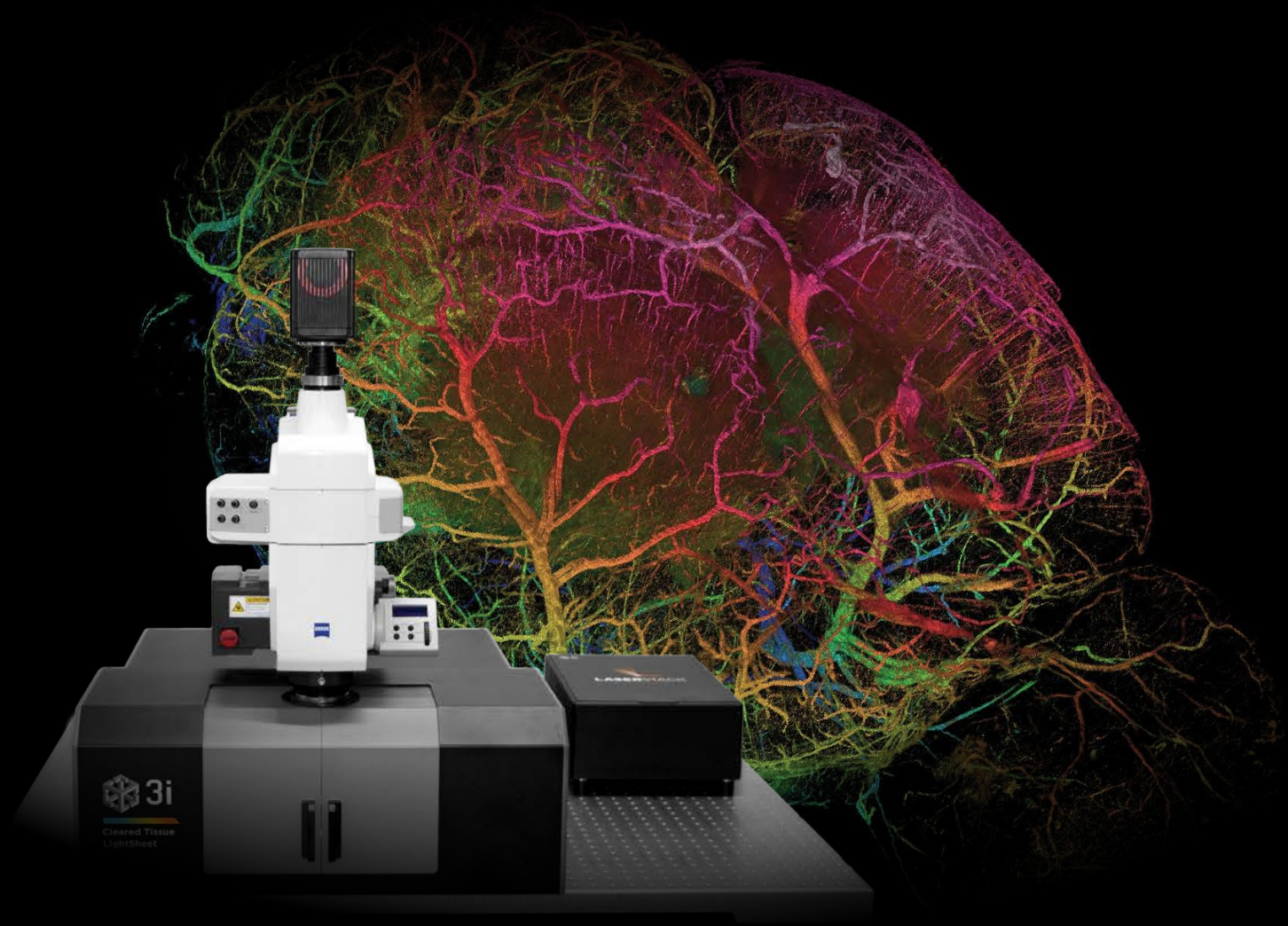
3i Intelligent Imaging Innovations

Cleared Tissue LightSheet

High-Speed High-Resolution Imaging of Cleared Tissue and Organs



Cleared Tissue LightSheet Microscopy System

Cleared Tissue LightSheet (CTLS) is a dual-side illumination lightsheet microscope for whole organ imaging. It incorporates a fully automated macro zoom microscope with high NA objectives and a spatial light modulator (SLM) to optimize the lightsheet for high-resolution imaging. Using a back-thinned sCMOS camera, CTLS images entire organs at high-resolution with low photobleaching. A volume of one cubic centimeter can be imaged in less than an hour.

Back-thinned sCMOS Camera

5.3MP 30fps 95% QE scientific CMOS detector

Automated Macro Zoom Microscope

Motorized focus, zoom and filter selection

Spatial Light Modulator

Dynamic lightsheet focus
Infinity Beam multi-directional illumination
Axial chromatic aberration correction

Chambers and Specimen Holders

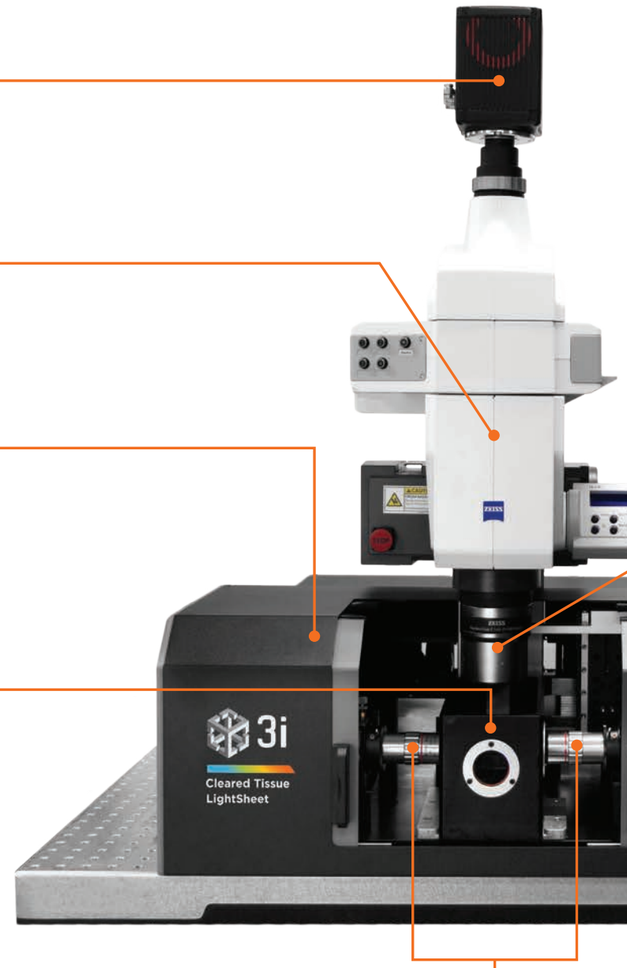
PTFE sample holders compatible with both aqueous and organic clearing solutions

Temperature controlled chamber

Multi-specimen holder for up to 7 different samples or a whole cleared animal

Chambers

Specimen Holders



SlideBook Software

Dedicated cleared tissue capture console

Hardware control, acquisition, processing, montage/stitching, segmentation, and volume rendering with storyboard support

Open file format for big data and high-performance computing applications

SlideBook

Computers and Storage

Computer workstations featuring Intel Xeon processors, NVIDIA Quadro GPUs and high-speed scalable SSD storage

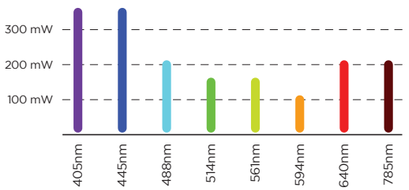
Petabyte data storage systems ranging from 500TB to over 2PB

Macro Fluorescence Objectives

PlanApochromat 0.5x/0.125NA
PlanNeoFluar 1.0x/0.25NA
Apochromat 1.5x/0.37NA
PlanNeoFluar 2.3x/0.57NA

LaserStack Laser Combiner

Modular Laser Combiner
Up to 8 lasers
Up to 300mW



Dual-Side Illumination

5x/0.14NA and 10x/0.28NA options

SlideBook

SlideBook manages every step in cleared tissue imaging. An intuitive workflow guides users through the collection of 3D stacks, 3D data montaging, volume rendering and finally movie making with story-board support. SlideBook is GPU optimized and readily handles the creation and processing of 3D datasets at over 1TB, making them ready for analysis and rendering. SlideBook SLD files can be accessed via any application supporting Bio-Formats OME, allowing seamless collaboration in any workflow.

