

*visions for  
better health care*

**Biophotonics**  
Research Program

FUNDED BY



Federal Ministry  
of Education  
and Research

Funded by the BMBF, the German Biophotonics research program brings together natural scientists, medical scientists, and engineers to realize practice oriented optical solutions for medical applications and life science research. This new column reports on the collaborative research projects, provides event and literature information, and keeps you up to date on trends and meetings in the field of Biophotonics. Connecting economy & science, developers & users – this ranks among the major aims of the funding initiative.



Speaker: Prof. Dr. Jürgen Popp, University of Jena and Institute of Photonic Technology  
E-mail juergen.popp@uni-jena.de

Public relations: Dr. Marion Jürgens, Dr. Andreas Wolff, Clemens Homann  
University of Jena and Institute of Photonic Technology  
E-mail info@biophotonik.org · www.biophotonik.org

## Photoswitches Pave the Way for Multicolour Super-Resolution Imaging

An important progress in super-resolution imaging was recently presented by Prof. Markus Sauer and his work group at Bielefeld University. The scientists introduced a universal and facile method for reversible photoswitching of commercially available Alexa Fluor and ATTO dyes spanning the entire visible range with an optical resolution of approximately 20 nm. The intriguing simplicity of the method facilitates applications and opens avenues for multicolour super-resolution imaging. The refined understanding of the photoswitching mechanism enables for the first time super-resolution imaging in fixed as well as in living cells with standard small organic fluorophores.



Multicolour super-resolution microscopy in living cells is now possible with standard small organic fluorophores. (Courtesy of Bielefeld Univ.)

This work completes the collaborative research project "Superresolution". From Feb 2007 to July 2009, the involved five academic partners successfully synthesized and investigated a series of optical molecular switches for fluorescence microscopy far below the diffraction barrier.

**Publication:**

**M. Heilemann, S. van de Linde, A. Mukherjee, M. Sauer, Super-resolution imaging with small organic fluorophores. *Angew. Chem. Int. Ed.* 48, 6903 (2009)**

## Ibidi Among the 10 Fastest Growing Technology Companies in Germany

ibidi GmbH, a provider of products for cell analysis, is one of the fastest growing high tech companies in Germany. The Munich based company was honored with the German FAST 50 Award by the business consulting firm Deloitte. The award is a ranking of the country's 50 fastest-growing technology companies, based on their percentage revenue growth over five years.

ibidi develops, manufactures and markets cell biochips ( $\mu$ -Slides) and accessories

for cell-based assays. The company's technology was funded by the State of Bavaria and by the German Ministry of Education and Research (BMBF). Particularly within the BMBF priority programs MEMS (BIOM) and optical technologies (Biophotonics), ibidi continues to be involved in collaborative projects.

[www.ibidi.de](http://www.ibidi.de)



The Biophotonics Research Program helped ibidi lay the basics for their series of advanced microslides and cell chambers for live cell microscopy, including this slide for the observation of directed cell motion ("chemotaxis"). (Courtesy of ibidi)

# Observing Living Cells in Their Three-Dimensional Environment

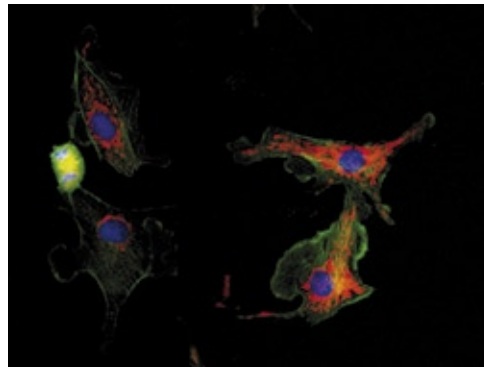
## “3D-Tissue Screen” project lays foundations for further investigation of cardiac arrhythmia and Alzheimer’s disease

Novel insight into the three-dimensional networks of living cells was gained within the “3D-Tissue Screen” research project. With a new microscope for live-cell imaging, the research network was able to observe complex dynamic processes in cardiac muscle cells at an unprecedented speed. This lays the foundation for a better understanding of cardiac diseases. A second microscope setup helped explore the mechanisms of Alzheimer’s more precisely than before.

