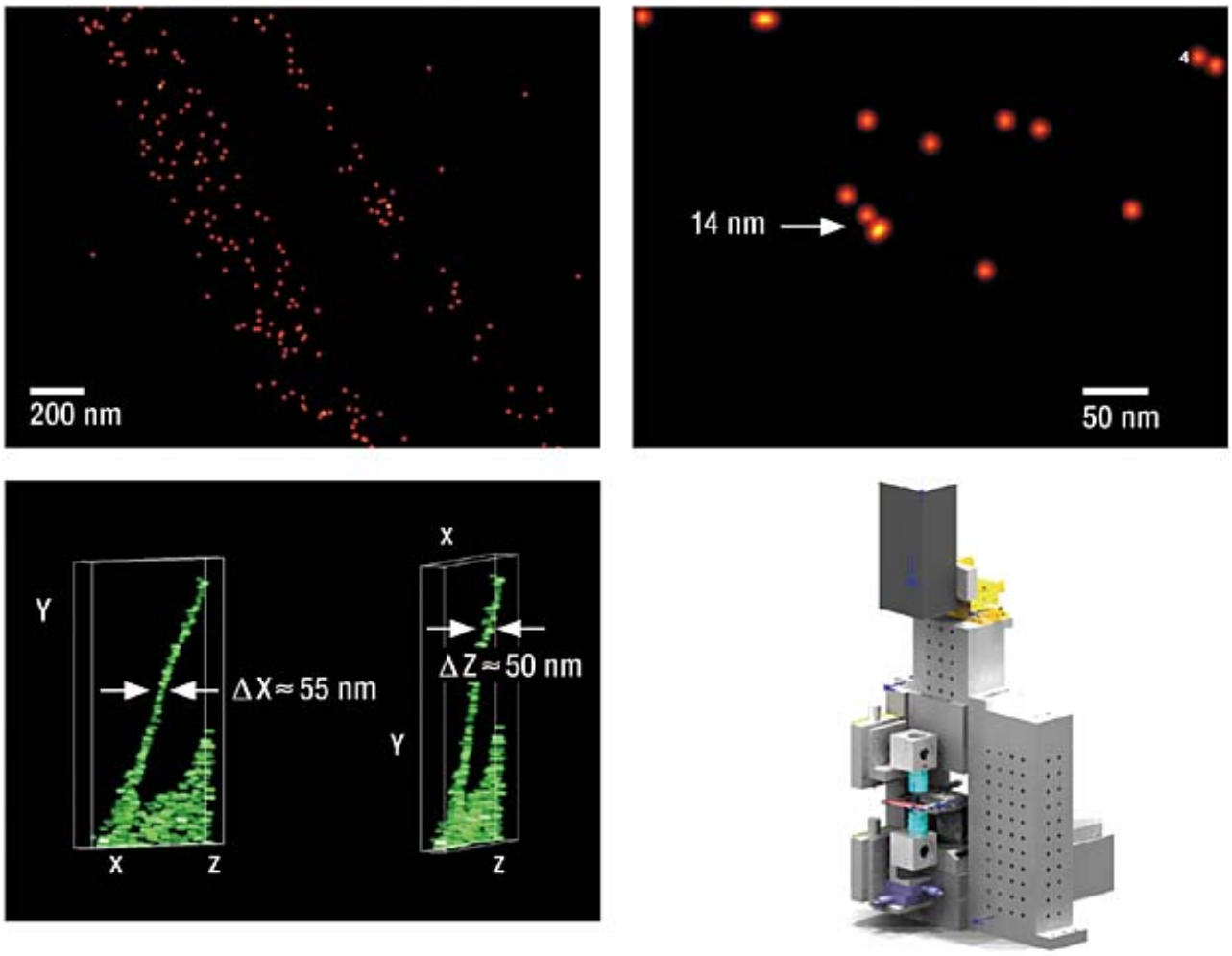
Healthcare industry BW

Living cells in focus

"Very deep, very large, in vivo and above all ultra fast," is how Prof. Dr. Dr. Christoph Cremer of the Department of Applied Optics and Information Processing at the Kirchhoff Institute of Physics at the University of Heidelberg describes the advantages of his optical Vertico-SMI nanoscope. Cremer hopes to use the nanoscope to decipher the molecular secrets of cells. This system is the follow-up to the 4Pi microscopy which he developed in 1971, and is the second development of his scientific career to break through the barrier of what has previously been possible in optical microscopy.

