

## scanR

**High-Content Screening** 

# High-Content Screening Station for Life Sciences



# HAVE A GOOD CHAT WITH YOUR CELLS AND LISTEN TO ALL THEIR SECRETS

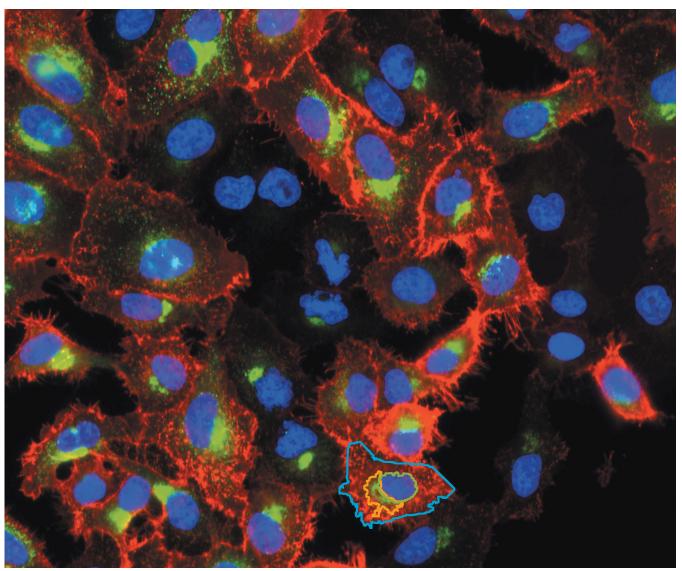


Image courtesy of EMBL, Heidelberg, Germany.

## **High-Content Screening Station for the Life Sciences**

For some challenges, hard work and motivation alone are not enough, and the ideal equipment is essential. The scanR screening station is the perfect solution to the challenge of microscope-based high-content screening. scanR perfectly combines the modularity and flexibility of a microscope-based setup with the automation, speed, throughput, reliability, and reproducibility demands of screening applications. The system is thus equally well suited to handling standard assays and assay development. Furthermore, the modular design allows the system to be adapted to the specific applications of an R&D lab as easily as to those of multiuser environments. Designed in collaboration with the EMBL (Heidelberg, Germany), scanR was developed as a powerful screening station with an extremely broad application range complemented by sophisticated image- and data-analysis software, which is based on a powerful, interactive, cytometry-oriented approach for handling and analyzing huge numbers of multidimensional data sets.

## **EXPAND YOUR SCANNING HORIZONS**

Designed for fully automated image acquisition and data analysis of biological samples, scanR can handle many different formats, e.g. multiwell plates, slides, and custom-built arrays. Its unmatched flexibility and open design make it equally adept at routine and advanced applications. With its powerful analysis module for biological functional assays, it is the perfect tool for assay development and high-content screening.

## **Research Fields**

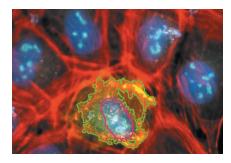
The system handles fixed and live cells with equal ease and is therefore the perfect screening platform for a wide cross section of research. scanR specifically targets the requirement for quantitative imaging and image analysis in modern cell biology, molecular biology, systems biology, and medical research. Examples include investigations on DNA damage, cell proliferation, and cell cycle analysis, or genome-wide screens using RNA interference, a key application to which scanR is specifically adapted.

For drug screening, a great many protocols have been developed to show the biochemical effects of compounds at a cellular level. For example, drug-induced changes in levels of gene expression can be accurately assessed using a range of standardized assays. scanR also excels at routine screens measuring apoptosis, micronuclei, or DNA fragmentation (comet assays).

