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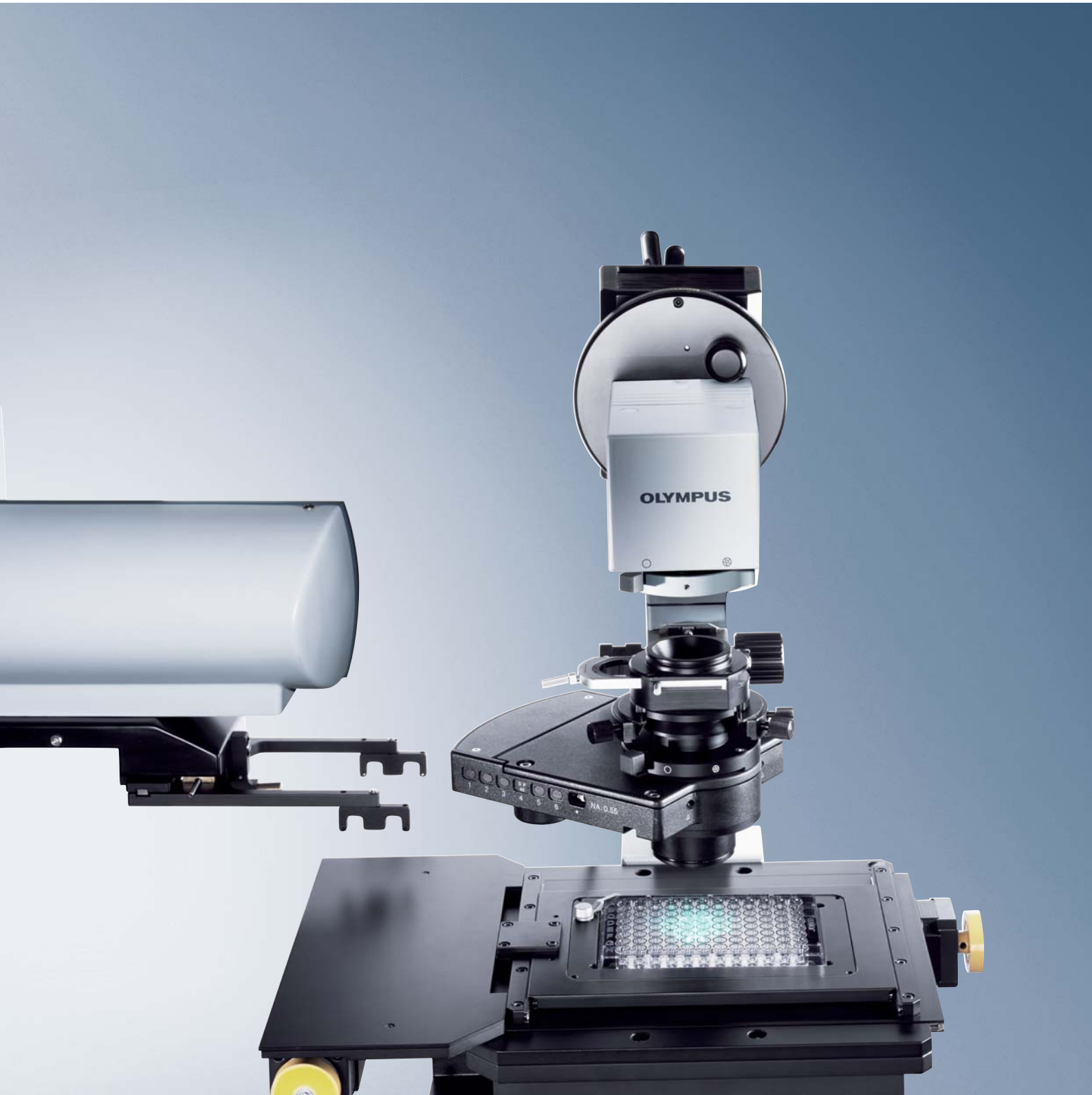
Your Vision, Our Future

