

Zentrum für Optische Technologien

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Optik Technologie



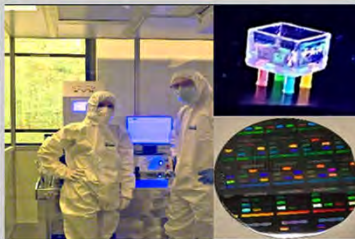
- Roboterbasierte
 - Polierverfahren
 - Messverfahren
 - 3D-Druckverfahren
- Prozesssimulation
- KI-Methoden
 - Prozessregelung
- Prozessmesstechnik

Licht - Materie Wechselwirkung



- Ultra-kurze Laser pulse
- Zeitaufgelöste Spektroskopie
- Nichtlinear Frequenzkonversion

Mikro- & Nanophotonik



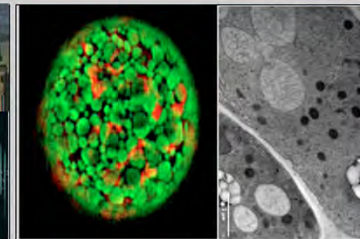
- Additive Fertigung
 - μ -Projektions Stereolithographie
 - Ink-Jet Druck
- Nano-Imprinting Lithographie
- Dielektrophorese
- Neuronale Netze

Vision Research Lab



- Wahrnehmung
- Fahrsimulation
- dynamische, sinnesmodalitätsübergreifende Erfassen des Explorationsvermögen

Bio-Photonik



- Visualisierung von Zellmechanismen von μm bis nm :
 - Fluoresz.mikroskop.
 - Korrelative Licht- & Elektronen-mikrosk.
 - Kryo-Tomographie
- Data Handling

Opto-Elektronik

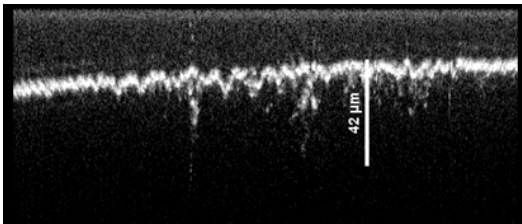


- Optoelektronische Komponenten
- Elektronische Messtechnik
- Sensorik

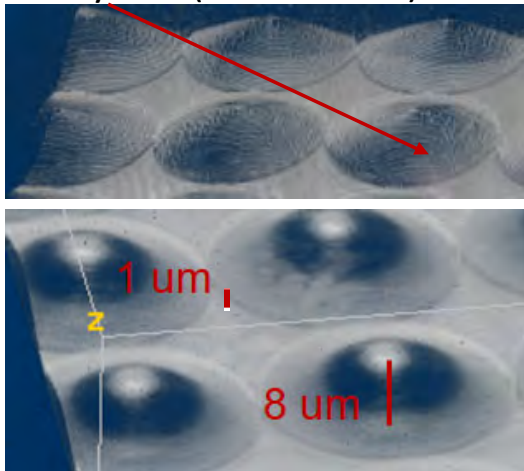
Analyse / Simulation

- Themenfeld 1

- Optical Coherence Tomography
- Ziel: Tiefenschädigungen beim Schleifen (Bsp Schleifen D64)

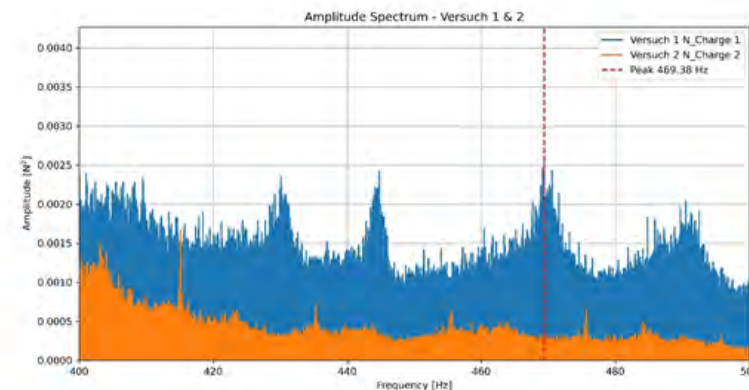


- Nano Scribe Layers? (AG Heinrich)



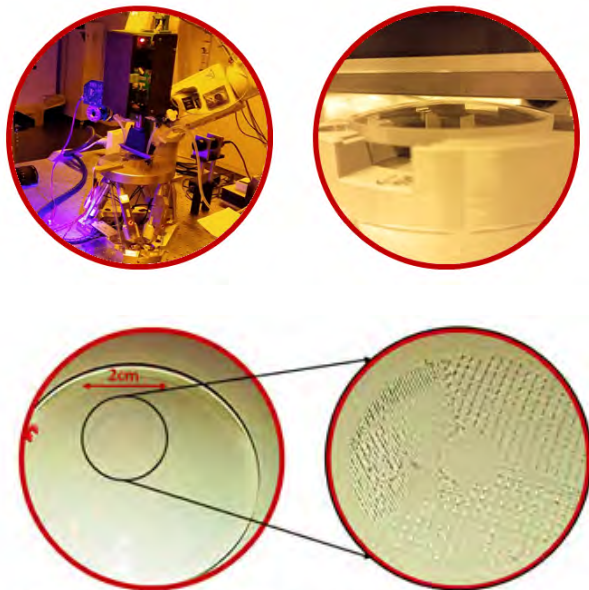
- Themenfeld 2

- Untersuchung Polierspalt
- ULE Optik mit Sensorik (Kraft, T, ..)



- Gute (orange) und schlechte (blau) Poliermittelchargen sind in Analyse Kraftdaten unterscheidbar
- Polierpads und Poliermittel in Temperaturdaten unterscheidbar

- Themenfeld 3
 - 3-D Druck Mikrolinsen mit AG Heinrich

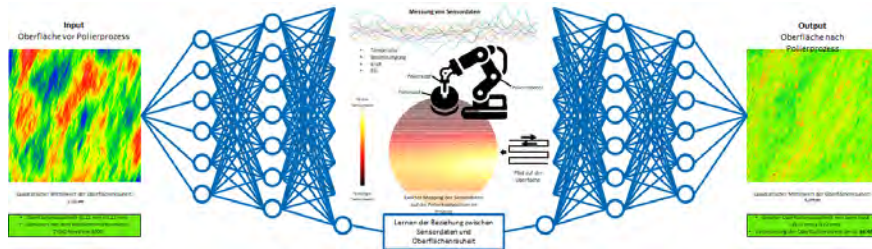


- Druck von Mikrolinsen auf Brillengläser
- Aktuell kleinstmögliche Auflösung 200 μm

- Themenfeld 4
 - Multi Aperture Positioning System (MAPS)

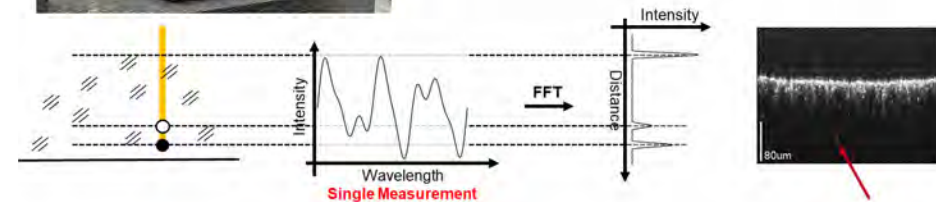


- Arbeitsgruppe Rainer Börret: Optik Technologie
 - Optimierung von Polierprozessen durch den Einsatz von Künstlicher Intelligenz



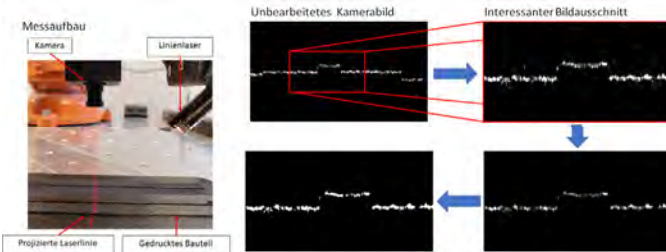
Optische Kohärenz Tomographie für Industrielle Anwendungen

- Zerstörungsfreie Messung von Optiken
- Defektanalyse in Halbleiteroptiken
- Beschleunigung von Fertigungsprozessen



Themenbereich
 (3 Doktoranden, 4 Duale Master, 2 Abschlussarbeiten)

- Massenstrommessung mit Lasertriangulation

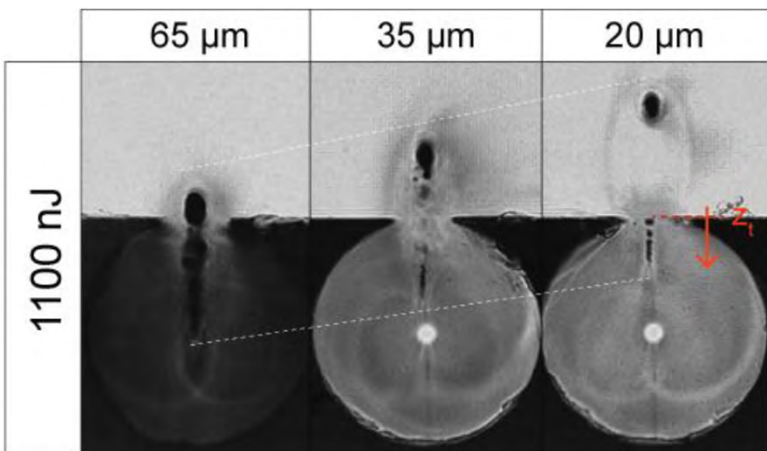


- Kraft- statt druckgesteuerter Roboterpolitur

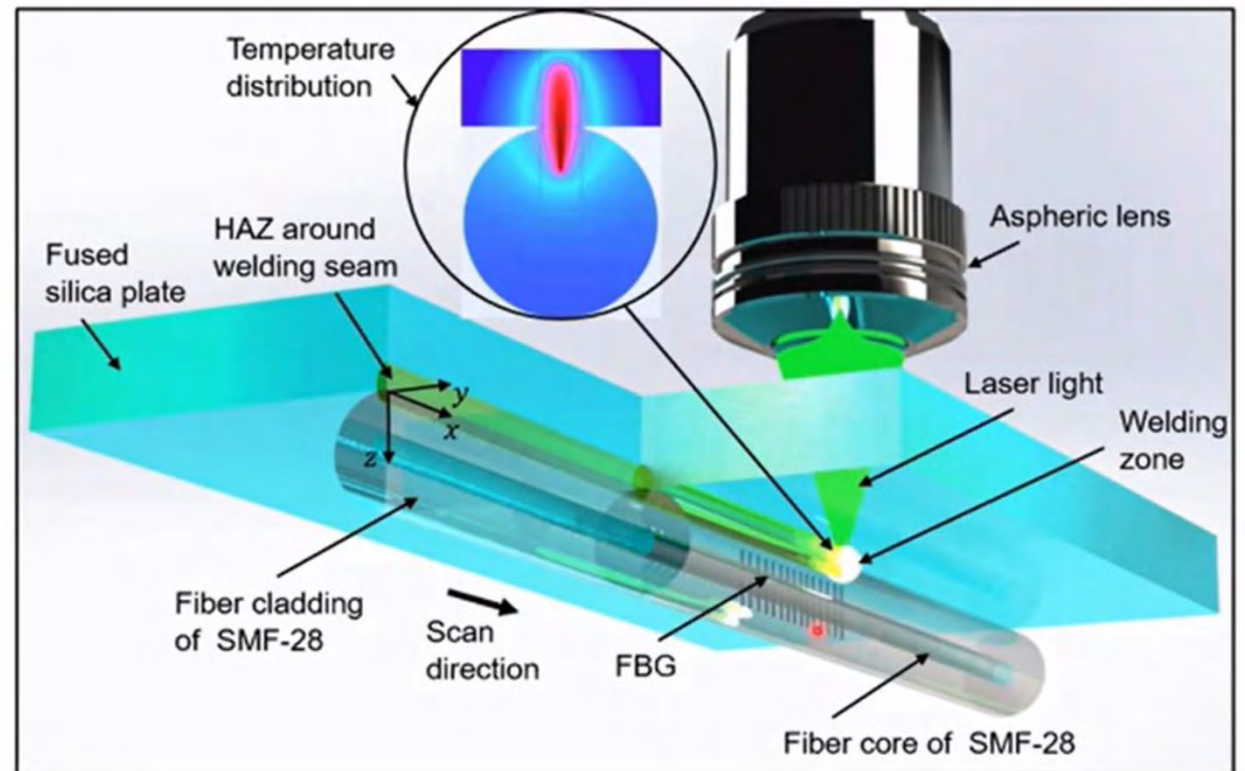


• Bulk-Fiber

- Focussing through a glass plate into the fiber
- Z-variation is critical:
- 125 μm fiber welding



Literatur



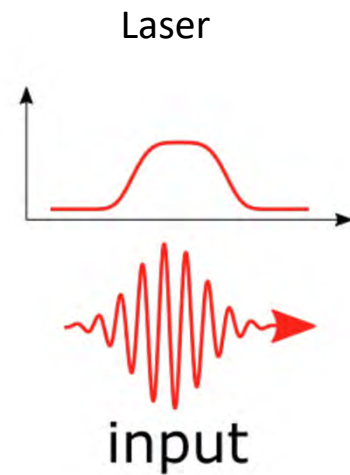
Vorobyev, Oleg B., et al. "Femtosecond laser welding of silica glass fiber for robust Bragg grating sensing in high temperature environment." *Frontiers in Ultrafast Optics: Biomedical, Scientific, and Industrial Applications XXI*. Vol. 11676. SPIE, 2021.



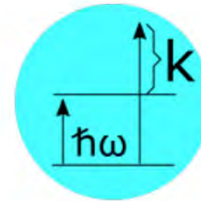
Research-Ma
Julian Jakob



Ma-Student
Cornelia Bauer



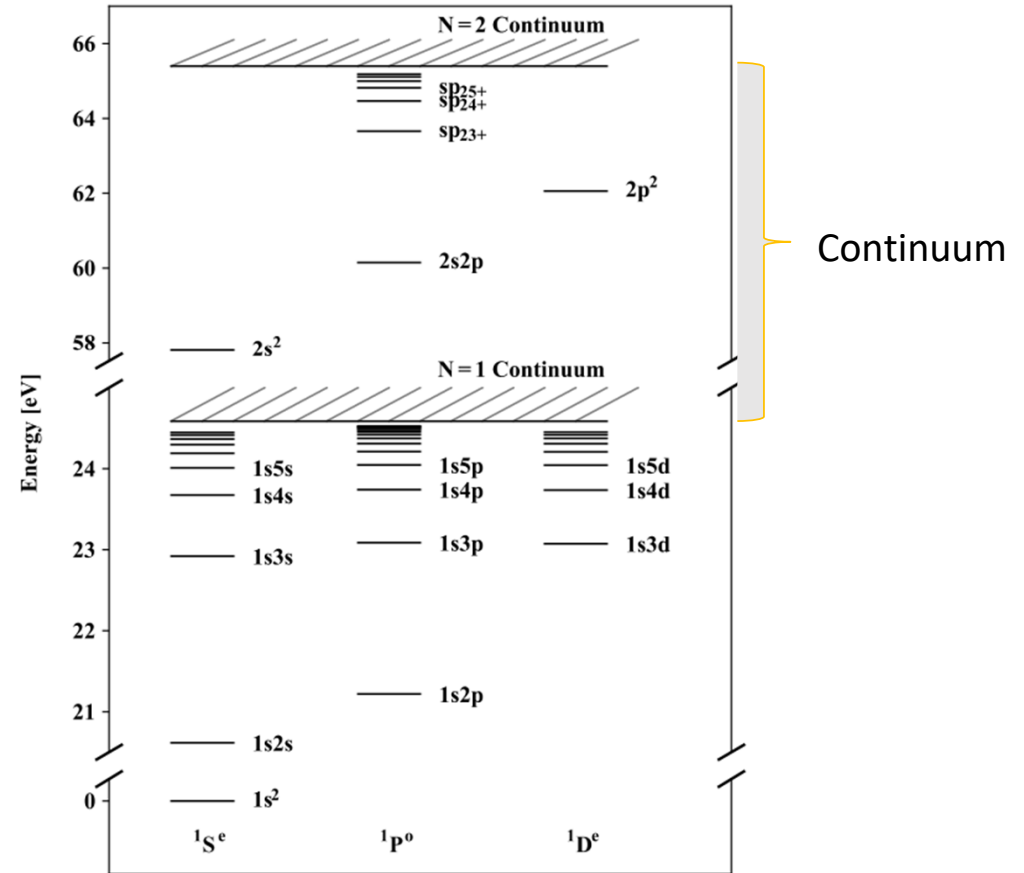
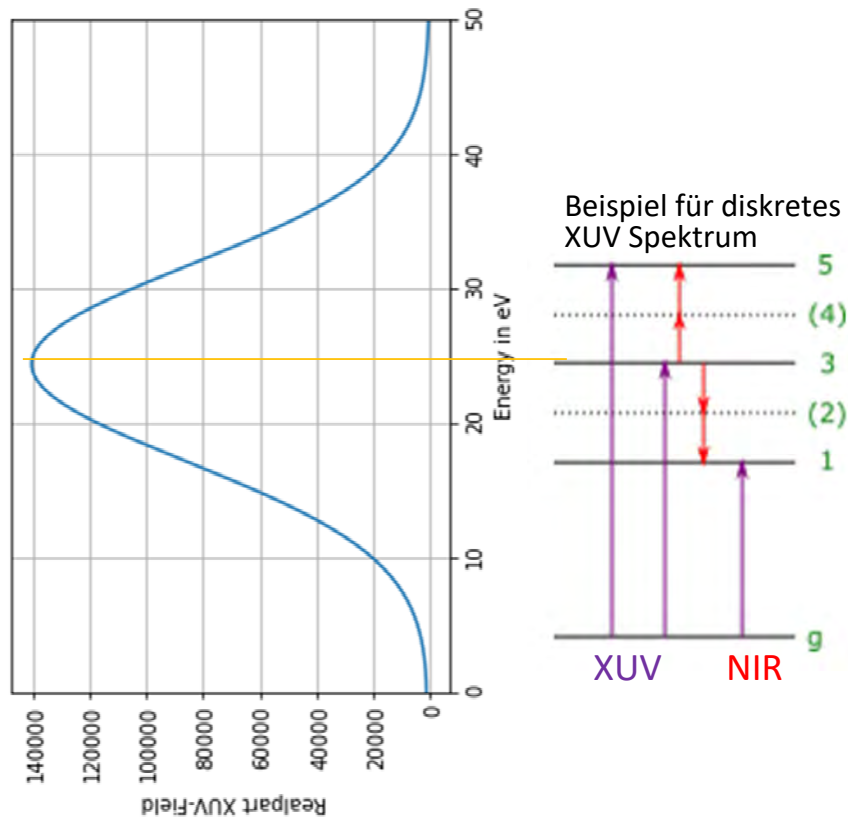
System



