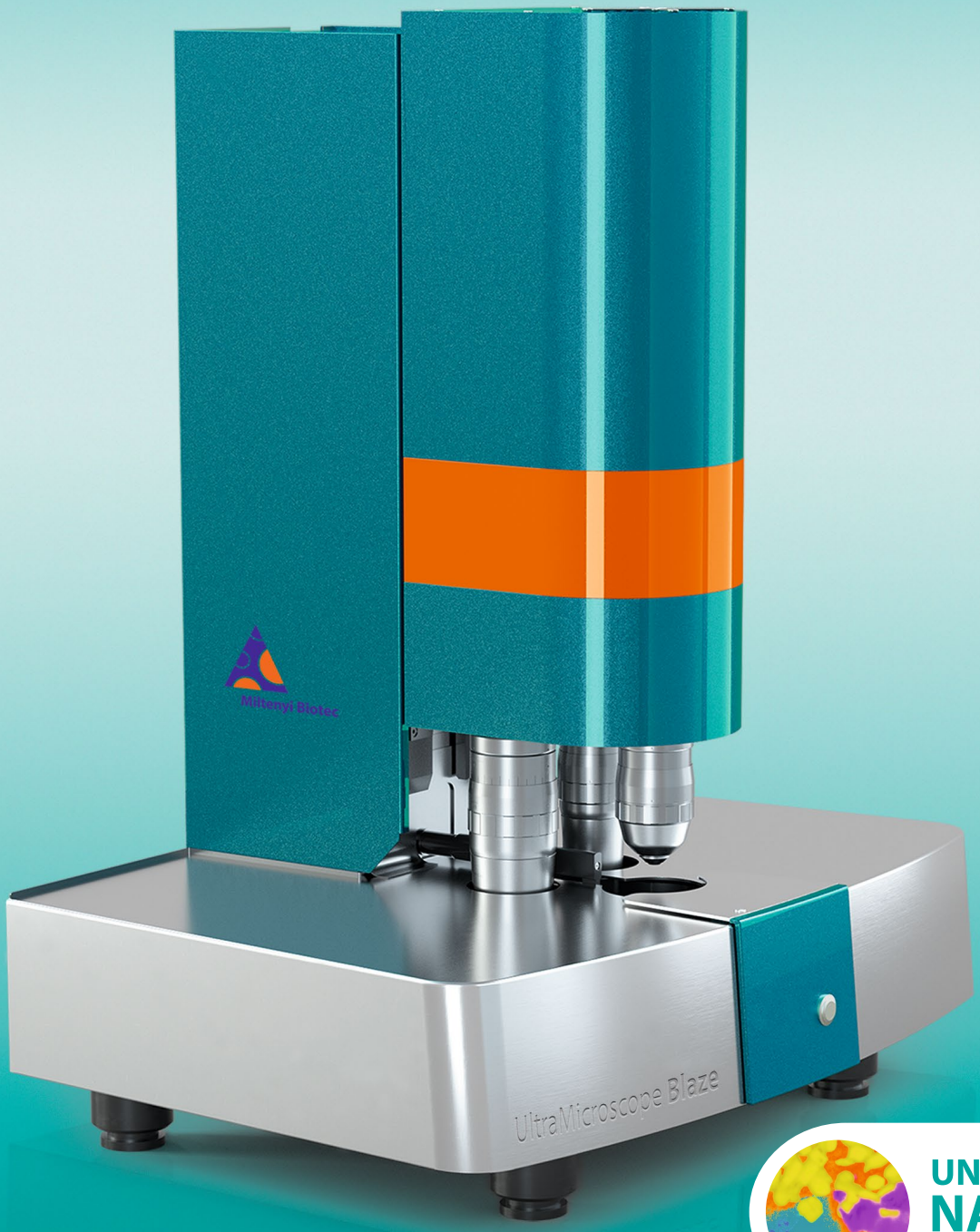
Miltenyi Biotec

UltraMicroscope Blaze™

The automation of light sheet microscopy



UNDERSTAND
NATURE'S
COMPLEXITY

Light sheet imaging from a new perspective

Discover our fully automated light sheet microscope UltraMicroscope Blaze for imaging multiple or very large samples with subcellular resolution. Explore microscopy at a different level to accelerate your projects and pave the way for new insights. The combination of our pioneering UltraMicroscope technology with the latest developments in the field of light sheet optics and sample preparation guarantees best data quality.