Bioscience Microscopes

scan^R

Advanced Imaging Systems

scan^R Screening Station for Life Science

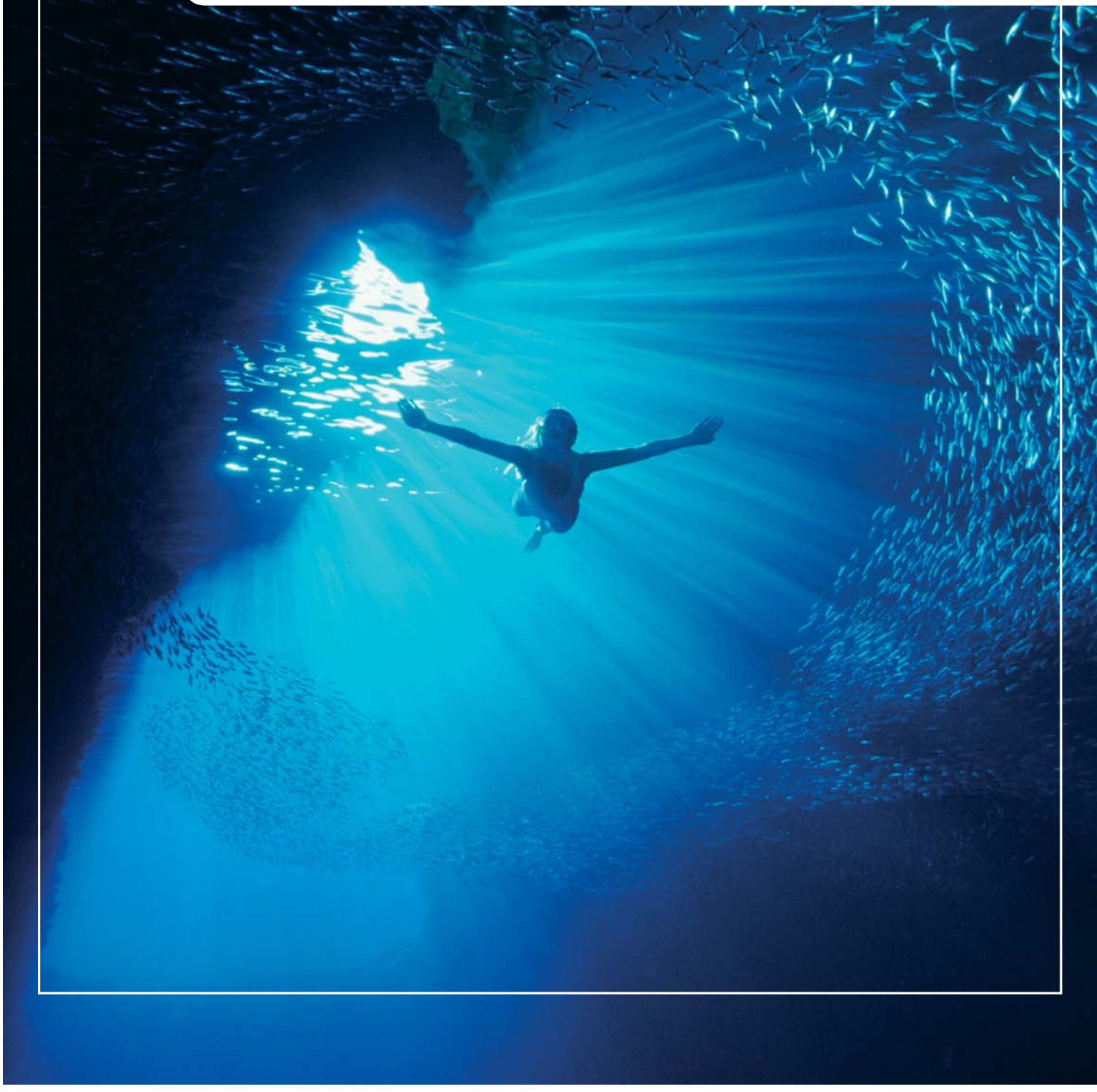


SCAN BEYOND YOUR HORIZON

Olympus scan^R screening station for life science

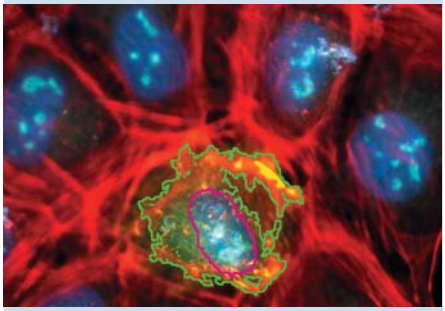
For some challenges, hard work and determination are not enough and the optimum equipment is essential. There is now the perfect solution to the challenge of cell-based screening: the new Olympus scan^R screening station for life science.

