

$Leica\ MacroFluo^{^{TM}}$

The fluorescence macroscope

Precision from the total picture down to the smallest detail



Studying Nature's Clues

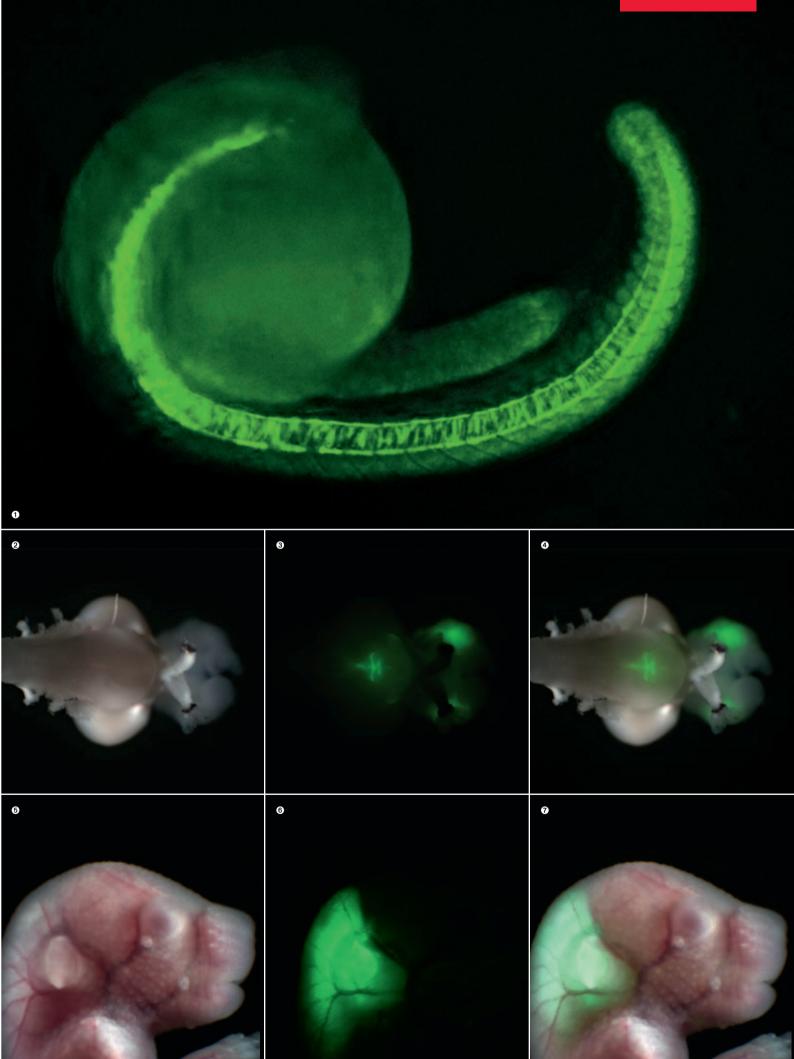
In modern developmental, molecular and cell biology, fluorescence technologies play a critical role in functional research of organisms and provide the researcher with enormous potential for gaining insight into a world that is usually hidden to the human eye. Complex genetic studies and cellular examinations of suitable model organisms are the prerequisites for understanding the molecular basis and complex correlations of life.

In many respects, the development, cell biology and physiology of the mouse are very similar to those of the human being. The mouse is therefore an ideal biological model for *in-vivo* studies that explore the causes of disease in humans and develop new therapeutic approaches. Cell and developmental biology are increasingly focused on understanding complex interrelationships in the organism. Therefore, a flexible microscope system is required that enables the causes of disease to be examined on living animal models with maximum precision and resolution in an intensely fluorescent image field and to be captured in digital images.

The Leica MacroFluo™ concept combines the advantages of macroscopy – large object fields, large working distances, parallax-free and precise imaging – with fluorescence technology at high resolution. The Leica MacroFluo™ provides brilliant images with maximum image precision and depth of information over a wide magnification range to capture all aspects of the complete image.

- Zebrafish embryo. GFP expression with control of Sonic hedgehog gene-regulatory sequences. GFP expression in anterior baseplate and notochord. Prof. Dr. Uwe Strahle, Research Center Karlsruhe, Germany and Cédric Vonesch, Imaging Centre IGBMC, Illkirch, France
- 2 • Expression of green fluorescence in an EGFP (Enhanced Green Fluorescent Protein) transgenic mouse, Dr. Massimo Pasqualetti, Università di Pisa and Dr. Filippo Rijli, Imaging Centre IGBMC, Illkirch, France

Special thanks to Jean Luc Vonesch and Didier Hentsch of the Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), Illkirch, France for their close cooperation in developing the Leica MacroFluo™



When Excellence Meets Brilliance

Parallax-free documentation

- Precise imaging of macroscopic specimens from the total picture down to the smallest detail
- · Detail-accurate analysis and 3D view

From macro to micro

- Apochromatically corrected manual or motorized 6:1 and 16:1 zoom systems for optimum adaptability
- 6:1 zoom with high numerical aperture for optimum light efficiency
- 16:1 zoom enables a wide range of research tasks to be carried out with just one microscope
- Optimal imaging of your specimens with a wide selection of high-quality objectives

With its consistently modular design, the Leica MacroFluo™ system enables individual adaptation to the task for precise imaging of all aspects of macroscopic specimens.

