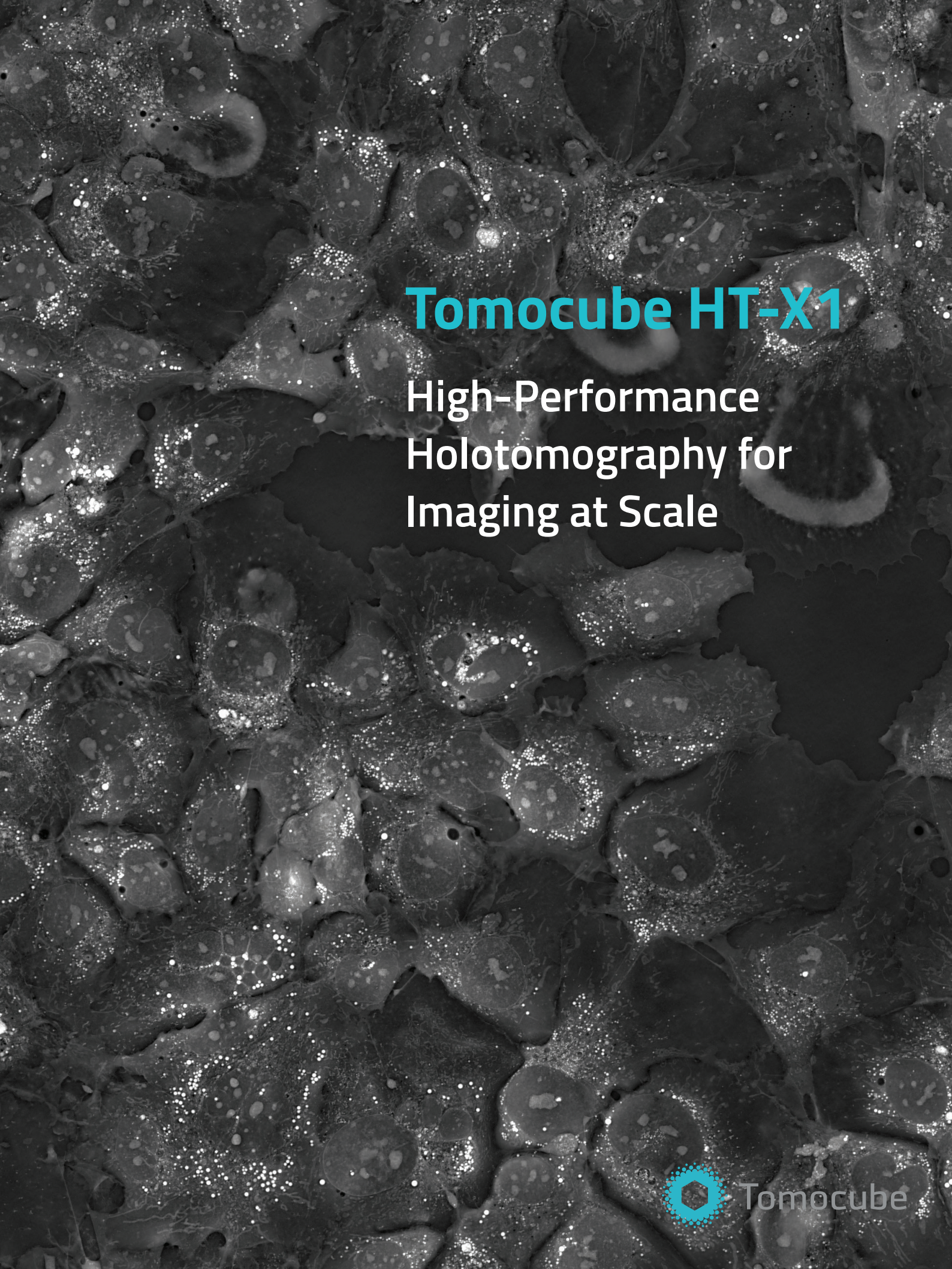


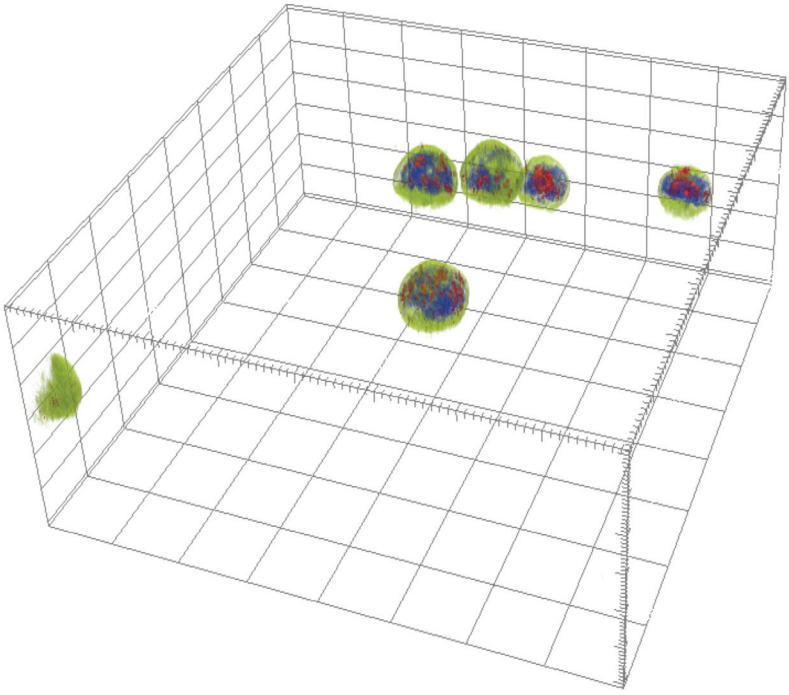
Tomocube HT-X1

High-Performance Holotomography for Imaging at Scale

Tomocube

Tomocube HT-X1 Holotomography

Multiplying Knowledge from 2D to 4D and Beyond



Holotomogram of K562 cells segmented and virtually stained.

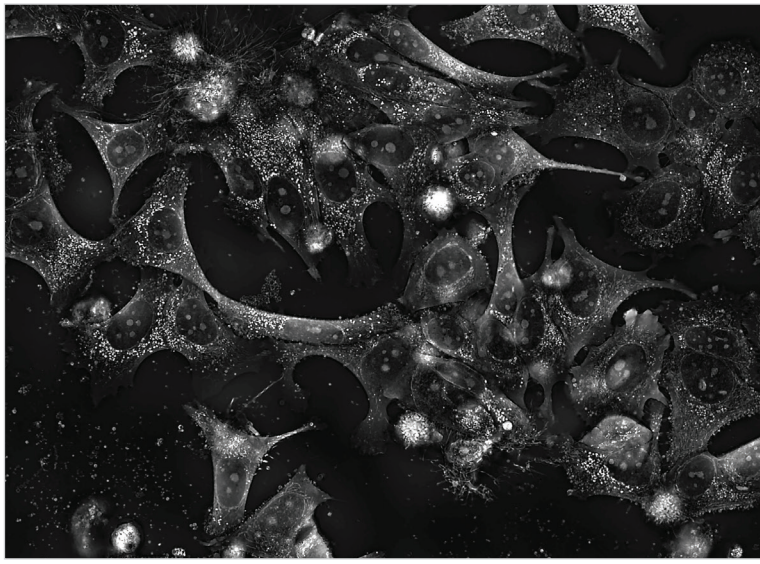
Observations of cellular morphology and activity are typically based on labeling of target molecules. These methods are invasive, affect the nature of the target molecules and potentially interfere with their biological relevance. In addition, these forms of label are not effective in providing quantitative information. The tools used to visualize labels are generally damaging to cells as often laser-based illumination is used to excite fluorochromes which in turn causes phototoxic damage to the cells.

The “holy grail” of imaging is to visualize cells without labeling to ensure the cells behave and grow normally. Holotomography (HT) does this by capturing the intrinsic light scattering properties of cellular materials using very low levels of light intensity, just enough to allow the light to pass through the cell. In doing so, the refractive index (RI) information of structures within the cell can be collected and selectively pseudo-colored to reveal the cell and its organelles.