User-Selectable App Appearance

Select a color scheme from dozens of options
Switch on-the-fly from dark to light themes

SlideBook Open File Format

Directory-based open file format for big data and high-performance computing applications

Volume Rendering

3D volume view visualization tools support a user-specified bounding box and a storyboard interface where multiple perspectives can be assembled into a single movie

NVIDIA CUDA GPU Acceleration

GPU acceleration of computationally-intensive operations such as deconvolution

Montage

Montaging of 3D data is built into SlideBook's workflow with spatial and frequency-based algorithms.

Prescan Roadmap

CTLS includes motorized zoom lenses to automatically zoom out and create a 3D map of the entire specimen. This map serves as virtual eyepieces, allowing inspection of the entire specimen at higher magnification and identification of regions of interest for zoomed-in high-resolution 3D imaging.

System Capture Console

The CTLS console is a single easy-to-use window featuring all frequent controls and status displays from laser selection to prescan roadmap to capture.

Capabilities

Capture

Control hundreds of devices including microscopes, stages, lasers, wheels, piezos, scanners, shutters and much more.

View

Visualize data through any numbers of portals, from single images to z-stacks, time lapse, color channels and 4D views.

Analyze

Analyze images and extract statistical data via a wide variety of algorithms while maintaining original data integrity.

Scripting

Macro scripting for capture and analysis enhances the flexibility and power available to users.

Communicate

Present and export data easily as 16-bit TIFFs, 3D movies, graphs or spreadsheets. Data is directly portable to MATLAB and Excel and adheres to Open Microscopy Environment (OME) standards.

Partners

MATLAB

Through hierarchical and conditional capture, user-supplied MATLAB programs can control experimental workflows.

Microvolution

Microvolution® software delivers nearly instantaneous deconvolution by combining intelligent software programming with the power of a GPU.

Aivia

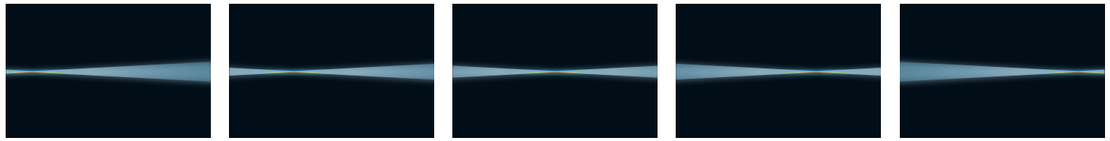
Aivia is an innovative and complete 2D-to-5D image visualization, analysis and interpretation platform with artificial intelligence-guided image analysis.

Dell

The latest high-power computer workstations control all microscope hardware and enable high-speed processing, segmentation and volume rendering of terabyte (TB) datasets.

Digital Lightsheet Focus

CTLS creates a dynamic lightsheet by sweeping a beam with a high-speed galvanometer while a spatial light modulator translates the waist of the sheet along the axis of propagation. Digital selection of the optimal region of focus results in thin optical sectioning with superior axial resolution.



BUMBLEBEE
A bumblebee cleared with iDISCO imaged with 1.5x/0.37NA shown as a high-resolution capture. Below: Magnified 3D view of the bumblebee's leg demonstrating Cleared Tissue LightSheet's flexibility from high-speed to high-resolution capture. Specimen courtesy of Dr. Ruth Hans, Light Microscopy Facility, Technische Universität Dresden, Center for Molecular and Cellular Bioengineering (CMCB) Technology Platform.

High-Speed

fastest imaging
without waist translation

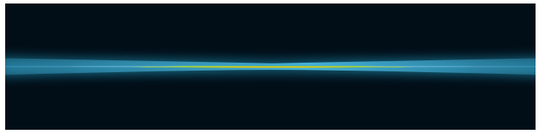
High-Resolution

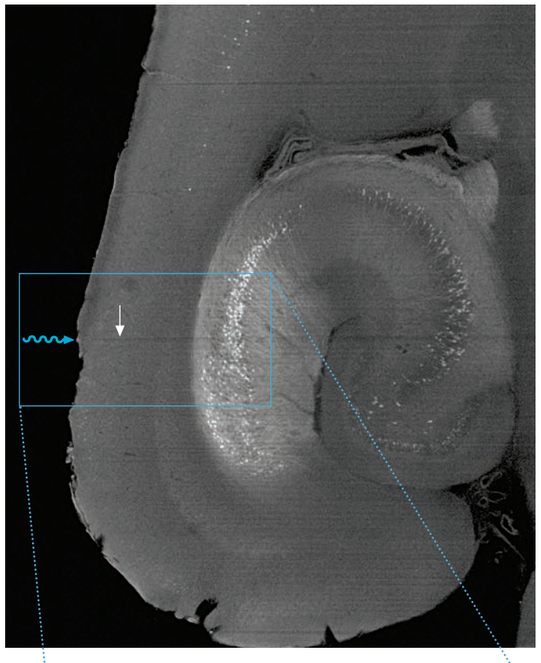
best resolution with
multiple-image waist translation

Shadow Reduction

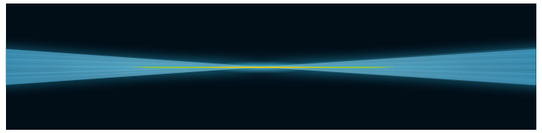
Infinity Beam is created by a special SLM pattern that converts the Gaussian beam into a beam multiplex. Similar to a flat fan nozzle, with Infinity beam the photons approach the specimen from a continuous distribution of angles in the plane of the sheet and are flattened axially in the plane of the objective's focus. Opaque objects in the specimen that would otherwise cause a shadow artifact instead will have their shadow reduced by the overlap of the continuous angles after the artifact.

