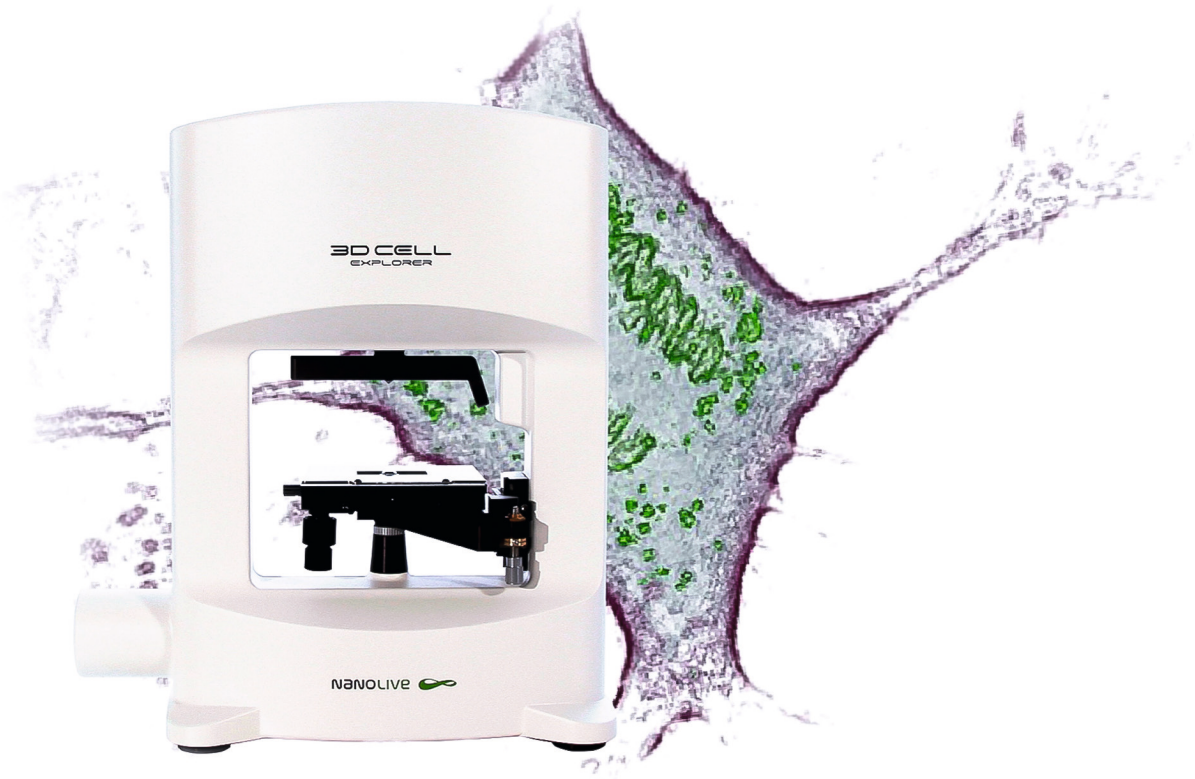
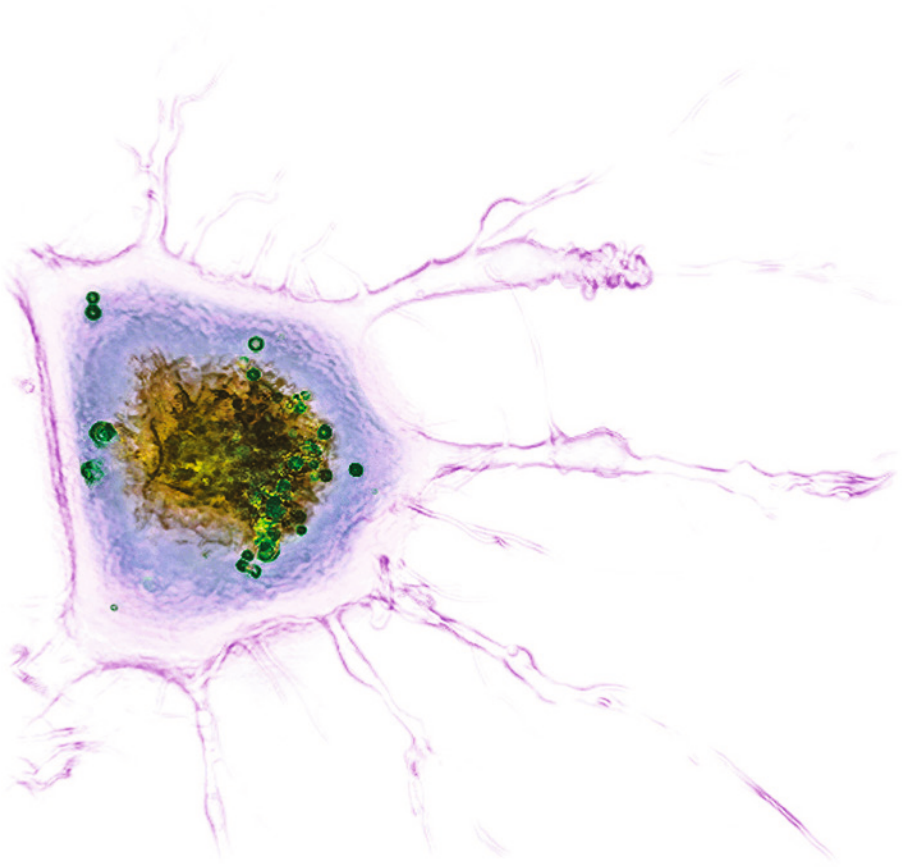
NANOLIVE
Looking inside life

3D CELL EXPLORER

A Revolutionary Tomographic Microscope To Look Instantly Inside Living Cells In 3D





Every Cell is unique and has its own complex structure

We have developed a disruptive technology which, for the first time, allows users to explore instantly the inside of a living cell in 3D without the need for any label or other invasive methods.

A self-adjusting, holographic & tomographic microscope

3D Cell Explorer

The 3D Cell Explorer is a non-invasive microscope that can image cells & tissues *in vitro* instantly and in 3D without any stain or label. Through a combination of holography and rotational scanning the system measures precisely the distribution of the physical refractive index (RI) within the cell (in 3D and time-lapse). Thanks to its completely self-adjusting optics, the best imaging results are always guaranteed – whatever the environment is (fundamental patent US 8,937,722 & EU WO 2011/121523).

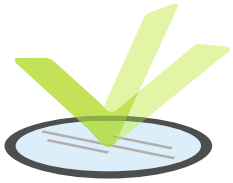
Inside the 3D Cell Explorer.

Technical Specifications	
Resolution	Δx,y = 200nm; Δz = 400nm
Field of view	~80µm
Depth of field	~30µm
Tomography frame rate	0.5 fps 3D image rate with full self-adjustement
Objective	air with 60x magnification, low power laser (λ=520nm, sample exposure 0.2mW/mm²)
Accessible sample stage	60 mm of free access to the sample stage for sample manipulation

Hardware highlights

UNIBODY CONCEPT

The revolutionary intuition we had at Nanolive, was to reduce structural complexity to one unique basic component – a unibody industrially derived from a single piece of aluminum. Thanks to this simple design, the 3D Cell Explorer is thin, light, simple and stable.



SELF-ADJUSTING LASER

To achieve optimal results for every measurement, the optics of our microscope are completely self-adjusting on sample conditions (e.g. media evaporation).

