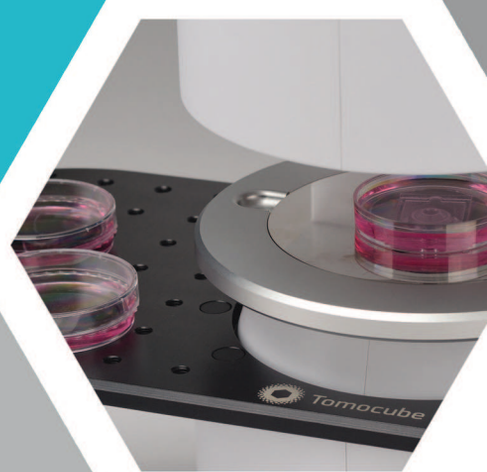
IMAGE DIFFERENT

Tomocube

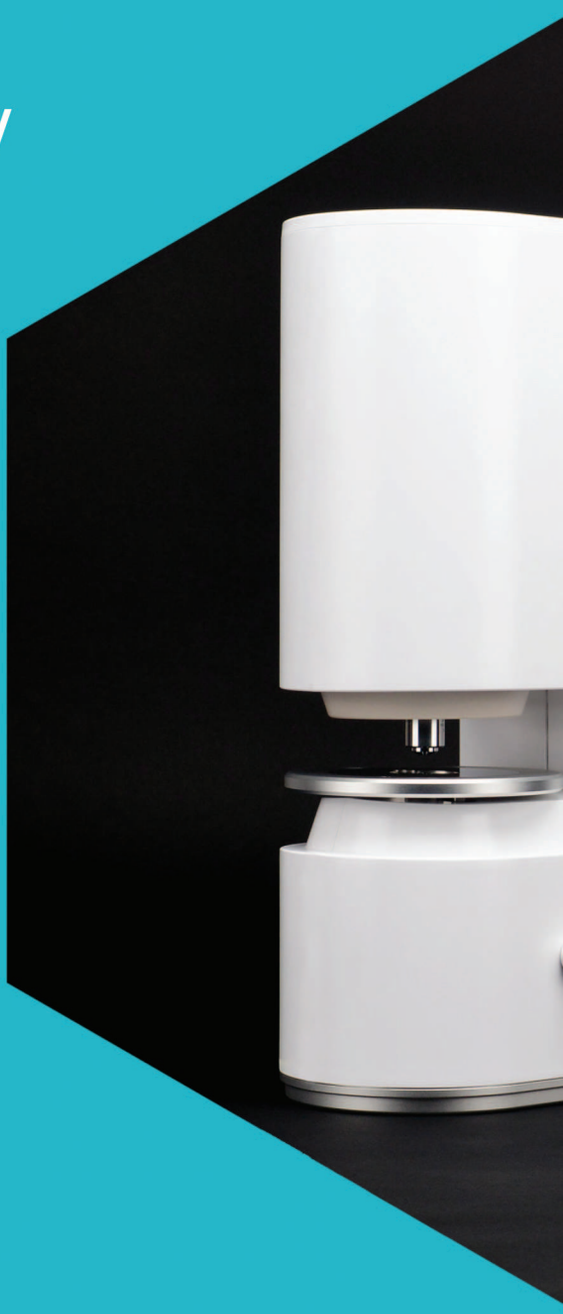
CONTENTS



Overview

Revolutionary holotomography (3D holographic microscopy) opens new era for label-free live cell imaging

Cellular analysis plays a crucial role in a wide variety of research fields and diagnostic activities in the life scien ces and medicine. However, the information available to researchers
and clinicians is limited by the current microscopy tech-niques. An innovative new tool – *holotomography* – can overcome many of these limitations and open new vistas for researchers and clinicians to understand, diagnose and treat human diseases.



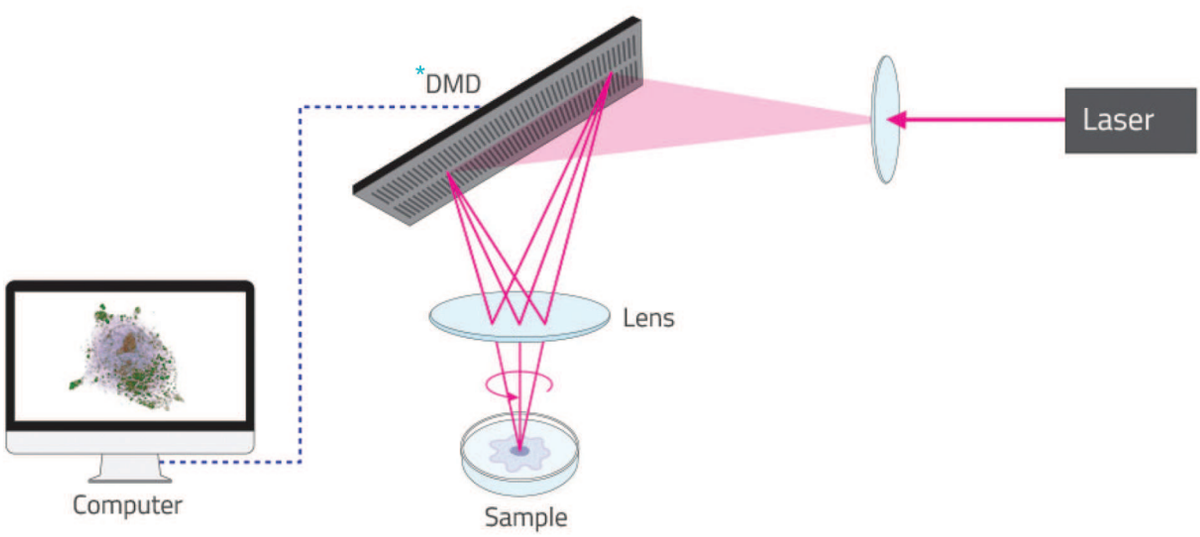
Holotomography (HT) - New era of microscopy

Tomocube's HT technology enable users to quantitatively and noninvasively investigate live biological cells and thin tissues in 3D. Holotomography reconstructs the 3D refractive index (RI) distribution of live cells and by doing so, provides structural and chemical information about the cell, including dry mass, morphology, and dynamics of the cellular membrane. This can be done very easy and fast, because RI is an instrinsic optical parameter of a material and thus HT does not require any preparation on samples.

