imaging, Broad Spectrum Detection and Hybrid Unmixing



Conventional 4 color fluorescence imaging

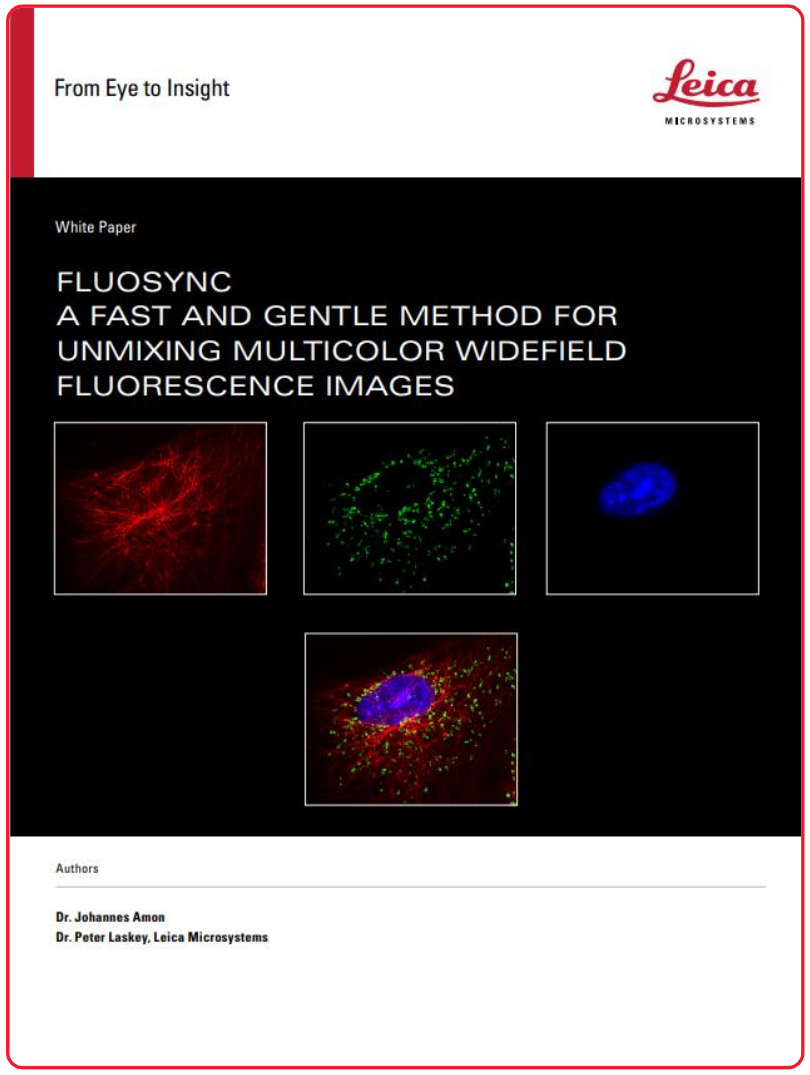
- Poor dye separation results in low localization accuracy
- Cut away signals to reduce cross talk
- Slow sequential imaging



FluoSync – Simultaneous true 4 label imaging

- Broad spectrum detection
- True dye separation
- 4 times faster imaging simultaneously