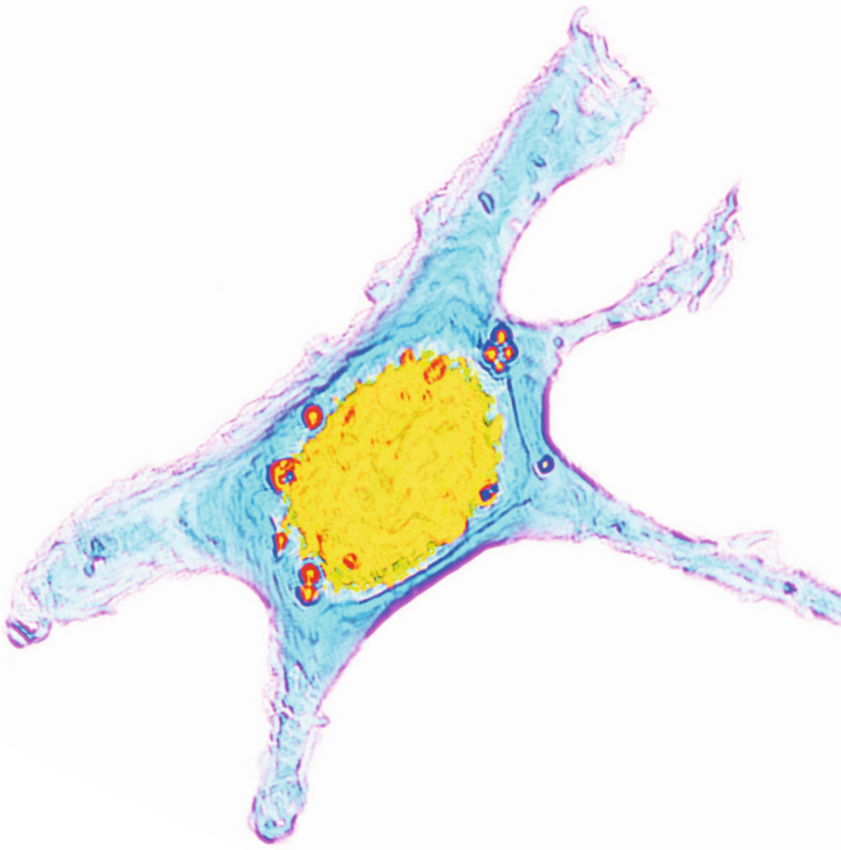
LOW POWER ILLUMINATION

Our 3D Cell Explorer uses a low power laser (Laser class 1: 0.2mW/mm2): No goggles required.

FAST ACQUISITION

A full 3D image of your cell will be loaded to your screen every two seconds.

The ultimate live cell imaging tool



With the 3D Cell Explorer, for the first time ever, you are free to perform long-term observations of your cells without any invasion and in a quantitative way, based on their own physical properties (refractive index).

User friendly

Cell friendly

Discovery friendly

User friendly

NO SPECIAL SAMPLE PREPARATION

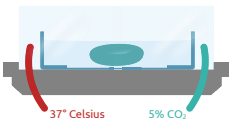
Our disruptive technology allows, for the first time, to explore instantly the inside of a living cell in 3D without the need for any labeling or other invasive methods. No risk for falsification, we measure the cell's structure itself and not attached molecules.

NO BLEACHING

You are able to take continuous images of your living cells as often as you want and for as long as you want without worrying of any bleaching effect.

INFINITE LIVE CELL IMAGING

The intensity of our laser light is comparable with environmental light. No safety goggles required. Observe your cells as long as you wish in their natural state, no phototoxicity.

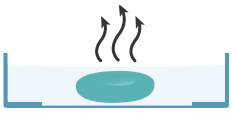


TOP STAGE INCUBATOR FRIENDLY

The microscope stage is perfectly compatible with classical top stage incubators. You are able to observe your cell's behaviour in their natural environment (5% CO_2 & 37°C).

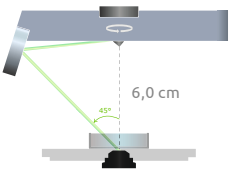
COMPATIBLE

Compatible with live cell imaging consumables (dishes or slides).



SELF-CALIBRATION

Self-adjusts on environmental changes: you do not need to worry for any environmental change of your sample. The microscope self-adjusts on your sample and adapts to changes in the imaging condition.



ACCESSIBLE SAMPLE STAGE

Open sample stage (60 mm). Change or move your samples easily.

WHITE LIGHT GUIDED SEARCH

Look for your ROI and focus on it through our white light mode.

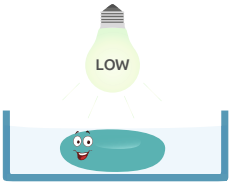
Cell friendly

NO STAINS

No need to kill (fix) your cells and no need to intrude them by adding chemical markers.

NO CELL SWELLING

No labeling derived cell swelling.



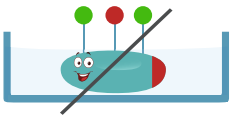
NO PHOTOTOXICITY

Our 3D Cell Explorer uses a low power green laser light (λ = 520nm, 0.2mW/mm^2). No photo-toxicity was observed even after days of continuous imaging in presence of a top stage incubator.

NO GENETICALLY MODIFIED CELLS (GMC)

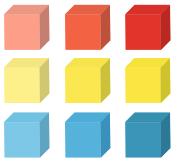
No need to genetically modify your cells to make them express exogenous proteins in order to see them.

Discovery friendly



NO MARKERS UNCERTAINITY

No result uncertainty due to stain efficiency or long linkers.



QUANTITATIVE 4D DATA

The different cell organelles have different compositions. The 3D Cell Explorer measures their different RI and allows quantitative analysis.

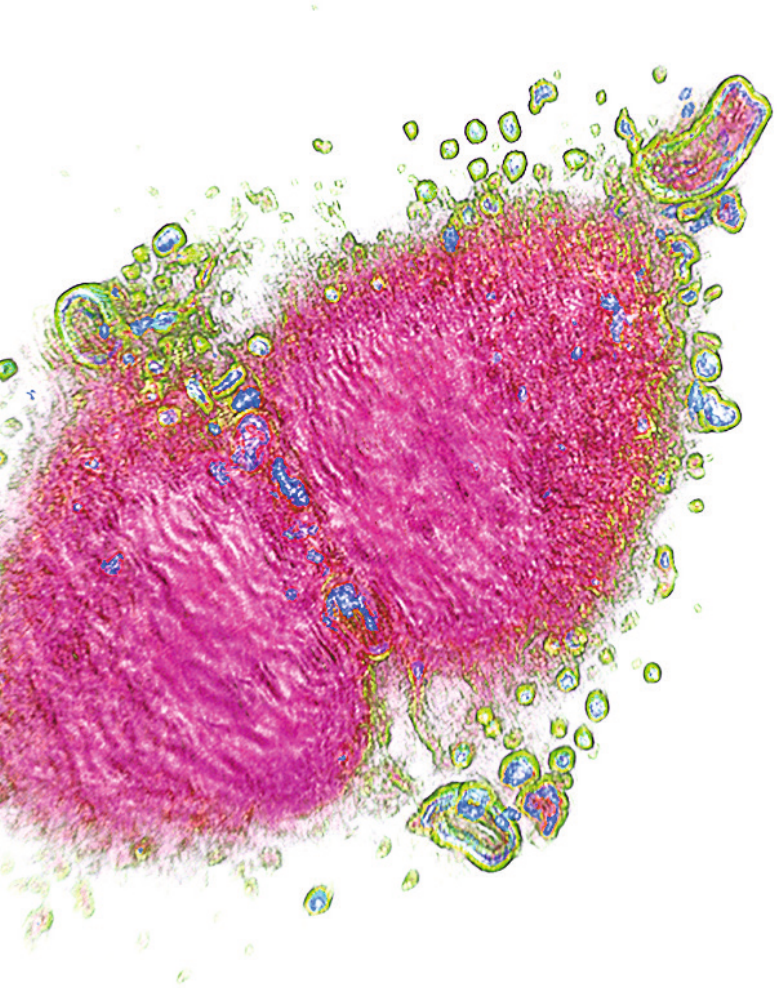
CORRELATIVE

You can compare our technology with other complementary technologies (e.g. Fluorescence, EM).

