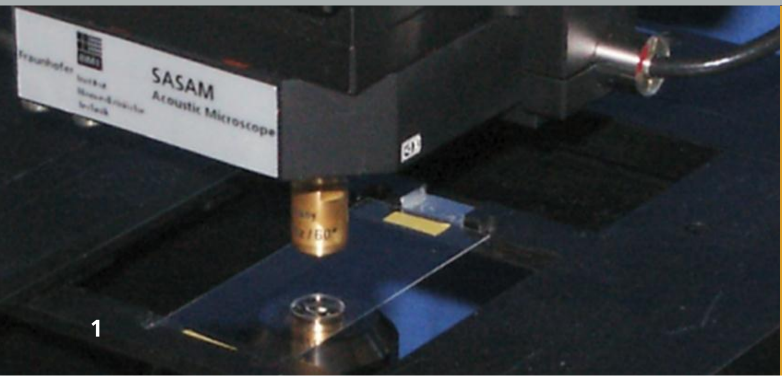
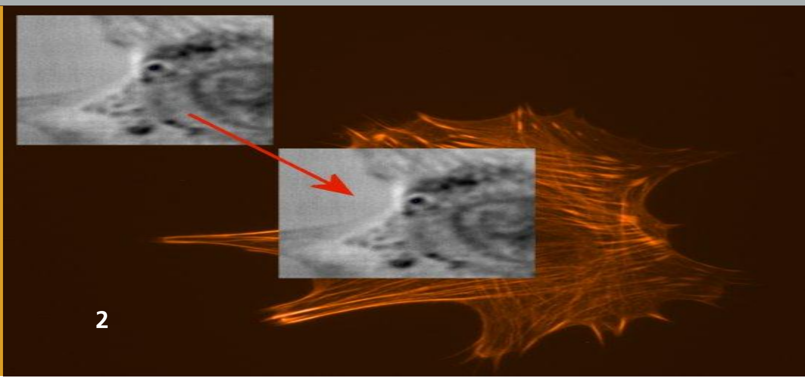
FRAUNHOFER-INSTITUT FÜR BIOMEDIZINISCHE TECHNIK IBMT





1 Measuring Head of the SASASM-Microscope consisting of Piezo-scanners and a GHz-lens

2 Superimposition of optic and acoustic images of a cell

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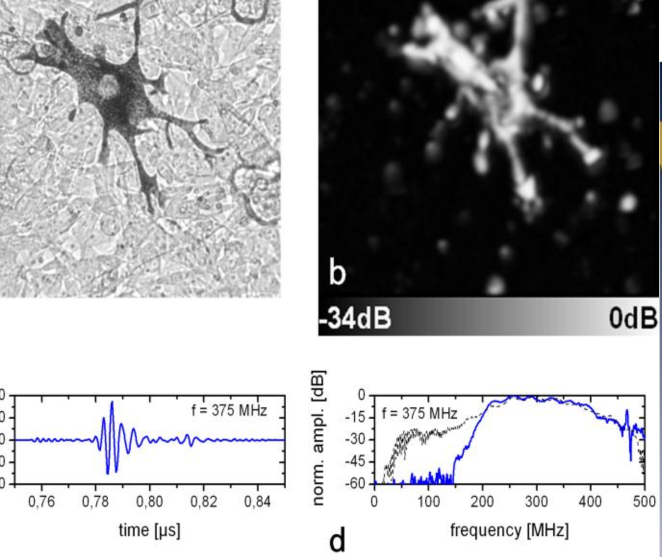
TIME-RESOLVED ACOUSTIC & OPTOACOUSTIC MICROSCOPY