Technology

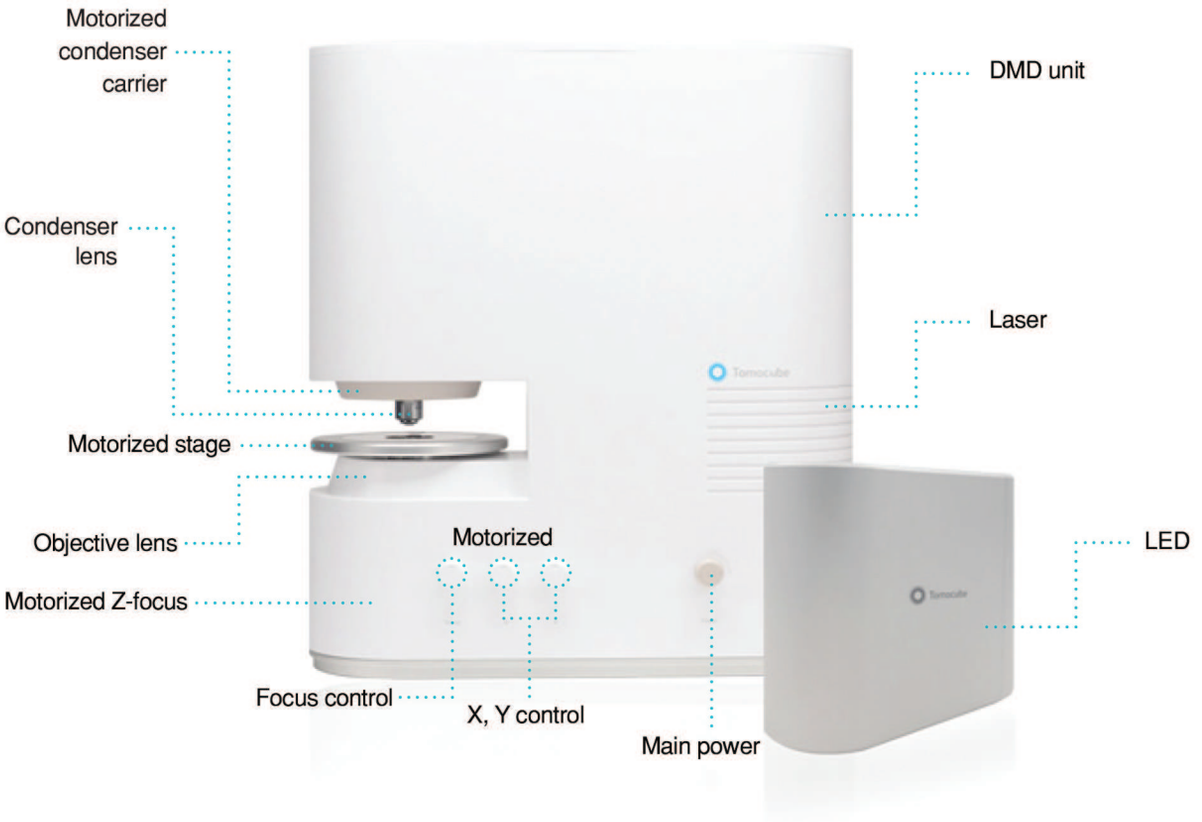
HT is an optical analgous to X-ray CT

RI is an intrinsic optical parameter that describes the speed of light passing through a specific material. Light passing through a cell is slower than light passing the surrounding medium. Analogous to X-ray CT (computed tomography), HT uses a laser beam to measure 3D RI distribution of cells. The system measures multiple 2D holograms of a sample in various illumination angles, from which a 3D RI tomogram is reconstructed via an inverse scattering algorithm. Tomocube presents unprecedentedly precise laser beam control, powered by Texas Instruments™ digital micromirror device (DMD) technology.



* Tomocube's patented technology utilizes a DMD, which allows to obtain multiple 2D images by every angle to reconstuct 3D RI Tomogram without any mechanical movement in the microscope.

HT Series components



HT-1S

60x Lens (dry)

Holotomography

HT-1H

60x Lens (water)

Holotomography
(High resolution)

HT-2S

60x Lens (dry)

Holotomography

3D fluorescence microscopy (3 ch.)

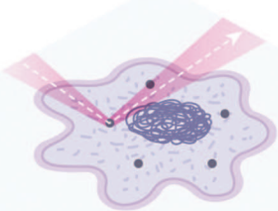
HT-2H

60x Lens (water)

Holotomography
(High resolution)

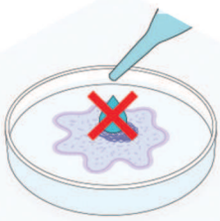
3D fluorescence microscopy (3 ch.)

Key features



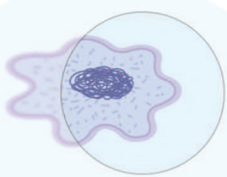
3-D Refractive index

New imaging contrast



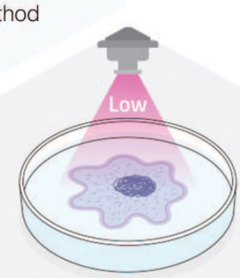
No label

Non-invasive method



High resolution

Beyond the diffraction limit



Low laser

532 nm, 0.05 mW

Fast imaging

In 2D, 3D and 4D

Efficient

High impact, Low cost

Benefits

01 Zero stress — Label-free imaging

02 Intact live cell imaging — Long-term image with short time interval

03 Time saving — No sample preparation and rapid 3D cell imaging (0.4 sec)

04 High quality 3D image — Optical resolution below 200 nm (Max. 110 nm)

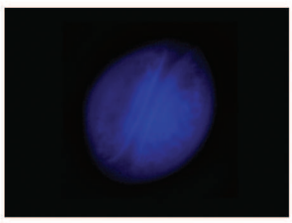
05 Quantitative bioimaging — RI enables quantitative bioimaging (Local cytoplasmic concentration, Dry mass)

HT-2: HT combined with 3D fluorescence imaging

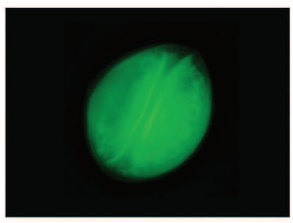
Holotomography powered with 3D fluorescence imaging

The HT-2 series opens a new era of 3D correlative imaging, combining the holotomography and fluorescence methods. The HT-2 allows the viewing of a 3D RI tomographic image of a living cell with minimal damage, while at the same time targeting consumer interest by allowing for fluorescence labeling in the very same cell.