In capturing the RI distribution, the Tomocube HT-X1 Holotomography can also provide quantitative data in 3D such as the volume, surface area, and dry mass of cells and their intracellular structures.

Holotomography Principle

Holotomography uses the refractive index (RI), an intrinsic optical parameter describing the speed of light passing a specific material, to visualize living cells and tissues. As light traverses through a sample, the various constituents scatter light differently based on their refractive index. By illuminating the sample with incoherent light beams specifically designed to retrieve the refractive index, we can capture a sequence of holograms from different positions. This new single beam technique keeps the imaging simple as it does not require background calibration on the sample and also reduces speckle noise. This also allows for imaging in more confluent samples without increasing the light intensity to pass through the samples.



MCF-7 cells imaged by the HT-X1. Minute structures extending from the cell membranes are visible from the holotomography image along with the subcellular compartments, showing the detection sensitivity.

Features

- High resolution, high contrast, and high sensitivity
- Large captured fields
- Programmable multi-well plate imaging
- Laser autofocus for well-to-well reproducibility
- Low noise, speckle-free imaging with no calibration step
- Bioimaging made quantitative
- Integrated incubation for long term time lapse
- Integrated 5 channel FL light engine
- Correlative holotomography with 3D fluorescence
- True multi-dimensional imaging across time, space and modality

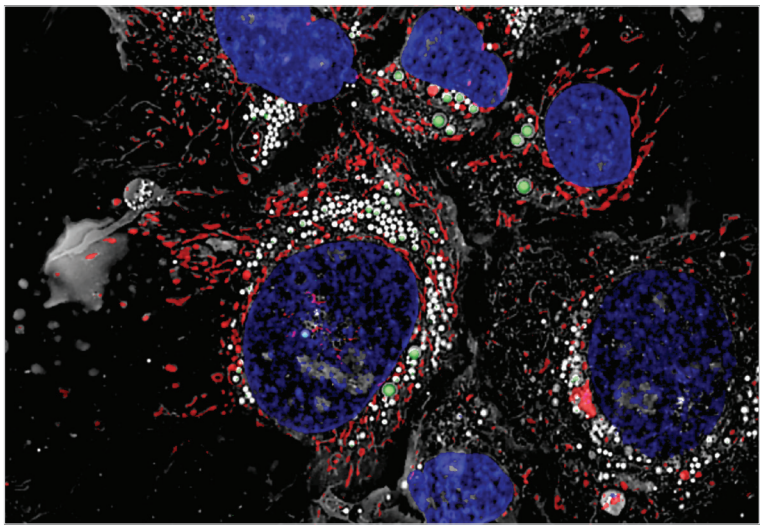
From 3D to Multi-Dimension in Time and Space

XYZT combined with correlative fluorescence and more

As an intrinsic property of materials refractive index (RI) values are non-specific. For imaging purposes beyond basic morphology there remains a requirement to apply some specific labelling.

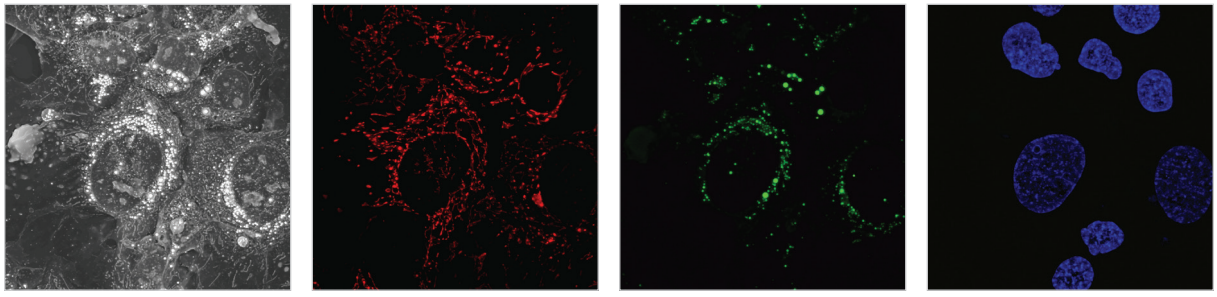
The HT-X1 combines holotomography (HT) with multi-channel fluorescence (FL) imaging for correlative 3D HT with 3D FL, allowing you to visualize the relative position of your target in 3D space.