Mica FluoSync Hybrid Unmixing



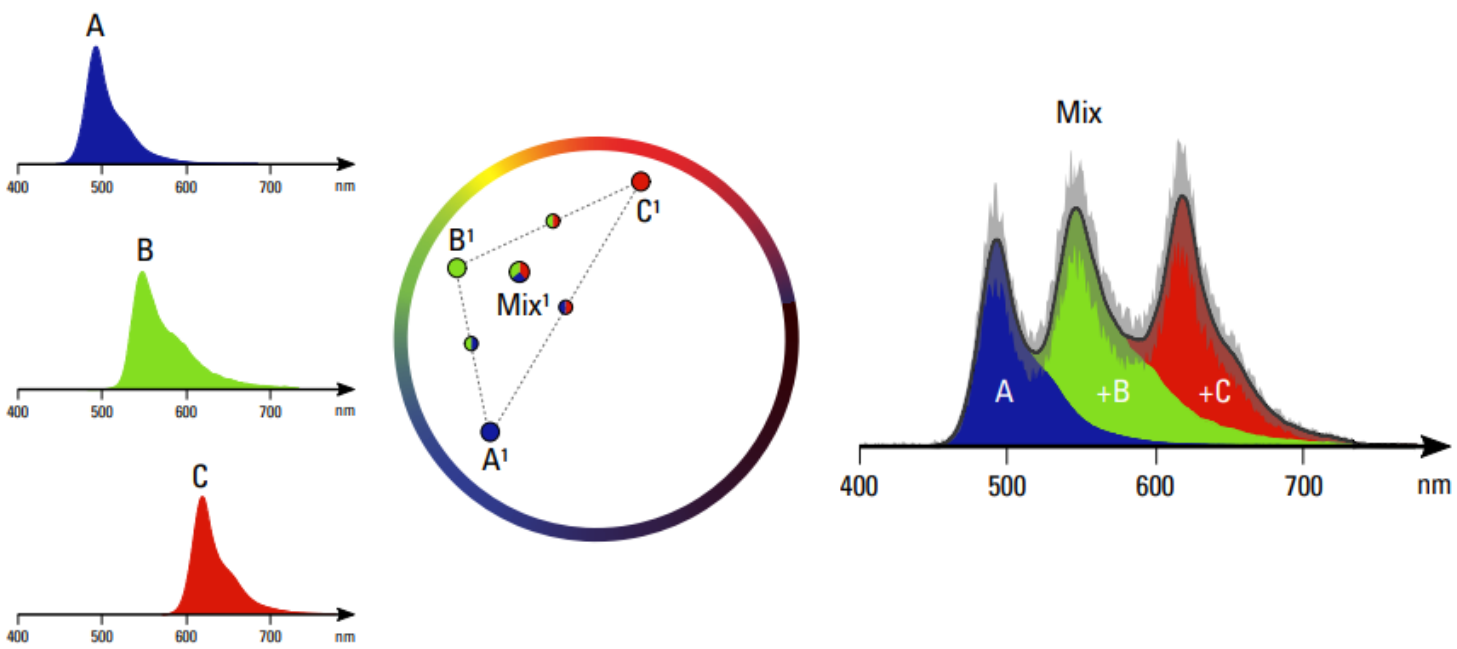


Figure 3. Depicted on the left are three individual spectra of a blue, green, and red fluorophore. By using the phasor analysis each pure spectrum will fall into a defined space in the phasor space where the color is represented on a circle and the sharpness of the signal determines the distance to the center (middle panel). Any combination of these fluorophores will also fall into a defined space. Depicted are one combination for each of the three fluorophores and a mix of all three. As possible combinations of fluorophores will also fall into "their" space, the spectra can be averaged for denoising. One example is shown in the right panel, where the black line represents the average ± the error (depicted as gray area). The noise-reduced spectrum represents a sum of all contribution fluorophores, that fills the area under the curve nicely.

References: Digman MA, Caiolfa VR, Zamai M, Gratton E. The phasor approach to fluorescence lifetime imaging analysis. Biophys J. 2008 Jan 15;94(2): L14-6.
F. Fereidouni, A. N. Bader, H. C. Gerritsen, Opt. Express 2012, 20, 12729.
Francesco Cutrale, Vikas Trivedi, Le A Trinh, Chi-Li Chiu, John M Choi, Marcela S Artiga & Scott E Fraser. Nature Methods 14, 149–152 (2017).

