CELLSENSE TECHNOLOGIES

DISCOVERER

BRILLOUIN MICROSCOPE

Mechanobiology Tools Made in Berlin

- Automated, high-resolution imaging
- Quantitative mechanical measurements
- Effortless integration with advanced light microscopes
- Revolutionary workflow-based software
- Ideal for studying mechanobiology in 3D

Studying mechanobiology in 3D with the Discoverer™ from CellSense

Brillouin microscopy is a label-free, non-contact, and non-invasive imaging technique

The CellSense Discoverer™ is a Brillouin microscope that combines the highest performance with revolutionary ease of use in an automated system. Its label-free, non-contact, and non-invasive nature allows users to measure mechanical properties of fragile biological samples, from cells to small organisms, without causing harm or damage. The Brillouin method provides clean and unaltered measurements without dyes or markers. The Discoverer™ bridges the gap between force techniques like AFM, indenter, or tweezers, and 3D techniques such as confocal, multiphoton, or light-sheet microscopy. It combines the ability to measure mechanical properties like stiffness or viscosity with the 3D capabilities of confocal, multiphoton, or light-sheet microscopy.

Brillouin microscopy is an optical method to measure mechanical properties in the sample volume

Technically, it is similar to confocal microscopy. Each pixel contains information about local stiffness or viscosity. Consequently, the user obtains a data cube filled with mechanical properties in 3D.

Perfect for living cells, organoids, tissues, and small organisms

The Discoverer™ system features a 780 nm laser with low phototoxicity that minimizes damage to samples during prolonged studies. Users can measure mechanical properties in 3D in a passive way, without any mechanical contact. This non-invasive optical measurement of mechanics is a significant benefit for living samples.

The Discoverer™: combining the latest Brillouin technology with superb flexibility and ease-of-use

The Discoverer™ is designed for maximum mechanical and thermal stability, compatible with both inverted and upright microscopes for long-term experiments on living samples. It features the latest Brillouin technology, including a multi-stage interferometric spectrum detector, optimized beam path, high-quality optical components with perfected coatings, and innovative automation features.

The Discoverer™ is a masterpiece of engineering. Its revolutionary software design enables users to obtain quick results without being experts. It offers a wide range of accessories, modes, and features, providing unparalleled flexibility for any application.

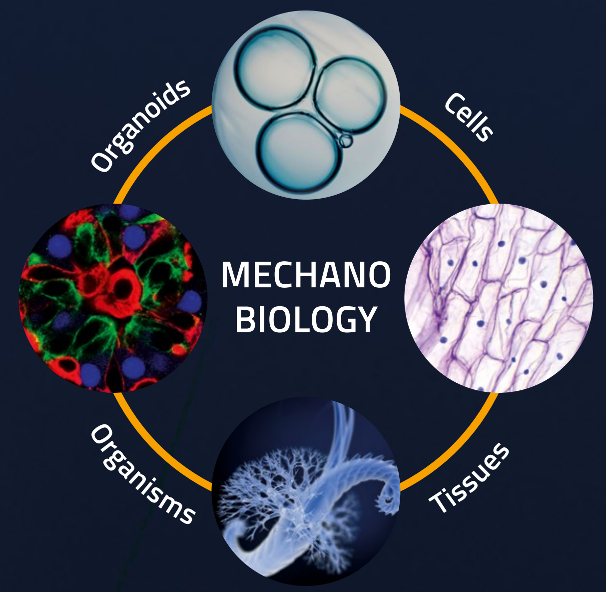
"For more than a decade, I've had the privilege of being part of the transformative journey of Brillouin microscopy. What began as breadboard setups is now on the way of becoming a sophisticated product with the promising work being done by CellSense. Our goal has always been to access the mechanical properties of complex biological samples in 3D. Due to its non-invasive and label-free nature, Brillouin microscopy is perfect for studying living specimens. While CellSense is still in the product launch phase, their efforts towards a turnkey design hold great promise for making this advanced technology user-friendly and widely accessible."