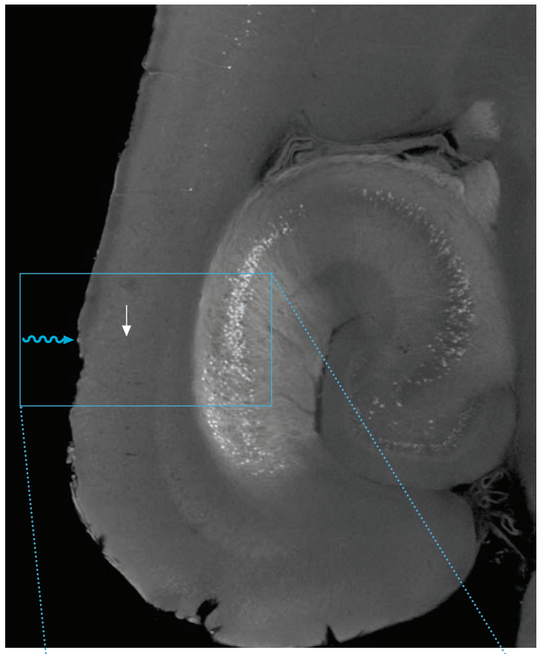
Conventional Light Sheet





Infinity Beam Light Sheet

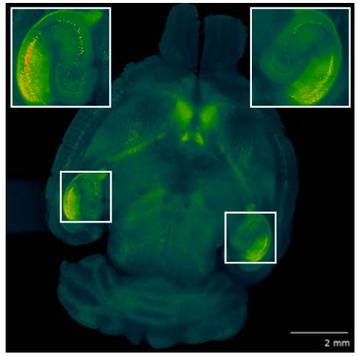




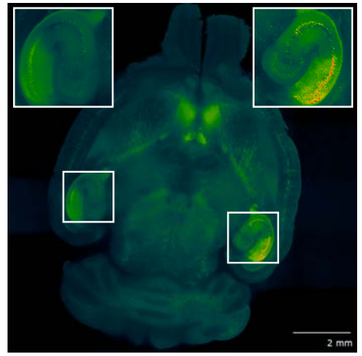
Dual-Side Illumination

A pair of excitation objectives are mounted in 3-axis focus mounts for easy beam centration and alignment. Illumination is toggled from the left side to right and back by the high-speed galvo. This allows for optimal sheet penetration across wide specimens with even illumination and neutralization of shadows caused by opaque structures.

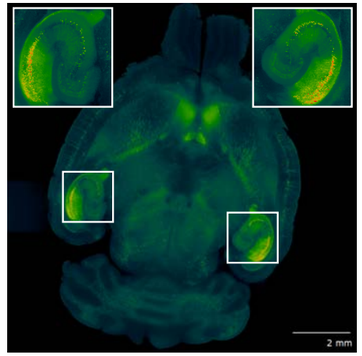
Left Side Illumination



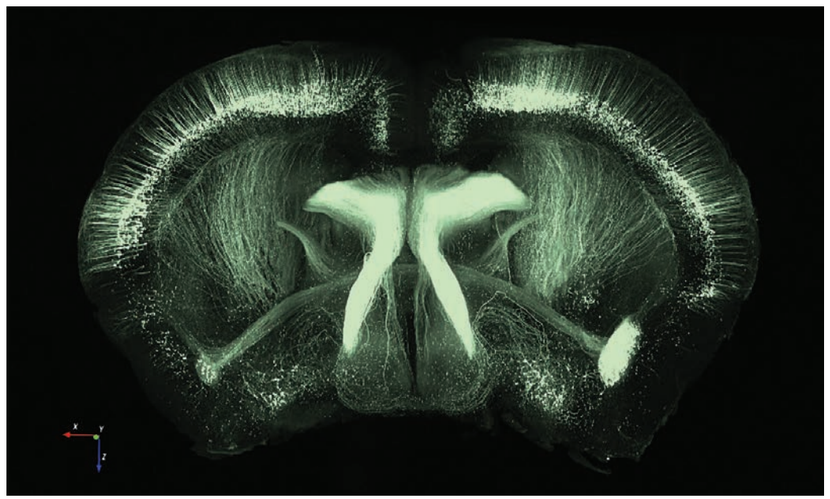
Right Side Illumination



Dual-Side Illumination



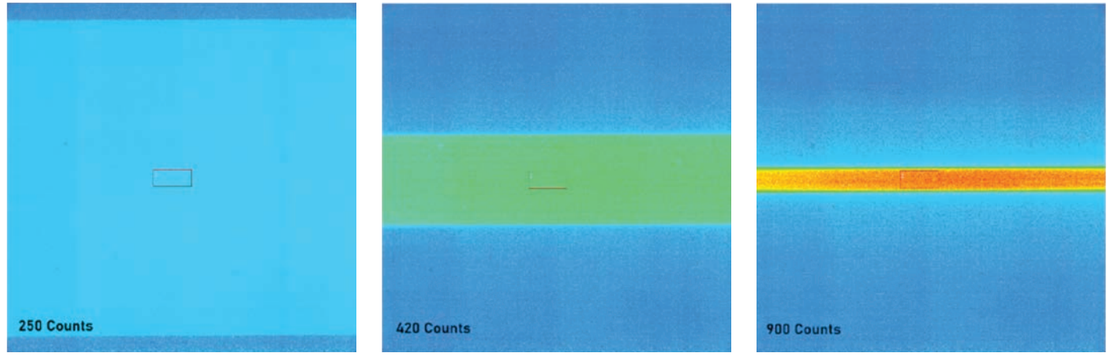
	5x/0.14NA	10x/0.28NA
Sheet Thickness	2.4 - 21µm FWHM	1.7 - 16µm FWHM
Sheet Length	0.5 - 4mm	0.5 - 2mm
Illumination Direction	Bi-directional	
Sheet Formation	Galvo mirror sweep	



BRAIN
Coronal section of Thy1-GFP mouse brain cleared with the PEGASOS method. Sample courtesy of Dr. H. Zhao, Beijing Institute for Brain Research

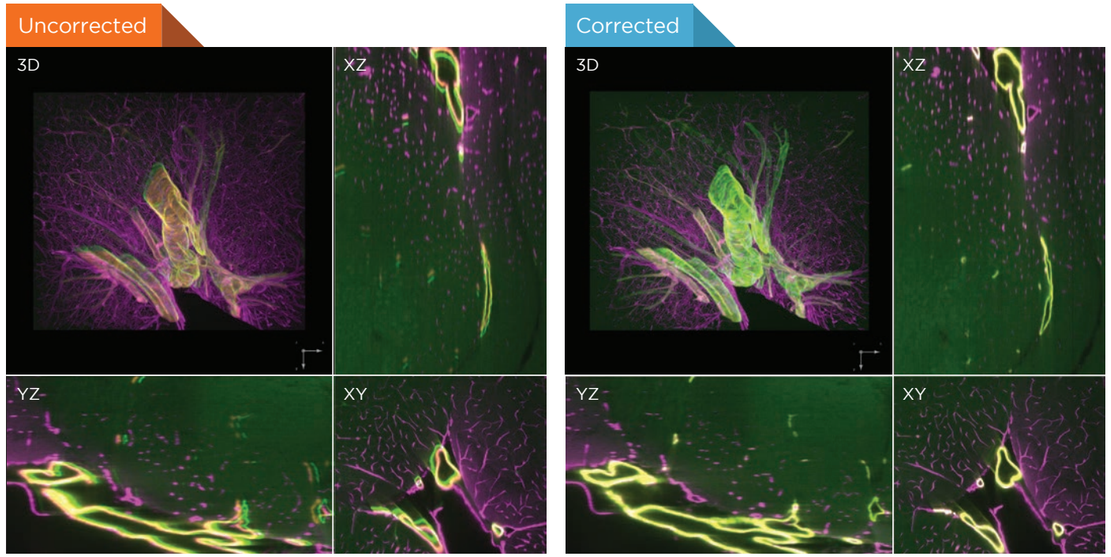
Galvo Swept Lightsheet

CTLS creates a dynamic lightsheet by sweeping the Gaussian laser beam with a high-speed galvo-controlled mirror. This method allows for a tightly focused uniform lightsheet whose width can be seamlessly expanded or contracted to manage photon budget.