Easy handling based on full automation

The UltraMicroscope Blaze enables seamless switching between different objectives and magnification lenses with the click of a button while keeping images sharp with the autofocus feature. Automated movement of the sample chamber greatly facilitates sample loading and exchange.

Image multiple samples together

Accelerate your research by imaging several different samples together. The large sample holder can either host a whole cleared mouse model or multiple samples at once, which can then be imaged sequentially and effortlessly. See the big picture without losing the subcellular details.

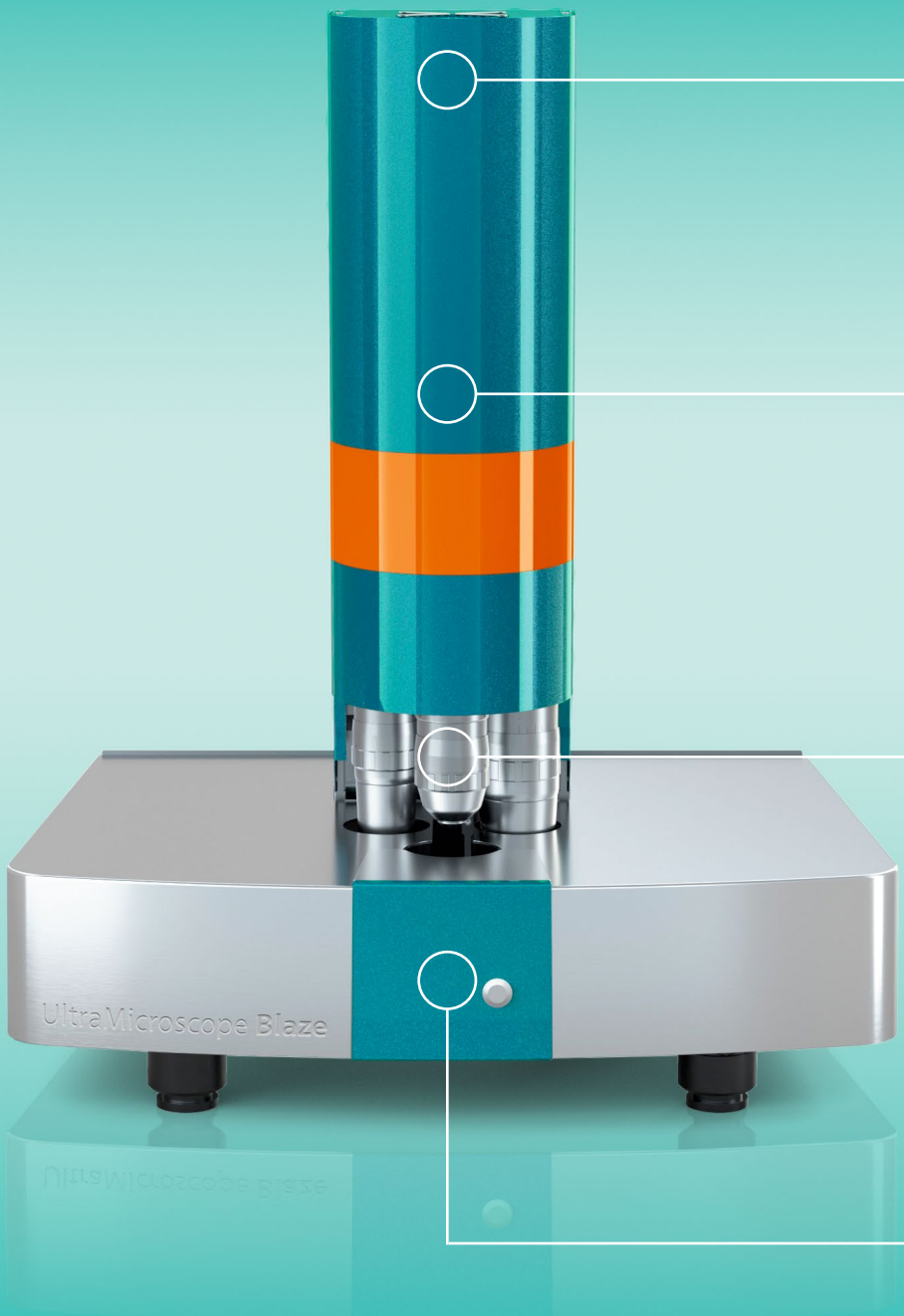
Next-level light sheet imaging

Cutting-edge illumination optics guarantee homogeneous excitation, and the specially developed MI Plan objective series delivers unprecedented image quality.

Easy handling based on full automation

The UltraMicroscope Blaze originates from a decade of experience and is designed to expedite your research projects. Our users' feedback has been the driving force to create this new member of the UltraMicroscope family.

Loading a sample into the microscope and switching between different magnifications has never been easier. Enter the fast lane with the new UltraMicroscope Blaze and pave the way for new insights.



Autofocusing

Keep your images sharp after sample and objective exchanges.

Automated magnification changer

Software-controlled exchange of magnification from 0.6× to 2.5×.

Motorized turret: From overview to subcellular imaging

Switch automatically between our MI Plan objective lenses.

Automated sample chamber release

The large sample chamber can be moved automatically allowing easy sample loading and exchange. It can hold a whole cleared mouse or multiple samples that can be imaged together.

Image multiple samples together

