Nikon

A1+

Confocal Microscope

Bring Imaging to Life!

Capturing high-quality images of cells and molecular events at high speed, Nikon's superior A1+ confocal laser microscope series, with ground breaking technology, enables you to bring your imaging aspirations to life.

A1+ with high performance and A1R+ with additional high-speed resonant scanner

The A1+ series dramatically improves confocal performance and ease of operation. The A1R+ with a hybrid scanner supports advanced research methods using photoactivation fluorescence protein. The ergonomic user-friendly design facilitates live-cell work and a huge array of new imaging strategies.

The ultimate confocal microscope

A1+ A1R+

Brightness

Fluorescence efficiency is increased by 30 percent, while the S/N (signal to noise) ratio of images is also increased. GaAsP detectors enable significantly brighter acquisition than traditional PMTs in standard and spectral imaging.

Dynamics

The high-speed resonant scanner allows imaging of intracellular dynamics at 30 fps (frames per second) (512 x 512 pixels). Image acquisition of 420 fps (512 x 32 pixels) is also possible.
The galvano (non-resonant) scanner has a high-speed acquisition capability of 10 fps (512 x 512 pixels) and 130 fps (512 x 32 pixels).

Interaction

Simultaneous imaging and photoactivation with the proprietary A1R+ hybrid scanner reveal intermolecular interaction. Analysis software for FRET is available as an option.

Spectrum

With a variety of spectral detector units, users can select from A1-DUS, the fast 32-channel PMT spectral detector unit, or A1-DUVB, the newly-developed high-sensitivity GaAsP PMT tunable emission spectral detector unit.

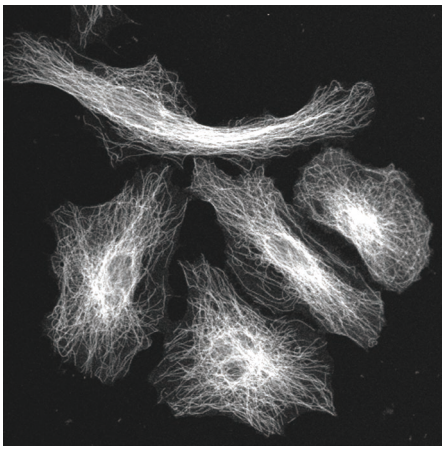
Brightness

Key Nikon innovations for improving image quality

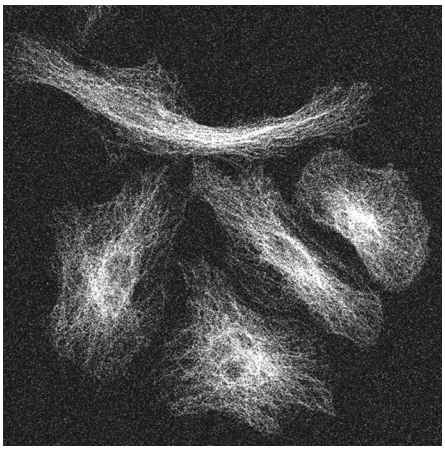
The highest standard of image quality has been realized by the development of a high-sensitivity GaAsP detector, in addition to increased light sensitivity resulting from comprehensive technological innovations in electronics, optics and software.

GaAsP Multi Detector Unit

The GaAsP detector uses gallium arsenide phosphide (GaAsP) in its PMT cathode. Since this enables it to achieve higher quantum efficiency than conventional detectors, brighter image acquisition with minimal noise and high-sensitivity is possible, even with very weak fluorescence specimens.



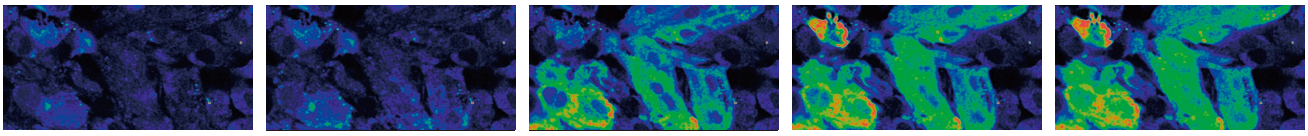
GaAsP detector



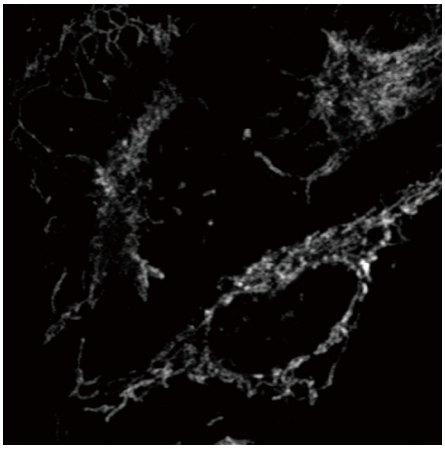
Normal detector

Bright high-speed imaging

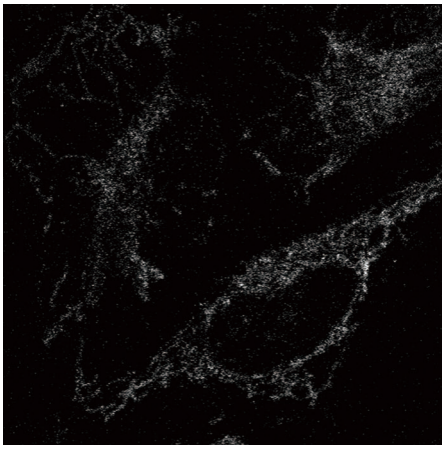
The high-sensitivity GaAsP detector enables bright imaging with minimal noise even during high-speed imaging, and is powerful for time-lapse imaging using a resonant scanner.



Calcium sparks in cardiomyocytes loaded with Fluo-8 are captured at 60 fps



GaAsP detector



Normal detector

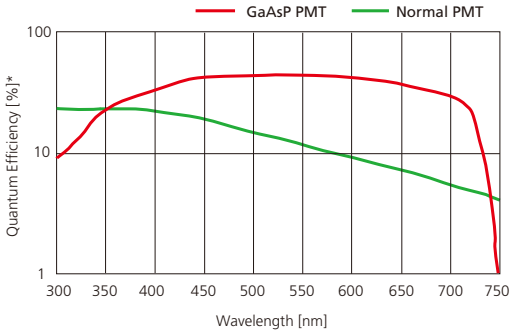
Images of HeLa cells labeled with MitoTracker, acquired using GaAsP PMT and normal PMT under the same conditions

Hybrid detector

The A1-DUG GaAsP multi-detector unit is a hybrid 4-channel detector which is equipped with two GaAsP PMTs and two normal PMTs.

Superior sensitivity

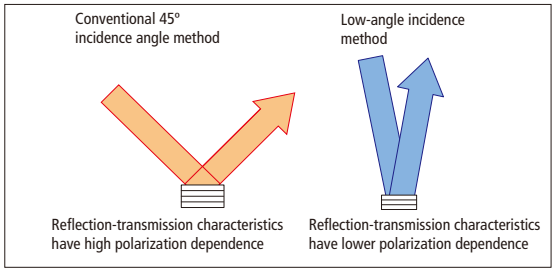
The GaAsP PMT is highly efficient at detecting the wavelength commonly used in confocal imaging. It dramatically enhances detection of fluorescence signals from specimens stained with dyes such as FITC, YFP and Alexa Fluor 568.

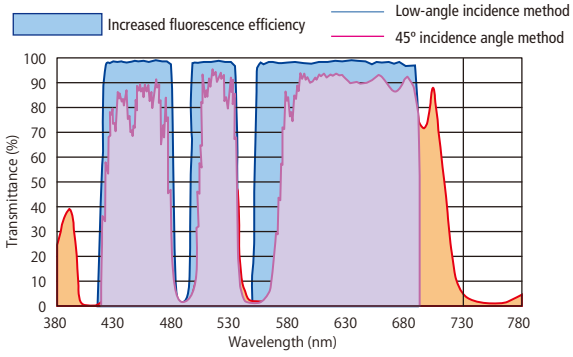


Sensitivity comparison of GaAsP PMT and normal PMT
GaAsP PMT realizes higher sensitivity than normal PMT, thus offering high quantum efficiency up to 45%.
* Quantum efficiency indicates logarithm

Low-angle incidence dichroic mirror creates a 30% increase in fluorescence efficiency

With the A1+ series, the industry's first low-angle incidence method is utilized on the dichroic mirrors to realize a 30% increase in fluorescence efficiency.

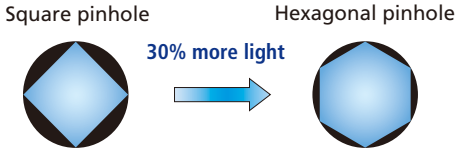




Comparison of fluorescence efficiency

Brighter images with continuous variable hexagonal pinhole

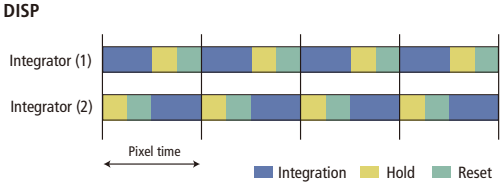
Instead of a continuous variable square pinhole, the industry's first hexagonal pinhole is employed. Higher brightness, equivalent to that of an ideal circular pinhole is achieved while maintaining the confocality.



64% of the area of a circle **83% of the area of a circle**

DISP improves electrical efficiency

Nikon's original dual integration signal processing technology (DISP) has been implemented in the image processing circuitry to improve electrical efficiency, preventing signal loss while the digitizer processes pixel data and resets. The signal is monitored for the entire pixel time resulting in an extremely high S/N ratio.



Two integrators work in parallel as the optical signal is read to ensure there are no gaps.

High-speed and high-quality imaging

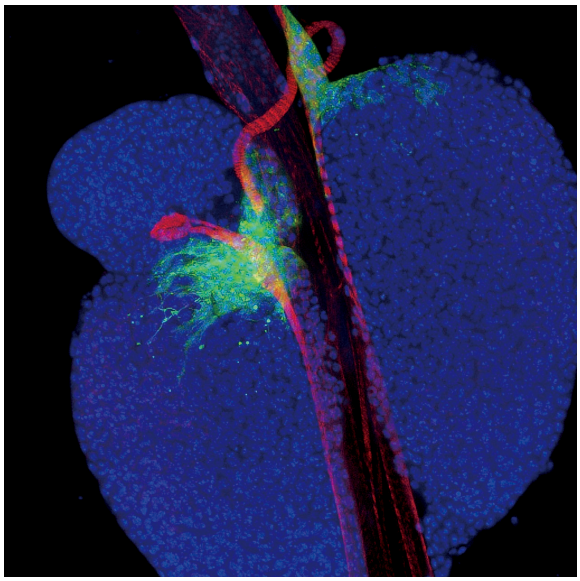
A1+ is equipped with a galvano (non-resonant) scanner for high-resolution imaging. A1R+ has a hybrid scanner that incorporates the advantages of both high-speed resonant and galvano scanners, offering ultrafast imaging and simultaneous photoactivation and imaging.

High-resolution imaging

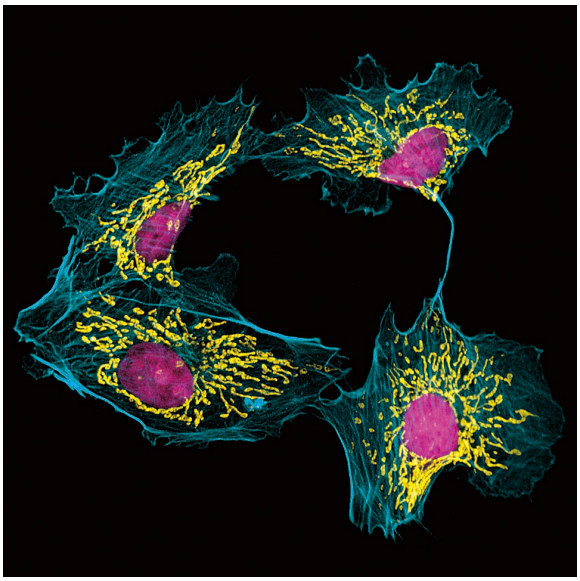
A1+/A1R+

Multicolor imaging

A four-channel detector (either A1-DU4 four-detector unit or A1-DUG GaAsP multi-detector unit) provided as standard equipment eliminates the necessity for an additional fluorescence detector and allows easy imaging of a specimen labeled with four probes.