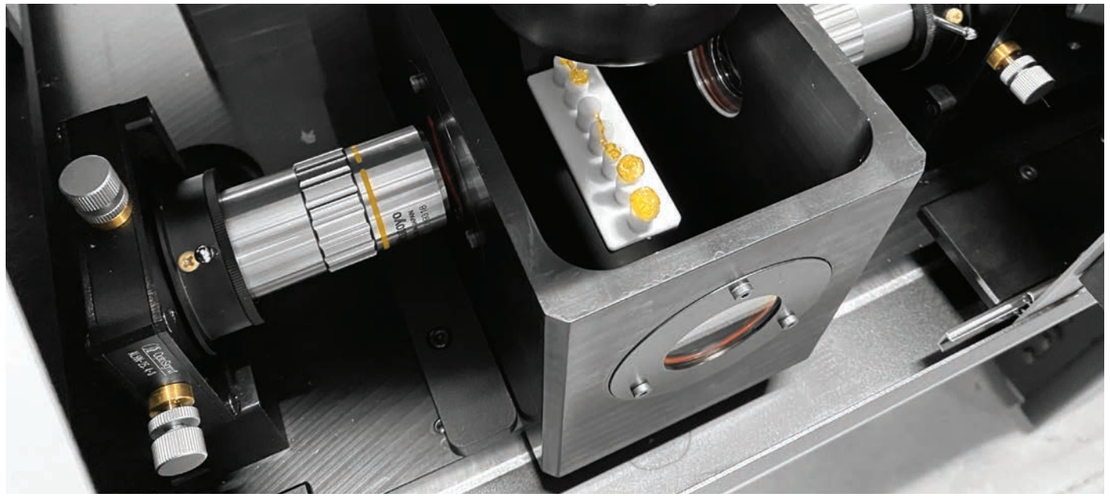
Axial Chromatic Aberration Correction

SlideBook creates an SLM pattern specific to each laser to correct for chromatic shift due to the refractive index of various clearing media. This figure shows epithelial cells lining the vasculature of a mouse brain imaged by 488nm, 561nm & 640nm lasers. Data are viewed in SlideBook's three-view tool showing XZ, YZ and XY perspectives of the gland before and after axial chromatic correction.

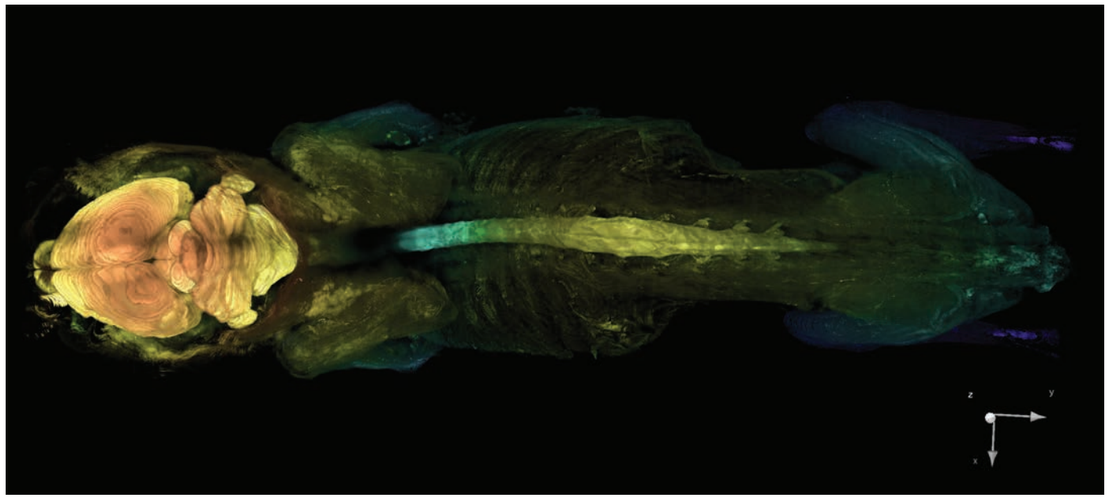


Cleared Tissue LightSheet XL

CTLS-XL incorporates a large chamber more than twice the size of standard chambers. The XL may be used to image an entire mouse or large organs roughly 20mm in width and 60mm in length. A 0.5x imaging objective with 114mm of working distance allows for exceptionally fast imaging of very large samples. All CTLS excitation and detection objectives and the smaller glass chambers are compatible with the XL microscope. CTLS-XL represents the ultimate toolkit for cleared tissue imaging of whole animals, large organs, or smaller specimens using chambers that require a modest amount of index matching media.

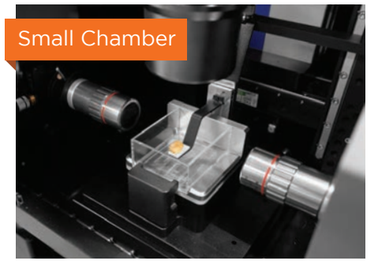


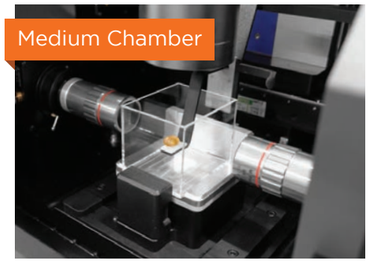
Shown below is a Thy1-YFP mouse measuring 4.5cm in length cleared with PEGASOS and imaged with Cleared Tissue LightSheet XL (sample Courtesy of Dr. H. Zhao, Beijing Institute for Brain Research). The ability to image whole, cleared animals is a useful investigatory tool in many areas of research including neuroscience, tumor biology, and more.

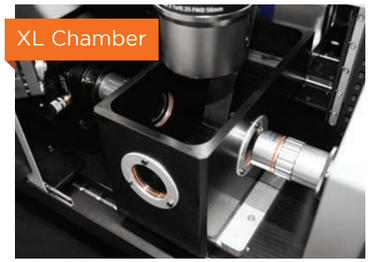


Stages, Chambers and Specimen Holders

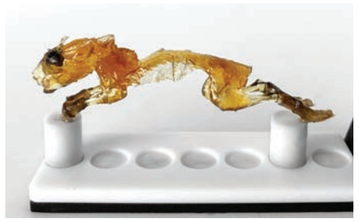
High-precision XYZ stages with sub-micron resolution allow for accurate positioning of the specimen. A variety of sample holders are optimized for cleared tissue and are non-reactive with both aqueous and organic clearing solutions.

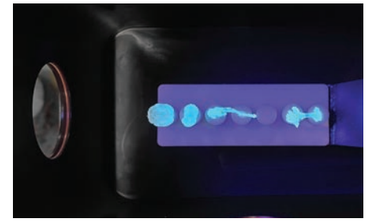






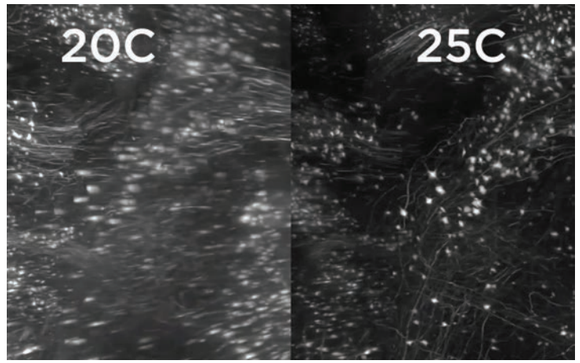
Up to 7 different samples, or a whole cleared animal, can be imaged with the multi-specimen holder. Samples are attached to magnetic pedestals that can be stored in index-matching media until they are ready to be imaged.





