



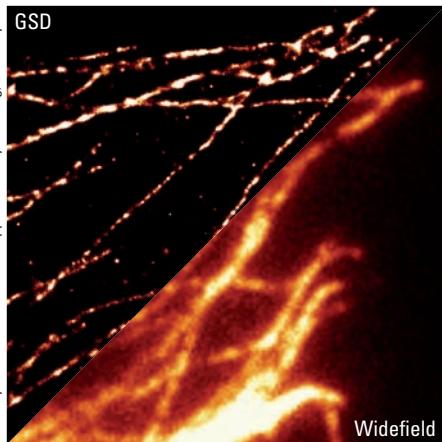
# Leica SR GSD

**Redefine the Limits of Microscopy**

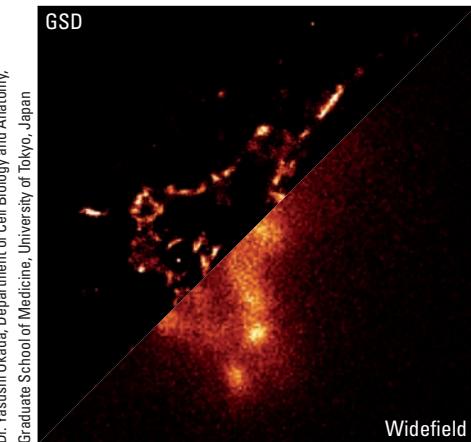
Widefield super-resolution with ground state depletion

Living up to Life

**Leica**  
MICROSYSTEMS

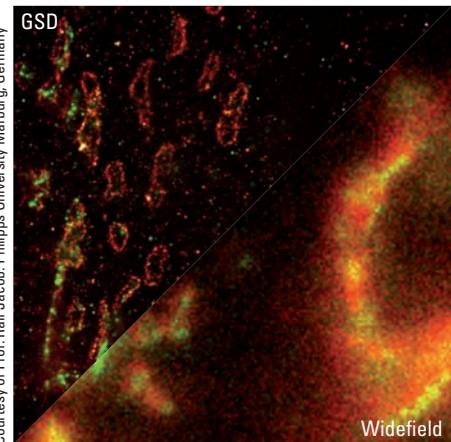


RCC-FG1 cells, immunofluorescence staining against  $\alpha$  tubulin with Alexa Fluor<sup>®</sup> 647.



Dr. Yasushi Okada, Department of Cell Biology and Anatomy,  
Graduate School of Medicine, University of Tokyo, Japan

Golgi body, B16 (Mouse melanoma cell line),  
Golgi targeting signal of  $\beta$  1,4-galactosyltransferase,  
fused to EYFP.

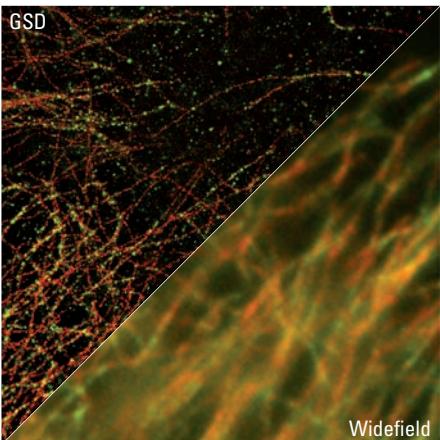


Courtesy of Prof Ralf Jacob, Phillips University Marburg, Germany

Golgi membrane protein Giantin and Golgi  
matrix protein GM130, immunofluorescence  
staining with Alexa Fluor<sup>®</sup> 647 and  
Alexa Fluor<sup>®</sup> 488, respectively.

- Resolve more – down to  $\sim 20$  nm
- Resolve online – see your super-resolution image build up on screen as it is acquired
- Resolve smartly – use standard dyes for highest flexibility





MDCK cells: Microtubules, Alexa Fluor® 642 (red) and TyrMicrotubules, Alexa Fluor® 488 (green).

# Bridging the Two Worlds of Light and Electron Microscopy

Fluorescence microscopy has developed into one of the most important tools in life science research. The ultimate aim is to examine single molecule and sub cellular components – structures that are too small to be resolved using standard light microscopy.

