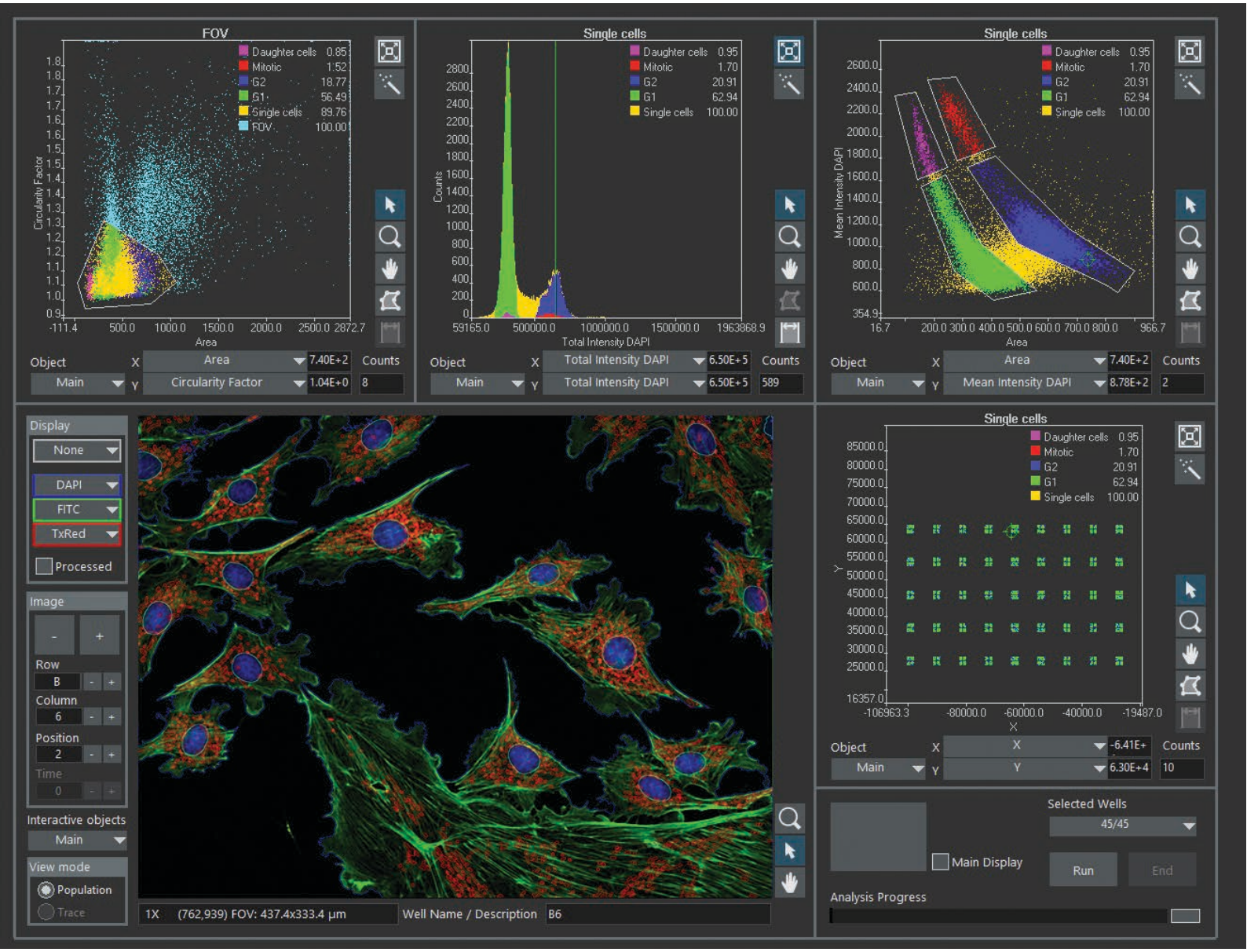
EVIDENT

High-Content Screening Station

scanR

Automated Image Acquisition and Data Analysis with Deep-Learning Technology



Much More Than Just High-Content Screening

Flexible, Modular, and Robust Hardware

The scanR screening station combines the modularity and flexibility of a microscope-based setup with the automation, speed, throughput, and reproducibility needed for high-content screening applications. The system is designed for a range of applications, including standard assays and assay development, and its modularity makes the scanR station adaptable for R&D lab applications and multiuser environments.