The new UltraMicroscope follows a simple rule: "Enable the easiest imaging of multiple or large samples for best data quality". Now you can reduce time-consuming sample exchanges and avoid sectioning artifacts to increase your output on high-quality data. Load all of your samples at once and run a pre-set program overnight. The UltraMicroscope Blaze will do the rest and your high-quality 3D data will be ready for you the next morning.

Figure 1: UltraMicroscope Blaze sample holder hosting five samples at the same time.

Next-level light sheet imaging

The combination of our successful UltraMicroscope technology with the latest developments in the field of light sheet optics guarantees the best data quality. The flat-field correction in addition to long working distances makes the MI Plan objective series well suited for high-resolution imaging of large samples. In addition, they are compatible with all imaging solutions from water to solvents with high refractive indices. Explore our broad range of magnification options, from panoptic imaging at 0.66× to subcellular imaging at 30×.

The UltraMicroscope Blaze uses cutting-edge illumination optics to slightly tilt 2×3 bidirectional light sheets with their Rayleigh lengths overlapping in the entire field of view (FOV). The Rayleigh length is where the light sheet is thinnest and where detection takes place. This helps to generate homogeneous illumination and high image quality. Get the most out of your sample with improved optical sectioning.

Figure 2: The MI Plan objective lens series is optimized for high-resolution light sheet microscopy.

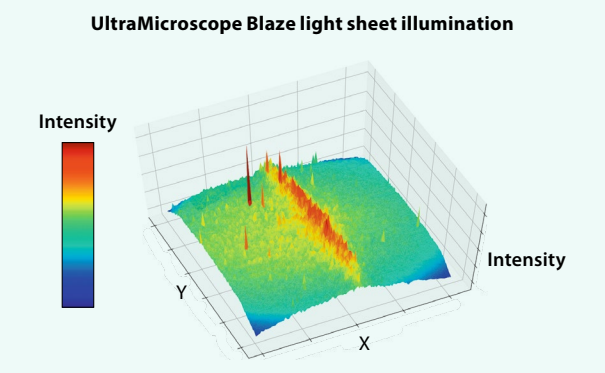


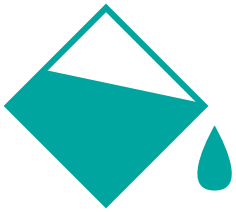
Figure 3: Intensity profile of the 2×3 bidirectional light sheets showing an overlap in the FOV. This optimized illumination generates uniform excitation that can achieve higher image quality and excellent optical sectioning.

