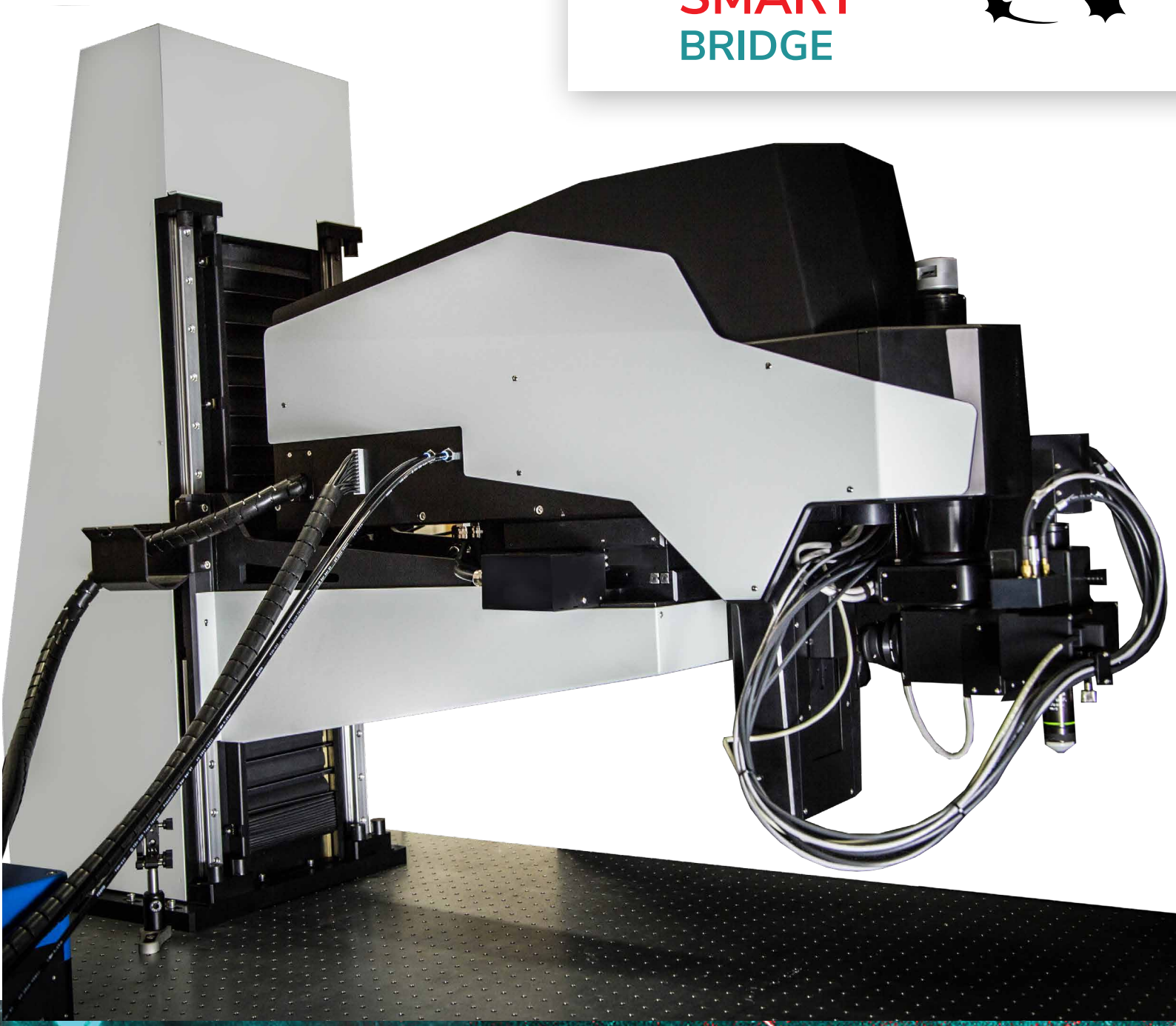
FEMTO SMART BRIDGE



THINKING AHEAD
FEMTONICS
MICROSCOPY

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YOUR PATH TO THE NEXT LEVEL

Thinking ahead

Our mission is to support the world's top-tier researchers with the most advanced two-photon imaging systems. Our innovative technologies address researchers' needs in a wide variety of *in vivo* and *in vitro* biological applications. Fueled by our collective, pioneering spirit since 2005, we aim to discover new approaches in the development of two-photon laser scanning microscopes, for the booming area of brain research and pharmaceutical development.

Femtonics holds more than 20 world records in laser scanning microscopy, which manifests in numerous high-impact publications and 44 international patents. As of today, we have sold more than 120 systems in 45 countries worldwide. We also nourish the next generation of neuroscientist though our popular PhD Program.

Why two-photon microscopy?

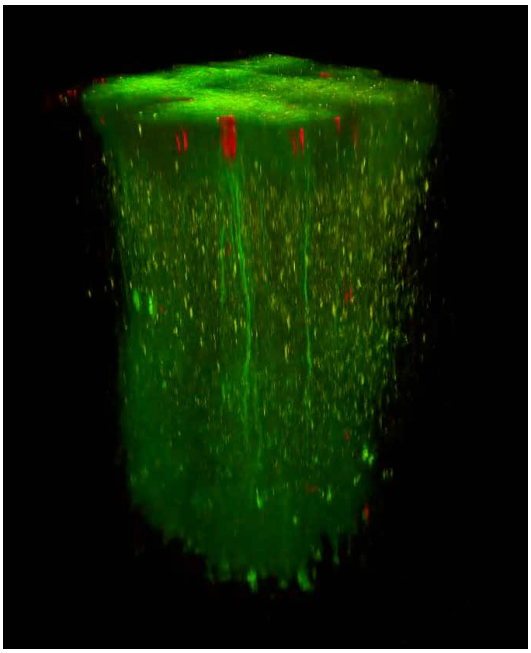
Every scientist, who aspires to get access to the smallest elements of the brain, desires to do so in the largest scanning volume possible, with the highest temporal and spatial resolution they can achieve. Multi-photon microscopy seems to be an ideal tool for them, as:

- two-photon and three-photon microscopy provides the deepest penetration for *in vivo* measurements (up to a depth of more than one millimetre) in the brain, embryos, whole organs and even entire animal models,
- it ensures a high spatial resolution, as two-photon absorption only occurs in the focal point, this way the resolution of small spines and axon boutons are preserved,
- it minimizes phototoxicity due to the low energy, high wavelength photons used, allowing for long recordings (up to several months),
- it can easily be combined with fast 3D scanning methods developed by Femtonics, reaching high spatiotemporal resolution with a high signal-to-noise ratio.

Choose Femtonics

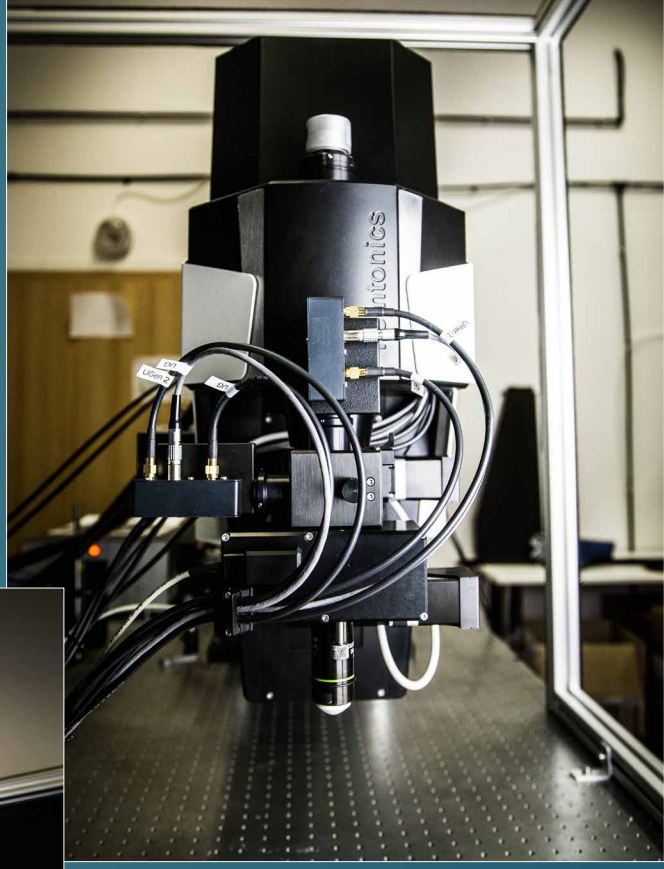
- Developed by scientists for scientists, focused on applications
- Fast 3D imaging of the activity of neuronal network, multiple dendritic processes, axons, and spines in behaving animal models
- 2D and 3D *in vivo* imaging technologies
- Specialized in custom-made integrated imaging systems
- Modular, easily upgradable instruments
- Ultrafast and Unique 3D random-access scanning modes

