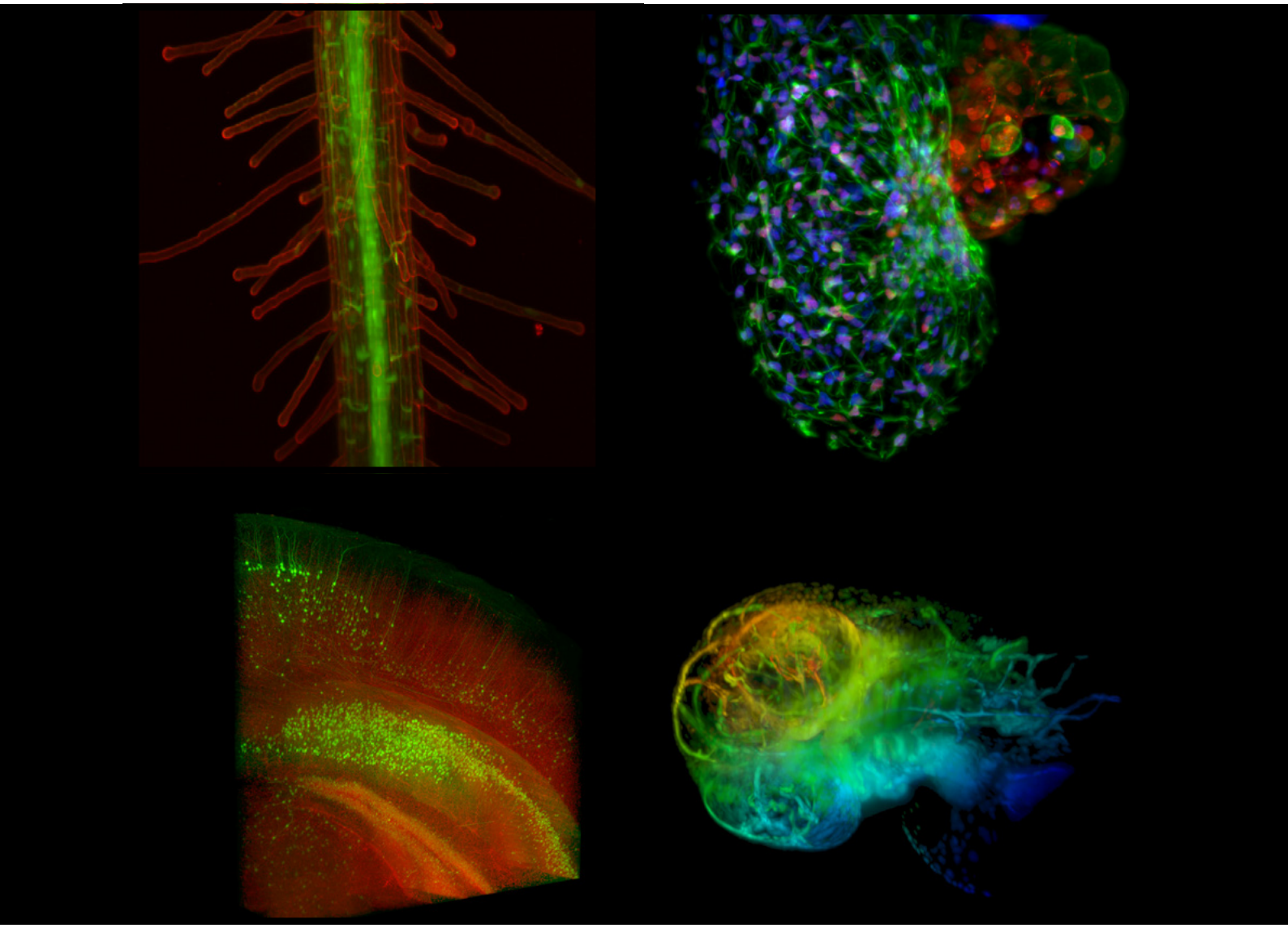
Application Note



ZEISS Lightsheet Z.1

Imaging Biological Samples – a Reference List

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Imaging Biological Samples – a Reference List

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Introduction

In Light Sheet Fluorescence Microscopy (LSFM), the detection beam path is placed perpendicular to the illumination beam path. By this means a fluorescently labeled sample is illuminated from the side, using laser-light that is formed into a thin sheet of light, exciting only fluorophores within the focal plane of the detection objective. Thus all fluorescent signal can be collected on a camera based detector.