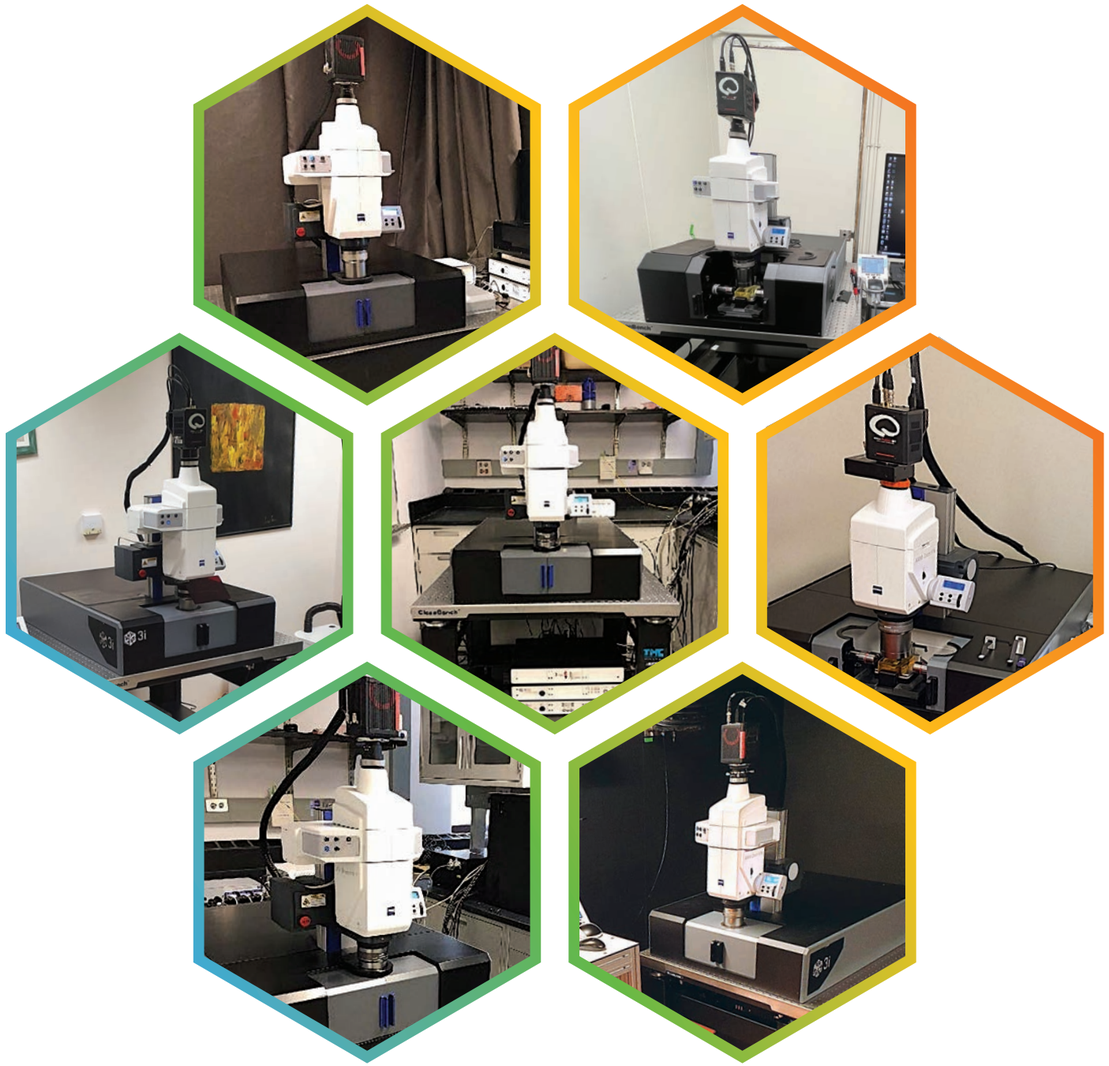
Temperature Controlled Media

Maintaining constant temperature over time is extremely important to data integrity in multi-hour acquisitions. Small changes in temperature will alter the refractive index of the immersion media, resulting in a shift in the beam above or below the plane of focus. The CTLS specimen chambers are thermally stable to +/- 1ºC.



Systems Engineering

3i's Systems Engineering department designs, builds and extensively tests every customer system. From spinning disk confocal to multiphoton to lightsheet and photomanipulation, 3i has delivered over a thousand custom, cutting-edge microscopy systems to help answer some of the most complex scientific questions.



Application Knowledge | Scientific Consulting

A team of PhD scientists meet with each client to document and better understand the scientific context of the user group to ensure that the capabilities of the delivered system match the underlying research goals.

Performance Criteria | Targeted to Experiments

Understanding key experiments and imaging paradigms allows Systems Engineering to apply targeted testing criteria to every system.

Customized Hardware | Novel Light Creation

No matter how complex or customized a light path may be for imaging or photostimulation, our engineers ensure that light is manipulated and directed to where it is needed, when it is needed.

Custom Test Plan | Assure Experiment Success

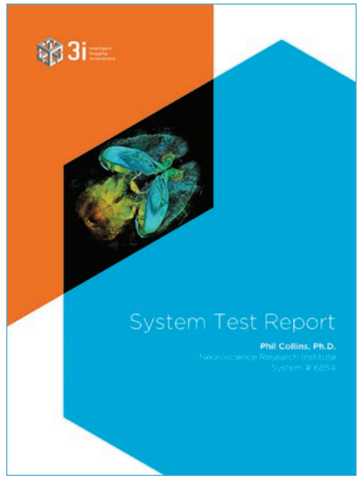
When a technically advanced experiment requires specific system performance to succeed in the lab, a custom test plan assures the system meets that mark prior to delivery.

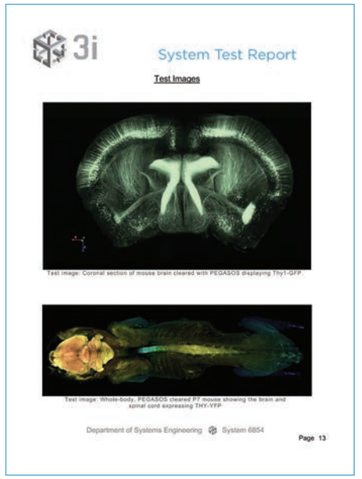
System Integration | Synchronization of Dozens of Instruments

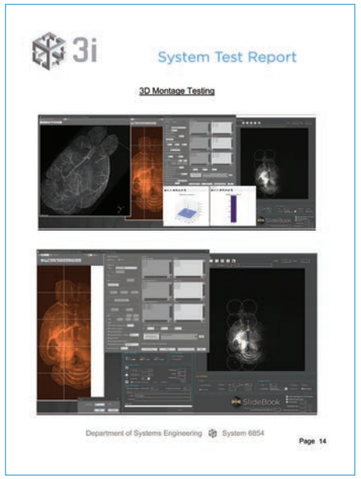
Systems Engineering combines institutional knowledge and scientific consultation to ensure that the instruments in each system are configured for experimental success in the lab.