Dr. Giuliano Scarcelli · Associate Professor · Robert E. Fischell Institute for Biomedical Devices
University of Maryland · College Park

Spatial biology meets mechanobiology

Mechanobiology across scales

In recent years, AFM has been established as the gold standard for mapping the mechanical properties of cells, gels, and tissues. However, its surface-bound capabilities limit its access to volume information. This is where the Brillouin method excels. By extending mechanical property mapping into 3D, it allows users to study the mechanics of three-dimensional objects, ranging from cellular organelles and cells to spheroids, organoids, complex tissues, and organisms like zebrafish or C. elegans. Brillouin microscopy enhances conventional volume methods with new capabilities.



The Discoverer™: Designed for multimodal imaging

The Discoverer™ system is a newly developed add-on for motorized inverted or upright research microscopes. It is compatible with major microscope brands, including Zeiss, Leica, Olympus/Evident, and Nikon. The installation is quick and straightforward, taking only minutes to complete. The OptiBridge™ module from CellSense connects to a side port of the microscope body, seamlessly integrating the system. The motorized microscope body is fully utilized and controlled via the Discoverer™ software, enhancing the light microscope's capabilities with a mechanical imaging channel for true multimodal imaging. Developed by experienced professionals in mechanobiology instrumentation, the Discoverer™ is ready to use.

Brillouin microscopy in plant physiology with Discoverer™

The Discoverer™ enhances the study of plant physiology by providing precise measurements of mechanical properties in plant tissues. With Brillouin microscopy, researchers can perform non-invasive, label-free analysis of cell wall stiffness and viscoelasticity in living plants. This high-resolution, quantitative data helps to understand the mechanical behavior of plant cells and tissues under different environmental conditions. By mapping these properties in three dimensions, the Discoverer™ allows the detailed study of complex plant structures, such as leaves, stems, and roots.

"Understanding mechanical properties of organoids and tissues is crucial as these complex structures develop and mature. Changes in the mechanical properties of tissues often accompany disease. Studying these changes in patient-specific organoids provide novel insights into disease mechanisms and lead to the development of more effective treatments. Brillouin microscopy is a promising tool to non-invasively explore these mechanics throughout the volume at a cellular level, opening new ways in biomedical research and clinical diagnostics."

Dr. Mina Gouti · Stem Cell Modeling of Development & Disease
Max Delbrück Center for Molecular Medicine (MDC) Berlin

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Smart system design for easy operation and fast results

Easy operation is key

The Discoverer™ microscope is designed with the user in mind. Its integrated design eliminates the need for manual adjustments of optical or mechanical components. Simply mount the sample on the sample stage as usual and control the microscope hardware through the intuitive software user interface. Time-consuming steps are minimized to save the user's time.

Intelligent stiffness mapping of large sample areas with new tiling functionality

