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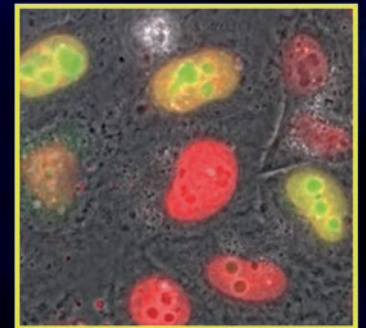
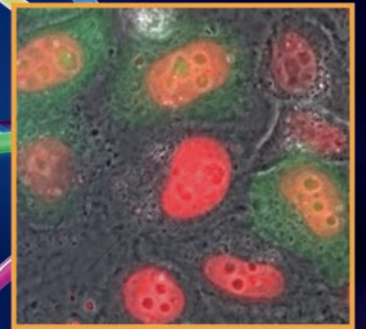
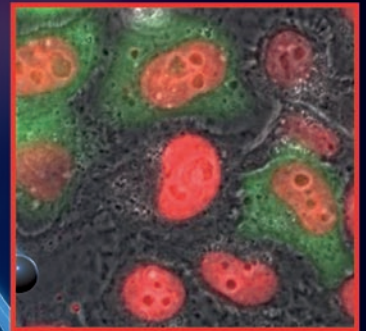
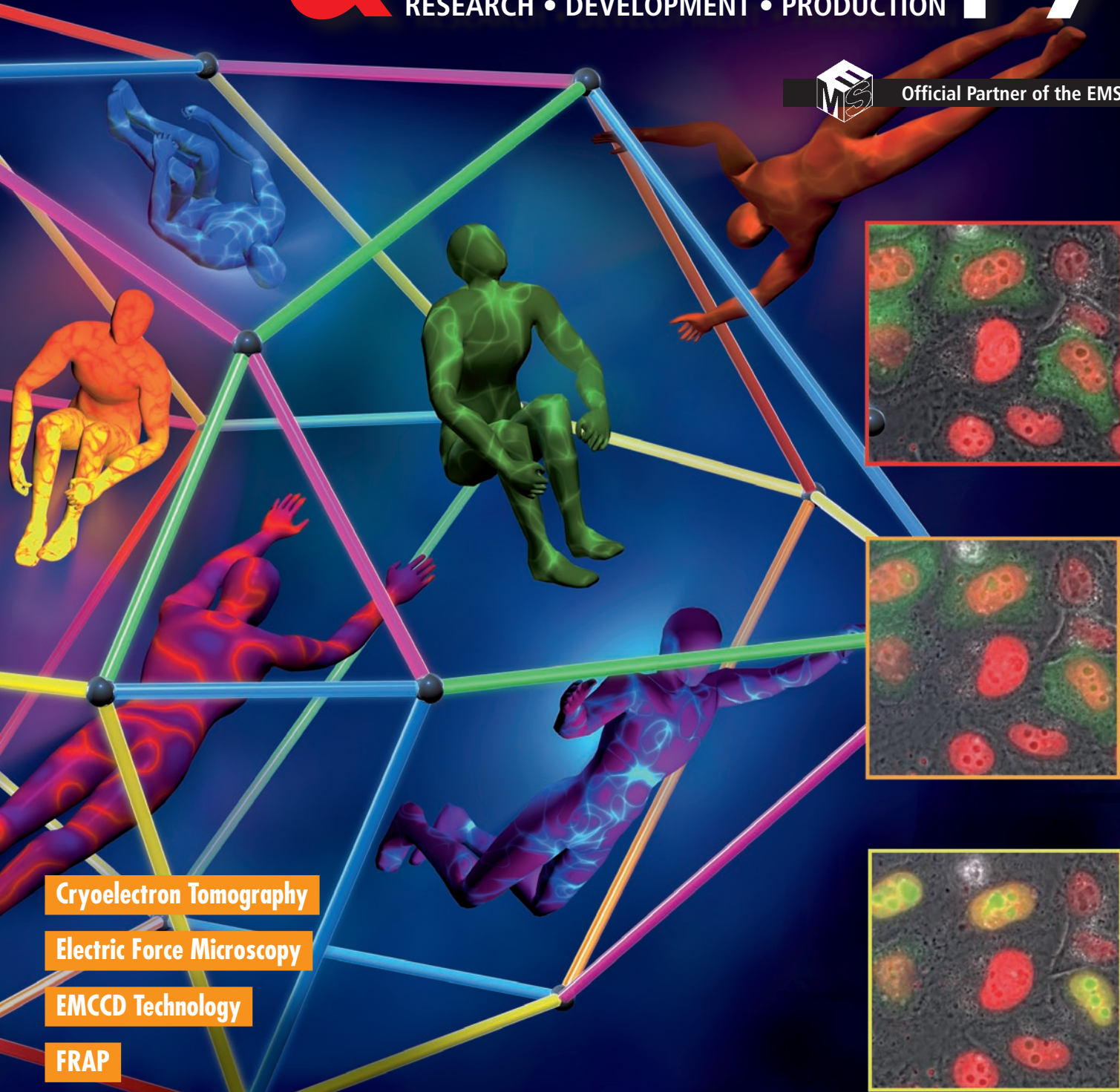
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# Imaging & Microscopy

