



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

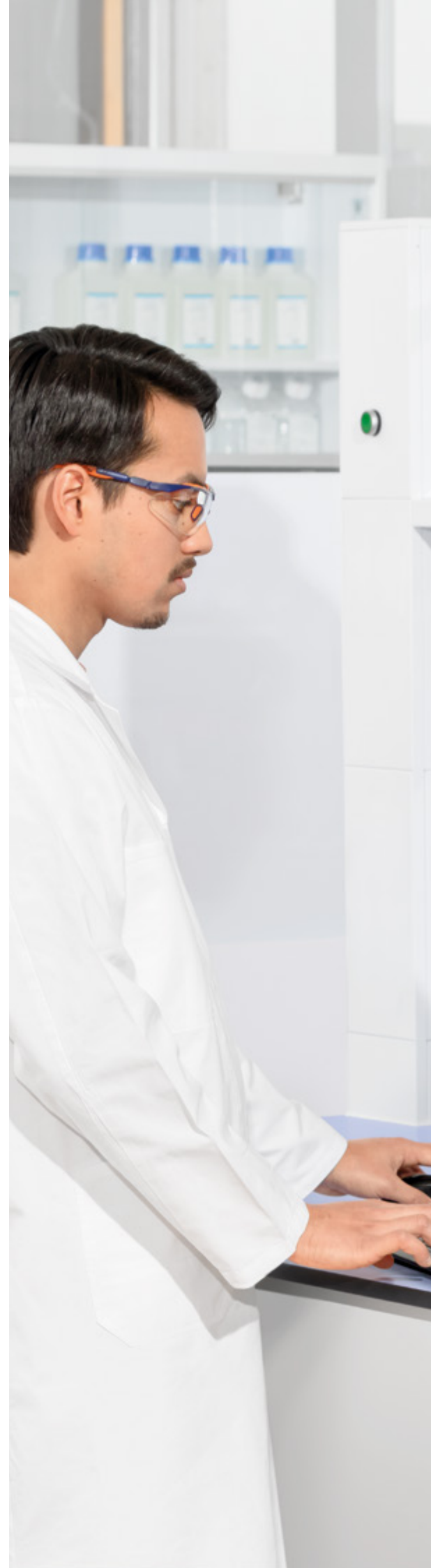
The UltraMicroscope Blaze enables seamless switching between different objectives and magnification lenses, and automated sample release with the click of a button, whilst keeping images sharp with the autofocus feature.

Image multiple samples together

Accelerate your research by imaging multiple samples together. The large sample holder can either host a whole cleared mouse model or up to five 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 homogenous 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 0.6x to 2.5x.

Motorized turret: From overview to subcellular imaging

Switch automatically between our MI Plan objective lenses.

Automated sample release

The large sample chamber can be automatically released for sample exchange. It can hold a whole cleared mouse or up to five 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.