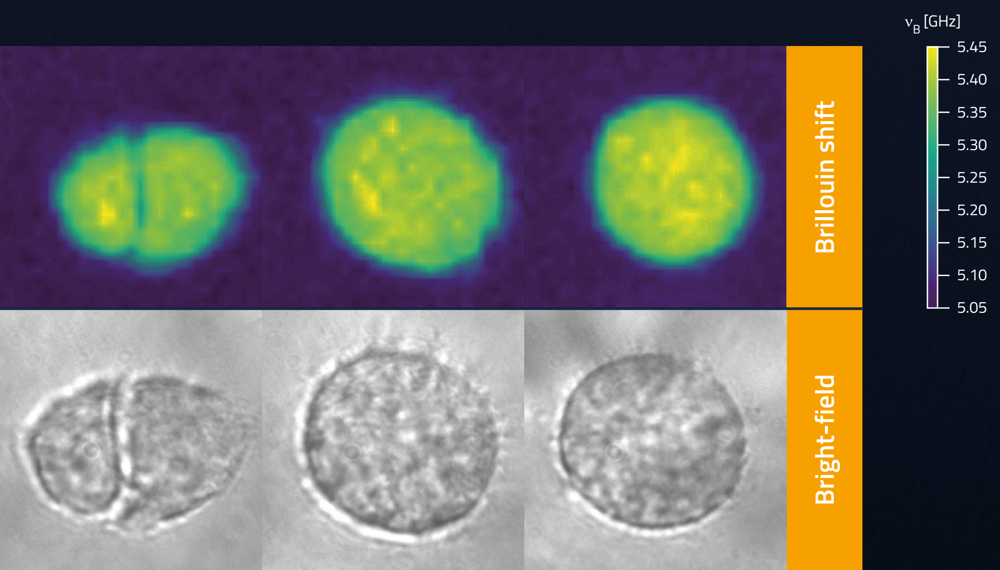
The control of the motorized sample stage allows direct access to large sample areas, with automatic movement to selected positions, grids, and mapping regions. The process begins with the PerfectOverlay™ mode, followed by selecting a region for optical tiling, which can extend up to millimeters in size. The whole sample is automatically brought into view by precise motor movements, making it easy to select regions and features for further investigation. Navigation from point to point is achieved with a single click, while MultiMap™ mode automates serial measurements across multiple maps.

Instrument setup and calibration routines are fully automated

Automation extends beyond position control, zooming, and focus. Time-consuming tasks, such as instrument setup and spectrum calibration, are fully automated, removing these burdens from the user's responsibilities.

"Brillouin microscopy holds great promise for biology and medicine by enabling detailed analysis of mechanical properties of complex biological samples in 3D. However, current home-made setups are not yet very user-friendly. The future establishment of this method in the field depends on bridging this gap. CellSense is on the way combining technical excellence with the development of a user-friendly and robust Brillouin microscope, making this advanced technique accessible to a broader range of researchers to enable challenging bio-imaging experiments."

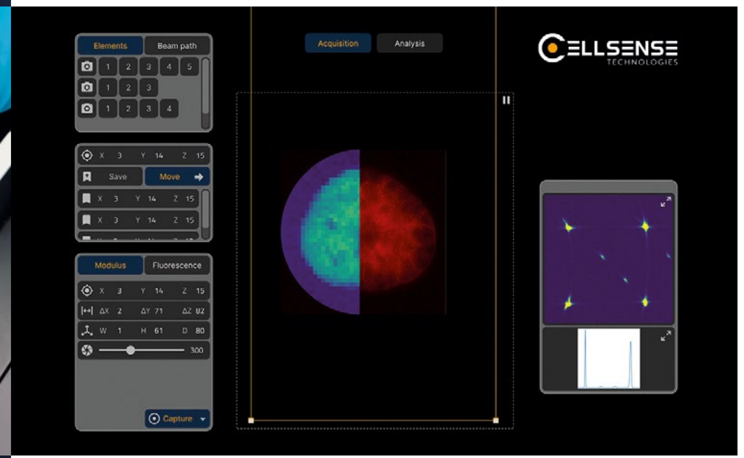
Dr. Robert Prevedel · Group leader EMBL Heidelberg



Brillouin microscopy scans and brightfield images of different mesenchymal stromal cells in a hydrogel matrix. The upper panel represent maps of the Brillouin frequency shift across cells, while the lower panel contains corresponding colocalized bright-field images, which were collected right before a Brillouin scan. For measurements, each hydrogel matrix sample containing cells was placed in a glass-bottom Petri dish and maintained at 37 °C using an on-stage incubator.

Sample courtesy: Prof. Dr. Georg Duda, Director Julius Wolff Institute, Berlin Institute of Health (BIH) at Charité – Universitätsmedizin Berlin, Germany

Powerful and intuitive workflow-based user interface



Software personalization developed for multi-user facilities

The needs of beginners and advanced users are different, so why should they use the same software? The range of experiments and options can be adapted to the experience level of the users. More advanced features can be unlocked as students progress, or options can be kept simple for those who have just booked a few hours in an imaging facility.

