From Microscopes to Universal Microanalysis Systems

Microscopy is Getting Easier and More Complex at the Same Time, Conquering New Markets

Much has happened since Abbe and Zeiss started to build microscopes industrially. New technologies manage to surpass the resolution limit defined by Abbe. Today's microscopes are complex technical systems that nevertheless have to be easy to use. This is a chance for microscope makers to open new markets and applications. Andreas Thoß of Optik & Photonik and Gunnar Schroeder, Department Manager Life and Materials Science Microscopy of Olympus Europa, talked about what the future will bring.

LTJ: Mr Schroeder, there have been impressive developments in the field of microscopy, such as confocal microscopy. What was the most important innovation in recent years?

SCHROEDER: In the field of confocal microscopy, an important development certainly is the improved temporal resolution that enables a more accurate observation of life processes, as well as the use of lasers to actively interfere in life processes. Microscope manufacturers are building fast scanners for this purpose. We at Olympus created the unique SIM scanner (Simultaneous Imaging and Laser Manipulation, two independent laser scanners integrated in a single scan head). The SIM scanner represents a substantial improvement of the essential functionalities: active manipulation of processes with a high temporal resolution and better documentation of these fast processes.

LTJ: Microscopy is used in many sectors of industry. Where do you still see new possibilities for applications?

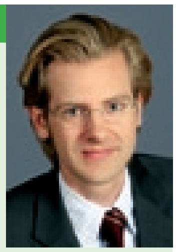
SCHROEDER: I don't think that industrial microscopy growth will depend much on new applications or pushed by outstanding innovations. I see more potential in the ways microscopy is used in established applications and the resulting future developments. A good example is the rising demand for quality assurance processes, especially in car manufacturing – not only because components are getting smaller and smaller, but because quality standards are rising. Service intervals for car engines have lengthened considerably during the last ten years; microscopy is an important factor in this development.

The trend is moving away from traditional microscopes and users whose main interests are optical properties and the resulting microscopic images. We see potential for new business models in analysis systems that provide results based on images, but without the necessity of understanding how microscopy works.

I think there is a lot of potential in this area. Industrial standards are sometimes even supporting this development, for example the ISO 16232 standard that came into effect this year. ISO 16232 deals with the cleanliness testing of automotive components. Microscopy is described as an efficient method for automated particle counting. After testing, the microscopic system automatically determines a standard-conforming degree of cleanliness. The result is based on microscopic images, but how the system actually works is completely irrelevant for most users.

LTJ: All this sounds very exciting. Does this mean that you are focussing on the application and on developing the necessary know-how at your company, so the user can concentrate on

THE PERSON



GUNNAR SCHROEDER

Gunnar Schroeder studied plastics technologies from 1988–1992 at the FH Darmstadt, Germany. From 1991–1994 he worked at the Ciba Vision GmbH in Grosswallstadt, Germany lastly as Leader High Tech. Since 1995 Gunnar Schroeder is working for Olympus. Firstly he started as Product Manager (Semiconductor Inspection Systems). After being Product and Section Manager of Materials Science Microscopy he is now responsible as Department Manager for Life and Materials Science Microscopy at Olympus Life Science Europa GmbH.

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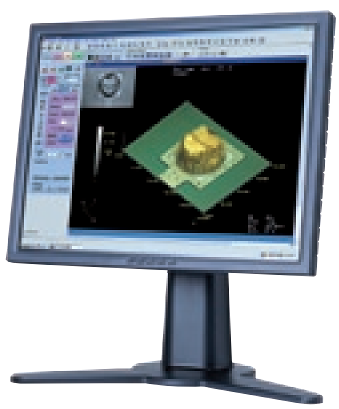

FIGURE 1: **Confocal laser scanning microscope for materials science.**

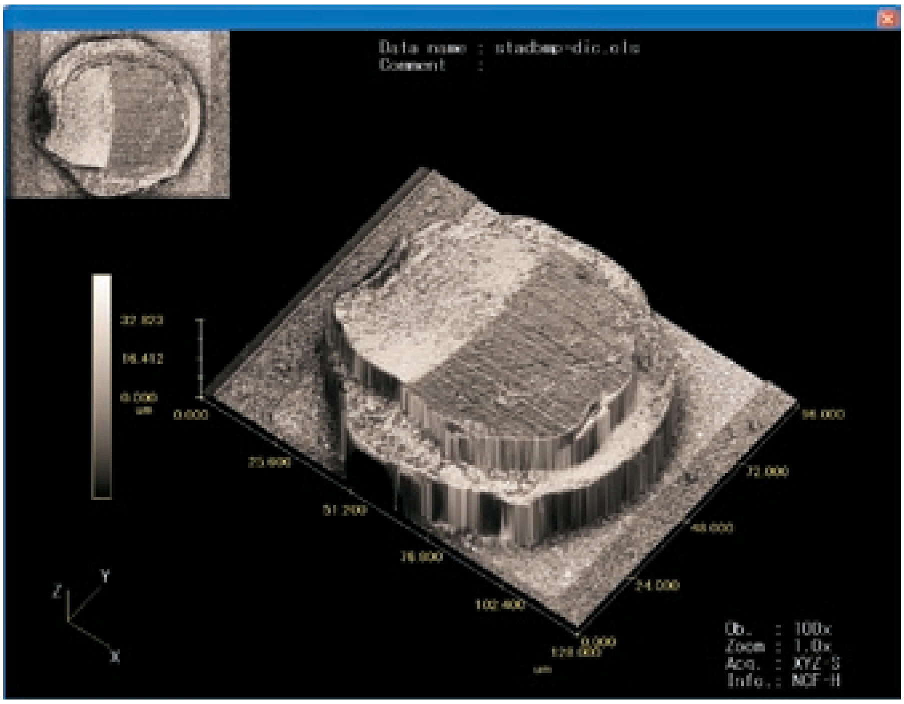

FIGURE 2: **Confocal laser scanning 3-D imgage of stud bump overlayed with confocal interference contrast surface.**