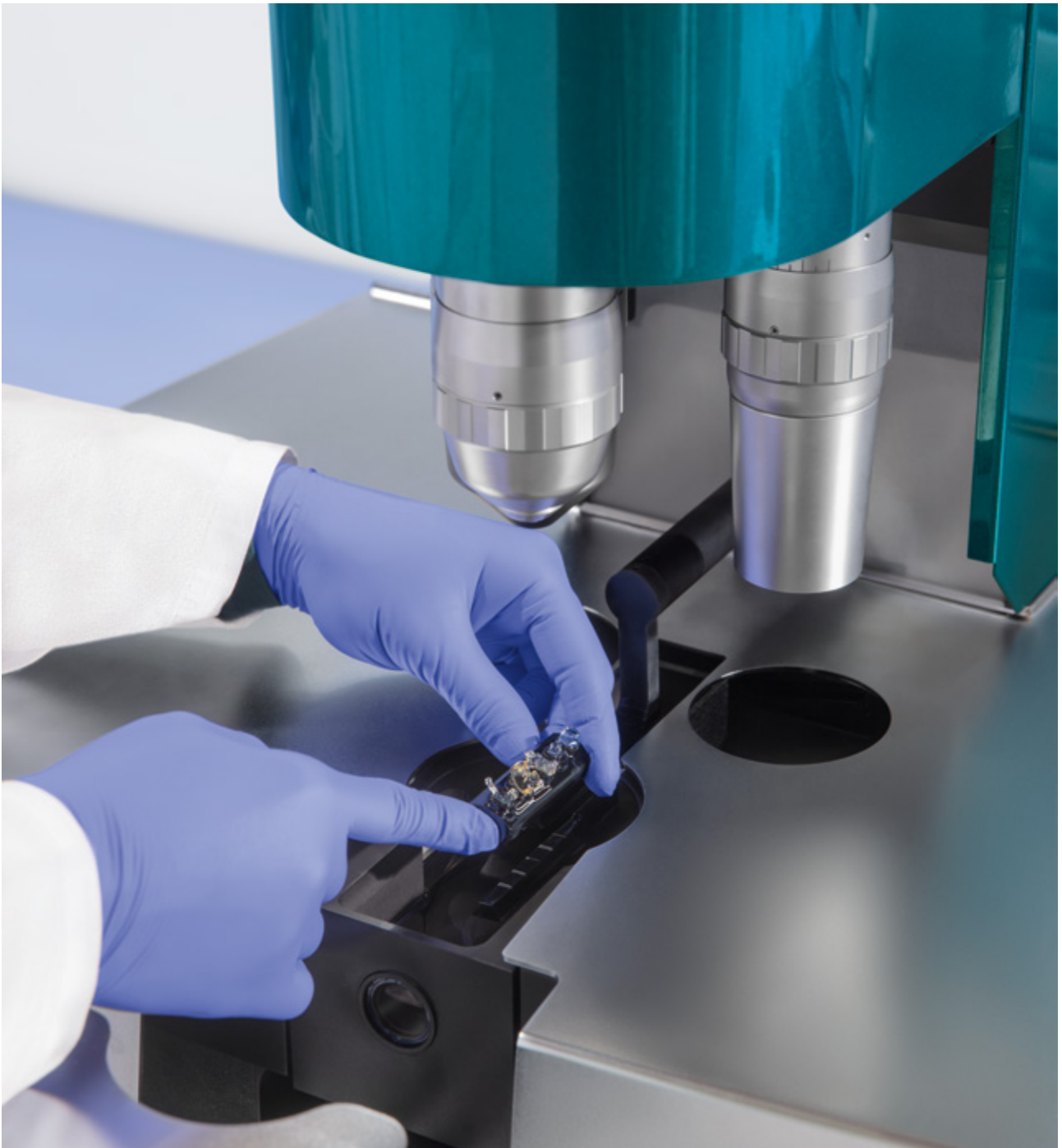


Figure 1: UltraMicroscope Blaze sample holder hosting five samples at the same time.

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 0.66x to subcellular imaging at 30x.



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

The UltraMicroscope Blaze uses cutting-edge illumination optics to slightly tilt 2x3 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 homogenous illumination and high image quality. Get the most out of your sample with improved optical sectioning.

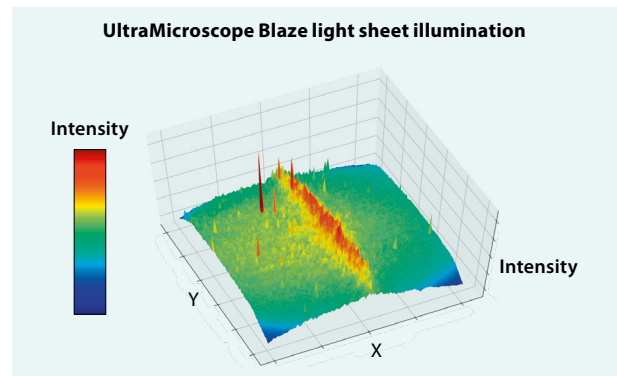


Figure 3: Intensity profile of the 2x3 bidirectional light sheets showing an overlap in the FOV. This optimized illumination generates uniform excitation that can achieve higher image quality and excellent optical sectioning.

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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.

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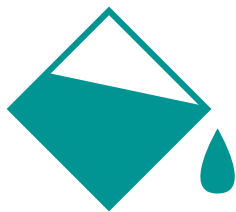
**Dr. Ali Ertürk, Director of
iTERM, Helmholtz Zentrum
München, Germany**



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

Pancreatic carcinoma, CAR T cells labeled with CD271 (LNGFR), human, Miltenyi clone: REA844 conjugated with Vio[®] 667 (violet) rhodamine lectin labeling vasculature (orange), GFP (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.