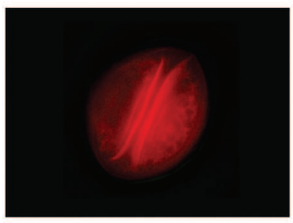
Pollen



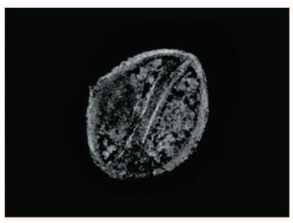
Auto fluorescence - Blue



Auto fluorescence - Green

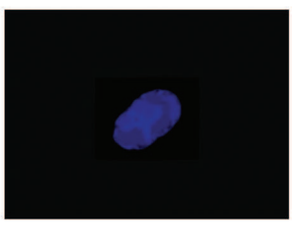


Auto fluorescence - Red

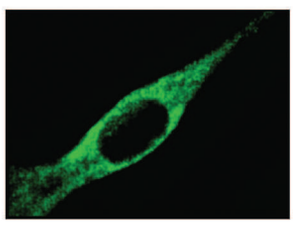


RI tomogram
(XY cross section)

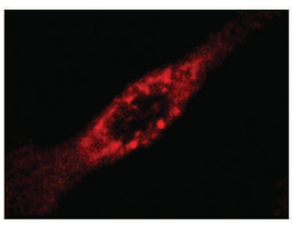
NIH-3T3



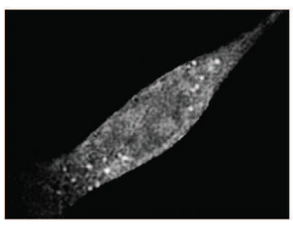
DAPI



GFP - tubulin



mCherry-actin



RI tomogram
(XY cross section)

Advantages

01 Correlative microscopy in one instrument

HT-2 provides high-quality 3D images of both holotomography and 3D fluorescence for each sample.

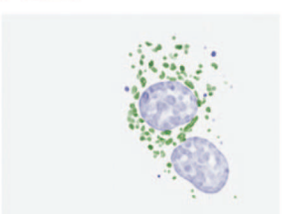
02 Quantitative data marked with fluorescence

HT-2 provides morphological (volume, surface area, projection area, sphericity and ellipticity), chemical (dry mass, concentration) and mechanical (cell deformability) properties of cells with 3D refractive index (RI) tomogram. Moreover, fluorescence image provides information about molecular specificity.

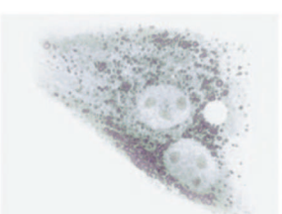
03 Live cell molecular and holographic imaging with minimal stress on cells

Simultaneous measurement capability of time-lapse 3-D RI tomography and fluorescence image allows long-time tracking of specific targets in live cells. The fluorescence image provides the position of specific target organelles or structures in live cell, and consecutive measurements of time-lapse 3-D RI tomography enables the monitoring of cells and their structures with minimal stress.

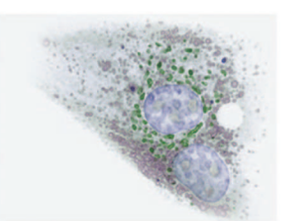
HeLa



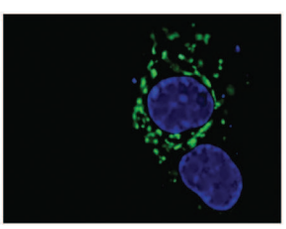
3D fluorescence
(DAPI, GFP-mitochondria)



3D RI tomogram



3D RI tomogram +
3D fluorescence



2D fluorescence
(DAPI, GFP)

Fluorescence capabilities

A three-channel LED light source (405 nm, 477 nm, 561 nm)
Wavelengths of the LED source can be customized

Z-stack images with a motorized Z-drive (step resolution: 150 nm)

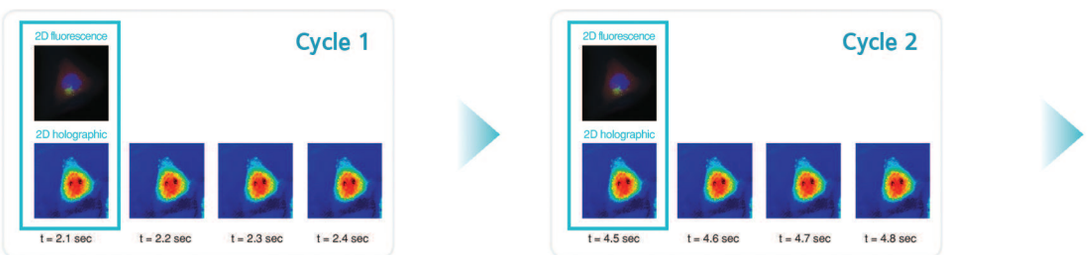
Correlative analysis in 2D, 3D and 4D with HT and fluorescence images

Upgradable: The HT-1 can be upgraded easily to the HT-2 (fluorescence version) in the field

Working scenarios

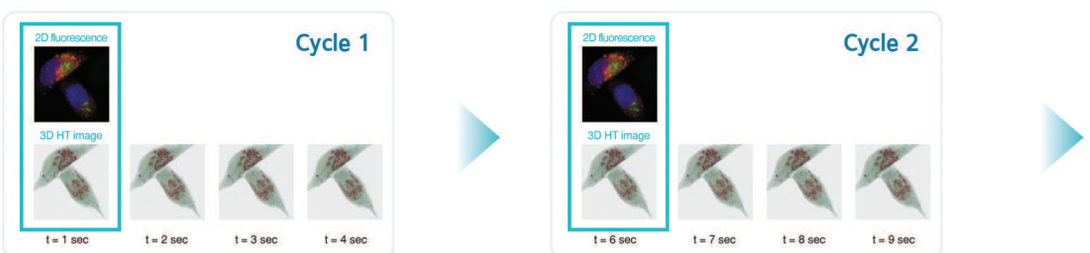
Scenario 1

Fast 2D fluorescence (FL) + 2D holography: enables the observation of very fast dynamics in the living cell through 2D holographic images (150 fps) after viewing the 2D FL image.



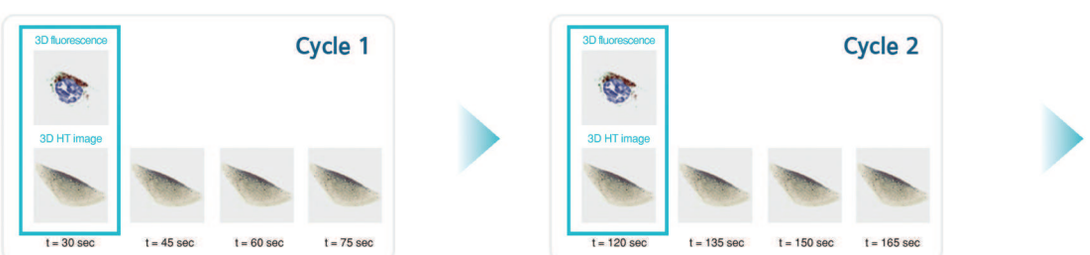
Scenario 2

Fast 2D FL + 3D HT: using a single 2D FL image, mark your target in the living cell and follow it across time using 3D HT images, without damaging the cell.