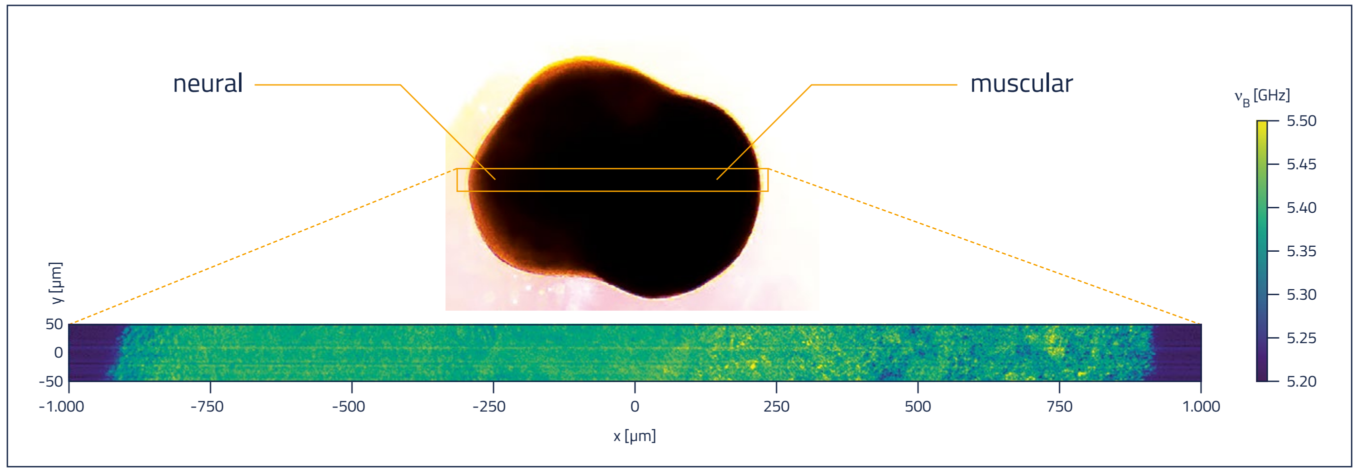
New workflow-based software design simplifies your work

Our intuitive software interface streamlines complex measurement tasks, making it accessible to users of all expertise levels. The workflow structure and task-based desktops organize all necessary information for different steps, guiding users naturally through the setup and acquisition process. This straightforward approach enables even those with minimal Brillouin experience to quickly achieve important results.

Experienced light microscopy researchers will appreciate the efficient experiment selection, predefined modes, favorites, and quick navigation. The revolutionary FlowPlanner™ software feature, with its step-by-step workflow structure, provides a logical progression for essential tasks. It guides users through experiment setup with intelligent help and status feedback for alignment and setup. This makes it simple, even for those with minimal experience, to confidently generate high-quality data in a short time frame.

Superior data correlation with the new PerfectOverlay™ feature

The advanced PerfectOverlay™ feature enables easy optically guided navigation to defined areas of interest directly in brightfield or fluorescence images. Smart integration maximizes the benefits of simultaneous Brillouin and optical measurements. Our calibration algorithms, visualization routines, and usability have all been optimized to offer the most user-friendly functionality available today.



Bright-field image and Brillouin microscopy scan of a live human neuromuscular organoid from a pluripotent stem cell derived neuromesodermal progenitor population. The left part of the neuromuscular organoid, as it is shown in the bright-field image on the top panel, corresponds to the tissue predominately consisting of neurons, while the right part of the organoid mainly consists of the muscular cells. The Brillouin microscopy image as a map of the Brillouin frequency shifts was acquired across the whole organoid spanning both types of tissues in a single scan (see bottom panel). Sample courtesy: Dr. Mina Gouti, the principal investigator in the "Stem Cell Modeling of Development & Disease" group, Max Delbrück Center for Molecular Medicine, Berlin, Germany

Seamless integration of Brillouin and light microscopy delivers perfectly aligned data

Plug and play system integration

The Discoverer™ builds on the expertise of renowned specialists in seamlessly integrating additional methods with light microscopy. This design is crucial for combining advanced optics, enabling the simultaneous use of standard condensers and epi-illumination microscopy alongside Brillouin on all major inverted or upright light microscopes.