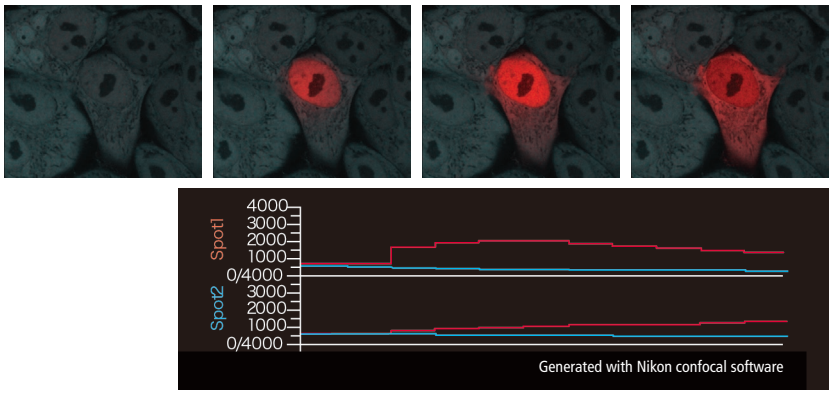
Drosophila sp. Embryonic heart

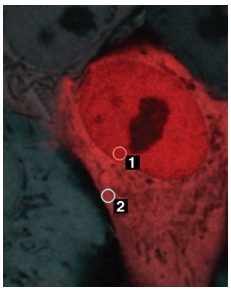


Bovine brain microvascular endothelial cells labeled with MitoTracker (mitochondria, yellow), phalloidin (actin, blue) and Hoechst (DNA, magenta).

Phamret (Photoactivation-mediated Resonance Energy Transfer)

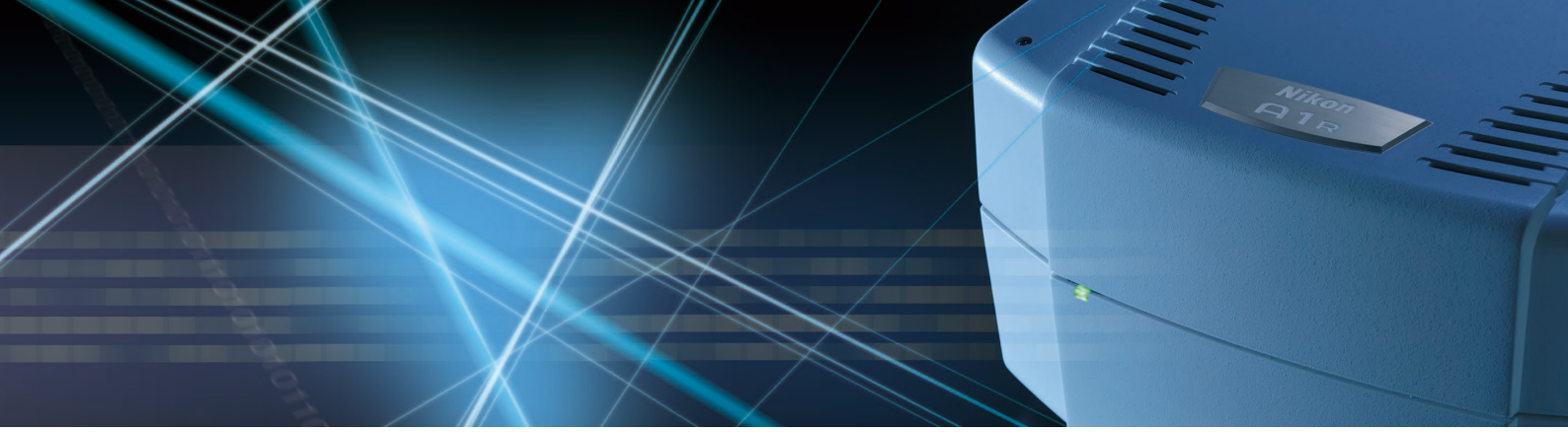
Photoconversion protein Phamret is a fusion protein of the CFP variant and the PA-GFP variant. When the PA-GFP variant is activated with violet to ultraviolet light, it changes light blue fluorescence to green fluorescence due to intermolecular FRET from CFP to PA-GFP.





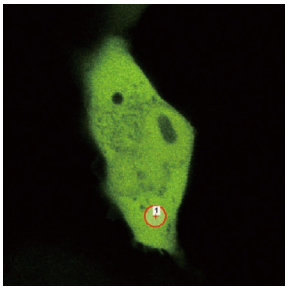
The graph indicates the changes of fluorescence intensity in each ROI. The blue line indicates the changes of fluorescence intensity of the CFP variant and the red line indicates the changes of fluorescence intensity of the PA-GFP variant.

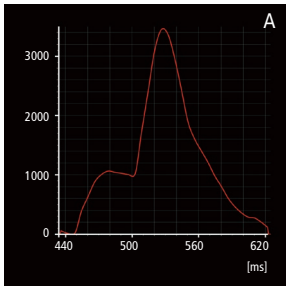
While imaging a HeLa cell expressing Phamret with light blue and green fluorescence using 457 nm laser as excitation light, the PA-GFP variant in an ROI is continuously activated with the 405 nm laser. The activated part observed in light blue fluorescence (shown in monochrome in the images) emits green fluorescence (shown in red in the images). And the dispersion of Phamret indicated by this green (shown in red in the images) is observed.
Activation laser wavelength: 405 nm, Imaging laser wavelength: 457 nm, Image size: 512 x 512 pixels, 1 fps (with galvano scanner)
Photos courtesy of: Drs. Tomoki Matsuda and Takeharu Nagai, The Institute of Scientific and Industrial Research, Osaka University

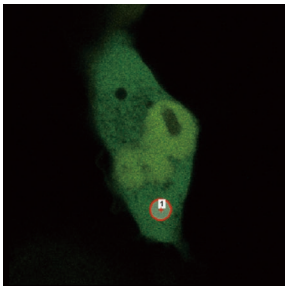


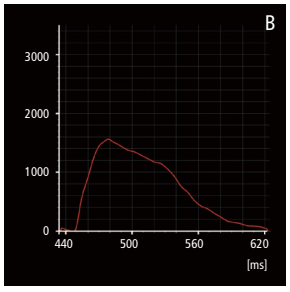
FRET (Förster Resonance Energy Transfer)

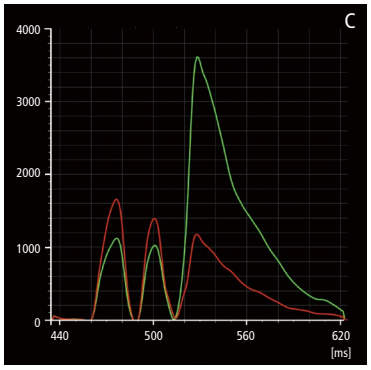
FRET is a physical phenomenon that occurs when there are at least two fluorescent molecules within a range of approximately 10 nm. When the emission spectrum of a fluorescent molecule overlaps with the absorption spectrum of another fluorescent molecule and the electric dipole directions of the two molecules correspond, then radiationless energy transfer from a donor molecule to an acceptor molecule may occur.







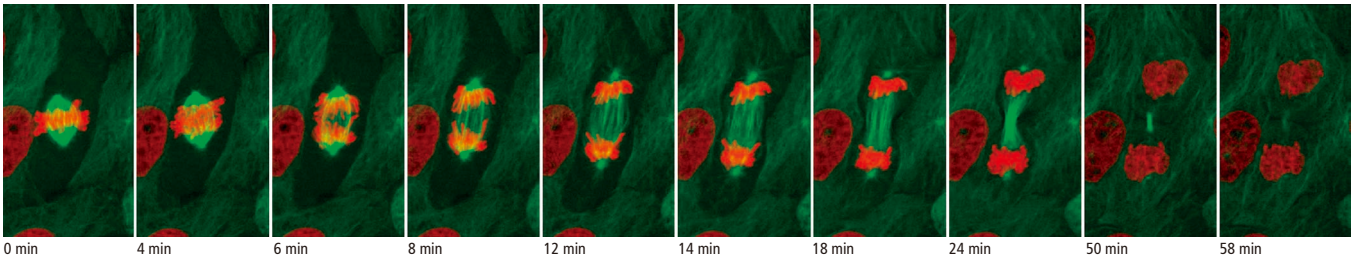




Spectral FRET acceptor photobleaching experiment using Venus and Cerulean-labeled probes.
Part A illustrates the baseline/pre-bleach emission spectral signature and Part B illustrates the post-bleach emission spectral signature. Measurement graphs indicate that the acceptor was photobleached, and there was a corresponding increase in donor intensity as a result.
C is a graph showing the spectrum before photobleaching (green) and after photobleaching (red); the Venus emission is bleached, and the Cerulean emission intensity has increased.

4D time-lapse imaging

A1+ acquires four-dimensional (XYZ-T) time-lapse images at high speed and high sensitivity, minimizing the damage to cells.

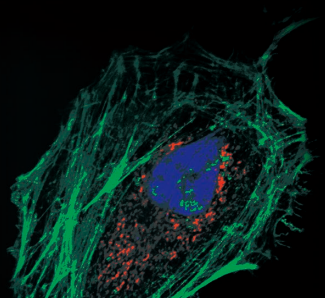


Z series projection of XYZ images of LLC-PK1 cell expressing EGFP-α-tubulin (green) and Histone H2B-mCherry (red) captured every 2 min (with galvano scanner)
Photos courtesy of: Dr. Keiju Kamijo, Department of Anatomy and Anthropology, Tohoku University Graduate School of Medicine

High-resolution A1+/A1R+ scan head

A1+/A1R+'s galvano scanner enables high-resolution imaging of up to 4096 x 4096 pixels. In addition, with the newly developed scanner driving and sampling systems, plus Nikon's unique image correction technology, high-speed acquisition of 10 fps (512 x 512 pixels) is also possible.

1D scanning	5,200 lps (lines per second)
2D scanning	130 fps (512 x 32 pixels)
Full frame scanning	10 fps (512 x 512 pixels)

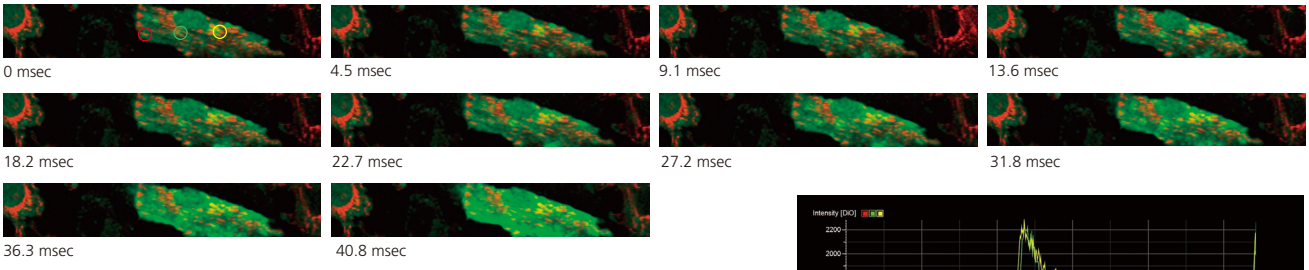


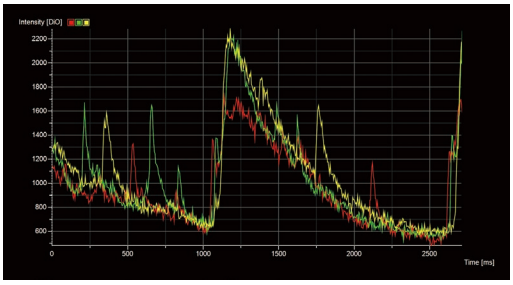
Ultrahigh-speed imaging

A1R+

Calcium sparks

A transient elevation of intracellular calcium (Ca^{2+}) concentration caused by ryanodine receptor (RyRs) is called a calcium spark. Ca^{2+} is released from sarcoplasmic reticulum (SR) to the cell by a calcium-induced calcium release (CICR) mechanism. Calcium sparks occur at local micro regions over a very short time.