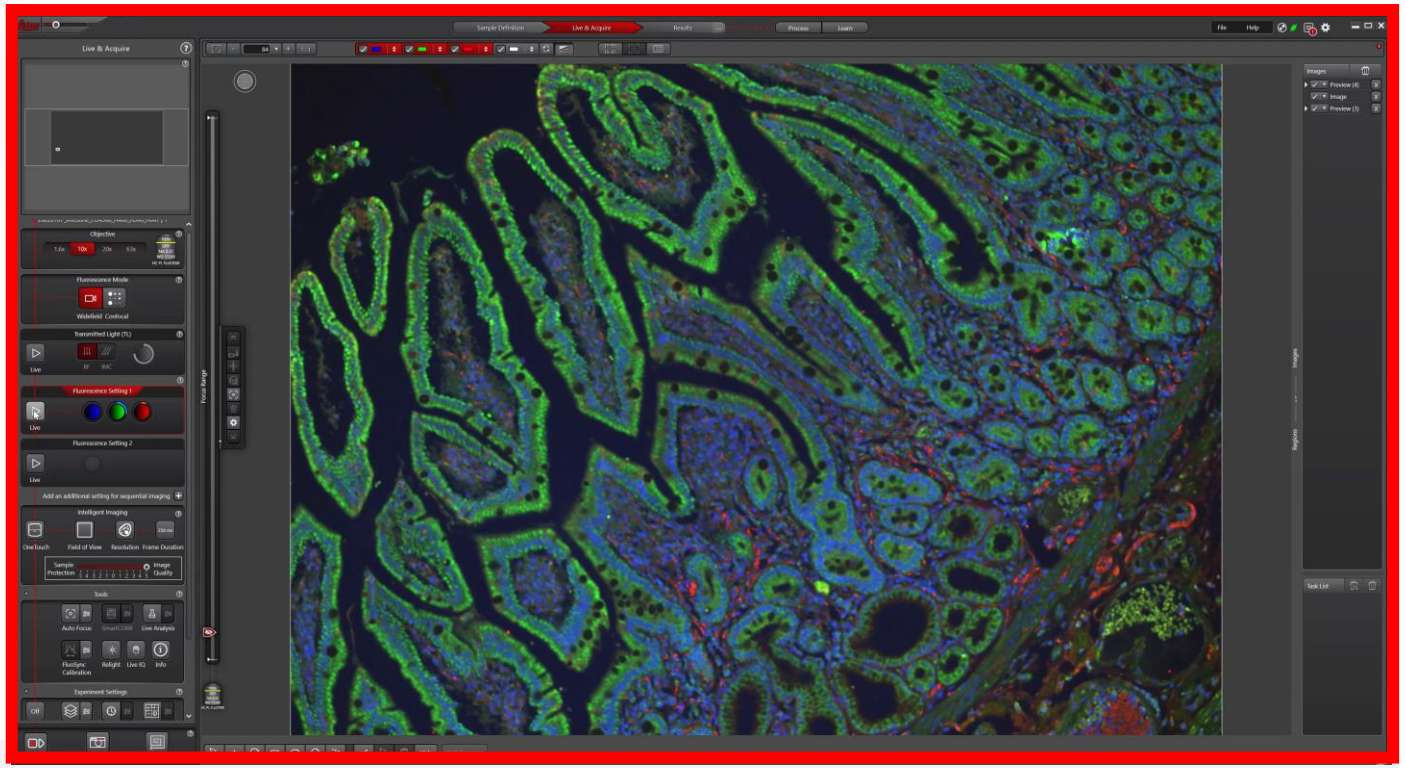
3D Tissue Imaging

Experiment description:

In this experiment we are creating a large overview of an intestine slide and increase the magnification to identify the right positions to acquire a confocal z-stack.

Experiment Challenges:

- Objects are not in focus when the objective is changed and user need to search.
- With increasing magnification it is difficult to keep the overview.
- With increasing magnification finding the same location is challenging.
- When using confocal, searching the right spot is very time consuming.
- When using a WF first and then a CF, finding the same location is difficult.
- Analyzing heterogeneous tissue with global thresholded parameters is prone to missing out objects.