System Test Report | Guaranteed Performance

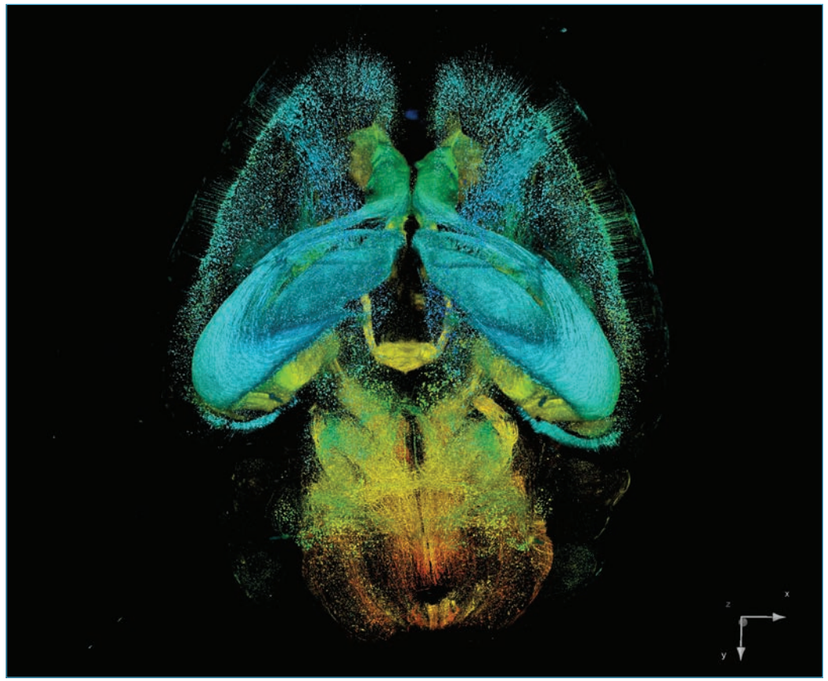
Performance metrics and results of the custom test plan are documented in a System Test Report delivered with each system.



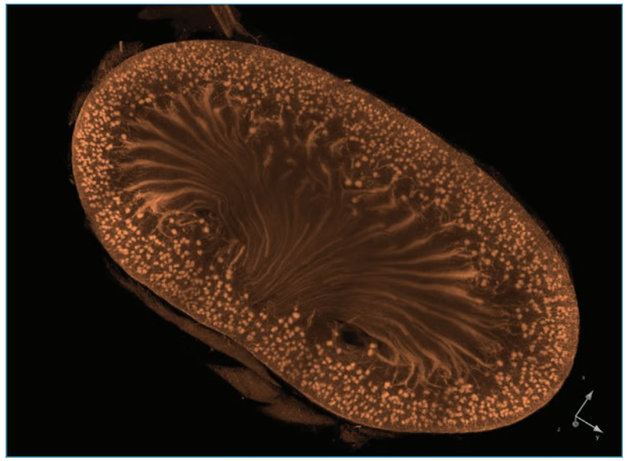




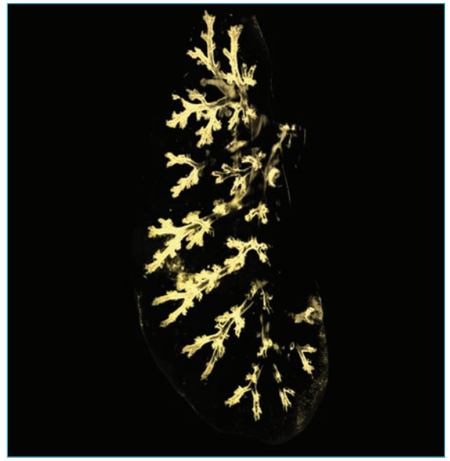
Data



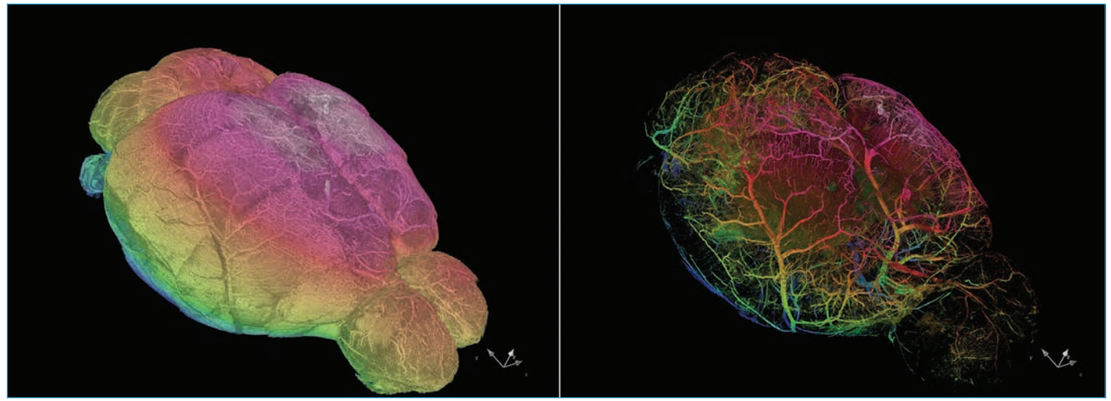
BRAIN
Thy1-GFP mouse brain cleared with PEGASOS and imaged with the 1.5x / 0.37NA objective in 90 minutes. SlideBook 3D visualization with lookup tables by depth. Sample courtesy of Dr. H. Zhao, Beijing Institute for Brain Research.



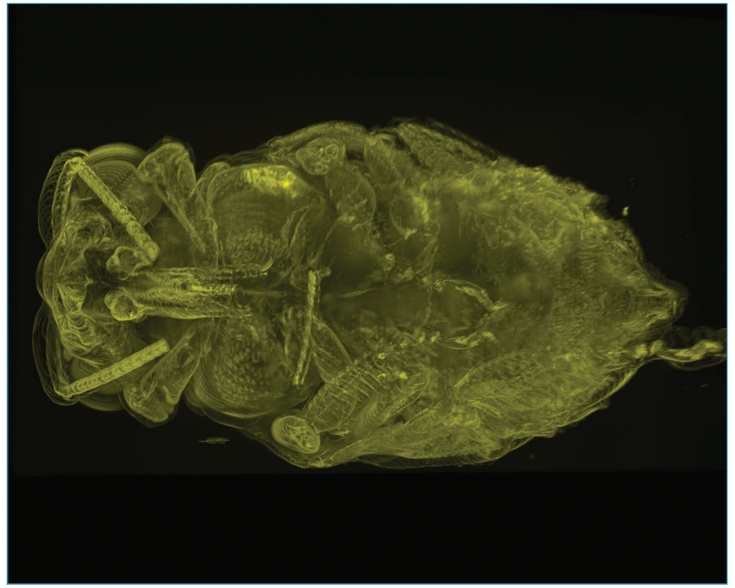
KIDNEY
Glomeruli are shown using td-tomato in a kidney cleared with PEGASOS. Sample courtesy of Dr. B. Shen, University of Texas Southwestern.



LUNG
Mouse lung cleared using the CUBIC technique showing the secondary and tertiary bronchi and bronchioles. Sample courtesy of Dr. L. Arispe, Northwestern University.