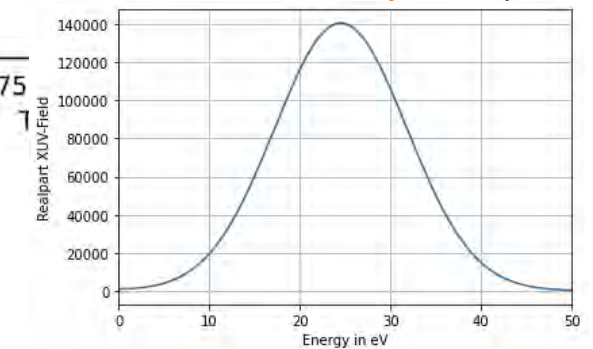
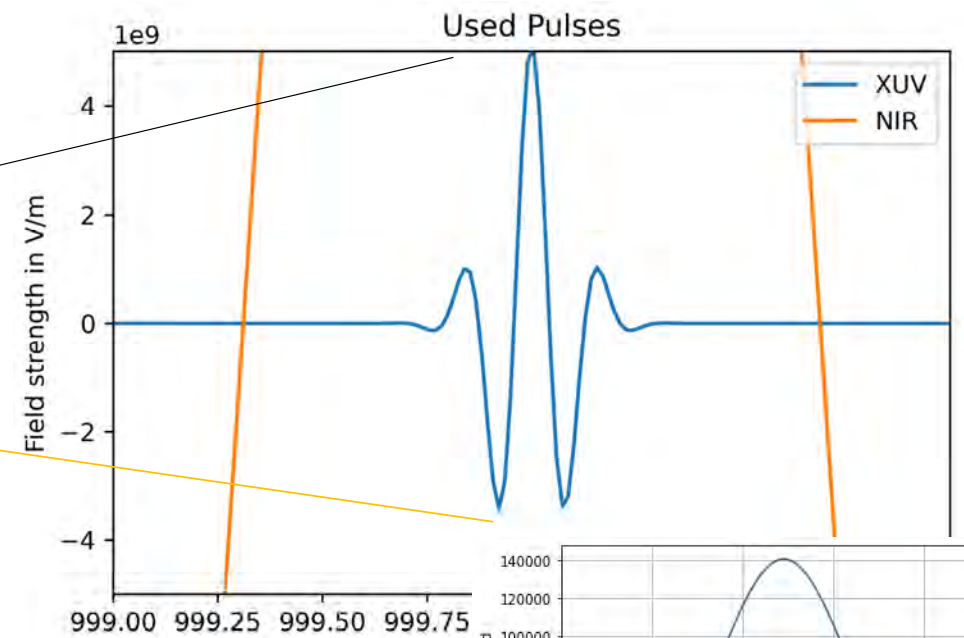
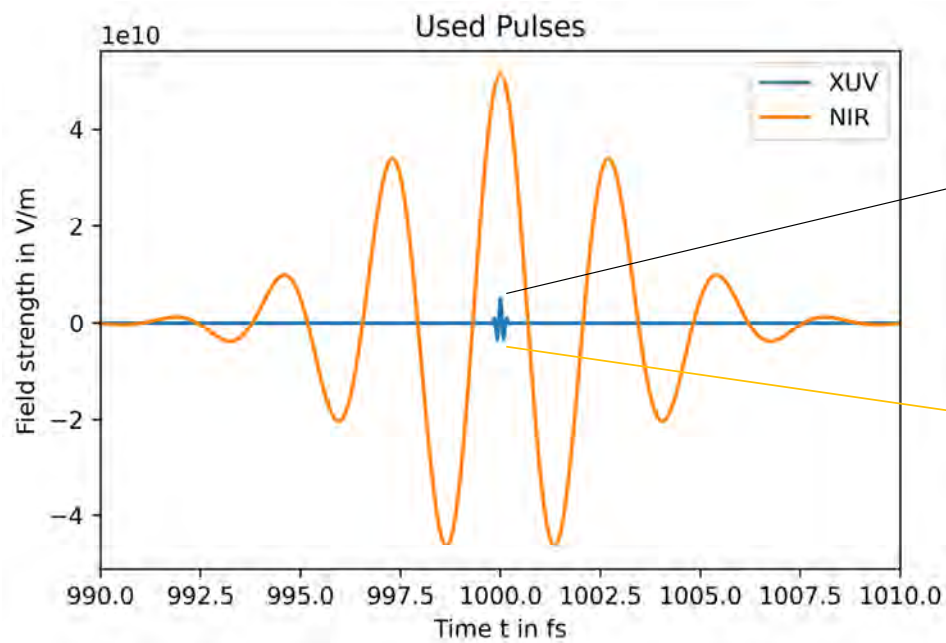
$$P(t) = \text{tr}\{\mu\rho\}$$

$$\sigma(\omega) \propto \frac{\omega}{c} \Im \left(\frac{P(\omega)}{E_{in}(\omega)} \right) \propto \frac{\omega}{c} \Im \left(\frac{FFT(P(t))}{FFT(E_{in}(t))} \right)$$

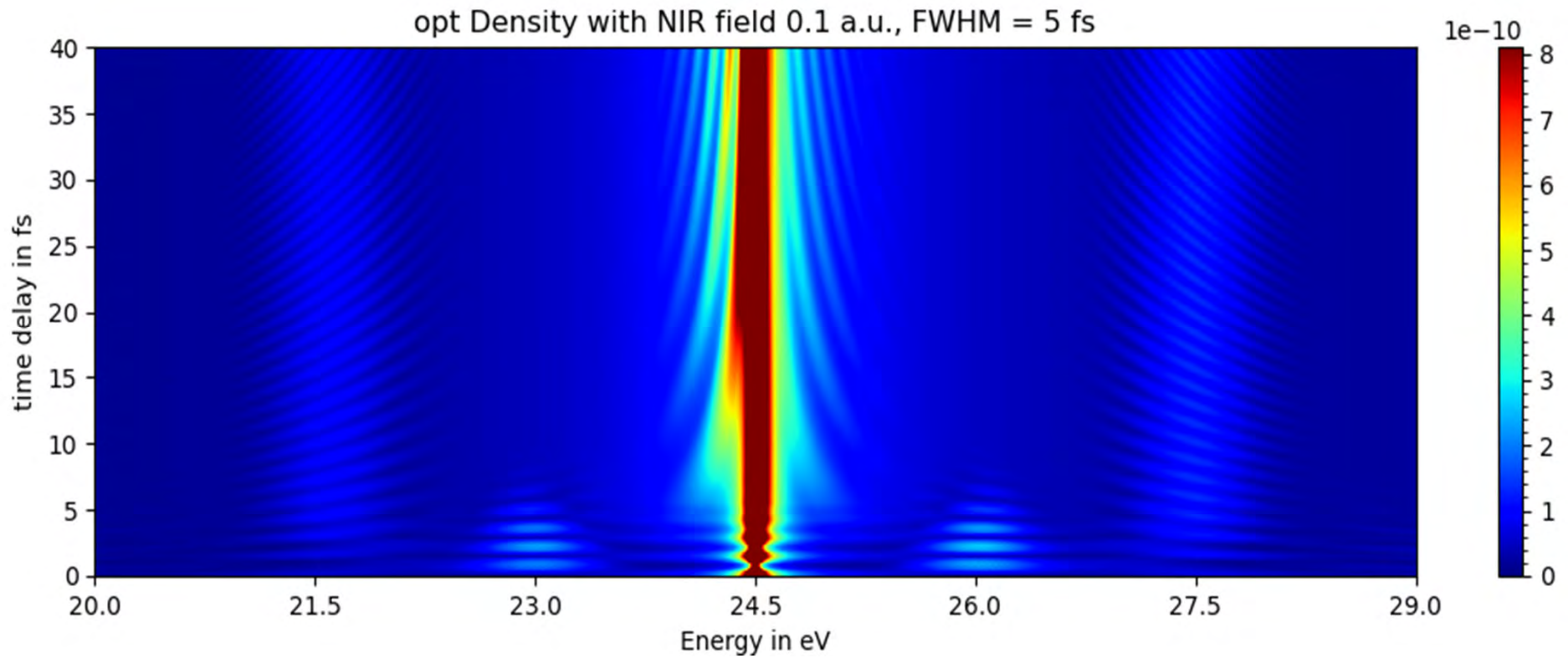
System: 3 Niveau –System (als Testsystem für Helium)



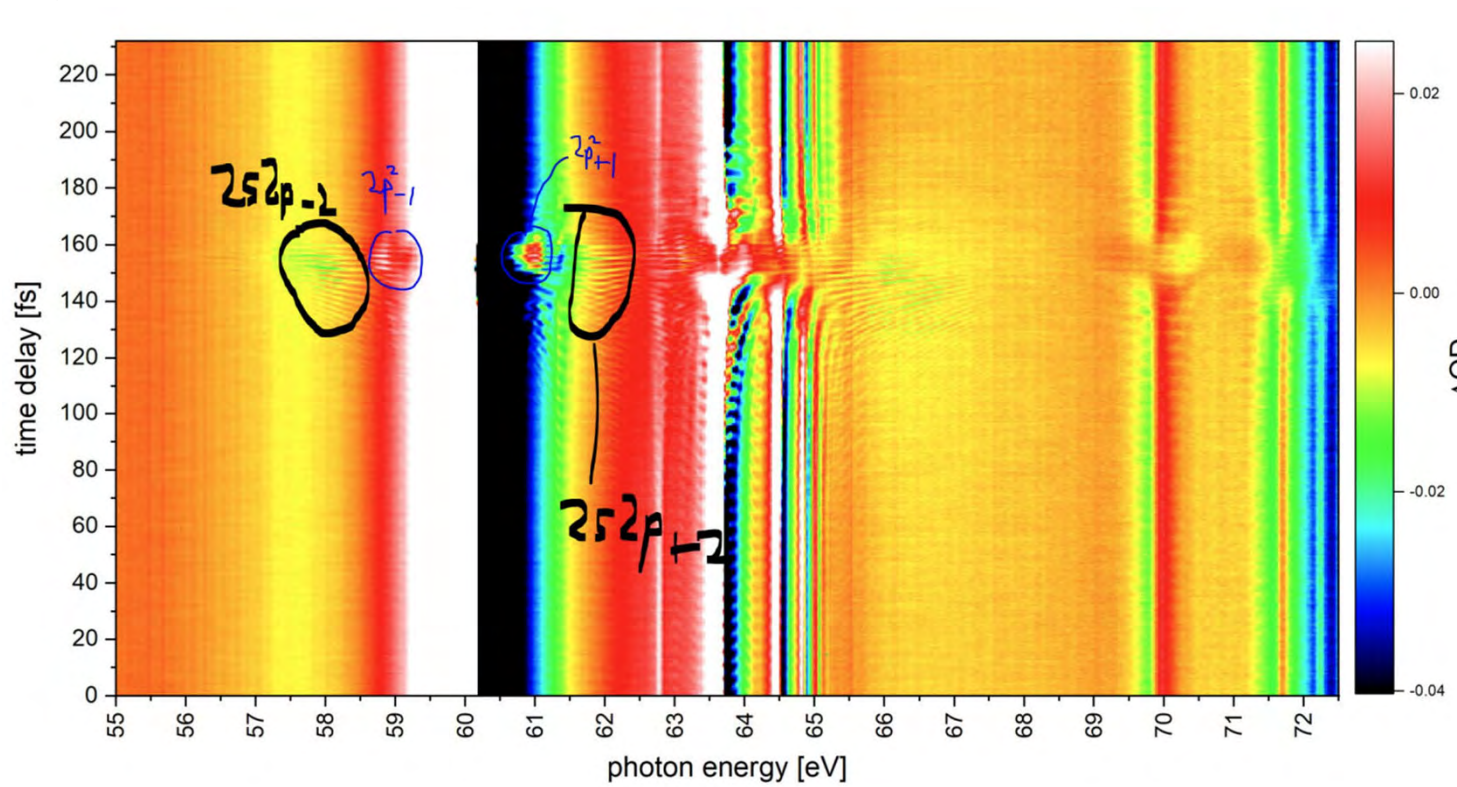
Laserpulse: input



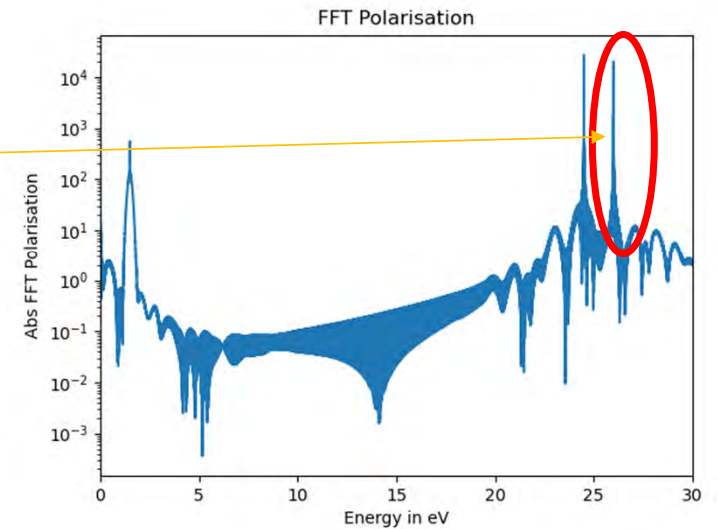
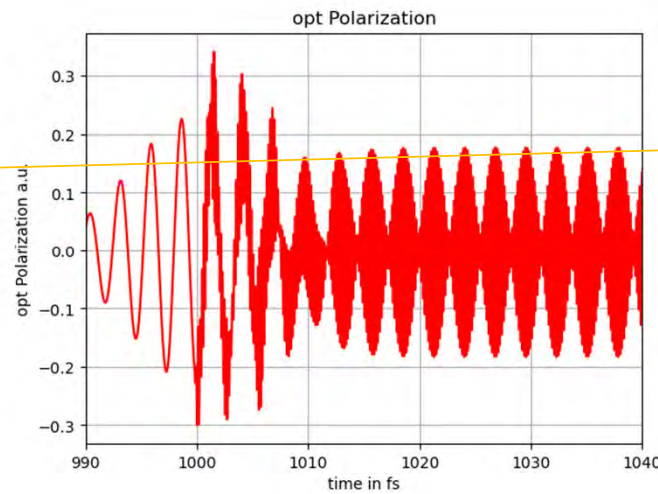
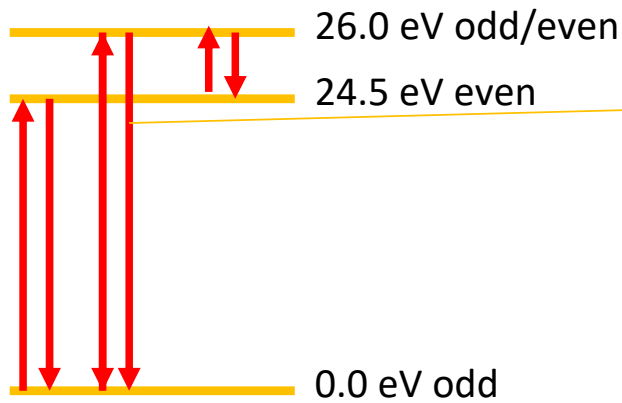
- 2 Nivea-System



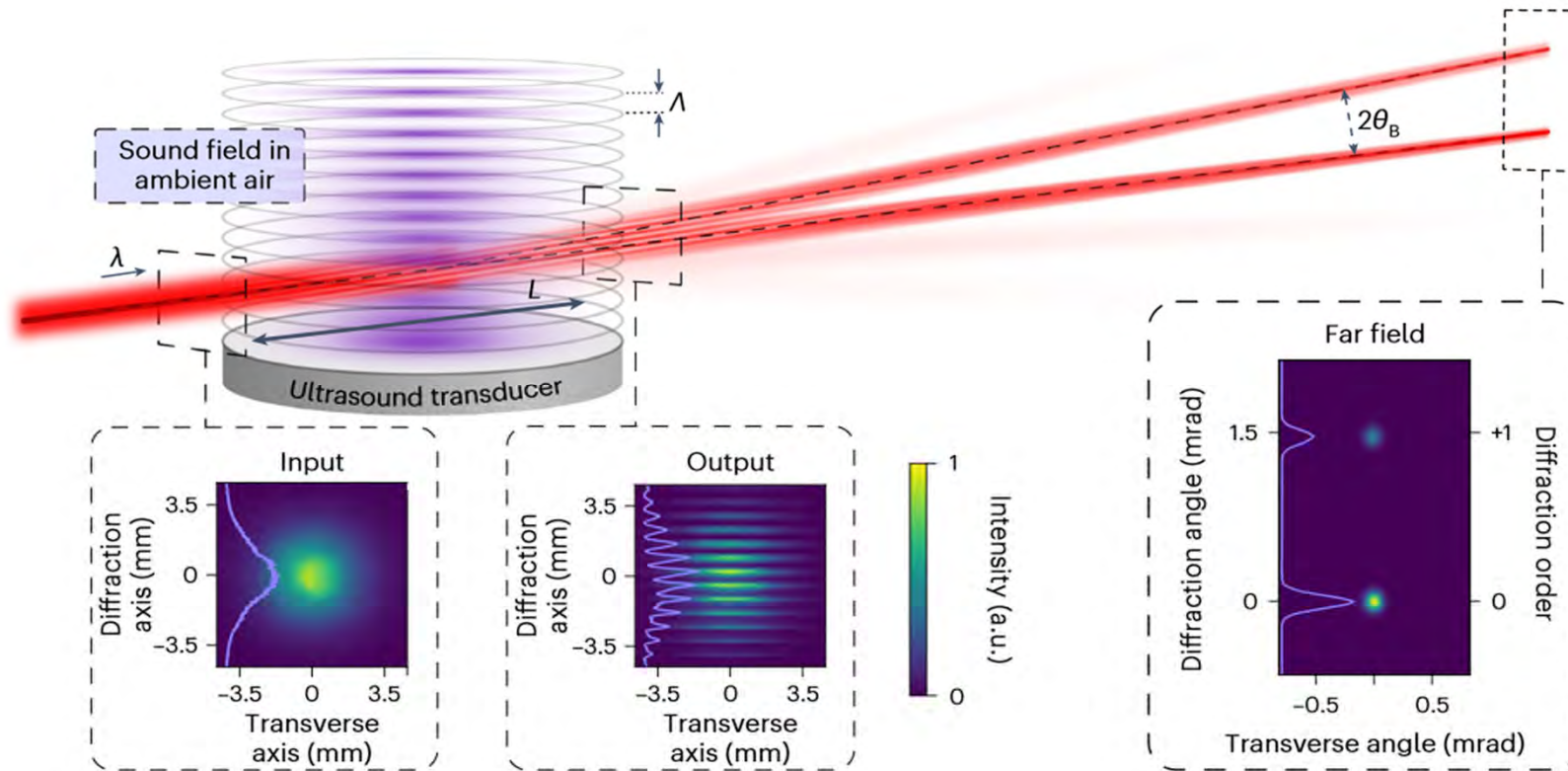
- System: Helium
- Zeitabstand – time delay zwischen XUV und IR Pulse
- Transmissionspektrum



- Kleine Tests



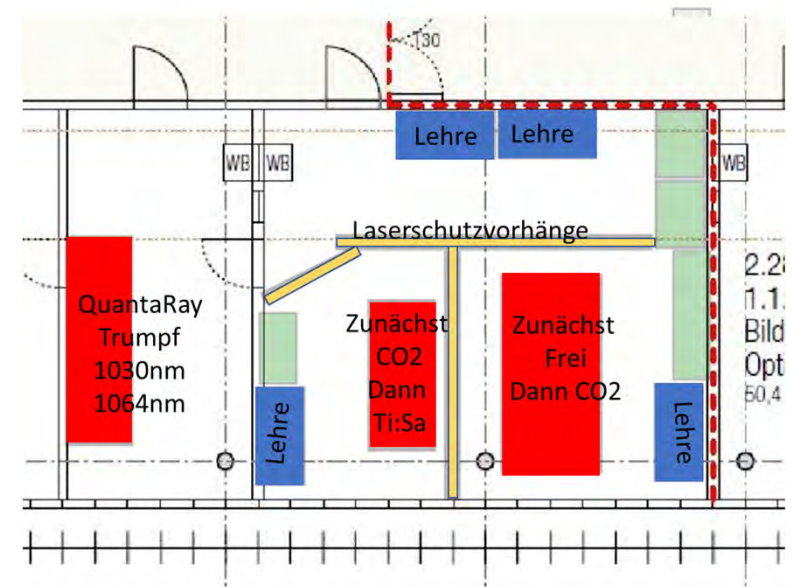
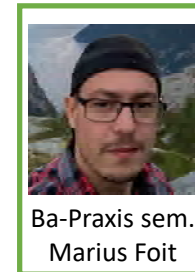
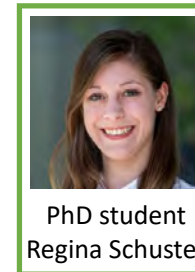
- Sono-phonic in Metamaterialien
- Akusto-Optischer Modulator in Luft