When the molecule-specific FL information is combined with the high-resolution 3D information from the physical properties, interpretation of the cellular activities can lead to deeper understanding of biological phenomena.



Hep3B cells observed by holotomography and 3-channel fluorescence (mitoDsRed, lipiDye, and Hoechst). The images from the two modalities are overlaid.

The HT-X1 acquires holotomography data simultaneously with fluorescence microscopy in 2D, 3D and 4D formats.
The flexibility in imaging can be even maximized by uncoupling the time scale of HT and FL. The uncoupling allows "hetero-timelapse" where a single FL image may be captured at a time frequency different to that of the HT, for example, one FL every ten HT, minimizing phototoxic damage without losing the temporal resolution.



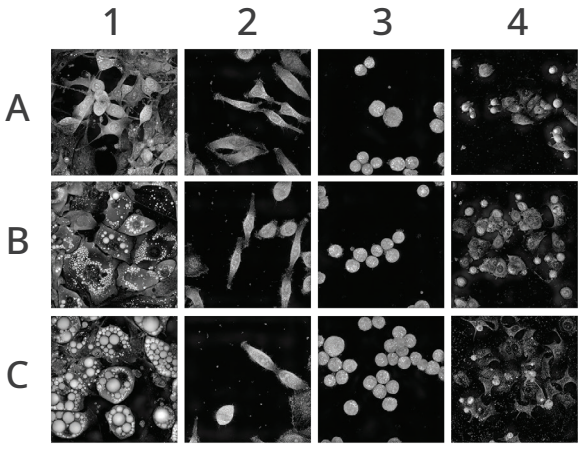
The individual channel images of the Hep3B cells shown top. From left to right, the holotomography image followed by the fluorescence images from mitoDsRed, lipiDye, and Hoechst.

Programmable Multi-well Imaging with Autofocus

In combining 2D, 3D and other dimensions, multi-well capability of the HT-X1 allows you to capture more relevant, more accurate and more quantitative information.

The HT-X1 has a motorized XY stage, a motorized Z drive, and a long-working distance condenser, giving full flexibility for imaging of multi-well formats.

The integrated laser-based autofocus ensures reproducibility from well to well and from time point to time point, which is particularly important in long term imaging. As a laser-based system it will find the correct focal plane even without cells present.