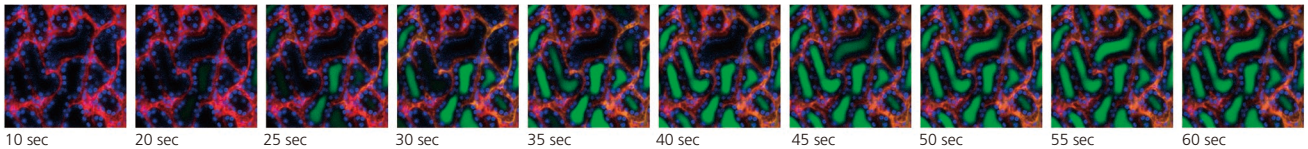




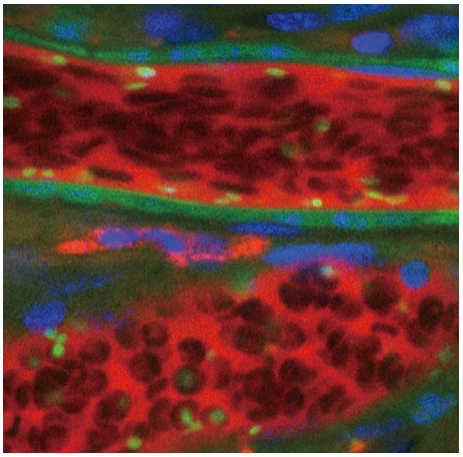
Ca^{2+} concentration changes in mouse's cardiomyocytes labeled with MitoTracker Red (for mitochondria, red) and Fluo-8 AM (calcium indicator, green), are captured at 240 fps (4 ms/frame). The graph indicates the change in intensity of the ROIs.

In vivo imaging

Imaging dynamic status of fluorescence labeled agents and intravital substances in live organisms under good physiological conditions is possible.



Proximal and distal tubules and peritubular capillaries in the kidney cortex are captured at 30fps with a resonant scanner. Blood flow is labelled with Evans Blue (red), and the nucleus with Hoechst (blue). 10 seconds after starting image capturing, FITC-Dextran (green) is administrated through the tail vein catheter. The entry of Dextran into the proximal and distal tubules after being filtered at the glomeruli is captured as a movie.
Photos courtesy of: Drs. Yu Matsumoto and Kazunori Kataoka, Division of Clinical Biotechnology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo

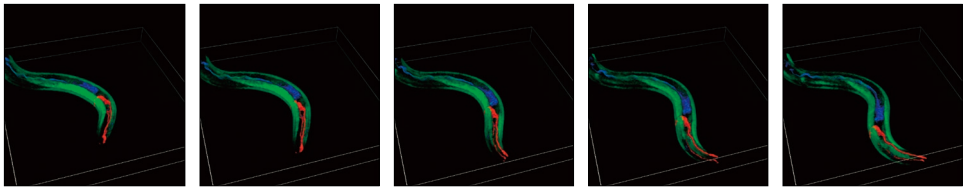


The cell dynamics in arterial and venous vessels of a testis are captured in real time at 30fps with a resonant scanner.
Red: blood flows (Texas Red-Dextran), blue: nucleus (leucocyte and vascular endothelial cells, Hoechst), green: cytoplasm (platelets etc., CAG promoter eGFP)
Platelets (green), erythrocytes (black) and leucocytes (blue) are identified.
Photos courtesy of: Dr. Satoshi Nishimura, Center for Molecular Medicine, Jichi Medical University, Department of Cardiovascular Medicine, TSBMI, the University of Tokyo

A1R+

High-speed 4D imaging

Using a resonant scanner and a fast piezoelectric device allows high-speed 4D (XYZT) imaging that captures the rapid change of samples with 3D information.



Images of a living nematode including its food (E. coli) expressing the fluorescent calcium sensor G-CaMP4 in the parietal muscle (green) and RFP in the AWC neurons (red), and stained with DAPI in the gut lumen (blue), are acquired using a confocal microscope.
Z-stack images are acquired using high-speed XYZ-T scanning at 1.1 sec. interval (35 images with 1 µm layer space).
Photos courtesy of: Drs. Keiko Ando and Junichi Nakai, The category of analysis of brain function, Brain Science Institute, Saitama University

Ultrahigh-speed A1R+ scan head

A1R+ is a hybrid scan head equipped with both a galvano scanner and a resonant scanner with an ultrahigh resonance frequency of 7.8 kHz. It allows ultrafast imaging and photoactivation at 420 fps (512 x 32 pixels), the world's fastest image acquisition.

1D scanning	15,600 lps
2D scanning	420 fps (512 x 32 pixels)
Full frame scanning	30 fps (512 x 512 pixels)

Stable, high-speed imaging

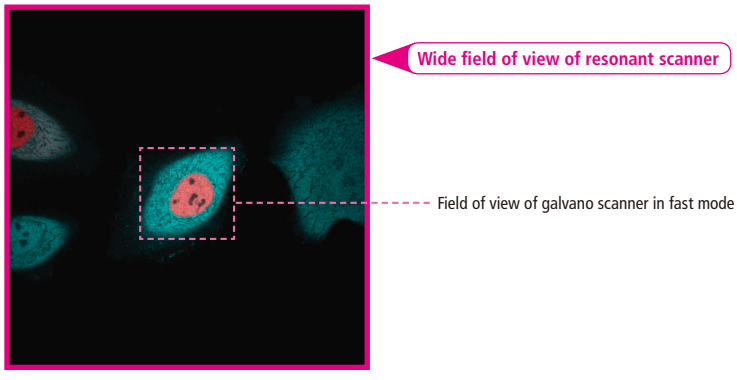
Nikon's original optical clock generation method is used for high-speed imaging with a resonant scanner. Stable clock pulses are generated optically, offering images that have neither flicker nor distortion even at the highest speed.

High-speed data transfer with fiber-optic communication

The fiber-optic communication data transfer system can transfer data at a maximum of 4 Gbps. This allows the transfer of five channels of image data (512 x 512 pixels, 12 bit) at 30 fps.

Wide field of view

Resonant scanners do not suffer from overheating of the motor during high-speed image acquisition. Therefore, it is not necessary to reduce the field of view of the scanned image in order to avoid overheating. This enables a wider field of view than with a galvano scanner.



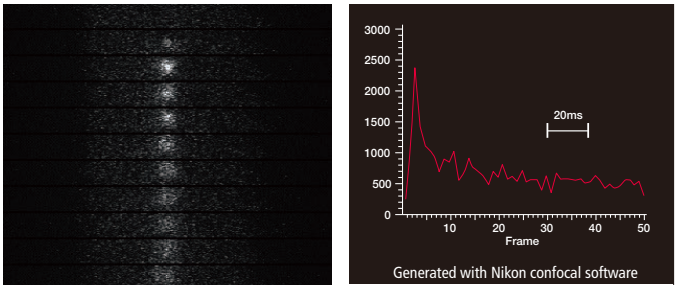
High-speed photoactivation imaging

A1R+

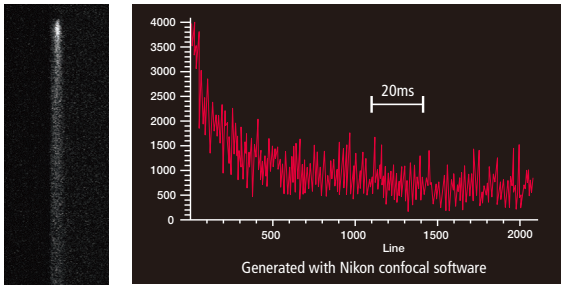
PA-GFP (Photoactivatable Green Fluorescence Protein)

PA-GFP irreversibly changes from a dark state to a bright state, while its absorption spectrum shifts to 488 nm wavelength, when exposed to 405 nm laser.

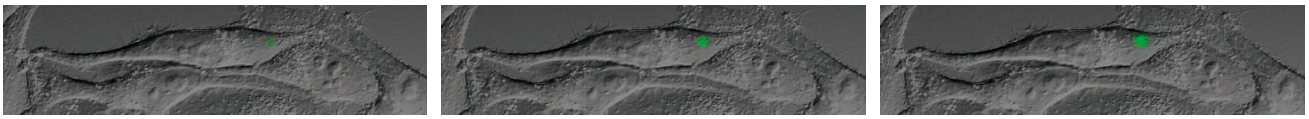
Observation with band scanning
Imaging at 420 fps (2.4 ms/frame, with resonant scanner)
Image size: 512 x 32 pixels



Observation with X-t scanning mode
Imaging with 64 µs time resolution (15,600 lps, with resonant scanner)



HeLa cells expressing PA-GFP are excited with 488 nm laser light. Directly after photoactivation (using 405 nm laser light) of a region of interest, the green emission (shown in grayscale) generated by photoactivated PA-GFP is detected and the subsequent distribution of the photoactivated protein is recorded at high speed. Note that photoactivation (with the 405 nm laser) and image acquisition (with the 488 nm laser) are performed simultaneously. Both XYt and Xt recordings are displayed. Graphs show fluorescence intensity (vertical) versus time (horizontal).
Activation laser wavelength: 405 nm, Imaging laser wavelength: 488 nm
Photos courtesy of: Drs. Tomoki Matsuda and Takeharu Nagai, The Institute of Scientific and Industrial Research, Osaka University



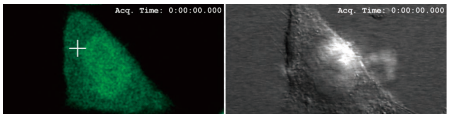
33ms | 99ms | 165ms

297ms | 429ms | 561ms

HeLa cell expressing PA-GFP was photoactivated for 1 second with a 405 nm laser while imaging at 30 fps (with resonant scanner) with 488 nm laser.
DIC images were captured simultaneously and overlaid.
Photos courtesy of: Dr. Hiroshi Kimura, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology

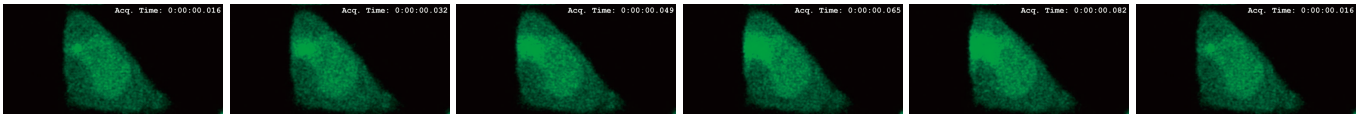
Caged compounds

Caged compounds are biologically active molecules that have been rendered functionally inert and can be instantly reactivated by near-ultraviolet light exposure. By controlling the light exposure, functionalized molecule expression in active form is possible in targeted intercellular sites with high spatial and time resolution.