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# Taking Us Closer to Life

## True Detail Imaging

Live cell imaging, the microscopic examination of living cells at the highest level, is currently the focus of cell research. As a rule, immortalised cell lines or stem cells in culture dishes are used for this purpose. The approaches taken often differ considerably. However, the cell is simultaneously seen as an autonomous unit and as a mirror of the processes taking place in the overall organism.

In live cell imaging, observation, manipulation and analysis are typical stages on the way to obtaining new explanations and knowledge. Here, optimum stipulations are essential. Carl Zeiss has set itself the task of offering total solutions in the form of the Axio Observer microscope and specific system components. These are aimed at supporting scientists at all stages and providing them with a decisive lead through a large number of benefits.

### Perfect Conditions for Observation

Irrespective of the approach taken, artifact-free microscopic observation is only possible if the ambient parameters are correct for the cells. Temperature, pH value and O<sub>2</sub> concentration must be regulated for this purpose. Here, absolute



Fig. 1: Optimum incubation conditions, more space: incubator PM S1 for Petri dishes and multiwell plates.

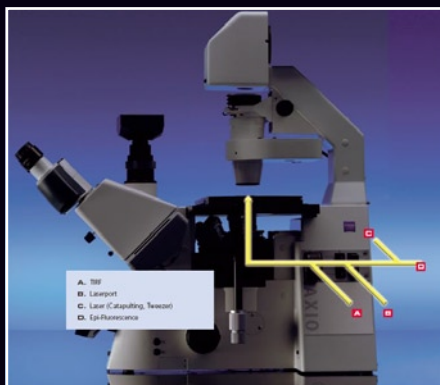


Fig. 2: Designed specifically for demanding laser applications such as FRAP, Uncaging, or for the targeted ablation of cellular structures. Also shown: illumination or manipulation options performed in combination (A, C, D).

precision is of the essence, particularly for long-time experiments.

Temperature repeatability is enabled by a thermal sensor that can be placed directly in the culture dish. This provides the actual temperature at the site of observation. Assumptions and difficult-to-interpret data are therefore a thing of the past. Thermally insulated objective lenses are additionally available for the Axio Observer. This interrupts the temperature flow into the nosepiece, ensuring that the target temperature is indeed achieved. The pH value is also of interest. This is regulated via the CO<sub>2</sub> concentration on the basis of a buffer system. However, the O<sub>2</sub> concentration must also be taken into account, as cells react sensitively to changed values.

The system is adapted to the exacting demands that must be met for regulating these parameters. The regulation of the incubation conditions is fully automated. Its performance is further enhanced by an intelligent stack and upgrade concept for the regulating modules. This overall concept for cell observation is unique and also provides also the acquisition of all incubation data.

### Finding Answers Through Manipulation

Observation is only one dimension. Often, new insights are only possible via direct communication with the cell. The cell is forced to respond. Here once again, the approaches taken are very different, and current possibilities are often inadequate.

Questions on protein folding, for example, are frequently clarified by molecular genetic means via temperature-sensitive folding mutants. In the experiment, the permissive and restrictive temperatures are specified. At the restrictive temperature, the cell responds by forming a protein that is differently folded and could therefore possibly be inactive. This is easy with this instrument via automatic temperature steps that are pre-programmed and saved beforehand.