Pioneers always want to push the limits, striving to learn more and demanding to see further. But when the diffraction limit stands in the way, another approach is needed.

Leica Microsystems is a pioneer in super-resolution microscopy. The 2007 introduction of the Leica TCS STED heralded a new era of products that break the barriers of diffraction limited imaging.

Building on the success of our confocal microscopy super-resolution systems, Leica Microsystems continues to work with the top scientists in the field to push the limits of resolution in widefield applications. Through collaboration with Professor Stefan Hell of the Max-Planck-Institute, Göttingen, we are proud to add the Leica SR GSD to our portfolio of super-resolution microscopy systems.

Based on the highly regarded Leica AM TIRF MC system and the Leica DMI6000 B inverted microscope, the Leica SR GSD harnesses a proven technique known as Ground State Depletion (GSD). This scientifically proven method improves resolution down to 20 nm, using a wide range of fluorophores.

With the Leica SR GSD, the limits of super-resolution are redefined. Open your research to a new world of possibilities in microscopy.



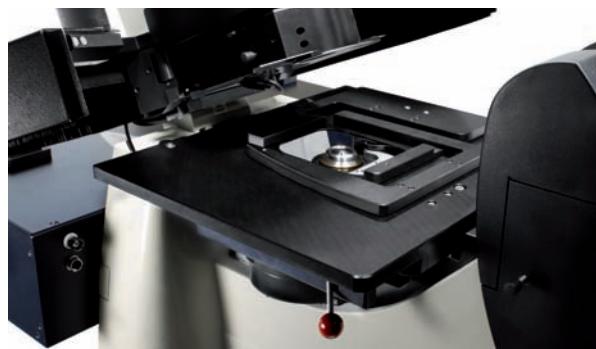
# Bring Previously Hidden Detail into Light



**“The GSDIM system from Leica Microsystems is an easy-to-use, straightforward super-resolution microscope that opens new possibilities for our research on membrane traffic that we could so far not achieve with alternative super-resolution systems.”**

**Dr. Rainer Pepperkok**

Team Leader and Head of Advanced Light Microscopy Core Facility, EMBL, Heidelberg, Germany



Latest technology for maximum performance:  
The SuMo Stage utilizes the latest technology for maximum performance and minimum lateral drift.

Visualizing the precise localization of cellular processes is crucial to understanding the interplay between molecules, structures and function. The additional insight given by Ground State Depletion super-resolution microscopy is extremely useful for a range of applications, since a number of structures currently in the research focus are smaller than the diffraction limit. This includes endo- and exosomes, viruses and nuclear pore complexes, to name but a few.

## Latest technology for maximum performance

The SuMo Stage (**S**uppressed **M**otion Stage) ensures maximum performance and minimum lateral drift, by closely coupling the objective with the sample holder.

## Bridging the resolution gap

The Leica SR GSD offers the highest lateral resolution with light microscopy and is a superb tool for determining the structure of fluorescently labeled specimens in neurobiology, cell biology, virology, microbiology and physiology. The Leica SR GSD provides detailed insights into cellular structures that cannot be seen with diffraction limited light microscopy and therefore bridges the resolution gap between light and electron microscopy.

## Integrated multi-purpose solution

The Leica SR GSD allows investigation of samples using high sensitivity super-resolution, as well as a wide range of fluorescence and transmitted light techniques: the Leica SR GSD system can also be a high sensitivity, high speed, multicolor, temperature-controlled widefield and TIRF microscope. This flexible multi-purpose system gives researchers the freedom to select the optimal combination of imaging techniques to build up a compelling set of images in support of scientific results. Use your established workflow!

## Integrates perfectly into existing workflows

The workflow for GSDIM (Ground State Depletion followed by Individual Single Molecule return) is based on standard immunostaining techniques and integrates perfectly into existing workflows for fluorescence microscopy. This enables the viewing of samples from the incredible perspective of super-resolution microscopy using a wide range of compatible fluorochromes including Alexa Fluor® 488, 532, 568 and 647, Atto 488 and 532, Rhodamine 6G and YFP. Use existing primary and secondary antibodies, adapt the staining protocol and start benefitting from the ultimate resolution in light microscopy!