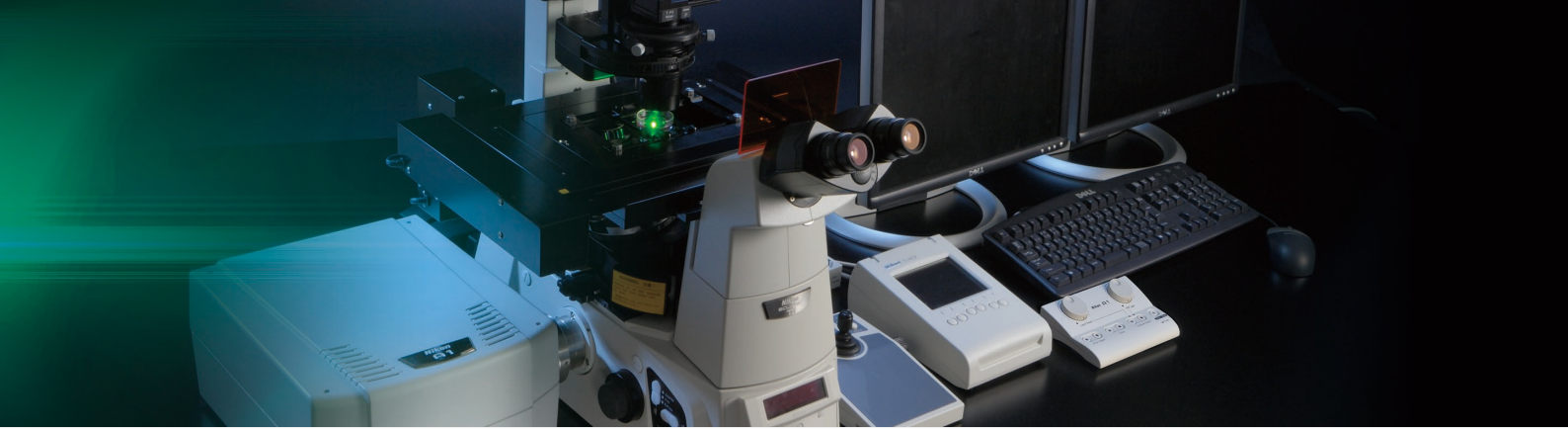


0 msec

HeLa cells are loaded with Fluo-4 (calcium indicator) and NP-EGTA (caged Ca^{2+} compound), and captured with DIC images and confocal images at 60fps. Ca^{2+} concentration changes are captured while the area indicated with a cross is stimulated for 100 ms using a 405 nm wavelength laser.

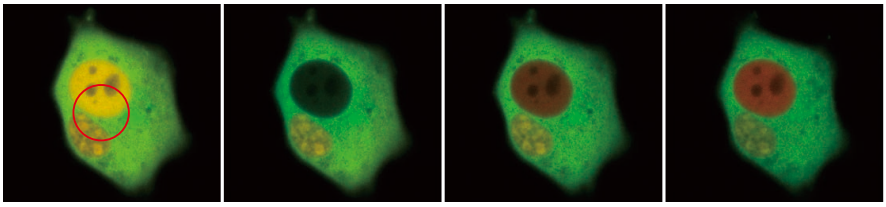


16 msec | 32 msec | 49 msec | 65 msec | 82 msec | 98 msec

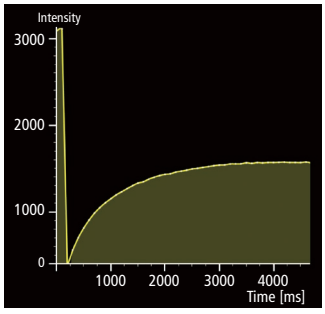


FRAP (Fluorescence Recovery After Photobleaching)

After bleaching fluorescence dyes within the ROI by strong laser exposure, the recovery process of fluorescence over time is observed in order for the molecule diffusion rate to be analyzed.
The A1R+' hybrid scanner allows high-speed imaging of fluorescence recovery during bleaching at a user-defined area.

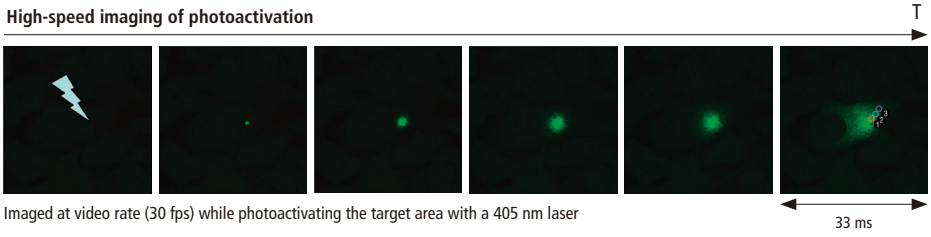


FRAP experiment observing nuclear transport of the YFP-label during a time-lapse acquisition sequence. The graph indicates the intensity change of the red ROI

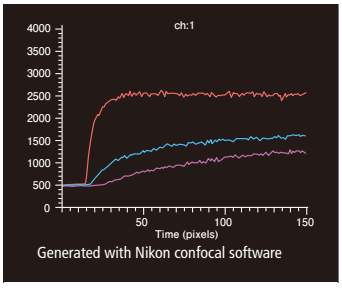


Simultaneous photoactivation and imaging

Simultaneous photoactivation and fluorescence imaging is conducted using galvano and resonant scanners. Because the resonant scanner can capture images at 30 fps, image acquisition of high-speed biological processes after photoactivation is possible.



Imaged at video rate (30 fps) while photoactivating the target area with a 405 nm laser



Points within the cell and changes of fluorescence intensity (From the point closer to the activated point: red, blue, violet)

Optical path in the A1R+ scan head

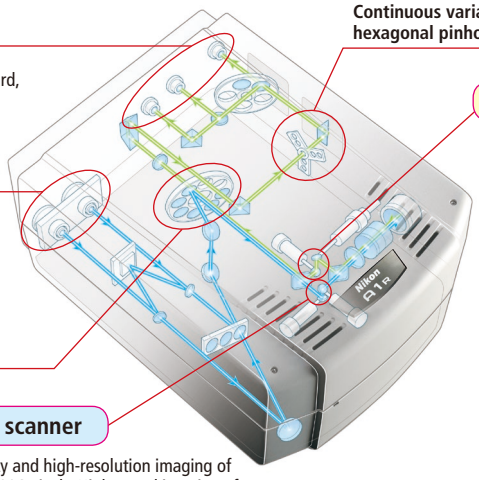
Optical output ports
The scan head has three ports for use with standard, spectral and optional detectors.

Excitation input ports
Up to seven lasers (maximum nine colors) can be loaded.

Low-angle incidence dichroic mirror

Continuous variable hexagonal pinhole

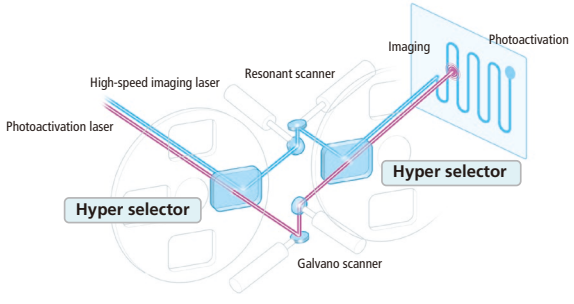
Resonant scanner
For high-speed imaging of up to 420 fps (512 x 32 pixels). During simultaneous photoactivation and imaging, the resonant scanner is used for image capture.



Galvano scanner
For High-quality and high-resolution imaging of up to 4096 x 4096 pixels. High-speed imaging of 10 fps (512 x 512 pixels) is also possible. During simultaneous photoactivation and imaging, the galvano scanner is used for photostimulation.

What is a hybrid scan head?

This mechanism allows flexible switching or simultaneous use of two scanners (resonant and galvano) with the use of a hyper selector.



Enhanced spectral detectors

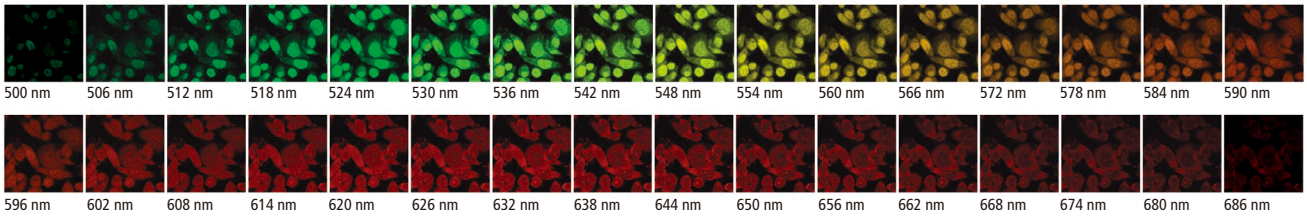
The fast 32-channel A1-DUS spectral detector unit and the newly developed high-sensitivity A1-DUVB GaAsP detector unit allow not only clean separation of overlapping spectra of fluorescent labels in multi-stained specimens but also unique a user-definable "Virtual Filter" emission filter mode.

A1-DUS spectral detector unit

The A1-DUS is a spectral detector unit with the capacity to acquire 32 channels of fluorescence spectra over a 320 nm wavelength range with a single scan. By precisely unmixing the overlapping spectra of fluorescent labels at a high wavelength resolution of at least 2.5 nm, the A1-DUS dramatically improves dynamic observations of live specimens and facilitates the acquisition of detailed data.

Fast 32-channel imaging at 24 fps

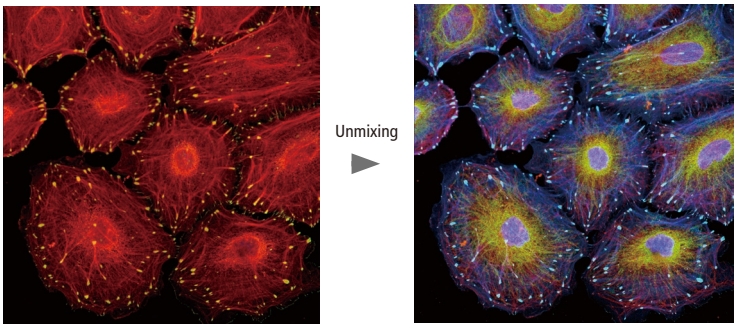
Unique signal processing technology and high-speed AD conversion circuit allow acquisition of a 32-channel spectral image (512 x 512 pixels) in 0.6 second. Moreover, acquisition of 512 x 32 pixels images at 24 frames per second is achieved.

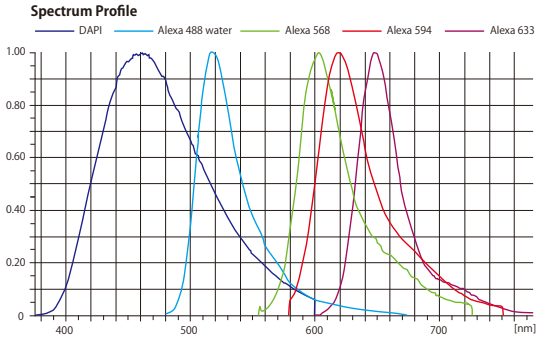


HeLa cells with DNA and RNA stained with Acridine Orange
Spectral images in the 500-692 nm range captured with 6 nm resolution using 488 nm laser excitation

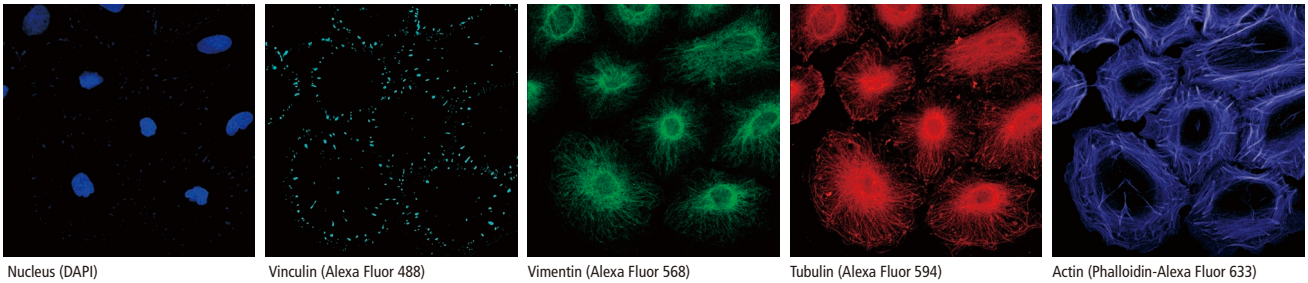
Accurate spectral unmixing

A1-DUS can acquire spectral images at a high wavelength resolution of at least 2.5 nm. Accurate spectral unmixing provides maximum performance in the separation of closely overlapping fluorescence spectra and the elimination of autofluorescence.