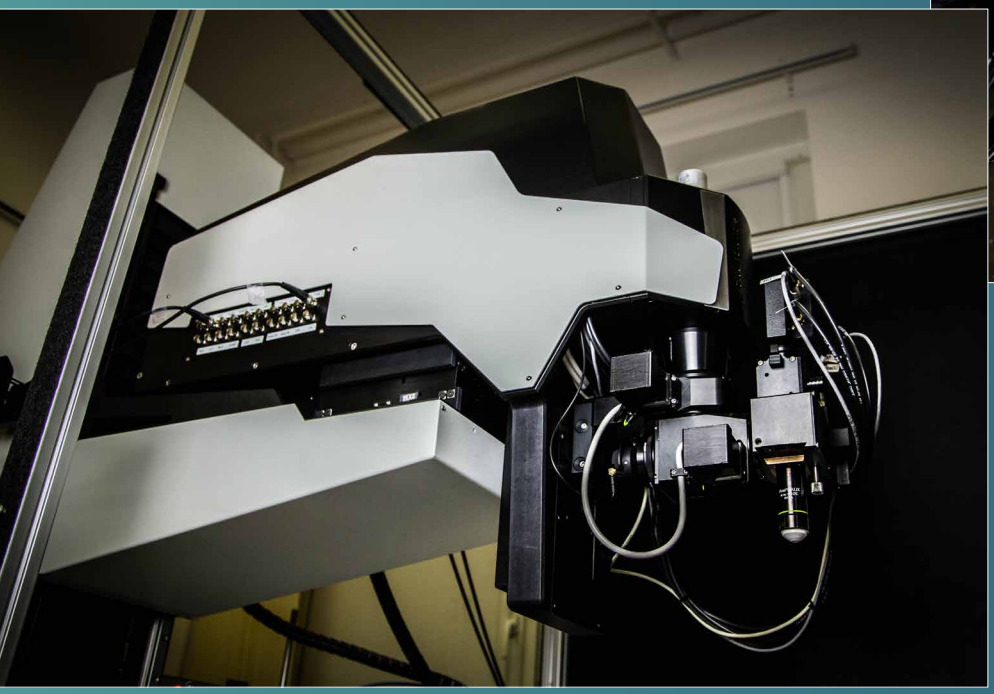
Gergely Katona PHD, CEO of Femtonics

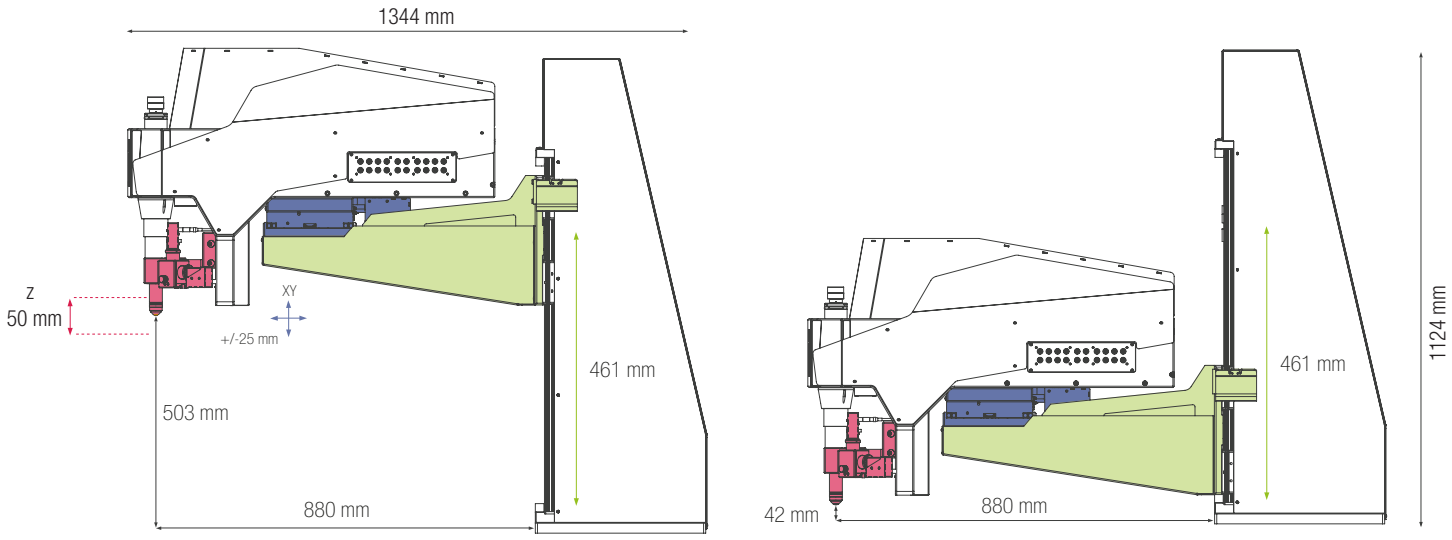


In vivo 3D recording in large volumes

FEMTO
SMART
BRIDGE





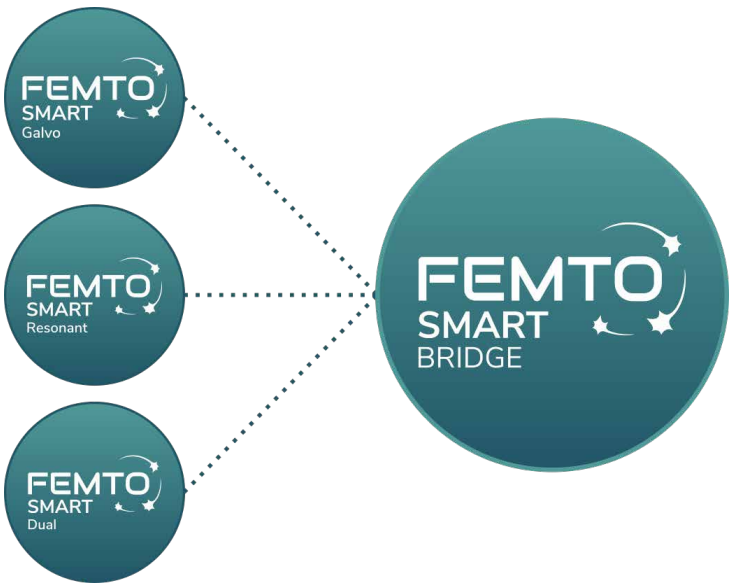


FEMTOSmart Bridge: a solution for many *in vivo* applications

The FEMTOSmart Bridge is a highly customized FemtoSmart microscope. It is equipped with a special lifting apparatus that provides large freedom and mobility in positioning the body in X, Y and Z directions, and secures an increased space under the objective for the sample or any accessories. The accessibility of the sample is supported also by the mobility of the objective, which can move in a 50 mm range in the Z-direction. The use of two further optional modules provides an even higher degree of freedom: a motorized tilting module can rotate the objective, reaching the sample from different angles, and a piezo objective positioner allows for the fast and fine movement of the objective in a 400 µm range. This complex appararatus makes these microscopes suitable for *in vivo* studies of model organisms ranging from zebrafish larvae, through mice navigating in a virtual reality to non-human primates.

Key features

- Moving range of 50 cm in X and Y directions, and a coarse Z adjustment of 1 mm provided by the lifting apparatus
- The objective can move in a 50 mm range by the objective arm
- The motorized tilting module rotates the objective in 180° around the horizontal and 100° around the vertical axis with 4%sec
- The Z movement with a piezo objective positioner module is 400 µm
- The distance between the foot and the objective is 880 mm
- Optimal for *in vivo* studies
- High level of modularity: upgrade possibility to photostimulation, gated detectors, piezo and more
- Patented imaging technologies, travelling detector system



FLEXIBLE STRUCTURE AND SCANNING METHODS

As to the design, the classic members of the FemtoSmart series stand on a static foot structure, which can be replaced by the bridge structure, creating the FEMTOSmart Bridge setup. The column-based X-Y-Z moving body of these microscopes houses the scanner unit, control circuits, and internal light path. The scanner can be galvanometric, with a focus on our elegant scanning patterns, resonant, with fast frame and volume scanning, or dual, a combination of both.

SUPERIOR IMAGING TECHNOLOGY

The fine-tuned optical construction allows imaging to a depth of 850 µm, and wavelength range from visible to the infrared regime allowing even 3P excitation. The scanners are delivering the highest resolution currently available. Detection is performed by our patented travelling detector system, where the highest quality GaAsP PMTs and associated optical elements are mounted on the objective arm as close as possible to the objective which helps to keep the photon collection ratio high.

MODULARITY

The microscope's modular nature allows us to assemble the components, and recombine and upgrade the system to perfectly fit the customer's needs. The system can be equipped with a lot of optional modules enabling it to be adapted to a wide range of biological applications, such as optogenetics, uncaging and dendritic imaging.

FOCUSING ON REGIONS OF INTEREST WITH HIGH SPEED AND SNR

FEMTO SMART Galvo

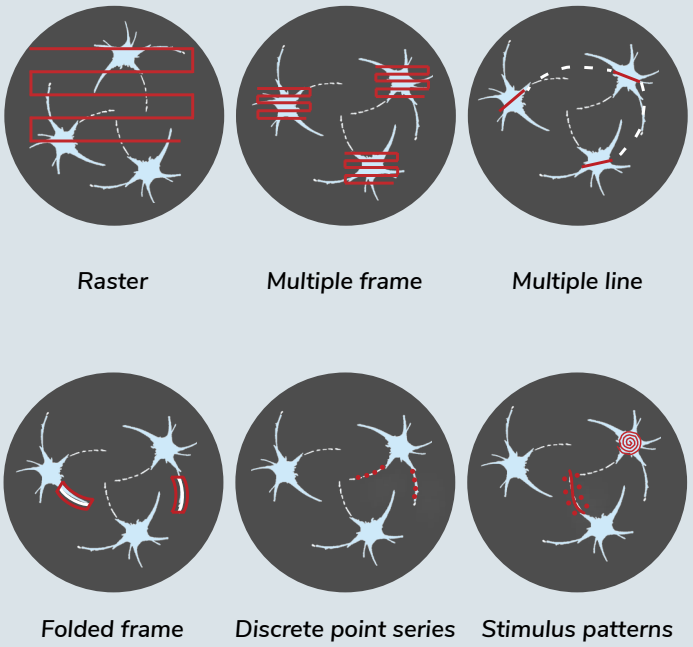
Galvo-based imaging

The galvo scanner combined with our intelligent control software enables the user to select numerous scanning patterns covering widely distributed ROIs. Multiple frame scanning allows focusing on cell bodies, multiple line scanning enables to follow action potentials along dendrites, scanning of discrete point series allows for the measurement or photostimulation of subcellular components with the highest temporal resolution. Our software features (real-time display, analysis functions, ΔF/F calculations, the integrated parallel data acquisition of electrical recordings) aid the understanding of physiological processes in your research focus.