# New Technology Breaks the Diffraction Barrier

## How to resolve below the diffraction limit

The resolution of a regular fluorescence microscope image is limited by diffraction to approximately half the wavelength of the emitted light. To separate fluorophores that are closer together, the solution is to ensure that not all illuminated fluorophores are able to emit simultaneously. To this end, the excitation light is used such that almost all fluorophores in the samples instantly turn dark.

The continuously shining excitation light removes fluorophores from their ground state, leaving only a few, sparsely distributed molecules capable of emitting fluorescence. These molecules are imaged on a camera so that their position can be localized with high precision – before being turned off. As other molecules return back to their ground state, the microscope registers the position of many sequentially emitting molecules. The position of each fluorophore is accumulated into a single image, revealing details with unmatched resolution down to 20 nm. This is the basic principle of the GSDIM technique.

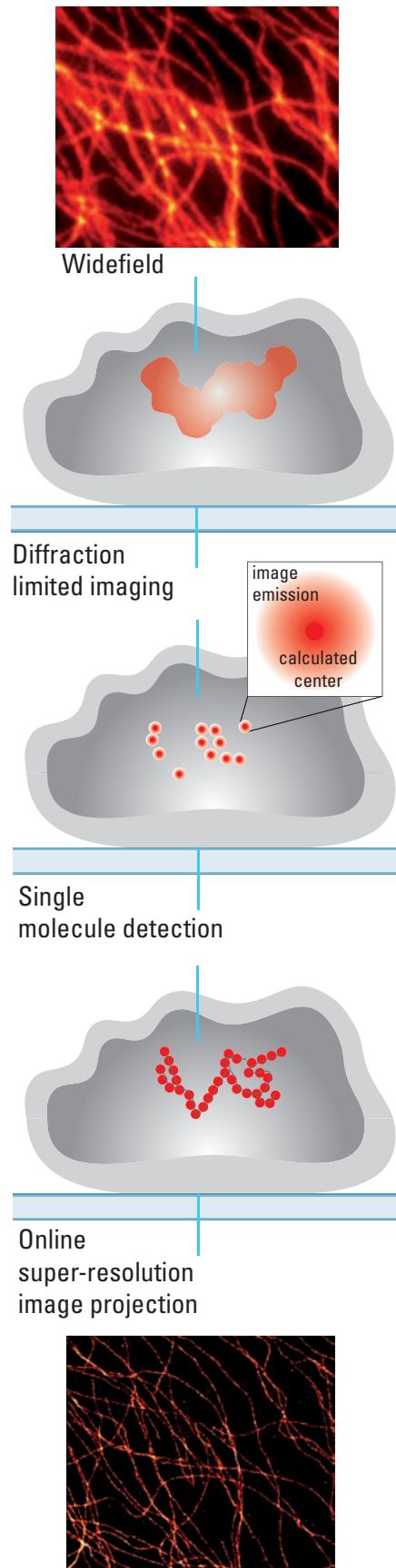
## The widefield solution for super-resolution

The Leica SR GSD is the latest addition to Leica Microsystems' portfolio of super-resolution products. Based on GSDIM technology, it surpasses the resolution limits previously set by other super-resolution systems. Following the successful technology transfer of STED, the Leica SR GSD extends the product line of cutting edge tools.

The new Leica SR GSD is based on the fully automated Leica AM TIRF MC system. It is possible to combine GSDIM super-resolution with TIRF evanescent field illumination to gain advantages from both sides. Three powerful lasers offer maximum flexibility so that you can choose the right fluorochrome for your work.

## Super-resolution on a multi-purpose imaging system

The Leica SR GSD puts the power of super-resolution into a user-friendly system, alongside a full range of widefield microscopy applications. The workstation allows you to perform everyday experiments, from high-speed imaging to time-lapse to TIRF, while expanding imaging into the sphere of super-resolution.