> The UltraMicroscope Blaze allows us to see every single cancer metastasis in the whole bodies of transparent mice and we can also see if drugs are targeting all those tiny micro-metastases. The UltraMicroscope Blaze will be a powerful tool for drug development in oncology.

Dr. Ali Ertürk, Director of iTERM, Helmholtz Zentrum München, Germany

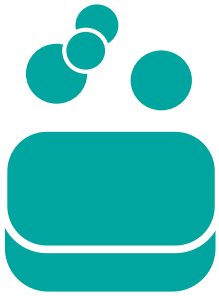
Obtain new insights in biology in three steps

With its cutting-edge optics, smart engineering, and intuitive interface, the UltraMicroscope Blaze offers a new perspective on organisms, how they are built, and how they function. Visualizing the three-dimensional architecture of complex biological systems is effortless thanks to the high-speed and automated imaging process. Since appropriate sample preparation is essential for this workflow, Miltenyi Biotec offers a complete portfolio of validated antibodies and antibody-fluorochrome conjugates, and an easy-to-use clearing kit. Start your experiments with the right tools to get the best results.



01 STAINING

Unique antibodies for reliable and reproducible staining. Explore our portfolio of REAfinity™ Recombinant Antibodies, validated for light sheet microscopy and optimized for our MACS® Clearing Kit.