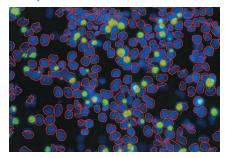
## **Examples of Cellular Screening Assays:**

- · Cell counting
- · Gene expression
- · Intracellular transport
- · Translocation
- · Cell proliferation
- · Promyelocytic leukemia (PML) body assay
- $\cdot$  Bacterial and viral infection assays
- · Cell cycle analysis
- · Protein localization and co-localization

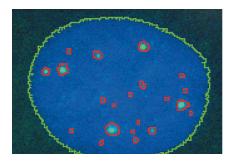
- · Cell array screens
- · Multicolor assays
- · Rare-event analysis
- · Automated FISH analysis
- $\cdot$  Fluorescence analysis in tissue sections
- · Live cell assays including kinetic analysis and gating on resulting response curves
- · Micronuclei and comet assays
- · Cell migration



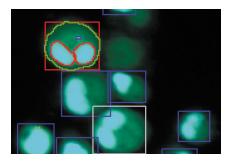
Genome-wide screen of cell arrays to identify novel genes involved in the intracellular transport mechanism. Image courtesy of Dr. R. Pepperkok, EMBL, Heidelberg, Germany.



Chlamydia trachomatis infection assay. Image courtesy of Dr. S. Hess, Max Planck Institute (MPI) for Infection Biology, Berlin, Germany.



Immunofluorescence staining of promyelocytic leukemia (PML) nuclear bodies in osteosarcoma cells.

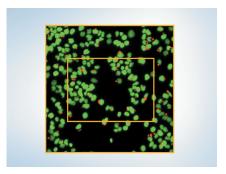


Segmentation of binucleated cells and micronuclei counting. Image courtesy of Department for In-Vitro Toxicology, Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hannover, Germany.

## **ADVANCED ACQUISITION**



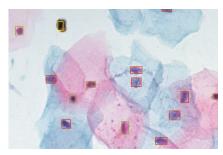
Automated high throughput. Cellular assays in microplates, slides, and self-defined cell arrays.



Equipped with a large sensor area, the Hamamtsu Orca Flash 4.0 camera increases the acquired field of view significantly.



U-RTC. The hyperprecise real-time controller ensures that all scanR devices and components are perfectly synchronized and parallelized to guarantee the necessary precision for high-throughout image analysis.



Fluorescence or transmitted-light images can be used for automated segmentation.

The Olympus scanR software features an intuitive graphical user interface based on a strictly workflow-oriented approach. This ensures simple handling in daily operation, reliable and stable image acquisition and straightforward system configuration. The scanR system design focuses specifically on quantitative measurements and on easy, reliable repeatability and flexibility, addressing the needs of scientific screening and assay development.

#### **Flexibility**

scanR is based on the latest Olympus high-end IX83 inverted microscope, providing the utmost flexibility, robustness, and stability. It handles all standard assay formats, such as micro well plates and slides, with ease and can also be configured to accept any custom designs, such as spotted arrays or biochips.

## **Highly Optimized Illumination**

scanR features a high-end LED illumination system for maximal switching speed and long-term intensity stability.

## **Hyperprecise Control**

The extreme demands for robustness, reliability, and throughput as well as minimized photobleaching are met by the perfect device synchronization and parallelization of the unique real-time controller (U-RTC) from Olympus.

#### **More Dimensions**

The advanced features of scanR allow truly multidimensional (X, Y, Z, t,  $\lambda$ ) screening. Time-lapse Z-stack images can be recorded at any number of locations on micro well plates, slides, or custom formats using all available observation methods, including fluorescence or brightfield, as well as differential interference contrast (DIC) or phase contrast.

## **Autofocus**

Fast and accurate autofocus is crucial for successful automated image acquisition. scanR provides a combination of hardware-based autofocus together with different software autofocus algorithms to meet the demands of extremely variable biological samples.

## **Large Field of View**

Equipped with a large sensor-area camera and an optimized fluorescence condenser, scanR can acquire huge areas of the sample with each camera image, increasing the amount of acquired data and decreasing the screening time dramatically.

## **Multi-level Acquisition**

Based on an initial pre-scan, the scanR Analysis software can determine all interesting objects with the complete image processing, image analysis, and cytometric data exploration engine available. In an automated workflow, the analysis results are employed to scan selectively only the objects-of-interest in a second, targeted screen. Typical scenarios where Multi-level Acquisition excels are large area samples with few cells which require high resolution or single cell events.