Scenario 3

3D FL + 3D HT: It is possible to obtain 3D FL and 3D HT images simultaneously, which allows researchers to investigate the 3D morphology of the cell with unprecedented imaging modalities. The quality and resolution of the 3D FL image can also be enhanced by using a deconvolution software.



TomoStudio™

2D/3D/4D holographic images

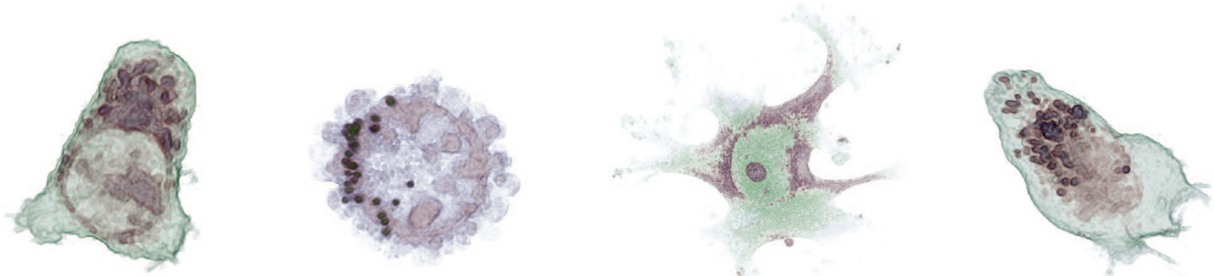
01 TomoStudio™, the HT-1 operating SW, controls the system and visualizes the captured image in various ways. The flexible user interface provides fast imaging capability and 2D/3D/4D visualization of cellular image based on 3D RI distributions of cells and tissues.

02 TomoStudio™ provides quantitative bioimaging information about morphological, chemical and mechanical properties of the sample. Quantitatative and label-free bioimaging capability will open a new avenue for the study of pathophysiology of cells and tissues.

03 Output parameters:

Morphological parameter	Chemical parameter	Mechanical parameter
Volume (μm^3)	Dry mass (pg)	Cell stiffness
Surface area (μm^2)	Concentration (pg/μm^3)	
Projection area (μm^2)	*RBC: Hb contents and concentration	
Sphericity		

* Red Blood Cell



TomoStudio™ provides

01

Work flow interface

User interface allows uninterrupted workflow from using the microscope to analyzing the data.

02

Data backup

Raw data can be stored in the computer for further analysis.

03

Fast image acquisition

HT-1 captures Holotomographic images every 0.4second (2.5 f/s) and 2D holographic images every 0.007second (150 f/s).

04

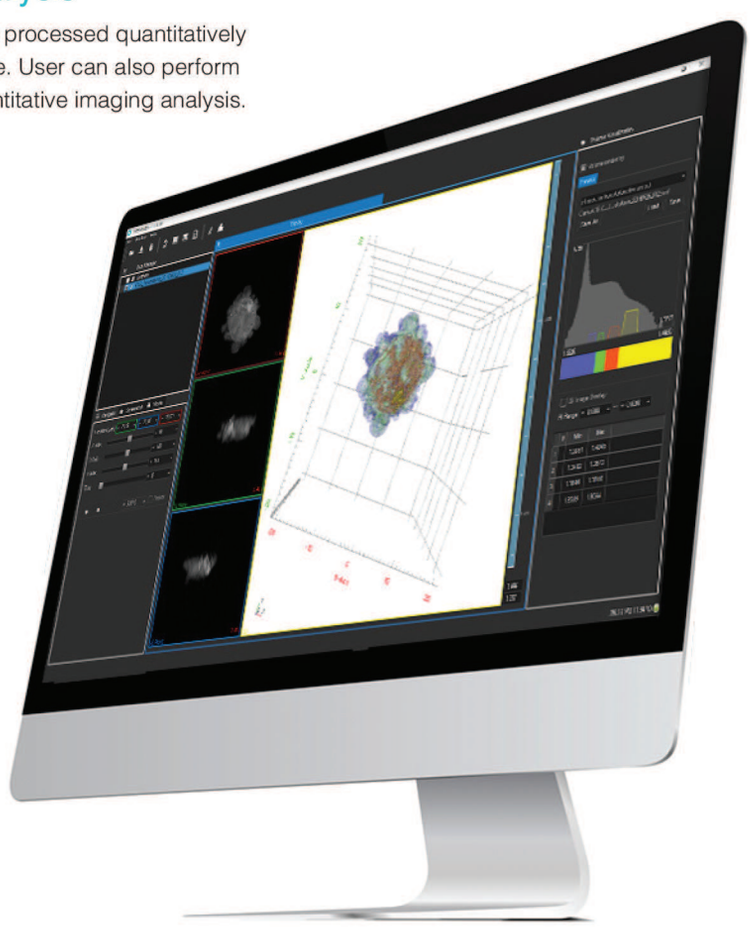
Holographic staining

Digital color coding controller (Transfer function) is a graphical user interface that stain the sample digitally based on RI information.

05

Data analysis

Data can be processed quantitatively and real-time. User can also perform various quantitative imaging analysis.