NOVELTY

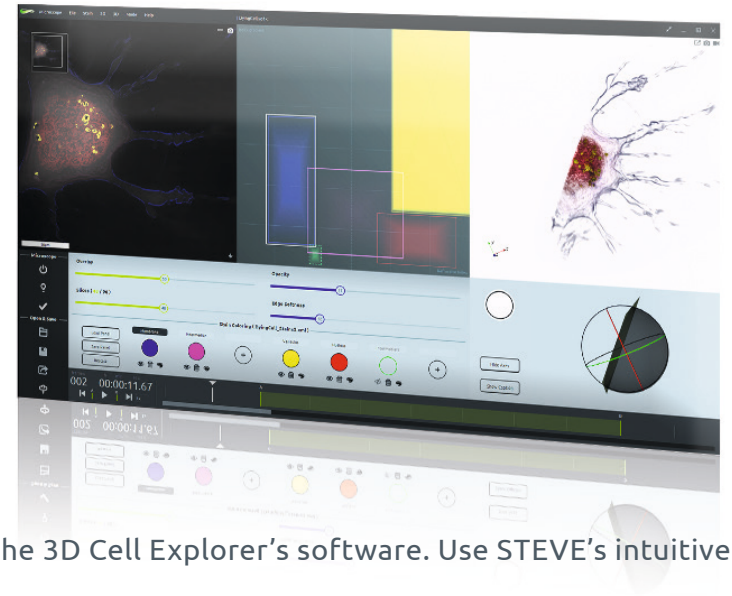
You will be able to investigate your cells as no one before:

- No alteration of their normal physiology
- No time limitation
- Digitally stain your cell's part of interest and compare them quantitatively

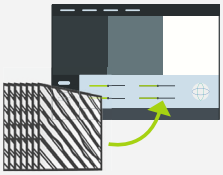


STEVE

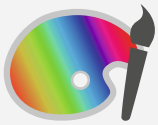
The intuitive and comprehensive software to explore your Cell data



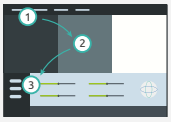
STEVE is the 3D Cell Explorer's software. Use STEVE's intuitive interface to control the microscope in real-time, explore your data using interactive digital stains and perform quantitative analysis on your measurements.



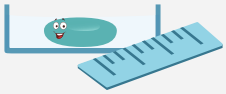
Real-time 3D visualization



Digital staining based on RI



Intuitive GUI

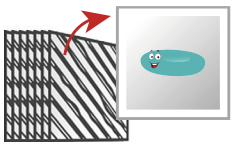


Cell metrics

DOWNLOAD AND TRY STEVE FOR FREE!

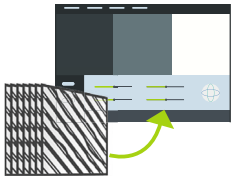
http://nanolive.ch/software/

Software features



COMPUTATIONAL IMAGING

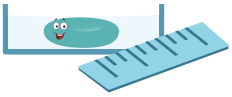
The microscope registers one hundred holograms per rotation. The holograms are raw data which are incomprehensible for the user. Nanolive's processing technique, based on complex deconvolution, treats these data and displays a comprehensible 96 z-stacks cell image in grey scale every two seconds. Furthermore, it corrects for many imaging errors that otherwise would require extremely expensive optical components and ultra-precise alignment.



REAL-TIME

STEVE allows for the acquisition and processing of cell data in real-time.

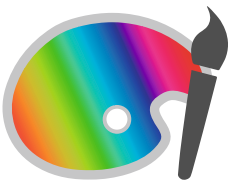
- One 3D cell image on the screen every 2 second
- Follow cell's kinetics and cell's dynamic live
- Instant verification of microscope alignment (self-calibration performed when necessary)



CELL METRICS

Measure and monitor your cell metrics during cell cycle or after the application of external stimuli:

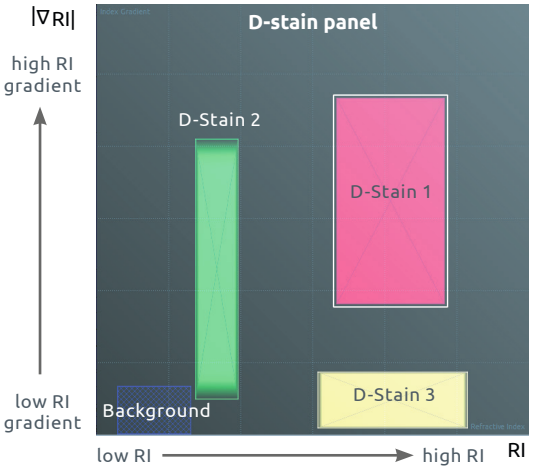
- Area
- Thickness
- Volume
- Texture/Roughness
- Activity (moving from frame to frame)

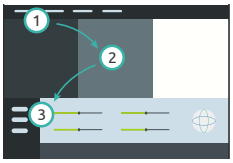


DIGITAL STAIN (D-STAIN)

Explore your data in 3D using our interactive digital stains and even perform quantitative analysis on your measurements.

- Quantitative staining based on physical markers (refractive index (RI) & RI gradient)
- Easy management of your digital stains (creation, edit, enable/disable, delete, export, save)
- Compare your results with other technologies, identify the exact refractive index range of your ROI
- Compatible exportation of digital stains for analysis and comparison