Key features

- For *in vivo* functional imaging in deep tissues
- Each cell body, axon, dendrite and spine can be measured separately
- Flexible imaging modes, patented solutions for fast imaging on the regions of interest
- High signal-to-noise ratio
- Intelligent control software

SCANNING MODES



850	800×800	4.1	200	40
µm deep	µm² FOV	fps 512×512 pixels 700×700 µm²	µs/point	lines/5 ms straight and curved lines

Specification

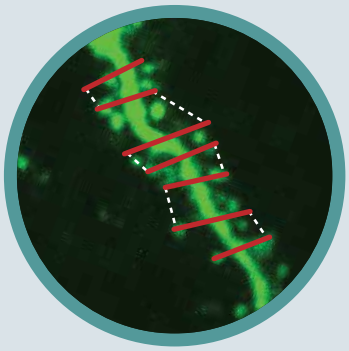
- *in vivo* deep brain imaging down to 850 µm
- 800 µm × 800 µm FOV (with a 20x obj.)
- 2D scanning modes
  - point and scanning of discrete point series with 200 µs/point
  - free hand line and multiple line: 40 lines/5 ms
  - frame with 4.1 fps at 512 x 512 pixel, 750 µm x 750 µm
  - folded frame, multiple folded frame
- pixel dwell time adjustable: 0.5 µs - 10 ms, pixel-based averaging
- minimized optical path length by patented travelling detector system
- non-descanned, ultrasensitive GaAsP PMT (quantum efficiency 40%<)
- high signal-to-noise ratio
- simultaneous detection of multiple wavelength
- custom-designed optical elements for maximal transmission efficiency
- MATLAB-based control software with analysis and upgrade possibilities
- ΔF/F, ΔG/R calculation
- parallel recording and analysis of electrophysiological data
- CMOS camera
- compatibility with extended IR wavelength range

Multiple line scanning

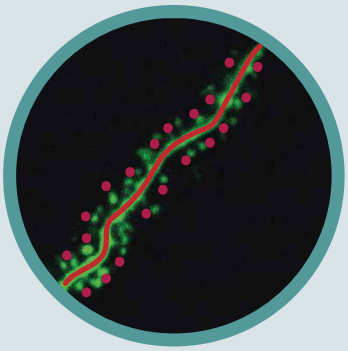
Multiple line scanning has been developed to record dendritic and spine activity of neurons in a near real-time mode. X and Y mirrors direct the laser beam, along straight lines or complex curves, and the scanner gathers signals from these lines, skipping the intermediate sections. Therefore, the scanning speed and the signal-to-noise ratio (SNR) from the multi-site ROIs increases 3- to 4-fold, compared to frame scanning.

Photostimulus patterns

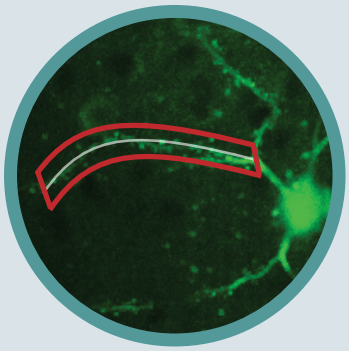
Our unique scanning patterns support optogenetics, uncaging, and other techniques of photostimulation. Scanning of discrete point series can be used for stimulation in femtoliter volumes, near dendritic spines. Stimulation can last from microseconds to seconds, accommodating the experiment. Signals can be followed along the dendrite by line scanning with photostimulation near simultaneously. Switching is achieved using a Pockels cell and gated detectors, on the microsecond scale.



Multiple line



Photostimulus patterns



Folded frame scanning

Folded frame scanning

This patented method allows for the imaging of an enclosed area along a line, where the shape of the selected regions can be straight or curved. Single cell bodies can be imaged in different regions, events can be followed along winding dendrites with their protrusions, even in moving tissues.

High signal-to-noise ratio

Subtle changes in the evoked signals can be revealed because of the following features:

- scanning only the relevant part of the field-of-view, and skipping the background, result in a very high SNR,
- photon collection efficiency is enhanced thanks to our patented travelling detector system, which uses the shortest possible optical path,
- the most sensitive GaAsP photomultipliers available (quantum efficiency 40%<) collect scattered photons.

HIGH-SPEED IMAGING IN A WIDE FIELD OF VIEW

FEMTO SMART Resonant

Resonant-based imaging

In the FEMTOSmart Resonant microscope, Femtonics combines high-speed and high-sensitivity imaging of living tissues by using a fast resonant scanner. Resonant-scanner-based raster scanning acquires images of the entire field-of-view ~5 times faster than galvanometric-based scanning: it is therefore the most appropriate choice for imaging the entire field-of-view at high frame rate.

Uninterrupted high-speed imaging

The resonant scanner consists of a fast oscillating mirror for x-axis deflection and a galvanometric mirror for y-axis sweep. Thanks to the 8 kHz oscillating speed of the fast x mirror, the microscope is capable of gathering images at 31 frames per second for hours.

High scanning rate with no image distortion

The velocity of the resonant scanner is non-linear: the speed is different in the center and at the edges of the frame. In the microscope, Pockels cell limits the scanning range to that portion where the scanning velocity is near linear, avoiding photobleaching/photodamage at the two sides of the image. Scan electronics performs dynamic pixel dwelling for data linearization and to cancel out image distortion.

3D volume scanning

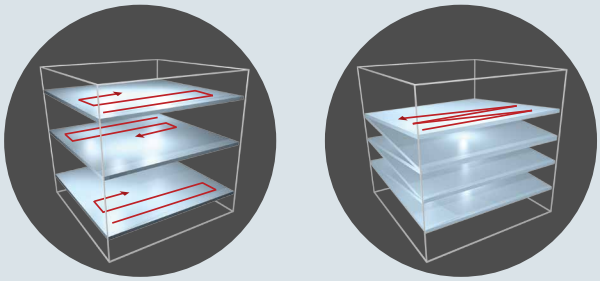
Fast XY-scanning, combined with fast Z-movement, ensure near real-time measurement of a 3D volume which enables us to study activity changes in 3D cellular networks or the morphology of organs. The fast Z movement can be performed by a Piezo objective positioner or a Liquid lens objective, and two scanning methods are available: frame by frame scanning and in-frame ramping.

850	600×600	31	500
µm deep	µm² FOV	fps 512×512 pixels 600×600 µm²	fps 32×512 pixels

Key features

- For *in vivo* high-speed functional imaging in deep tissues
- Rapid image acquisition
- Long-term measurements
- Time-lapse imaging
- 3D volume scanning upgrade
- Intelligent control software

SCANNING MODES



Fast frame and frame by frame volume scanning

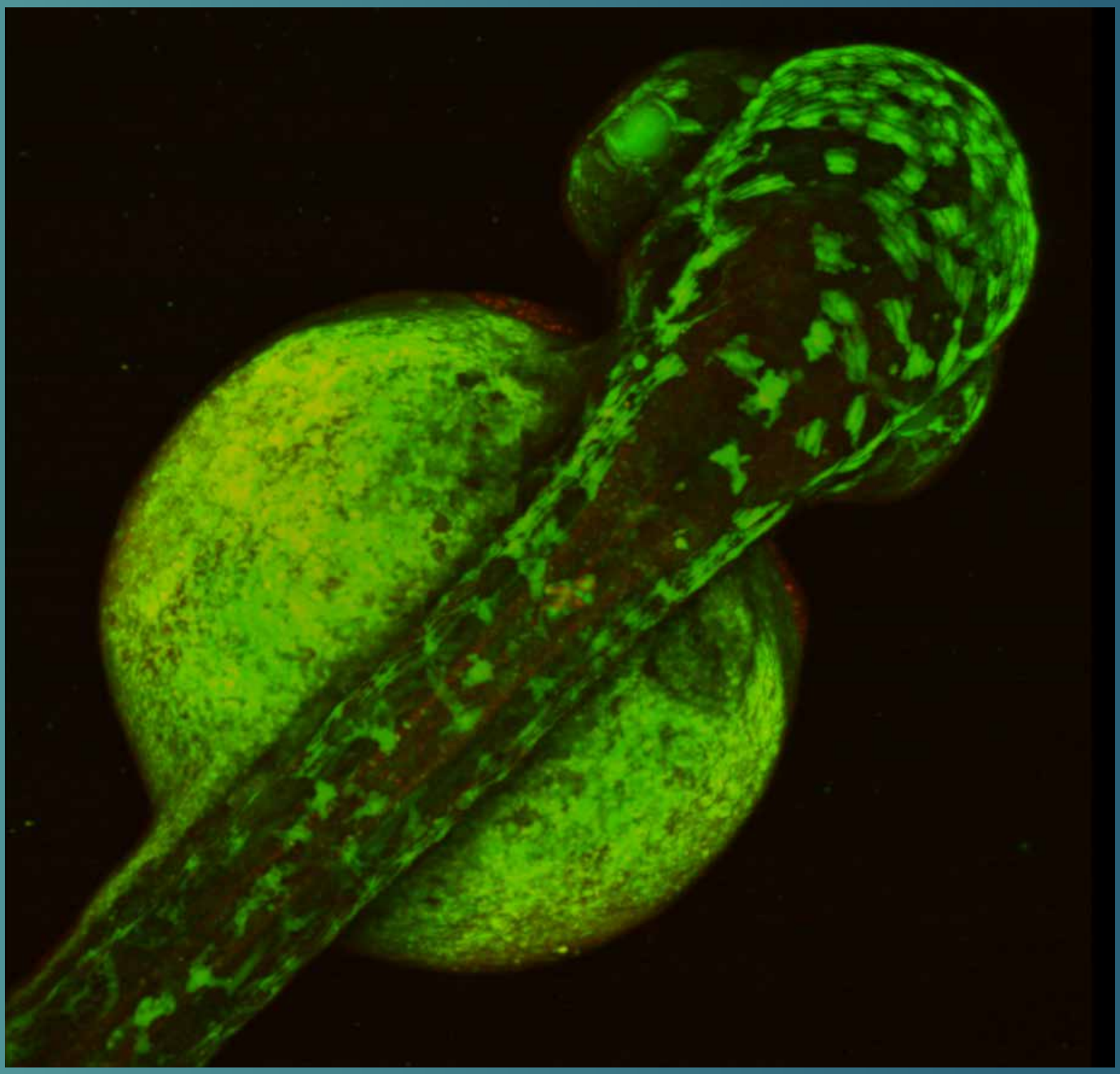
In-frame ramping scanning

Specification

- *in vivo* deep brain imaging down to 850 µm
- 600 µm × 600 µm FOV (with a 20x obj.)
- scanning modes
  - raster scanning with 31 fps at 512x512 pixels and 500 fps at 512x32 pixels
  - 16 000 lines/sec (straight, parallel with x-axis)
  - 3D volume scanning with 3 Hz by Piezo objective positioner
- dynamic pixel dwell time to avoid image distrortion
- minimized optical path length by patented travelling detector system
- non-descanned, ultrasensitive GaAsP PMT (quantum efficiency 40%<)
- high signal-to-noise ratio
- simultaneous detection of multiple wavelenghts
- custom-designed optical elements for maximal transmission efficiency
- C++-based control software with analysis and upgrade possibilities
- dedicated software efficiently handling large datasets
- nearly unlimited measurement times
- ΔF/F calculation
- parallel recording and analysis of electrophysiological data
- CMOS camera
- compatibility with extended IR wavelength range

Time-lapse imaging or long-term measurements

While two-photon excitation provides in-depth imaging and high spatial resolution, the high frame scanning rate provides high temporal resolution. This enables us to measure rapid events in living cells, neuronal networks, or other circuits. Automated measurements with a high frame scanning rate and unlimited video streaming support long-term studies: following learning processes, memory retrieval, associative learning, development of model organisms, etc. The figure below shows an early stage of the development of a zebrafish embryo.