scan^R perfectly combines the modularity and flexibility of a microscope-based set-up with the automation, 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 multi-user environments. scan^R was developed as a powerful screening station with an extremely broad application range on the basis of experimental screening systems designed by the European Molecular Biology Laboratory (EMBL).

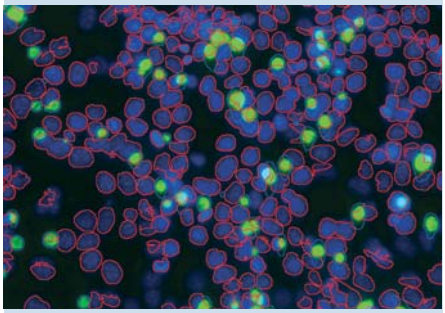


TOUGH CHALLENGES NEED SMART SOLUTIONS

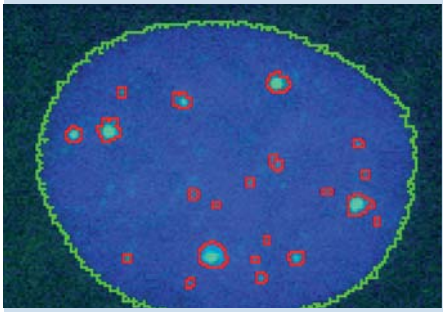
Designed for fully automated image acquisition and data analysis of biological samples, scan® can handle many different formats, e.g. multi-well plates, slides or custom-built arrays. The unmatched flexibility and open design make it equally adept at routine and advanced applications. With its powerful analysis module for biological functional assays, it is the perfect tool for assay development and high-content screening. scan® provides complex image analysis and advanced data evaluation, which enable it to complete a whole range of standard and bespoke assays.



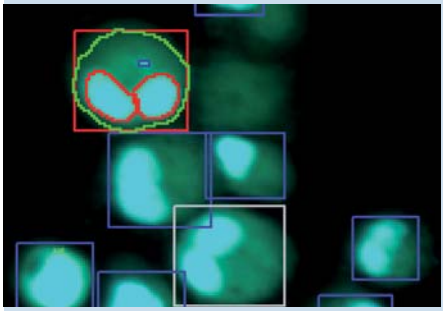
Genomic-wide screen on cell arrays to identify novel genes involved in intracellular transport machinery.
Image courtesy of Dr R. Peperkok, EMBL, Heidelberg, Germany.



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 Toxicology and Experimental Medicine (ITEM), Hannover, Germany

Research fields

A The system handles fixed and live cells with equal ease and is therefore the perfect screening platform for a wide cross section of research. scan® specially targets the need for quantitative imaging and image analysis in modern cell biology, systems biology and medical research. For example, cancer research involves investigations on many levels, such as DNA damage, cell proliferation and cell cycle analysis. Furthermore, novel genome-wide screens using RNA interference are a key application to which scan® is specially adapted (developed in close cooperation with the EMBL).

For drug screening, a great many protocols have been developed to show the biochemical effects of compounds on the cellular level. For example, drug-induced changes in gene expression levels can be assessed accurately via a range of standardised assays. scan® also excels at routine screens measuring apoptosis, micronuclei or DNA fragmentation (comet assays). Additionally, scan® covers a huge range of screening applications (selected examples are listed below) which are implemented in many research areas.