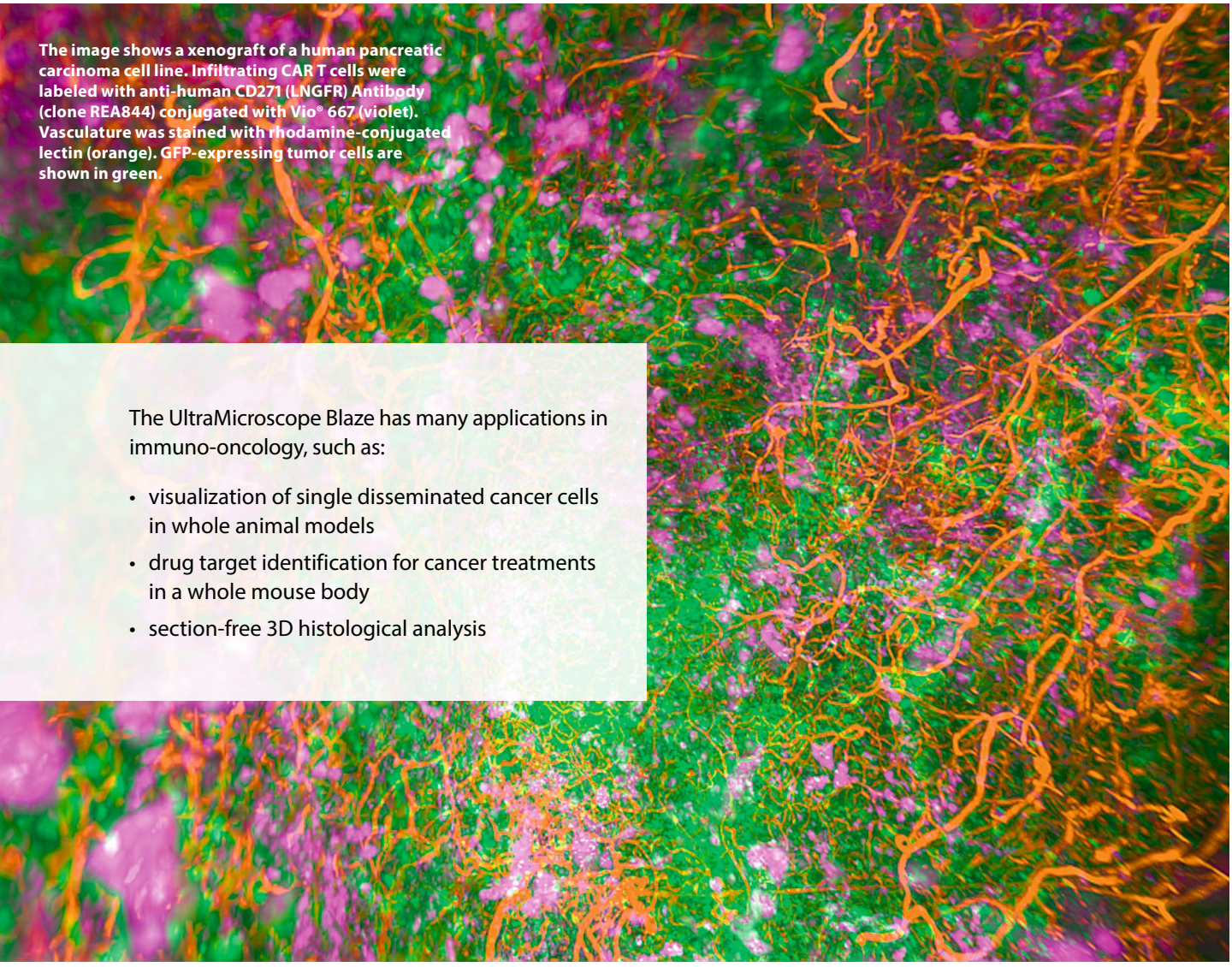
02 CLEARING

The MACS Clearing Kit provides a clearing process that is straightforward to use: fast, non-toxic, cost-effective, and easy. Clearing renders the optical properties of opaque organs, like brains and tumor tissues, and even entire mouse models, transparent while keeping their structure intact.

03 AUTOMATED IMAGING

Multiple cleared samples can be imaged at once; each sample is excited by six focused light sheets and the resulting fluorescence is recorded. One sample after another is moved through the focal plane, exciting fluorophores at each layer and creating 3D image stacks while keeping photodamage and bleaching to a minimum.

Visualize details inside tumor cells in whole animal models and organs



The image shows a xenograft of a human pancreatic carcinoma cell line. Infiltrating CAR T cells were labeled with anti-human CD271 (LNGFR) Antibody (clone REA844) conjugated with Vio® 667 (violet). Vasculature was stained with rhodamine-conjugated lectin (orange). GFP-expressing tumor cells are shown in green.

The UltraMicroscope Blaze has many applications in immuno-oncology, such as:

- visualization of single disseminated cancer cells in whole animal models
- drug target identification for cancer treatments in a whole mouse body
- section-free 3D histological analysis

Cellular and molecular probing of intact human organs.
Zhao, S. *et al.* (2020) Cell 180, 1–17.

Deep learning reveals cancer metastasis and therapeutic antibody targeting in the entire body.
Pan, C. *et al.* (2019) Cell 179: 1661–1676.e19.