This unique setup allows for extremely light efficient optical sectioning and unprecedented imaging speed, causing only minimal phototoxicity or bleaching. Image acquisition with high spatial and temporal resolution over long periods of time becomes a feasible task. Lightsheet Z.1 offers a horizontal LSFM setup, in which a sample is suspended from above and placed into a liquid-filled sample chamber, providing the sample with environmentally (temperature, medium) stable conditions over long periods of time. Additionally, the sample can be rotated in front of the detection objective to image from the perfect angle or to combine different viewing perspectives into one dataset, known as Multiview imaging.

The many advantages of Lightsheet Z.1 have been used by scientists of different specialties to advance their research. Imaging live specimens clearly benefits from the combination of advantages LSFM offers. Therefore, many publications featuring Lightsheet Z.1 are reporting in vivo imaging of whole organisms (e.g. model organism in developmental biology) or three-dimensional cell- and tissue-cultures.

But fixed and chemically cleared tissues, such as whole mouse brains, also make use of the fast, sensitive and stable imaging conditions of Lightsheet Z.1.

This document is a collection of the published research using Lightsheet Z.1, over the past three years. It shows the vast opportunities of a multi-purpose LSFM within different areas of research.

Further Reading

1. Olaf Selchow and Jan Huisken (2013). Light sheet fluorescence microscopy and revolutionary 3D analyses of live specimens. Photonik international, 2013 (Originally published in German in BioPhotonik 1/2013). For download click here.
2. Reynaud, E. G. et al (2015). Guide to light-sheet microscopy for adventurous biologists. Nature Methods 12, 30–34. doi:10.1038/nmeth.3222
3. Pampaloni, F. et al (2015). Light sheet-based fluorescence microscopy (LSFM) for the quantitative imaging of cells and tissues. Cell and tissue Research Volume 360, Issue 1 (129–141). doi 10.1007/s00441-015-2144-5
4. White Paper: Sample Preparation for Light Sheet Microscopy, Protocols and Guidelines for ZEISS Lightsheet Z.1. For download click here.

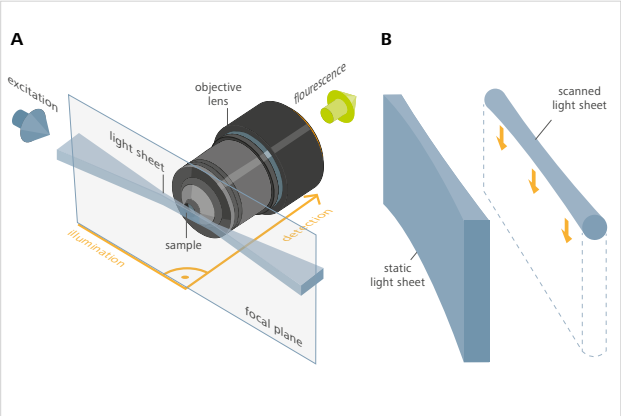

Figure 1 *The light sheet is projected onto the sample form the side (A), i.e. perpendicular to the optical axis of the detection lens, hence illuminating the microscope's entire focal plane. (B) The light sheet is generated either statically using a cylindrical lens or dynamically by high-frequency scanning of a laser beam. (Taken from Olaf Selchow and Jan Huisken, 2013)*