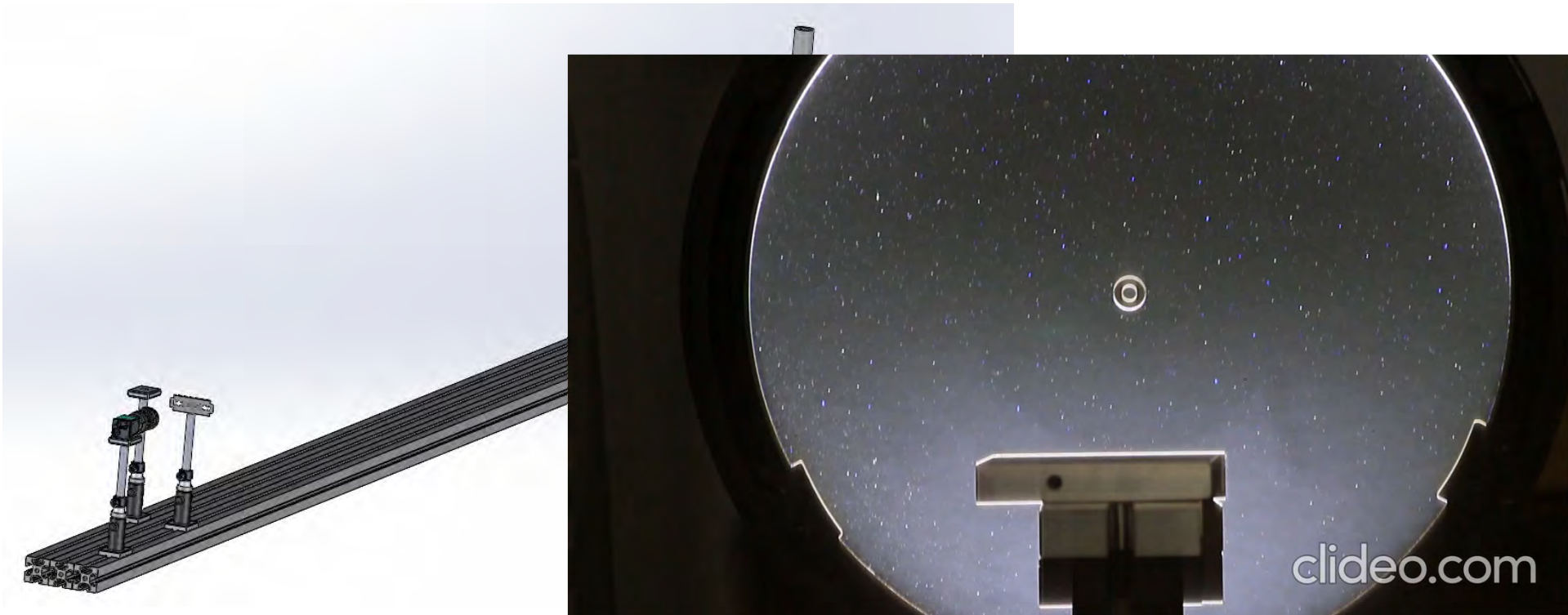
Schrödel, Y., Hartmann, C., Zheng, J. *et al.* *Nat. Photon.* (2023).

Arbeitsgruppe Harth - SOPHIMA

Parameter	Hamburg	Aalen
Wavelength of light	1.030 μm	10 μm
Acoustic frequency	490 kHz	40 kHz
SPL	140 dB	?
Gaussian beam radius ($1/e^2$)	3.25 mm	?
Diffraction-limited beam divergence	0.1 mrad	?
Beam path in sound field	7 x 70 mm	?
Laser operation mode	pulsed ($t_{\text{pulse}} = 500 \text{ fs}$, $E_{\text{pulse}} = 10 \text{ mJ}$)	CW
Ambient temperature	21.1°C	?
Relative humidity	42.5 %	?

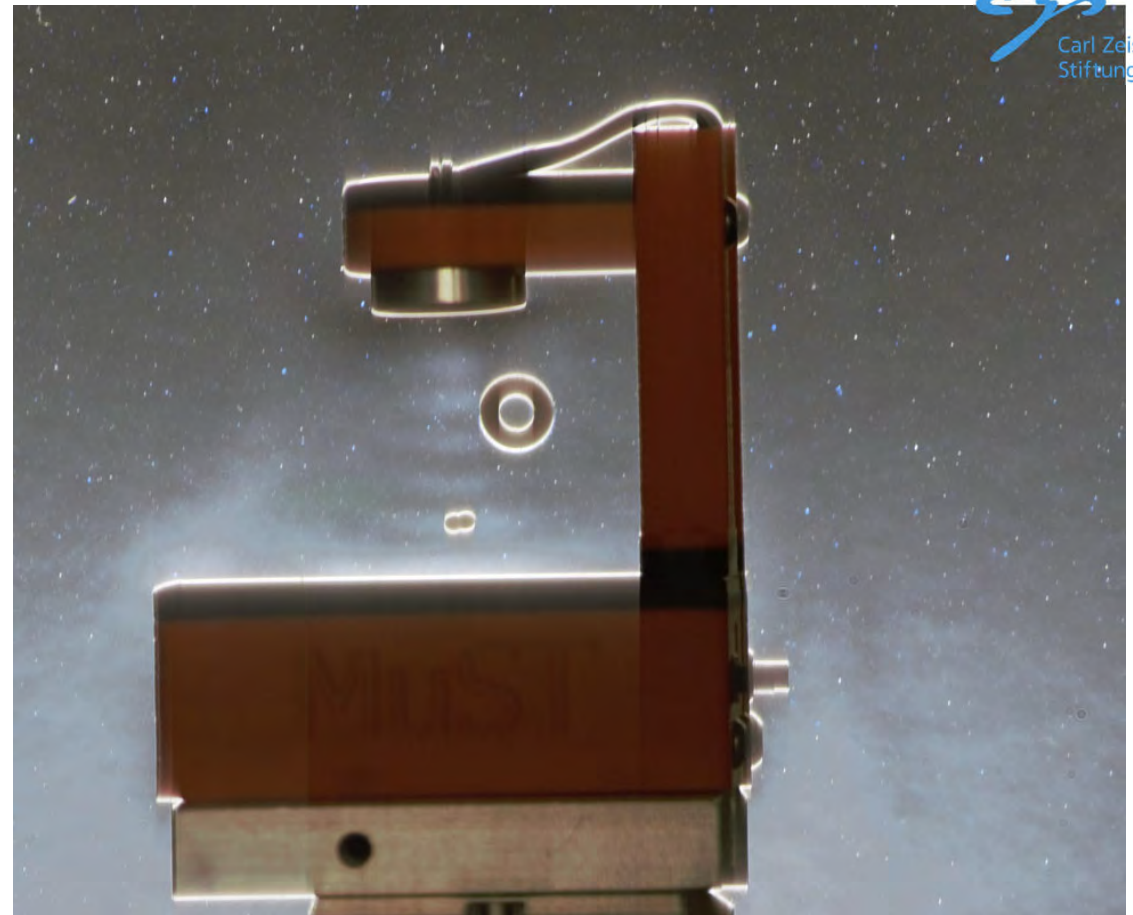


- Schlieren Setup zur Beobachtung und Charakterisierung der Ultraschallfelde



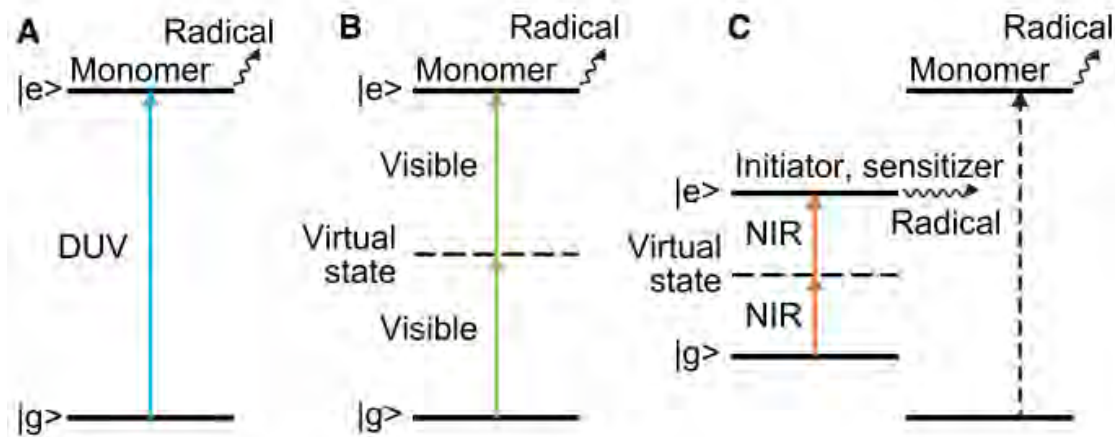
- Stehende akustische Welle

$$\lambda_m = 6.8\text{mm} \quad f = 44\text{kHz}$$



Bei der Aushärtung von Harzen für die Herstellung von optischen Komponenten

- 2 Photonen Polymerisation mit kurzen Pulse
- Herstellung von kleinsten innen-liegenden Strukturen (siehe AG Heinrich)

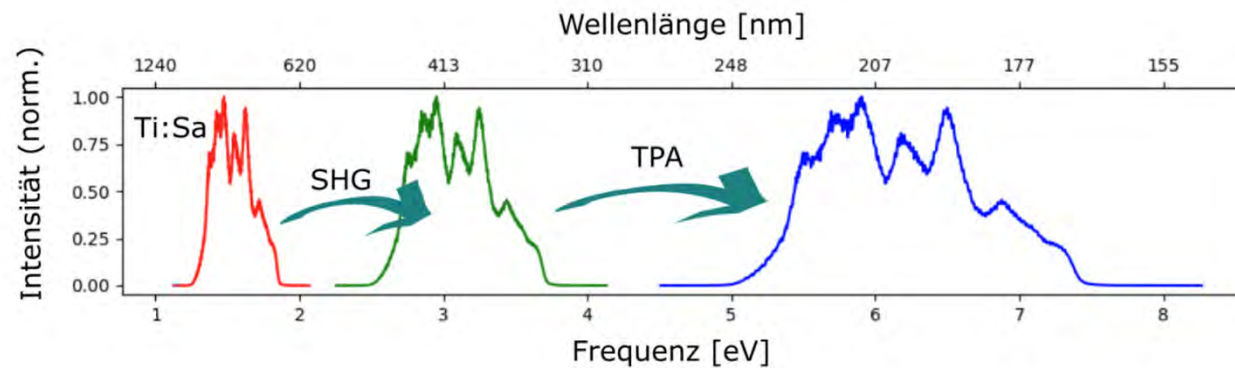
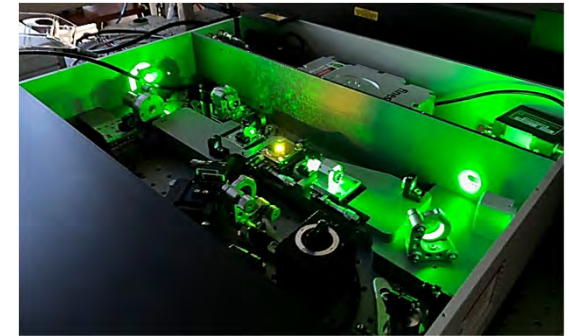


Ein Ansatz:
Vereinfachen
des
Moleküls

Was sind die physikalischen Prozesse bei der Brechungsindexänderung während der Polymerisation?

Bei der Aushärtung von Harzen zur Optikherstellung

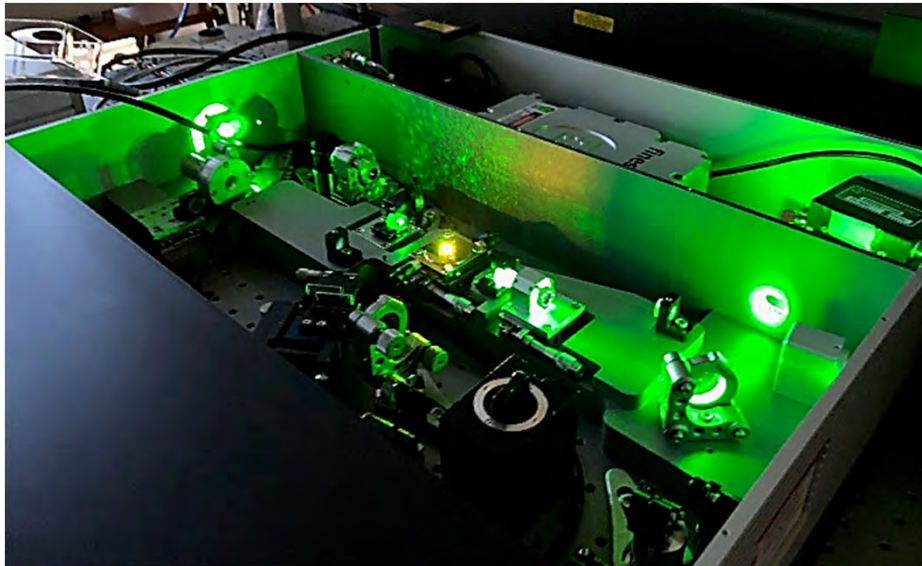
- 2 Photonen Polymerisation mit kurzen Pulse
- Herstellung von kleinsten innen-liegenden Strukturen (siehe AG Heinrich)



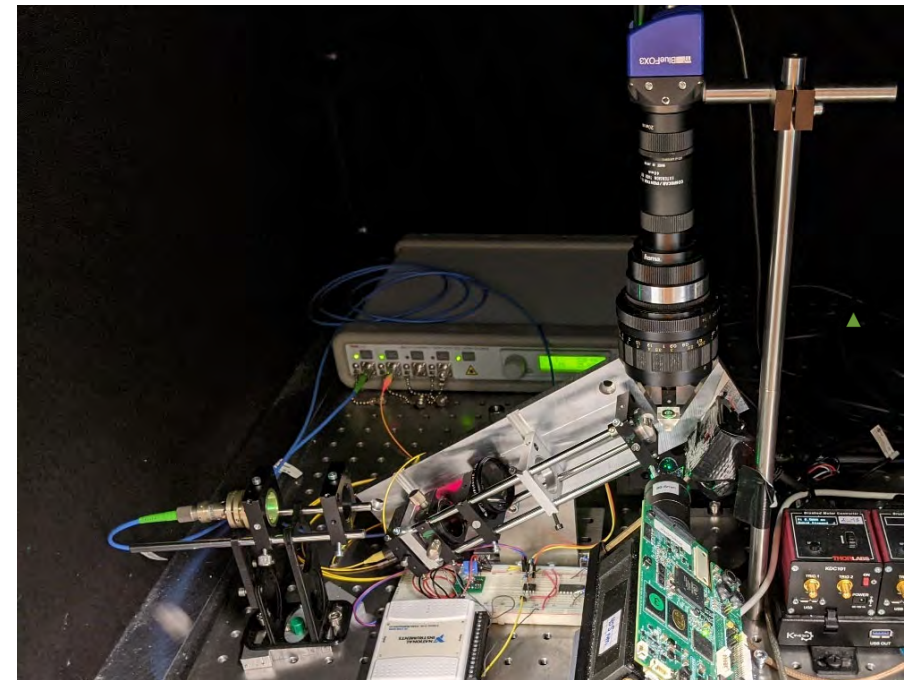
Was sind die Physikalischen Prozesse bei der Brechungsindexänderung während der Polymerisation?

Bei der Aushärtung von Harzen zur Optikherstellung

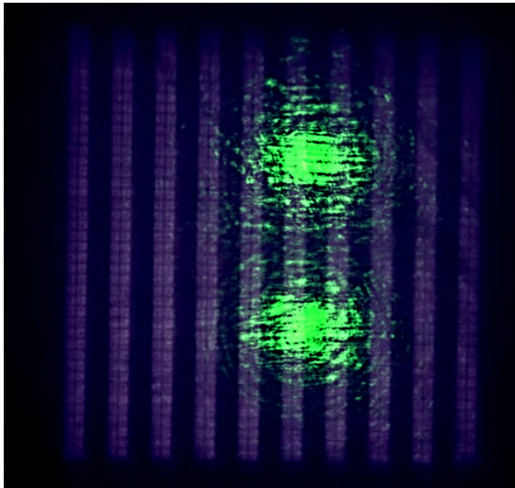
- Ultra-kurzpulse Laser
 - 20 fs, 3W
 - 800 nm, 80 MHz



- Scanning Focused Refractive Index Microscopy (SFRIM)



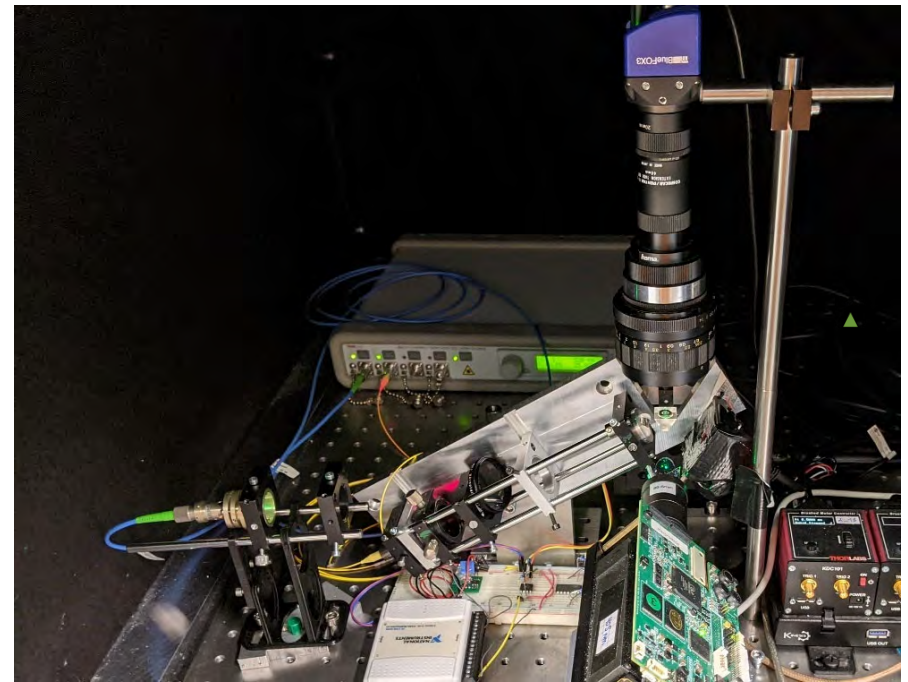
- Aufspalten des Spots in 2 spots → dadurch ist ein Abtasten des Gitter bzw. eine Ortsauflösung möglich



Andreas Heinrich
Professor

Forschungs-Semester
2023 😊

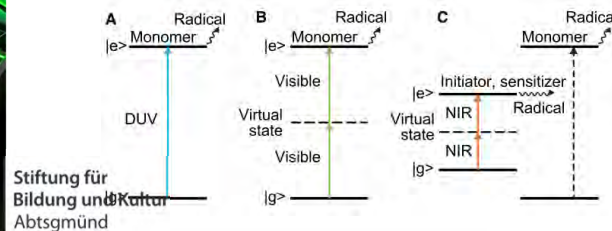
- Scanning Focused Refractive Index Microscopy (SFRIM)



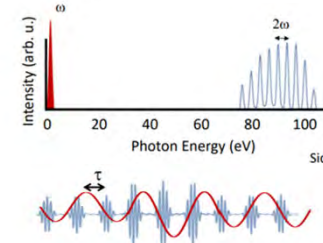
Arbeitsgruppe Anne Harth: Licht-/ Materie Wechselwirkung