# Leica SR GSD – The Fast Way to

## Your Benefits

- Maximum resolution down to 20 nm
- The SuMo Stage, with **Suppressed Motion** technology, minimizes drift for accurate localization of molecules
- Online super-resolution image projection – see results as they are acquired
- Full application flexibility offered by combining super-resolution with TIRF and epifluorescence on a multi-purpose live cell imaging system
- Standard fluorochromes can be used – no need to change protocols
- Powerful lasers for the highest flexibility in fluorochrome selection
- Large set of powerful image processing tools

## Redefine the limits of microscopy

In microscopy, it is always necessary to minimize drift. This is of paramount importance in super-resolution imaging, due to the resolution and the acquisition times in question. The Leica SR GSD introduces brand new technology in drift reduction, which puts the maximum system drift below the resolution during acquisition. This simplifies sample preparation – gold beads or other fiducial markers are not needed.

## Breaking the barrier between reality and resolution

Maximum resolution depends on the number of photons you can collect for calculation. With three high power lasers, the Leica SR GSD can switch all fluorochromes into the dark state very rapidly. The maximum number of photons per frame can then be collected to get the best possible resolution.

## Clarity without compromise

For resolution beyond diffraction limits you need tools that reach far beyond standard. With a high NA and correction over the full aperture, the objective is perfect for both TIRF and super-resolution imaging with unmatched performance.



# Super-resolution Imaging

## Resolve previously hidden details

GSDIM super-resolution imaging needs time to acquire a sufficient number of single molecule events. The image acquisition runs in the background – but how long do you collect images before stopping the experiment?

To help answer this question, the Leica SR GSD offers online image projection of the super-resolution image. During acquisition, the user sees the image building up online. This feature puts you in full control of the experiment – you can decide to stop or continue the image acquisition to achieve the best result. There is no need to repeat the experiment because the acquisition stopped too early or too late.

## Redefine the way you image

Leica Microsystems' super-resolution platform offers an easy-to-use, fully automated experiment wizard. The software guides you step by step to the perfect super-resolution image. Many automated functions are available to help with settings or alignments, but can be switched off to keep operation as simple as possible. The system software is Leica Application Suite for Advanced Fluorescence (LAS AF), offering the familiarity and ease of use already appreciated on our confocal and widefield systems.

## Extend imaging possibilities with super-resolution

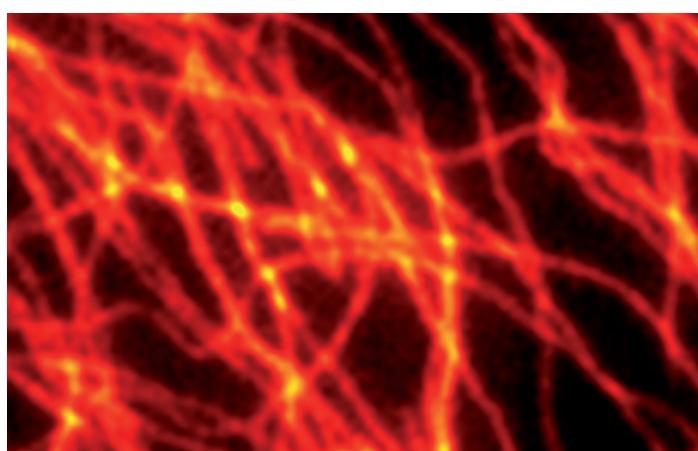
A whole range of powerful offline tools such as filter functions, recalculations of pixel size or different thresholds are available to fine-tune acquisition settings or optimize the super-resolution image for specific purposes.



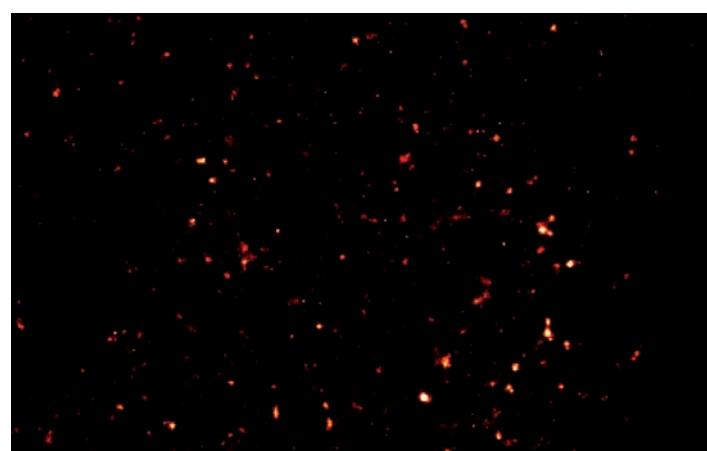
**“Leica Microsystems turned our idea of switching standard fluorophores by ground state depletion into a nanoscope that delivers stunning images.”**