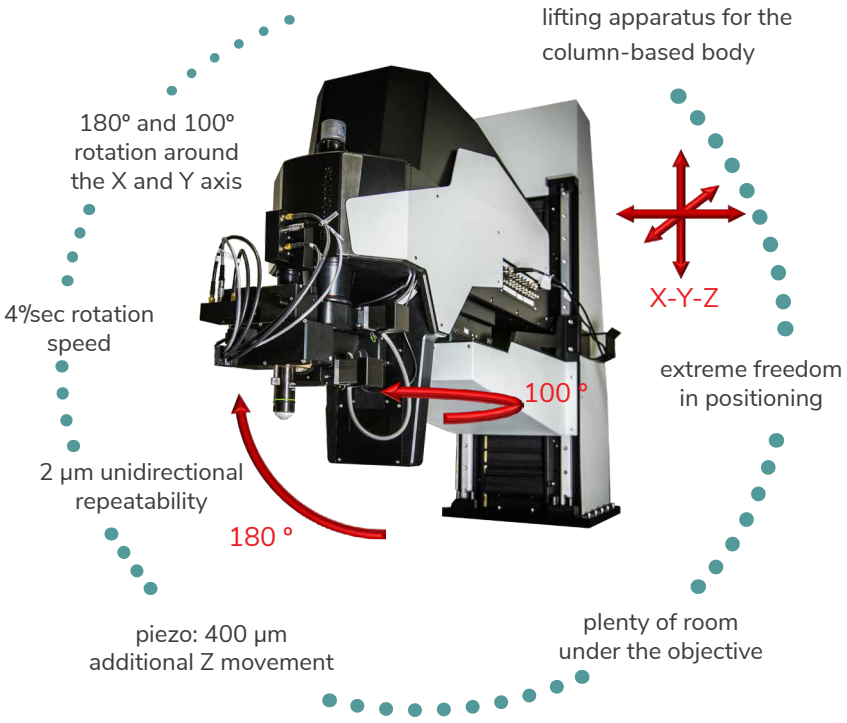


FEMTOSMART DUAL
WITH BRIDGE STRUCTURE AND TILTING OBJECTIVE

A fully customized setup for a higher level of positioning freedom for small and large animal samples

TILTING OBJECTIVE

BRIDGE STRUCTURE



BENEFITS OF THE FEMTOSMART

- functional deep brain imaging up to 850 µm
- galvo and resonant scanners working in tandem
- flexible and fast ROI scanning possibilities
- frame scanning with 31 fps
- intelligent measurement and analysis software functions

BENEFITS OF THE BRIDGE STRUCTURE

- very large space for the sample or accessories
- high-range mobility
- chronic imaging spot location within craniotomy

BENEFITS OF THE TILTING OBJECTIVE

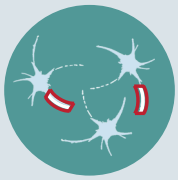
- high-level of accessibility to the sample
- motorized tilting unit for rotating the objective
- fast Z-stack acquisition from tilted positions
- flexible, backlash-free, precise objective positioning
- 2 or 3 detectors are equipped on the tilting unit intelligent software control

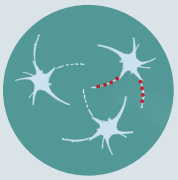
Scanning methods

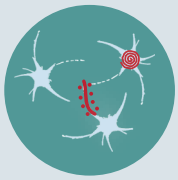

raster

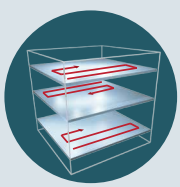

multiple frame

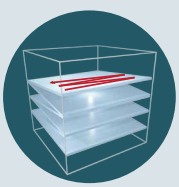

multiple line


folded frame

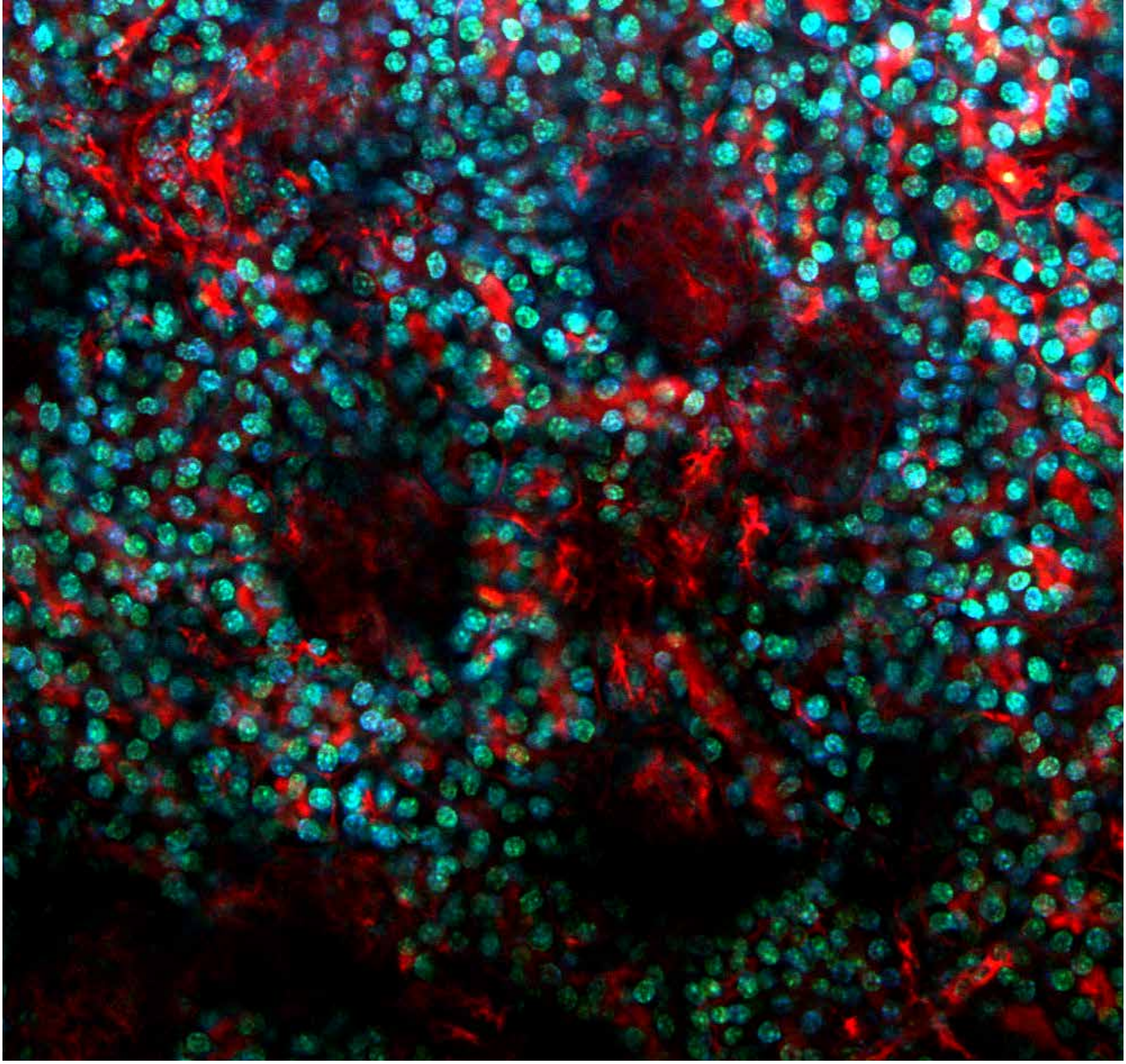

discrete point-series


stimulus patterns


volume scnanning by frame by frame mode


volume scanning by continuous ramping mode


functional imaging in small and large models



Renal glomeruli were imaged from a anesthetized rat model. Nuclei were labeled with Hoechst dye (blue), blood vessels were labeled with rodamine dextran (red).
Image courtesy of Katalin Kis-Petik, Semmelweis University, Hungary.

"Femtonics provides state of the art equipment which is flexible and suit many experimental setups. In addition, the scientific background of the company and in-house experimental expertise makes them the ideal commercial partner for the design and development of customized setups to fit your requirements. Their team is professional, responsive and very skilled."

Nenitha Dagslott, PhD, Kavli Institute for Systems Neuroscience, NTNU, Norway
FEMTOSmart Bridge user

MESC MEASUREMENT CONTROL AND DATA ANALYSIS SOFTWARE

The FEMTOSmart microscope family is driven by the MESc measurement control and data analysis software. MESc is under active development for performing cellular and network imaging measurements supporting more and more features and Femtonics hardware.

New MESc features

- Dual scanning: resonant-scanner-based imaging with simultaneous galvanometric scanner based photostimulation
- MESc Application Programming Interface (API) for no-limit custom data processing and measurement control

Key features

- Measurement configuration and control
- Live data display and processing
- Efficient data streaming to disk in HDF5 format
- Data exporting into standard file formats
- Convenient and fast measurement display and data processing
- Remote control through the MESc Application Programming Interface

Test drive MESc with a free download from our website!