Light-RESIN interaction



Light-ATOM interaction



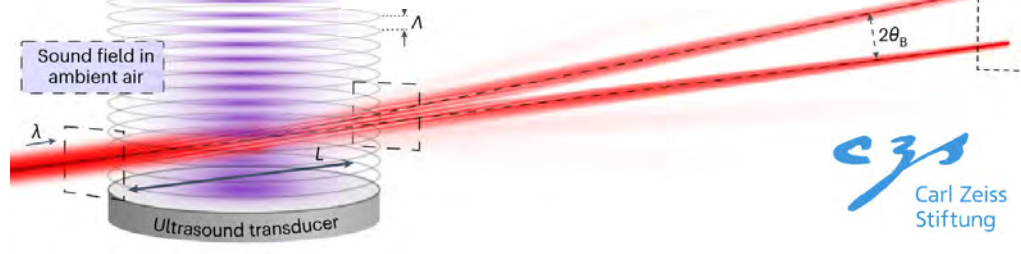
$$\rho = \begin{pmatrix} \rho_{11} & \rho_{12} \\ \rho_{21} & \rho_{22} \end{pmatrix}$$

TA : $P \approx \mu\rho_{12}$
 RABBITT : $SB \approx \rho_{22}$

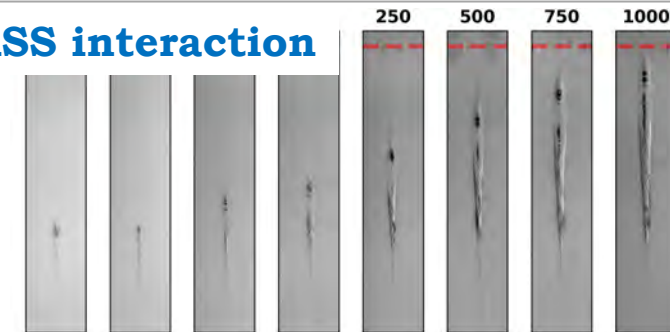


Glass-glass welding, deflection on ultrasonic fields, n-Photon polymerisation
 (3 Doktoranden, typ.: 1 Dualer Master, 2 Abschlussarbeiten, 1 Praxissemester, 3 Projekte)

Light-GAS interaction

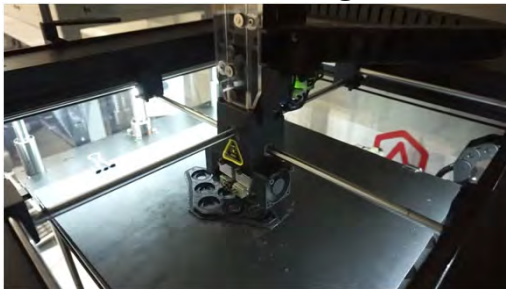


Light-GLASS interaction



- Commercial Printing Technologies @ ZOT

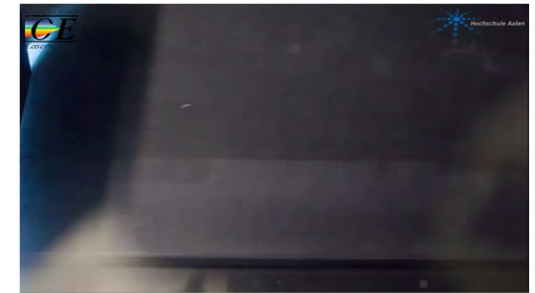
FDM Printing



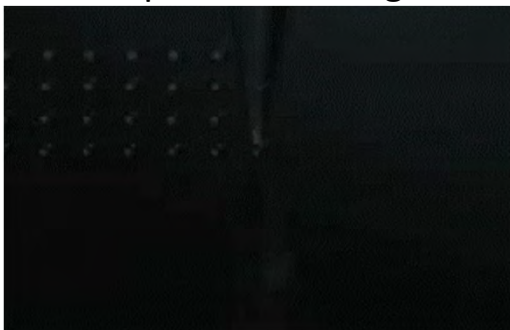
STL Printing



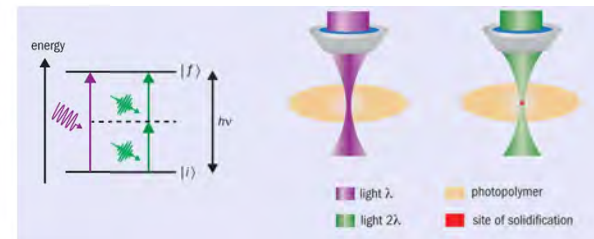
Ink-Jet Printing



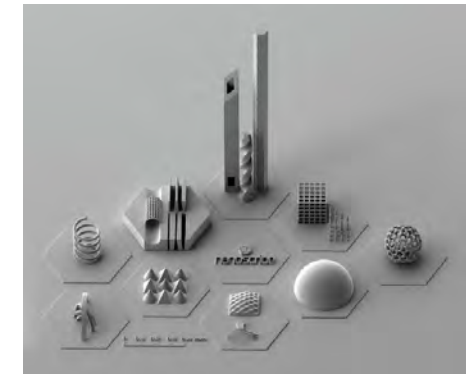
Dispenser Printing



2PP (Nanoscribe Quantum X)

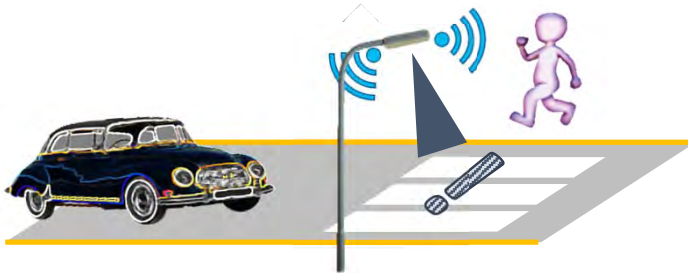


Ref.: S. Steenhusen, Fraunhofer ISC



Ref.: Nanoscribe

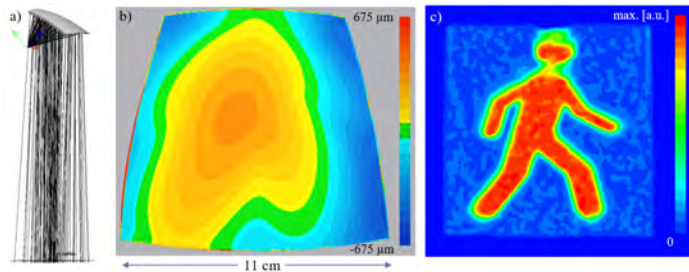
- 3D printed reflector – Task



- Realization



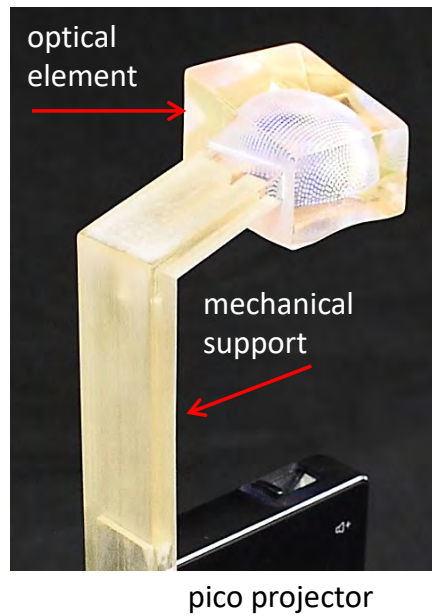
- Design



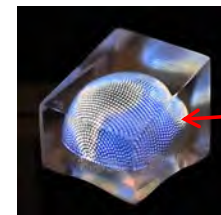
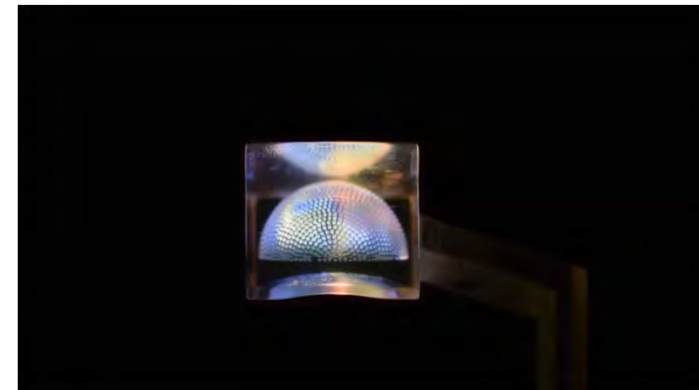
- Result



- Volume Display

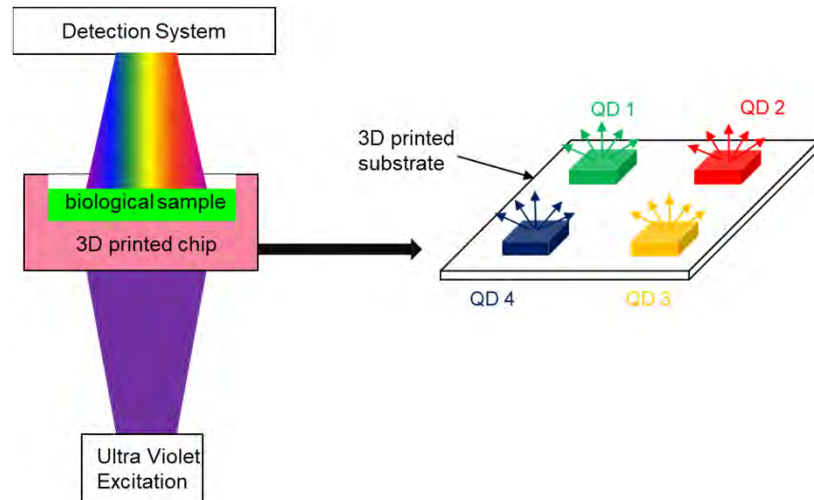


- realization

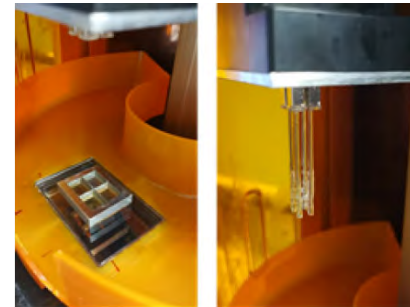


scatter centers

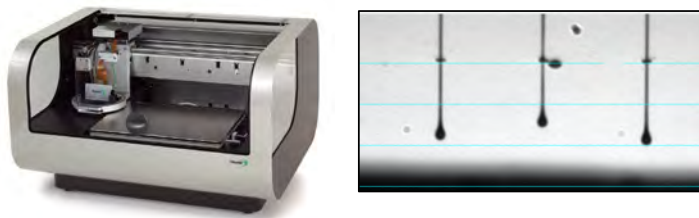
- Luminescent Optics - idea



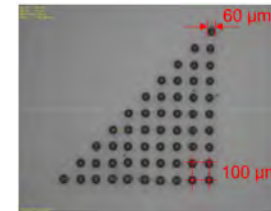
- Realization



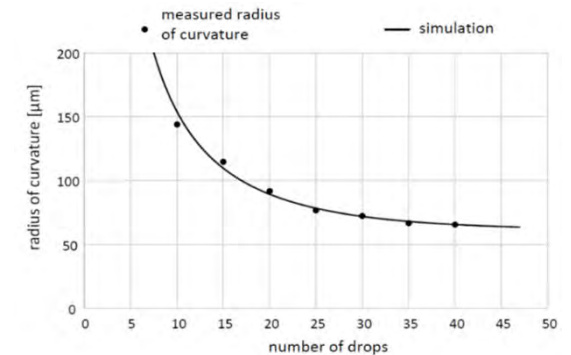
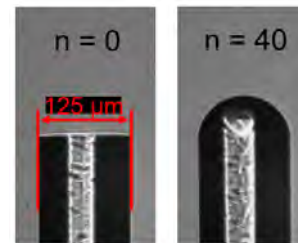
- Issues with printed macrooptics
 - Volume scattering
 - Rough surface needs to be polished
 - Non homogeneous refractive index distribution
- Can we overcome this issues?
- Solution: ink-jet printing of micro optics: accumulation of droplets ($\sim 10\text{pL/drop}$)



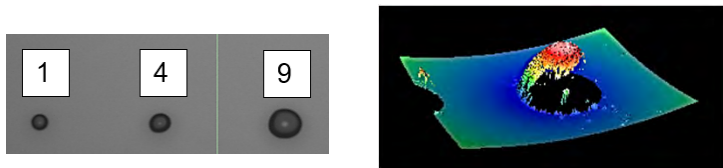
- Result
 - Lenses printed on a plane substrate



- Lens printed on a glass fiber

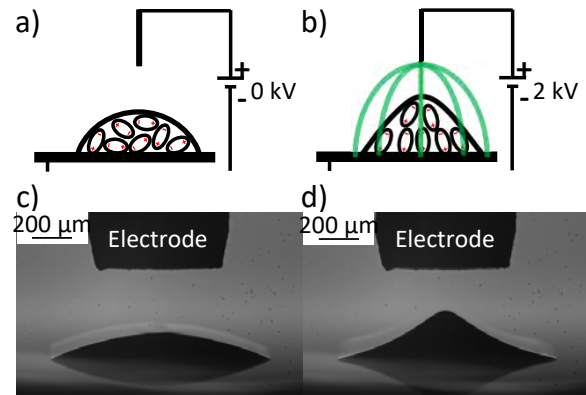


- But: spherical drops only!

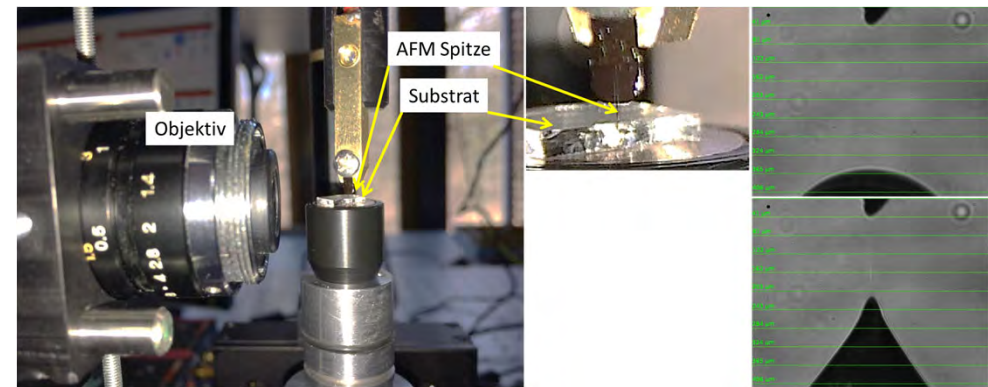


- How to generate an asphere?

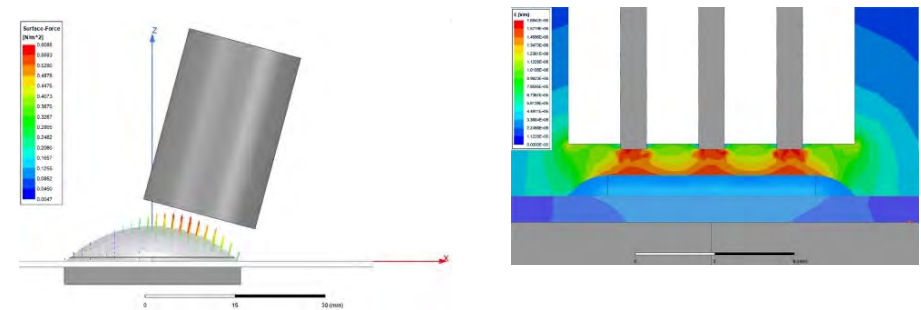
- Dielectrophoresis



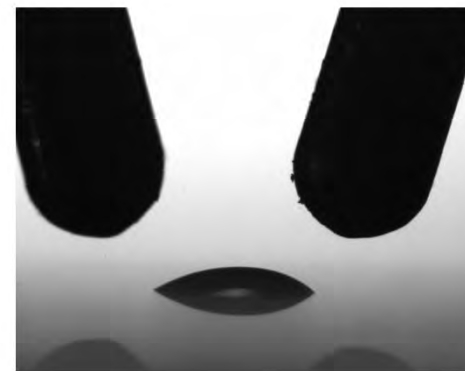
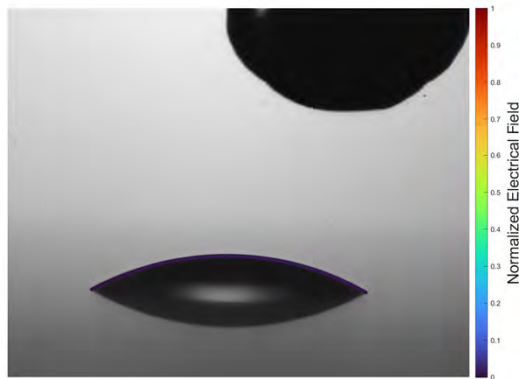
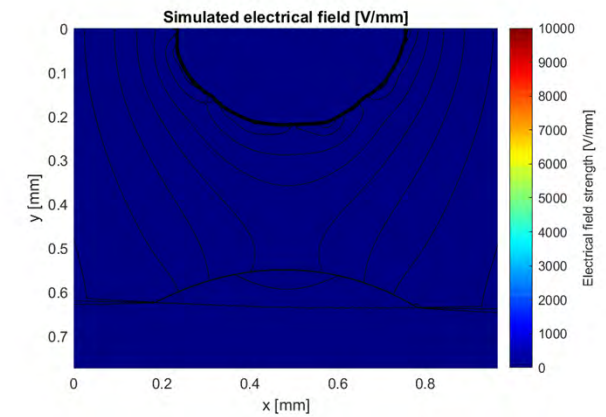
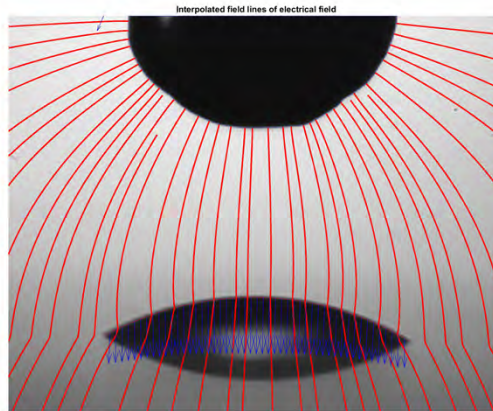
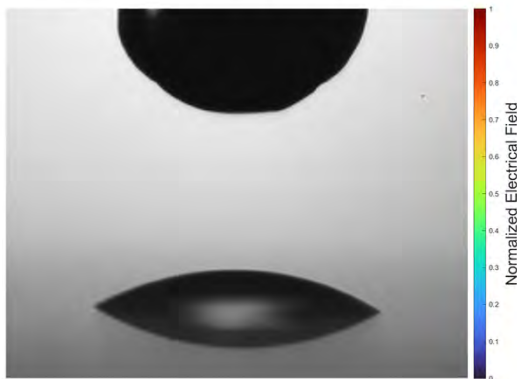
- Experimental Set-up



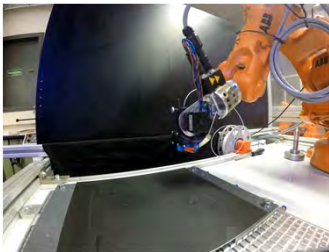
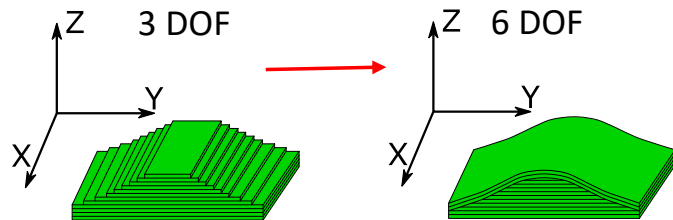
- Shape and position of tip matters!