Cell Culture / In Vitro Imaging

Publication	Sample	Application
Polanski, R. et al (2015). Caspase-8 activation by TRAIL monotherapy predicts responses to IAPi and TRAIL combination treatment in breast cancer cell lines. Cell Death and Disease (2015) 6, e1893. doi:10.1038/cddis.2015.234	Spheroids using 31 different breast cancer cell lines	High throughput application screen Multicolor imaging on fixed tissue
Sethi, P. et al (2015). 3D tumor tissue analogs and their orthotopic implants for understanding tumor-targeting of microenvironment-responsive nanosized chemotherapy and radiation. Nanomedicine Vol. 11 No. 8 pages 2013-2023. doi:10.1016/j.nano.2015.07.013	4T1-mCherry tumor cells, C166-GFP endothelial cells, murine embryonic fibroblasts (MEF)	3D co-culture spheroid model, representing the milieu of triple negative breast cancer in vitro
Hagiwara, M. et al (2015). In vitro reconstruction of branched tubular structures from lung epithelial cells in high cell concentration gradient environment. Scientific Reports 5, Article nr. 8054. doi:10.1038/srep08054	Primary lung epithelial cells	3D cell culture in Matrigel Multicolor imaging on fixed tissue
Janisch, K.M. and Dwyer, N.D.(2015). Imaging and quantitative analysis of cytokinesis in developing brains of Kinesin-6 mutant mice. Methods in Cell Biology, available online 2nd September 2015. doi:10.1016/bs.mcb.2015.06.008	Mouse *Mus musculus*	Embryonic mouse cerebral cortex, whole mount "slabs"

Clearing

Publication	Sample	Application
Kim, S.-Y. et al (2015). Stochastic electrotransport selectively enhances the transport of highly electromobile molecules. PNAS November 2, 2015. doi:10.1073/pnas.1510133112	Mouse *Mus musculus*	Clearing, CLARITY; of whole organs Staining of cleared tissue with stochastic electrotransport
Hama, H. et al (2015). Sca/eS: an optical clearing palette for biological imaging. Nature Neuroscience 18 (10). doi:10.1038/nn.4107	Mouse *Mus musculus* Human	Clearing, Sca/eS, of brain tissue slices Fluorescence imaging TEM imaging after Clearing
Menegas, W. et al (2015). Dopanine neurons projecting to the posterior striatum from an anatomically distinct subclass. eLife 2015;10.7554/eLife.10032. doi:10.7554/eLife.10032	Mouse *Mus musculus*	Clearing, CLARITY, of brain tissue Whole brain imaging, mapping neuron projections
Chen, J.Y. et al.(2016), Hoxb5 marks long-term haematopoietic stem cells and reveals a homogenous perivascular niche, Nature, February 11, 530 (7589): 223-7. doi:10.1038/nature16943.	Mouse Bone Marrow Haematopoietic stem cells (HSCs)	Cleared Bone Marrow (CUBIC)
Eunsoo, L. et al. (2016), ACT-PRESTO: Rapid and consistent tissue clearing and labeling method for 3-dimensional (3D) imaging, Scientific Reports, 6: 19103, doi:10.1038/srep19103	Mouse Brains	ACT-PRESTO Clearing method

Plant Imaging

Publication	Sample	Application
Perochon, A. et al (2015). TaFROG encodes a Pooideae orphan protein that interacts with SnRK1 and enhances resistance to the mycotoxigenic fungus Fusarium graminearum. Plant Physiol. Nov 9 (2015). doi:10.1104/pp.15.01056	Plant *Arabidopsis thaliana*	Functional characterization of a gene as a component of resistance to the important disease (Fusarium head blight9 in wheat (Triticum aestivum) in vivo imaging
Ovecka, M. et al. (2015). Preparation of plants for developmental and cellular imaging by light-sheet microscopy. Nature Protocols 10, 1234-47. doi:10.1038/nprot.2015.081	Plant *Arabidopsis thaliana*	Sample preparation of seedlings Root growth and development in vivo imaging
Berson, T. et al (2014). Trans-Golgi network localized small GTPase RabA1d is involved in cell plate formation and oscillatory root hair growth. BMC Plant Biology 14:252. doi:10.1186/s12870-014-0252-0	Plant *Arabidopsis thaliana,* *Allium porrum,* *Nicotiana benthamiana*	Root development Root hair formation In vivo imaging Time lapse experiments