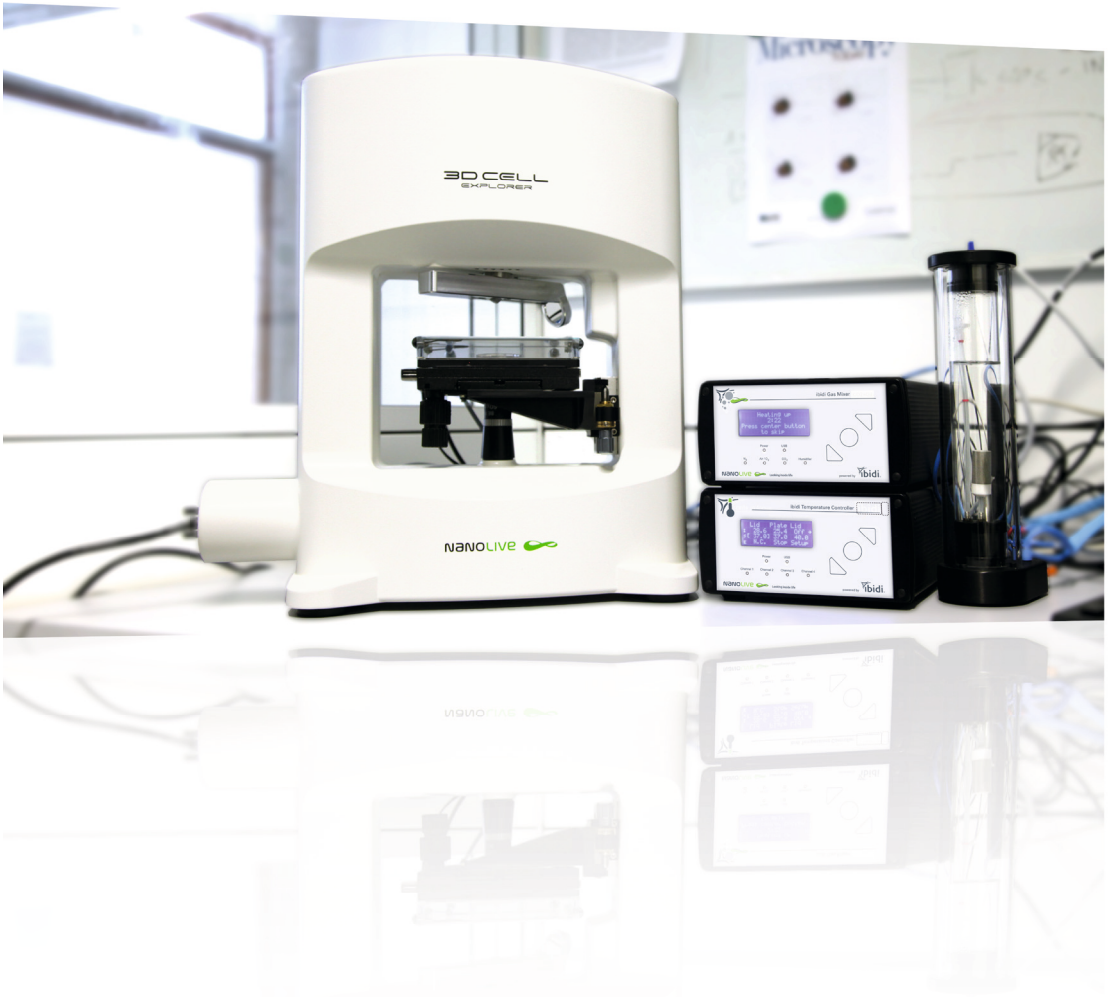




INTUITIVE GUI

STEVE's intuitive graphical user interface has been specifically conceived for fast learning. All options and commands necessary for acquiring and staining images are displayed on the main screen.

Accessories



The Nanolive-ibidi top-stage incubator

This novel combination allows for non-invasive 4D live cell tomography (every two seconds) for several days in physiological environmental conditions.

The Nanolive-ibidi top-stage incubator brings all the required incubation controls directly on the stage of your 3D Cell Explorer. Temperature, humidity and CO_2 and O_2 gas concentrations can be meticulously regulated during your time-lapse cell experiments to give you the most accurate live cell results!

The Nanolive-ibidi incubator is an especially adapted solution:

- "plug & play" by perfect fit on the microscope stage
- High stability by magnetic adhesion to the 3D Cell Explorer stage
- Best imaging quality through self-calibration and optical quality
- Works on any cell confluency (up to multi-layers)
- Compatible with traditional live cell consumables (e.g. fluordish & slides)
- Exceptional customer support provided by ibidi

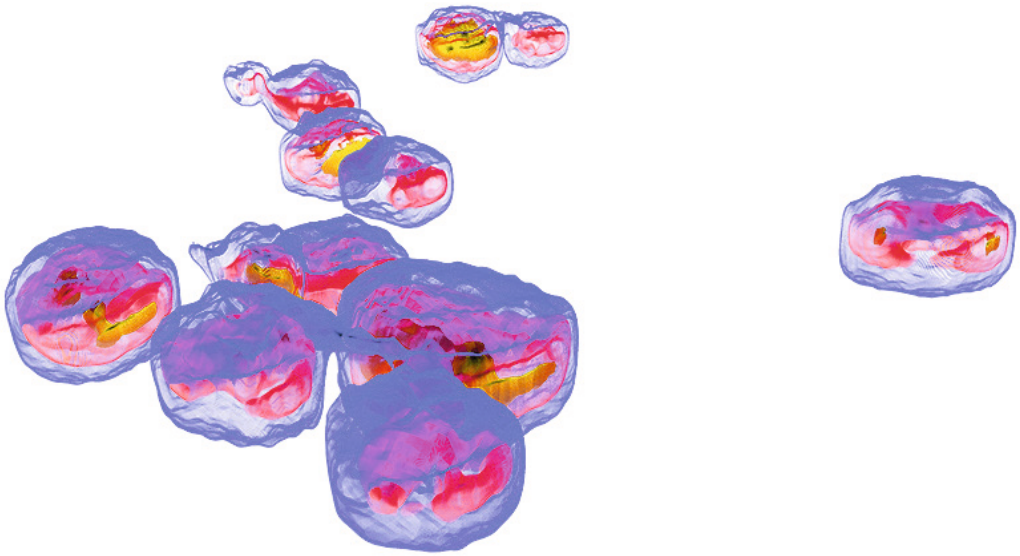
Computer Technical Specifications

Each of the requirements are absolutely necessary for the 3D Cell Explorer to operate correctly. *

PC recommendation & specifications	
CPU	1.5 GHz or faster multi-core CPU
CPU Memory	minimum 8GB DDR3 RAM
Hard disk	450 MB free space for STEVE and 1 TB for acquisition data
GPU**	NVIDIA GTX or Quadro card with a minimum **2 GB GPU RAM (dedicated)**
USB ports	2 ports, minimum one **USB 3.0 port**
Operating System	64-bit versions of Windows Vista, 7, 8 or 10. (**Updated drivers:** you need to have the latest Nvidia Graphics Card drivers, USB 3.0 drivers and fully updated Windows)
In addition	Internet access for STEVE installation and for the newest updates.

*We are happy to provide you with a list of computers and laptops that we have tested and validated. Please contact us.
**If you are unsure about the minimal requirements, please contact us for an updated list of tested GPU cards.

A tool for discovery

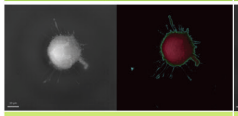
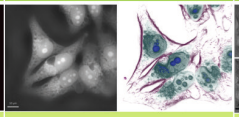
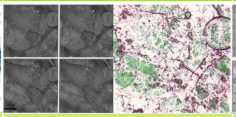
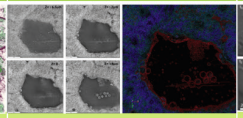
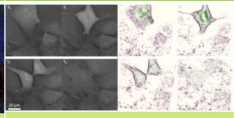


Applications

The 3D Cell Explorer is a tool for discovery and we are just at the beginning of exploring all the potential fields of application. There are no boundaries.

Thanks to this new technology, we believe that many discoveries on living cells will be done and will extend our understanding of life, diseases and effect of drugs.