Measurement control

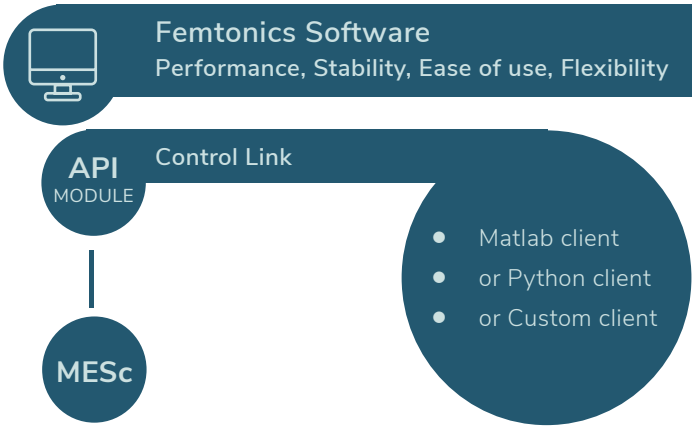
- Integrated control of all hardware units: focusing, resonant and galvo scanners, PMTs, Pockels cells, light path actuators, auxiliary digital and analog channels, pipette manipulators, XY(Z) stages, etc.
- Live preview mode with on-the-fly measurement parameter adjustment
- Real-time measurement data display with live analysis functions
- Digital lab-book philosophy: entire measurement series with different types of measurements can be saved into one HDF5 file, including measurement metadata
- Unlimited measurement time, unlimited video streaming to the hard drive
- Pervasive auto-save and rescue

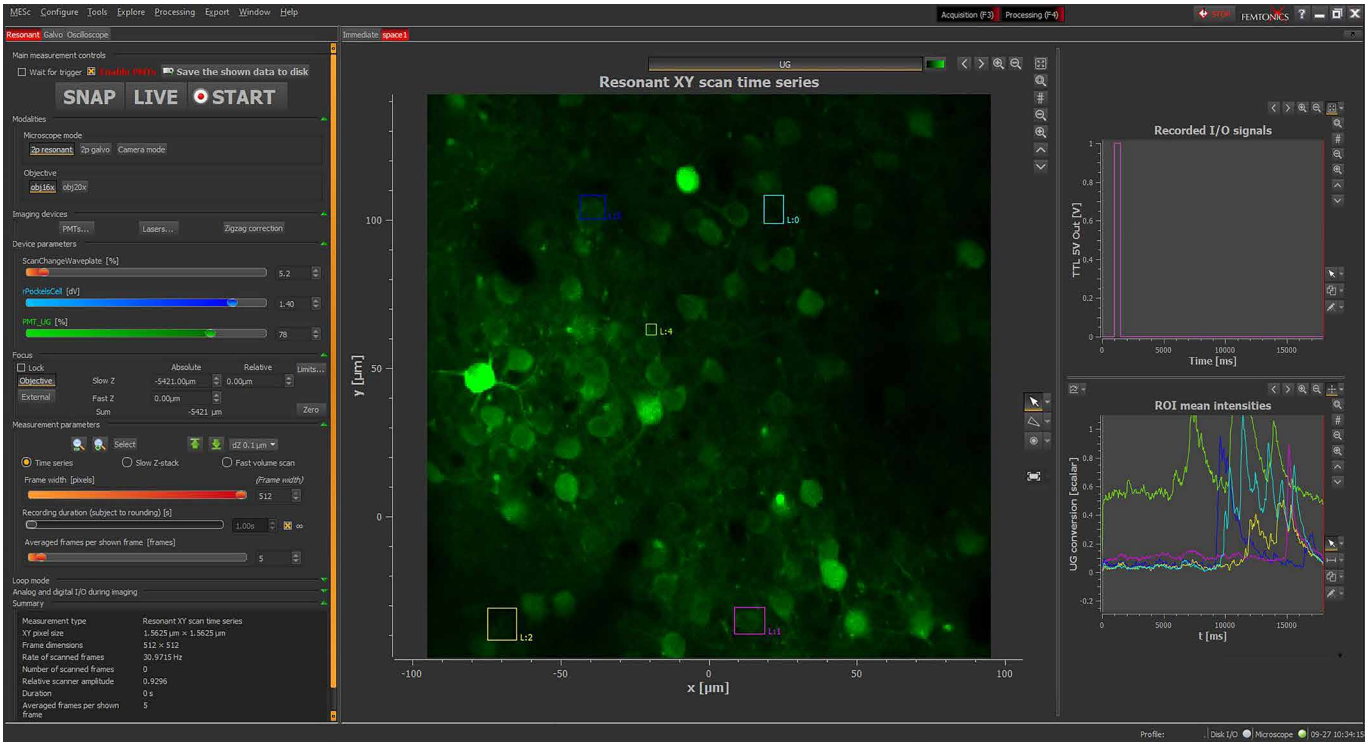
Data analysis

- Composite display of color-coded multi-channel data
- Polygonal and rectangular ROIs for intensity change calculations
- Recorded imaging data exportable to common image and video formats
- Electrical recordings exportable to common spreadsheet software

MESc API Application Programming Interface Programming Femtonics microscopes

The MESc API is a set of clearly defined instructions that can be given to MESc from various software systems like MATLAB or Python. It lets the experimenter perform data analysis with external tools and control measurements with a freely designable protocol.





"The two-photon excitation scopes we got from Femtonics had immediately placed us on a different level of experimental probing, in terms of fluorescence sensitivity and optical and imaging design flexibility. Their engineers have been quick and smart with fixing any technical issues arising. Looking forward to seeing the next wave of advanced instruments from them."

Prof. **Dmitri Rusakov**, Institute of Neurology, UCL, England

OPTIONAL MODULES

3P WAVELENGTH EXTENSION

for three-photon excitation

It allows non-invasive functional imaging of the deeper tissues with higher axial resolution compared to the 2P excitation. Use it for SHG and THG.

MULTIPLE BEAM PATH

for uncaging and optogenetics

We offer secondary, fine-tuned laser sources utilizing the same light path of the scope for a wide range of biophotonics applications.

TILTING OBJECTIVE UNIT

for free rotation of the objective

It rotates the objective, giving a higher level of freedom to reach the sample from different angles. Built-in piezo objective positioner ensures additional Z-movement.

PIEZO OBJECTIVE POSITIONER KIT

for fast Z-stack and 3D imaging

It positions mechanically, rapidly the objective enabling the microscope to collect signals from different depths with up to 200 Hz.

FLIM EXTENSION

for Fluorescence Lifetime Imaging

Time correlated single photon counting and the derived fluorescence lifetime imaging provide intimate information about molecular dynamics.

LED LIGHT SOURCE

for ful-field optogenetics

Full-field illumination allows molecules and cells to be stimulated over the whole FOV homogeneously.

GREEN ILLUMINATION

for vessel pattern visualization

Green illumination allowing high-contrast visualization of blood vessels helps to navigate on the surface of any organs under *in vivo* conditions.

IN VITRO EXTENSION

for cultured cells or acute brain slices

Gradient contrast illumination eases camera guided patch-clamping while transmitted fluorescence detectors enhance signal collection and SNR.

AND ACCESSORIES

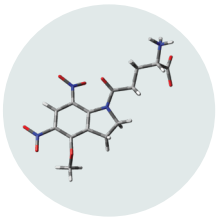
GRAMOPHONE

FOR BEHAVIOR STUDIES

Gramophone is a locomotion tracking device which allows a head restrained mouse to run on the disk and to respond to visual or other stimuli.

HEAD HOLDERS FOR RODENTS

Head holders fix the rodent's head in different positions, enabling, precise measurements in the brain of anesthetized and behaving animal models.



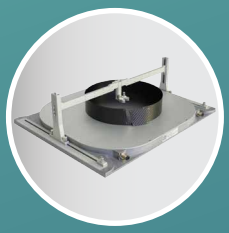
DNI-GLU

for uncaging

This masked form of glutamate releases the bioactive glutamate rapidly and requires less irradiation for release than other caging scaffolds.

LUIGS & NEUMANN TREADMILL WITH VR

The Luigs & Neumann treadmill was designed to investigate the integration of sensory and spatial information in the brain, while the animal is moving a treadmill belt and navigating in a virtual environment (VR).