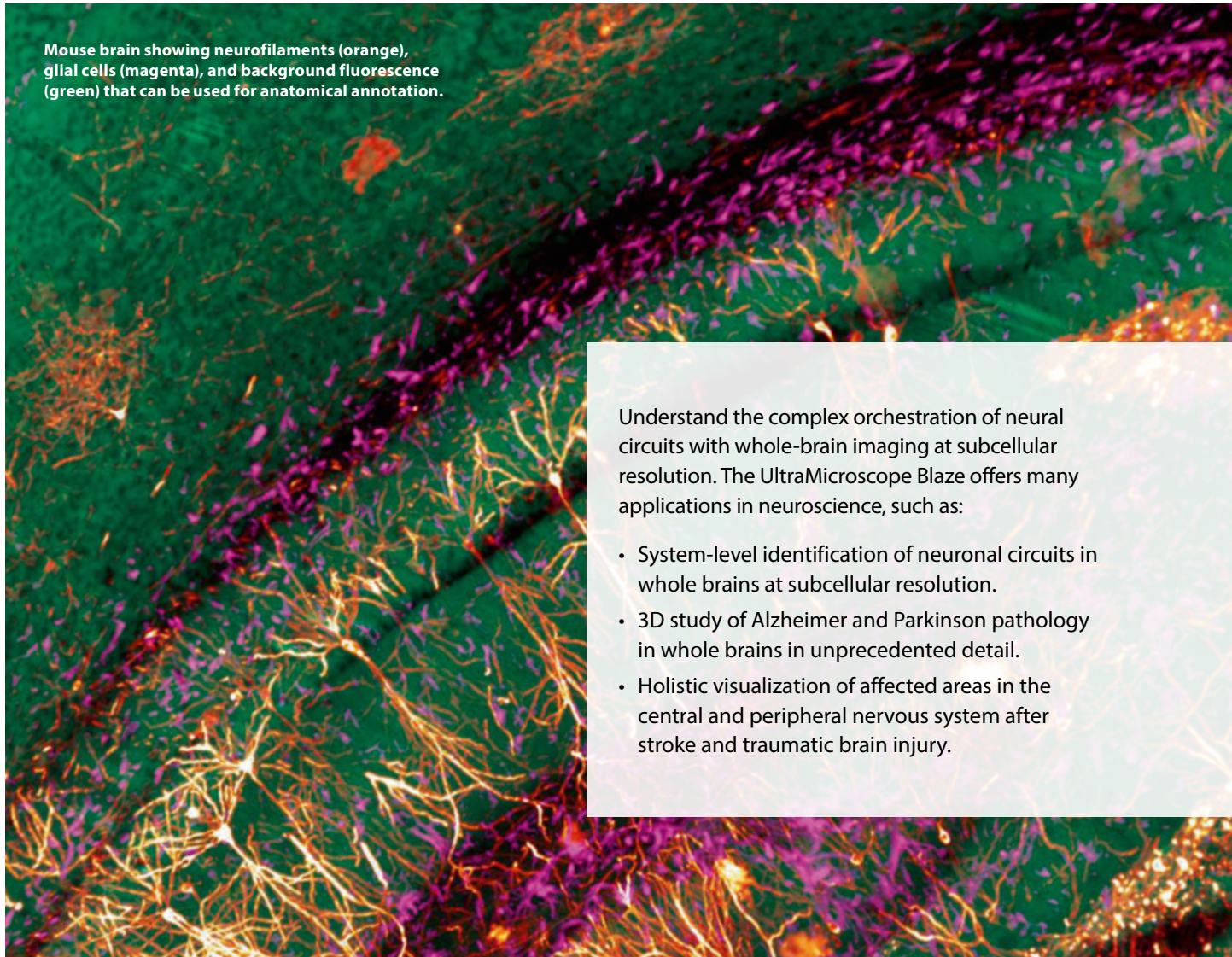
Correlated MRI and Ultramicroscopy (MR-UM) of brain tumors reveals vast heterogeneity of tumor infiltration and neoangiogenesis in preclinical models and human disease.

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 Alzheimer and Parkinson pathology 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 comes in two configurations. The zoom configuration is equipped with a manually controlled zoom optics reaching from 1.26x to 12.6x.

The automated objective (AO) configuration can host the MI Plan objective lenses and provides a total magnification from 0.6x to 30x thanks to its automated magnification changer. Both versions can be equipped with either 4.2 MP or 5.5 MP sCMOS camera.