### Prof. Dr. Stefan Hell

Director at the Max-Planck-Institute for Biophysical Chemistry, Department of NanoBiophotonics, Göttingen, Germany



Accurate detection in all types of illumination: widefield reference image



Single molecule image

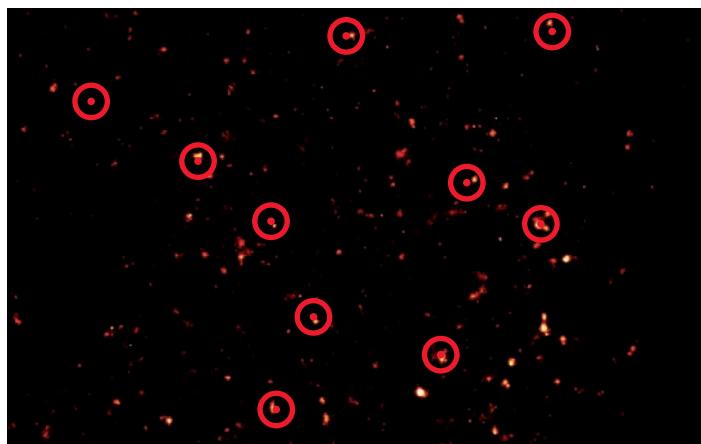
# Technical Specifications

<b>Lateral resolution*</b>	<ul style="list-style-type: none"> <li>– Maximum 20 nm</li> <li>– Typical 40 nm</li> </ul>
<b>Laser</b>	<ul style="list-style-type: none"> <li>– 488 nm/300 mW</li> <li>– 532 nm/500 mW</li> <li>– 642 nm/500 mW</li> <li>– 405 nm/30 mW</li> </ul>
<b>Imaging modes</b>	<ul style="list-style-type: none"> <li>– GSD super-resolution</li> <li>– TIRF (also available with GSD)</li> <li>– EPI fluorescence (also available with GSD)</li> <li>– Brightfield</li> <li>– DIC/PH</li> </ul>
<b>Laser safety</b>	System class 1
<b>Field of view</b>	<ul style="list-style-type: none"> <li>– 18 x 18 µm (GSD mode)</li> <li>– 50 x 50 µm (standard TIRF)</li> </ul>
<b>Supported dyes</b>	<ul style="list-style-type: none"> <li>– Alexa Fluor® 488</li> <li>– Rhodamine-6G</li> <li>– Atto 532 and 488</li> <li>– Alexa Fluor® 532</li> <li>– Alexa Fluor® 546</li> <li>– Atto 565 and 568</li> <li>– Alexa Fluor® 568</li> <li>– Alexa Fluor® 647</li> <li>– YFP</li> </ul>
<b>Imaging</b>	Real-time image processing and display of results as they are acquired
<b>Software</b>	Full set of software tools for configuration, acquisition, processing and image analysis

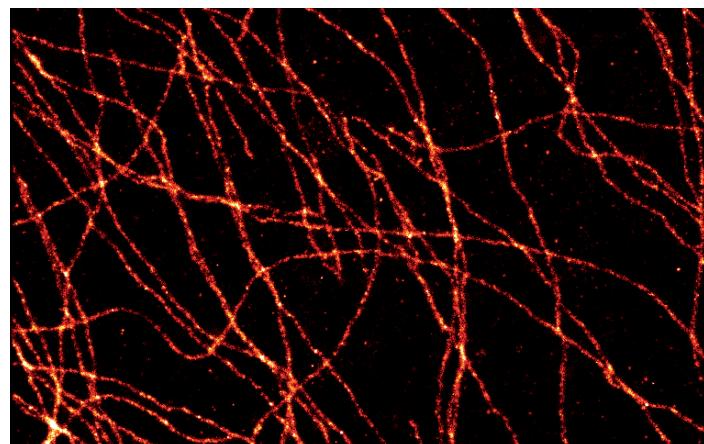
\* Performance of the system is dependent on the appropriate room and sample conditions