The scanR system features sophisticated image-analysis and data-analysis software that uses an interactive, cytometry-oriented workflow, enabling it to analyze large numbers of multidimensional data sets.

Versatile

Get the benefits of a high-content screening station and high-end research microscope in one system

Live Cell Solution

Seamless environmental control, reliable drift compensation, and analysis of kinetic parameters

Spinning Disk Confocal System

Acquire high-resolution, high-contrast images using the scanR system with the Olympus IXplore SpinSR super resolution microscope, including the Yokogawa CSU-W1 scanner unit. Micro-lens-based disks and laser excitation provide seamless confocal image quality at high speed.

Robot Loading System Setup

For automated high-throughput screening, the scanR system can be combined with a plate-loading robot system.

Incubation System Setup

Combining the scanR high-content screening solution with an incubation system provides strict temperature, humidity, and CO_2 level control.

TIRF and FRAP System Setup with cellSens Software

The scanR platform is compatible with the Olympus IXplore family of microscopes, which, combined with cellSens software, enables users to perform advanced imaging experiments such as TIRF and FRAP.

Comprehensive Life Science Solution

Designed for fully automated image acquisition and data analysis, the scanR solution accommodates multiwell plates, slides, and custom-built arrays. The system can handle fixed and live cells, and the screening station specifically targets the requirements for quantitative imaging and image analysis in modern cell biology, molecular biology, systems biology, and medical research.

Acquisition

High-speed and high-throughput acquisition with advanced imaging and sample flexibility

Workflow

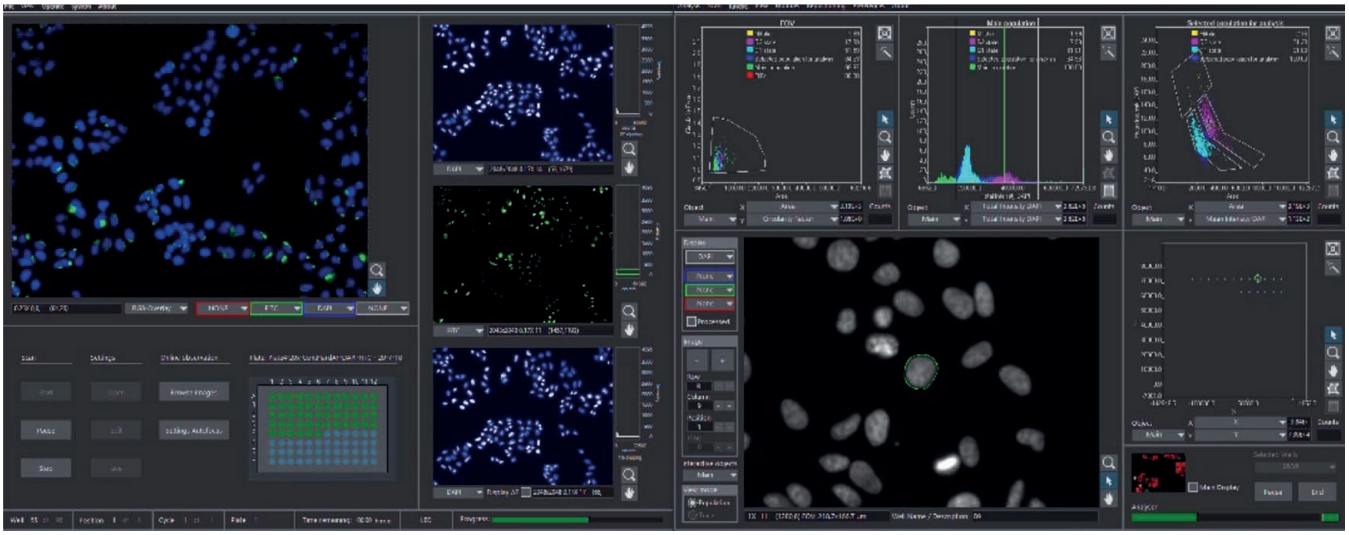
Full automation, from image acquisition to results, with online analysis

Analysis

Unique cytometric data analysis, gating, and classification using data-linked scatter plots and histograms

Set Up Your Analysis During Acquisition

Most of the analysis features are available on the fly during acquisition. This enables users to perform immediate quality control during long screening experiments and generate statistics of thousands of cells in just a few seconds.