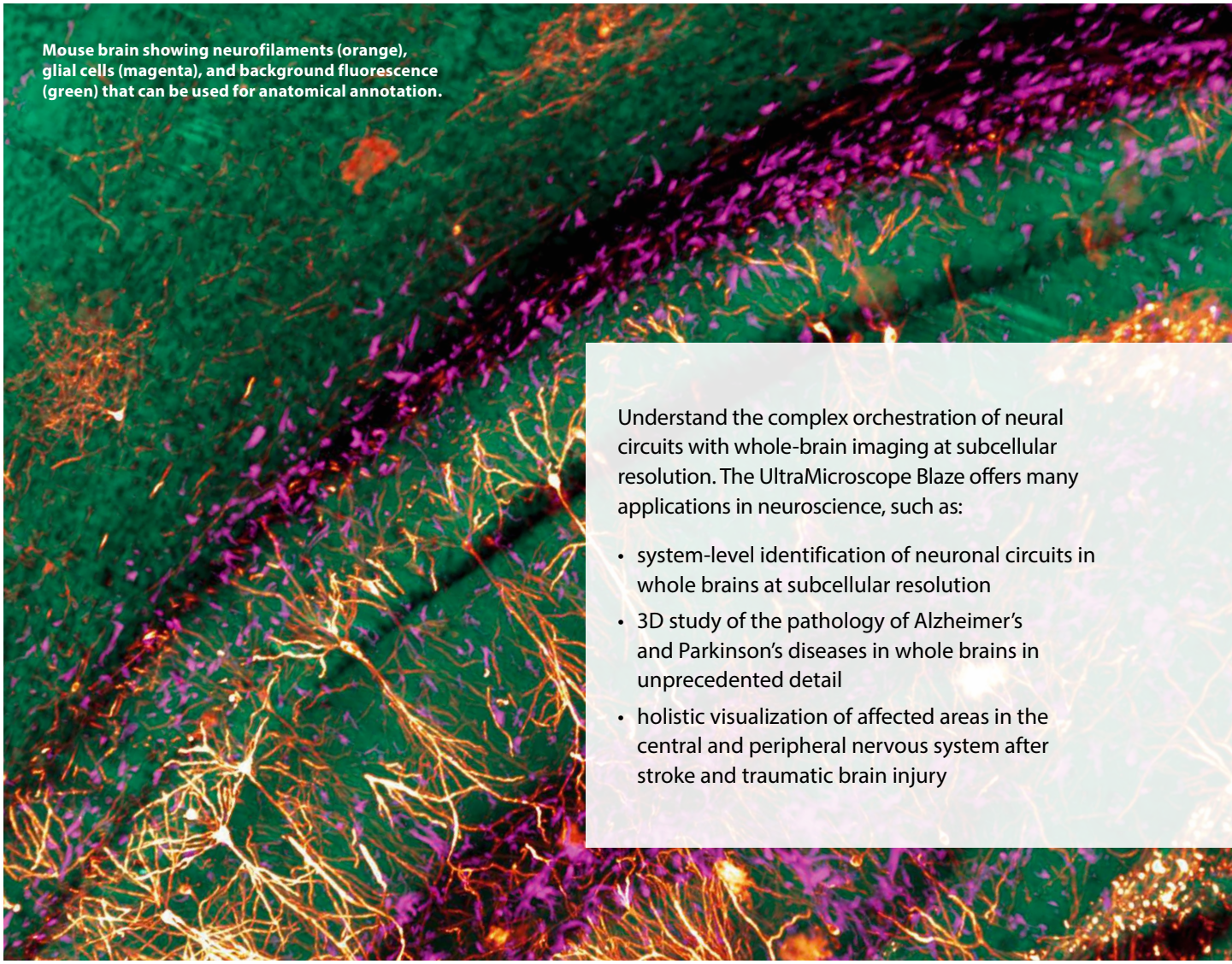
Locally renewing resident synovial macrophages provide a protective barrier for the joint.
Culemann, S. *et al.* (2019) Nature 572: 670–675.

Glioblastoma multiforme restructures the topological connectivity of cerebrovascular networks.
Hahn, A. *et al.* (2019) Scientific Reports 9, 11757.

Correlated MRI and Ultramicroscopy (MR-UM) of brain tumors reveals vast heterogeneity of tumor infiltration and neoangiogenesis in preclinical models and human disease.
Breckwoldt, M.O. *et al.* (2019) Front. Neurosci. 12, 1004.

Tumor uptake of anti-CD20 fabs depends on tumor perfusion.
Mendler, C.T. *et al.* (2016) J. Nuc. Med. 57: 1971–1977.

Neuroimaging of large samples with subcellular resolution



Mouse brain showing neurofilaments (orange), glial cells (magenta), and background fluorescence (green) that can be used for anatomical annotation.