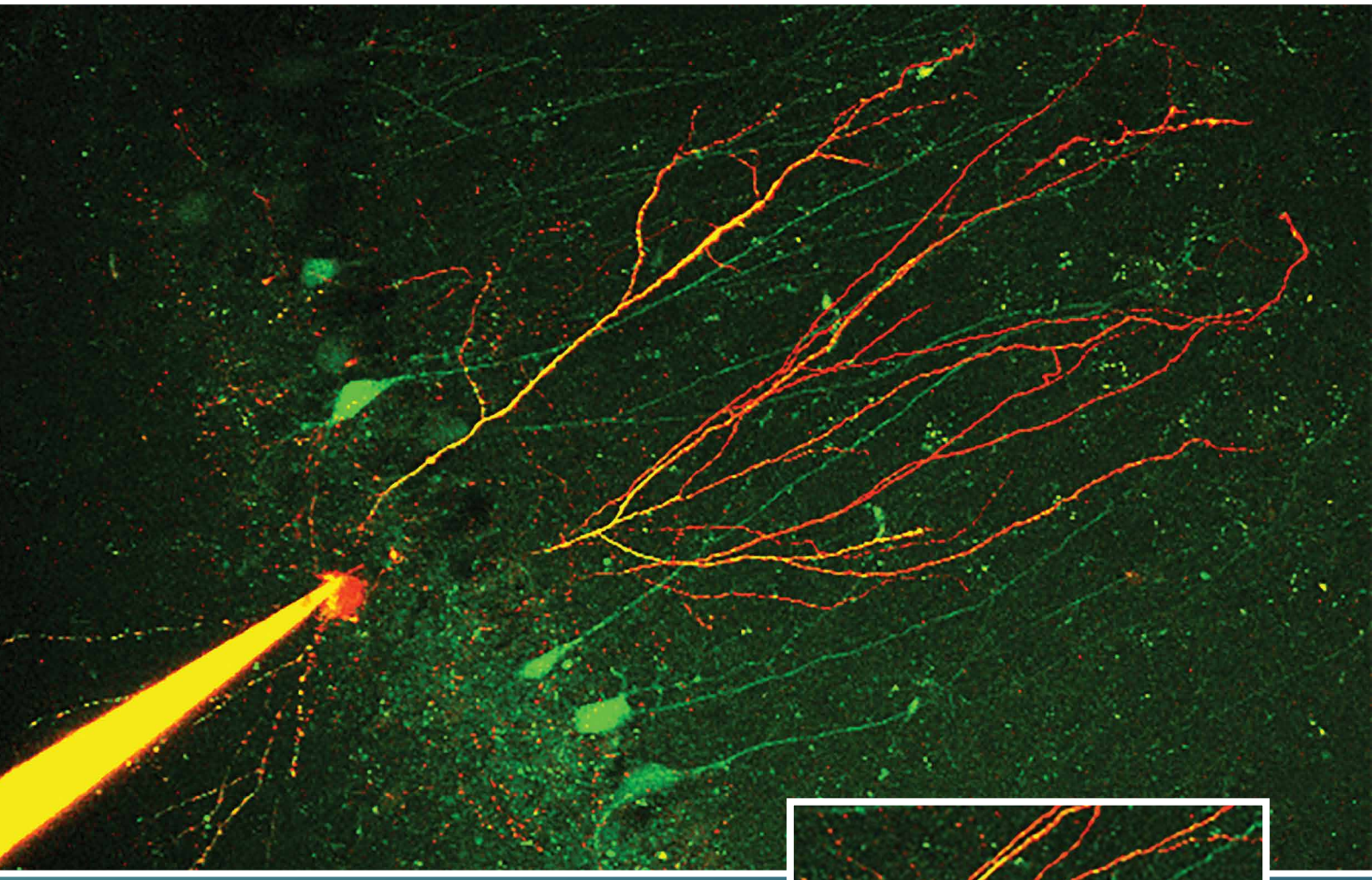
NEUROTAR VIRTUAL REALITY SYSTEM

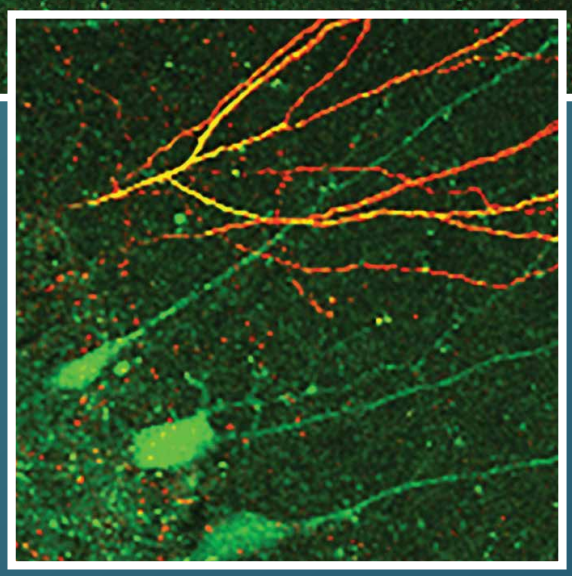
In the Neurotar Mobile HomeCage, a head-fixed, awake rodent can walk freely on a flat-floored, air-lifted cage that moves according to the animal's locomotion, to study brain function.

PHENOSYS VIRTUAL REALITY SYSTEM

The JetBall-TFT contains a TFT surround monitor system and a spherical treadmill with optional operant devices, that allows a restrained animal to navigate virtual space for investigating cognition, learning, etc.

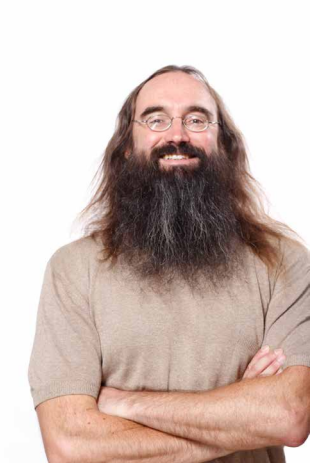
BIOLOGICAL
APPLICATIONS





An *in vitro* patch-clamped interneuron labeled with Alexa-594 from a hippocampal slice of a GCaMP-expressing mouse model.

BIOLOGICAL APPLICATIONS



Tamas

Application specialist, college professor
PhD in Neural Sciences

Fields of expertise: primate visual cortex, human visual system, dopaminergic signaling, voltage sensitive dye imaging.

Denes

Application specialist, research scientist
PhD in Neural Sciences

Fields of expertise: 2D and 3D microscopy, in vivo and in vitro electrophysiology, patch clamp recordings.

Zsolt

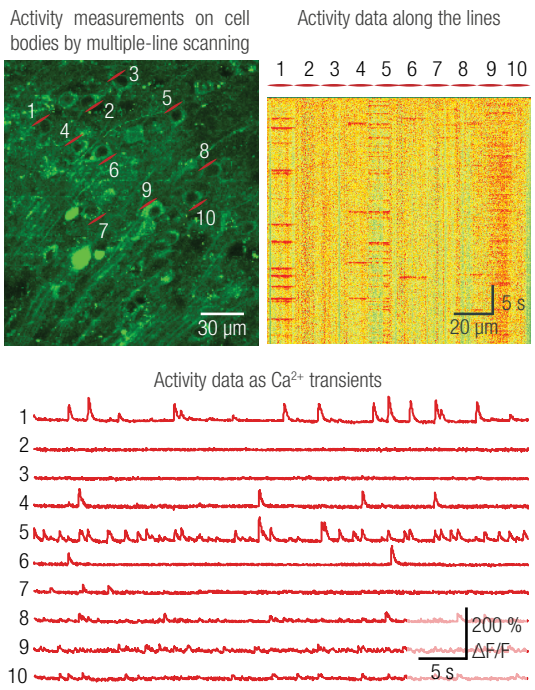
Application specialist, research scientist
MSc in Biology

Fields of expertise: calcium imaging, hippocampal cicuits, behavioral protocols, surgical methods, electrophysiology.

OUR APPLICATION SPECIALIST TEAM consists of scientists with profound research experience and understanding in the field of neuroscience and two-photon technology.
They are always ready to support researchers by providing them with all the needed information about our microscopes, through online and on-site demonstrations, and to aid them in finding the most appropriate system for their needs.
Femtonics microscopes offer the most innovative technologies, while addressing researchers' needs in a wide variety of in vivo and in vitro biological applications.

NETWORK IMAGING

All sensations and behaviors are encoded in the dynamic activity patterns of neural networks. In other words, complex networks of many individual neurons respond to environmental features, visual or auditory stimuli, reward or punishment, etc. Neural networks extend over 3D space and, in most cases, cross many cortical layers of the brain. Two-photon microscopy has made it possible for neuroscientists to reach the deep regions of the cortex or other structures (down to 850 µm) and study them at a high spatiotemporal resolution by using many new scanning methods, and reveal the function of neuronal populations.



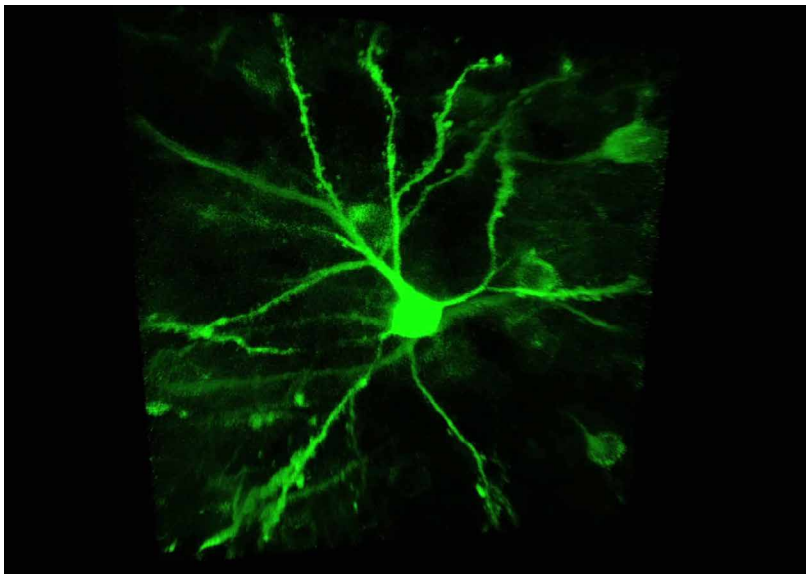
Imaging of somata as ROIs in 2D FEMTOSmart Galvo

The FEMTOSmart Galvo, with its flexible scanning patterns such as 2D scanning of discrete point series, 2D multiple-line, and folded-frame scanning, supports the manual selection of individual cells in a 2D plane. By skipping measurement of the entire field, it is possible to maintain a high signal-to-noise ratio.

Using the TravellingSalesman software module, it is possible to determine the shortest pathway to visit the defined points arbitrarily dispersed on the field of view. The short round-trip time results in a high measurement repetition speed, up to 100 Hz for about 30 cells.

Fast scanning of the entire FOV or a volume FEMTOSmart Resonant equipped with Piezo objective positioner kit

Fast-frame scanning based on a resonant scanner combined with fast Z-focusing performed by a Piezo objective positioner kit, is a well-known approach for studying three-dimensional neural networks. In this case, the entire field of view is imaged continuously by the fast scanner, while the objective positioner moves between planes. Different (cortical) layers might be recorded simultaneously this way, or the frames may be assembled to volumes resulting in a four-dimensional dataset.



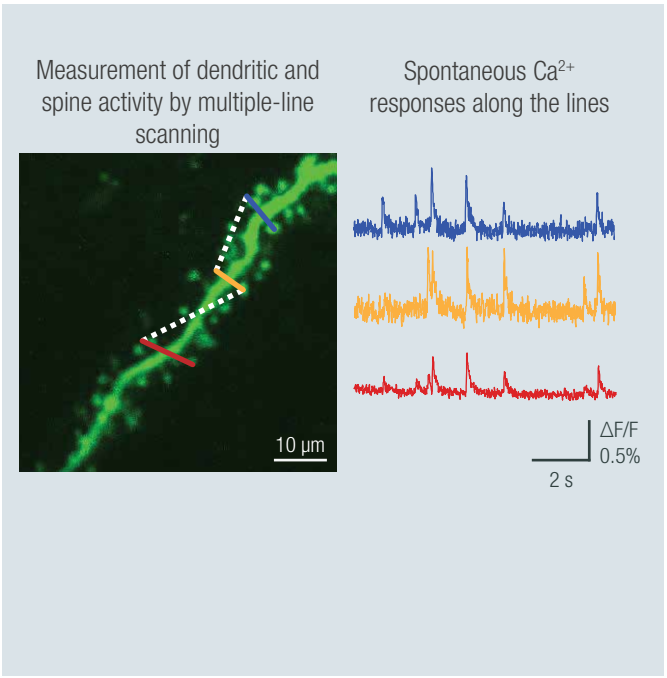
DENDRITIC IMAGING

Dendrites and dendritic spines are thin, sensitive processes and are therefore difficult to study. Using two-photon laser scanning technology, however we are able to collect signals from femtoliter volumes of deeper regions of the brain, while at the same time avoiding phototoxicity. In addition, the spatially confined scanning of axons, dendrites, and spines as regions of interest (ROIs) makes it possible to detect even sub-threshold signals because of the high signal-to-noise ratio (SNR). There are several configurations which make it possible to visualize dendritic arborization and perform functional measurements under *in vitro* and *in vivo* conditions in 2D and 3D samples.