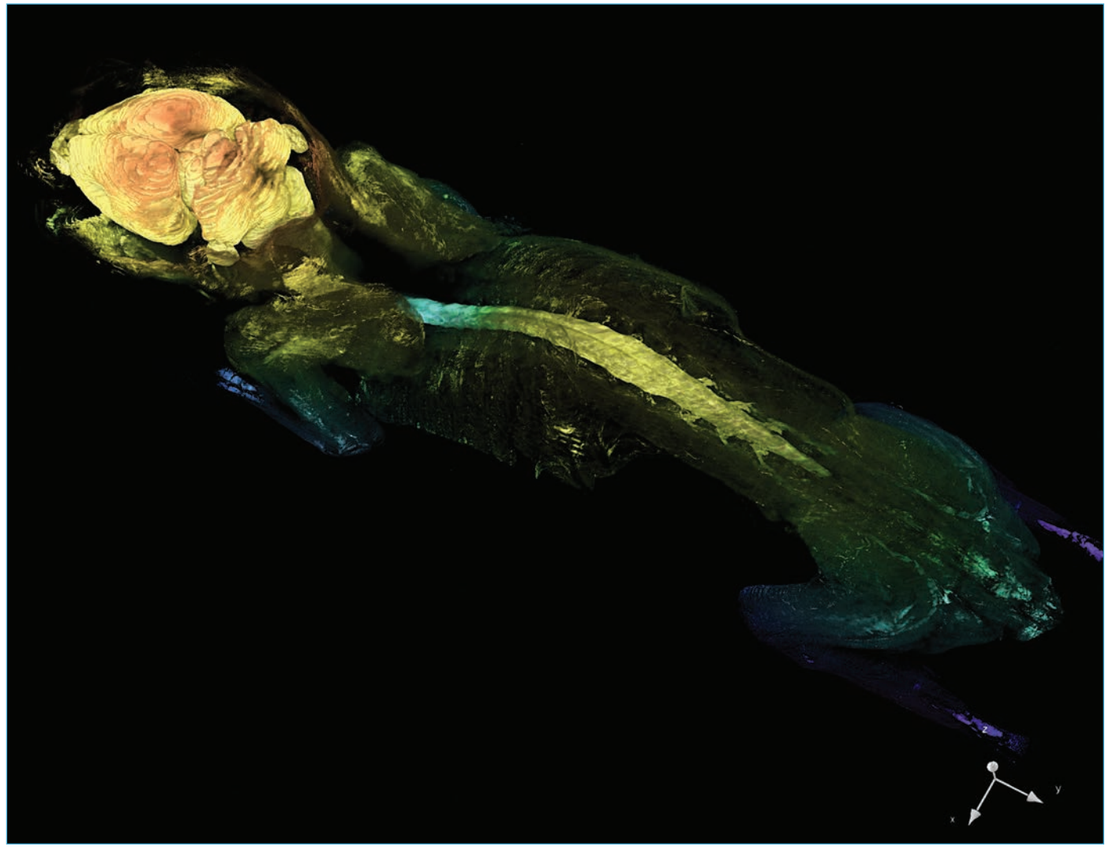


BRAIN
Mouse brain index-matched in ethyl cinnamate showing vasculature as revealed by tomato-lectin. Sample courtesy of Dr. J. Wythe, Baylor College of Medicine.

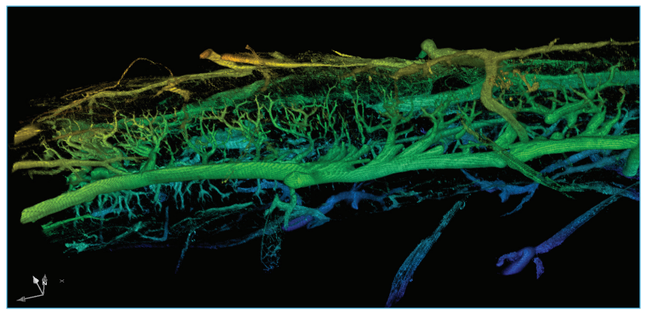


WHOLE ANIMAL
Autofluorescent bee cleared with ethyl cinnamate. Sample courtesy of Dr. K. Mackenzie, University of Aberdeen.

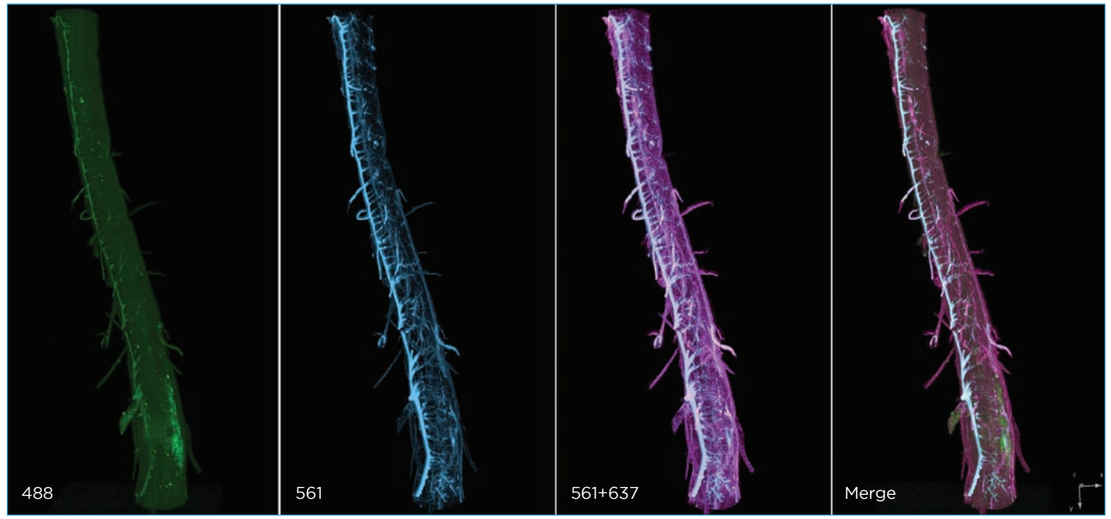
Data



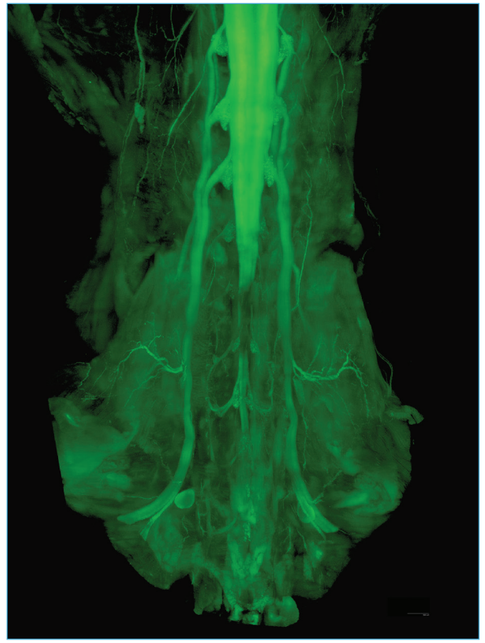
WHOLE ANIMAL
Thy1-YFP mouse measuring 4.5cm in length cleared with PEGASOS and imaged with Cleared Tissue LightSheet XL.
Sample Courtesy of Dr. H. Zhao, Beijing Institute for Brain Research.



SPINAL CORD
Epithelial cells in a mouse spinal cord cleared with iDISCO.
Sample courtesy of Dr. V. Lemmon, University of Miami.