Whole Organisms / In Vivo Imaging

Publication	Sample	Application
Yokota, Y. et al (2015). Endothelial Ca^{2+} oscillations reflect VEGFR signaling-regulated angiogenic capacity in vivo. eLife 2015; 10.7554/eLife08817. doi: 10.7554/eLife08817	Zebrafish embryo *Danio rerio*	Ca^{2+} imaging in endothelial cells during angiogenesis In vivo imaging
Francisco, J. et al (2015). SPARC triggers a cell-autonomous program of synapse elimination. PNAS October 27, 2015. doi: 10.1073/pnas.1512202112	Western clawed frog tadpole *Xenopus tropicalis*	Neuronal development Excess synaptic contacts elimination Fixed tissue
Park, O.K. et al (2015). 3D Light-Sheet Fluorescence Microscopy of Cranial Neurons and Vasculature during Zebrafish Embryogenesis. Mol. Cells 38(11). doi:14348/molcells.2015.0160	Zebrafish embryo *Danio rerio*	Cranial vasculature and nervous system morphogenesis Time lapse experiments
Bajoghli, B. et al. (2015). Noninvasive in toto imaging of the thymus reveals heterogeneous migratory behavior of developing T cells. The Journal of Immunology vol. 197 no5 2177-2186. doi: 10.4049/jimmunol.1500361	Medaka *Oryzias latipes*	T-cell migration in the juvenile thymus In vivo imaging
Chittajallu, D.R. (2015). In vivo cell-cycle profiling in xenograft tumors by quantitiative intravital microscopy. Nat Methods Jun;12(6):577-85. doi: 10.1038/nmeth.3363	Mouse *Mus musculus*	Automatization of cell – cycle profiling in vivo imaging
Chow, C.L. et al (2015). Characterization of a unique cell population marked by transgene expression in the adult cochlea of nestin-CreER(T2)/tdTomato-reporter mice. J Comp Neurol. 2015 Jul 1;523(10):1474-87. doi: 10.1002/cne.23747	Mouse *Mus musculus*	Whole mount cochlear Multicolor imaging
Wu, X. et al. (2015). Innovative delivery of siRNA to solid tumors by super carbonate apatite. PLoS One. Mar 4;10(3):e0116022. doi: 10.1371/journal.pone.0116022	Mouse *Mus musculus*	In vivo siRNA delivery into solid tumor tissue Multicolor imaging of fixed tissue
Meyen, D. et al (2015). Dynamic filopodia are required for chemokine-dependent intracellular polarization during guided cell migration in vivo. eLife 2015;4:e05279. doi:org/10.7554/eLife.05279	Zebrafish embryo *Danio rerio*	Chemokine-directed migration of primordial germ cells, in vivo imaging
Deirdre, C. et al (2015). Spiralian gastrulation: germ layer formation, morphogenesis, and fate of the blastopore in the slipper snail Crepidula fornicate. EvoDevo, 6:24. doi:10.1186/s13227-015-0019-1	Snail (slipper snail) *Crepidula fornicata*	Gastrulation in a spiralia Time lapse experiments
Zecca, A. et al (2015). The Order and Place of Neuronal Differentiation Establish the Topography of Sensory Projections and the Entry Points within the Hindbrain. J Neurosci. May 13;35(19):7475-86. doi: 10.1523/JNEUROSCI.3743-14.2015	Zebrafish embryo *Danio rerio*	Mapping neurosensory network, Axon navigation In vivo imaging
Amat, F. et al (2014). Fast, accurate reconstruction of cell lineages from large-scale fluorescence microscopy data. Nat Methods Sep;11(9):951-8. doi: 10.1038/nmeth.3036	Fruit fly embryo *Drosophila melanogaster*	Cell tracking and cell lineage reconstruction, In vivo imaging Time lapse experiments
Pauli, A. et al (2014). Toddler: An Embryonic Signal That Promotes Cell Movement via Apelin Receptors. Science Vol 343 no. 6172. doi:10.1126/science.1248636	Zebrafish embryo *Danio rerio*	Gastrulation In vivo imaging Time lapse experiments
Krug, R.G. et al.(2014). A transgenic zebrafish model for monitoring glucocorticoid receptor activity. Genes, Brain and Behavior Jun; 13(5): 478-487. doi:10.1111/gbb.12135	Zebrafish embryo *Danio rerio*	Stress responses In vivo imaging
Udan R.S., et al (2014). Quantitative imaging of cell dynamics in mouse embryos using light-sheet microscopy. Development 141: 4406-4414. doi:10.1242/dev.11102	Mouse *Mus musculus*	Post-implantation embryogenesis Sample preparation Time lapse experiment
Dong, J. et al. (2016) Discovery and expression of 3 siglecs-like in Oreochromis niloticus neutrophil, and their interaction with group B streptococcal sialylated capsular polysaccharides, Molecular Immunology - online, February 1, 2016, doi:10.1016/j.molimm.2016.01.005	Nile Talpia (Fish) *Oreochromis niloticus* and Zebrafish *Danio rerio*	Infection of fish with bacteria *Streptococcus agalactiae* (GBS) in free neutrophils and live fish
Barry, J. D., et al., (2016), TimerQuant: a modelling approach to tandem fluorescent timer design and data interpretation for measuring protein turnover in embryos, Development, Jan 1;143(1):174-9. doi:10.1242/dev.125971	Zebrafish *Danio rerio*	Investigation of fluorescent protein dynamics in live fish
Zanoni, M. et al., (2016) 3D tumor spheroid models for in vitro therapeutic screening: a systematic approach to enhance the biological relevance of data obtained, Scientific Reports, Jan 11;6:19103. doi:10.1038/srep19103.	Cell Spheroids Tumor models	Developed a Spheroid Tumor model for use in a cytotoxicity test
Incha, J., et al., (2016), Using Light Sheet Fluorescence Microscopy to Image Zebrafish Eye Development, J. Vis. Exp. (110), e53966, doi:10.3791/53966.	Zebrafish *Danio rerio*	Live Zebrafish eye development
Felker, A., et al., (2016) In Vivo Performance and Properties of Tamoxifen Metabolites for CreERT2 Control, PLoS One. 2016 Apr 14;11(4):e0152989. doi:10.1371/journal.pone.0152989	Zebrafish *Danio rerio*	Used Zebrafish to study Cre/lox system activation with Tamoxifen and Endoxifen via ERT2