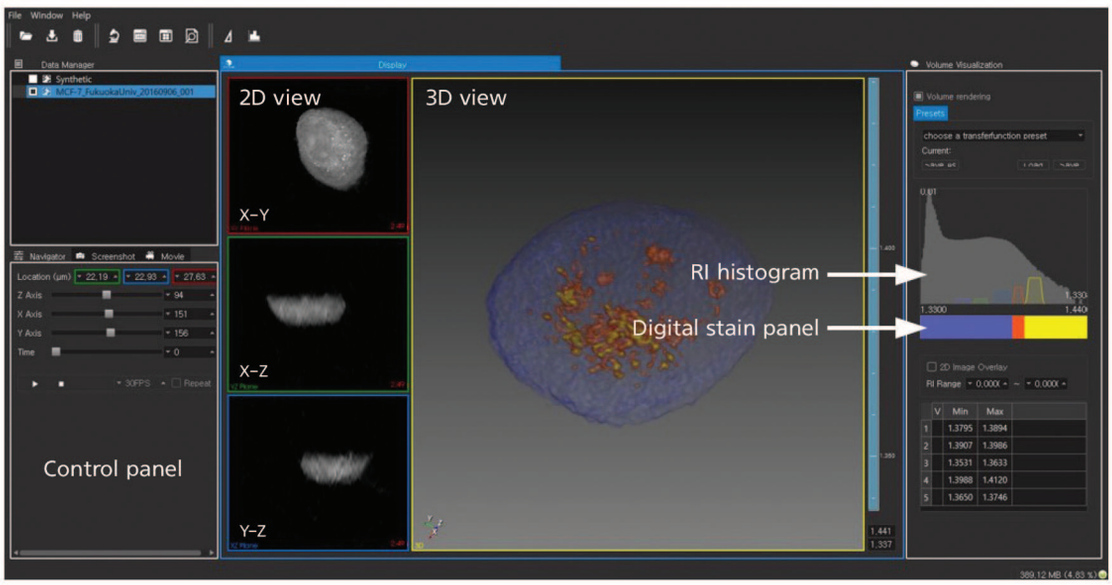


06

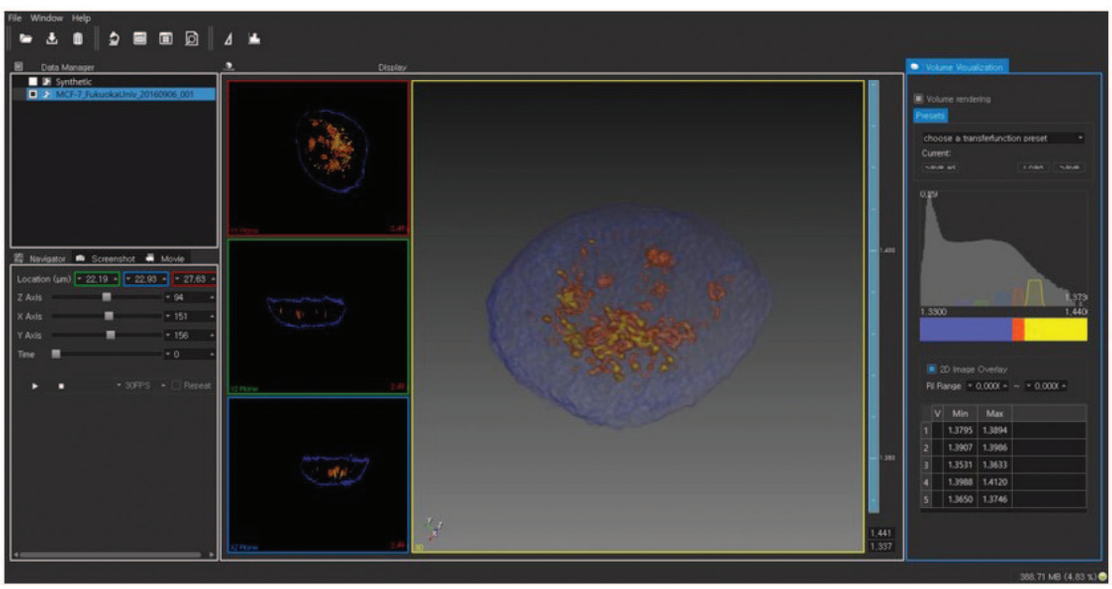
Dynamic image processing

Data processing does not interfere with the image acquisition process. Selective data processing is possible any time.

3D view with digital color coding



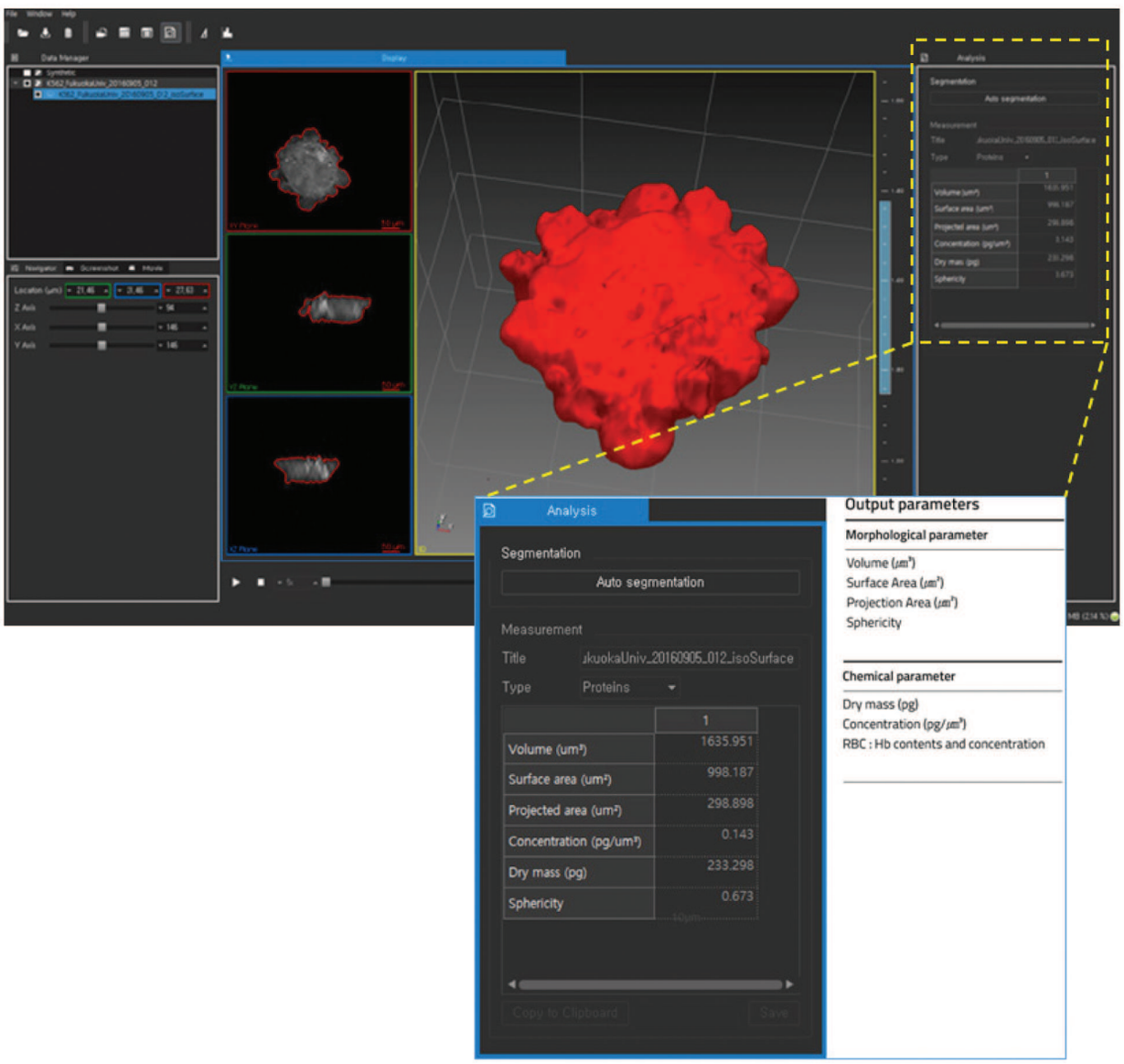
2D overlay



Analysis

Auto segmentation and analysis data

(Volume, Surface area, Concentration, Dry mass..)