Example of cellular screening assays

A	Cell counting
	Gene expression
	Intracellular transport
	Translocation
	Cell proliferation
	Promyelocytic leukaemia (PML) body assay
	Bacterial infection assay
	Cell cycle analysis
	Protein localisation and co-localisation
	Live cell assays
	Multicolour assays
	Rare event analysis
	Automated FISH analysis
	Fluorescence analysis in tissue sections
	Cell array screens
	Micronuclei and comet assays

ACQUIRE MORE

See your assay in action

Each cell-based experiment produces a plethora of information, most of which is not fully collected because many assays are completed as end-point studies with fixed cells. What is missed, though, are the dynamic cellular and sub-cellular events that are key to understanding the causes or effects on the molecular level. scan® provides time-lapse screening functionality to track the dynamic changes over time in tens of thousands of living cells.

scan® incorporates advanced modular software and hardware, controlled through an easy-to-use interface that provides access to all image acquisition and image analysis parameters. The system includes a unique real-time controller which synchronises the scan® hardware and the special multifunctional Olympus MT20 illumination system. The combination of these innovative devices ensures maximised acquisition speed, minimises bleaching as well as phototoxicity, and provides the basis for true quantitative measurements. The system is designed to produce multidimensional (X, Y, Z, t, λ) images with great ease. Once acquired, images can be automatically analysed by the powerful scan® image and data analysis software that is based on a cytometry-oriented approach towards the handling and analysis of huge amounts of multi-dimensional data sets. The scan® analysis software allows for full image processing (e.g. background correction), object and sub-object detection, parameter calculation as well as sophisticated gating and classification schemes.

To extend the functionality of scan®, a series of optional components can be added. For example, the Olympus cell^cubator advanced environmental control chamber enables long-term live cell imaging. An optional plate-loading robot greatly enhances automation. Other optional features such as an IR laser-based autofocus, terabyte data storage systems and a professional workbench add even more flexibility. Additionally, scan® is available as a special development version that provides LabVIEW® source code interfaces for researchers in need of the ultimate experimental screening development platform. LabVIEW® is a powerful graphical development environment for automation from National Instruments.

ADVANCED AUTOMATED ACQUISITION

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

Flexibility as standard

A scan^R is based on inverted or upright Olympus high-end microscopes, providing the modularity of an open microscope set-up and can be fitted with a large set of optional devices. It handles all standard assay formats, such as microplates and slides, with ease and can also be configured to accept any custom designs such as spotted arrays and biochips. scan^R can be precisely adapted to any application and fulfills the requirements of multi-user environments.

Highly stabilised illumination

B The revolutionary MT20 illumination system developed by Olympus has, at its core, a highly stabilised xenon or mercury/xenon burner, a fast filter wheel, an achromatic and absolutely reproducible attenuator, as well as a fast shutter with an exceptional on/off time of less than 1 ms. The MT20 is coupled to the microscope via a flexible quartz light guide, eliminating the effects of heat and vibration, and has optimised optics for homogeneous illumination. Based on the innovative MT20 illumination system and the real-time controller described below, highly reproducible, consistent image data are generated and photobleaching is reduced to a minimum.

Hyper-precise control

C The extreme demands on robustness, reliability and throughput are met by perfect device synchronisation and parallelisation via the unique Olympus real-time controller.

More dimensions

The advanced features of scan^R enable true multidimensional screening. Time-lapse, Z-stack images can be recorded at any number of locations on multi-well plates, slides or custom formats, using all available colour channels.

Contrast imaging

D In addition to fluorescence techniques, scan^R supports brightfield imaging including contrast-enhancing methods, such as differential interference contrast (DIC) or phase contrast, to provide further detail.

Software autofocus

Fast and accurate autofocus is crucial for successful automated image acquisition. To meet the demands of the extremely variable biological sample, scan^R provides different autofocus algorithms. The scan^R 'object-based' autofocus uses specific features to distinguish relevant cellular objects from cell debris, dirt or dust. For highly variable samples, an 'image-based' autofocus is available, which focuses based on information from the entire field of view. Image acquisition can be performed with a Z-offset, with respect to the autofocus plane, so that structures that are located in different focal planes can be imaged in focus.

Image (left page) courtesy of EMBL, Heidelberg, Germany.