The 780 nm laser used for Brillouin excitation also permits simultaneous fluorescence use without bleaching dyes during long-term experiments.

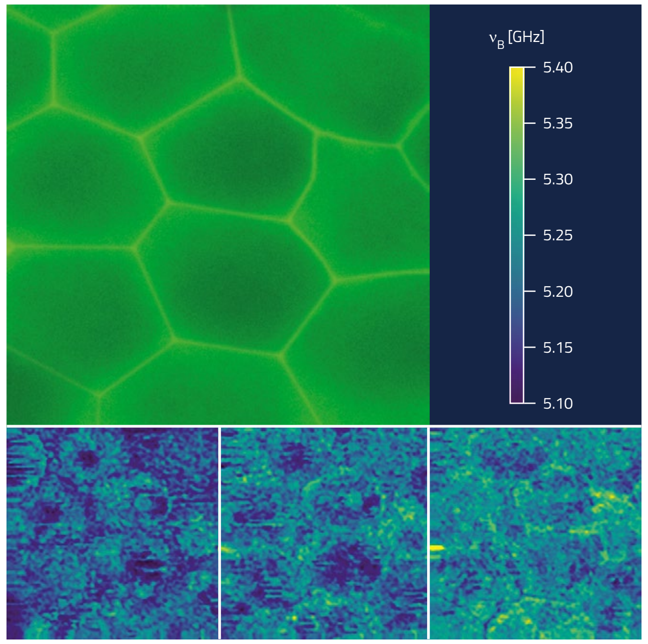
Easy integration with environmental control systems for live cell imaging

The new system is designed for maximum compatibility with a wide range of environmental solutions from various suppliers. Just add a stage incubator for example from Ibidi, TOKAI HIT or Okolab to your inverted microscope or use a large incubator solution to keep your samples under a controlled environment. This is a straightforward integration into the CellSense workflow.

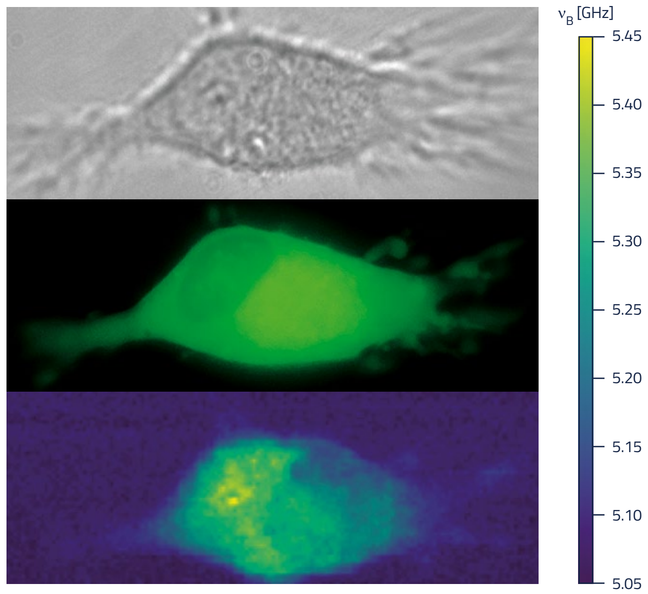
With the flexible FlowPlanner™ tool, users can control environmental conditions via a USB connection directly from the CellSense user interface, ensuring optimal conditions for live cell imaging.