TomoStudio™ 2.0 optimized for the HT-2 series

Operating

01
Full control of the motorized stages, condenser and Z-drive

02
Full control of the laser source and camera

03
Full control of 3 color LED light sources(405 nm, 477 nm, 561 nm)

Features

Obtaining 3D RI Tomogram 1

'Mark' and 'Find' function for recoding the position of multiple cells 3

2 Obtaining 3D fluorescence images up to 3 colors

4 Control of fluorescence and tomogram with different time series
(Hetero time-lapse: e.g. 1 FL in every 10 tomogram)

Visualization

01

Digital color coding of RI tomogram with high flexibility

02

Gradient transfer function displays the additional differentiation factor of RIs in the cell

03

Digital 3D overlay of FL and HT images

Accessories

01

TomoChamber

For long-term live cell imaging, it is necessary to secure specific environment to keep cells alive. TomoChamber is an incubation chamber designed to perform time lapse imaging with HT-1. It can be installed in the sample stage, where it maintains the temperature and supplies CO_2 to maintain the required condition.

02

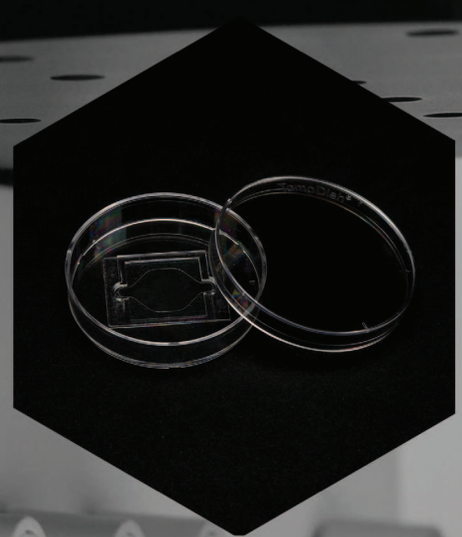
TomoPlate

The laboratory is constantly exposed to mechanical vibrations.
TomoPlate is a magnetic type compact anti-vibration table specially designed for higher resolution imaging, minimizing the effects of vibration.

03

TomoDish

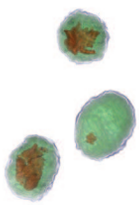
Specially designed dish for live cell imaging, allowing easy sample preparation and high-resolution sample imaging. Both adherent and floating cells can be cultured and prepared for imaging very easily.



Applications

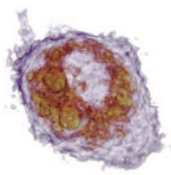
Hematology

- Malaria infection
- Sickle cell identification
- Blood analysis



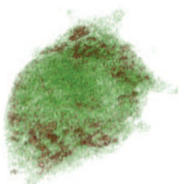
Microbiology

- Bacteria classification
- Microorganism imaging
- Microorganism lipid content test



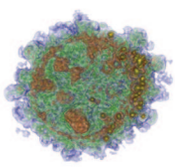
Immunology

- White blood cell classifcation
- Immune response



Nanotechnology

- Nanoparticle imaging
- Cell organelle tagging with nanoparticle



Cell biology

- Intracellular trafficking
- Cell division
- Live cell imaging
- Quantification
- Cellular structure analysis

Capabilities

01 Observe the cellular changes without any labeling or staining

02 Multidimensional acquistion : 2D time (150 fps) / 3D time (2.5 fps)

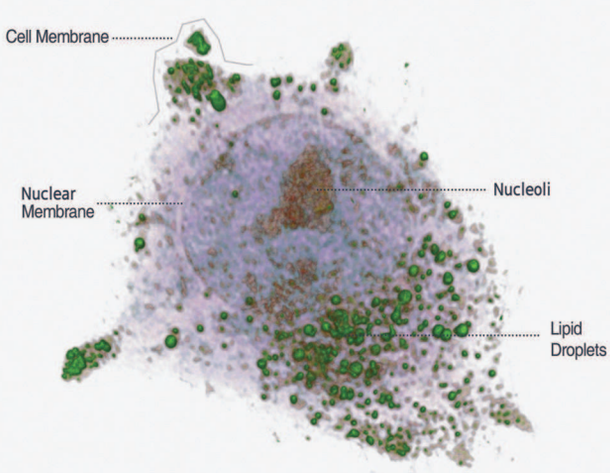
03 Visualize the cellular organelles with 3D RI distribution

04 Identify the changes of the quantitative properties of cells

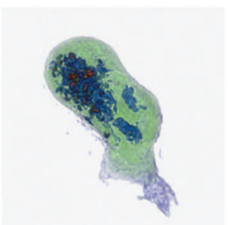
05 Detect the cellular organelles tagged by nanoparticles

06 Observe the vesicle movement in timelapse

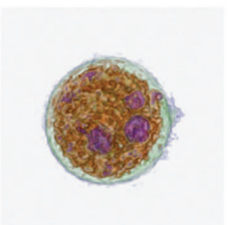
07 2D/3D/4D correlative images with fluorescence



