BioMed
BioMedizinisches
Technologiezentrum
TECH

Label-Free Cell & Tissue Characterization

medizinische fakultät
Westfälische
Wilhelms-Universität Münster

WWU
MÜNSTER

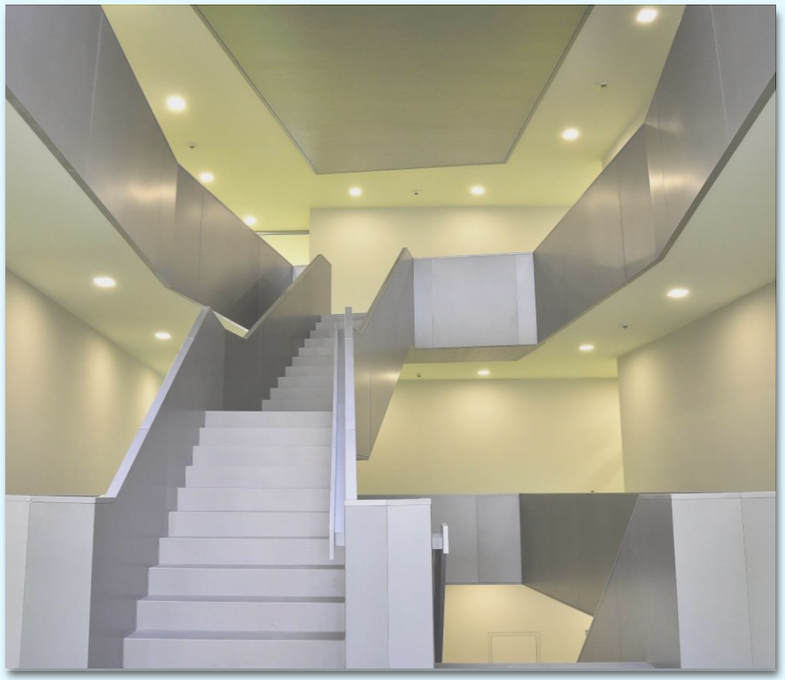
Label free optical imaging

Get new sights on your cells

Label-free optical technologies are enabling methods for numerous biomedical, industrial and healthcare applications.

Label-free imaging allows the individual and native characterization of cells & tissues.

The Biomedical technology Center (BMTZ) is closely linked to the clinics and institutes of Muenster University Hospital and connected with various national & international research institutions.



Label-free imaging at BMTZ

- Quantitative Phase Imaging - QPI
- Optical Coherence Tomography - OCT
- Holographic Tomography - HT
- Multispectral QPI
  - from visible to near-infrared light

Application areas

- Label-free Bio-Imaging
- Toxicology Screening
- Tumor & Cell Biology
- Nanostructure Analysis
- Biotechnology
- Industrial Cooperations
- Technology Transfer

Label-free imaging concept

- Fast, easy and markers without additional costs.
- Uses intrinsic material markers.
- Based on biophysical cell & tissue properties with parameters as refractive index, light scattering, reflection, dry mass & volume.

Label-free imaging advantages

- Direct access to cell & tissue phenotypes and patho-physiological alterations.
- Native cell & tissue analysis – no fixation or staining required.
- Non-destructive and non-invasive – samples can be further analyzed with other analytical methods.
- Methods are complementary and can be combined with bright-field & fluorescence microscopy.

Microscopic Technologies

The **Biomedical Technology Cente**r (BMTZ) is a unit of the Medical Faculty of the Westfaelian-Wilhelms-University and provides most modern technologies for cell and biomedical research, photonics and nanotoxicology. It forms a core unit of the NanoBioanalytik Center (NBZ), an association of the Muenster Economic Development Agency, analytical companies and the medical faculty of the University of Muenster

The BMTZ has broad experience in the development and evaluation of innovative optical technologies for life sciences, drug screening & diagnostics with medical, industrial and pharmaceutical partners. Main competence is the label-free & non-invasive characterization of diverse cell types and tissues. BMTZ has a unique interdisciplinary team of biologists, physicists, engineers, physicians and chemists and leading expertise for high-resolution, label-free digital quantitative holography processes.