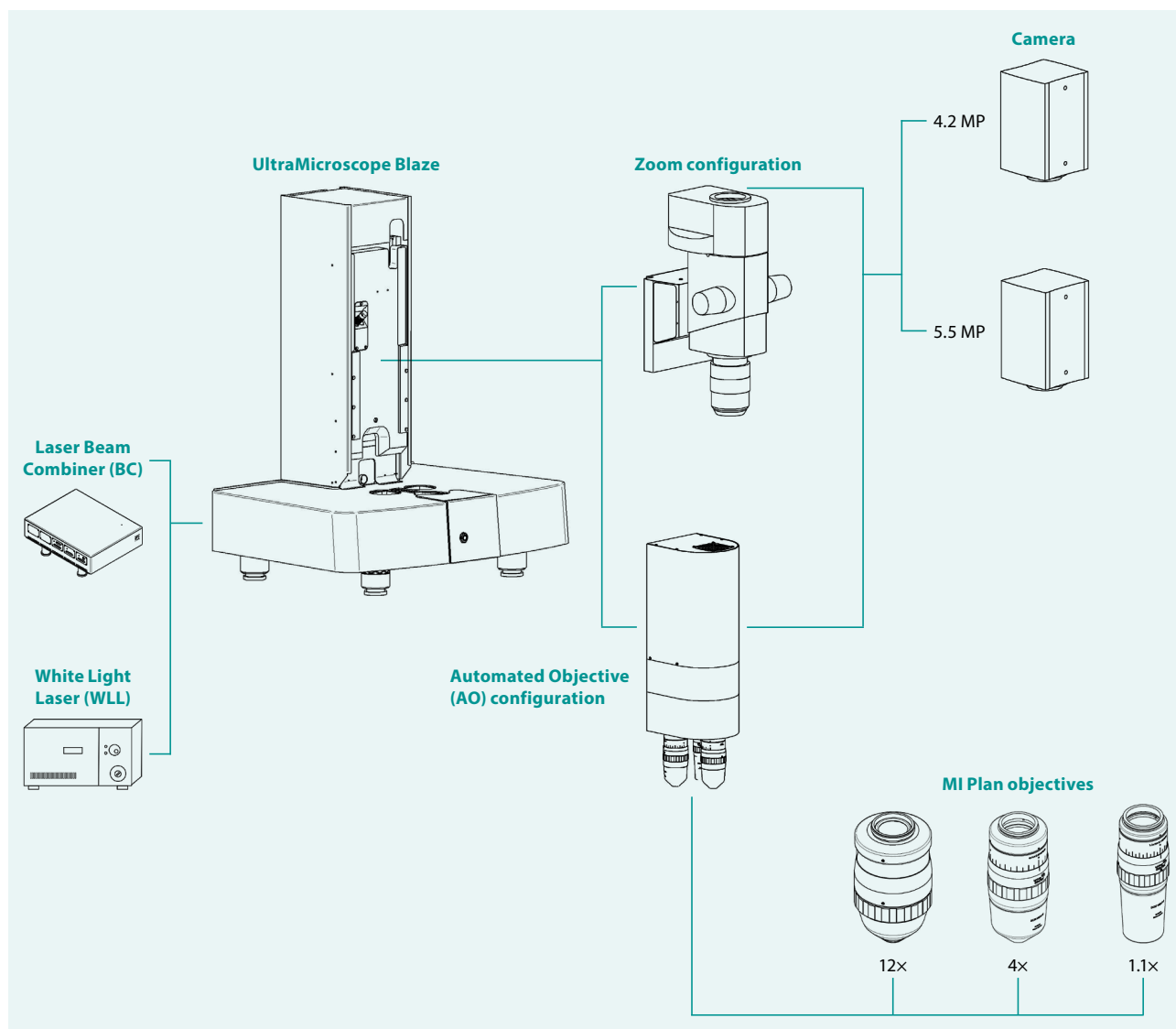


Figure 4: Overview of the UltraMicroscope Blaze configurations.

UltraMicroscope Blaze 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

Detection optics

Zoom configuration AO configuration

	2 \times	1.1 \times	4 \times	12 \times
Objective lenses	2 \times	1.1 \times	4 \times	12 \times
Zoom Magnification changer	1.26–12.6 \times	0.66–2.75 \times	2.4–10 \times	7.2–30 \times
Resolution at detector	1–10.4 μm	4.8–19.6 μm	1.3–5.4 μm	0.44–1.8 μm
Numerical aperture	0.5	0.1	0.35	0.53
Working distance	>5.7 mm	\leq 17 mm	\leq 16 mm	\leq 10.9 mm
FOV diagonal (5.5 MP camera)	1.7–17.3 mm	7.9–33 mm	2.2–9.1 mm	0.73–3 mm
Emission filters	Seven filters \varnothing 32 mm	Seven filters \varnothing 43 mm		
Chromatic correction	Dynamic 400–850 nm			

Image chamber

Imaging solution	Aqueous buffers and organic solvents
Sample travel range (x, y, z)	12.5 mm, 43.7 mm, 25 mm
Chamber size	129 mm \times 51 mm \times 64 mm
Multiple sample capacity	Up to five samples at once
Refractive index matching	1.33–1.56

General information

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

Light sources

Laser BC	Max. 5 laser lines (405, 488, 561, 639, 785 nm)*, 50–100 mW per diode
Supercontinuum WLL	460 nm–800 nm, 1 mW/nm–3 mW/nm

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

Camera specifications

	4.2 Megapixel sCMOS camera	5.5 Megapixel sCMOS camera
Detector	4.2 Megapixel sCMOS camera	5.5 Megapixel sCMOS camera
Active pixels (w \times h)	2048 \times 2048	2560 \times 2160
Pixel size	6.5 μm \times 6.5 μm	6.5 μm \times 6.5 μm
Sensor size	13.3 mm \times 13.3 mm; 18.8 mm diagonal	16.6 mm \times 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%



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