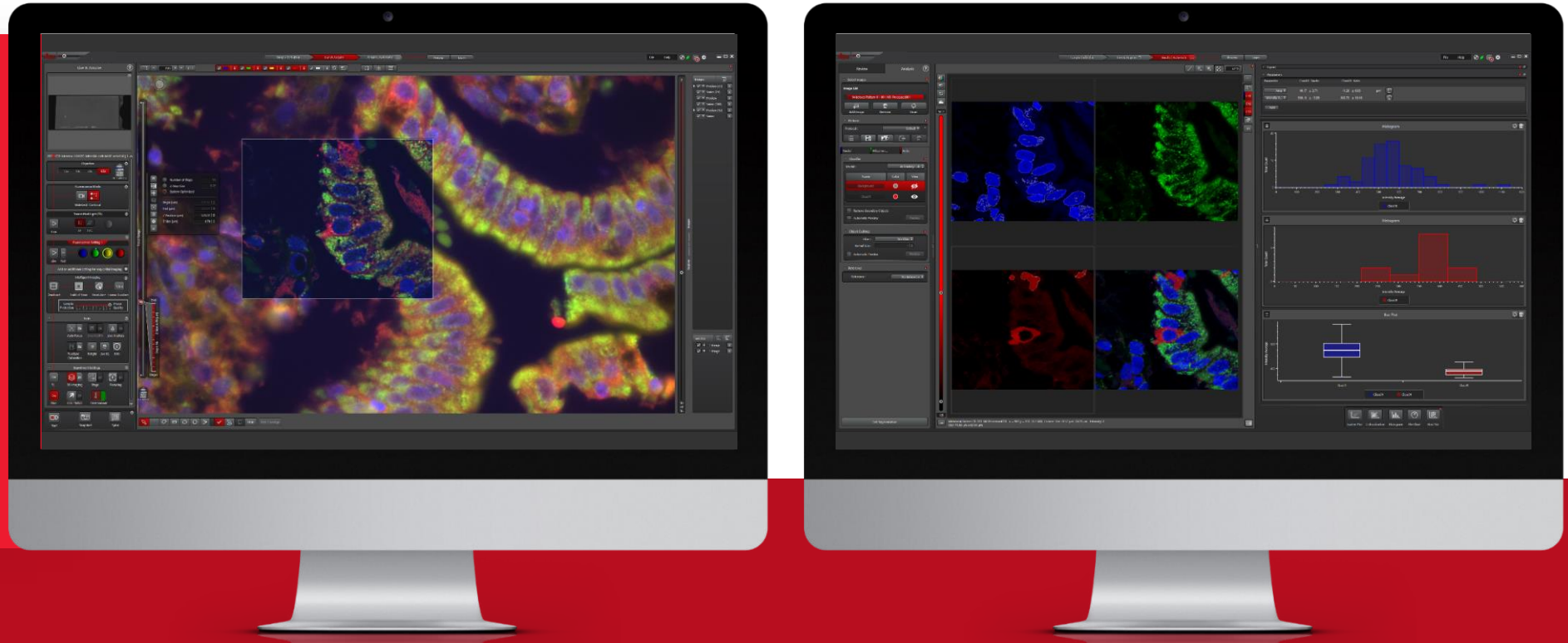


Mica's benefits:

- **Access for all :** Mica provides a clear sample overview and allows to easily change observation conditions with just a few clicks.
- **No constraints :** Mica seamlessly combines transmitted and fluorescence widefield with confocal imaging.
- **Radically simplified workflows :** Mica allows to effortlessly transit from a large sample overview to highly resolved images and provides AI based analysis within the same workflow.

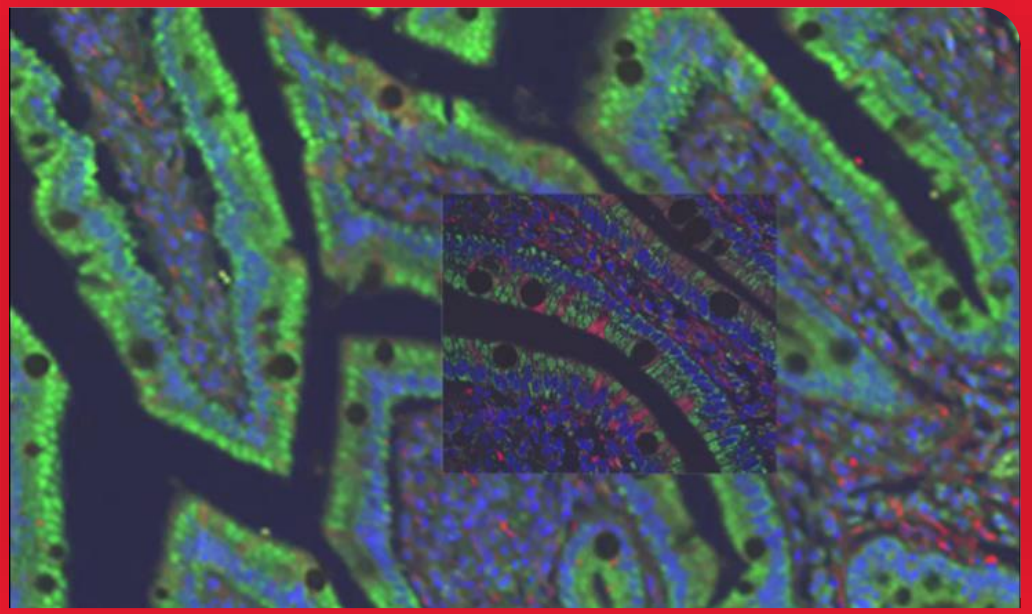
3D Tissue Imaging

Seamlessly move from fast overview to high resolution when required by your experiment.