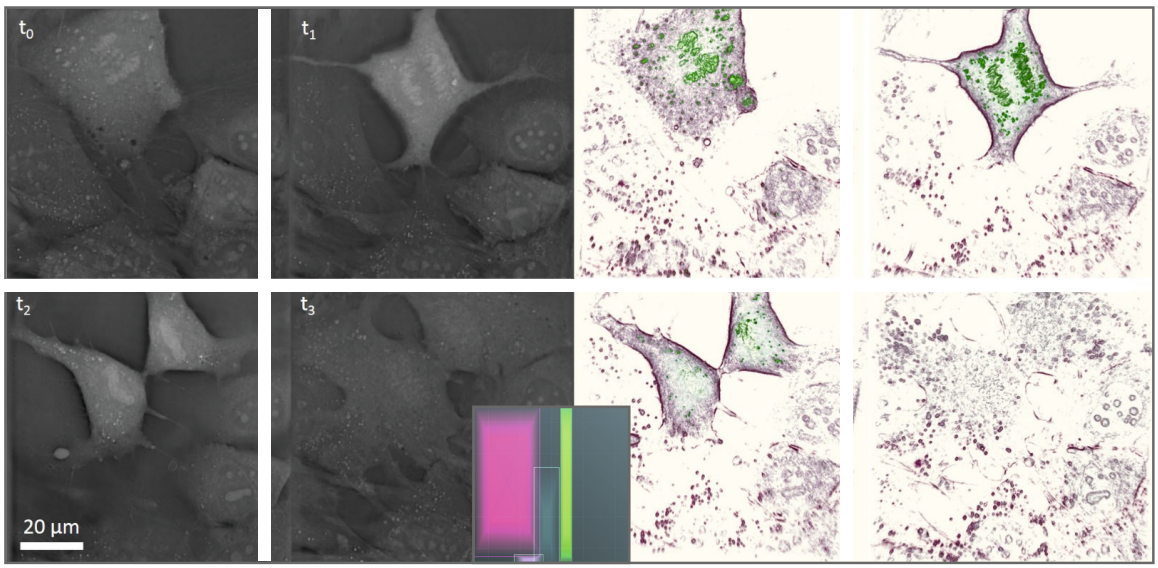
Cell imaging conditions enabled by the 3D Cell Explorer:

Single cell	Cell culture	Cell's multi-layer	Tissue slices	Time-lapses
				
Live	Low confluent	Live	Paraffin	Single cell
Fixed	High confluent	Fixed	Frozen	Cell cultures

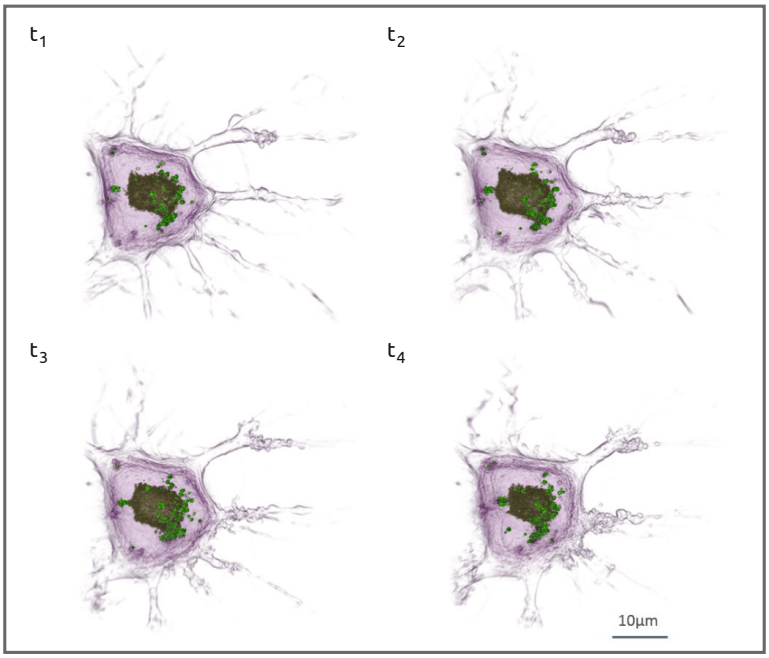
The 3D Cell Explorer performs 3D and real-time *in vitro* cell imaging on

A. SINGLE CELL MORPHOLOGY, KINETICS & DYNAMICS

- Death
- Remodeling
- Migration
- Adhesion
- Intracellular trafficking
- ...



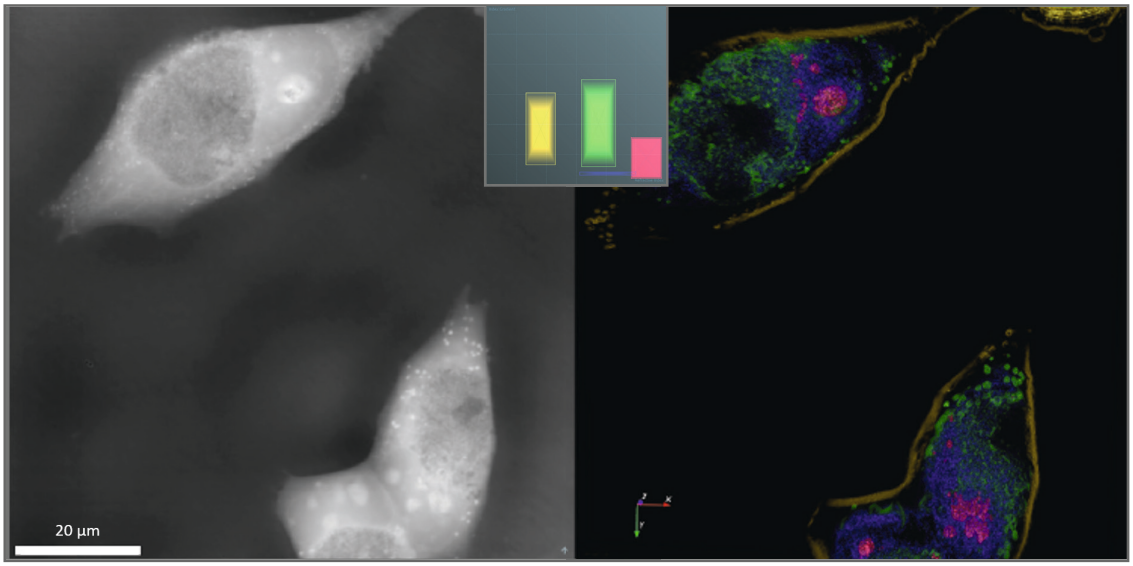
Mouse Fibroblastic Reticular Cell (FRC) during mitosis. On the left 2D slice (refractive index map by 3D Cell Explorer). On the right, 3D reconstruction obtained with STEVE. Colors are RI specific. D-stain panel: membrane is pink, condensed DNA is green and normal DNA is light blue.



Mouse Fibroblastic Reticular Cell (FRC) during apoptosis.

B. INTERACTIONS & REACTIONS

- Cell-cell
- Cell-bacteria
- Cell-virus
- Inorganic material
- Stimuli
- Drugs & Toxicity
- Nanomaterial internalization/ trafficking
- ...

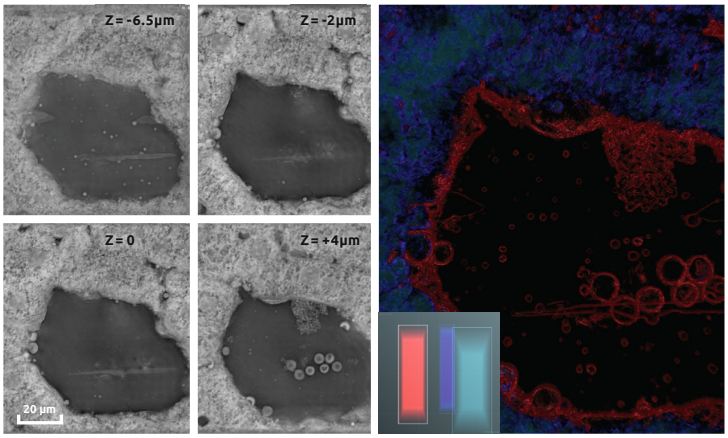


HeLa cells infected with Chlamydia. On the left 2D slice (refractive index map by 3D Cell Explorer).
On the right, 3D reconstruction obtained with STEVE. Colors are RI specific. D-stain panel: Chlamydia is green, the nuclei blue, the nucleoli are red and the membrane yellow.

Paraffin fixed Mouse skin sections (8 µm).