The Leica HCX PL APO 100/1.47 – highest correction for maximum resolution

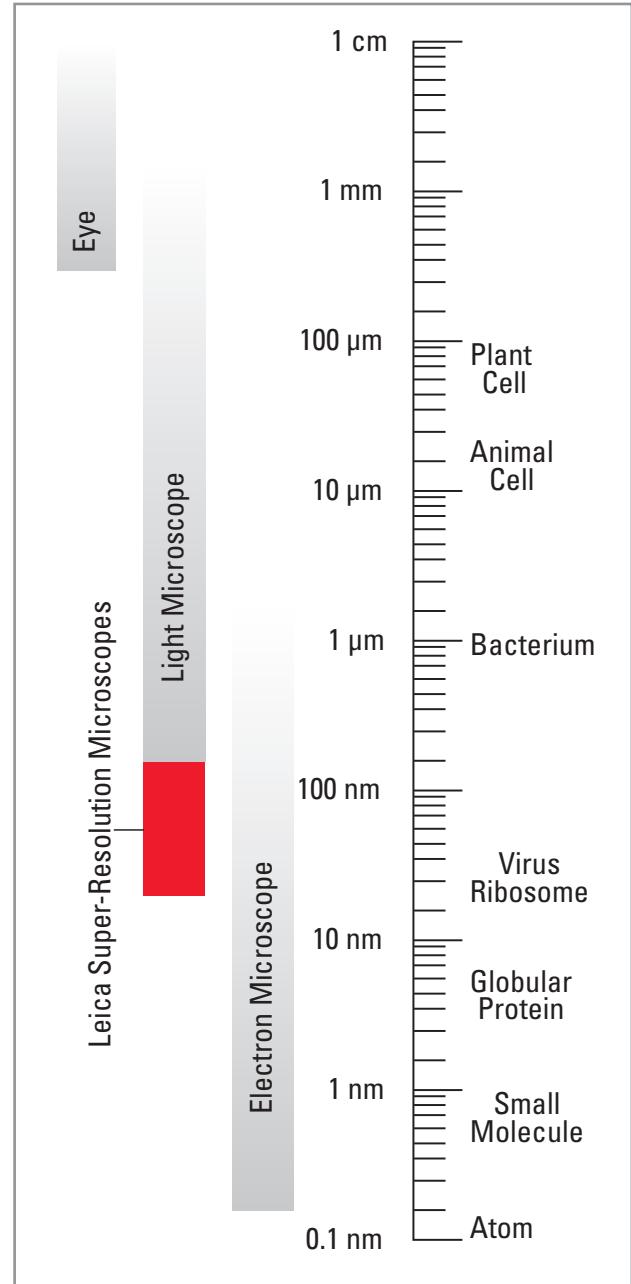
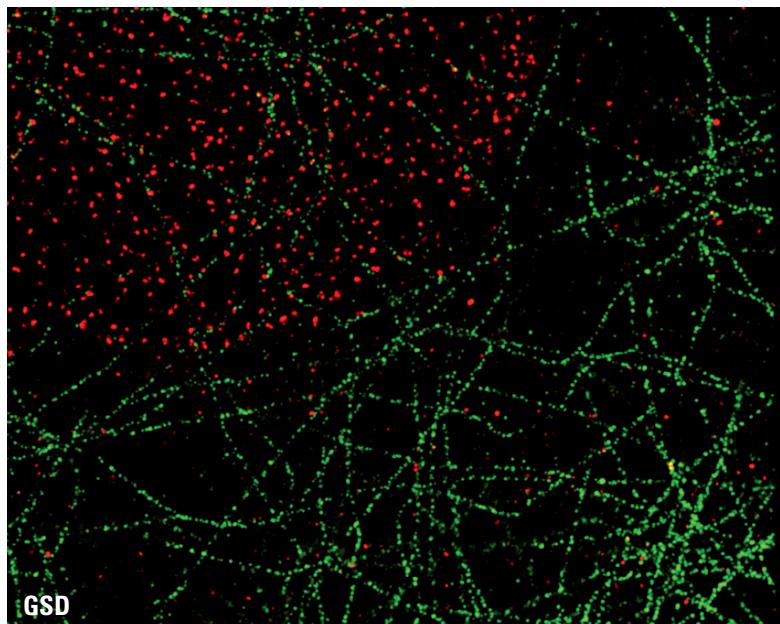
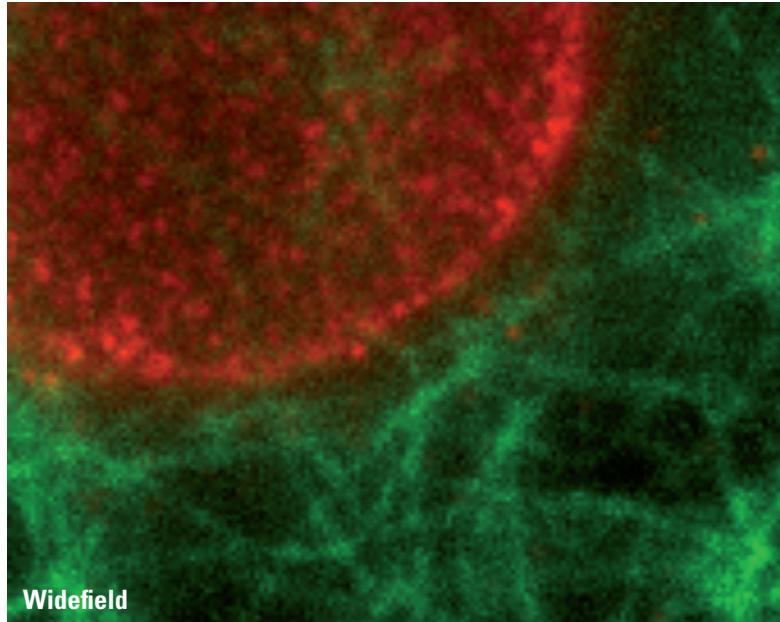