A better understanding of the causes and mechanisms of diseases is considered as a key to the development of novel, targeted therapies. Here, light microscopy is an ideal tool as it allows to study the functional interaction of molecules and structures in their native environment, i.e. in living cells and tissues. While commercial microscopes are not optimized for automated high-throughput applications in live cell research, the research network has investigated and validated several concepts as a basis for a suitable 3D reader platform. The functional model allows to keep living cells in their native three-dimensional environment by using special cell chambers, to manipulate them e.g. by electrical stimulation, and to observe their behavior in great detail. The concept is tailored for high sample throughput and combines several microscopic technologies, including laser scanning, fluorescence lifetime measurements, and marker-free quantitative phase contrast microscopy using digital holography. Under the guidance of Prof. Dr. Rainer Uhl (TILL Photonics GmbH/LMU Munich), five industrial partners and six research partners contributed their expertise. They could demonstrate the benefits of their novel solutions in a number of applications.

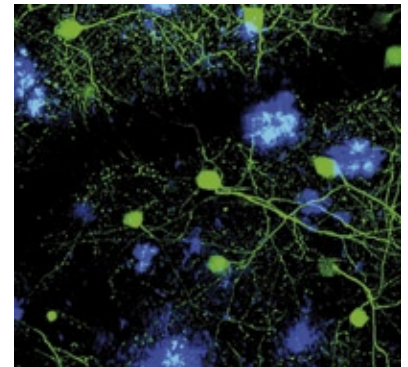
**Understanding cardiac arrhythmia:** At Saarland University, the 3D reader platform was optimized and applied for the investigation of cardiac muscle cells. Using its 3D cell model of human cardiac myocytes, the Institute of Molecular Cell Biology (MCB) explores cellular origins and mechanisms of cardiac arrhythmia in order to find novel approaches for pharmacological therapies.

**Migrating cells:** The three-dimensional movement of red blood cells was observed at the Center of Biomedical Optics and Photonics at Muenster University, using the novel microscope together with a module

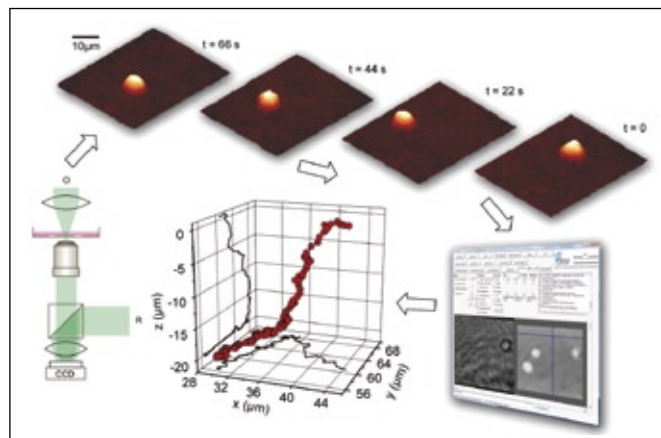


Heart muscle cells imaged with the new reader platform.

(Courtesy of Saarland Univ., MCB)



Amyloid plaques (blue) between the neurons of transgenic Alzheimer’s mice. (Courtesy of LMU Munich, ZNP)



Digital holographic 3D-cell tracking of sedimenting red blood cells.

(Courtesy of Muenster Univ., CeBOP)

for digital holography. This imaging procedure is especially gentle on the cells, as it does not require to treat them with fluorescence markers, and might provide further insights into the directed motion (“chemotaxis”) of cancer cells in the future.

**Alzheimer plaques:** As an additional setup, a two-photon intravital microscope was assembled at the LMU Munich, Center of Neuropathology and Prion Research (ZNP). It enabled the scientists to study mechanisms of Alzheimer’s disease more exactly than before. Now they assume that the characteristic Alzheimer plaques in the brain grow slower than expected so far.

Other applications explored in the course of the project include two-photon endoscopy for intraoperative tissue diagnostics and the investigation of plant root cells for ecological pest control. The research network is active since May 2007. While several partners successfully conclu-

ded their projects in fall 2009, the functional model and its components are still being optimized. After project wrap-up in April 2010, TILL Photonics plans to refine them into a marketable system. The German Ministry of Education and Science (BMBF) has supported the research project with about 3.3 Million Euro; another 2.2 Million Euro were invested by the involved companies.

### List of the 11 project partners:

[www.biophotonik.org](http://www.biophotonik.org)

**Project coordinator:**

**Prof. Dr. Rainer Uhl,**

**TILL Photonics GmbH,**

**E-mail: [rainer\\_uhl@me.com](mailto:rainer_uhl@me.com)**