Accredited biomedical Laboratories
_ biosafety level BSL-1
_ Genetic-Engineering safety level 1 (S1)
_ industry audited

Standard Operating Procedures (SOPs)
_ standardized SOPs for imaging, cytotoxicity & immunology testing
_ individual SOP development

Sample Preparation
_ individual and standardized preparation of *ex vivo* samples
_ technology targeted samples and standards (OCT, Raman, Infrared-Spectroscopy)

Instrument development and manufacturing
_ Development and manufacturing of standardized or customized QPI systems.

Software and algorithm development
_ Python-based algorithm and software development for image acquisition, reconstruction & evaluation.

Microscopic Technologies

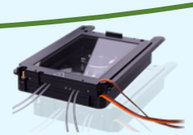
Characterization of cells & tissues

Systems for:

- standard light & fluorescence microscopy
- **holographic** and **tomographic** imaging systems
- **live-cell imaging** with stage top incubator systems
- quantitative evaluation of label-free image data (customizable)
- single cell analysis, **high throughput** and **high content screenings**

Compliant technology (GxP, ISO, FDA)

- multi-parametric analysis of unstained cells & tissues
- automated data acquisition
- application development & validation
- customized optical solutions
- cell culture quality check



Multiparametric cell analysis

QPI - Quantitative Phase Imaging

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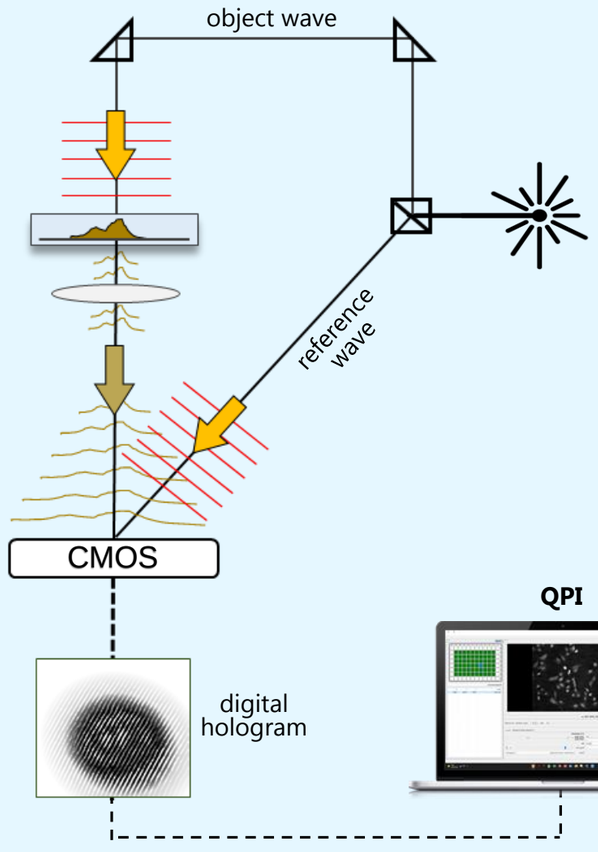
Label-free quantitative microscopy

Quantitative phase Imaging (QPI) allows non-invasive & label-free optical visualization & quantification of biophysical parameters of living cells & tissues with minimized efforts on sample preparation. QPI based on DHM microscopy, as developed at BMTZ, generates high-contrast and information-rich images by measuring changes of the optical path length delay changes of light that passes through transparent biological specimens. The resulting interference pattern or hologram includes information about sample morphology, density and optical properties such as the refractive index (RI).

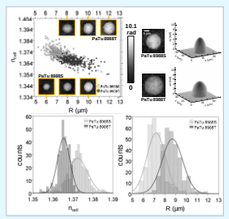
Automated QPI system can be used for kinetic cell characterization and phenotyping. The marker-free imaging technology shows the native, unaffected state of the sample. QPI is a versatile tool for long-term cell studies as no staining is required and due to the imaging concept, the interaction with the sample is minimized (low light exposure, no phototoxicity).