Designed for workflow: scanR offers image acquisition and image analysis in parallel

Examples of Cellular Screening Assays

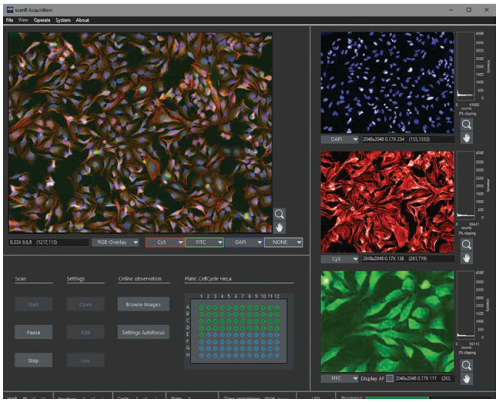
- Cell counting
- Gene expression
- Intracellular transport
- Translocation
- Cell proliferation
- Promyelocytic leukemia (PML) body assay
- Bacterial and viral infection assays
- Cell-cycle analysis
- Cell-array screens
- Multicolor assays
- Rare-event analysis
- Automated-FISH analysis
- Fluorescence analysis in tissue sections
- Live-cell assays including kinetic analysis and gating on resulting response curves
- Micronuclei and comet assays
- Cell migration
- Protein localization and colocalization

Advanced Acquisition

Incorporating Olympus' high-end IX83 inverted microscope, the scanR system has the flexibility to handle all standard assay formats, including microwell plates and slides, and can be configured to accept custom designs, such as spotted arrays or biochips.

Clear Guidance

The software's workflow is easy to use, enabling reliable image acquisition and straightforward system configuration. The system delivers accurate, repeatable quantitative measurements to address the needs of scientific screening and assay development.



Layout of acquisition software

Reduced Phototoxicity

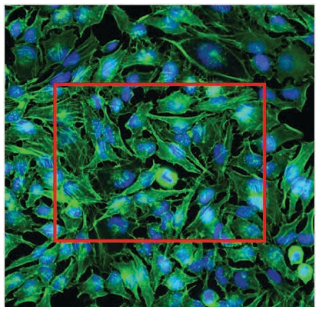
The real-time controller (U-RTCE) synchronizes the laser and camera with microsecond illumination accuracy to reduce photobleaching and phototoxicity, helping cells remain healthy during complex experiments.

Optimized for X Line Objectives

Outstanding image quality is a fundamental requirement for quantification. The scanR system supports Olympus X Line objectives to deliver broad chromatic aberration correction, uniform images, and a high numerical aperture (NA).

Large Field of View

The scanR camera's high-performance image sensor and optimized fluorescence illuminator offer a wide field of view to capture more of the sample with each image, significantly decreasing screening time.



Equipped with a large image sensor, the Hamamatsu Orca Flash 4.0 camera significantly increases the acquired field of view

Maintain Your Focus

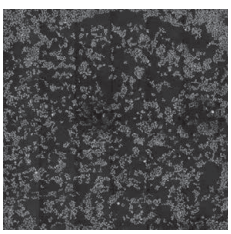
Fast and accurate autofocus is crucial for successful automated image acquisition. Throughout the automated image acquisition, the scanR system maintains the focus plane using a combination of software algorithms and hardware, including TruFocus.

More Dimensions

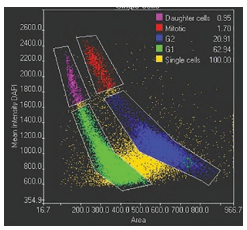
The system's advanced features enable truly multidimensional (X, Y, Z, t, l) screening. Time-lapse Z-stack images can be recorded at numerous locations on microwell plates, slides, or custom formats, using all available observation methods (fluorescence, brightfield, differential interference contrast (DIC), and phase contrast).

Multilevel Acquisition

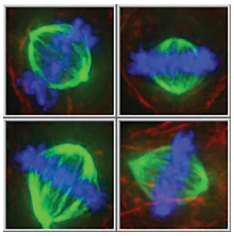
Based on an initial prescan, the scanR analysis software can identify all the potential objects of interest. In an automated workflow, the analysis results are used to selectively scan the objects of interest in a second, targeted screen. This multilevel acquisition is especially beneficial for single-cell events or high-resolution imaging of large-area samples with few cells.