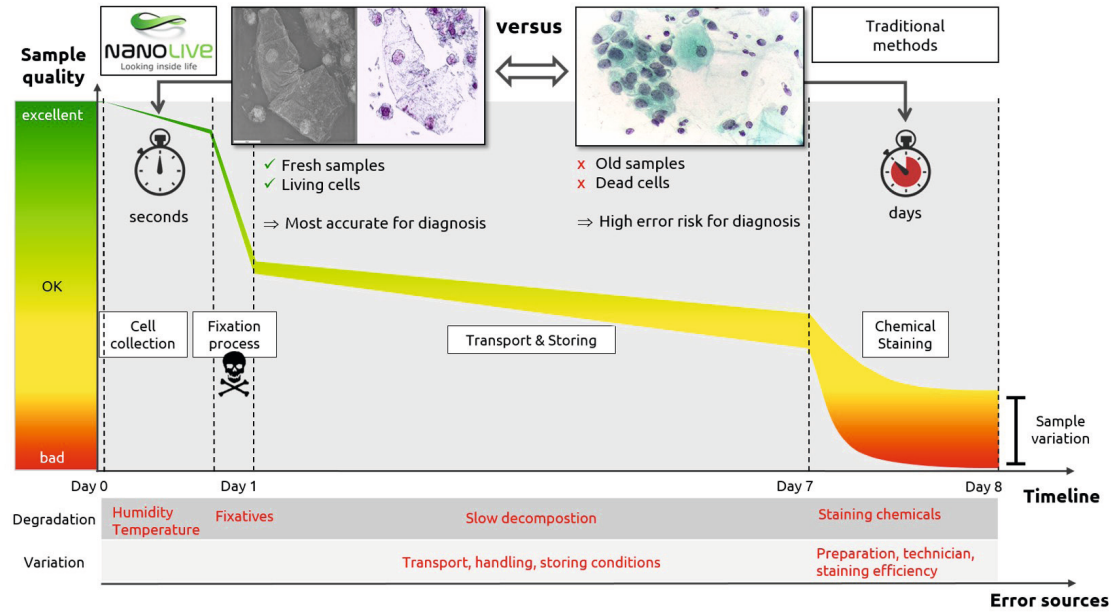
C. STAIN-FREE HISTOLOGY & HISTOPATHOLOGY

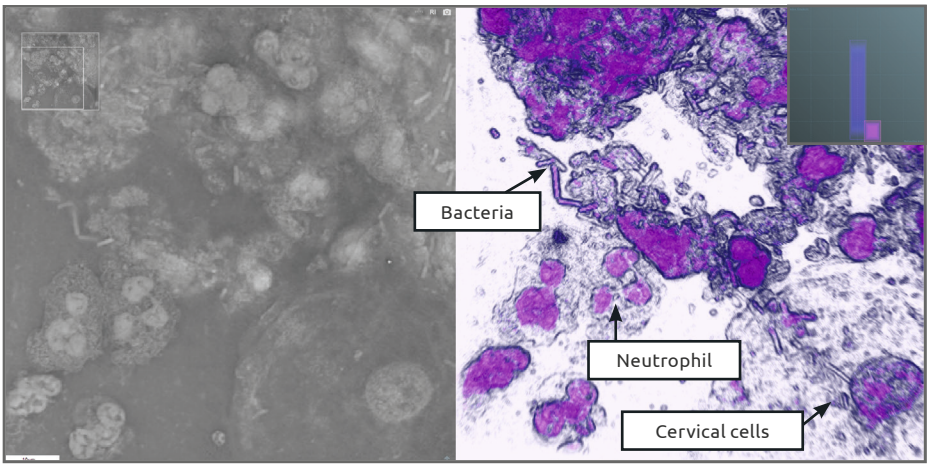
- Tissues morphological analysis
- 3D Tissue characterization
- Cancer diagnosis
- ...

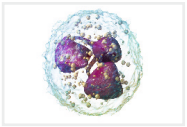


Fixed 8um slice of mouse liver with a blood vessel. Sample was fixed in 4% PFA and embedded in OCT.
On the left 2D slices at different depth of field (refractive index map by 3D Cell Explorer). On the right, 3D reconstruction obtained with STEVE. Colors are RI specific. D-stain panel: Blood is red, and hepatic tissue is blue.

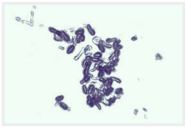
D. STAIN-FREE CYTOPATHOLOGY



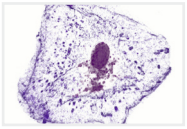




Neutrophil



Bacteria

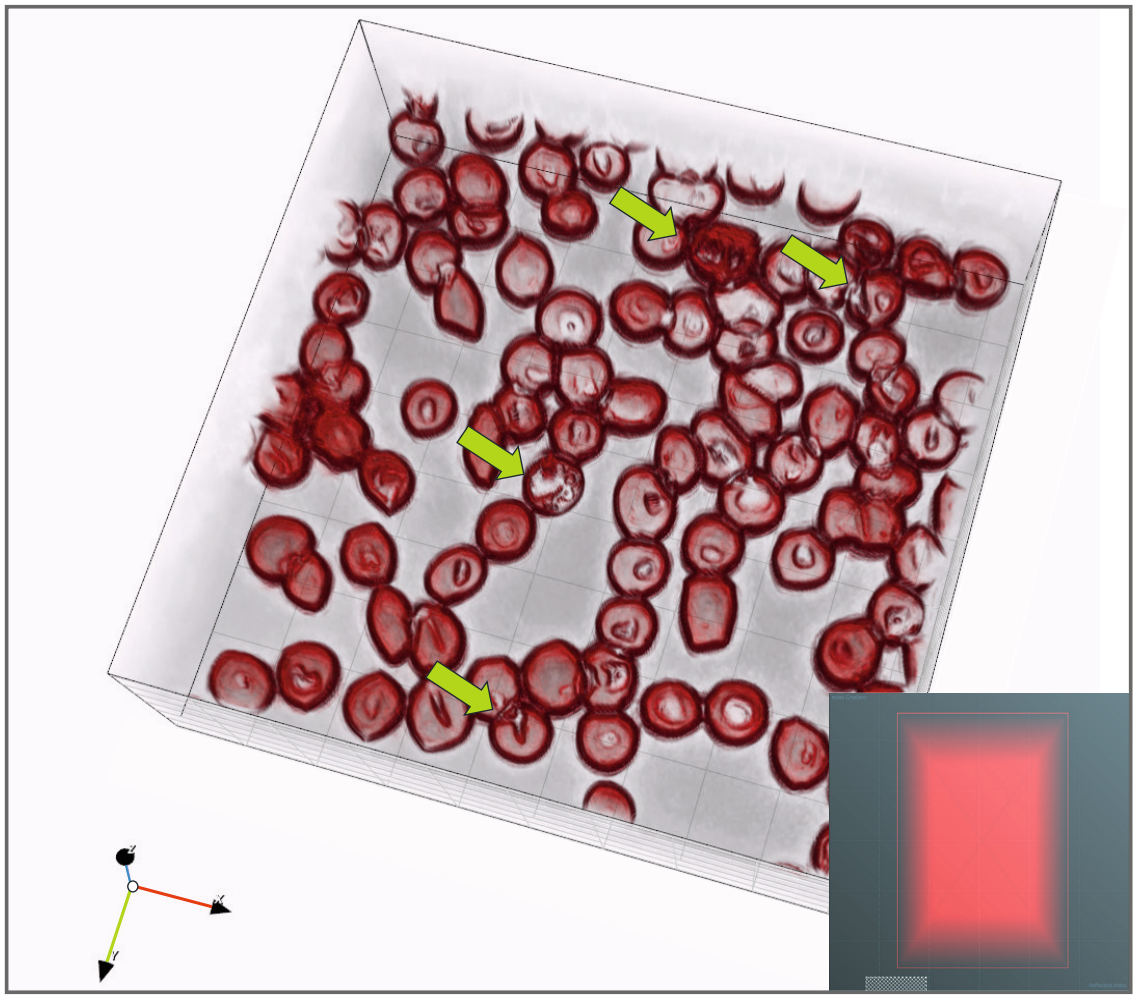


Cervical cells

A micrograph of an cytopathology specimen (Pap-test). Inflammatory cells fighting bacteria among normal cervical cells. On the left 2D slice (refractive index map by 3D Cell Explorer). On the right, 3D reconstruction obtained with STEVE. Colors are RI specific. D-stain panel: membrane is purple, nuclei are pink.