KEO one
QPI-system

Principle of QPI



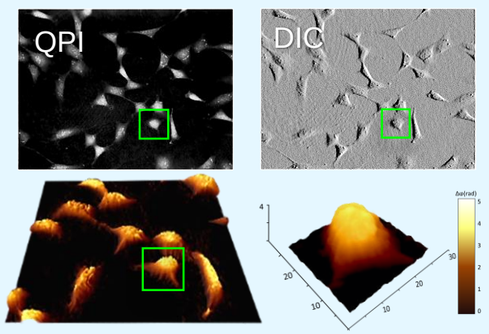
3D images & parameters



Biophysical cell parameters of QPI

- volume
- dry mass
- refractive index (RI)
- morphology
- density of cells & tissues
- thickness

NIH 3T3 cells



3D plot

Features

- non-invasive & label-free
- full-field imaging
- fast single shot
- base for automated segmentation and 2D/3D single cell tracking
- post acquisition refocusing
- HTS & HCS
- physiological
- cost and time-efficient

QPI - Quantitative tool for **native** cell analysis

Holotomography

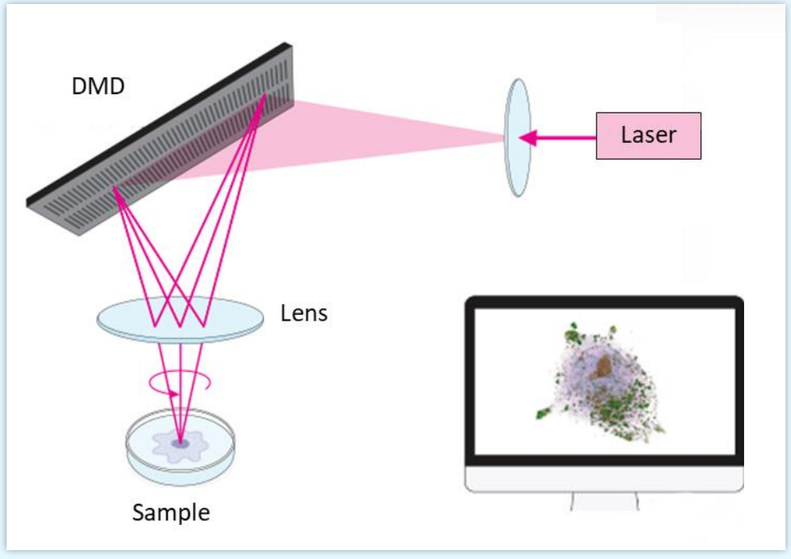
Holotomography for label-free 3D cell imaging

The technology of holotomography is a laser-interferometric QPI-technology for 3D imaging of single cells, cell popuation and tissues.
Biophysical parameters such as volume, refractive index or dry mass are spatially recovered.

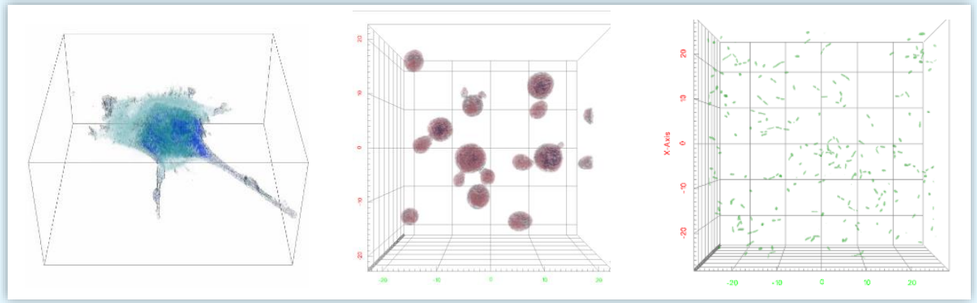
Principle:

Multi-angle illumination by using a digital mirror device (DMD) is utilized to acquire hologram series from which refractive index tomography are reconstructed.

Principle of Holotomography



Exemplary applications



Biophysical Parameters

morphological

- volume
- surface area
- projection area
- sphericity

biochemical

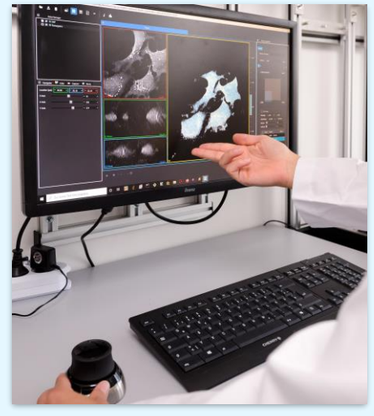
- dry mass (pg)
- Hb conc. red blood cells

mechanical

- cell stiffness
- membrane fluctuation

Features

- Non-invasive & label-free imaging
- 3D visualization of cells/tissue sections
- Refractive Index (RI) determinations
- Automated stiching of areas
- Analysis of cellular interactions
- Cost & time-effective
- TomoStudio visualization & analysis software