Low-resolution scan covering a large area



Automated target identification



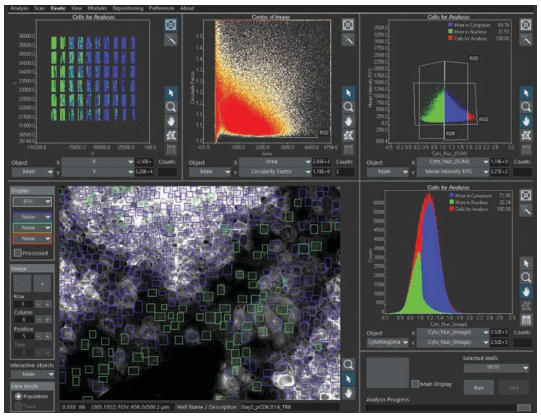
High-resolution acquisition

Powerful Data Visualization and Quantitative Analysis

The large amount of data you can collect from your assays necessitates coherent and careful automated quantitative analysis. Analysis can be performed online during acquisition, when the system is connected to a local network, or offline on previously acquired datasets.

Analyzing Data

Analytical techniques can be as simple as counting cells on display or as complex as ratiometric feature-based analysis of multilabeled objects and subobjects in different cell types or cell compartments. Image analysis is carried out as a logical multistep procedure consisting of image processing, object detection, feature extraction, and data analysis using gating and classification.



Layout of analysis software

Image Processing

Before nuclei, cytoplasm, and other subcellular objects are contoured, the raw images are preprocessed, if necessary. For example, adaptive size background correction or calibration-based shading correction is used to automatically and rigorously remove heterogeneous background and shading while retaining the relevant intensity information. Spectral unmixing can effectively remove potential bleed-through of different fluorophores.

Object Detection and Analysis

Powerful object detection modules are optimized to segment nuclei, cells, or other structures. Several detection algorithms can be selected and adapted to the objects of interest. Based on the segmentation results, features to be extracted can be selected from a list of over 100 object parameters. Additional mathematical operations can be performed on the parameters. Owing to this highly flexible data output, the scanR system can facilitate a wide range of cell-based assays.

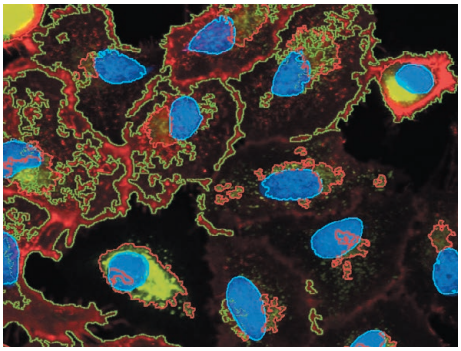
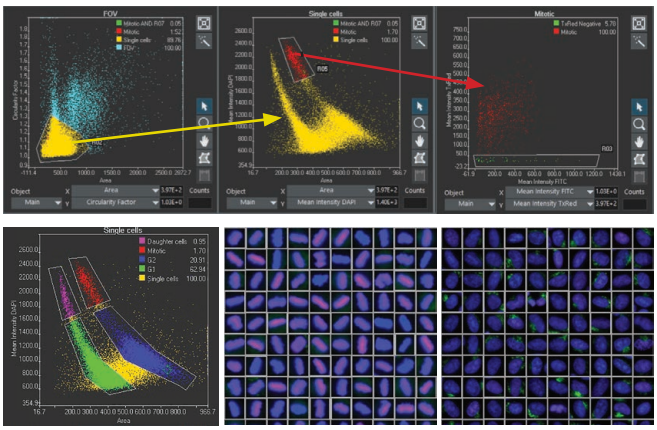


Image screenshot detail following data acquisition by scanR demonstrating the detection and separation of labels (courtesy of Dr. R. Pepperkok, EMBL Heidelberg, Germany)

Gating and Classification

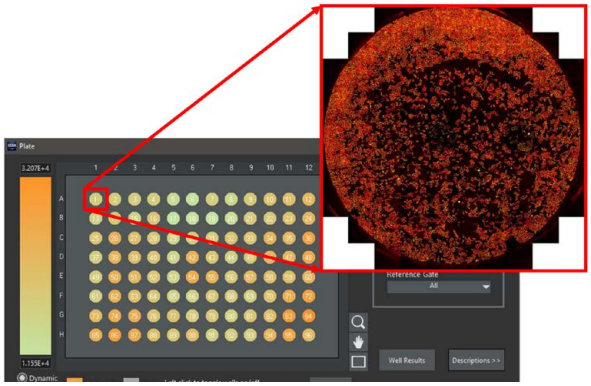
The scanR system adapts the powerful data analysis approach used in cytometry to suit the specific demands of large-image dataset analysis. Multidimensional image data are displayed in two-dimensional scatter plots or one-dimensional histograms, from which clustered data populations of interest can be selected using graphical tools. Gates from different plots can be combined with Boolean operators to create complex classification schemes—for example, gated objects can be rescanned to perform automated rare-event analyses.