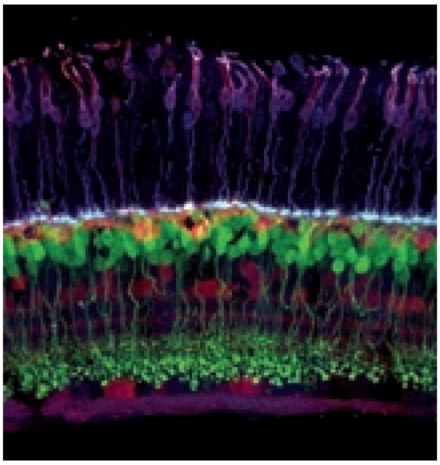

FIGURE 3: **Multi colour confocal image of cortical cell layers of mouse brain.**

THE COMPANY

Olympus Microscopy

Hamburg, Germany

With European headquarters in Hamburg, Olympus is one of the world's leading manufacturers of professional opto-digital products for medicine, science and industry. As a result, Olympus provides a comprehensive range for all market requirements. From microscopes for training and routine tasks to high-end system solutions in the fields of life and materials science, there is a system for every need. The product line is complemented by innovative laboratory equipment for cellular research applications.

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the actual task at hand and does not have to think about the system he or she is using?

SCHROEDER: Exactly. We are basically moving away from what is commonly considered a microscope and towards analytical systems that don't require microscopic know-how. This is how we try to make microscopic technology accessible to new user groups.

LTJ: Can you see possibilities for further development in academic research?

SCHROEDER: The establishment of confocal laser microscopy in materials science is a good example how known light microscope technologies can create new business opportunities if applied smart with a new concept idea.
Confocal laser scanning microscopy is nothing new in itself. We only made it acceptable by focussing on applications in materials science and by developing a product concept geared towards the special requirements of this group of users.

Confocal laser scanning microscopy used to be limited to niche applications. We managed to make this familiar technology accessible to a much larger range of applications. I think this trend will continue, although confocal microscopy, just like any other technology, has its disadvantages as well as its advantages. Scientists want to achieve resolutions as high as possible and to generate as much information on the examined products as possible. Every available method, be it SPM, AFM, interferometry or electron microscopy, has its benefits but also its individual disadvantages. The decisive factor will be how well the various techniques can be combined to overcome the limitations of each individual system.

LTJ: Let's talk about overcoming limitations: The STED technology developed by Professor Hell in Göttingen/Germany is a further step towards an even higher resolution. How much resolution do we need? Are there limits? Is it really useful to push technology forward, to achieve smaller and smaller observable structures?

SCHROEDER: Professor Hell's motivation for developing STED and the lively interest it created show that there is great demand for high-resolution methods. Take for example the visualization of motion processes, of motor proteins. We would need a resolution of 16 nm for that. If we move further down the scale and ask what a protein's crystal structure looks like or how it changes, we would need a resolution in the angstrom range. These examples show that it makes sense to attempt even higher resolutions.

However, STED as a method has its limitations that severely constrict the possibilities for application. The high level of energy affects the specimens, handling is relatively difficult, and image recording is significantly slower, especially when compared to conventional confocal microscopes.

This is exactly where it becomes obvious that lateral resolution is not the be-all and end-all. The crucial task will be to observe living cells in an environment that is as natural as possible. This is going to be an exciting challenge for microscope manufacturers and people like Professor Hell who are working on developing completely new technologies. The goals are not just a high lateral resolution, but also a high z-resolution and especially a high temporal resolution. This means documenting very small temporal intervals, to understand for example protein-protein interactions. Humans on the other hand have relatively long cycles, such as the 24-hour day cycle. This requires to observe a cell for 24 hours under natural conditions which should not change from the first to the last hour. Here is a great opportunity to develop and use completely new technologies for the examination of living specimens in an environment that is as natural as possible. Fluorescence technology for example does not work here, because the high energy of the excitation light interferes with natural conditions.

Bioluminescence certainly is a method with a lot of potential, as it allows the observation of cells for long periods of time and without energy input.

LTJ: Does this mean that you are concentrating on optical microscopy because it allows to work with the living cell, as opposed to X-ray diffraction or electron microscopy?

SCHROEDER: Yes, that is precisely the point.

LTJ: Now a question regarding the economic side of things: How has business been for you in life sciences and material sciences during the last twelve months?

SCHROEDER: Our business has developed according to our expectations; growth has been weak.

LTJ: With the financial crisis everywhere in the media, are you expecting any consequences for your business, your markets?

SCHROEDER: We are expecting considerable repercussions. Budgets are getting tighter, investments are deferred. The effects are felt much faster in the industrial markets than in the scientific sector, because time-to-market periods are significantly shorter. We hope to maintain profits in the coming financial year by introducing new products.

LTJ: What are your expectations for the academic sector?

SCHROEDER: The financial crisis will probably change purchasing criteria. I think that, in the scientific sector as well as in other sectors, there will be much greater emphasis than before on investment protection. Reliability and cost-of-ownership will be much more important than has been the case, especially in science. This concerns top-quality systems such as confocal laser scanning microscopes with investment volumes between EUR 150,000 and 800,000. Everyone who owns such a system today and is aware of the service costs will think very hard and look very closely at the service costs for comparable systems and whether it is possible to save money in the long run.

LTJ: Thank you very much for the interview.

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