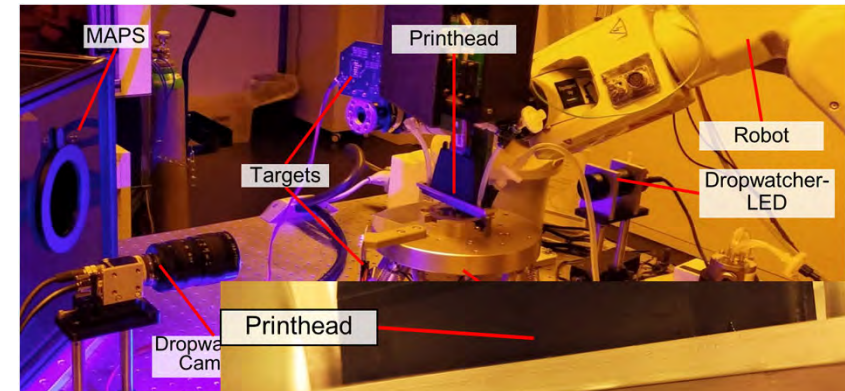
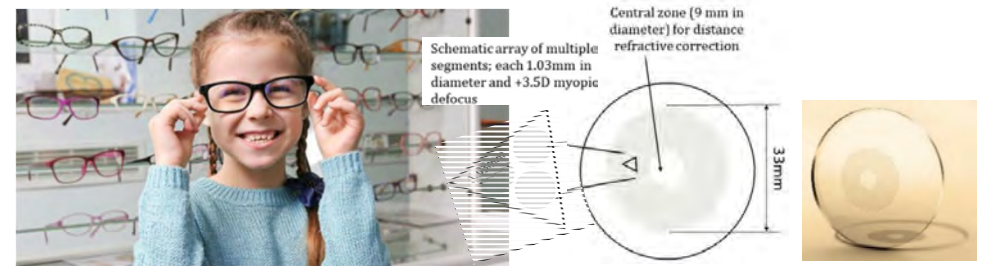
- Example Micro lens



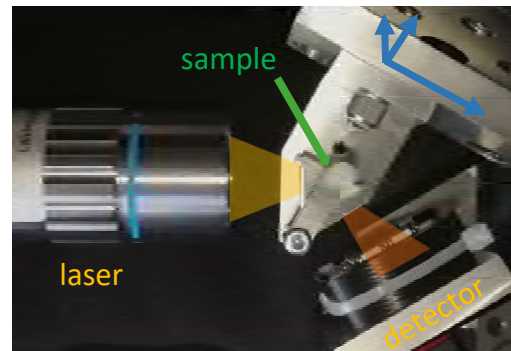
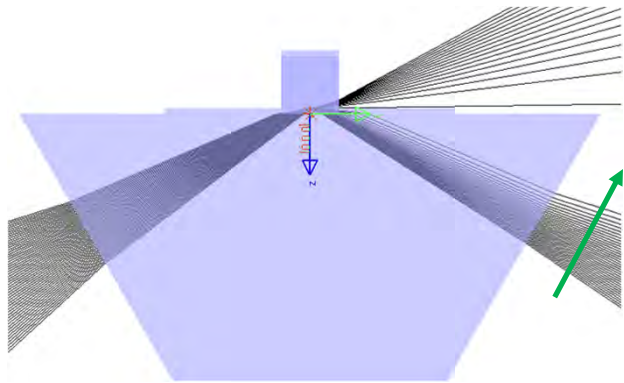
- 6DOF printing platform - kinematic



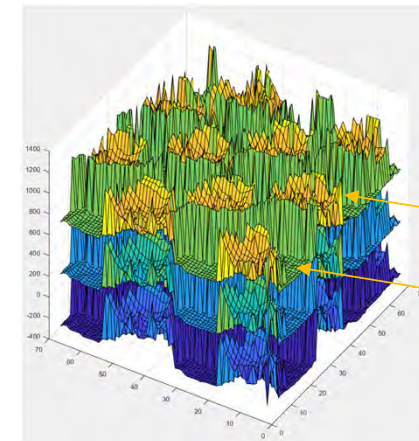
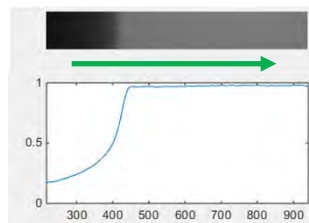
- Example: Ink-Jet print on spectacle lenses



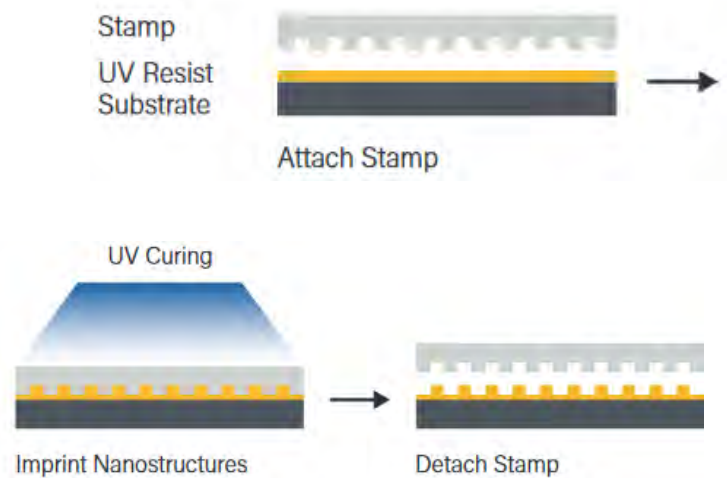
- Metrology:
scanning focused refractive index microscopy



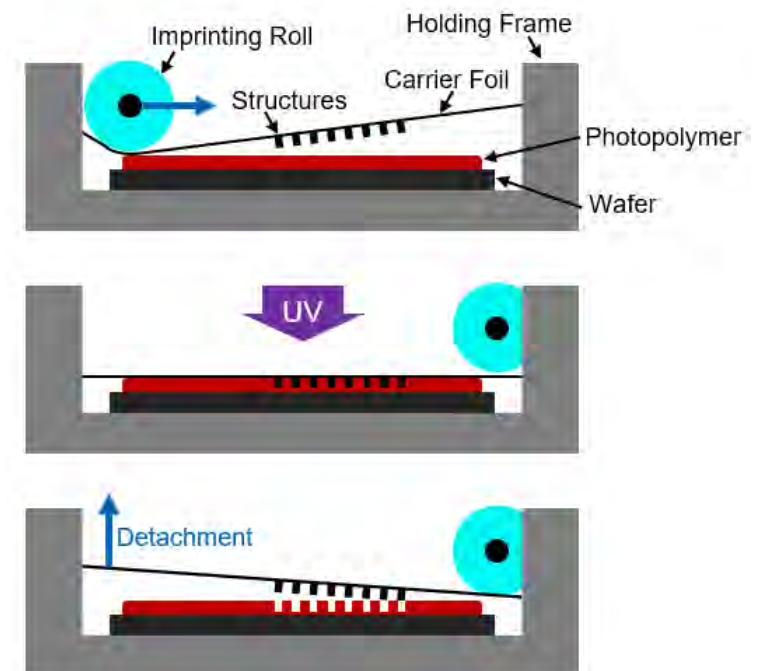
Total internal reflection
creates dark-bright edge



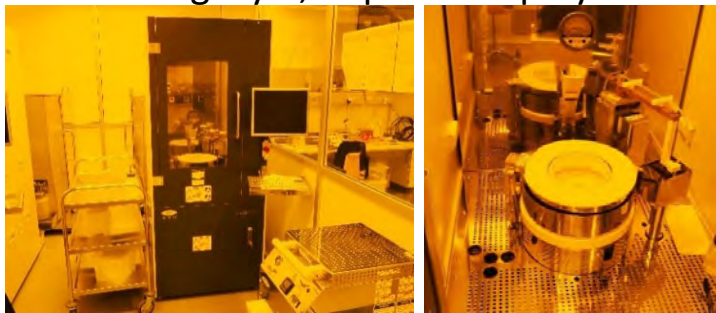
- Principle
 - Soft NIL



- Principle
 - Smart NIL



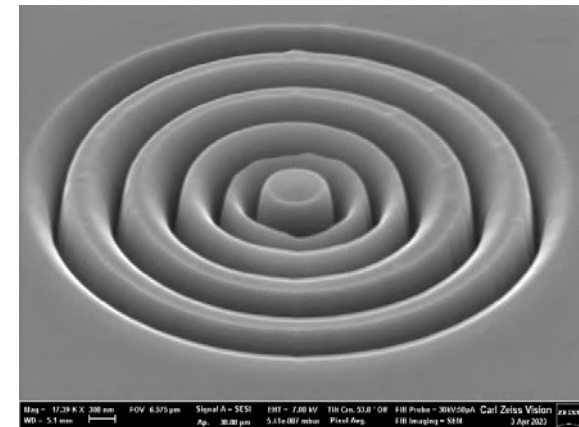
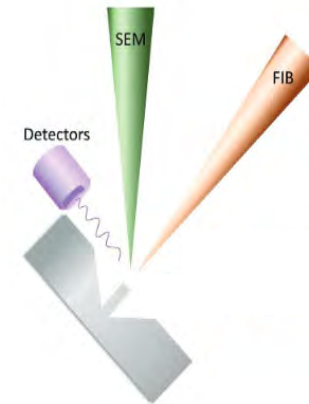
- System: EVG 620
 - Spincoating and (pre)bake for
 - Anti Sticking layer, Replication polymers etc.



- Replication:



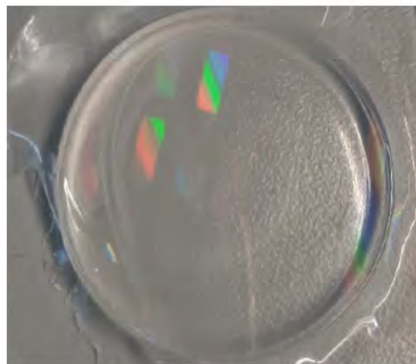
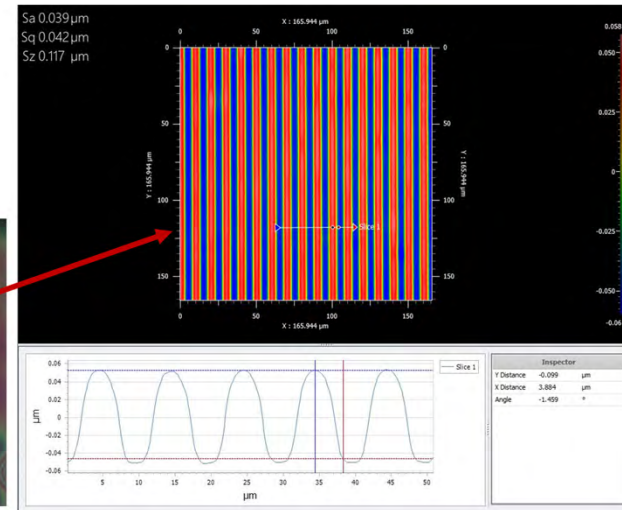
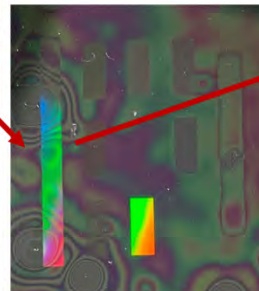
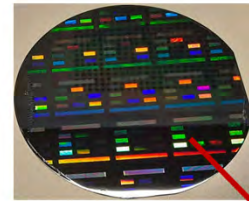
- How to create the master?
 - FIB (collaboration with Carl Zeiss Vision)



- 2PP System

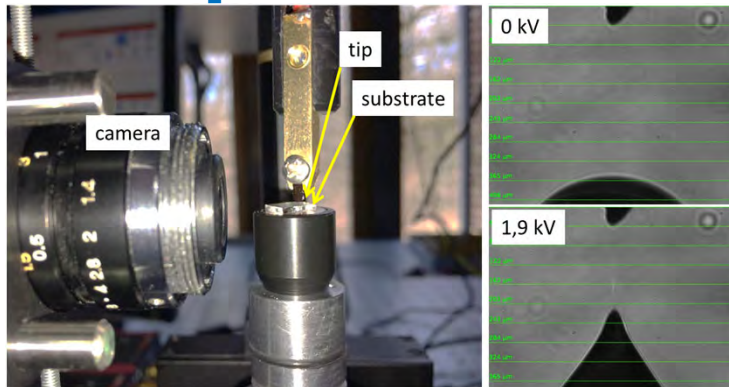


- Examples
 - Replication of Microlenses and gratings

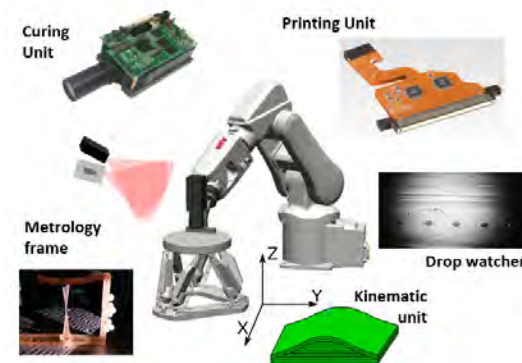


Arbeitsgruppe Andreas Heinrich: Mikro- und Nanophotonik

Dielektrophorese



Ink-Jet 3D Druck



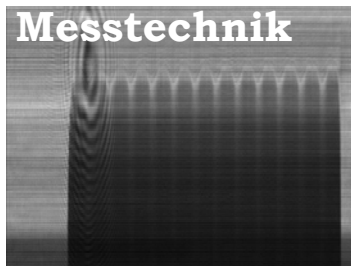
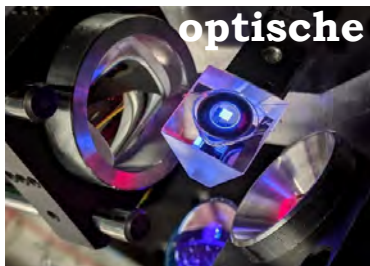
2-Photonen-Polym.



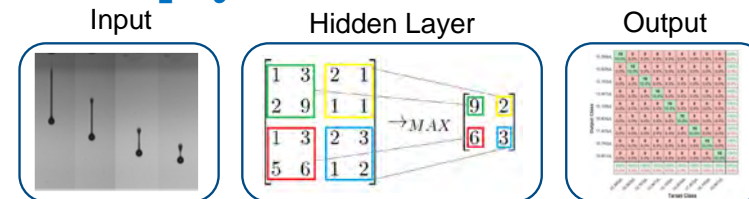
Nanoimprint Lithographie



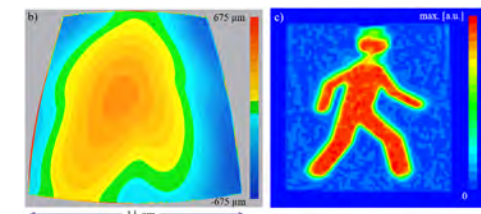
Design, Entwicklung und Realisierung (AM & NIL) von optischen Elementen
(7 Doktoranden, typ.: 3-5 Duale Master, 3-5 Abschlussarbeiten)



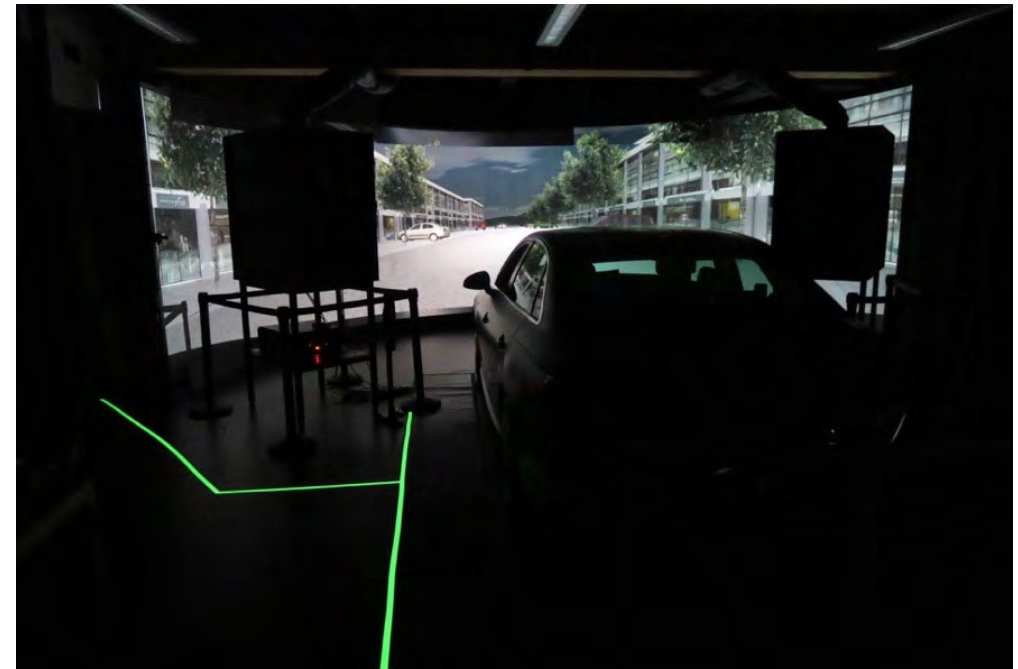
KI für physik. basierte Probleme



Optik Design

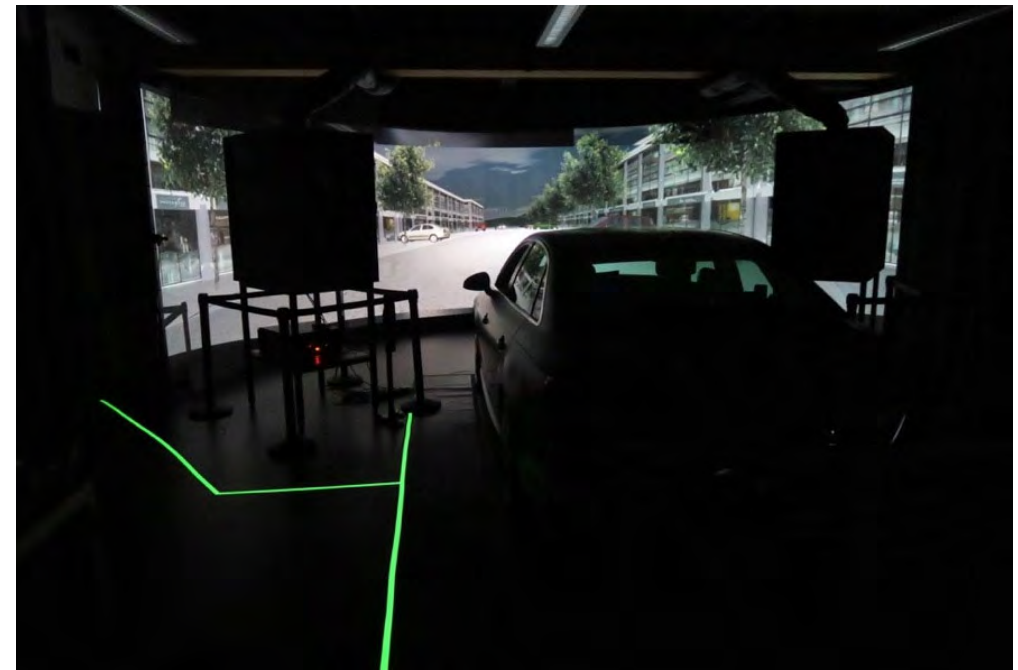
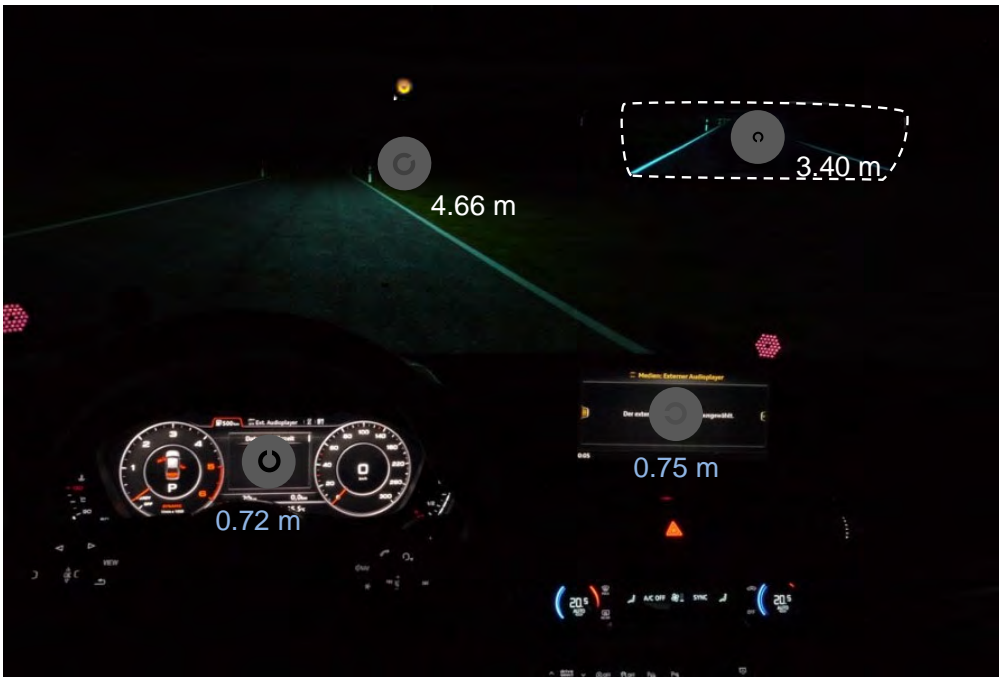


