LEICA MICROSYSTEMS - "WITH THE USER, FOR THE USER"

PIONEERING INNOVATIONS AND CLEVER SOLUTIONS FOR EVERYDAY MICROSCOPY COMBINED WITH WORLD-CLASS OPTICS

To understand structure and function of cells, brains or other complex biological systems, the method of choice is microscopy. Leica Microsystems is a pioneer in the field of innovative high-tech precision optic systems for the analysis of microstructures. The company has made technological history numerous times; innovative products and technologies from Leica Microsystems have received several awards in recent years. Its super-resolution microscopy such as STED (STimulated Emission Depletion) and GSD (Ground State Depletion) systems can, for the first time, make details as small as 20 nanometers visible and will provide new insights into molecular cell processes, paving the way for the fight against diseases such as cancer, Alzheimer's or Parkinson's.

A TRADITION OF INNOVATION

The company was founded by Carl Kellner in Wetzlar, Germany, in 1849. Its name developed from various brand names, all with a long tradition: Wild, Leitz, Reichert, Bausch + Lomb, Jung and Cambridge Instruments. Thus, Leica Microsystems unifies tradition and progress to support groundbreaking research projects with new instruments for new insights. These high-tech precision instruments are used for medical and industrial research, in clinical practice, in quality inspection, forensic science and environmental technology. The company is represented in over 100 countries with six manufacturing facilities in five countries, service and sales units in 20 countries and a global network of dealers. The company is headquartered in Wetzlar, Germany. Leica Microsystems operates globally in three divisions – Life Science, Industry and Medical Division – where it ranks with the market leaders.

LIFE SCIENCE DIVISION

Leica Microsystems supports the imaging needs of the scientific community with innovation and expertise for the visualization, measurement, and analysis of microstructures. The microscopy systems including cameras and software are used in research laboratories and universities. Confocal microscopes from Leica Microsystems are partners in top-level biomedical research, offering unprecedented precision in three-dimensional imaging and exact examination of subcellular structures and dynamic processes. As excellent sample preparation is a prerequisite for perfect microscopy, Leica Microsystems Life Science Division also offers the most comprehensive product portfolio for the preparation of biological, clinical, medical and industrial samples in the electron microscope.

INDUSTRY DIVISION

The Leica Microsystems Industry Division provides high-quality and innovative imaging systems for industrial applications and material sciences. Its solutions are used in quality control and in forensic science investigations. Digital microscopes from Leica Microsystems open up new horizons in mobility and speed to support R&D and quality assurance as they combine high-end optics with innovative digital technology for macroscopic and microscopic imaging. State-of-the-art inspection microscopes for the semiconductor industry ensure higher resolution and throughput for the inspection of 8 and 12 inch wafers.

MEDICAL DIVISION

The Medical Division provides surgeons in neurosurgery, ophthalmology, otolaryngology and dentistry with high-class surgical microscopes, digital medical imaging and data management solutions. Leica Microsystems' ophthalmic surgical microscope, with enhanced Red Reflex, combines world-class optics with an innovative dual illumination system that dramatically improves the surgeon's view when performing cataract surgery. The most compact surgical microscope currently available on the market originates from the idea pool of Leica Microsystems.

"WITH THE USER, FOR THE USER"

This statement by Ernst Leitz I in 1907 still describes what matters most in Leica Microsystems' product development: It is the fruitful collaboration with users and the strong focus on understanding their applications which at the same time is the driving force of innovation. While a number of groundbreaking products and technologies have found their way to the market, innovative products by Leica Microsystems also make a difference in everyday microscopy and education.

CLEVER SOLUTIONS FOR EVERYDAY MICROSCOPY



With Leica DMshare, microscope images can be transferred onto the iPad in real time. This means they are available anywhere any time – even on the move and independently of the microscope.

With Leica DMshare, microscope images can be transferred onto the iPad in real time. This makes it easy to visualize images and share the microscope experience with others. This feature is enhanced further when several users are connected to the same camera – an excellent setup for teaching and discussion.

As in clinical or routine applications long working hours are spent at the microscope, Leica Microsystems pays special attention to the ergonomic design of its products. The company offers the most comprehensive portfolio of ergonomic accessories like variable binocular tubes, heightadjustable elements and options for left-handed users. Within seconds, the microscope can be adjusted to the individual body size of each user. In the end, working in a comfortable posture leads to more quality.