Parallax-free fluorescence macroscopy

While in stereomicroscopy, changing the Z position of the observer is associated with a parallax error (an apparent lateral shift of the specimen when acquiring z-stacks), the Leica MacroFluo™ combines macroscopic viewing with a vertical beam path typical of microscopes. This enables parallax-free images with simultaneously large working distances and object fields with a maximum of precision. The result is much greater accuracy in digital image processing, analysis and measurements.

Leica MacroFluo™ Z6 APO (A) — high macroresolution and powerful fluorescence

The Leica Z6 APO (A) is available as a fully apochromatically corrected manual or motorized 6.3:1 zoom body, which, depending on the objective equipment, can reach a macro resolution from 351 lp/mm (planapochromat 1×) up to 1500 lp/mm (planapochromat 5× HR) and thus can resolve specimens up to a structural width of 330 nm. The wide range of planapochromatically corrected objectives creates sufficient free room for specimen manipulation and, due to the high numerical aperture, enables high-performance fluorescence documentation at low magnification.

Motorization of the zoom, iris diaphragm and built-in fine focus and the new motorized focus make it easy to automate experiment procedures. Results can be reproduced at any time.

Leica MacroFluo™ Z16 APO (A) — fluorescence analysis at the highest level

The Leica Z16 APO (A) is available as a manual and a motorized instrument. With the large zoom range from $7.1\times$ to $115\times$ (planapochromat $1\times$), fluorescent specimens up to a structural width of 330 nm (planapochromat $5\times$ HR) can be observed and documented. Thus the Z16 APO (A) permits the study of clearly contoured overviews of chicken embryos and neural systems, but also selected details such as the expression of proteins at high magnification and resolution.



Brilliant fluorescence images, rich in detail and contrast

- Coupling of illumination and zoom optics – maximum light efficiency and uniformly illuminated object fields
- Filters individually matched to your specimens – maximum flexibility in selecting fluorescent dyes
- Specimen-optimized transmission properties and filters with Zero Pixel Shift – for pin-sharp images

Adjustment-free light sources – the best light for your specimens

- Leica EL6000: Uniformly illuminated object fields with software-controlled shutter control for documenting image series
- Leica SFL100: Durable, cost-effective and compact LED illuminator with adjustable light intensity for optimum image quality
- Leica SFL4000: 5 LED modules that can be combined as desired for specific excitation of fluorochromes – high light efficiency for high-contrast images with simultaneously low phototoxicity

Powerful, Even with Weak Fluorescence

Fluorescence without compromises

The Leica MacroFluo™ is equipped with a high-quality fluorescence axis that ensures an optimum light stream and thus the greatest brightness and homogeneity. Up to five filter blocks can be inserted into the easy-to-rotate turret disk. The illumination is coupled into the zoom optics. This guarantees precise illumination, maximum light efficiency, and homogenous object fields at any zoom position.