## **ANALYSIS AND VISUALIZATION**

The huge amount of data you can now collect from your assays creates the need for coherent and careful automated quantitative analysis. Installed on either the same or different workstations, connected via a local network, image and data analysis can be performed online at the same time as acquisition, or offline on previously-acquired datasets.

#### **Analyzing Data**

Analytical techniques can be as simple as counting labeled 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 by means of gating and classification.

### **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 are used to remove heterogeneous background and shading automatically and rigorously while retaining the relevant intensity information. Spectral Unmixing can remove potential bleed through of different fluorophores effectively.

## **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. This highly flexible data output enables the scanR system to be used for almost any current and future cell-based assay.

## **Gating and Classification**

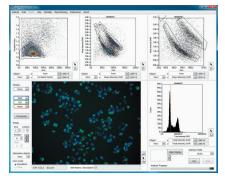
scanR specifically excels in subsequent data analysis and evaluation. For this purpose, the powerful data analysis concepts that are successfully applied in cytometry are adapted to suit the specific demands pertaining to the analysis of large image data sets. The multidimensional image data generated 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. Gated objects can be re-scanned to perform automated rare-event analyses, for example.

## **Immediate Quality Control**

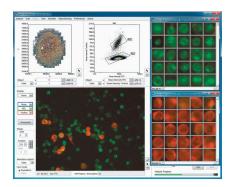
Images and objects are reciprocally linked to any data point related to them. Clicking on a data point loads the relevant image in the display window and highlights the object in question. Clicking on an object in the image display window highlights the related data points in the scatter plots and histograms.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



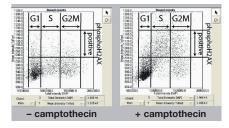
<sup>\*\*</sup> Courtesy of Dr. M. Jager, Clinical Research, TRION Research GmbH, Martinsried, Germany.



Cell cycle distribution of chlamydia trachomatis-infected



Diagnostic screening of tumor markers in cytospin preparations.\*\*



Correlation between H2AX phosphorylation and the cell cycle phase in a DNA repair assay.\*\*\*

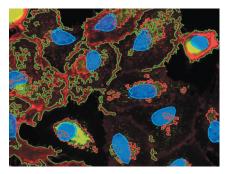


Image screenshot detail following data acquisition by scanR demonstrating the detection and separation of

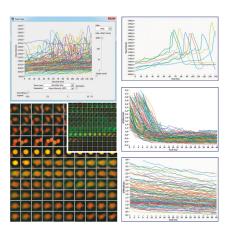
<sup>\*\*\*</sup> Courtesy of Dr. F. Buchholz, MPI for Molecular Cell Biology and Genetics, Dresden, Germany.

<sup>\*\*\*\*</sup> Courtesy of Dr. R. Pepperkok, EMBL Heidelberg, Germany.

## **FLEXIBLE MODULE OPTIONS**



Automated image analysis runs at the same time as acquisition or uncoupled on a separate analysis system.



Time-lapse cytometry. Impression of kinetic analysis.



cellVivo - the Olympus Incubation system.

scanR was designed not only to satisfy the specific speed, endurance, and reliability requirements of a fully automated high-content screening system but also to provide unmatched flexibility and adaptability coupled with extensive expansion capabilities. This enables scanR to perfectly match the specifications of any application and budget.

## **Time-lapse Cytometry – Measuring Kinetic Parameters**

The scanR kinetic module allows objects to be classified by their kinetic properties. Tracking curves are evaluated on the basis of values (mean static parameters such as intensity, area, ratio, shape factor, etc.) measured over time. The curves are condensed into single characteristic values. Finally, kinetic parameters can be plotted in 1D or 2D histograms, and populations can be gated based on their specific kinetic properties.

### **3D Deconvolution**

The 3D Deconvolution module is a powerful processor which uses known experimental parameters (e.g. numerical aperture, wavelength) to optimize image quality, remove out-of-focus light and improve optical sectioning.

## A Tale of Two Systems

ScanR is compatible with the Olympus cellSens live cell imaging software, which can run on the same system. The same setup can thus be used both as the dedicated scanR screening system and at the same time as a high-end imaging system.