PIONEERING IN SUPER-RESOLUTION MICROSCOPY

Widefield *versus* GSDIM. Ptk2-cells. NPC-staining: anti-NUP153/AlexaFluor 532 Microtubule-staining: anti-β-tubulin/AlexaFluor 647. Courtesy: Wernher Fouquet, Leica Microsystems



in collaboration with Anna Szymborska and Jan Ellenberg, EMBL, Heidelberg, Germany (http://www.leica-microsystems.com/science-lab/widefield-super-resolution-with-gsdim/).

In the field of super-resolution microscopy Leica Microsystems is a pioneer, offering both widefield and confocal super-resolution technology. With the Leica SR GSD widefield super-resolution microscope, scientists can now achieve resolutions far below the limit of diffraction that have never been attained before in widefield fluorescence microscopy. The system is capable of resolving details as small as 20 nanometers. It is used as a reliable research tool for a wide range of biomedical applications, providing neuroscientists, cell biologists, virologists, structural biologists, microbiologists, and physio-

logists with new opportunities for studying the function and interaction of single molecules and visualization of sub-cellular structures.

CONFOCAL PLATFORM FOR SUPER-RESOLUTION

The Leica TCS SP8 super-resolution microscope has been designed for confocal microscopy with optimal photon efficiency and high speed. It combines high-performance optics, the fastest true confocal scanner and the most sensitive detection system available. The result truly benefits from super-resolution for live cell imaging – revealing detailed high contrast images down to a resolution of <50 nm and at reduced laser power for improved cell viability and with live imaging of the dynamics of cells.



Visualization of lytic granules imaged by CW-STED and confocal on F-actin. NK92 cells were adhered to glass coated with antibody to activating (NKp30) and adhesion (CD18) receptor then fixed, permeabilized and stained for perforin and actin. Cells were imaged using CW-STED (actin, green) and either CW-STED or confocal (perforin, red). The image shows the same cell with granules detected by STED (A) or confocal (B). A region of interest is enlarged to show greater resolution of granules (center panel). (C) Full width half maximum (FWHM) measurements of confocal (green line) and STED images (red line). Horizontal dashed lines show half maxima, vertical dashed lines show width at half maxima. (D) Representative line profile of pixel intensities of actin (green line) and perforin (red line) taken from a line bisecting a single granule (shown in white in STED image enlargement). AU: arbitrary units. Courtesy: Emily M. Mace and Jordan S. Orange, Children's Hospital of Philadel-

phia, Research Institute, Philadelphia, PA, USA (http://www.leica-microsystems.com/science-lab/visualization-of-the-natural-killer-cell-immune-synapse-by-super-resolution-nanoscopy/).

Based on STED technology, the Leica TCS STED CW received several important awards and scales down the scanning spot to sub-diffraction size by switching off fluorescence in the periphery of the excited area. Stimulated emission is based on a well-thought-out interplay of fine optics and photophysical processes and delivers super-resolution in a purely optical way – on a confocal platform. The workflow, which was designed in cooperation with leading scientists, and the easy operation of the system make super-resolution accessible to a broad field of research. With the Leica TCS STED CW, super-resolution has already become an indispensable method in many life science research institutes working with light microscopes. A recent investigation of the time-course of the fluorescence emission probability in CW-STED has revealed the benefit of using a gated fluorescence detection – Gated STED – to further improve the resolution of CW-STED and/or to reduce the STED intensity in the sample for a given resolution.



Effect of light-gated reflection suppression. The left image shows a profile (xz-) section of a fluorescently labeled cell. Light was collected in the emission band and in the excitation band. The reflections at the slide surface and at the coverslip are obvious (strong horizontal lines). Right image: Without changing emission bands, the light gate fully suppresses these reflections (http://www.leica-microsystems.com/science-lab/gates-open-for-improved-confocal-fluorescence-and-super-resolution-sted/).

"Leica Microsystems continues fusing latest technology with a deep understanding of users' applications to provide uniquely innovative and easy-to-use solutions which are optimized to produce best possible results with as little effort as possible", says Sebastian Tille, Director Widefield Imaging at Leica Microsystems Life Science Division. "We are constantly on a journey of evolution and have added to our traditional core competencies in optics and mechanics a profound expertise in electronics and software, thus building the basis for continued leadership in the markets we serve."

LEARN, SHARE, CONTRIBUTE IN LEICA SCIENCE LAB

For experts, beginners and those who just want to know more, there is Leica Science Lab, the knowledge portal of Leica Microsystems. It offers scientific research and teaching material on the subjects of microscopy. The content is designed to support beginners, experienced practitioners and scientists alike in their everyday work and experiments. Users can explore interactive tutorials and application notes, discover the basics of microscopy as well as high-end technologies and become part of the Leica Science Lab community by sharing their expertise. http://www.leica-microsystems.com/science-lab/