Understand the complex orchestration of neural circuits with whole-brain imaging at subcellular resolution. The UltraMicroscope Blaze offers many applications in neuroscience, such as:

- system-level identification of neuronal circuits in whole brains at subcellular resolution
- 3D study of the pathology of Alzheimer's and Parkinson's diseases in whole brains in unprecedented detail
- holistic visualization of affected areas in the central and peripheral nervous system after stroke and traumatic brain injury

Mapping the fine-scale organization and plasticity of the brain vasculature.
Kirst, C. *et al*, (2020) Cell 180, 780–795.e25.

Circuit asymmetries underlie functional lateralization in the mouse auditory cortex.
Levy, R.B. *et al.* (2019) Nat. Commun. 10: 2783.

GABAergic inhibition in dual-transmission cholinergic and GABAergic striatal interneurons is abolished in Parkinson disease.
Lozovaya, N. *et al.* (2018) Nat. Commun. 9: 1422.

Three-dimensional study of Alzheimer's disease hallmarks using the iDISCO clearing method.
Liebmann, T. *et al.* (2016) Cell Rep. 6: 1138–1152.

Mapping of brain activity by automated volume analysis of immediate early genes.
Renier, N. *et al.* (2016) Cell 165: 1789–1802.

Whole-brain imaging with single-cell resolution using chemical cocktails and computational analysis.
Susaki, E.A. *et al.* (2014) Cell 157: 726–739.

Specifications

The UltraMicroscope Blaze can host three MI Plan objective lenses that can be exchanged automatically. Total magnification ranges from 0.66× to 30× thanks to the automated magnification changer. The instrument can be equipped with either a 4.2 MP or a 5.5 MP sCMOS camera.