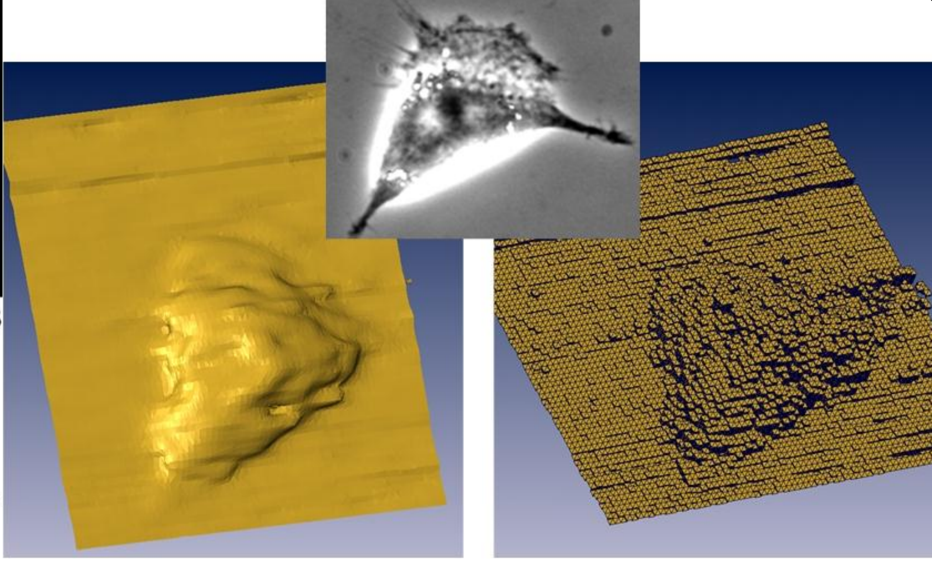
Situation

The interrelation between biochemical and mechanical properties of cells during processes like apoptosis, proliferation or migration is of fundamental interest to biological and medical research.
While it is possible to sample the biochemical properties of cells or tissues by optical microscopy methods, high-frequency ultrasound allows to examine their mechanical properties.
To utilize the advantages of both methods, the Fraunhofer IBMT developed an acoustical microscope that is integrated into an inverted optical microscope. This setup allows to capture the optical and the mechanical properties of cells synchronously.
Furthermore, IBMT´s acoustic microscopy technology can be modified for optoacoustic imaging. In this hybrid technology, acoustic signals are generated by absorption of short laser pulses in cells or tissue. In conjunction with appropriate nanoscale biologically functionalised contrast agents, optoacoustics can be used for molecular imaging.

Solution

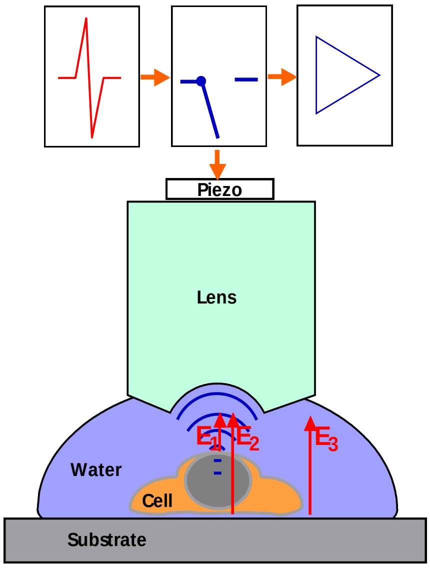
In acoustical microscopy short ultrasonic pulses are generated and focused unto the sample by an acoustical lens. When hitting the sample, the pulse is partially reflected by the sample and its substrate. The reflected ultrasonic pulses are acquired by the same lens that is focusing the original pulses.
The reflected ultrasonic waves are amplified and then digitalized by fast AD-converters.
In the optoacoustic mode, pulsed NIR-laser light is coupled into the optical path of the microscope and focused unto the sample.
Due to the strong focusing even pulse energies in the nJ-range are sufficient to generate detectable ultrasonic signals.





Technical Data

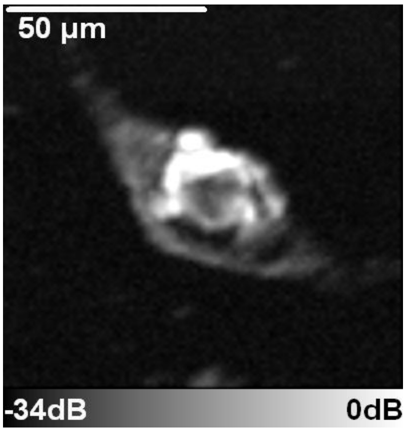
Digitalization with up to 8 GSamples/s,
lateral resolution down to 1 µm,
at a frequency of 1 GHz,
image range scaleable from
50 µm up to 50 mm



A short ultrasonic pulse is focused unto the sample. Different signal components are reflected by the sample and by the substrate.

Different Applications – cell imaging

Regulation of cell volume is an essential mechanism of homoeostasis. It is also of vital importance for various physiological processes, like for example for the coordination of transepithelial transport, or for gene expression.
In acoustical microscopy the local height of a cell can be calculated from the signal run-time difference between the echoes of cell and substrate at known speed of sound. With sufficient sampling it is possible to reconstruct the three-dimensional cell morphology and to calculate the cell volume.
Since in acoustical microscopy there are only very low sound levels in the lens focus it is considered to be a non-invasive method that leaves the examined cells undamaged.
A further preparation of the sample, i.e. a staining, is not required. So, the method is suitable for long-term measurement.



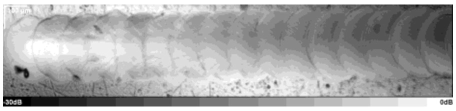
Optoacoustic image of A549 cells after incubation with magnetite nanoparticles

In optoacoustic imaging, the distribution of intrinsic chromophores or contrast agents within a single cell layer can be imaged with sub-cellular resolution. Due to the high sensitivity for the detection of NIR-absorbing structures it is possible to visualize nano-particle contrast agents that are difficult to detect optically due to their small size or their low concentration.

Material testing

Acoustical microscopy is suitable for various high resolution non-destructive material testing applications, including:

- Detection of delaminations and inclusions
- depth-resolved imaging of defects
- local measurement of elasticity
- Determination of porosity
- Measurement of layer adhesion
- Characterization of polymers



Visualization of welding seams by means of a 300 MHz –lens (total width 15mm)

Compared to other methods, acoustical microscopy provides the advantage of completely non-invasive and non-destructive probing.

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

2 *three-dimensional reconstruction of the cell surface based on high resolution acoustic microscopy signals.*