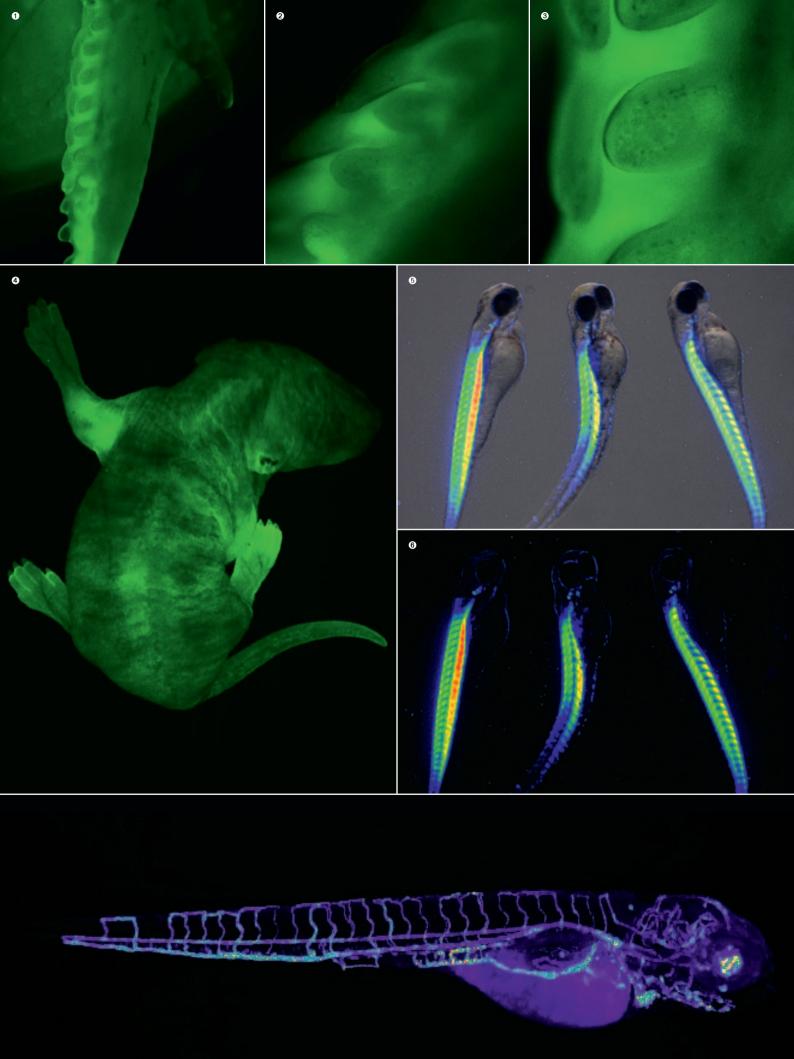
Filter your specimens for best results

New fluorescent dyes and staining methods are continually opening new possibilities for the study of development stages, reactions, signal transduction and metabolic pathways. For this purpose, the wide range of Leica filter blocks can be expanded even further by adding individualized filter block combinations to ensure optimum transmission properties for almost any application. With Zero Pixel Shift technology, when the filter blocks are switched, no undesirable pixel shifts occur between the individual images of the different spectral ranges — an ideal prerequisite for digital multicolor fluorescence experiments.

Let there be light

With the Leica EL6000, Leica Microsystems offers an external light source equipped with a long-life metal halide lamp — a cost-effective and time-saving alternative to mercury vapor lamps. Furthermore, the available Leica SFL100 is a compact, cost-effective LED fluorescence illuminator that enables optimum excitation at 470 nm with adjustable light intensity. For easily combining different wavelengths in multi-fluorescence experiments, the Leica SFL4000 offers five high-performance fluorescence modules, which can be controlled via an intuitive user interface. All light sources listed here enable adjustment-free adaptation to the microscope and thus guarantee uniformly illuminated, high-contrast fluorescence images: the best light for your research.

- ◆ S Chicken with GFP expression in the wing. Institut Albert Bonniot, Grenoble, France
- Transgenic mouse with GFP expression. Dr. Daniel Metzger, Prof. Pierre Chambon, Imaging Centre IGBMC, Illkirch, France
- **⑤** − **⑥** Zebrafish. View of polarization contrast in false colors. Imaging Centre IGBMC, Illkirch, France
- Zebrafish larva. CD41-GFP expression in thrombocytes. Time-lapse image of thrombocyte circulation to illustrate the vascular system. Dr. Philippe Herbomel, Institut Pasteur, Paris, France



Equipped for Future Tasks



Motorized focus and SmartTouch™: reliable, precise focus made 100% reproducible by control using the Leica LAS software



Objective slide (here, with 2× and 5× objective): convenient extension of the range of applications by simply toggling between the required magnifications



Binocular photo tube with image correction: easy handling and accurate adjustment of the image section for documentation

Solid basis for your research

Advanced documentation, particularly of fine details, requires a solid basis. The design of the new focusing column and the carrier of the fluorescence axis reliably absorbs shocks and vibrations. This prevents impairment of image quality even when obeserving specimens in liquid medium.

The high-quality mechanical engineering of the coarse/fine focus adjustment enables convenient, uniform focusing and enables accurate adjustment of the focus position at all times, even in the micrometer range. With the new Leica motorized focus, you can focus on your specimen not only quickly and precisely, but also reproducibly. The motorized focus of the Z series makes parallax-free and accurate documentation as easy as child's play.

Supreme performance for your research

With the wide range of planapochromatically corrected objectives and the ability to adapt DM objectives, the Leica Macro-Fluo™ provides enormous flexibility with regard to magnification and working distance. In particular, the high-performance 5× planapochromatic objective enables brilliant, true-to-detail reproduction of your research results with a numerical aperture of 0.5 and a resolution of 1500 lp/mm. The objective slide for manual zooming allows you to combine the 2× and 5× planapochromat objectives to conveniently expand the range of applications. From low magnification to fine details – the Leica MacroFluo™ offers high-performance converging lenses for brilliant fluorescence with sufficient free room for specimen manipulation.