Laser experiments are slightly more complex. In many cases, this can be de-

scribed as a new dimension in living colors. These are specifically bleached, for example, in FRAP. On the basis of the manner in which the fluorescence signals are regenerated, the scientist distinguishes between free diffusion, active transport processes and hindered diffusion due to membranes. It is also possible to use the laser to convert cellular proteins or fluorophors to the active form (uncaging). If these are enzymes, an entire process chain can be activated on site in the cell at a desired time, for example. What is important in all these processes is simultaneous monitoring with fluorescence or also with transmitted light. With its laser port, the microscope is open for all laser applications, and there is no need for any enlargement of the infinity space. This rules out the possibility of a loss in optical quality.

Another way of manipulation is the artificial change in the location of the cell. Laser tweezers make it possible to isolate cells or to deliberately combine them. Microdissection and laser catapulting permit the highly pure isolation of organelles, cells or entire organisms. The Palm Microbeam system features all these options.

### Efficient Editing and Combination of the Raw Data in the Analysis

It is essential for raw data to be condensed to what is absolutely essential. Only in this way is it possible to meaningfully interpret contents and achieve decisive scientific progress. The microscope in the system allows this in many different ways: the storage of environmental data in the image data for even more safety, the calculation of emission intensities in ratio experiments during the experiment or the range of highly advanced downstream modules in Axiovision. The latter, including deconvolution, unmixing, colocalisation up to the detection of image areas in which motion is taking place, are options for special applications and round off the complete, incredibly diverse software package.

### The Axio Observer System

At all levels, maximum performance is expected of the microscope and the system. These are precisely the needs on



Fig. 3: Targeting the result more purposefully: analysis with AxioVision.

which the system is focused. Questions facing scientists can now be answered considerably more quickly.

The microscope – at the center of the overall system comes with many new functions. Major optimisations in the contrasting techniques include a new level of DIC quality with a clearly homogenous background, the apochromatic fluorescence ray path with homogenous excitation in fluorescence for better contrasting in the periphery of the field of view and, finally, the variable phase contrast that combines negative and positive phase contrast in one objective lens. All optimisations provide that little extra information that can be so important today. The enhancements are rounded off by a completely new operating concept that is effective at all levels. For example,

it includes various motorised diaphragms in fluorescence, a 6x reflector nosepiece that can be equipped without any need for its removal and AKE (automatic component recognition) for even more safety and ease of use. Another unique feature is the touch-screen TFT display for the complete, optional operation of the instrument as a docking station. Therefore, it can be directly positioned at the PC. The three different stand types of the Axio Observer – A1, D1 and Z1 – cover the entire range of possible applications.

The main principle behind the system is simple upgrading and reconfiguration for maximum flexibility in order to meet the rapidly changing needs of users. This is essential, for the requirements to be met by the individual workplace change very quickly. The highest quality de-

mands were fulfilled in the selection of external components. Typical features include, for example, the quickly upgradeable TIRF system with space-saving slider, the Cell Observer now also in the HS version (high speed) for the observation of rapid motion (e.g. vesicle transport) or highly advanced confocal versions, e.g. the new LSM Duo (for the detection of the spectral signature in each image point beside the option of scanning with > 100 frames per second for the observation of very dynamic events like the movement of blood cells).

Last but not least, with this microscope Carl Zeiss is remaining true to the pledge and commitment of the company made with the name Carl Zeiss: Fluorescence years ago, i. e. to provide leading microscope systems for applied and basic research that would offer maximum contrast and exhaust all technical possibilities for fluorescence applications.

All to take us a little closer to the cell and to life itself.

**Contact:**

**Dr. Eugen Wehner**

Carl Zeiss MicroImaging GmbH, Göttingen, Germany

Tel.: +49 551 5060 660

Fax: +49 551 5060 464

micro@zeiss.de

www.zeiss.de/fluorescence

Fig. 4: Axio Observer A1 is the manual stand (left), Axio Observer D1 the semi-motorised stand (in the middle) and Axio Observer Z1 the fully motorised stand with all options (right).