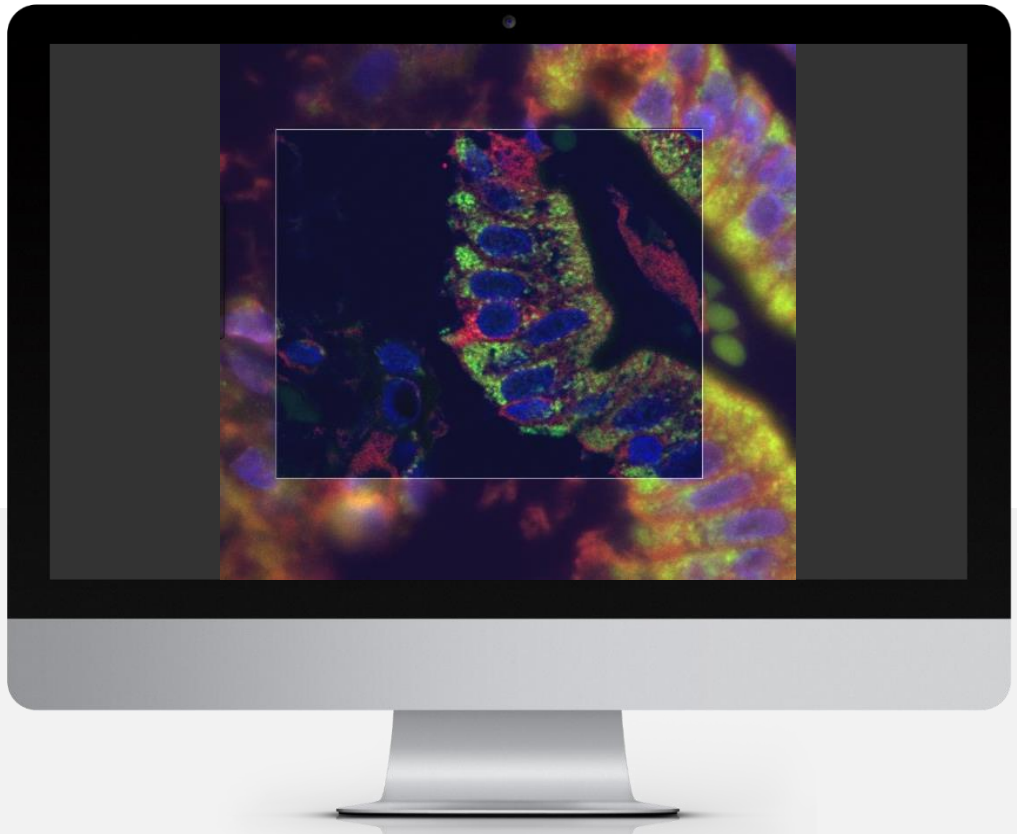


We can observe how the overview is rapidly created in widefield and a more detailed view of areas of interest is created with 10X and 20X magnification. This is followed by a high magnification view (63X) in widefield and followed by acquisition of a confocal image. The acquired confocal image is then segmented to quantify sizes.

Seamlessly connecting modalities



Without an integrated system with widefield and confocal imaging, you have to either carry your sample between systems or compromise on the efficiency. And the alignment of image data after moving from one system to another adds an extra step.



Mica provides you with widefield and confocal imaging seamlessly connected in a contained system – use the optimally fitting imaging modality when it is needed.