- (Nacht-)Fahrsimulation



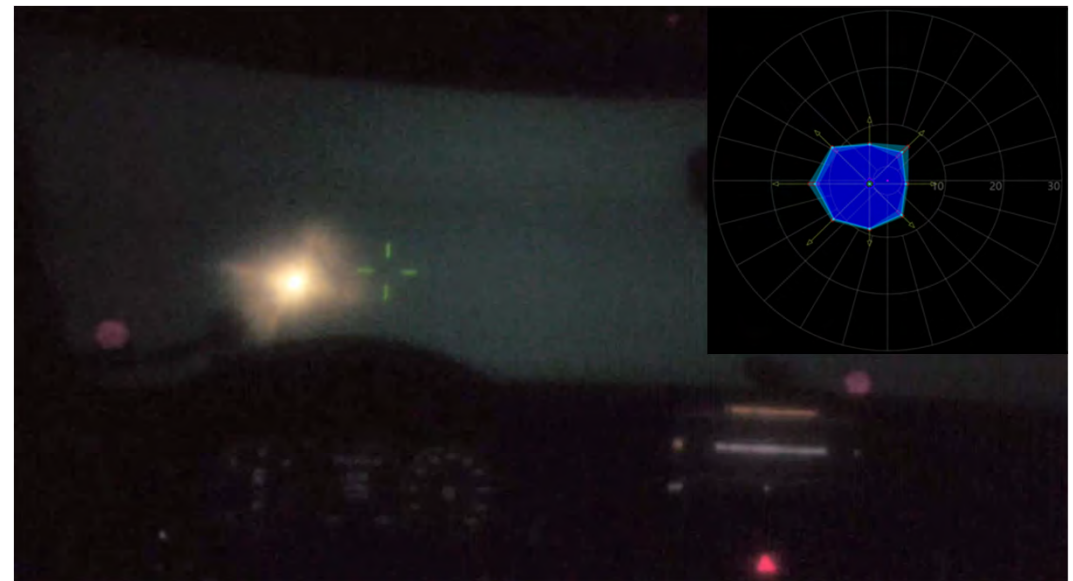
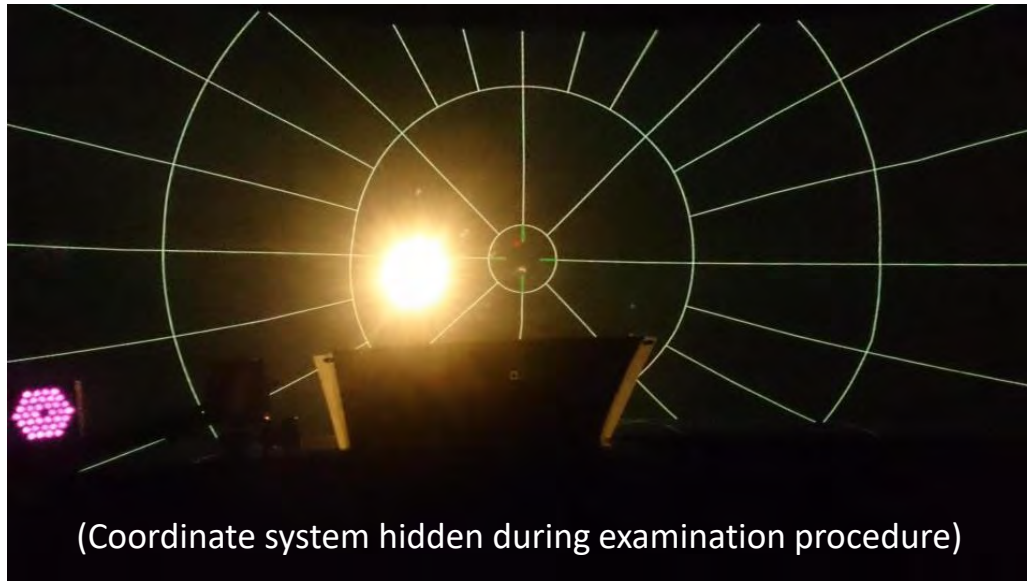
Untersuchungsbedingungen hoch standardisiert, unabhängig von Umweltbedingungen, hoch immersiv, realitätsnah, ungefährlich, reproduzierbar, skalierbar

- (Nacht-)Fahrsimulation

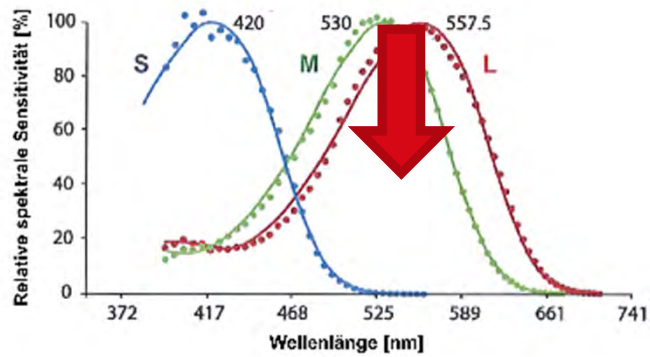


Untersuchungsbedingungen hoch standardisiert, unabhängig von Umweltbedingungen, hoch immersiv, realitätsnah, ungefährlich, reproduzierbar, skalierbar

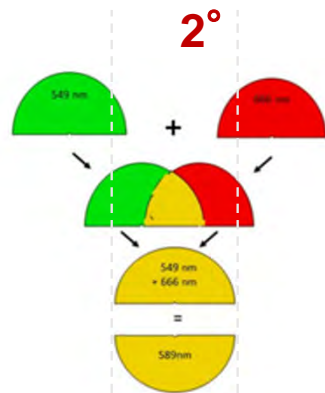
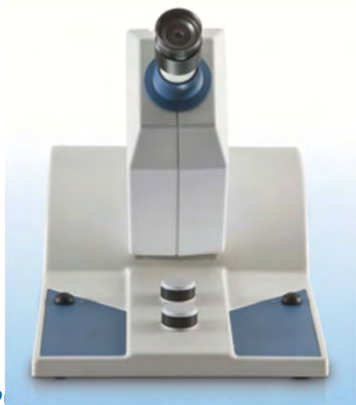
- Blendung



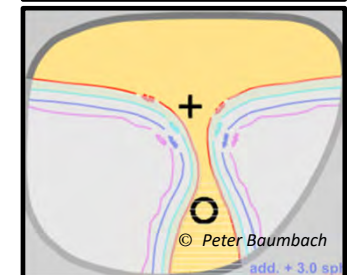
- Farbsehen



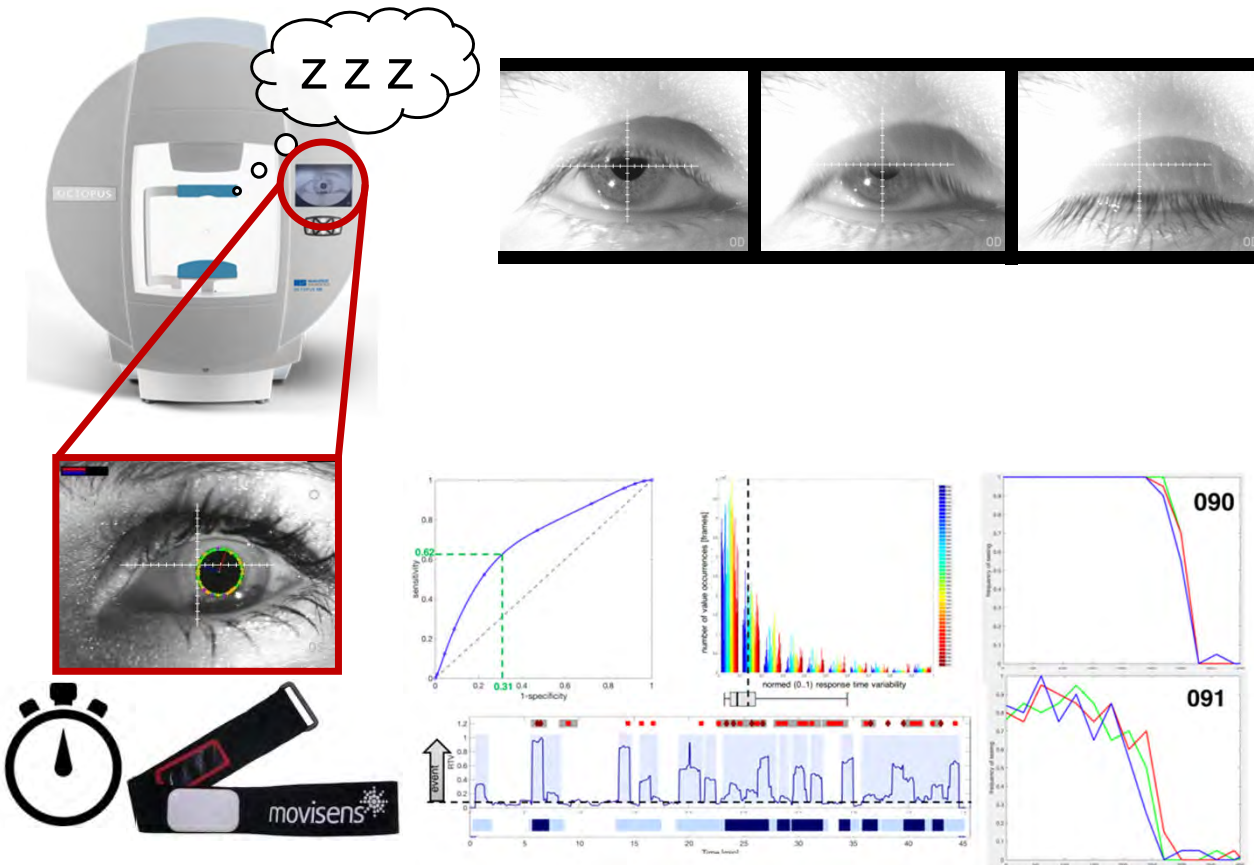
Anomaloskop



- Benchmark optischer Korrekturen



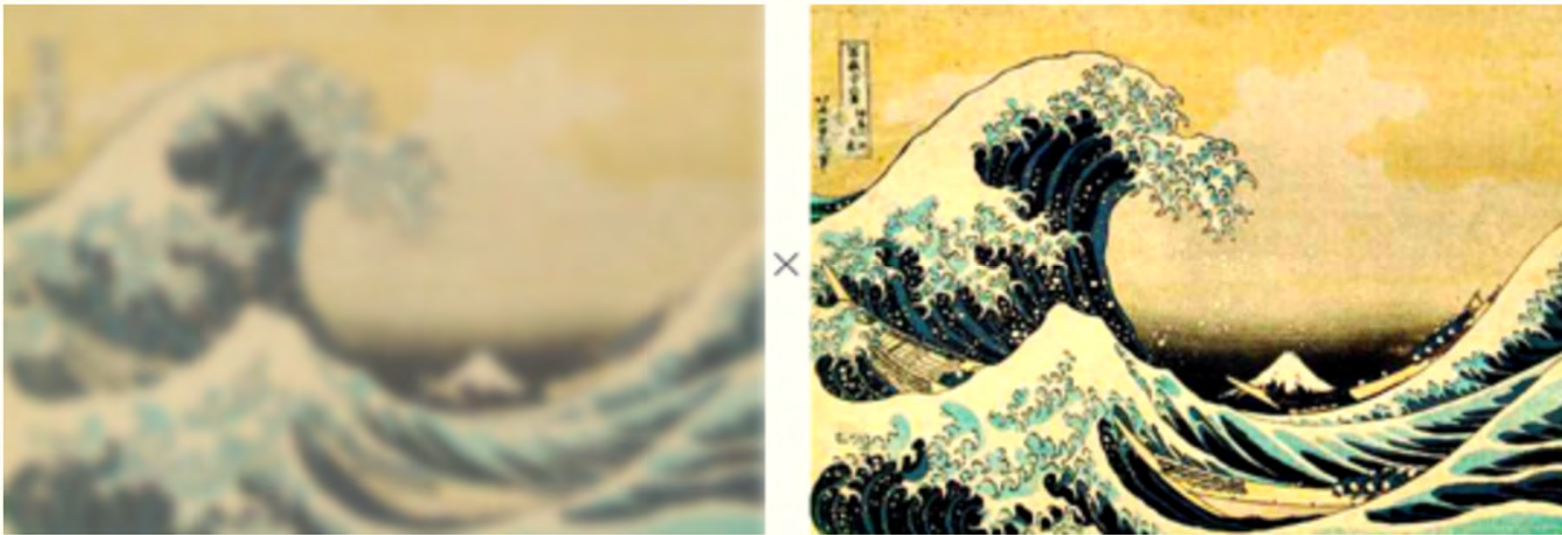
- Wachheit und Aufmerksamkeit



Ziele:

- Dosierter Monotonie-Belastungstest
- Identifikation robuster Vigilanz-Marker

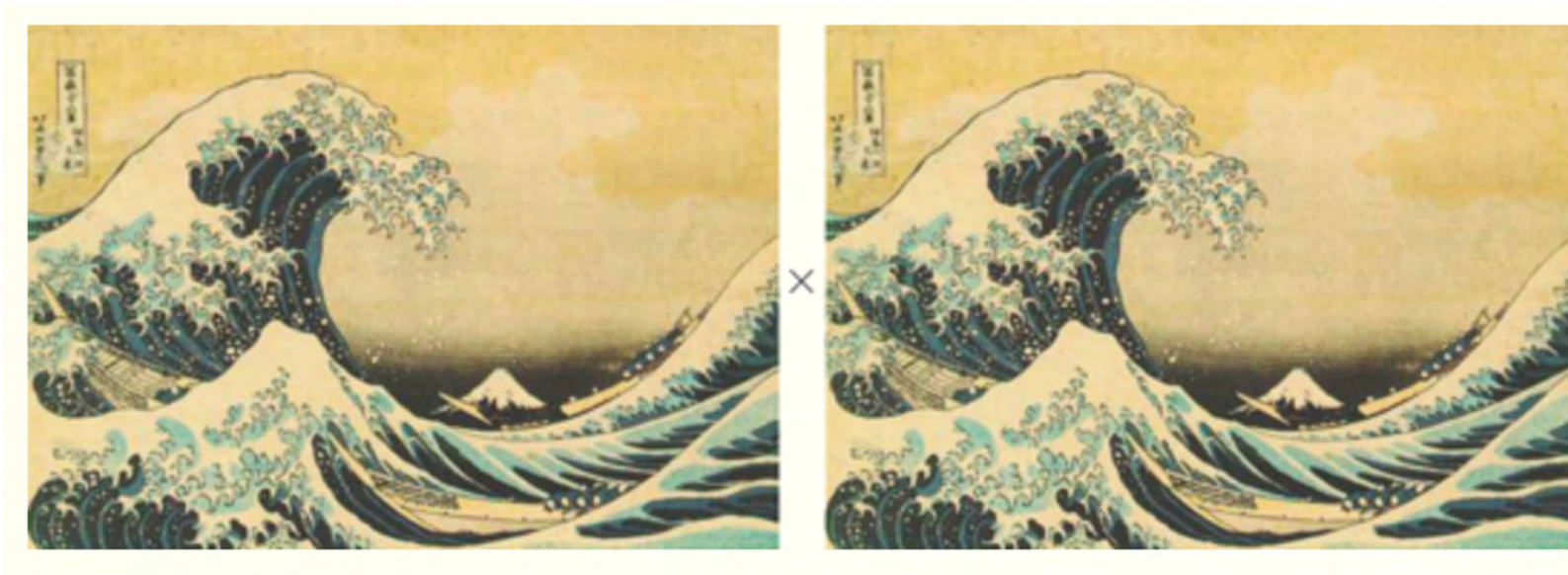
- Relevanz der sinnesphysiologischen Untersuchung



*“The braking wave off Kanagawa”
Katsushika HOKUSAI (1831-1833)*

<https://michaelbach.de/ot/lum-contrastAdapt/index.html>

- Relevanz der sinnesphysiologischen Untersuchung

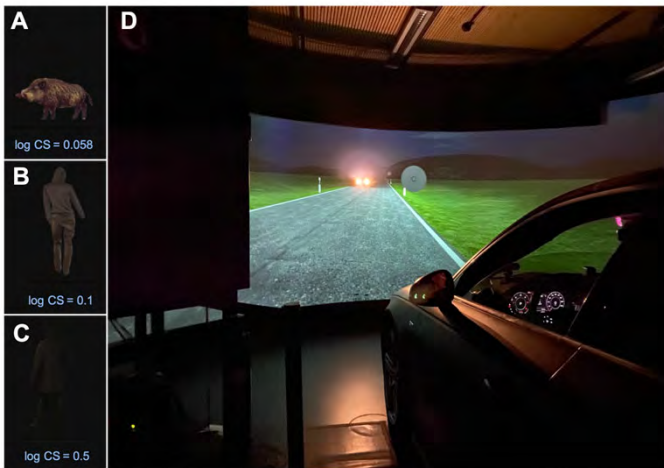


*“The braking wave off Kanagawa”
Katsushika HOKUSAI (1831-1833)*

<https://michaelbach.de/ot/lum-contrastAdapt/index.html>

- Arbeitsgruppe Judith Ungewiß: Vision Research

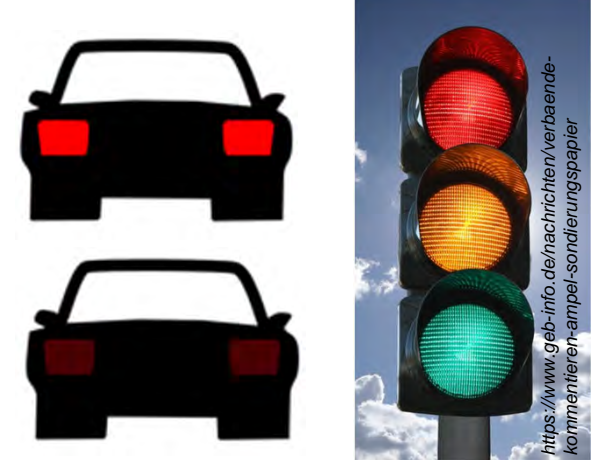
Nachfahrsimulation



Beeinträchtigung durch Blendung



Farbensehen

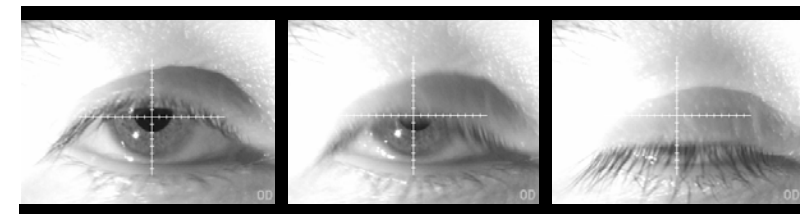
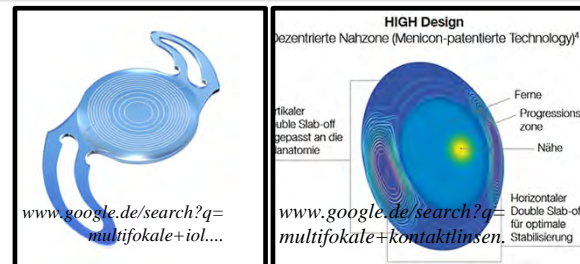