Spectral and unmixed images of five-color-fluorescence-labeled HeLa cells
Specimen courtesy of: Dr. Tadashi Karashima, Department of Dermatology, Kurume University School of Medicine



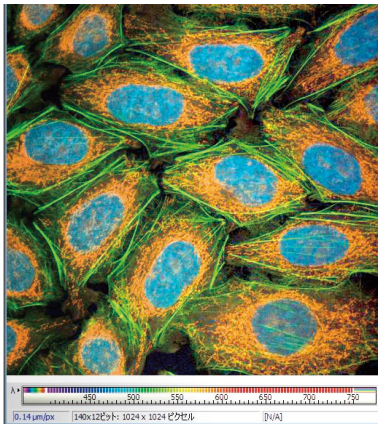
Nucleus (DAPI) | Vinculin (Alexa Fluor 488) | Vimentin (Alexa Fluor 568) | Tubulin (Alexa Fluor 594) | Actin (Phalloidin-Alexa Fluor 633)

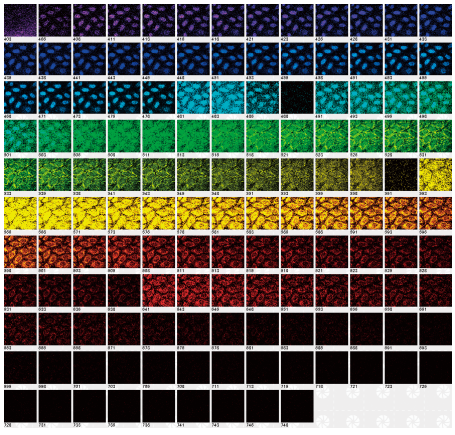
Real time unmixing

Superior algorithms and high-speed data processing enable real time unmixing during image acquisition. Unmixing processing used to be performed after spectral imaging. Real time unmixing is highly effective for FRET analysis, since probes with adjacent spectra such as CFP and YFP, GFP and YFP that were difficult to unmix in real time can be easily unmixed.

Wide band spectral imaging

Simultaneous excitation with four lasers selected from a maximum of eight wavelengths is available, enabling spectral imaging across wider bands.

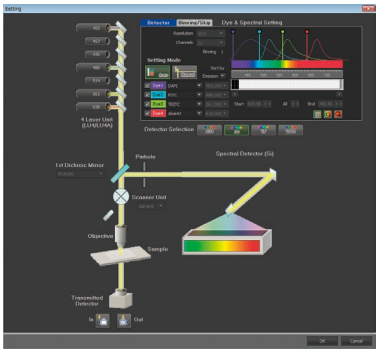


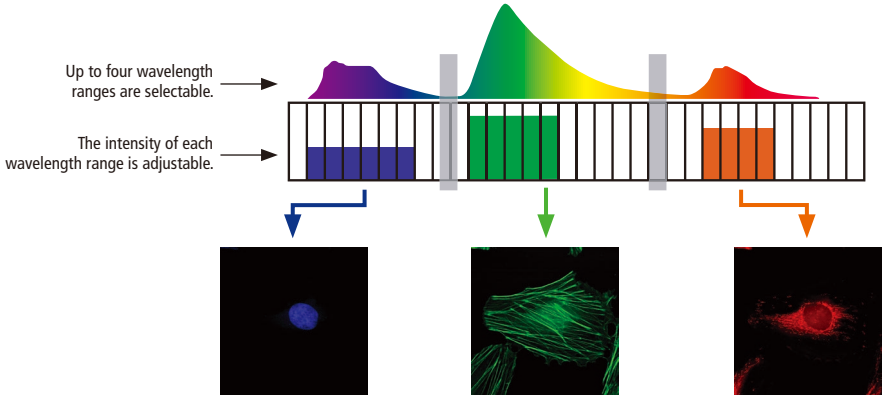


The λ scanning function of ND acquisition software allows image capturing of a wide wavelength range of up to 350 nm (140 channels) with a high wavelength resolution of 2.5 nm.

Filter-less intensity adjustment is possible with V-filtering function

Desired spectral ranges that match the spectrum of the fluorescence probe in use can be selected from 32 channels and combined to perform the filtering function. By specifying the most appropriate wavelength range, image acquisition with the optimal intensity of each probe is possible in FRET and colocalization. Up to four wavelength ranges can be simultaneously selected. The sensitivity of each range can be individually adjusted, which supports applications using various probe combinations.





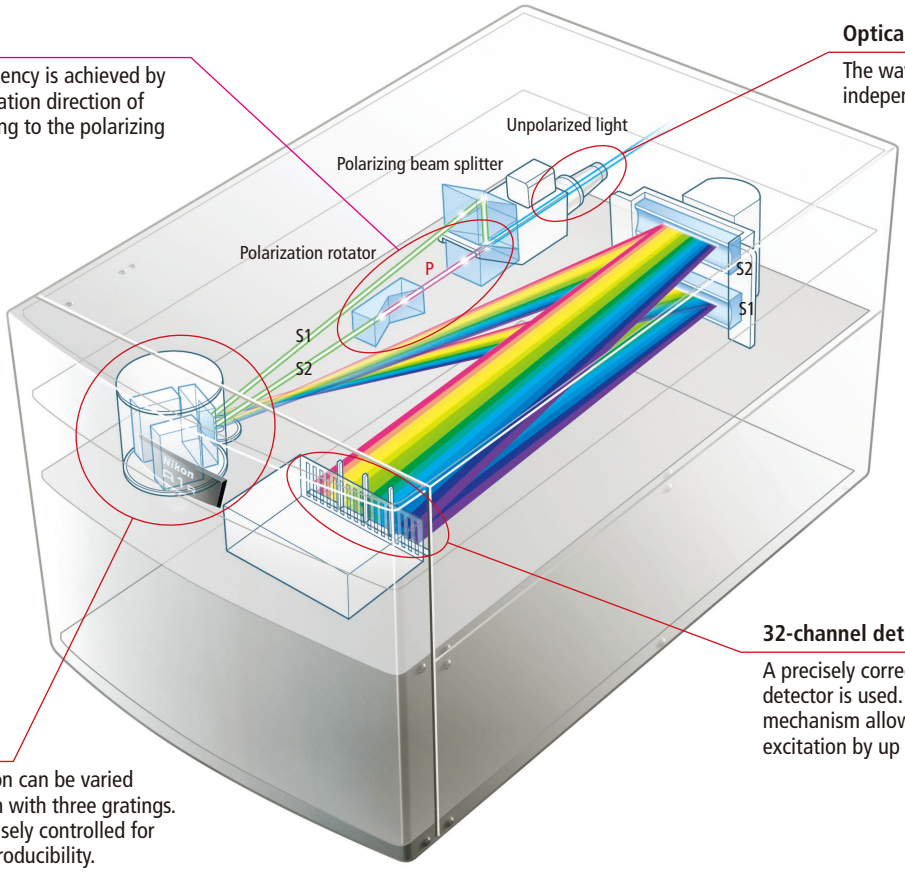
Spectrum

DEES system

High diffraction efficiency is achieved by matching the polarization direction of light entering a grating to the polarizing light beam S.

Optical fiber

The wavelength resolution is independent of pinhole diameter.



32-channel detector

A precisely corrected 32-PMT array detector is used. A three-mobile-shielding mechanism allows simultaneous excitation by up to four lasers.

Multiple gratings

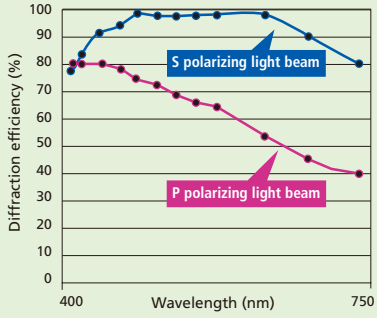
Wavelength resolution can be varied between 2.5/6/10 nm with three gratings. Each position is precisely controlled for high wavelength reproducibility.

High-quality spectral data acquisition

Diffraction Efficiency Enhancement System (DEES)

With the DEES, unpolarized fluorescence light emitted by the specimen is separated into two polarizing light beams P and S by a polarizing beam splitter. Then, P is converted by a polarization rotator into S, which has higher diffraction efficiency than P, achieving vastly increased overall diffraction efficiency.

Characteristics of grating



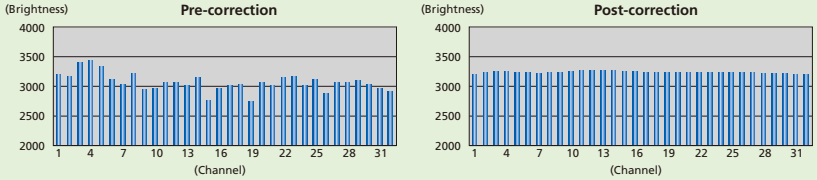
High-efficiency fluorescence transmission technology

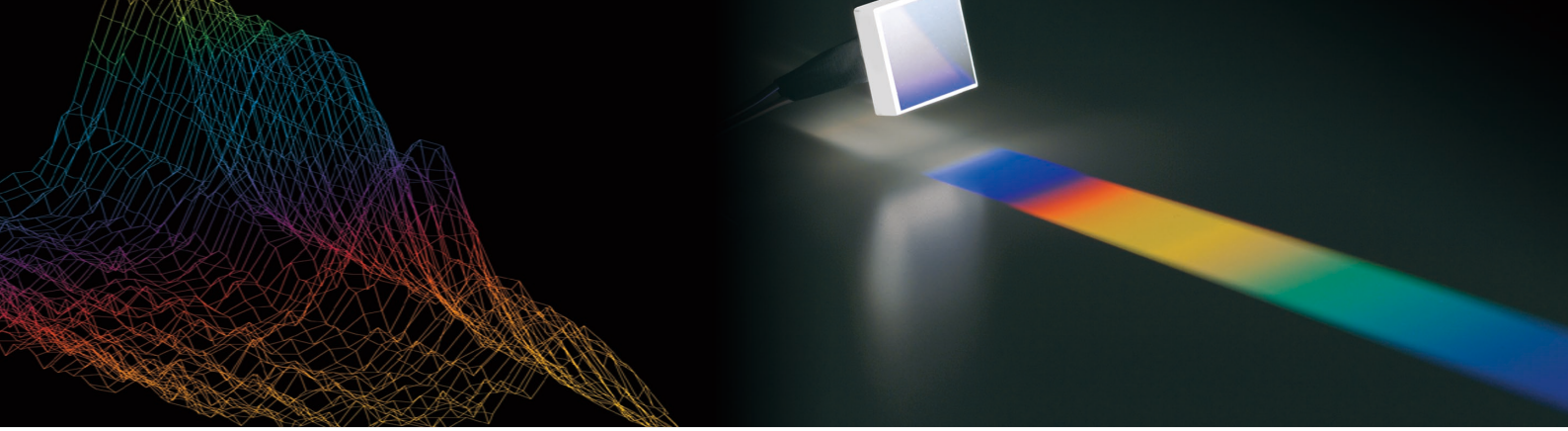
The ends of the fluorescence fibers and detector surfaces use a proprietary anti-reflective coating to reduce signal loss to a minimum, achieving high optical transmission.