With this invention, Professor Cremer, whose stem cell research project in the "Cell-Based & Molecular Medicine" biotech cluster was one of the five winners in the German Top Cluster Contest, makes an important contribution to the University of Heidelberg's excellence initiative.

"Cremer's nanoscope is a winner for four reasons: first, it enables the investigation of large cell areas with a resolution of up to 10 nanometres; second, it has a very high image acquisition and processing speed which, and this is the third reason, enables the recording of three-dimensional images of entire living cells in real-time. Fourth, common fluorescent dyes can be used. All these are ideal prerequisites for the routine application of the nanoscope," said innovation manager Dr. Andrea Nestl from the Technologie-Lizenz-Büro (TLB) GmbH, which is exploiting the patent portfolio.



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The Vertico-SMI (pictured bottom right) is the first optical nanoscope for routine applications which is fast enough to look at living cells. It enables a broad panoramic view (pictured top left) on fluorescent membrane proteins, combined with a sharp view deep into the cells. It has a resolution 20 times higher than that of normal light microscopes. Molecules with a distance of only 14 nanometres can be clearly differentiated from each other (pictured top right; section of top left picture). The sensational 3D resolution of 50 nanometres shows green fluorescent membrane proteins of a cancer cell (pictured bottom left; recently published in Applied Physics) (Figure: Kirchhoff Institute of Physics, University of Heidelberg)

This innovative, patent-protected method (SMI: spatially modulated illumination) with a sensational resolution of 10 nanometres in 2D and 40 nanometres in 3D therefore has the potential to revolutionise the entire field of molecular biological, medical and pharmaceutical research and can be used for the prevention, risk reduction and therapy of diseases. The Vertico-SMI prototype enables the analysis of living liquid cell cultures in Petri dishes. The appropriate gas atmosphere is generated by an incubation chamber that can be connected to the nanoscope.

Similar nanoscopy methods such as the American developments PALM and SIM/OMX also use far-field microscopy techniques, but they do not have this extraordinary high image acquisition speed, thereby making it impossible to image living cells with high molecule densities. The STORM technology, which was developed in Harvard, can only work with a pH that damages living cells.

Focussing nanoscopy methods such as STED and ISOSTED achieve the fast imaging of small areas, but would take too long to image large areas that can for example be investigated with far-field microscopy, as many images need to be taken of small areas and assembled into a whole.

The Vertico-SMI is the only nanoscope in the world that is able to acquire three-dimensional data of living cells in two minutes. The highly resolved picture is assembled by a computer using several thousand individual images.

The potential applications of such a fast, user-friendly and very robust optical nanoscope go far beyond the limits of biomedical applications. Potential applications include its use in materials research, the quality control of nanocoatings, or in the field of electronics, especially in high-throughput methods because it is possible to detect the tiniest deformations in 3D viewing.

Cremer - pioneering inventions in optical physics

Cremer's scientific career is an ideal combination of knowledge in the fields of optical physics and molecular biology. With the Vertico-SMI, he launched a sensational system that pushed back the barriers of optical resolution.

Back in 1971, Cremer was the first to break through the optical limit of resolution established in 1873 by Ernst Abbe (who defined 200 nm as the theoretical limit of light microscopy; Abbes law), co-founder of Zeiss, when he and his brother Prof. Dr. med. Thomas Cremer (Ludwig Maximilian University of Munich) developed the 4Pi microscopy (DE patent application publication 2116521). The development of the first radiation technique used to create specific DNA damage in surviving cells in order to subsequently identify the function of genes, especially of genes involved in embryonic development, led to a very successful cooperation with Prof. Dr. Christiane Nüsslein-Volhard who received the Nobel Prize in Medicine in 1995. The inventive brothers also made another important intervention: they developed the confocal laser scanning microscope (CLSM) which is used for the analysis of fluorescent objects and which is found in almost all molecular biology institutes around the world.

Prof. C. Cremer is involved in three ongoing excellence projects at the University of Heidelberg. He is also adjunct professor at the University of Maine where he is involved in the establishment of the Institute for Molecular Biophysics (IMB) at the renowned Jackson Laboratory.

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Further information

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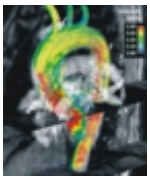

Molecular imaging - a close look inside the human body