A Automated, high throughput

Cellular assays in microplates, slides and cell arrays.

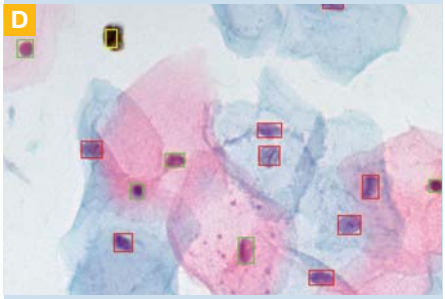
B MT20 illumination

Highly stabilised sytem for reproducible fluorescence excitation.

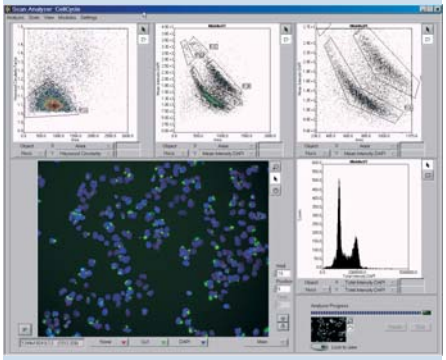
C IX2_FRFACA

Like all components of scan^R the fast mirror unit is controlled by the hyper-precise real-time controller.

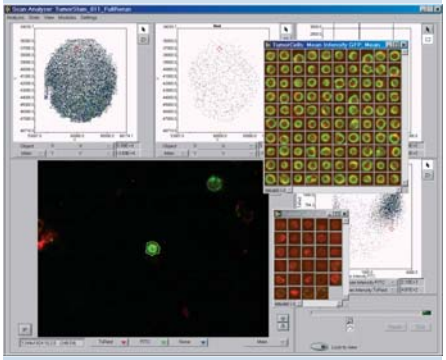
D



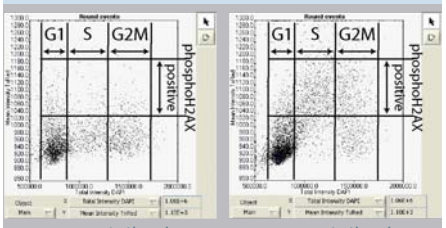
Fluorescence or transmitted light images can be used for automated segmentation.



Cell cycle distribution of chlamydia trachomatis-infected HeLa cells.*



Diagnostic screening of tumour markers in cytospin preparations.**



– camptothecin + camptothecin

Correlation between H2AX phospholylation and the cellcycle phase in a DNA repair assay.***

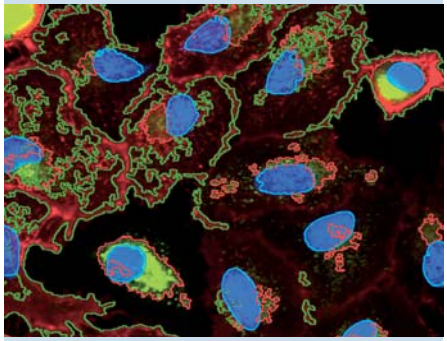


Image screenshot detail following data acquisition using scan^R, demonstrating the detection and separation of labels.****

ANALYSIS AND DISPLAY

With the huge amount of data that you can now collect from your assays comes the need for coherent and careful quantitative automated analysis. The powerful scan^R analysis software package is completely independent from the scan^R acquisition software. This enables both modules to be installed on either the same or different workstations, connected via a local network. In both cases, image and data analysis can be performed "online" at the same time as acquisition or "offline" on previously acquired data sets.

By collecting more data, you are also increasing the number of analytic techniques that can be carried out on your samples. These can be as simple as counting the labelled cells on display or as complex as ratiometric feature-based analysis of multi-labelled objects and sub-objects in different cell types. Image analysis is carried out as a logical multi-step procedure consisting of image processing, object detection, feature extraction and data analysis by gating and classification. A workflow-oriented user interface guides users through all steps.

Image processing

Before contouring nuclei, cytoplasm and other sub cellular objects the raw images are, if necessary, pre-processed. For example an Adaptive Size Background Correction is used that automatically and robustly removes heterogeneous background and shading while keeping the relevant intensity information.