Accurate, reliable spectral data: three correction techniques

Three correction techniques allow for the acquisition of accurate spectra: inter-channel sensitivity correction, which adjusts offset and sensitivity of each channel; spectral sensitivity correction, which adjusts diffraction grating spectral efficiency and detector spectral sensitivity; and correction of spectral transmission of optical devices in scan heads and microscopes.

Multi-anode PMT sensitivity correction





A1-DUVB GaAsP detector unit

The A1-DUVB is a compact fully tunable emission detector unit capable of spectral imaging with user-defined emission bandwidths, in both galvano and resonant imaging modalities.

NEW

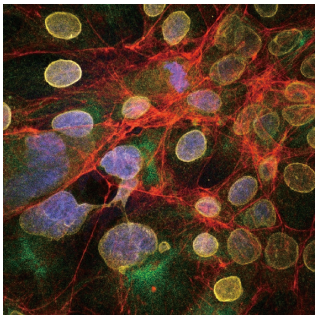
High-sensitivity spectral image acquisition

With a GaAsP PMT, the A1-DUVB tunable emission detector delivers flexible detection of fluorescent signals with higher sensitivity.

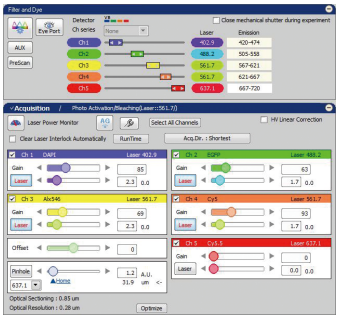
Variable acquisition wavelength range

User-defined emission bands can collect images within a selected wavelength range, replacing the need for fixed bandwidth emission filters. Users can define the emission bandwidth range to as little as 10nm. Spectral images of multi-labeled specimens can be acquired by capturing a series of spectral images while changing detection wavelengths.

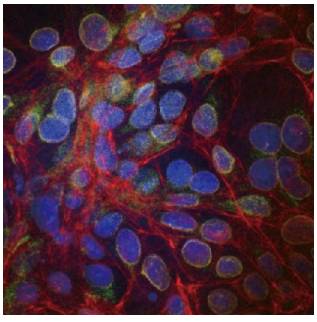
Based on the application, virtual bandpass mode and continuous bandpass modalities are selectable on the A1-DUVB.



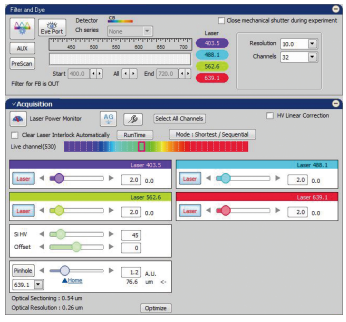
VB (Variable Bandpass) mode



VB (Variable Bandpass) mode allows maximum 5ch color image



Unmixed Image
CB (Continuous Bandpass) mode



CB (Continuous Bandpass) mode allows maximum 32 ch spectrum imaging

HeLa cells labeled with five-color fluorescence, Nucleus: DAPI, Vimentin: Alexa Fluor 488, Lamin: Alexa Fluor 568, Tubulin: Alexa Fluor 594, Actin: Alexa Fluor 633
Specimen courtesy of: Dr. Tadashi Karashima, Department of Dermatology, Kurume University School of Medicine

Optional second channel detector

An optional second GaAsP PMT provides flexibility in detection. Users can divert selected wavelengths to the second fixed bandwidth emission channel by inserting a dichroic mirror, while simultaneously utilizing the user-definable emission band on the first channel. The second detector allows FRET, ratio imaging and other applications requiring simultaneous multi-channel imaging.

Accurate spectral unmixing

Multi-channel images acquired with the A1-DUVB can be spectrally unmixed by using the spectra of reference samples, or the spectra within the acquired images.

Ease of Use

Increased flexibility and ease of use

NIS-Elements C/C-ER control software features easy operation and diverse analysis functions. Combined with a remote controller and other hardware, NIS-Elements C/C-ER provides a comprehensive operational environment.

NIS-Elements C

Detailed operability based on the analysis of every possible confocal microscope operation pattern ensures an intuitive interface and operation, satisfying both beginners and experienced confocal users. By taking advantage of the hybrid scanner, the software enables a complicated sequence of experiments such as photoactivation to be carried out with simple-to-use settings.

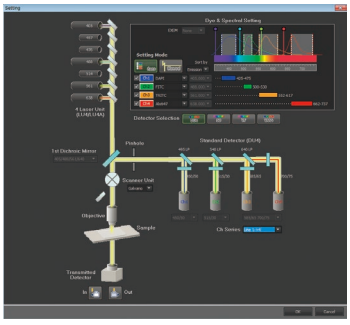
Simple image acquisition

• Basic operation

Parameters for basic image acquisition are integrated in a single window, allowing simple image acquisition.

• Optical setting

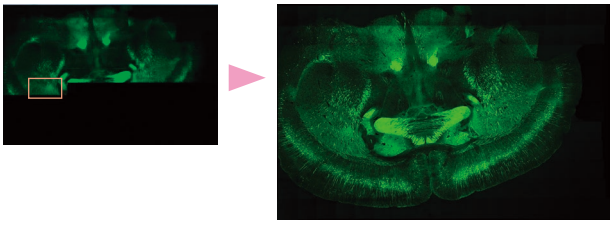
By simply selecting a fluorescence probe, an appropriate filter and laser wavelength are set automatically. Microscope setup is also conducted automatically.



Diverse application

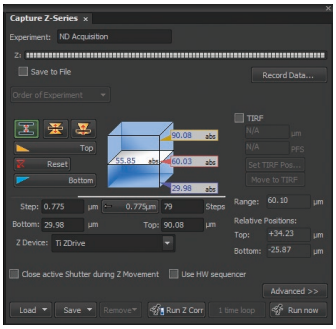
• Large imaging (image tiling)

Images of adjacent fields that are continuously captured with the motorized stage are automatically stitched to produce a whole high-resolution image of the tissue.



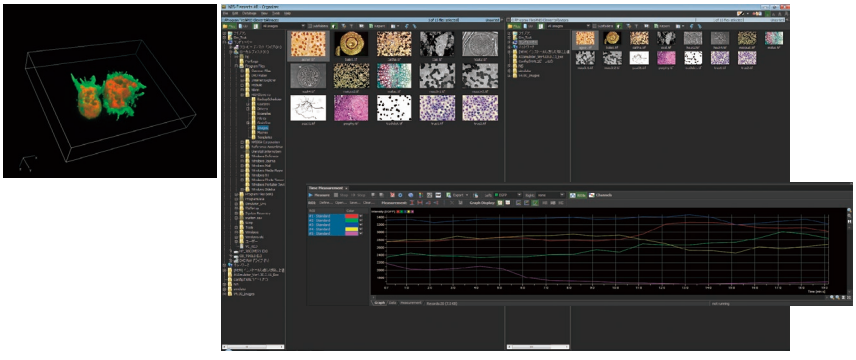
• Multidimensional image acquisition

Acquisition of images with a free combination of multidimensional parameters including X, Y, Z, t, λ (wavelength), and multipoint is possible.



Reliable analysis functions

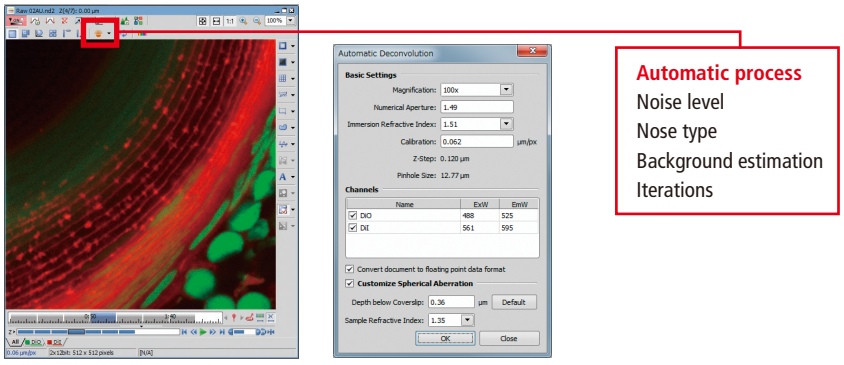
- Real-time ratio display
- Deconvolution
- High-speed 3D rendering
- Multidimensional image display (nD Viewer)
- Synchronized display of multidimensional images (View synchronizer)
- Diverse measurement and statistical processing
- Powerful image database function
- Colocalization and FRET



NIS-Elements C-ER

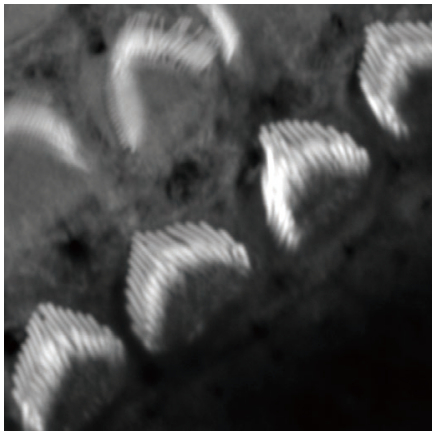
Automatic enhanced resolution imaging

Higher resolution confocal images can be generated with a single click using the NIS-Elements C-ER package. The software assesses the captured image and automatically determines processing parameters to achieve enhanced resolution without sacrificing high imaging operability. In addition, the resolution of previously captured confocal images can be improved using pre-processing technology.

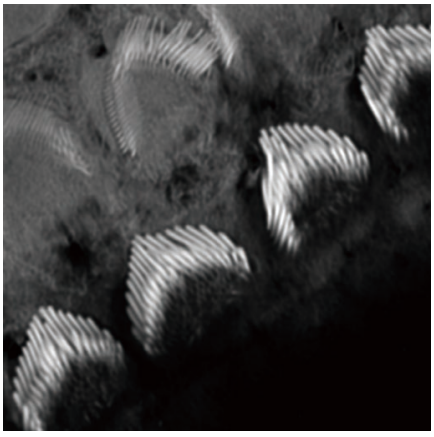


Automatic process
Noise level
Nose type
Background estimation
Iterations

Confocal microscopes potentially possess the capability of acquiring images at a higher resolution than the theoretical limit of resolution for an optical microscope of 200 nm, but this has not been effectively achieved. With newly-developed image processing technology, the NIS-Elements C-ER package enables an increase in image resolution beyond that of a conventional confocal image (resolution can be improved 1.5 times (XY), 1.7 times (Z)).



Conventional confocal microscope image



NIS-Elements C-ER processed image

Apical surfaces of auditory epithelia of mouse cochleae were stained by Atto-565-phalloidin at postnatal day 2.
Photographed with the cooperation of: Dr. Hideru Togashi, Division of Molecular and Cellular Biology, Department of Biochemistry and Molecular Biology, Kobe University Graduate School of Medicine.

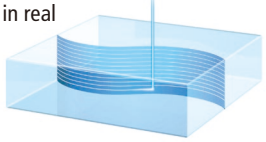
User-friendly hardware

Exchangeable fluorescence filters

The 4-channel detector is provided as standard, enabling simultaneous four-color imaging. Up to six filter cubes commonly used for microscopes can be mounted on each filter wheel and are easily changeable.

Spline Z scans

High-speed image acquisition in the Z direction is possible. By using the piezo-motorized Z stage, an arbitrary vertical cross-sectional view can be achieved in real time without acquiring a 3D image.



Easy setting operation

The remote controller provides simple button or dial operation of laser, detector, and scanner settings.

Laser units with great flexibility and efficiency

The two laser unit series are compatible with A1+/A1R+. The LU-NV series supports up to eight wavelengths and switching of seven fiber outputs. The LU-N4/LU-N4S/LU-N3 comes with pre-installed lasers, and achieves both high efficiency and simple set-up.