Detection of single molecule events



Final super-resolution image

# GSD (Ground State Depletion)



Resolving power of different microscopy techniques: The Leica SR GSD is advancing light microscopy to a new level of resolution.

Ptk2-cells. NPC-staining: anti-NUP153/Alexa Fluor® 532

Microtubule-staining: anti-β-tubulin/Alexa Fluor® 647

Courtesy: Wernher Fouquet, Leica Microsystems in collaboration with Anna Szymborska and Jan Ellenberg, EMBL, Heidelberg, Germany.

# “With the user, for the user”

# Leica Microsystems

Leica Microsystems operates globally in four divisions, where we rank with the market leaders.

## ● Life Science Division

The Leica Microsystems Life Science Division supports the imaging needs of the scientific community with advanced innovation and technical expertise for the visualization, measurement, and analysis of microstructures. Our strong focus on understanding scientific applications puts Leica Microsystems' customers at the leading edge of science.

## ● Industry Division

The Leica Microsystems Industry Division's focus is to support customers' pursuit of the highest quality end result. Leica Microsystems provide the best and most innovative imaging systems to see, measure, and analyze the microstructures in routine and research industrial applications, materials science, quality control, forensic science investigation, and educational applications.

## ● Biosystems Division

The Leica Microsystems Biosystems Division brings histopathology labs and researchers the highest-quality, most comprehensive product range. From patient to pathologist, the range includes the ideal product for each histology step and high-productivity workflow solutions for the entire lab. With complete histology systems featuring innovative automation and Novocastra™ reagents, Leica Microsystems creates better patient care through rapid turnaround, diagnostic confidence, and close customer collaboration.

## ● Medical Division

The Leica Microsystems Medical Division's focus is to partner with and support surgeons and their care of patients with the highest-quality, most innovative surgical microscope technology today and into the future.

The statement by Ernst Leitz in 1907, “with the user, for the user,” describes the fruitful collaboration with end users and driving force of innovation at Leica Microsystems. We have developed five brand values to live up to this tradition: Pioneering, High-end Quality, Team Spirit, Dedication to Science, and Continuous Improvement. For us, living up to these values means: **Living up to Life.**

## Active worldwide

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and representatives in more than 100 countries