A hierarchical gating approach enables intuitive selection of populations, which may also be visualized in galleries

Immediate Quality Control

Images and objects are reciprocally linked to their related data points. Clicking on a data point loads the relevant image in the display window and highlights the object in question. Clicking on an object in the image display window highlights the related data points in the scatter plots and histograms. A gallery view of all the images of a selected or gated data population can also be created to enable a direct and visual comparison of larger image sets with relevant information.



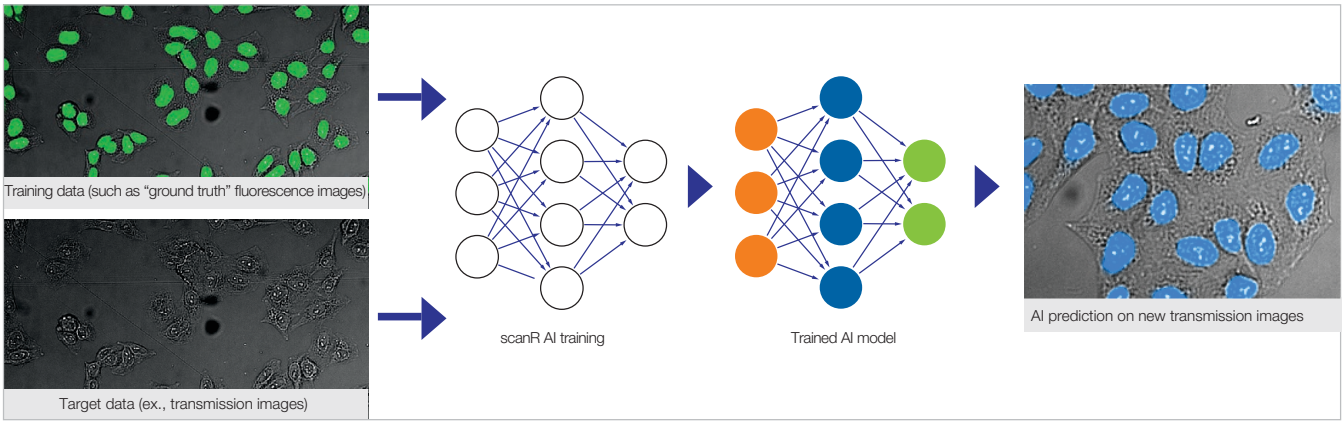
Results are visualized in heatmaps or exported to tables; displaying an overview of full wells is simple

scanR AI—The Power of Deep Learning

Olympus' self-learning microscopy technology makes it possible to establish assays with groundbreaking analysis capabilities. The powerful learning capacity of scanR AI reduces photobleaching and improves acquisition speed, measurement sensitivity, and accuracy, facilitating longer observations with reduced influence on cell viability. What until recently seemed impossible to perform is now feasible with deep learning.

Self-Learning Microscopy

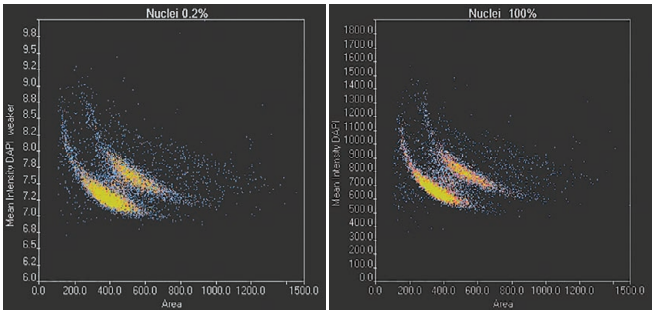
The system's fully automated and integrated workflow acquires pairs of images for example data, which the software processes to generate an image analysis model. Olympus' optimized deep-learning technology, which is based on a dedicated convolutional neural network architecture, provides powerful and flexible learned analysis protocols. No human data annotations are required throughout the training phase, making it easy to use a large number of examples, so you can fully exploit the deep-learning technology's potential.