LU-NV series

Multiple laser light sources can be mounted to the laser units, and up to eight wavelengths are available. Output through up to seven fibers is possible. Switching them allows a single laser unit to support a microscope system that combines multiple laser applications, such as the A1+/A1R+ confocal microscope, TIRF, photoactivation, and N-SIM/N-STORM super resolution microscope.

- Lasers available for this series are: 405 nm, 445 nm, 458 nm, 488 nm, 514 nm, 532 nm, 561 nm, 594 nm, 640 nm and 647 nm.
- High-power lasers for the N-SIM/N-STORM super resolution microscope and confocal microscopes are available.
- Lasers can be individually turned on and off, boosting their efficiency.
- The optical axis of each laser is adjusted at the time of shipping, making the system easy to set up.
- The monolithic laser combiner prevents alignment shift even after long-term use.
- The AOTF allows laser power to be controlled and modulated.

LU-NV Laser Unit with LU Controller Box B (top)

LU-N4/N4S 4-laser unit/LU-N3 3-laser unit

The LU-N4/LU-N4S is equipped with four lasers (405 nm, 488 nm, 561 nm, and 640 nm), while the LU-N3 has three lasers (405 nm, 488 nm, and 561 nm). The LU-N4S is compatible with spectral imaging.

- Lasers can be individually turned on and off, boosting their efficiency.
- The optical axis of each laser is adjusted at the time of shipping, making the system easy to set up.
- The monolithic laser combiner prevents alignment shift even after long-term use.
- The AOTF allows laser power to be controlled and modulated.

LU-N4/N4S/N3 Laser Unit

High-performance objectives for confocal imaging

High-NA objectives have been developed that highly correct chromatic aberrations over a wide wavelength range, from ultraviolet to infrared. Transmission is increased through the use of Nikon's exclusive Nano Crystal Coat technology. CFI Apochromat λS series objectives provide chromatic aberration correction over a wide wavelength ranging from 405 nm and are powerful enough for multicolor imaging. In particular, LWD 40xWI λS has an extremely wide chromatic aberration correction range of 405 nm to near-IR. The high NA, long working distance CFI75 Apochromat 25xW MP also corrects up to near-IR. The CFI Plan Apochromat IR 60xWI corrects chromatic aberration up to 1,064 nm and accommodates laser tweezers.


CFI 75 Apochromat 25xW MP


CFI Apochromat LWD 20xWI λS


CFI Apochromat 40xWI λS

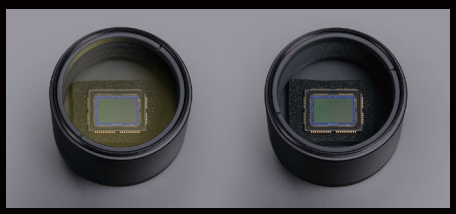

CFI Apochromat LWD 40xWI λS

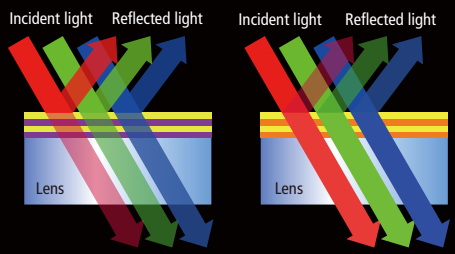

CFI Apochromat 60x oil λS


CFI Plan Apochromat IR 60xWI

Nano Crystal Coat technology

With its origins in Nikon's semiconductor manufacturing technology, Nano Crystal Coat is an anti-reflective coating that assimilates ultra-fine crystallized particles of nanometer size. With particles arranged in a spongy construction with uniform spaces between them, this coarse structure enables lower refractive indices, facilitating the passage of light through the lens. These crystallized particles eliminate reflections inside the lens throughout the spectrum of visible light waves in ways that far exceed the limits of conventional anti-reflective coating systems.


Conventional multi-layer coating　　Nano Crystal Coat



Conventional multi-layer coating　　Nano Crystal Coat

Recommended objective lenses

CFI Plan Apochromat λ 10x	NA 0.45, W.D. 4.00 mm	N
CFI Plan Apochromat VC 20x	NA 0.75, W.D. 1.00 mm	
CFI Apochromat LWD 20xWI λS	NA 0.95, W.D. 0.95 mm	N
CFI 75 Apochromat 25xW MP	NA 1.10, WD 2.00 mm	N
CFI Plan Apochromat λ 40x	NA 0.95, W.D. 0.21 mm	N
CFI Apochromat 40xWI λS	NA 1.25, W.D. 0.18 mm	N
CFI Apochromat LWD 40xWI λS	NA 1.15, W.D. 0.60 mm	N
CFI Apochromat 60x oil λS	NA 1.40, W.D. 0.14 mm	N
CFI Plan Apochromat VC 60xWI	NA 1.20, W.D. 0.29 mm	
CFI Apochromat TIRF 60x oil	NA 1.49, W.D. 0.12 mm	
CFI Plan Apochromat IR 60xWI	NA 1.27, W.D. 0.17 mm	N
CFI Apochromat TIRF 100x oil	NA 1.49, W.D. 0.12 mm	

N : Nano Crystal Coat-deposited


CFI Plan Apochromat λ 10x


CFI Plan Apochromat VC 20x

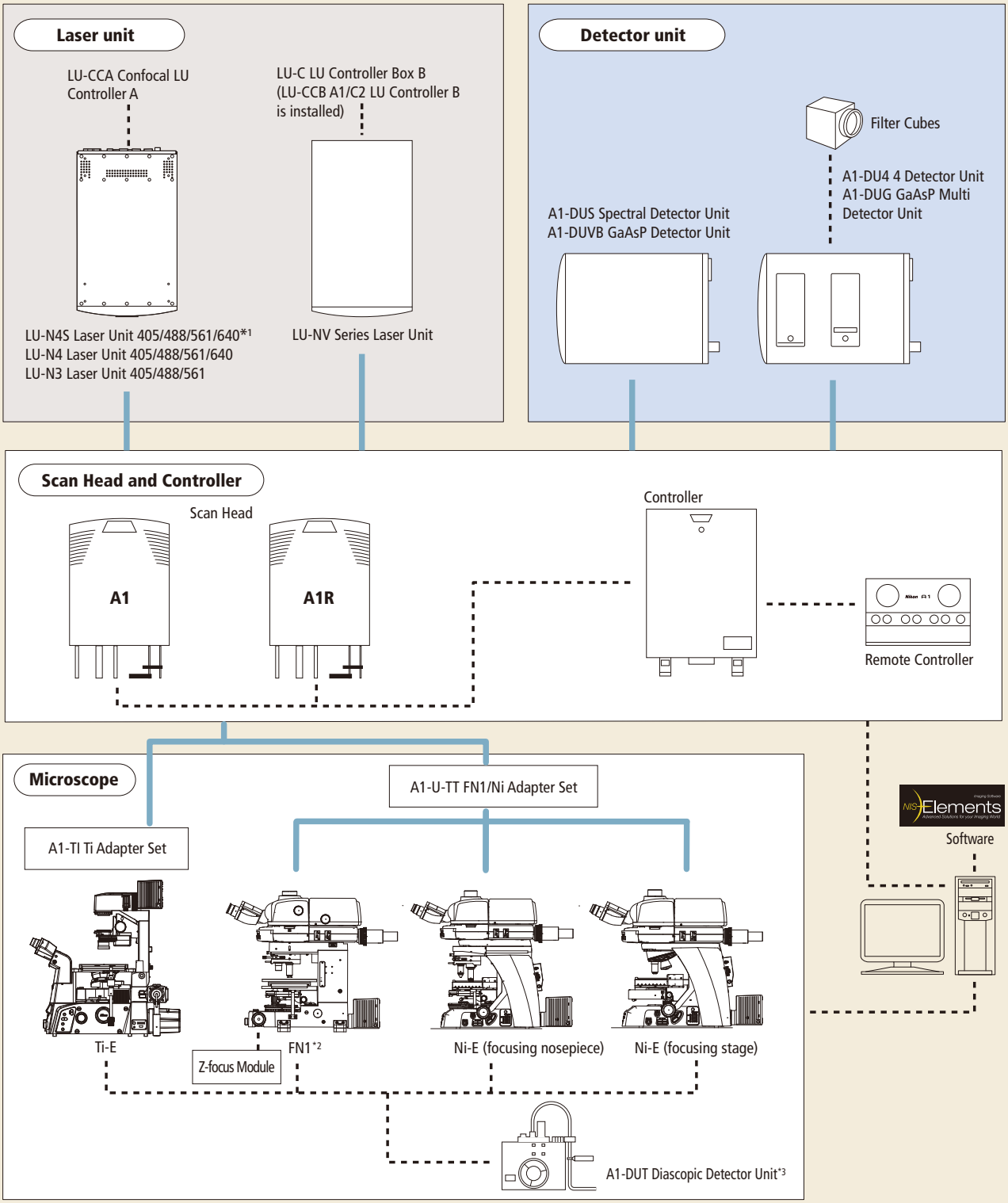

CFI Plan Apochromat λ 40x


CFI Plan Apochromat VC 60xWI


CFI Apochromat TIRF 60x oil

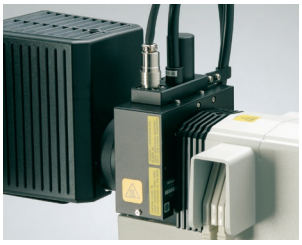

CFI Apochromat TIRF 100x oil

System diagram



*1 When using Spectral Detector Unit. *2 NI-TT Quadrocular Tilting Tube can be used. *3 Dedicated adapter may be required, depending on microscope model.