Object detection and analysis

Powerful object detection modules are optimised to segment nuclei, cells or other structures. Several detection algorithms can be selected and adapted to the objects of interest. Based on this, segmentation-relevant features can be selected out of a list of more than 100 object parameters. The selected parameters are extracted for evaluation and classification. Additional mathematical operations can be performed on the parameters. This highly flexible data output enables the scan^R system to be used for almost all current and future cell-based assays.

Gating and classification

scan^R 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 the specific demands of analysing large image data sets. The multidimensional image data generated are displayed in two-dimensional scatter plots or one-dimensional histograms. From these, clustered data populations of interest can be selected via graphical tools. Selected data sets can be repeatedly gated for further investigation. Gates from different plots can be combined with Boolean operators to create complex classification schemes.

Immediate quality control

Images and objects are linked reciprocally to any data point related to them. By clicking on a data point, the respective image is loaded into the display window and the respective object is highlighted. By clicking on an object in the image display window, the related data points in the scatter plots and histograms are highlighted. Additionally, a gallery view of all images of a selected or gated data population can be created to allow a direct and visual comparison of larger image sets with relevant information.

* Image courtesy of Dr S. Hess, Max Planck Institute (MPI) for Infection Biology, Berlin, Germany.
** Courtesy of Dr F. Buchholz, MPI of Molecular Cell Biology and Genetics, Dresden, Germany.
*** Courtesy of Dr M. Jäger, Clinical Research, TRION Research GmbH, Martinsried, Germany.
**** Courtesy of Dr R. Peperkok, EMBL Heidelberg, Germany.

FLEXIBLE MODULE OPTIONS

scanR was not only designed to comply with the specific demands of speed, endurance and reliability that are required for a fully automated high-content screening system, but also to provide unmatched flexibility and adaptability coupled with extensive expansion capabilities. This enables scanR to fit the exact specifications of any application and budget.

Whatever you need

A tale of two systems

A scanR is compatible with the Olympus cellR imaging station, since both systems are based on the same hardware components. The cellR software can run on the scanR workstation. The same set-up can thus be used as the dedicated scanR screening system and additionally as the cellR research imaging station.

Environmental control

B For live cell screening, the Olympus cellcubator advanced environmental control chamber can be added for precise maintenance of temperature, humidity and pH.

Plate-loading robot

C The scanR supports a plate-loading robot. The robot enables fully automated screening of multi-well plate stacks and extends screening to 24/7 operation.

IR laser autofocus

To maximise autofocus accuracy, reliability and speed, an infrared laser-based autofocus system that does not interfere with fluorescence imaging and cell viability is available for scanR. The laser autofocus can be combined with the software autofocus to enhance accuracy.

Extended storage tools

Automated screening produces huge amounts of image data, and storage solutions therefore need to be considered. Olympus can provide professional terabyte data storage systems, which integrate seamlessly with the software.

Professional workbench

scanR can be fitted into a customised professional workbench that is available as a table top platform, an open bench or a fully enclosed box to shield the system from dust and ambient light.

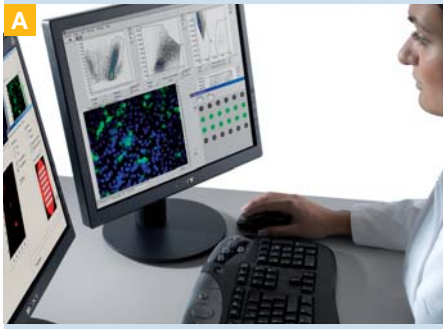
scanR development version

For leading-edge research and screening development applications, scanR is available as a special development version. Via defined LabVIEW® source code interfaces, the full acquisition functionality of scanR is accessible. Moreover, the scanR analysis software package provides interfaces that allow the addition of new custom-built image processing and object detection modules that can be programmed by the user in National Instruments LabVIEW® and Vision graphical development environments.

Customisation

The scanR team of application specialists will be happy to customise your system exactly to your needs and applications.