Example workflow using self-learning microscopy to generate an AI model for label-free analysis of challenging brightfield images; the cell nuclei of Hela cells are GFP-labeled for the training phase to show the system how to analyze the brightfield images

Analyzing Your Data

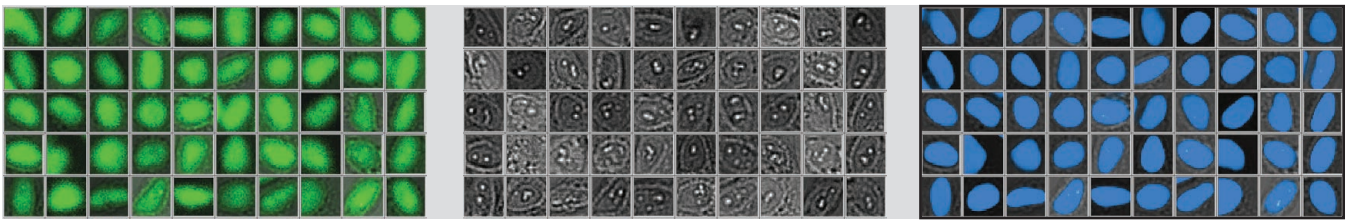
After a one-time training phase, scanR AI enables the system to automatically analyze new data by incorporating the learned analysis protocol into its assay-based workflow. Because the user has full control in designing the training experiment and many challenging analysis conditions can be covered during the training phase, the accuracy and robustness of the analysis results are improved. The learned AI analysis protocol can be validated in depth and with ease with the software's unique data exploration and analysis interface, so you can be confident in the AI results.



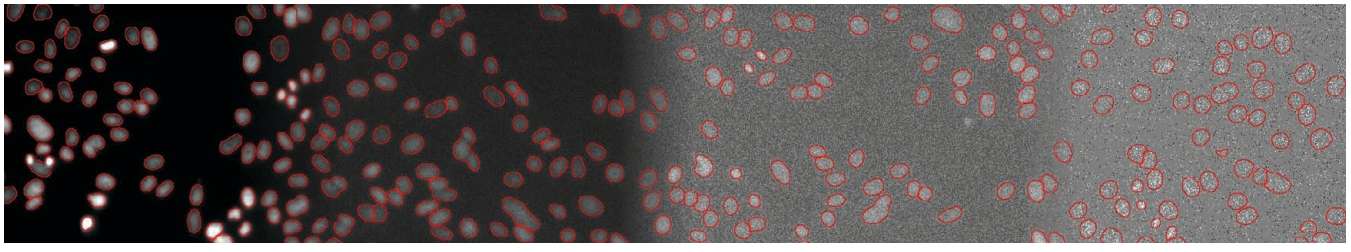
Validation of AI-enabled low-light exposure (0.2%) cell cycle assay (left) in comparison to established assay (right)

A New Way of Thinking

Self-learning microscopy opens new horizons in high-content analysis. Applications range from previously impossible image segmentation and classification tasks to quantitative analysis of extremely low signal levels, simplifying staining protocols, label-free analysis, and more.



Example application: Label-free analysis (blue overlay) of brightfield images (background) with GFP label shown as reference (right); the analysis is highly robust even in difficult imaging conditions as can occur in brightfield screening



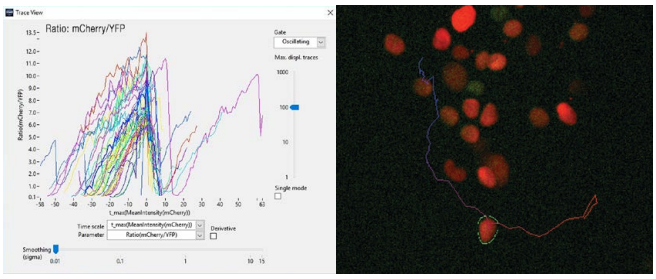
Example application: Robust segmentation of cell nuclei at different signal levels, enabling a dramatic reduction of light exposure for quantitative analysis

Flexible Module Options

The scanR system is flexible, so you can choose the capabilities that match your application and budget.