## **Plate-Loading Robot and Integration Interface**

The scanR platform supports a plate-loading robot. The robot facilitates fully automated screening of multi well plate stacks and extends screening to 24/7 operation. scanR offers flexible support for integration into automated sample preparation lines.

## IR Laser Hardware Autofocus based on IX83 ZDC

The latest Olympus infrared laser-based z-drift compensation system (ZDC), which interferes with neither fluorescence imaging nor cell viability, is available for scanR to maximize autofocus accuracy, reliability, and speed. The ZDC perfectly complements the distinct autofocus options of the software to ensure the best focus accuracy and reliability.

## **Olympus Incubation System**

The Olympus cellVivo provides stringent control of temperature, humidity, and CO2 levels for sample integrity and focus position when working with living cells.

## Customization

The scanR team of application specialists will be happy to customize your system to suit your needs and applications precisely.

scanR Specifications	
	Microscope-based screening system platform for life science applications
scanR screening system	Flexibility: system configuration can be adapted precisely to suit the application
	Performance and endurance: a highly integrated system concept and real-time synchronization unites the advantages of an open
	platform with the demands of screening applications for throughput and reliability
Microscope frame	Olympus inverted high-end microscope IX83, one or two decks
	Motorized stage, Märzhäuser SCAN IM 120x80 for IX83
Lumencor Spectra X	6 independent LED channels, turn on/off $\sim$ 10 $\mu s$
LED illumination	Application-optimized bandpass filters
	Lifetime >20,000 hours with more than 70% initial intensity
Transmitted-light	Transmitted-light illumination for visual inspection only (no transmitted-light screening)
illumination options	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	Real-time controller with additional CPU, independent of the OS of the imaging PC
system synchronization	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 V2 QE80, high-sensitivity cooled sCMOS camera with large 18.8 mm sensor chip
	Hamamatsu ORCA-FLASH 4.0 LT, economic sCMOS camera with large 18.8 mm sensor chip
	Hamamatsu ORCA R2, high-sensitivity cooled CCD camera, recommended for long exposure times
	Hamamatsu C8484, high-sensitivity CCD camera
Objective options	Objectives for "thin" (0.1–0.2 mm) substrates, cover slips, and glass bottom plates (2x, 4x, 10x, 20x, 40x, 60x,100x)
	Objectives for "thick" (~1 mm) substrates, plastic bottom plates, and slides (2x, 4x, 10x, 20x, 40x, 60x)
	Phase contrast objectives for "thin" (0.1-0.2 mm) substrates, cover slips, and glass bottom plates (10x, 20x, 40x)
	Phase contrast objectives for "thick" (~1 mm) substrates, cover slips, and glass bottom plates (10x, 20x, 40x)
Filter sets	Single-band filter sets (specifications as requested)
	Multiband filter sets (specifications as requested)
	2 independent software modules: scanR Acquisition software and scanR Analysis software
scanR system	Shading correction workflow to compensate for shading and optimize spatial intensity homogeneity during and post-acquisition
software	The software modules can be installed on the same or on different workstations (Windows 7 32-/64- bit, Windows 10 32-/64-bit)
scanR Acquisition software	Work-flow-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
	Versatile 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, e.g. scriptable interfaces for liquid handling
scanR Analysis	Automated image and data analysis for standard assays and assay development
software	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 work flow and advanced scientific assay development functionality
Computer	Imaging computer (latest generation PC), Windows 10 64-bit
Additional options	Time-lapse kinetic analysis module – a unique cytometric approach for better analyzing and understanding live cell dynamics
	IR laser hardware autofocus function based on the ZDC of the latest Olympus IX83 microscope series
	3D Deconvolution module (64-bit operating system required)
	cellVivo incubation system
	Plate-loading robot
	Encoded magnification changer IX3-CAS
	Fast emission filter wheel (FFWO) for high-speed imaging in "Sedat" configuration
	Customization: hardware, software, assays
	Additional scanR Analysis workstation
	2 <sup>nd</sup> license for scanR Analysis software
2 systems in one setup	Can be combined with cellSens live cell imaging software for full versatility of a high-end imaging system