Image Processing

Publication	Sample	Application
Schmied, C. et al (2014). Open-source solutions for SPIMage processing. Methods in Cell Biology Vol. 123, pages 505-529. doi:10.1016/B978-0-12-420138-5.00027-6	Fruit fly embryo *Drosophila melanogaster*	Multiview imaging Bead-based registration Image processing
Amat, F. et al (2014). Fast, accurate reconstruction of cell lineages from large-scale fluorescence microscopy data. Nat Methods Sep;11(9):951-8. doi: 10.1038/nmeth.3036	Fruit fly embryo *Drosophila melanogaster*	Cell tracking and cell lineage reconstruction In vivo imaging Time lapse experiments
Chittajallu, D.R. (2015). In vivo cell-cycle profiling in xenograft tumors by quantitiative intravital microscopy. Nat Methods Jun;12(6):577-85. doi: 10.1038/nmeth.3363	Mouse *Mus musculus*	Automatization of cell – cycle profiling in vivo imaging

Sample Preparation

Publication	Sample	Application
Flood, P. et al.(2015) Using hydrogels in microscopy: a tutorial. Micron, Online - February 8, 2016, doi:10.1016/j.micron.2016.02.002	Using hydrogels to mount samples for microscopy	Review on sample mounting including Lightsheet Z.1

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