Measuring Kinetic Parameters

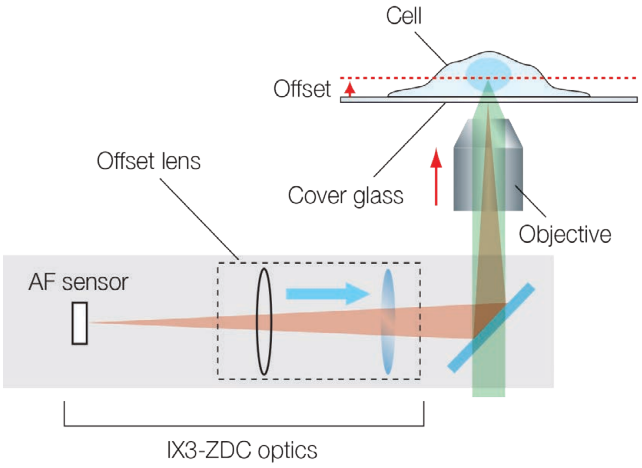
The scanR kinetic module enables live cells, nuclei, and other objects to be classified by their time-variant properties. Tracking curves are evaluated based on values (mean static parameters such as intensity, area, ratio, shape factor, etc.) measured over time. All static parameters, such as intensity or the ratio of fluorescence markers, position, size, or shape, can be evaluated and analyzed over time. The curves are condensed into single characteristic values, the “kinetic parameters” of the object. Finally, the kinetic parameters can be plotted in 1D or 2D histograms, and populations can be gated based on their specific time-variant properties.



hES cells expressing FUCC (CA) biosensor (Courtesy of Dr. Silvia Santos, The Francis Crick Institute, London, UK)

TruFocus with Infrared (IR) Laser Hardware Autofocus

The TruFocus system’s infrared laser does not interfere with fluorescence or cell viability. TruFocus complements the scanR system’s autofocus capabilities while improving focusing accuracy, reliability, and speed.



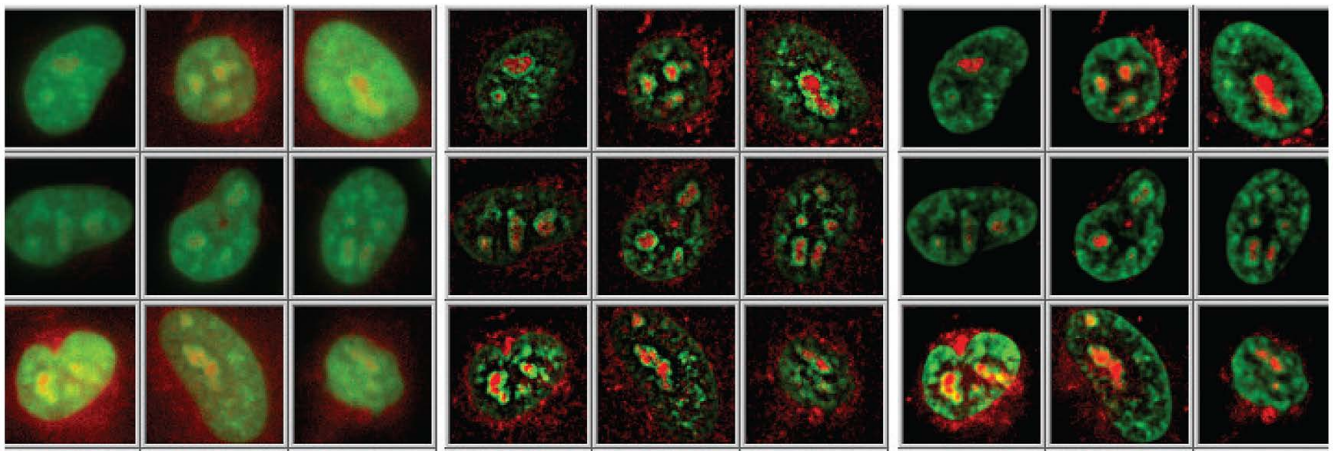
The enhanced continuous AF mode, keeps the desired plane of observation precisely in focus, even when adding reagents or during changes in room temperature

A Tale of Two Systems

Olympus cellSens live cell imaging software can run on the same system as the scanR high-content screening solution. This enables the same setup to be used simultaneously as the scanR screening system and a high-end imaging system.

High-Speed TruSight Deconvolution

The scanR system can obtain near-confocal-quality image detail for the most demanding screening applications using 2D and 3D constrained iterative deconvolution algorithms. The fast and easy-to-use algorithms accurately remove out-of-focus blur and background and can reveal essential structural details, even for very blurry images. The scanR system’s deconvolution is a helpful tool for in-depth analysis requiring high-resolution structural details.