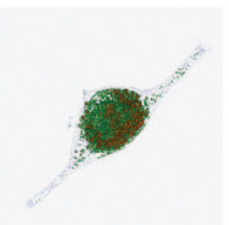
3D HT images of various cell types



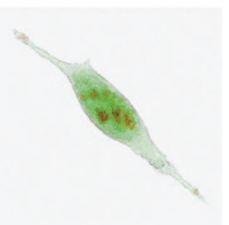
Lymphoma



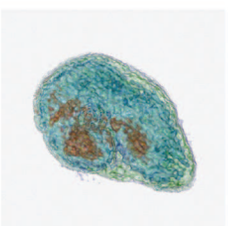
Leukemia cell



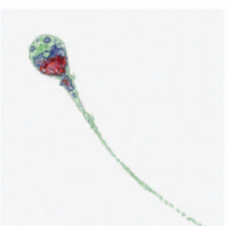
Melanoma



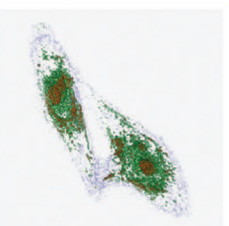
Neuron



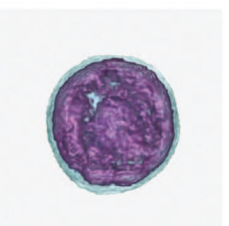
Stem cell



Sperm

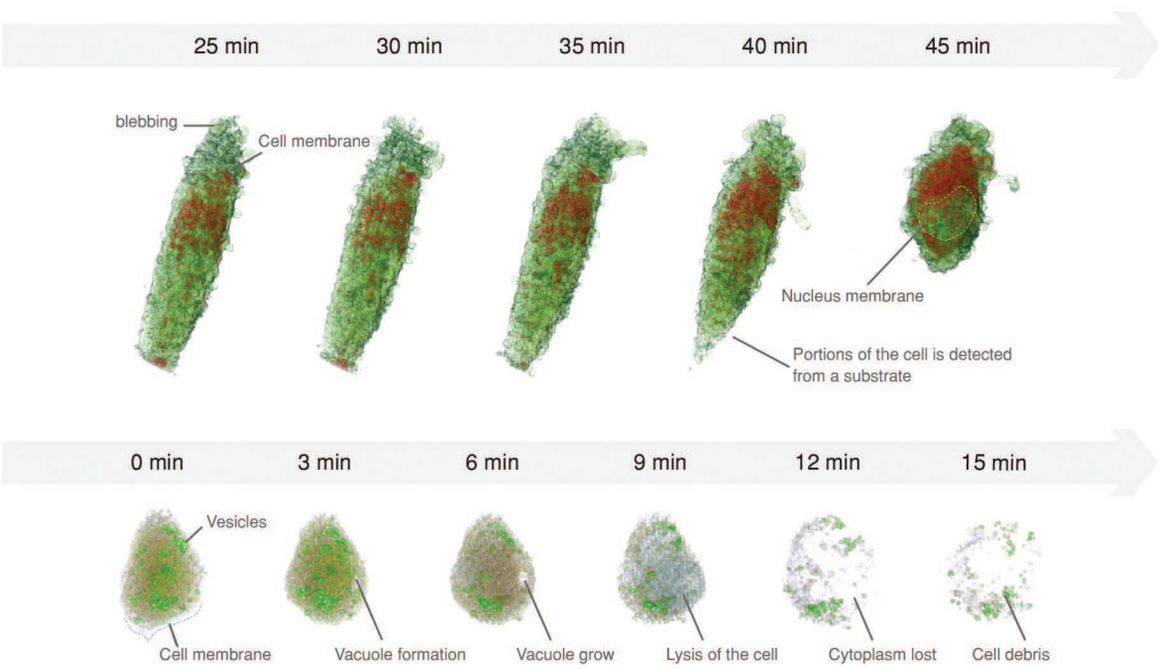


HeLa

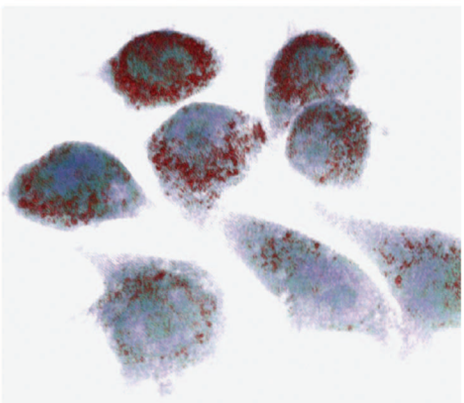


B cell

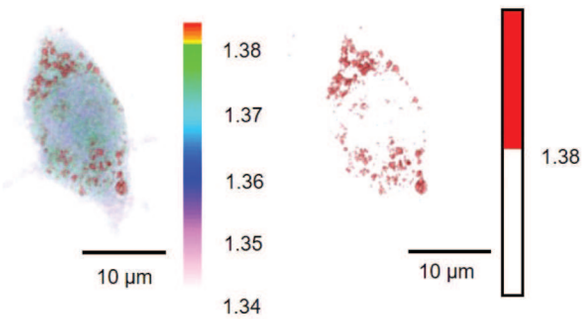
4D HT timelaps



Nano particle imaging

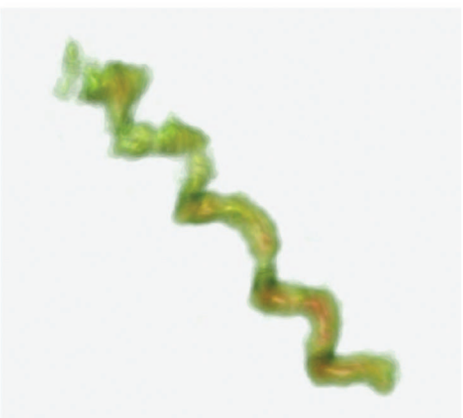


3D RI tomogram of HeLa cells treated with GNPs



GNPs segmentation from 3D RI tomogram

3D HT image of bacteria

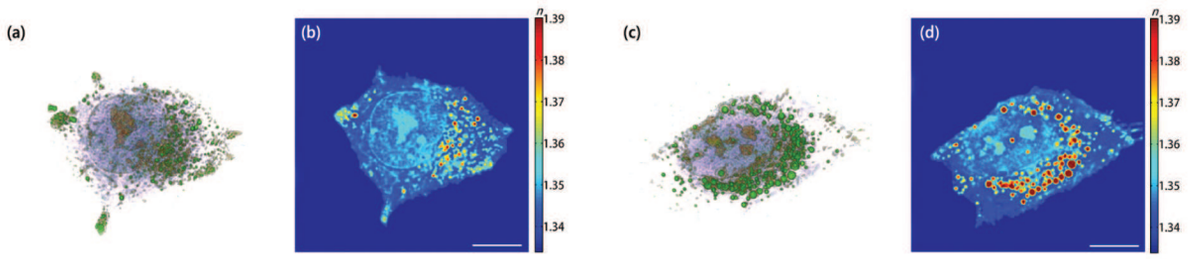


Advanced Optical Materials, DOI: 10.1002/adom.201600617

3D HT image of plankton

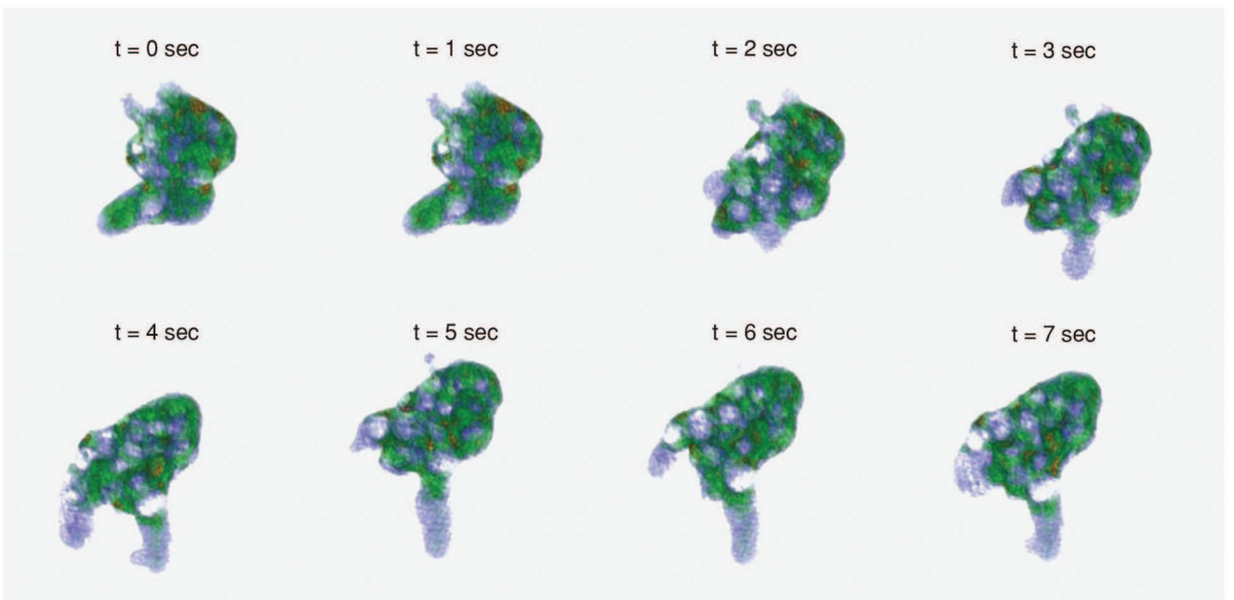
Journal of the Optical Society of Korea Vol. 18, Issue 6, pp. 691–697 (2014)

Lipid imaging



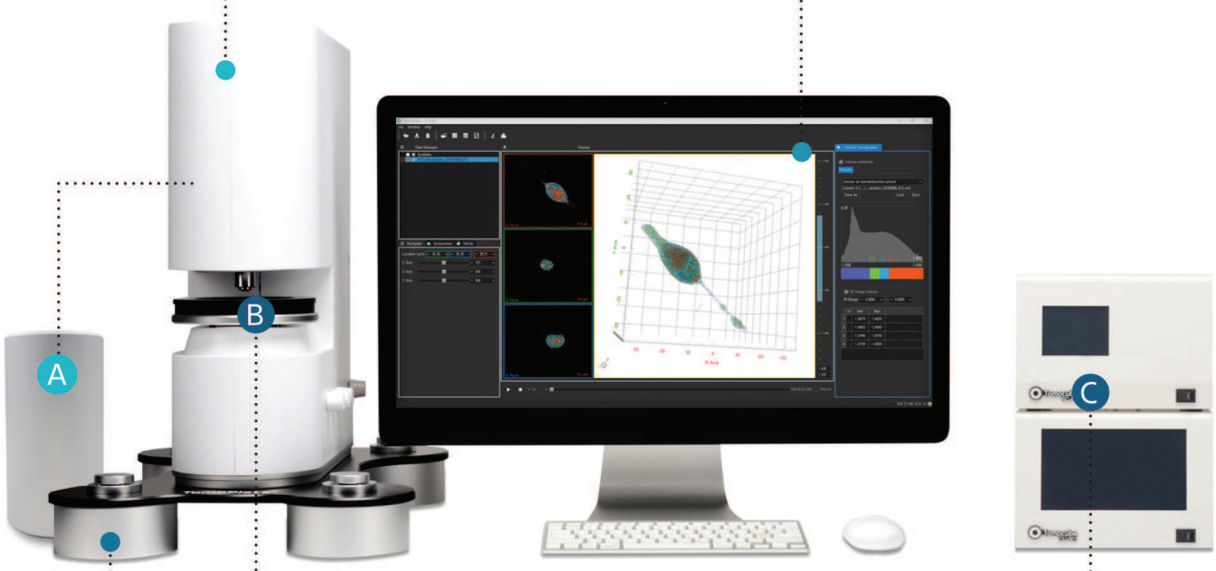
3D RI tomograms of lipid droplets in live hepatocytes. (a,c) 3-D rendered isosurface image (b,d) Cross-sectional slice phase images of 3-D RI distribution (Scientific Reports 6:36815 (2016))

Micro organisms



HT Timelaps images : Amoeba movement

System



01 HT-1
Microscope Body, HT-2, LED **A**

02 TomoStudio™
Software for HT series

03 TomoPlate