- Cell nuclear evaluation
- Fast Pap-smear analysis
- Needle aspiration biopsy
- Cancer diagnosis
- Infection diagnosis
- Microbial infections: parasitic, viral, and/or bacterial
- Reactive changes
- Immune reactions
- Cell aging
- Amyloidosis
- Autoimmune diseases
- ...

E. STAIN-FREE BLOOD CYTOLOGY



Human Blood sample infected with Plasmodium malariae. Green arrows indicate few infected cells. Colors are RI specific. D-stain panel: red blood cells were D-stained in red, Background is grey.

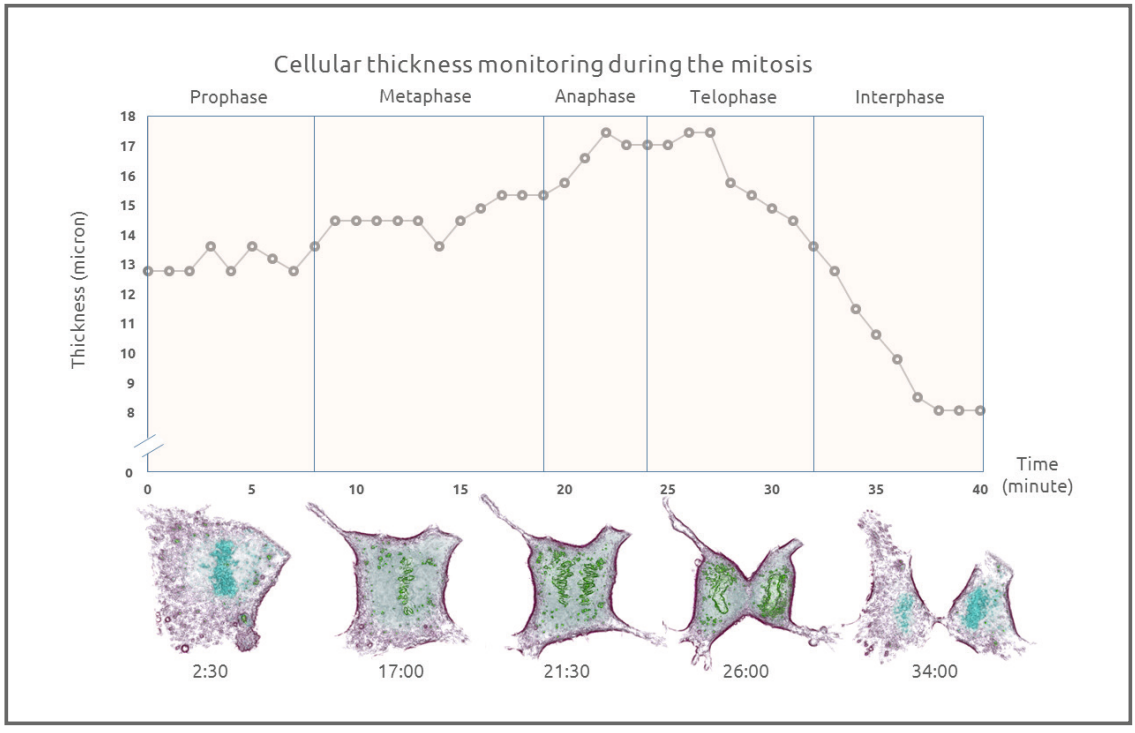
Drop of blood based diagnosis of:

- Red blood cells count (CBC) (e.g. Anemia)
- White blood cells count (e.g. Mononucleosis)
- Platelets count (e.g. Leukemia, Myeloma)
- Microorganism infections (e.g. Malaria, Chlamydia trachomatis)
- Monitor size and shape of the red blood cells (e.g. Anemia)
- Shape, size, and relative numbers of white blood cells (e.g. Sickle-cell disease, G6PD deficiency)