Erfassung sinnesphysiologischer Parameter unter herausfordernden Bedingungen
 aktuell 3 studentische Projektarbeiten (als Teil des Masterstudiums), typischerweise ca. 3-4 Abschlussarbeiten pro Jahr

Benchmark optischer Korrekturen (links)

Wachheit und Aufmerksamkeit während sinnesphysiologischer Untersuchungen (rechts)

17.02.2024



Who we are: Team & Main Funding



*Correlated Multimodal
Imaging in Life Sciences
(COMULIS)*



*Implementierung von suprauflösender
Kryo-Fluoreszenzmikroskopie unter Abbes
Beugungslimit & deren korrelative
Kombination mit
Rasterelektronenmikroskopie*

Chan Zuckerberg Initiative

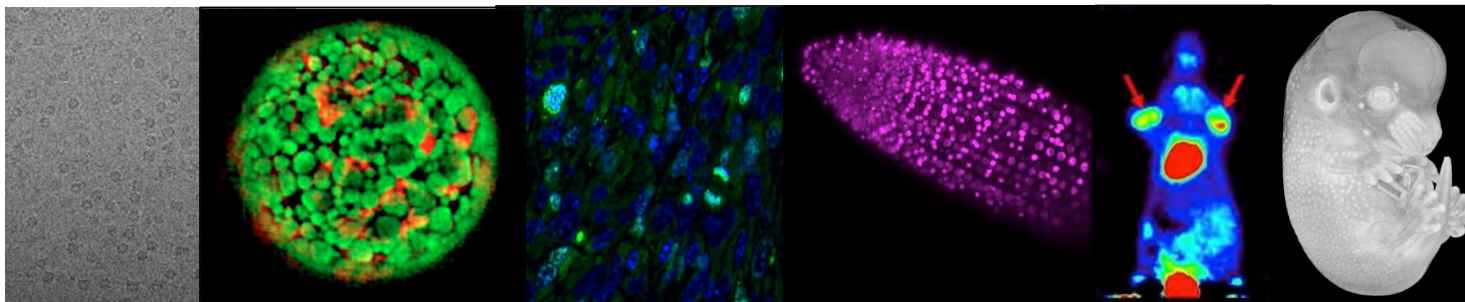
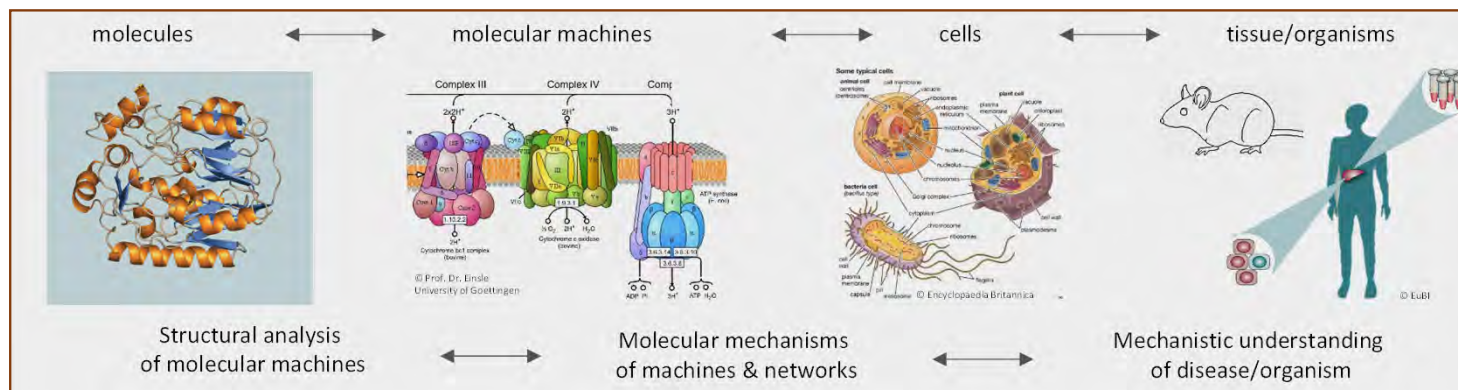
*Advancing Imaging Through
Collaborative Projects
(COMULISglobe)*



*Correlative Light, Electron
and X-ray Microscopy
(CLEXM) to progress research
into the understanding and
treatment of diseases.*

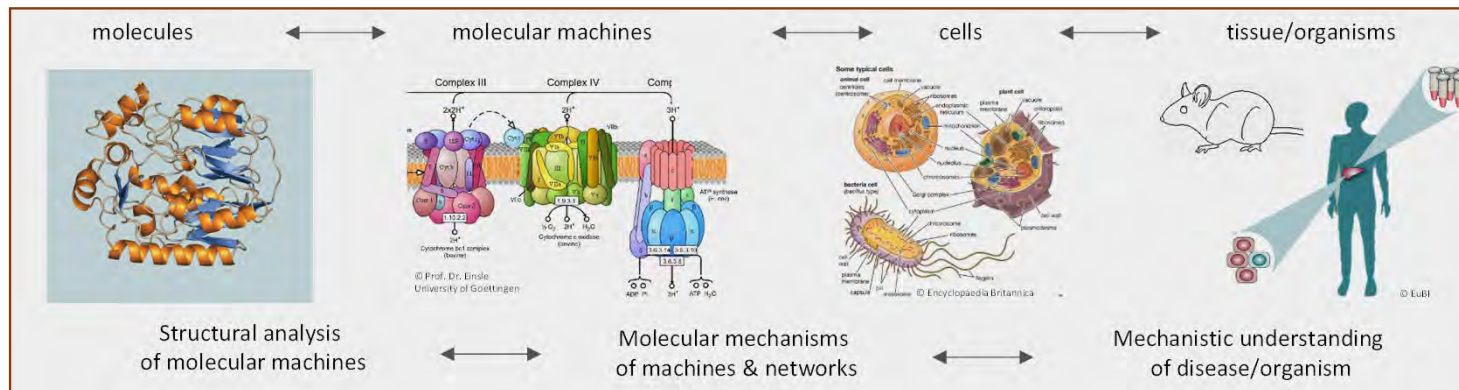
Vision: Help unravel the secrets of life & facilitate diagnostics by **correlative bioimaging across scales**

The whole is more than its sum. (Aristoteles)



Vision: Help unravel the secrets of life & facilitate diagnostics by **correlative bioimaging across scales**

The whole is more than its sum. (Aristoteles)



(cryo-)TEM
Mass Spec Imaging

Electron Microscopy

AFM
Super-resolution
(PALM/STORM/STED)

Superresolution

SIM
TIRF
SEM
Confocal

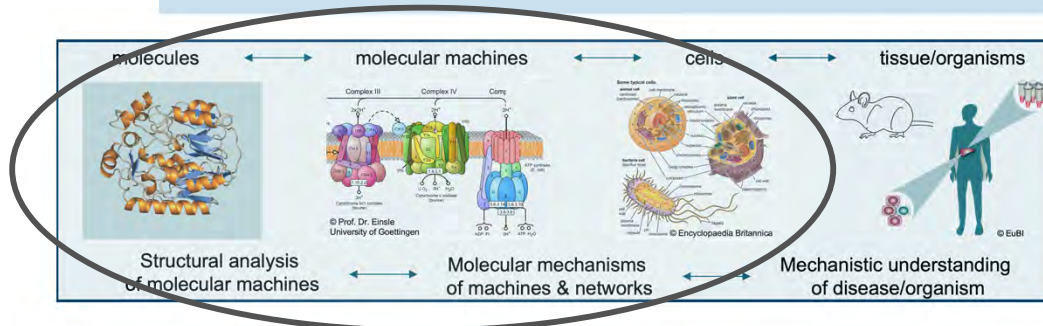
Fluorescence Microscopy

Raman
Light Sheet
Multiphoton

Thick Tissue Microscopy

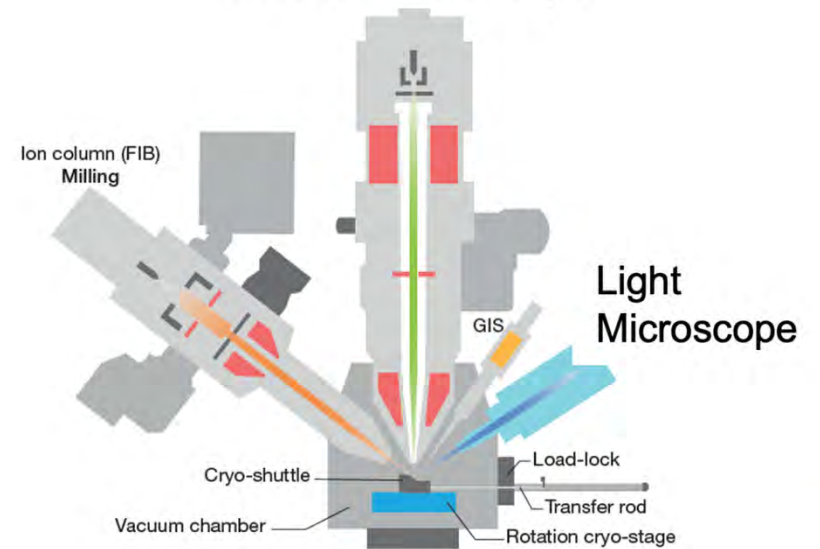
OCT
PAI
CT
MRI
PET/SPECT
Ultrasound

Goal: An advanced **cryogenic CLEM** instrument – Bringing Cell Biology and CLEM to the next level



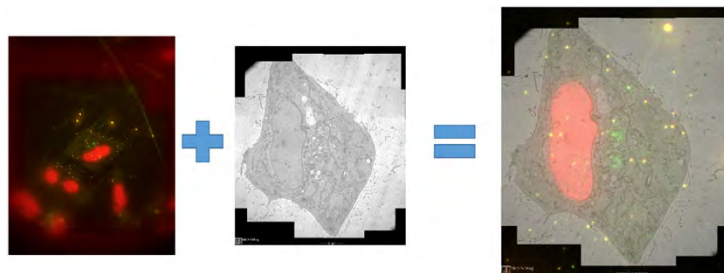
Aim: Hybrid CLEM instrument

Electron Microscope



© ThermoFisher Scientific

Correlative Light & Electron Microscopy (CLEM)



Light

Electron

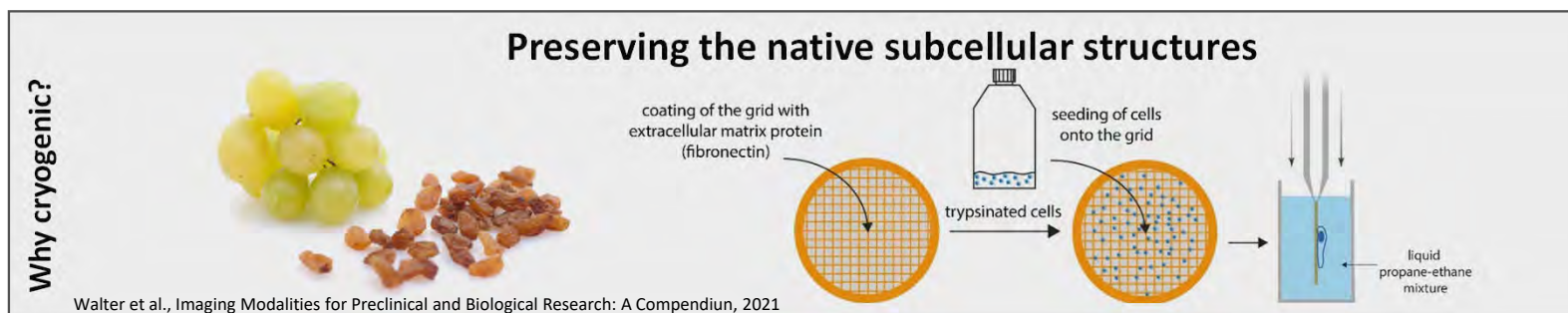
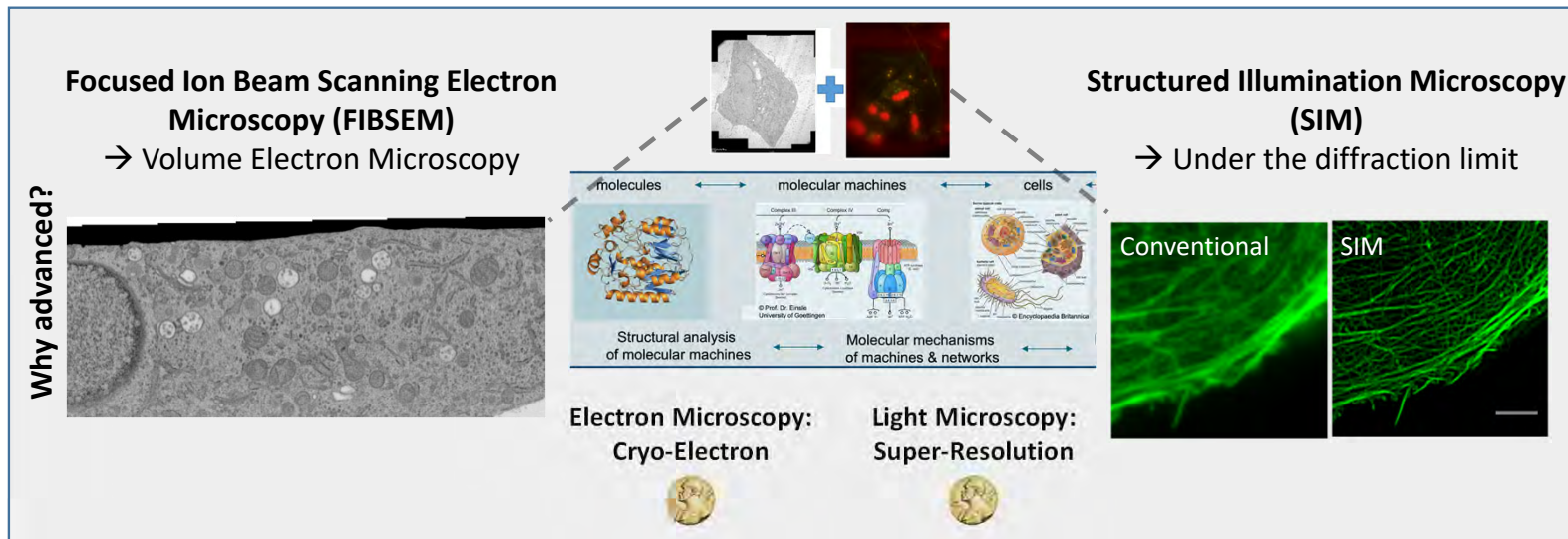
CLEM

Molecular function
at >250 nm

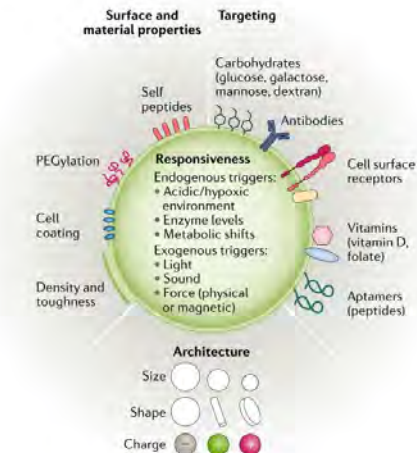
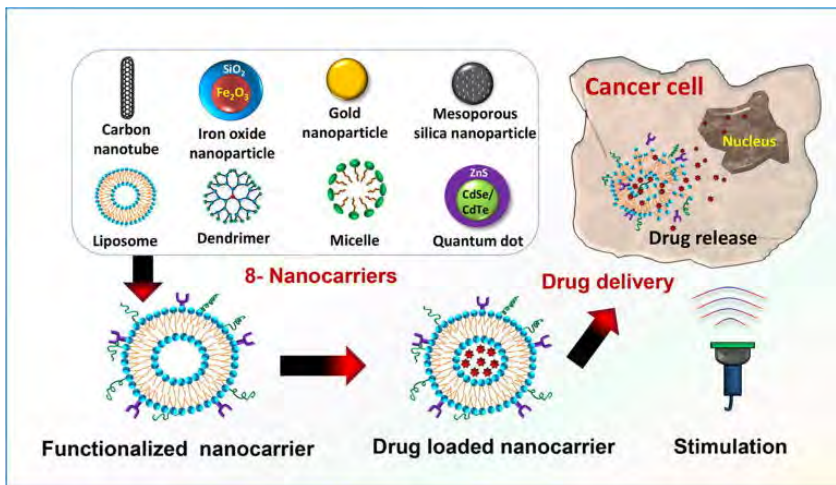
Subcellular archi-
tecture at >1 nm

Molecules within
structural context

Our Implementation: Advanced cryogenic CLEM - Correlative Super-Resolution Light & Scanning Electron Microscopy

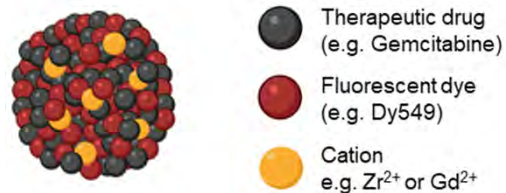


Biomedical Showcases: Diagnosing uptake, mechanisms of action, and effects of nanoparticles in cancer therapy

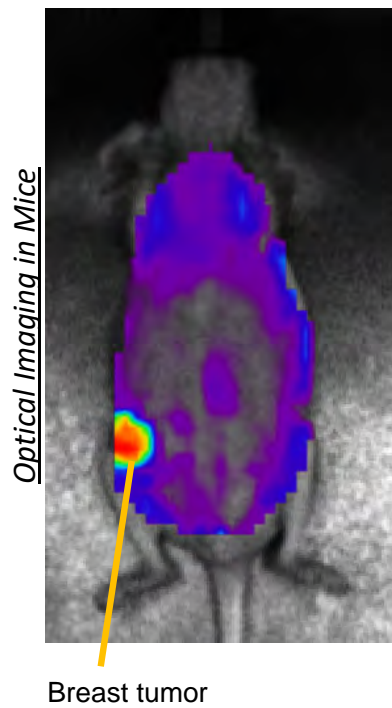


Visualizing expected clinical advantages of novel nanoparticles with extraordinarily high (multi)drug load (in collaboration with MPI Göttingen)