4 Detector Unit/GaAsP Multi Detector Unit



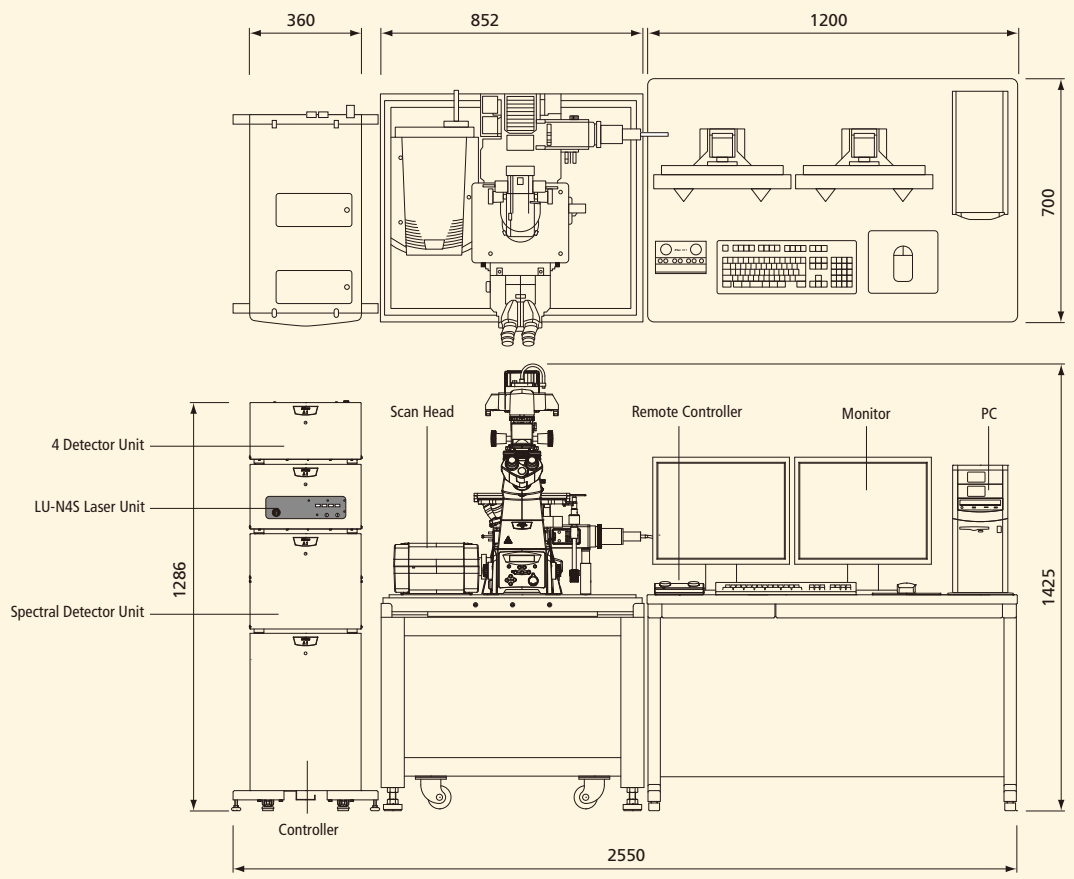
Diascopic Detector Unit

Specifications

		A1+	A1R+
Scan head input/output port		2 laser input ports 3 signal output ports for standard, spectral and optional detector*1	
Laser	LU-N3 3-laser unit	405 nm, 488 nm, 561nm lasers are installed; built-in AOTF *Cannot be used with A1-DUS spectral detector	
	LU-N4/N4S 4-laser unit	405 nm, 488 nm, 561 nm,640 nm lasers are installed; built-in AOTF *Use LU-N4S when using A1-DUS spectral detector	
	LU-NV series laser unit	Compatible lasers : 405 nm, 445 nm, 458 nm, 488 nm, 514 nm, 532 nm, 561 nm, 594 nm, 640 nm, 647 nm ; built-in AOTF	
Standard fluorescence detector	Wavelength	400-750 nm	
	Detector	A1-DU4 4 Detector Unit: 4 normal PMTs A1-DUG GaAsP Multi Detector Unit: 2 GaAsP PMTs + 2 normal PMTs	
	Filter cube	6 filter cubes commonly used for a microscope mountable on each of three filter wheels Recommended wavelengths: 450/50, 482/35, 515/30, 525/50, 540/30, 550/49, 585/65, 595/50, 700/75	
Diascopic detector (option)	Wavelength	485-650 nm	
	Detector	PMT	
FOV		Square inscribed in a ø18 mm circle	
Image bit depth		4096 gray intensity levels (12 bit)	
Scan head	Standard image acquisition	Scanner: galvano scanner x2 Pixel size: max. 4096 x 4096 pixels Scanning speed: Standard mode: 2 fps (512 x 512 pixels, bi-direction), 24 fps (512 x 32 pixels, bi-direction) Fast mode: 10 fps (512 x 512 pixels, bi-direction), 130 fps (512 x 32 pixels, bi-direction)*2 Zoom: 1-1000x continuously variable Scanning mode: X-Y, X-T, X-Z, XY rotation, Free line	
	High-speed image acquisition	—	Scanner: resonant scanner (X-axis, resonance frequency 7.8 kHz), galvano scanner (Y-axis) Pixel size: max. 512 x 512 pixels Scanning speed: 30 fps (512 x 512 pixels) to 420 fps (512 x 32 pixels), 15,600 lines/sec (line speed) Zoom: 7 steps (1x, 1.5x, 2x, 3x, 4x, 6x, 8x) Scanning mode: X-Y, X-T, X-Z Acquisition method: Standard image acquisition, High-speed image acquisition, Simultaneous photoactivation and image acquisition
	Dichroic mirror	Low-angle incidence method, Number of positions: 8 Standard filter: 405/488, 405/488/561, 405/488/561/638, 405/488/543/638, 457/514, BS20/80 Optional filter: 457/514/561	
	Pinhole	12-256 µm variable (1st image plane)	
Spectral detector (option)	A1-DUS spectral detector unit	Number of channels: 32 Wavelength detection range: 400 - 750 nm Spectral image acquisition speed: 4 fps (256 x 256 pixels) Maximum pixel size: 2048 x 2048 (Spectral mode/Virtual filter mode) Wavelength resolution: 2.5/6.0/10.0 nm, wavelength range variable in 0.25 nm steps Compatible with galvano scanner only	
	A1-DUVB GaAsP detector unit	Number of channels: 1 GaAsP PMT with variable emission plus 1 optional GaAsP PMT (A1-DUVB-OP) with a user-defined dichroic mirror and barrier filter Wavelength detection range: 400 - 720 nm, narrowest: 10 nm, broadest:320 nm Maximum pixel size: 4096 x 4096 (CB mode/VB mode) Wavelength resolution: 10 nm, wavelength range variable in 1 nm steps Compatible with galvano and resonant scanners	
Z step		Ti-E: 0.025 µm, FN1 stepping motor: 0.05 µm Ni-E: 0.025 µm	
Compatible microscopes		ECLIPSE Ti-E inverted microscope, ECLIPSE FN1 fixed stage microscope, ECLIPSE Ni-E upright microscope (focusing nosepiece type and focusing stage type)	
Option		Motorized XY stage (for Ti-E/Ni-E), High-speed Z stage (for Ti-E), High-speed piezo objective-positioning system (for FN1/Ni-E)	
Software	Display/image generation	2D analysis, 3D volume rendering/orthogonal, 4D analysis, spectral unmixing	
	Image format	JP2, JPG, TIFF, BMP, GIF, PNG, ND2, JFF, JTF, AVI, ICS/IDS	
	Application	FRAP, FLIP, FRET(option), photoactivation, three-dimensional time-lapse imaging, multipoint time-lapse imaging, colocalization	
Control computer	OS	Microsoft Windows® 7 Professional 64bits SP1	
	CPU	Intel Xeon E5-2643v3 (3.40 GHz/20 MB) or higher	
	Memory	16 GB or higher	
	Hard disk	300 GB SAS (15,000 rpm) x2, RAID 0 configuration	
	Data transfer	Dedicated data transfer I/F	
	Network interface	Gigabit Ethernet x2	
	Monitor	1600 x 1200 or higher resolution, dual monitor configuration recommended	
Recommended installation conditions		Temperature 23 ± 5 ºC, humidity 70 % (RH) or less (non-condensing)	

*1 FCS/FCCS/FLIM is possible in combination with third-party systems
*2 Fast mode is compatible with zoom 8-1000x and scanning modes X-Y and X-T. It is not compatible with Rotation, Free line, CROP, ROI, Spectral imaging, Stimulation and FLIM.

Layout



* Layout sample

Dimensions and weight

Scan Head	276(W) x 163(H) x 364(D) mm	Approx. 10 kg
Controller	360(W) x 580(H) x 600(D) mm	Approx. 40 kg
A1-DU4 4 Detector Unit	360(W) x 199(H) x 593.5(D) mm	Approx. 16 kg
A1-DUG GaAsP Multi Detector Unit	360(W) x 199(H) x 593.5(D) mm	Approx. 16 kg
A1-DUS Spectral Detector Unit	360(W) x 323(H) x 593.5(D) mm	Approx. 26 kg
A1-DUVB GaAsP Detector Unit	360(W) x 91(H) x 595.5(D) mm	Approx. 9 kg
LU-N4/N4S/N3 Laser Unit	360(W) x 210(H) x 593.5(D) mm	Approx. 16 kg
LU-NV Laser Unit	400(W) x 781(H) x 685(D) mm	Approx. 70 kg
LU Controller Box B (for LU-NV)	400(W) x 123(H) x 687(D) mm	Approx. 7 kg

Power source

A1$^+$/A1R$^+$ System	Scan Head and Controller	Input 100-240V ± 10%, 50-60Hz, 5A-2A
	Computer Unit	Input 100-240V ± 10%, 50-60Hz, 12A-10A
Laser Unit	LU-N4/LU-N4S/LU-N3	Input 100-240V ± 10%, 50-60Hz, 2A max.
	LU-NV Series	Input 100-240V ± 10%, 50-60Hz, 4.8A max.
	LU Controller Box B (for LU-NV)	Input 100-240V ± 10%, 50-60Hz, 1A max.
Microscope	Inverted Microscope Ti-E with HUB-A and HG Fiber Illuminator Intensilight	Input 100-240V ± 10%, 50-60Hz, 5.7A max.

Note: When an air compressor is used with a vibration isolated table, an additional power source is necessary.

Diverse peripherals and systems for pursuit of live cell imaging

A1+ with N-SIM, A1+ with N-STORM and A1+ with TIRF

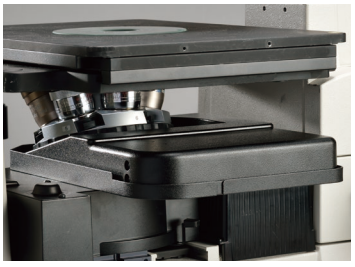
A1+/A1R+ can be equipped with the TIRF system and super resolution microscope systems N-SIM, N-STORM on a single inverted microscope and all controlled from Nikon's integrated software. This meets the demands of multi-perspective cellular analysis.
N-SIM provides super resolution of approximately double that of conventional microscopes, while N-STORM provides approximately 10 times higher super resolution. TIRF enables visualization of ultra-thin optical specimen sections of approximately 100 nm, enabling the observation of single molecules.

Configured with N-SIM, N-STORM and confocal microscope A1+

Confocal microscope with Perfect Focus System

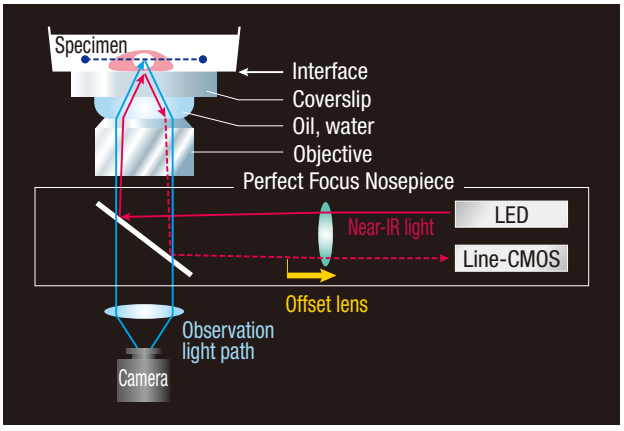
With the inverted microscopes Ti-E, an automatic focus maintenance mechanism—Perfect Focus System (PFS) can be used. It continuously corrects focus drift during long time-lapse observation and when reagents are added.

*Use with glass bottom dish is recommended.



Perfect Focus Unit with motorized nosepiece

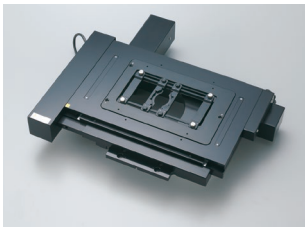
Concept of the Perfect Focus System



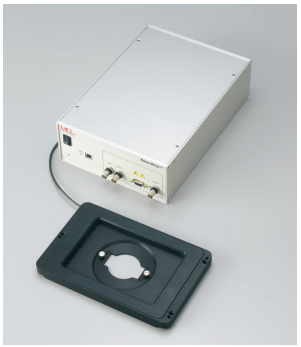
The diagram shows the case when an immersion type objective is used.
A dry type objective is also available.

Motorized stages

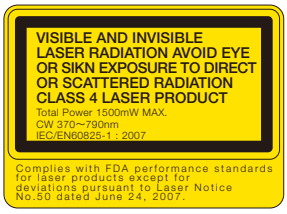
The motorized stages make multipoint observation easy. It allows multipoint XYt (4D), multipoint XYZ (4D), multipoint XYZt (5D) and multipoint XYZt (6D, including spectral information) observations. By using the standard motorized stage or motorized XY stage equipped with a linear encoder with enhanced positioning repeatability in combination with the optional motorized piezo Z stage with high-speed Z-direction scanning capability, high-speed line Z scans are possible.



Standard motorized XY stage



Motorized Piezo Z stage



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