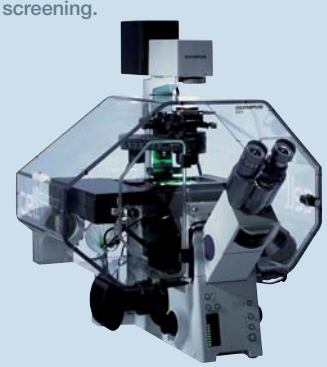
A



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

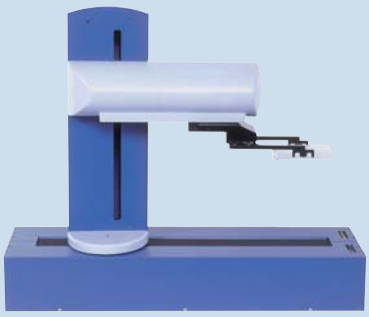
B cellcubator

Incubation chamber for live cell screening.



C **Plate loading robot systems**

Supported by scanR



scan^R system specifications

Item	Specification
scan^R screening system	Microscope-based screening system platform for life science applications
	Flexibility: system configuration can be adapted exactly to the application
	Performance and endurance: a new highly integrated system concept and real-time synchronisation unites the
	advantages of an open platform with the demands on throughput and reliability of screening applications
Microscope frame	Olympus inverted microscope IX81
	Motorised stage Märzhäuser SCAN IM IX2
	Olympus upright microscope BX61 (optional)
MT20 fluorescence illumination system	Short arc burners, 150 W, xenon or mercury-xenon
	Highly stabilised light output, intensity fluctuations < 0.1%, feedback loop stabilised burner current
	Fast filter wheel with 8 filter positions for standard 25 mm optical filters that can be easily exchanged without tools
	Filter switch < 58 ms (neighbouring positions)
	Attenuation, 14 levels, from 1% to 100%, achromatic, with high repeatability
	Attenuation switch, min. 58 ms (neighbouring positions)
	Shutter, on/off time < 1 ms
	Operation: all modes simultaneously
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	Real-time control board with additional CPU, independent from imaging PC
synchronisation	Temporal resolution: 1 ms
	Timing precision: < 0.01 ms
	Multi-task acquisition with hardware switch (Z-position, exciter filter, etc.),
	Camera control: trigger
Camera options	Hamamatsu ORCA-AG, high-sensitivity cooled CCD camera, recommended for long exposure times
	Hamamatsu C8484, high-sensitivity CCD camera
	Intensified and EMCCD cameras (Hamamatsu) on request
Objectives 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)
	Multi-band filter sets (specifications as requested)
scan^R system **software**	2 independent software modules: scan^R acquisition software and scan^R analysis software
	The software modules can be installed on the same or on different workstations
scan^R acquisition software	Automated image and data analysis for standard assays and assay development
	Workflow-oriented configuration and user interface
	Variable powerful software autofocus procedures that can be combined with an optional IR laser hardware autofocus,
	2-step coarse and fine AF, object-based AF, image-based AF
	Plate manager with predefined formats (slides, multi-well plates) and editing interface to create and edit customised formats (spotted arrays)
	Online display
	Time-lapse screening, Z-stack screening, multicolour screening (no limit on number of acquisition channels)
	User interaction: pause, resume, reconfigure software autofocus
scan^R analysis software	Automated image and data analysis for standard assays and assay development
	Online and offline analysis
	Image processing, image analysis and particle detection, parameter extraction and calculation
	Cytometric data analysis, gating and classification
	Direct link between data points, objects and images
	Predifined assays and advanced scientific assay development functionality
Computation	Imaging computer (latest generation PC), 2 hard disks (80 GB and 250 GB), 2GB RAM
Additional options	IR laser hardware autofocus based on ZDC
	Plate-loading robot
	Open or closed system bench
	Environmental control by cell^cubator
	Fast mirror unit turret IX2-FRFACA
	Professional data storage systems
	Customisation: hardware, software, assays
	Development version with LabVIEW® source code interfaces
	Service contract
	Additional scan^R analysis workstation
	2nd licence for scan^R analysis software
2 systems in one set-up	cell^R imaging station

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