Optical Coherence Tomography (OCT)

OCT 3D imaging of cell clusters, tissues & animals

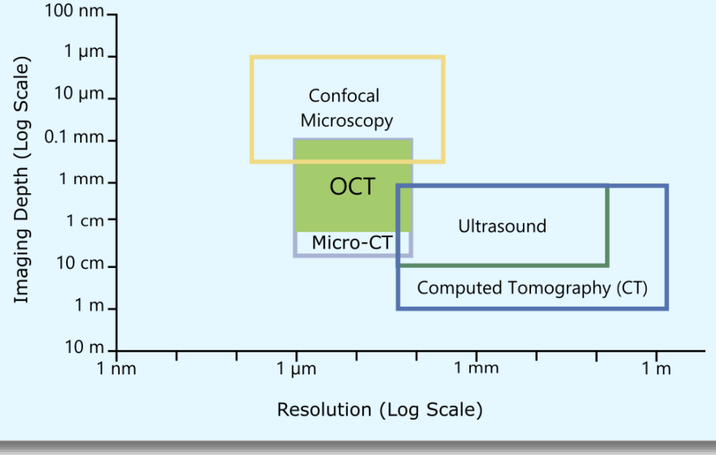
BMTZ research on biomedical applications with label-free optical methods includes investigation of partly transparent samples with OCT imaging. OCT is a non-invasive and non-destructive imaging technique that provides real-time, 1D depth, 2D cross-sectional and 3D sub-surface volumetric imaging of structural features with micron-level resolution.

OCT images are generated by detecting light that is backscattered or reflected from the different interfaces inside the sample. Thus, it is ideal for investigations on semitransparent samples.

Daphnia magna (juv.) with microspheres

Features

OCT bridges the resolution gap between confocal microscopy and ultrasound imaging



OCT at BMTZ

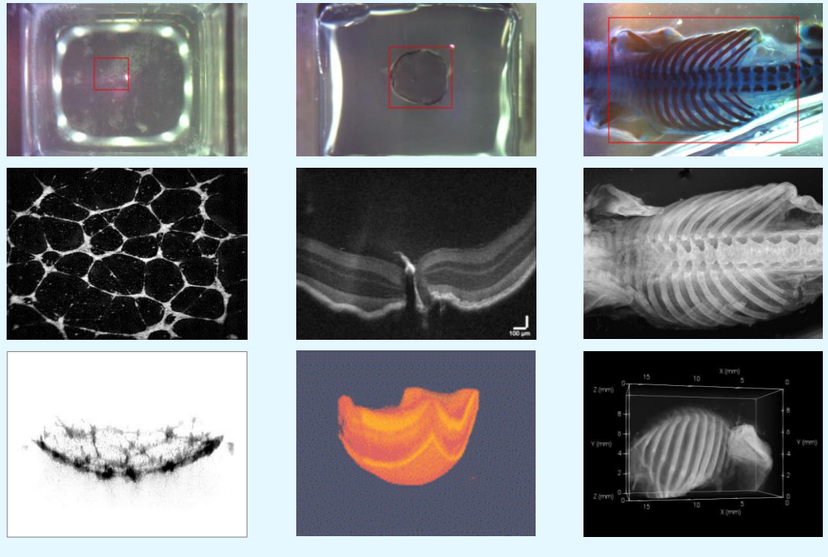
- State-of-the-art high resolution OCT system
- No specific sample preparation required
- Flexible probe head

Application support

BMTZ has broad application experience investigation of biological samples and materials with OCT and in the preparation of in-vitro and in-vivo models for OCT imaging.

From the analysis of samples with commercial state of the art OCT systems to the development of test standards for OCT imaging. BMTZ offers our expertise and support with individually tailored solutions.