Anti-vibration plate for HT series

04 TomoChamber
TomoChamber, the incubator for HT-1, consists of **B**. stage top incubator and **C**. controller

Technical specification

Technical specification			
Model		HT-1S	HT-1H
Objective lens		60x NA 0.8	60x NA 1.2 (Water immersion)
Optical resolution	Lateral resolution	166 nm	110 nm
	Axial resolution	1 ㎛	356 nm
Reconstructed voxel resolution	Lateral resolution	166 nm	110 nm
	Axial resolution	332 nm	220 nm
Field of view		max. 80 ㎛	
Depth of field		max. 40 ㎛	
Imaging speed		150 fps (2D holography)	
		2.5 fps (3D holography)	
Light source (Laser)		532 nm, 0.05 mW, laser class 1	
Max. illumination angle in the sample plane		53°	63°
Microscope body		Fully motorized	
Size (W x D x H, mm)		445 x 180 x 500	
Weight		23 kg. / 51 lbs.	
Power requirement		100~240 V, 50 / 60 Hz, 1.5 A, 100 W	

HT-2 fluorescence speicification		
Model	HT-2S	HT-2H
Light source	Three LEDs for triple channel (λcenter = 385 nm, 470 nm, 570 nm)	
Lateral resolution	~ 350 nm	~ 220 nm
Axial resolution	~ 1.6 ㎛	~ 0.7 ㎛
Field of view	80 ㎛ x 80 ㎛	
Imaging	2D/ 3D/ 4D	
Maximum exposure	1 sec	
Life time	> 10,000 hrs	

Environmental requirement	
Temperature	15℃ ~ 30℃, It has to be ensured that the airflow of the air-conditioner is not directed toward the system
Humidity	< 65%

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