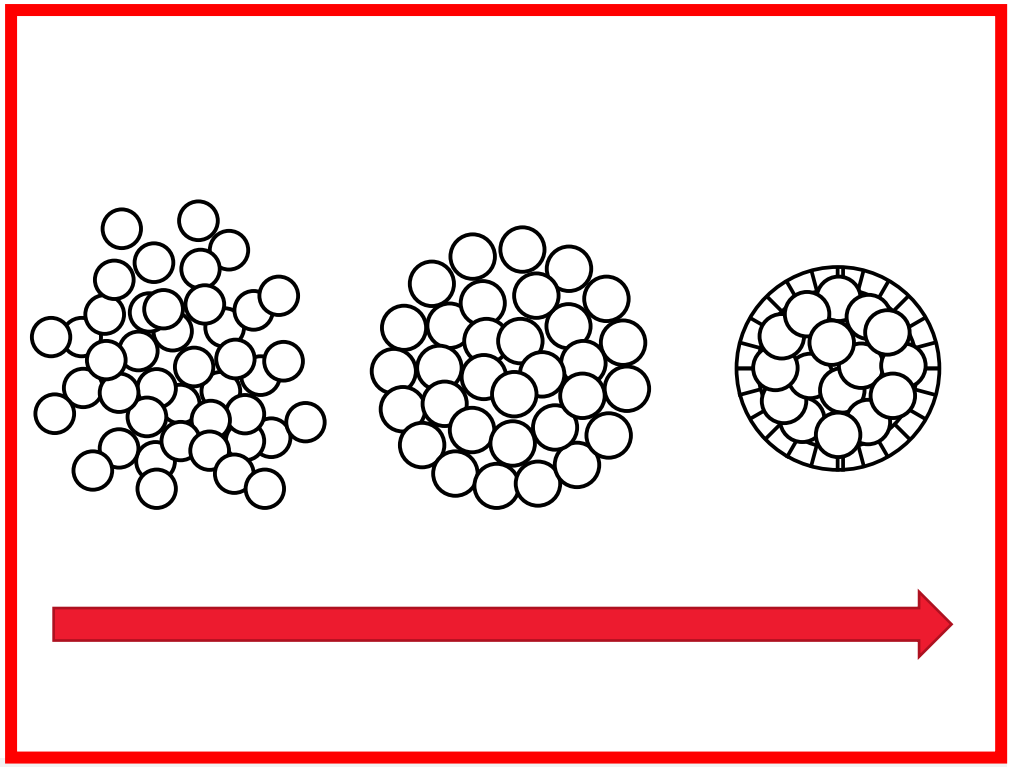
Long-term Time-lapse experiment

Experiment description:

In this experiment we see the formation of spheroids starting from a mono-cell layer. The formation of a spheroid requires optimal physiological conditions – ensuring undisturbed cell cycles and proliferation.

Experiment Challenges:

- Prolonged sample survival, ensuring physiological conditions.
- Low expression levels of markers, endogenous levels need to be kept to not impair cell homeostasis.
- Stable supply of nutrients and unchanged concentration in the medium – impaired by evaporation.
- Staying in focus and adapt imaging to changing sample characteristic like lateral and axial growth.



Mica's benefits:

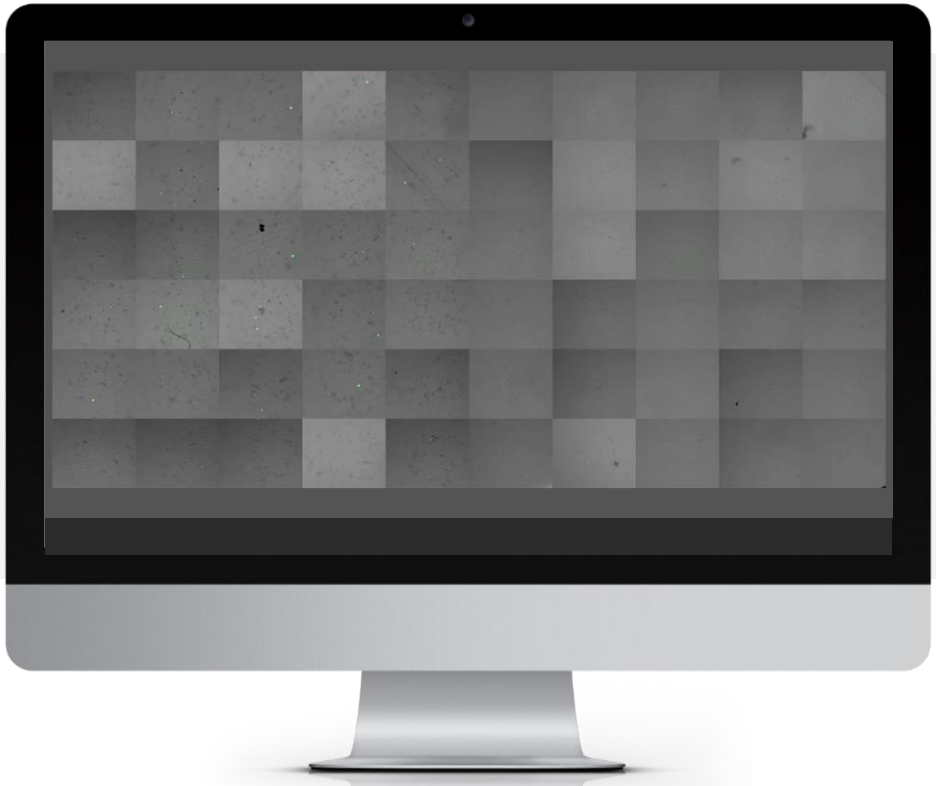
- **Access for all :** Easy setting up of controlled environmental conditions and matching focus strategy.
- **Radically simplified workflows :** On screen annotation and extraction of multiple parameters.
- **No constraints :** Optimal environmental conditions and multiple modalities (BF, WF, and CF) to match experimental needs and intelligent automation for water immersion and focus strategies.

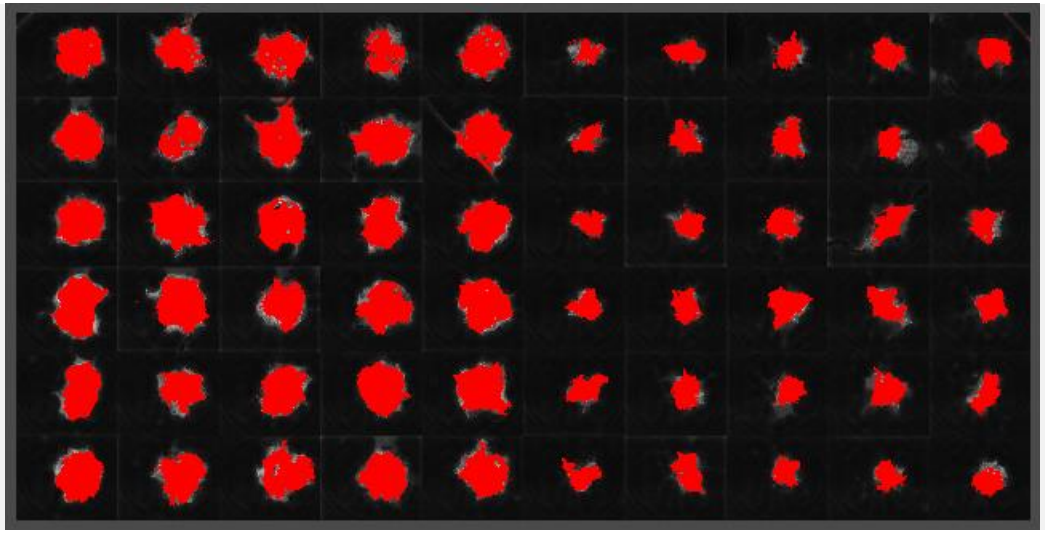
Long-term Time-lapse experiment

Spheroid growth

- MX1-GFP stably transfected cells (left half)
- U2OS cells (right half)
- Formation of 3D Spheroids
- 1000 cells per well

- Time-lapse over 72 hrs. every 30 minutes
- Green, GFP
- Black and white, integrated modulation contrast





Long-term Time-lapse experiment

Spheroid growth

- Formation of 3D Spheroids of
  - stably transfected MDCK MX1-GFP (upper row)
  - U2OS cells (lower row)
- 1000 cells per well
- Time-lapse over 60 hrs. every 30 minutes (or what ever the correct spelling of timelapse is)
- Green, GFP. Gray, integrated modulation contrast

The Microhub era is now!
Experience the future

- Access for all
- No constraints
- Radically simplified workflows

Meet Mica