High scanning speed along dendrites and spines in 2D FEMTOSmart Galvo

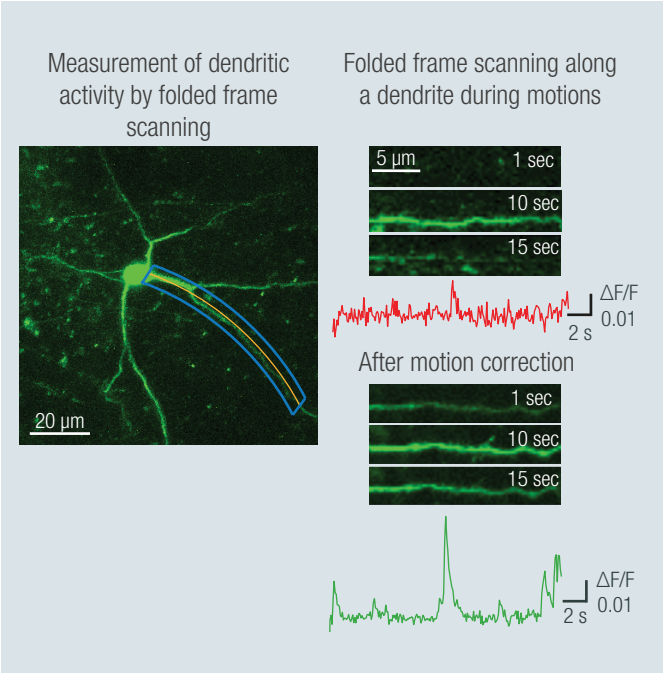
2D MULTIPLE-LINE SCANNING

The adaptable X and Y mirrors of the galvanometric scanner, coupled with the special electronic boards from Femtonics, can follow the tortuous protrusions of the dendritic arbor precisely using the 2D multiple-line scanning method. By limiting the scanning to the spines and omitting the space between them, both the scanning speed (up to 2 kHz) and the SNR can be increased.



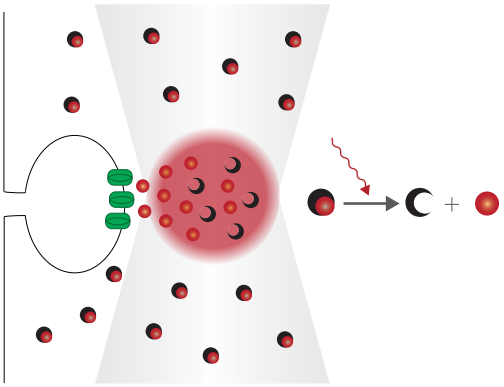
FOLDED FRAME SCANNING

Using folded-frame scanning, an area along a pre-selected line can be imaged. The selected regions can take many shapes, from areas around straight lines to complex bent curves. This advanced scanning method is useful for following events along curved dendrites with spines, and can also be advantageous for dendritic measurements in behaving animals where motion artefacts are a common problem. The images are corrected for motion offline by the control software, as long as the dendrite remains in the scanned area.



PHOTOSTIMULATION/ UNCAGING

Uncaging means the activation of biochemically masked ('caged') molecules via photolysis, which mimics the physiological release of bioactive compounds. This technique is widely used in neuroscience, where the bioactive molecule is usually glutamate or another neurotransmitter. Using two-photon photostimulation, made possible by the secondary laser beam in the FEMTOSmart Galvo, very precise release of these compounds can be elicited in extremely small volumes. Two-photon imaging is a powerful opportunity to follow the changes evoked in dendrites or spines, even receptor distribution can be studied this way on the neurons.

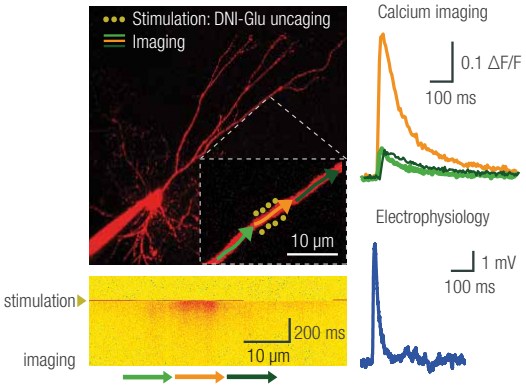


In vivo uncaging at well-defined points

FEMTOSMART GALVO EQUIPPED WITH A MULTIPLE BEAM PATH EXTENSION

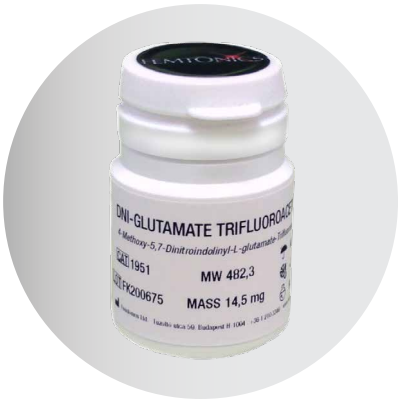
The accuracy of the excitation point, and the highly flexible scanning patterns, mean that the FEMTOSmart Galvo is the best choice for uncaging experiments. The secondary laser beam, essential for the stimulation, is coupled to the existing light path. Thus the stimulation and the imaging can be performed near simultaneously using the galvo scanner. Multiple-point scanning (yellow points on the figure) is used for stimulation around spines, while multiple-line scanning (arrows) makes high-speed imaging along the dendrites possible.

Uncaging experiment using DNI-Glu performed by FEMTOSmart Galvo



DNI-GLU-TFA

Femtonics Chemistry designs and develops new caged neurotransmitters for frontier neuroscience research. The main product is a glutamate derivative, but custom-synthesized compounds can also be generated to meet customers' specific needs. This dinitro-indoline-masked form of glutamate releases the bioactive glutamate more rapidly than any other commercially available compound. It was developed for high-quantum yield, requiring less irradiation for release, so its effective concentration is lower than other caging scaffolds. DNI-Glu is a compound developed in-house, only available from Femtonics. See also Chiovini et al., Neuron, 2014.

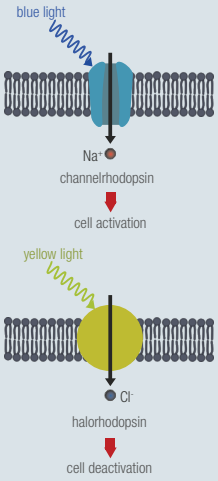


Features of DNI-GLU-TFA

- Photostimulation with two-photon laser
- High quantum-yield
- Effective at low concentration
- Seven-fold higher quantum yield than any other caged form
- High excitatory postsynaptic potential and high Ca^{2+} transient as a response to the photorelease
- Less illumination is sufficient to elicit the same response as with alternative compounds
- Elicits large transients or regenerative activity

PHOTOSTIMULATION/OPTOGENETICS

The essence of optogenetics is introducing light-activated recombinant ion channels such as channelrhodopsin (ChR2) or halorhodopsin (NpHR) into excitable cells. Light activation of these molecules lead to an influx or outflow of ions which excites or inhibits neurons selectively. Halorhodopsin and channelrhodopsin together enable multicolor optical activation, silencing, and desynchronization of neural activity, creating a powerful neuroengineering toolbox.



STIMULATION AND IMAGING

The photostimulation can be induced using visible or infrared light, while imaging is performed by a femtosecond IR laser. Switching between the stimulation and imaging is done at a sub-millisecond scale. Importantly the detectors are protected during the stimulation by a built-in gating system.

FULL-FIELD ILLUMINATION FEMTOSMART RESONANT EQUIPPED WITH LED LIGHT SOURCE

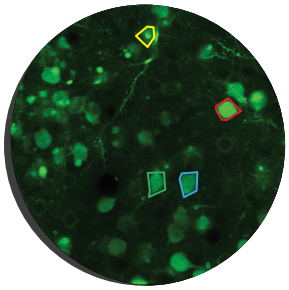
The entire FOV can be stimulated with the LED source above the objective. LEDs are available at different wavelengths, exciting ChR2 at 473 nm or NpHR at 561 nm. The light impulses are precisely timed and highly repeatable. The FEMTOSmart Resonant microscope follows the changes over the whole field of view at a resolution of 31 frames per second.

STIMULATION ALONG ROIS FEMTOSMART GALVO EQUIPPED WITH MULTIPLE BEAM PATH EXTENSION

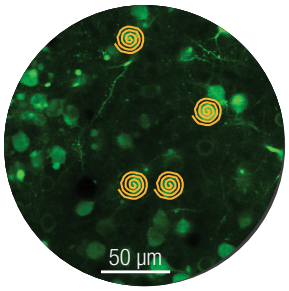
To stimulate cells or subcellular components selectively, the best solution is using the FEMTOSmart Galvo to steer the laser beam rapidly through optimized scanning patterns, such as a spiral, zigzag, etc. We offer a continuous laser tuned to 473 or 561 nm for ChR2 or NpHR activation, respectively. Precise two-photon activation of these molecules is also a viable option.

SIMULTANEOUS PHOTOACTIVATION AND IMAGING FEMTOSMART DUAL

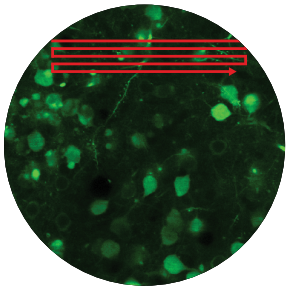
The FEMTOSmart Dual microscope contains a galvo and a resonant scanner which function in tandem to combine the advantages of both the galvo and resonant microscopes. This is the best solution for simultaneous photostimulation and high-speed imaging.



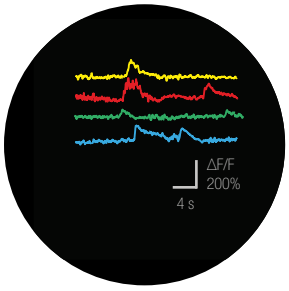
Offline ROI selection



Stimulation along ROIs using spiral scanning pattern with galvo scanner on ChR2 expressing neurons



Full-field imaging by resonant scanner



Calcium responses from the selected ROIs

BEHAVIORAL STUDIES

Behavioral processes are paired with patterns of brain activation. The neural basis of a behavioral trait such as visuomotor learning, memory retrieval, associative learning, or spatial navigation can be mapped by controlled, multiform experimental manipulation. This can be a change in stimulus information, task instruction, or reward and punishment which alter the underlying pattern of brain activation. Monitoring or evoking behavioral data, and parallel imaging of neuronal circuits in a living animal's brain can reveal the connections between changes at cellular and behavioral levels.