The basis for successful documentation

Leica Microsystems offers you a selection of powerful transmitted-light bases that always present your specimens in the best light, with brightfield illumination with high or low diffusion, oblique transmitted-light illumination, and darkfield. The Rottermann Relief contrast method also ensures excellent display, even of unstained living cells.

The optional gliding stage ensures the necessary sensitivity when positioning specimens. Furthermore, the integration of the motorized Leica IsoPro™ stage enables you to carry out multiposition experiments accurately, all the way to TileScan for particularly large specimens. The Leica MATS Thermocontrol System with a heated specimen stage made of optical glass provides gentle, absolutely uniform temperature across the entire stage surface. This temperature stability over long periods lets you perform time-lapse experiments on temperature-sensitive specimens with precision.

Investment for the future

In multiuser environments, adaptability is an important characteristic for satisfying all the requirements posed by various fields of research. Particularly in this regard, the MacroFluo™ system is an investment that will pay off in the long run. Thanks to the modular design, a complete range of accessories for manual and motorized zoom systems is available for you to choose from.



Leica TL bases: whether simple transmitted light, oblique illumination or relief contrast – the Leica bases allow you to get the best out of your specimens.



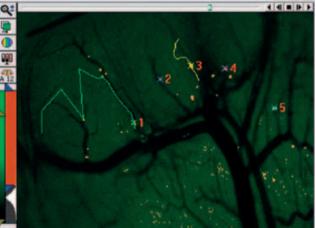
Automated specimen scans are child's play with the $\mathsf{IsoPro}^{\mathsf{\tiny{TM}}}$ motorized cross-stage

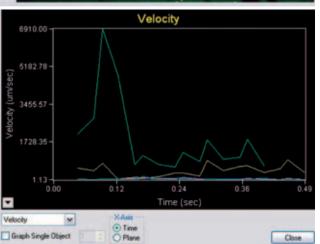


Leica SmartTouch™: easy control and overview of the motorized microscope functions via touch panel and individually programmable control buttons

Well-conceived and Customized System Solutions







Integrated complete solution

In the Leica Application Suite (LAS), automated microscopes, digital cameras and software are combined to create one user-friendly, consistent imaging solution. Versatility and a consistent, modular construction mean that you have enormous flexibility in building your microscope system, which in turn is perfectly adapted to your applications. Thus LAS is an intuitive solution that makes both routine and research analysis easier.

Leica MM AF

Leica MM AF powered by MetaMorph® is available as an MM AF online version for image processing and analysis and as a complete software package for image acquisition and analysis. The latter offers the highest flexibility and versatility in integrating the microscope, peripherals and camera for multidimensional image acquisition, processing and analysis.

Optional modules such as 3D deconvolution or 3D measurements as well as various application modules for automatic fluorescence analysis provide you with everything you need to adapt the microscope system to the requirements of your research.

Screenshots from the Leica LAS and MM AF powered by Metamorph® (from top to bottom):

LAS Multifocus module: Drosophila melanogaster. Compound eye.
Dr. Tricoire, Institut Jacques Monod, Université de Paris, France
Leica MM AF 3D motion analysis: Trajectories of five identified
particles. Prof. Marianne Quiding-Järbrink, Department of Microbiology and
Immunology, The Sahlgrenska Academy, University of Gothenburg, Sweden
Leica MM AF 3D motion analysis: Graphic display of the analysis

The expert in fluorescence applications

Leica Microsystems has cooperated with leading scientists to develop the Leica AF6000, an exceptionally ergonomic fluorescence software program. The intuitive operating concept guides you reliably and easily to brilliant results. In combination with the motorized MacroFluo™ zoom modules, the Leica AF6000 E is an entry-level software program that enables easy documentation, image overlay and time-lapse images.

The modular design of the software means that you can add to your system at any time as your needs grow and change. Thus the Leica AF6000 fulfills additional requirements of fluorescence applications: The software-controlled EL6000 shutter control allows manual multichannel fluorescence with time and Z series. The integration of the motorized Leica IsoPro $^{\text{TM}}$ cross-stage enables multi-position experiments and TileScanning as well as optional WellPlate acquisition.

A wide variety of functions for image documentation, quantification, optimization and analysis can be expanded by adding software options such as 3D reconstruction of image information or deconvolution. Thus the MacroFluo™ becomes an integrated microscope system that is capable of growing along with your research requirements.

Screenshots from the Leica AF6000 software

(from top to bottom)

AF6000: Image gallery in acquisition mode
AF6000: TileScan in configuration mode

AF6000: WellPlate acquisition module in configuration mode