Exemplary applications

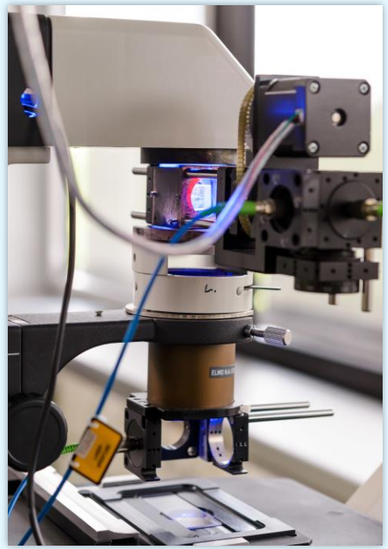


HUVECs cells in 3D Matrigel | Murine retina tissue | Rat skeleton

Multispectral QPI

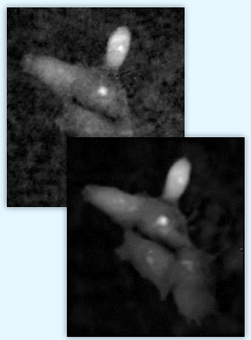
Quantitative information from the visible to the infrared range

QPI combined with spectrally broad emitting super continuum laser sources and fast continuously tunable acousto-optic tunable filters (AOTFs) enables the analysis of biological samples at different wavelengths from the visible (VIS) to the near infrared (nIR) spectral range.
This feature extends QPI to spectroscopic phase microscopy, e.g. for investigations of partially absorbing samples in histopathology and for determining the chromatic dispersion of biological cells and particle properties.

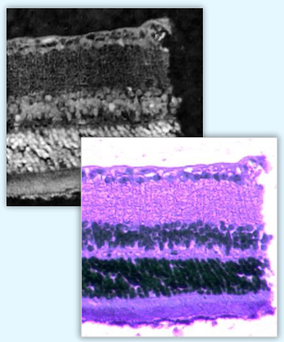


Exemplary applications

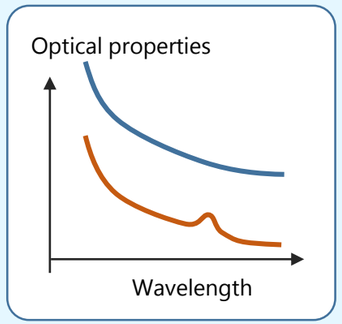
Noise reduction



Histopathology



Chromatic analysis



Unique features

- Multispectral imaging in the wavelength range: l=500-1700 nm
- Correction of chromatic aberrations by numerical refocusing.

Multispectral (VIS-nIR) QPI

Our Services: Measurements, Research & Development for Science & Industry

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Label-free imaging technologies at BMTZ :
advanced access to phenotypes of cells, tissues & small organisms

We offer

- Measurements and collaborations with BMTZ available label-free imaging systems.
- Evaluation of samples and research interests to find the most suitable imaging solution.
- Development of sample preparation and standardization methods, targeted to specific needs.
- Consulting and arrange contacts to external imaging partners from our network for additional technologies.
- Setting up or participate in new projects involving biomedical label free imaging methods.
- Customized OEM QPI systems for various microscopes and suitable biomedical instruments.
- Contract research & development for industrial partners.
- Evaluation of new imaging technologies for biomedical applications and targeted customer needs and requirements.

Funded Projects

Cooperation Partners

Applications

Cellular Processes

- Cell adhesion
- Cell confluence
- Cell viability
- Cell proliferation
- Cell water content & osmotic processes
- Cell morphology
- Cell-cell interactions

Cellular Processes

- Migration & Invasion
- Wound Healing
- 2/3/4D Cell Motility
- Apoptosis
- Phagocytosis
- Long term live-cell imaging
- Cytotoxicity

Phenotypic Assays

- Cardiomyocyte function
- Macrophage particle uptake
- Endothelial tube formation
- Tissue density & structure
- Inflammatory processes

Application Fields

- Oncology
- Immunology
- Neurobiology
- Angiogenesis
- Dermatology
- Regenerative Medicine
- Stem Cell Research
- Microbiology

Application Fields

- Liquid biopsy
- Blood testing
- Drug response
- Toxicity testing
- Nanoparticle analysis
- Cell Culture Quality Management
- Environmental toxicology

Keep in touch with us

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