Advanced optical techniques parallel to Brillouin with the same light microscope base

- Transmitted light modes like brightfield, phase contrast, and DIC
- Epi-fluorescence
- Confocal laser scanning
- Spinning disk imaging
- Advanced imaging techniques like super resolution or single molecule imaging
- Raman imaging



A single-cell layer of the retinal pigmented epithelium of a mouse eye imaged using epi-fluorescence microscopy (upper image) and 3D Brillouin microscopy of the same area scanning at three heights (bottom panel). Scanning at different position along z-axis allows to find better the desired imaging plane in the single-cell layer of the retinal epithelium. After dissecting the mouse eye the sample of the retina epithelium was fixed and immobilized by "flat-mounting" between a microscopy slide and a glass coverslip. Sample courtesy: Dr. Jacopo Di Russo, the group leader at the Interdisciplinary Center for Clinical Research of the RWTH Aachen, Germany



A live adherent dendritic cell imaged in vitro using three light microscopy modalities under physiological conditions: bright-field (top), epi-fluorescence (middle), and Brillouin frequency shift (bottom). The cell nucleus, which has darker appearance in the fluorescent image comparing to the rest of the cell, produces higher Brillouin frequency shifts, indicating lower compressibility of the organelle. Sample courtesy: Prof. Dr. Georg Duda, Director Julius Wolff Institute, Berlin Institute of Health (BIH) at Charité – Universitätsmedizin Berlin, Germany

Quantitative data from cells, organoids, tissues, and organisms

Delivering precise, reproducible results to enhance scientific research

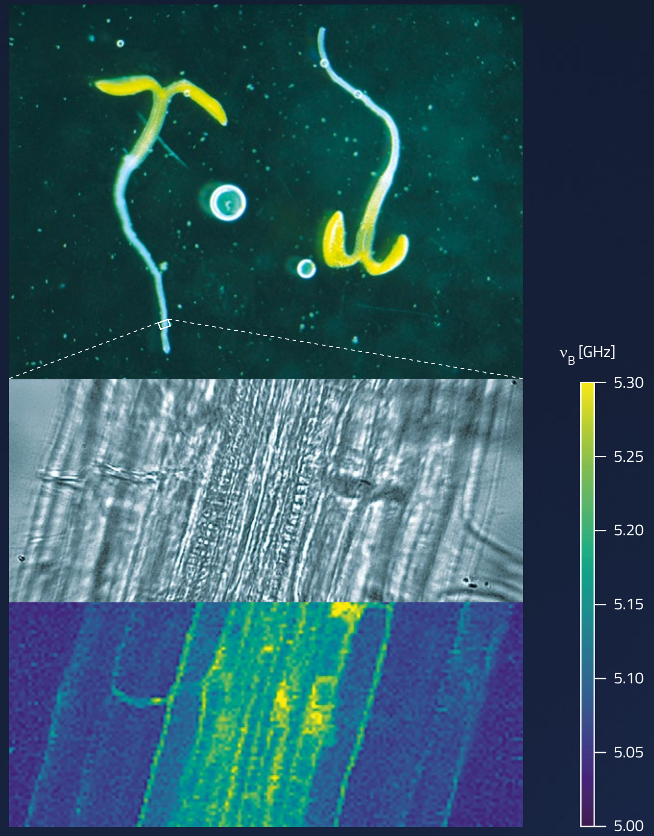
The Discoverer™ provides comprehensive solutions for mechanical property mapping, specifically designed for biological materials.

It addresses a wide range of scales, from organelles and single cells to larger structures like spheroids, organoids, tissue samples, and entire organisms.

Applications include stiffness mapping and viscoelasticity measurements over extended time periods.