BEHAVIORAL EXPERIMENT CONTROL

Bpod is an open-source behavior-recording system and real-time environment controller for rodent experiments. Using high-level programming environments (MATLAB/Python), it provides a low-latency closed-loop link between behavioral events, stimulus delivery, and stimulation. Using its built-in liquid reward delivery system, it can be used to power go/no-go discrimination, two alternative forced choice, and CS/US behavioral paradigms. Bpod data acquisition is fully synchronized with the microscope, and the behavioral events can be precisely aligned to the recording of Ca^{2+} transients.

SOFTWARE-CONTROLLED TRIGGERING OF STIMULI

Different forms of stimulation can be triggered or driven directly using the analog and digital output signals of the microscope, planned and controlled from the measurement control software. Visual, auditory, tactile, whisker or odor stimuli can be generated this way. The Stim Visual software module of the control software enables videos or images for visual stimulus to be loaded and played sequentially, and the stimuli synchronized with the evoked neural responses.

VIRTUAL REALITY SYSTEMS

Virtual Reality (VR) systems enable head-fixed but free-to-move rodents to enter a VR environment and perform complex behaviors, and provide a user-friendly experimental protocol for investigating cognition, navigation, learning, memory, and operant conditioning.

Luigs & Neumann treadmill with virtual reality

The Luigs & Neumann treadmill was designed to investigate the integration of sensory and spatial information in the brain of mice. The system allows tactile, visual or olfactory stimulation of a head-fixed mouse, while the animal is moving a treadmill belt and navigating in a virtual environment. In parallel all established optical and electrophysiological measurements or manipulations for head-fixed animals can be performed e.g. to study navigation strategies.

Neurotar Mobile HomeCage provides a real and familiar moving VR environment. A head-fixed, awake rodent walks freely on a flat-floored, air-lifted cage that moves according to the animal's locomotion, while exploring and navigating during *in vivo* recordings and imaging experiments.

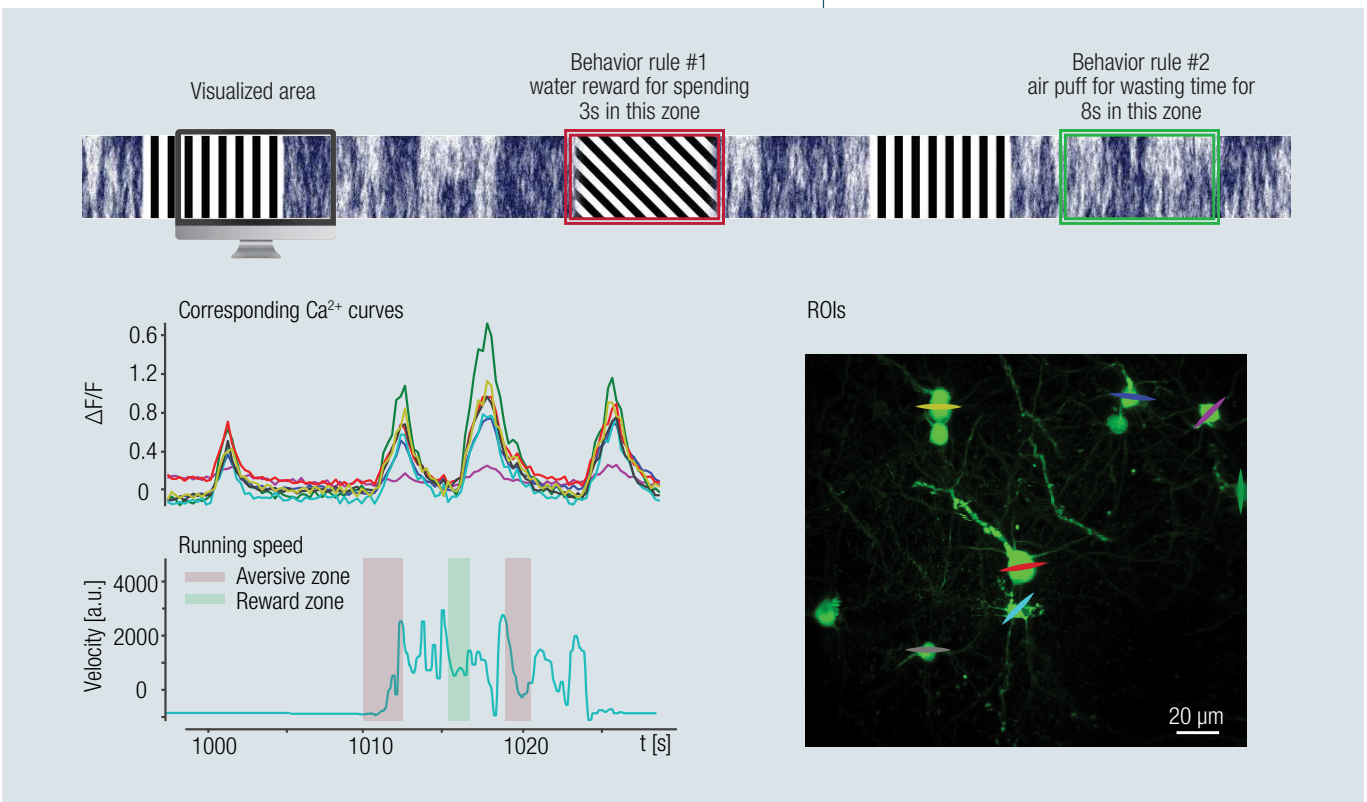
Phenosys JetBall-TFT consists of a TFT surround monitoring system focusing on 200° around the animal, and a spherical treadmill which make unobscured field or maze designs possible. This device can be coupled with optional operant devices, and allows a restrained animal to navigate in virtual space.

GRAMOPHONE

Gramophone is a single-dimension locomotion tracking device. It consists of a rotating disk, an electric registration system, a stabilized head holder and a monitor. It allows a head restrained mouse to run on the disk and to respond to visual or other stimuli. The speed and the direction of the running are registered by software controlled manner.

How does it work?

The monitor shows visual stimuli such as predefined patterns or customizable linear mazes that change in accordance of the mouse's movement on the rotating disk, creating a virtual reality where the animal can navigate itself by moving the disk. It can be used for high accuracy velocity recording in conjunction with a two-photon microscope, or as a control interface for behavioral training in a virtual linear maze.
The behavior response and the two-photon Ca^{2+} signals can be recorded simultaneously and aligned to each other. The Gramophone can be coupled with multiple operant devices such as a water reward, air puff, etc., and the spinning speed of the disk is recorded in a triggered manner.

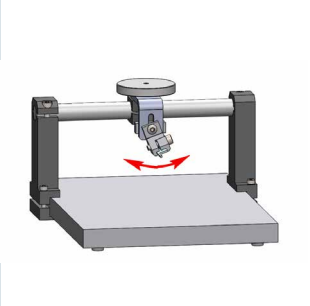


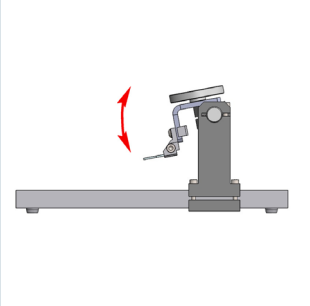
HEAD HOLDERS FOR RODENTS

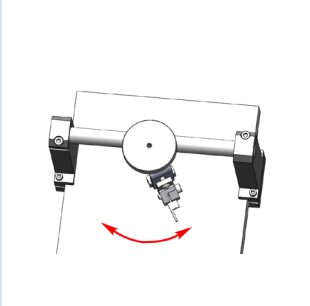
Head holder stands and head plates fix the rodent's head in different positions, enabling precise measurements in the brain. Three types of head holders are available with different dimensions. For anesthetized rodents, we offer a heating pad coupled to a holder, or for behaving animals a stand that ensures access to jetballs, treadmills, or other devices.

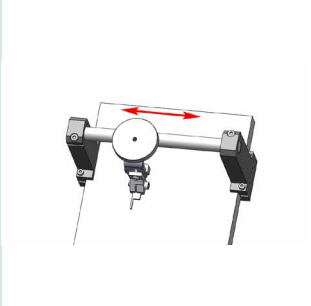
Flexible head holder

Offering maximum flexible adjustment for positioning the head, this holder fixes the skull from one side. The head plate can be moved in three directions of the space and also along the bridge. It is offered for difficult to access parts such as eyes or auditory cortex, and anesthetized rodents.









Elevated head holder

The elevated head holder is recommended primarily for VR applications such as jetballs and treadmills. The height of the stand is adjustable, and similarly to the flexible head holder, the plate can be moved in three directions and also along the bridge.

Stabilized head holder

Stabilized head holder is attached to the rodent's head at two sides. It is ideal for craniotomy or other surgery where the head of the animal model has to be fixed. It can be coupled to the Gramophone.

SUPPORT

CONTACT REMOTE SUPPORT

We provide remote technical support that allows our technical team to test the hardware and modify the software from afar.

CUSTOMER SERVICE PORTAL

Our online customer service portal enables users to contact the Femtonics support team directly.

DOWNLOAD

Download the microscope control and analysis software and take it for a test drive!

Our mission is to make readily available high quality technical support pre and post microscope selection. We can enhance your work by custom optimizing the software and/or the hardware. Femtonics support team consists of mechanical, optical and software engineers as well as application scientists who are ready to provide technical advice and technical guidance with the microscope which starts at production and continues through assembly, installation and maintenance. We aim to keep your system healthy, up-to-date and operating at the highest level of its performance.

Online service desk

Femtonics provides remote technical support with each newly installed Femtonics microscope in which we include an internet camera and a microphone along with remote control software. This allows our technical team, with customer's permission, to remotely test the hardware, to modify the software and to find solutions to any unexpected issues. This is like having your own technical support person next to you proving to have a high customer satisfaction.

Service follow-up

An online management tool at our website receives the incoming service tasks and lists them as traceable processes. In this way, the user always knows about the current state of the service process.

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