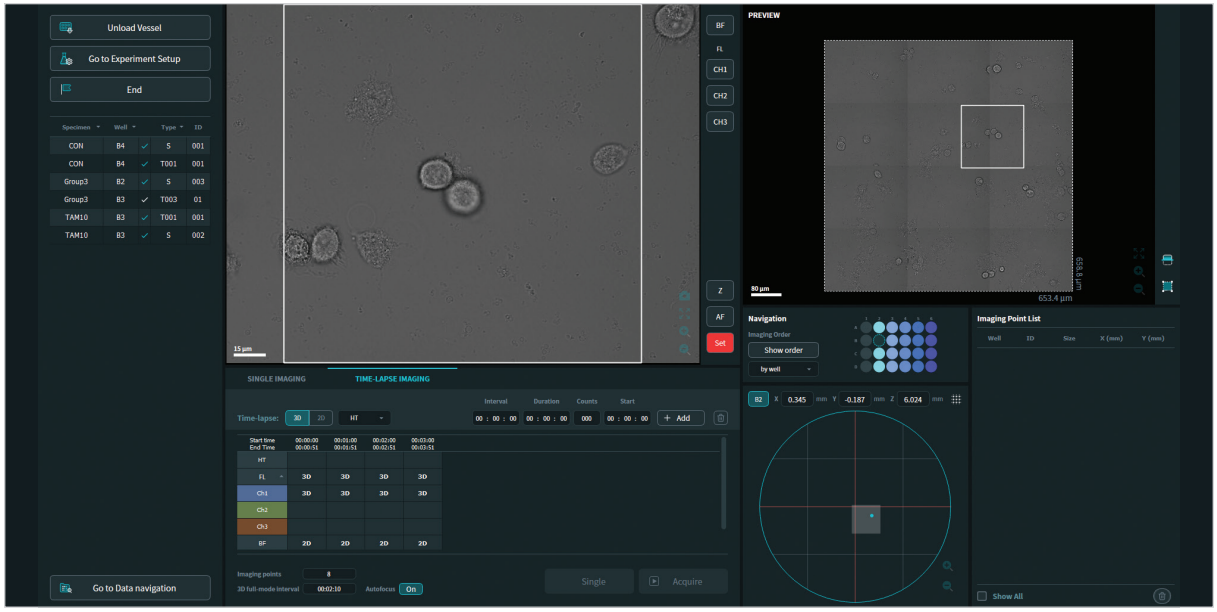
Integrated Environmental Chamber

For timelapse live cell imaging, the HT-X1 comes with an integrated active environmental control chamber for temperature and CO_2, which works with the motorized sample and focus stages that accommodate multi-well plates.

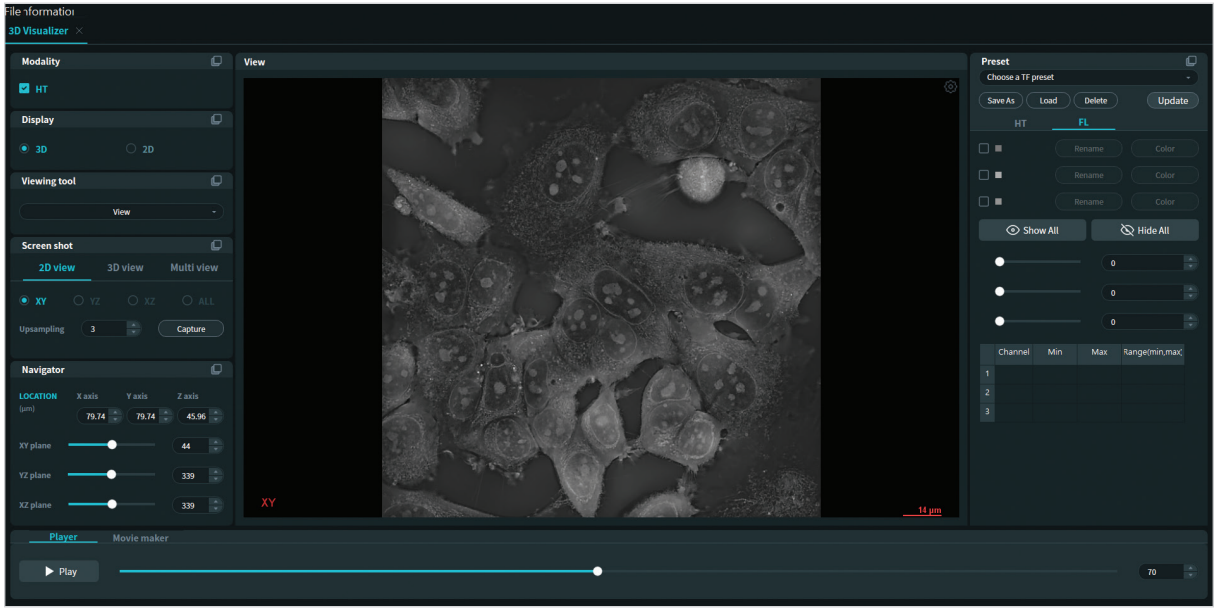
Intuitive Software to Drive Your Experiments

Designed with flexibility and efficiency in mind

As the control software for the HT-X1 TomoStudio X is designed to operate the system as you design the experiment. TomoStudio X offers flexible workflows for multi-dimensional image acquisition of holotomography and fluorescence in multi-well imaging conditions. All the essential control and status of the system are displayed all at one glance.



Visualization of your acquired data is available through TomoAnalysis. Acquired data can easily be clustered visualized and downloaded to other platforms for your specific analysis.



System Configuration

1. HT-X1 main unit

- Holotomography illumination
- Detection
- Sample holder
- Environmental chamber
- Positioning stages
- Fluorescence light engine

2. Environmental control unit

- External controller for temperature and gas

3. Software

- TomoStudio X for control of acquisition
- TomoAnalysis for data analysis and report

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