Discoverer™ key features

- Highest resolution, quantitative data using the latest Brillouin technology
- Advanced algorithms for experimental workflow with the **FlowPlanner**™
- Powerful and fast batch-processing with comprehensive fitting routines
- Viscoelastic sample properties at specific locations or as maps for probing polymers, gels, and living cells
- Full range of accessories for environmental control, essential for live samples
- Automated mapping of sample properties over a large range with the **MultiMap**™ for bio-printed substrates, cells, and tissue samples



Seedlings of Arabidopsis (thale cress) plant. Colocalized bright-field image (middle panel) and Brillouin microscopy scan (bottom panel) were acquired for the area close to the tip of the plant's root as it is shown in the stereoscopic image (top panel). The sample, immobilized between a microscopy slide and a glass coverslip, was imaged at room temperatures in an aqueous buffer. Higher frequency shifts observed in the Brillouin-microscopy scan correlate well with the cells wall structure of the root observed in the bright-field image, indicating elevated mechanical properties of designated areas. Sample courtesy: Dr. Laura Bacete, Assistant Professor in the Plant Science Centre, Department of Plant Physiology, Umeå University, Sweden

"In the realm of biomechanics, technologies such as AFM, optical traps, and microfluidic deformability cytometry have provided valuable insights into the origin and biological relevance of cell and tissue mechanical properties. As pioneers of BioAFM, the ex-JPK founders are now on the way to developing the next-generation Brillouin microscope within CellSense. This is a logical step towards 3D mechanobiology. Our group shares a long relationship with the CellSense team and the same passion to drive the understanding of mechanical aspects in biology and medicine. We are happy that CellSense is transferring Brillouin technology from the optical bench to a turnkey, user-friendly product. Based on our knowledge and their expertise in instrumentation, we are confident that this collaboration will significantly advance the field."

Prof. Dr. Jochen Guck · Director Max Planck Institute for the Science of Light Erlangen
Department Biological Optomechanics

Specifications for the Discoverer™ Brillouin microscope

Basic configuration	· Laser module · Spectrometer module	· OptiBridge™ module · PC and software
System specifications	· Integrated closed-box system, with highest mechanical and thermal stability · Advanced fiber coupling to existing inverted or upright light microscopes · Near IR laser excitation with 780 nm for lowest phototoxicity and uncompromised fluorescence · Spectral resolution < 1 pm	· Highest detector sensitivity for fastest signal capture · Transmission illumination with standard condensers for precise brightfield, DIC and phase contrast · Fully automated system setup and calibration · Dimensions of laser module and spectrometer module both stackable with 110 × 65 × 24 cm^3 · Dimension OptiBridge™ with 42 × 40 × 15 cm^3
Optical configurations	· Fits on inverted motorized microscopes from · Zeiss (Axio Observer line) · Olympus/Evident (IXplore line) · Nikon (Ti2 line) · Leica (DMi line) · For upright motorized fluorescence microscopes combined with Brillouin from · Zeiss (Axio Imager) · Olympus/Evident (BX) · Leica (DM line) · Nikon (Ni line)	· Brillouin simultaneously with other light microscopy methods · Fully simultaneous operation with optical phase contrast and DIC using standard condensers · Combine Brillouin with advanced commercial confocal microscopes and all advanced fluorescence optical techniques ZEISS OLYMPUS EVIDENT Leica Nikon
Stages and sample holders	· Compatibility with motorized stages is available for all major inverted optical microscope manufacturers such as Zeiss, Nikon, Olympus/Evident and Leica	
New workflow-based Discoverer™ software	· Revolutionary user experience with the new interface design · True multi-user platform, perfect for imaging facilities · New PerfectOverlay™ for combined optical and Brillouin or other information · MultiMap™ for multiple area mapping	· FlowPlanner™ for designing a specific measurement workflow · Powerful Data Processing (DP) with full functionality for data export, fitting, filtering, edge detection, 3D rendering, and cross section, etc. · Powerful batch processing of images including and other analyses
Standard operating modes	**Brillouin operation** · Brillouin mapping with Brillouin shift and linewidth · Advanced stiffness and viscosity mapping · PerfectOverlay™ for combining Brillouin and other optical images	**Optical imaging modes** · Brightfield imaging · Basic widefield fluorescence
Optional modes and accessories	· FlowControl™ feature for remote experiment control · Wellplate mapping function · Epi-Fluorescence import function	· Environmental control options · Additional XY or Z sample movement stages available

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