

1 3-D reconstruction of optoacoustic signals from A549-cells after incubation with magnetite nanoparticles.

2 Nd:YAG-laser utilized for optoacoustical signal generation.

## OPTOACOUSTIC MICROSCOPY

### Situation

Optoacoustic imaging is a new hybrid modality that combines the advantages of acoustics and optics. Ultrasound signals are generated when laser emission is absorbed by intrinsic or synthetic chromophores in cells or tissue. The absorption process generates heat, which causes spatial expansion, which in turn generates ultrasound signals that can be utilized for imaging purposes. Thus the high contrast of optics can be combined with the high resolution of acoustics.

In combination with appropriate biologically functionalized nanoscaled contrast agents, optoacoustic techniques can be used for macroscopic molecular imaging. In order to examine contrast agents on the single cell level, a very high resolution is required. However, contrast agents that are generally applicable for optoacoustics are not necessarily detectable with every microscopic imaging setup.

For this reason, Fraunhofer IBMT has developed an optoacoustic microscope that is intended to bridge the gap between the chemical and biochemical processes in contrast agent synthesis and their actual use in preclinical animal models.

### Solution

For optoacoustic microscopy, a hardware platform is used which is comparable to the acoustical microscopy (SASAM) with respect to signal detection. Images are generated by pointwise scanning of an object and acquisition of the time-resolved high-frequency ultrasound signals generated by the thermoelastic effect. The emission of a pulsed NIR-laser is coupled into the optical path of a microscope and focused onto the sample. Due to the strong focusing even pulse energies in the nano-Joule-range allow to generate ultrasound signals with adequate SNR.

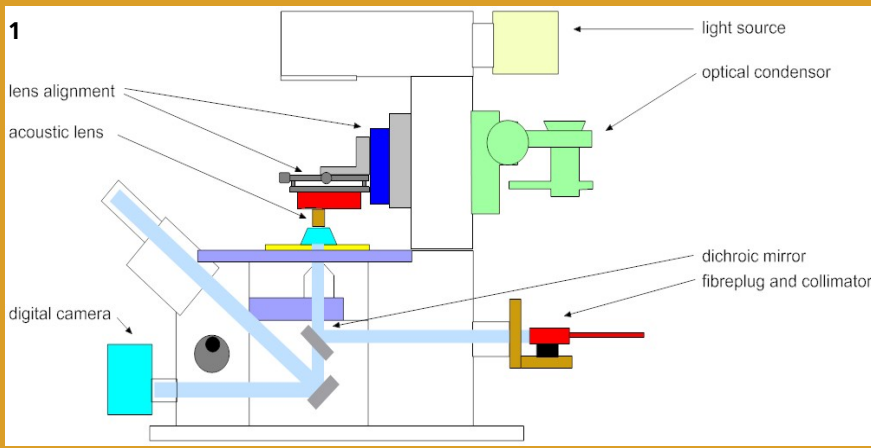
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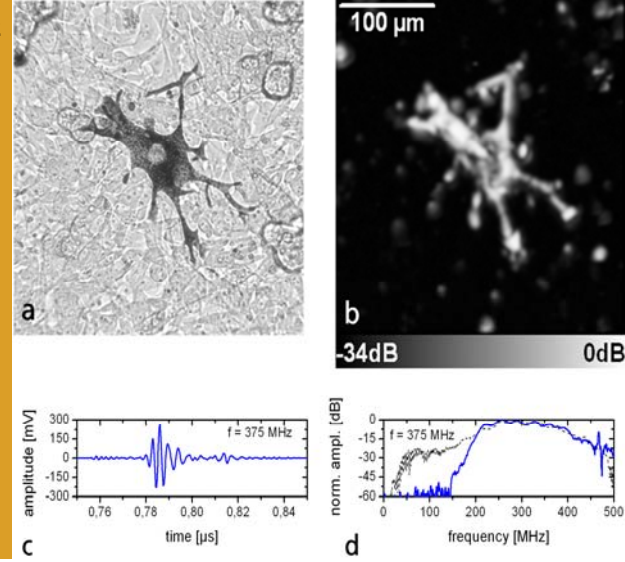
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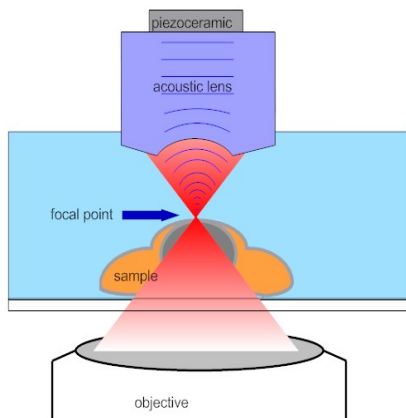
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### Technical data

The optoacoustic microscope developed by Fraunhofer IBMT is based on the SASAM platform.

Acoustic lenses with frequencies ranging from 100 MHz to 1 GHz are utilized for signal acquisition. The system can be used in different imaging modes. A focused and an unfocused imaging mode are selectable for optical excitation as well as for acoustic detection. The optimum resolution of 3 μm is achieved when optical excitation and acoustical detection are performed in a confocal mode.

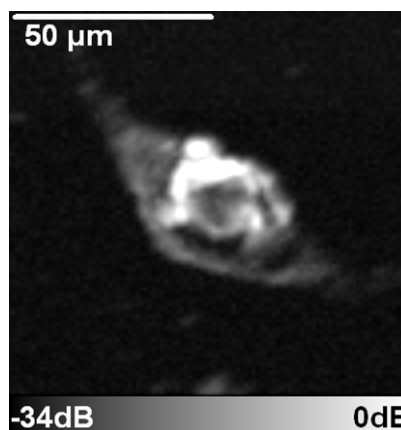
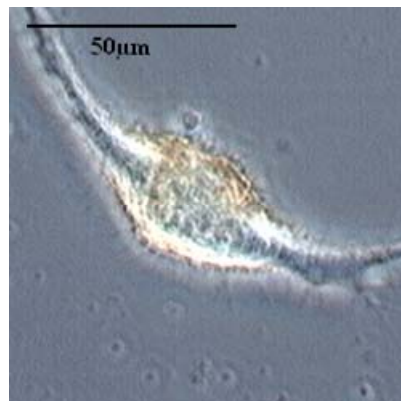


Measuring setup of the optoacoustic microscope operated in confocal mode.

### Applications

Optoacoustic microscopy allows the imaging of intrinsic or synthetic chromophores within a single cell.

Like conventional ultrasound, optoacoustic techniques are scalable in terms of resolution. Structures can be imaged by the same method macroscopically as well as microscopically.



A549-cells after incubation with magnetite nanoparticles (optical and optoacoustical).

Thanks to the high sensitivity for the detection of NIR-absorbing structures, it is possible to visualize nanoparticle contrast agents that can hardly be detected optically as a result of their small size or their low concentration.

Furthermore material or tissue properties like the absorption coefficient  $\mu_a$  can be detected with subcellular resolution.

Optoacoustic microscopy can attend the development of new nanoparticles and characterize their usability as molecular contrast agent for macroscopic optoacoustic imaging.

1 Setup of the optoacoustical microscope as add-on module for an inverted optical microscope.

2 Optical (a) and optoacoustic image (b) of a single B16F1-cell (melanoma). High-frequency optoacoustic signals of the cell, time-resolved and frequency-resolved (c, d).