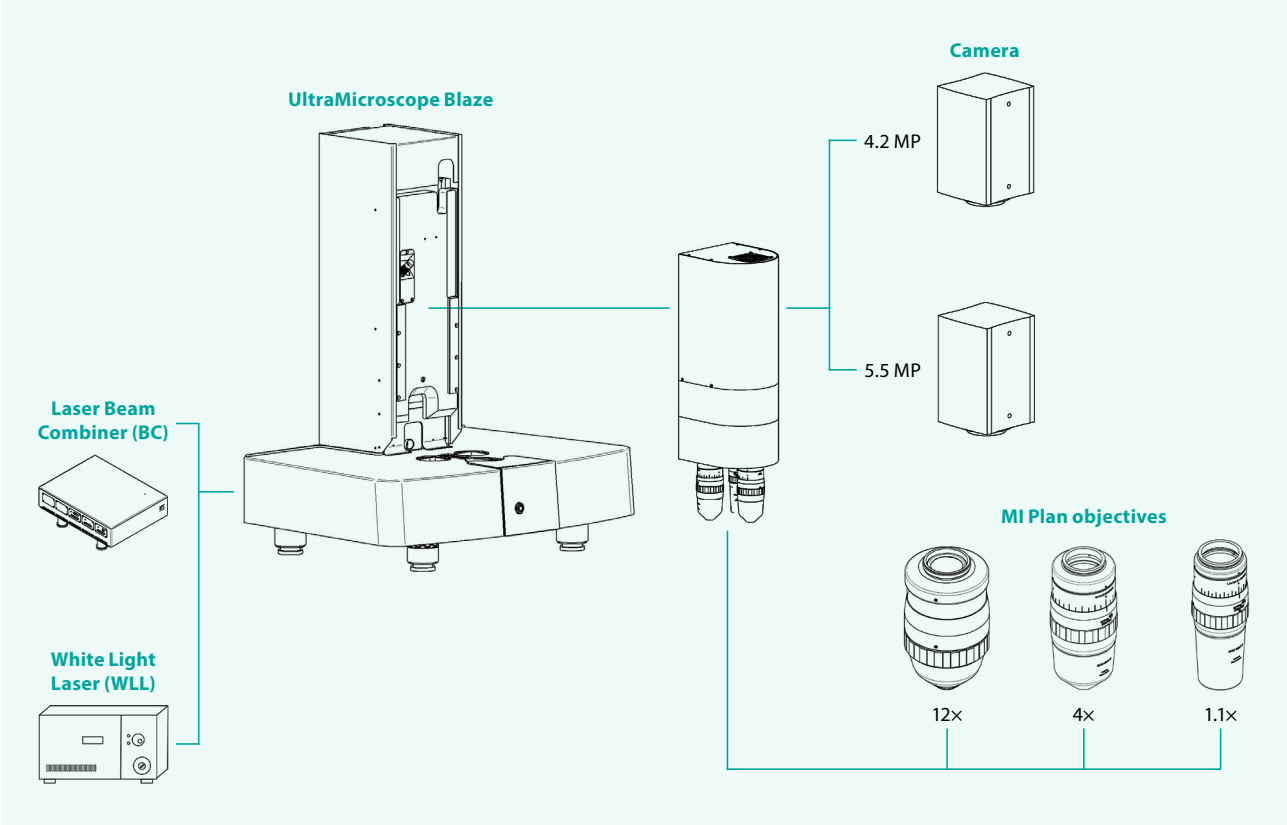


Figure 4: Overview of the UltraMicroscope Blaze configurations.

UltraMicroscope Blaze Instrument specifications	
Sheet optics	
Illumination	Uni- and bidirectional
Number of light sheets	1–6
Thickness	4–24 µm
Width	1–20 mm
Numerical aperture	0.0135–0.135
Focus positioning	Dynamic
Refractive index (RI) compensation	Software-controlled automated RI compensation over the range of 1.33–1.56, covering all clearing media

UltraMicroscope Blaze Instrument specifications (cont.)

Light sources

Laser BC	Max. 5 laser lines (405, 488, 561, 639, 785 nm)*, 50–100 mW per diode
Supercontinuum WLL	Spectral range depending on the laser module (e.g. 410–800 nm)

Detection optics

Objective lenses	1.1×	4×	12×
Total magnification	0.66–2.75×	2.4–10×	7.2–30×
Numerical aperture	0.1	0.35	0.53
Max. theoretical resolution at detector	4.8 µm	1.3 µm	0.5 µm
Working distance	≤17 mm	≤16 mm	≤10.9 mm
FOV diagonal (5.5 MP camera)	7.9–33 mm	2.2–9.1 mm	0.73–3 mm
Emission filters	Seven filters Ø 43 mm		
Chromatic correction	Software-controlled automatic chromatic correction in the range of 400–850 nm		
Focusing	Software-controlled autofocus		
Objective change	Motorized turret allows automated change of objective lenses.		
Magnification change	Software-controlled automated magnification changer for all objective lenses		

Camera specifications

Detector	4.2 Megapixel sCMOS camera	5.5 Megapixel sCMOS camera
Active pixels (w×h)	2048×2048	2560×2160
Pixel size	6.5 µm × 6.5 µm	6.5 µm × 6.5 µm
Sensor size	13.3 mm × 13.3 mm; 18.8 mm diagonal	16.6 mm × 14 mm; 21.8 mm diagonal
Readout noise	0.8 med e^-	1 med e^-
Maximal frame rates	100 fps	100 fps
Maximum quantum efficiency	82%	60%

Image chamber

Imaging solution	Aqueous buffers and organic solvents
Sample travel range (x, y, z)	24 mm, 50 mm, 23 mm
Chamber size	51 mm × 129 mm × 64 mm
Sample mounting assistance	Easy access to sample holder by automated movement of the sample chamber from measurement to parking position
Multisample measurement	Batch measurement mode for automated sequential imaging of multiple samples in one experiment

General information

Dimensions (w×h×d)	67 cm × 91 cm × 52.5 cm
Weight	98 kg (w/o controller and laser)

*Five out of eleven available laser lines can be chosen for the Beam Combiner.

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