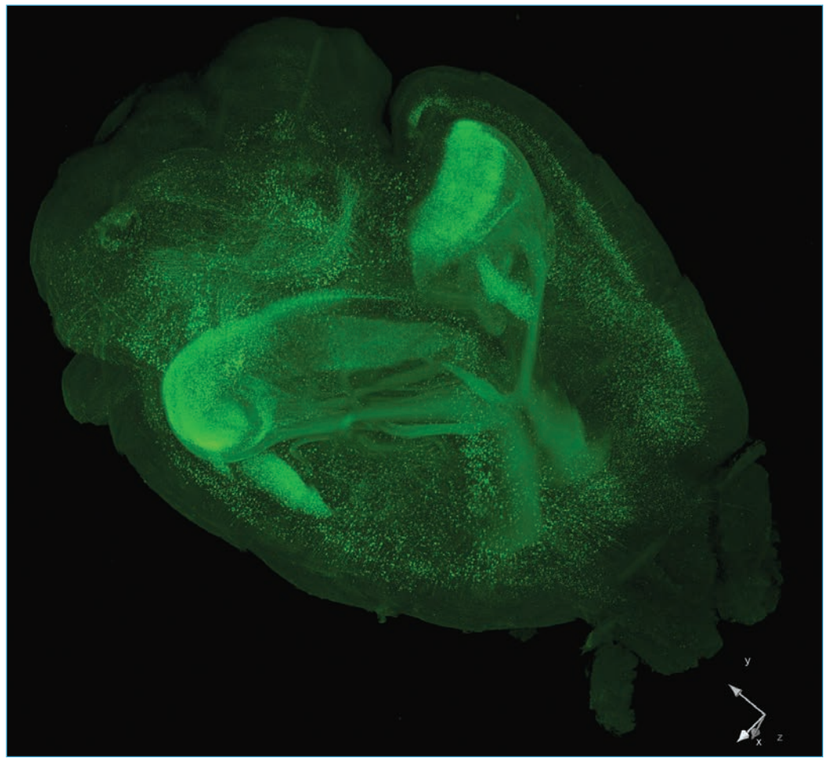


SPINAL CORD
3 different epithelial markers were used to interrogate the vascular morphology of the mouse spinal cord. This specimen is 1.8cm long and cleared with iDISCO. Sample courtesy of Dr. P. Tsoulfas, University of Miami, Miami Project to Cure Paralysis.

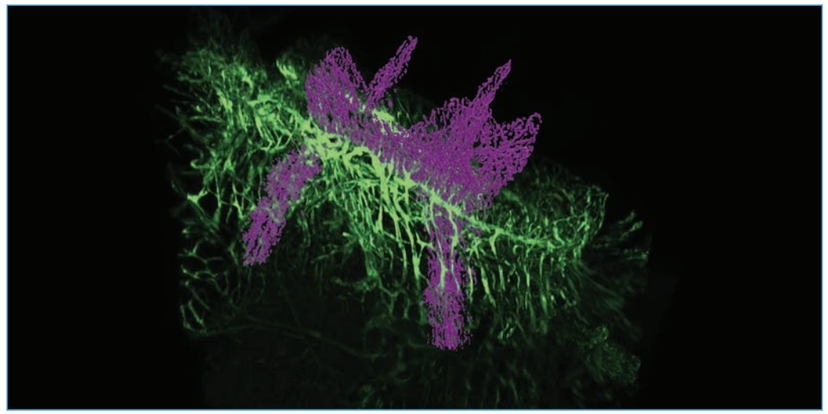


SPINAL CORD
Sacral region of the spinal cord from a Thy1-YFP mouse cleared with PEGASOS with intact dorsal root ganglia and its axons projecting into the hind limb.
Sample courtesy of Dr. H. Zhao, Beijing Institute for Brain Research.

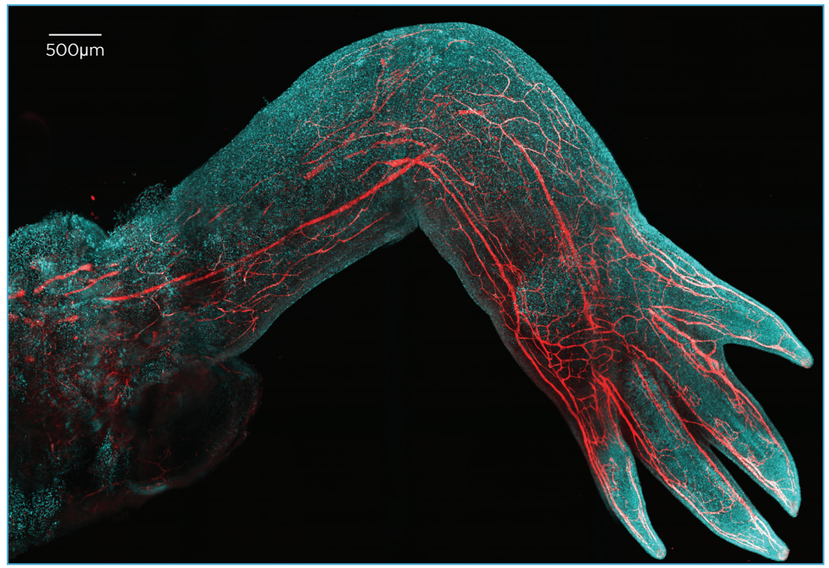
Data



BRAIN
Thy1-GFP mouse brain cleared with PEGASOS. Sample courtesy of Dr. H. Zhao, Beijing Institute for Brain Research.

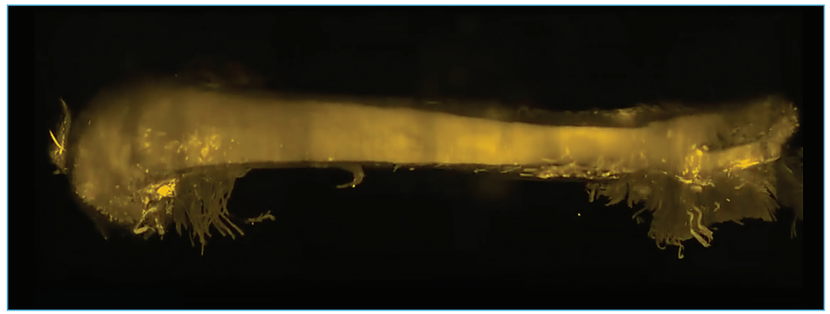


MANDIBLE
Mouse mandible cleared with PEGASOS showing vasculature and dentin in the molar teeth reported by endogenous fluorescence cdh5cre. Sample courtesy of Dr. D. Jing and Dr. Y. Li, Sichuan University, Department of Orthodontics.



LIMB
Axolotl limb from the transgenic line CNP-EGFP, which labels the nervous system. Stained for GFP with an Alexa-Fluor 594 secondary antibody, and nuclear staining with Sytox Green. Image courtesy of Maximina Yun Lab, Center for Regenerative Therapies TU Dresden (CRTD). Clearing protocol: Subiran Adrados C, Yu Q, Bolaños Castro LA, Rodríguez Cabrera LA, Yun MH. (2020) Salamander-Eci: An optical clearing protocol for the three-dimensional exploration of regeneration. Developmental Dynamics. https://doi.org/10.1002/dvdy.264

HIND PAW
Mouse hind paw labeled with Thy-1 YFP and cleared with PEGASOS. Specimen courtesy of Dr. Wenjing Luo, Texas A&M Health Sciences Center.



FEMUR
Mouse femur cleared with PEGASOS and labeled with Thy1-YFP. Sample courtesy of Dr. Weijing Luo, Texas A&M Health Science Center.

Support and Maintenance

A variety of software and equipment support levels help keep systems running well for years. A Software Support Agreement allows labs to run the latest version of SlideBook with new acquisition and analysis features. It includes direct access to 3i staff via email, phone and video chat. A System Maintenance Agreement adds an annual preventative maintenance visit, 3i service visits and 3i coordination of any repairs, although repair and replacement parts are not included. A System Extended Warranty adds full coverage for repairs and replacement parts. Additionally, 3i application scientists may provide in-person and webinar-based application training.

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Repairs Coordinated by 3i			
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3i designs and manufactures technologies for living cell, live cell, and intravital fluorescence microscopy including superresolution, computer-generated holography, spinning disk confocal, multi-photon and lightsheet. SlideBook software manages everything from instrument control to image capture, processing and data analysis. 3i was established in 1995 by a group of cell biologists, neuroscientists, and computer scientists to provide advanced multi-dimensional microscopy platforms that are intuitive to use, modular in design, and meet the evolving needs of investigators in the biological research community.

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