Comparison of widefield, 2D deconvolution, and 3D deconvolution

Customization

Contact the scanR team of application specialists to customize your system to suit your needs and applications.

scanR Specifications

scanR Screening System	Microscope-based screening system platform for life science applications Flexibility: system configuration can be adapted to suit the application Performance and endurance: the integrated system and real-time synchronization combine the advantages of an open platform with the demands of screening applications for throughput and reliability
Microscope Frame	Olympus IX83 inverted microscope, one or two decks Motorized stage, Märzhäuser SCAN IM 120 × 80 for the IX83 microscope
LED Illumination Options	Lumencor SPECTRA X light engine with six independent LED channels CoolLED pe300 ultra with three independent LED channels Application-optimized bandpass filters
Transmitted-Light Illumination Options	Transmitted-light illumination for visual inspection only (no transmitted-light screening) Transmitted-light illumination for screening and visual inspection including fast shutter (transmitted-light screening supported) Optional DIC (differential interference contrast) or phase contrast
Hardware Control and System Synchronization	Real-time controller with additional CPU, independent of the OS of the imaging PC Temporal resolution: 1 ms Timing precision: <0.01 ms Hardware-synchronized multitask acquisition (illumination control, exciter filter, shutters, etc.) Precise camera control via external trigger
Camera Options	Hamamatsu ORCA-Flash 4.0 V3, high-sensitivity cooled sCMOS camera with large 18.8 mm (0.74 in.) sensor chip Hamamatsu ORCA-Flash 4.0 LT, an economic sCMOS camera with large 18.8 mm (0.74 in.) sensor chip Hamamatsu ORCA-Fusion, sCMOS camera with large 21.2 mm (0.83 in.) sensor chip
Objective Options (Supports Olympus X Line Objectives)	Objectives for “thin” (0.1 mm–0.2 mm [0.004 in.–0.008 in.]) substrates, cover slips, and glass bottom plates (2X, 4X, 10X, 20X, 40X, 60X, 100X) Objectives for “thick” (~1 mm [0.04 in.]) substrates, plastic-bottom plates, and slides (2X, 4X, 10X, 20X, 40X, 60X, 100X) Phase contrast objectives for “thin” (0.1 mm–0.2 mm [0.004 in.–0.008 in.]) substrates, coverslips, and glass-bottom plates (10X, 20X, 40X) Phase contrast objectives for “thick” (~1 mm [0.04 in.]) substrates, coverslips, and glass-bottom plates (10X, 20X, 40X)
Filter Sets	Single-band filter sets (specifications as requested) Multiband filter sets (specifications as requested)
scanR System Software	Two independent software modules: scanR acquisition software and scanR analysis software Shading correction workflow to compensate for shading and optimize spatial intensity homogeneity during and post-acquisition The software modules can be installed on the same or different workstations (Windows 10 32-/64-bit)
scanR Acquisition Software	Workflow-oriented configuration and user interface Variable, powerful software autofocus procedures that can be combined with an optional IR laser hardware autofocus function, 2-step coarse and fine autofocus, object-based autofocus, or image-based autofocus Flexible plate manager with predefined formats (slides, multiwell plates) and editing interface to create and edit customized formats (spotted arrays) Shading correction to compensate for shading and optimize spatial intensity homogeneity Time-lapse screening, Z-stack screening, multicolor screening (unlimited number of acquisition channels) Support for integration into automated sample preparation lines, ex, scriptable interfaces for liquid handling
scanR Analysis Software	Automated image and data analysis for standard assays and assay development Online and offline multicore analysis Image processing, image analysis, particle detection, and parameter extraction and calculation Cytometric data exploration, analysis, gating, and classification Powerful and flexible gating concept including automated population detection Direct link between data points, objects, and images Assays-based workflow and advanced scientific assay development functionality
Computer	Imaging computer (latest generation PC), Windows 10 64-bit
Additional Options	scanR AI deep-learning solution Time-lapse kinetic analysis module—a unique cytometric approach to better analyze and understand live-cell dynamics 3D deconvolution module (64-bit operating system required) Confocal option with Yokogawa CSU-W1 with one or two cameras Two-camera simultaneous acquisition TruFocus incubator system IR laser hardware autofocus function Incubation system Plate-loading robot Encoded magnification changer IX3-CAS Fast-emission filter wheel (FFWO) for high-speed imaging in “Sedat” configuration Additional scanR analysis workstation Second license for scanR analysis software
2-in-1 System Setup	Can be combined with cellSens live cell imaging software for full imaging system versatility

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