F. CELL'S METRICS

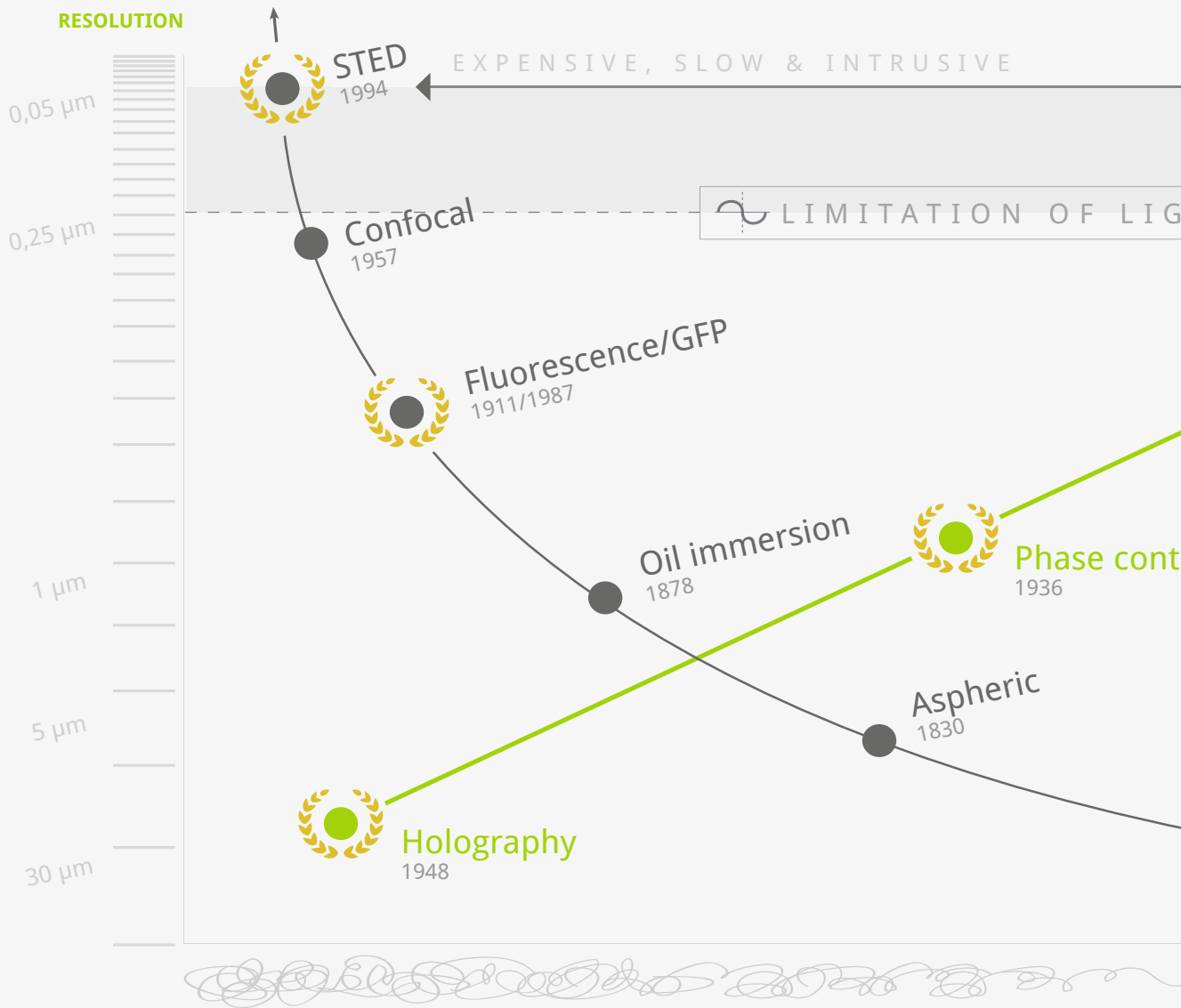
Metrics

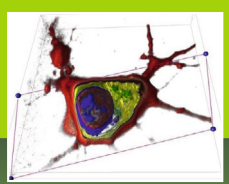
- Area
- Thickness
- Volume
- Texture/Roughness
- Irregularity
- Activity (moving from frame to frame)
- Density distribution *histogram of RI
- RI segmentation (d-stains)



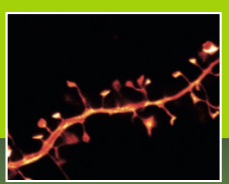
Cellular thickness monitoring during mitosis. The cell rounds up, gets thicker, reaches a maximum of 17 um during late anaphase and then goes back to be flat (8um) when replication is completed. Cell thickness was monitored during the mitotic process with high precision (500 nm axial resolution).

History of Optical Microscopy & Cell Biology

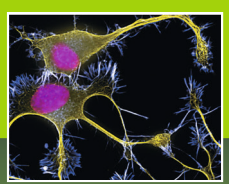




3D Cell Explorer
Nanolive , 2015
Neuron

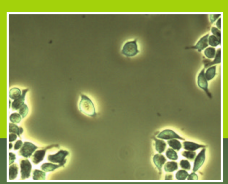


STED
Hell, 1994
Nerve cell
Nobel Prize 2014

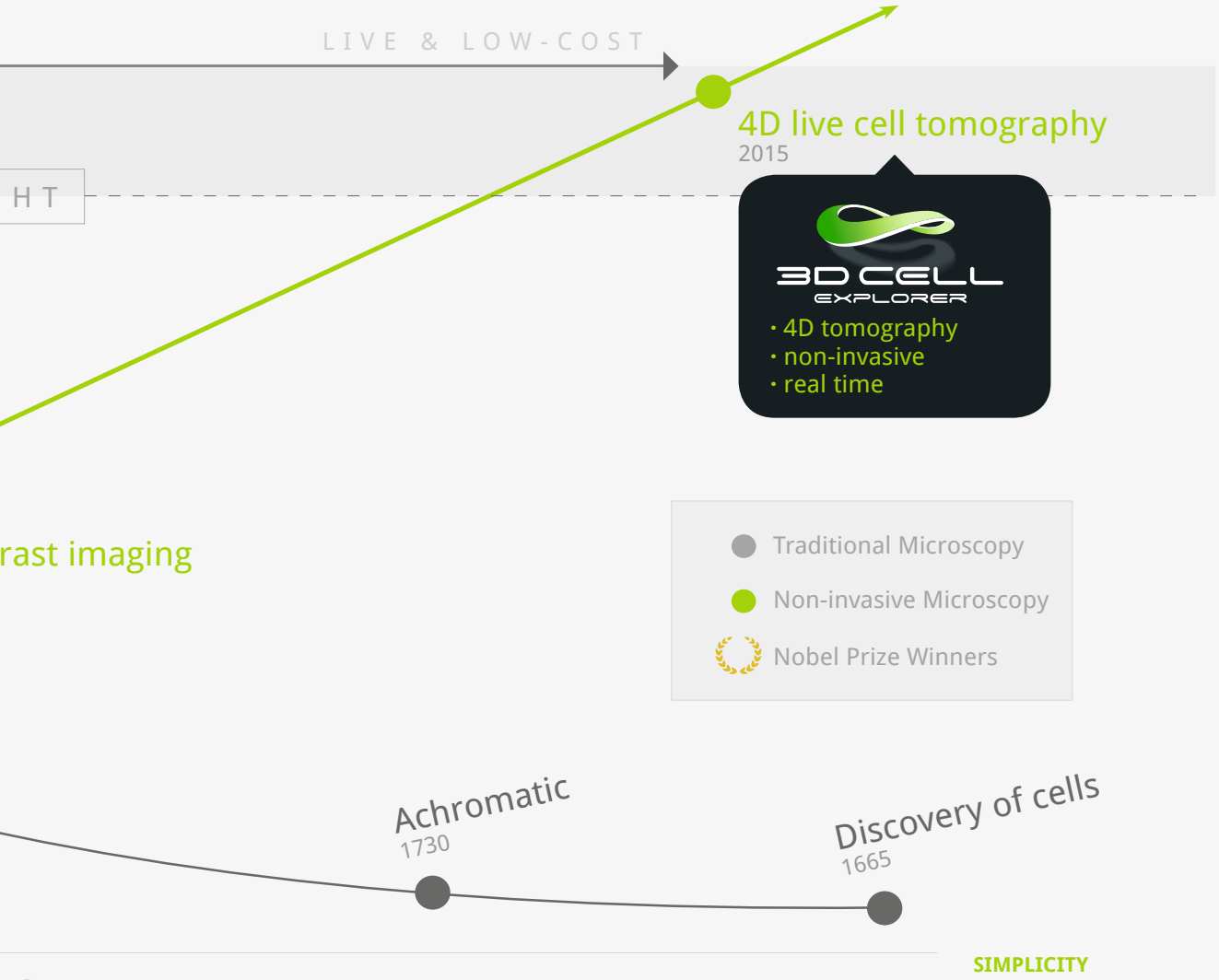


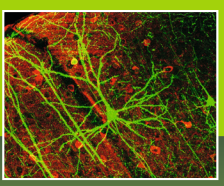
Confocal
Minsky, 1957
Neuron

Holography
Gabor, 1948
Fibroblasts
Nobel Prize 1971

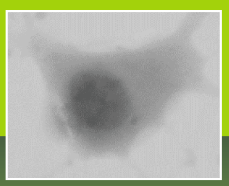


Phase contrast
Zernike, 1933
S. cerevisiae
Nobel Prize 1953



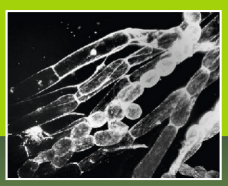


Fluorescence/GFP
Heimstadt, 1911 & Prasher, 1987
Neuron
Nobel prize 2008



Oil immersion
Abbe, 1878
Neuron

Aspheric
Lister, 1830



Achromatic
Hall, 1730
staminal hairs of Tradescantia virginiana

Discovery of cells
Hooke, 1665
Cork cells

Our Vision

WE ARE SCIENTISTS, WORKING FOR SCIENTISTS.

Our belief is that each and every biologist, researcher and physician should be able to explore and interact instantly with living cells without damaging them.

We want to support the study of how living cells and bacteria work, evolve and react, thus building a solid base for new drugs and therapies, in order to enable breakthrough researches.

This is the reason why we have developed the 3D Cell Explorer: with the 3D Cell Explorer, researchers, students and medical doctors can directly experience what happens inside the living cell – in real time!

NANOLIVE
Looking inside life

AWARDS

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