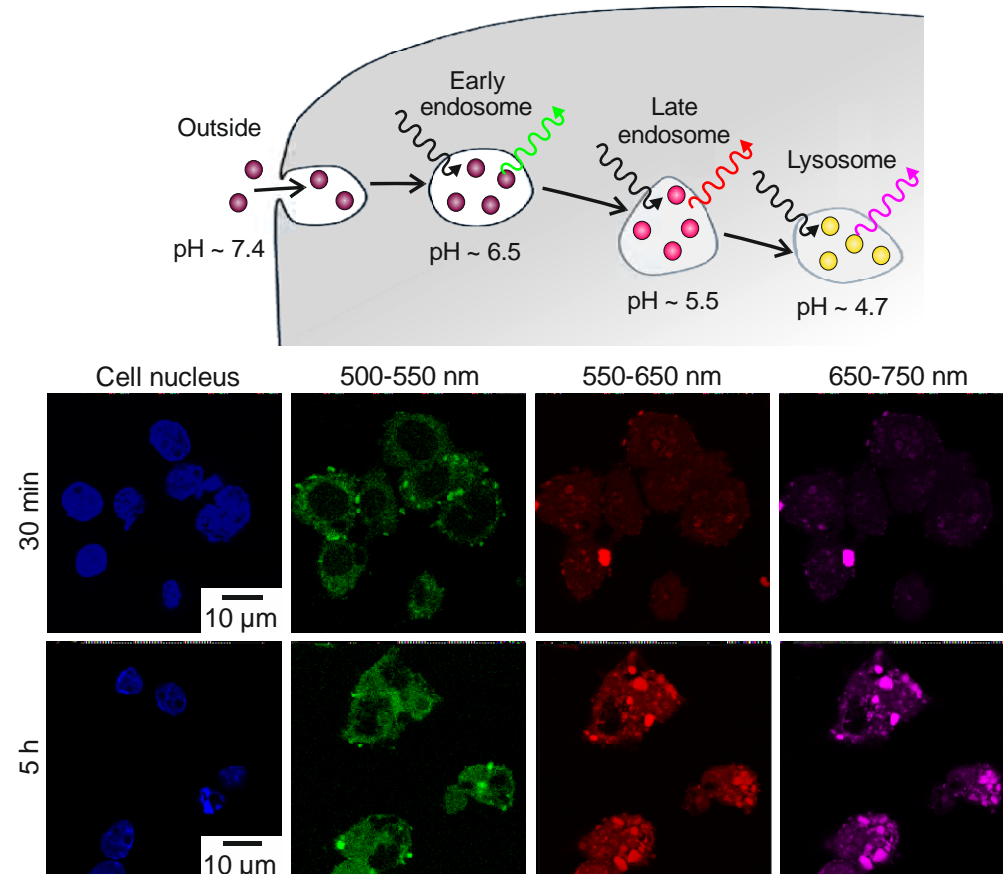
Hybrid NPs



Biomedical Showcases: Preliminary Studies in Mice & Cells

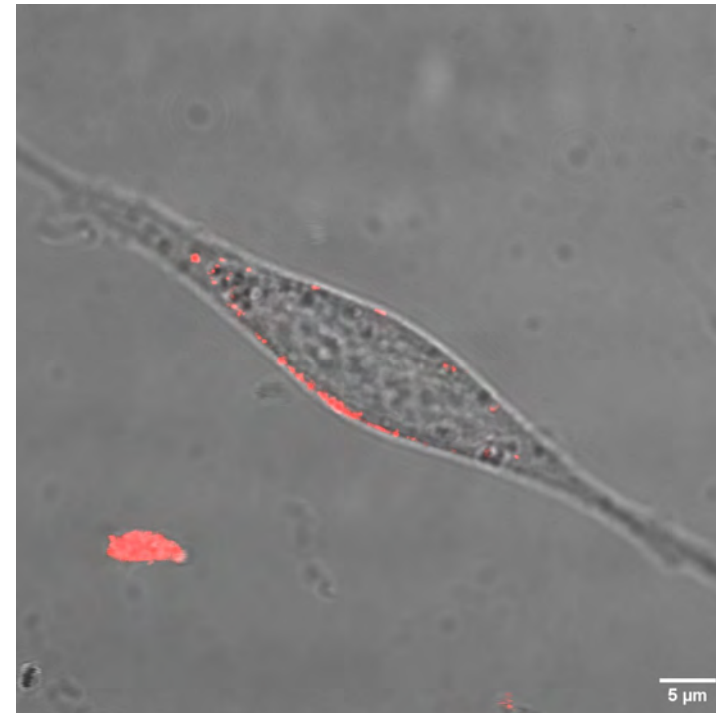
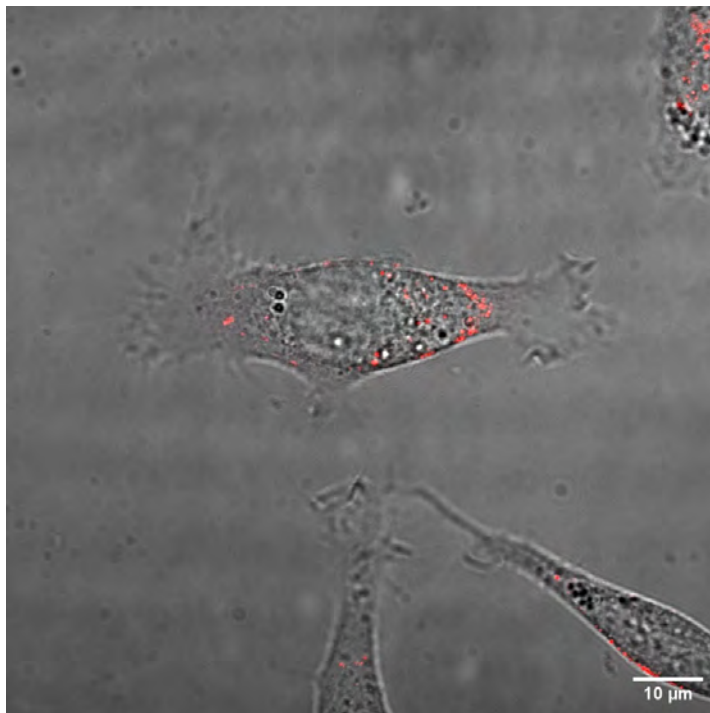


pH-sensitive Fluorescence microscopy of nanoparticles in cells



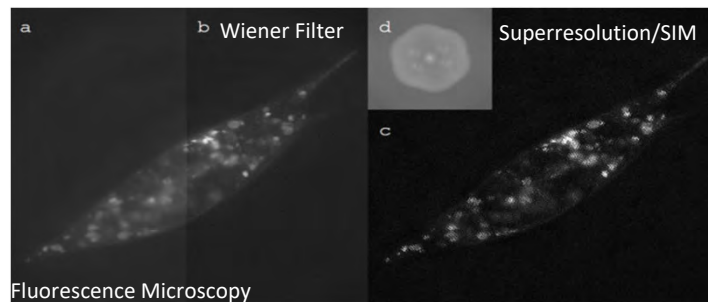
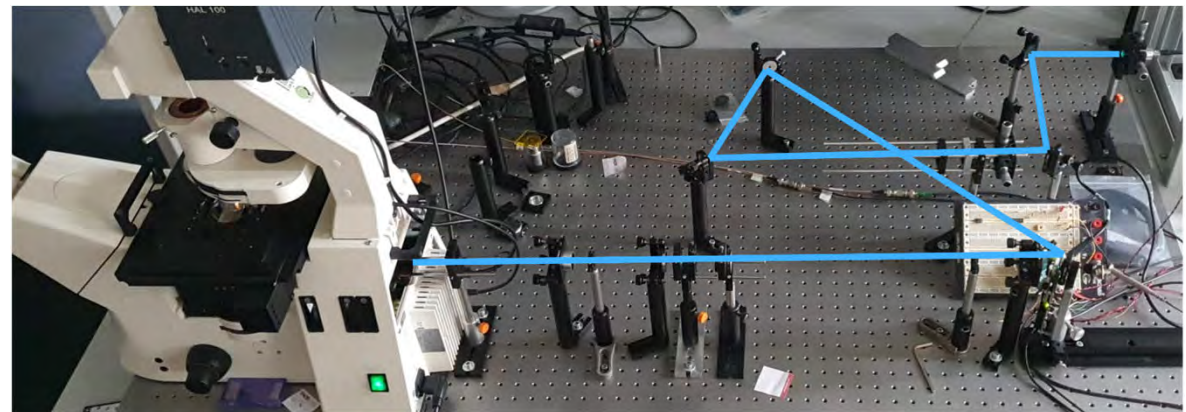
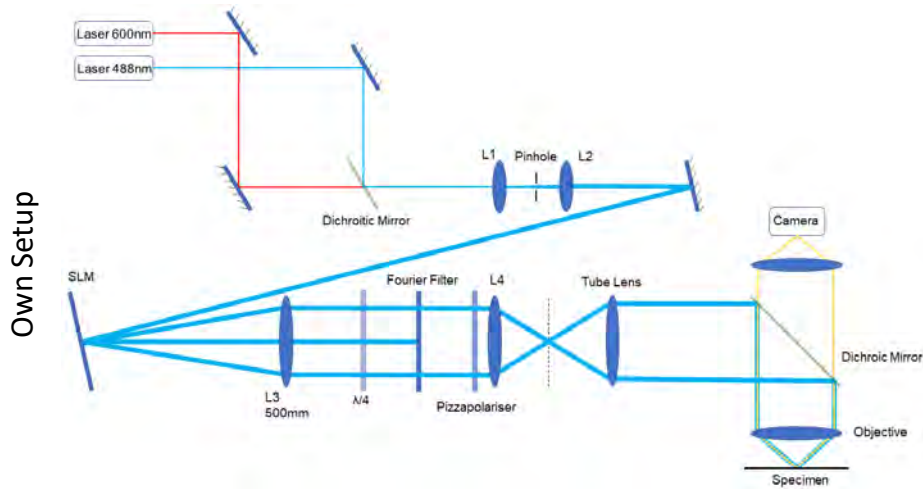
Biomedical Showcase: Preliminary studies to visualize nanoparticle-based drug therapy below the diffraction limit

Confocal microscopy of nanoparticles (Zeiss LSM 700)



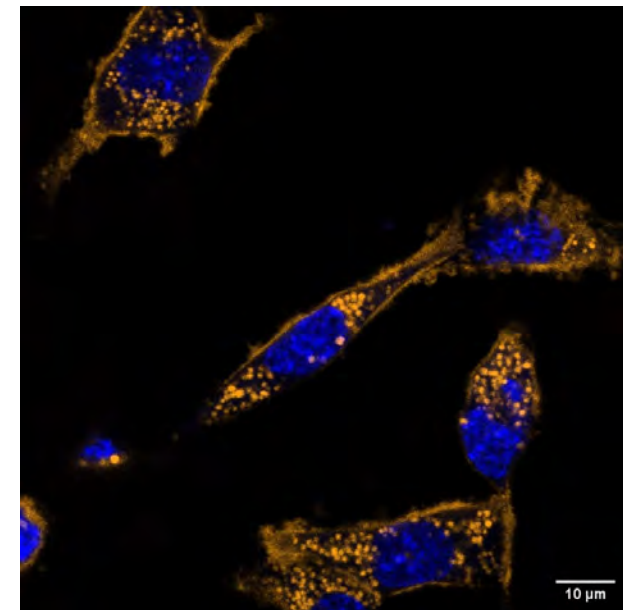
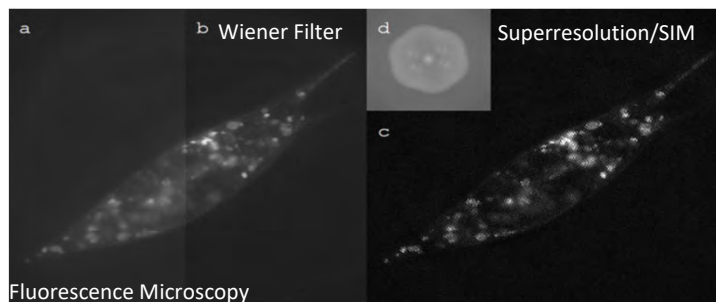
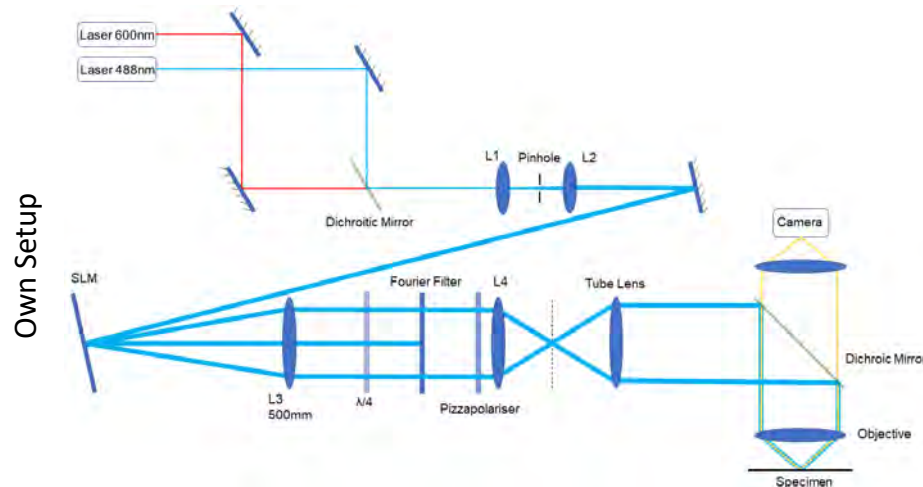
Towards Superresolution: Preliminary studies to visualize nanoparticle-based drug therapy below the diffraction limit

Structured illumination superresolution microscope at room temperature



Towards Superresolution: Preliminary studies to visualize nanoparticle-based drug therapy below the diffraction limit

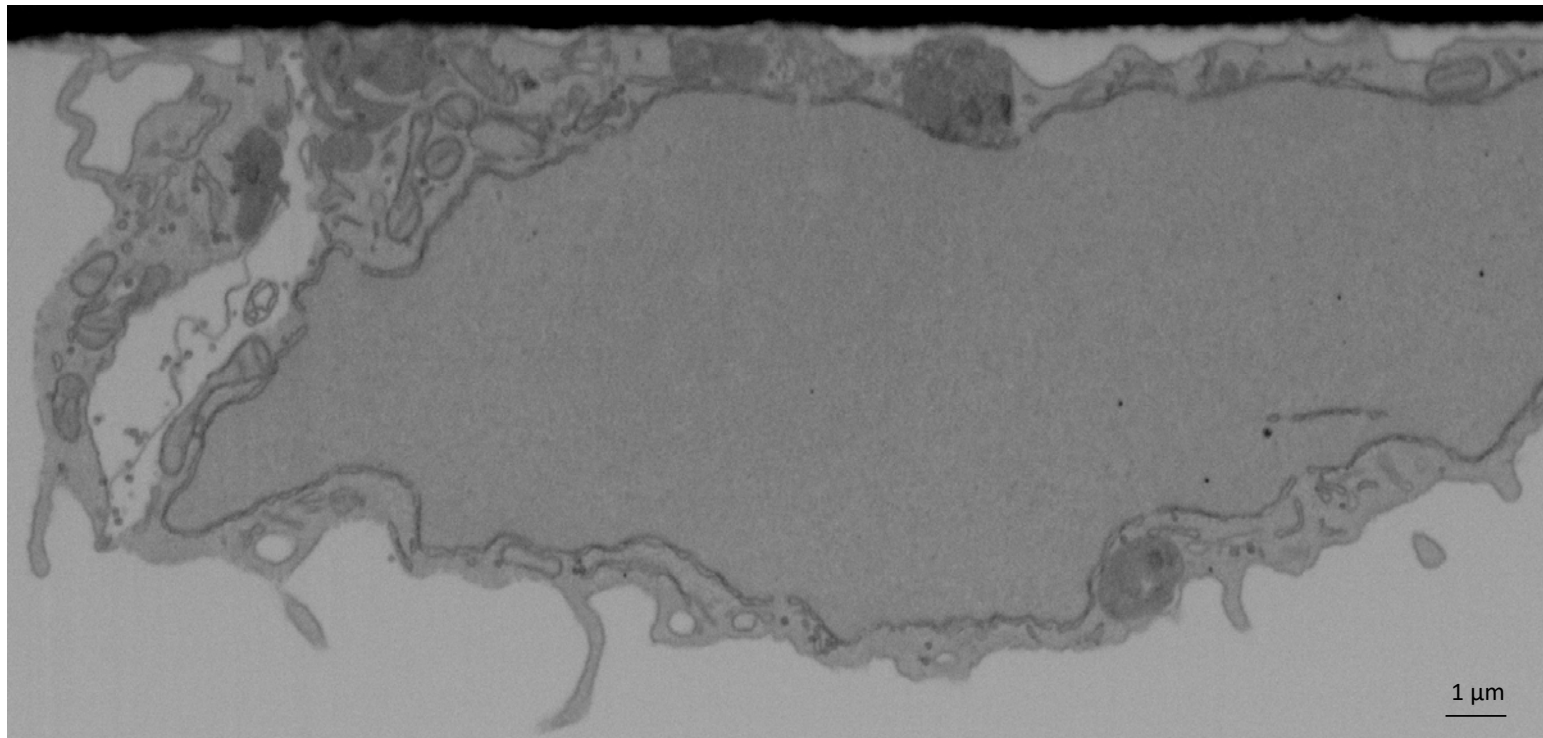
Structured illumination superresolution microscope at room temperature



nucleus/Hoechst (blue); nanoparticles (orange)

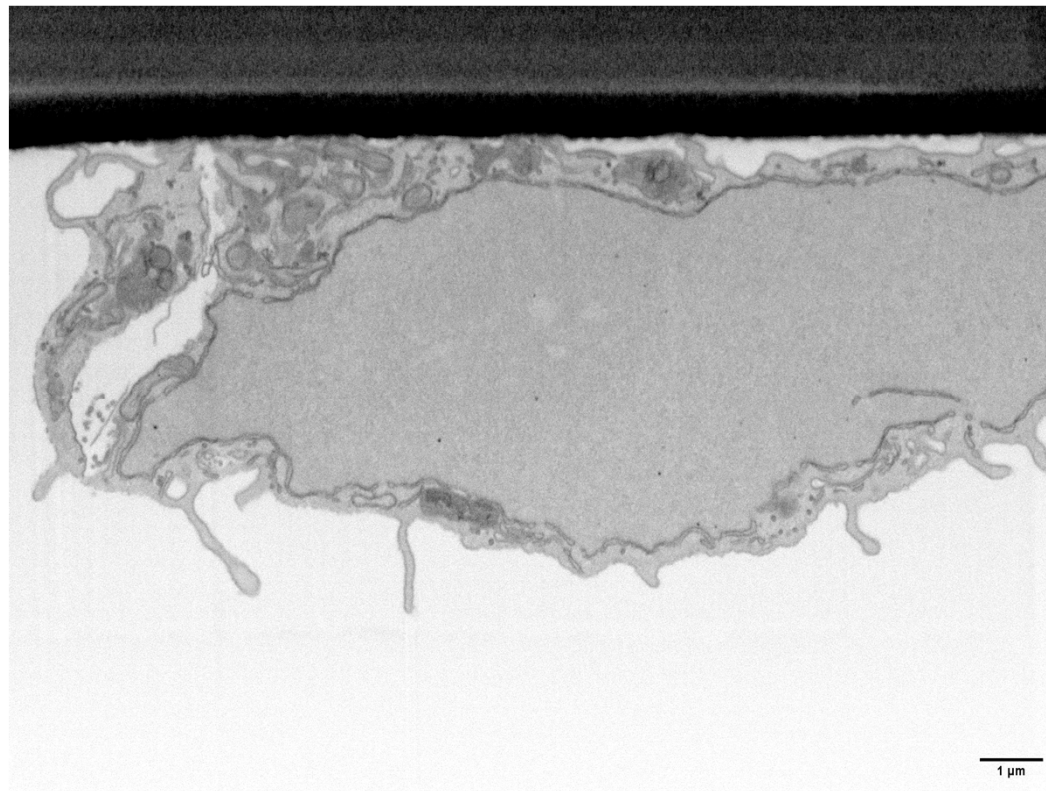
Towards Advanced CLEM: Control H8N8 cancer cells without nanoparticles using FIBSEM

FIBSEM at room temperature (Zeiss Crossbeam)

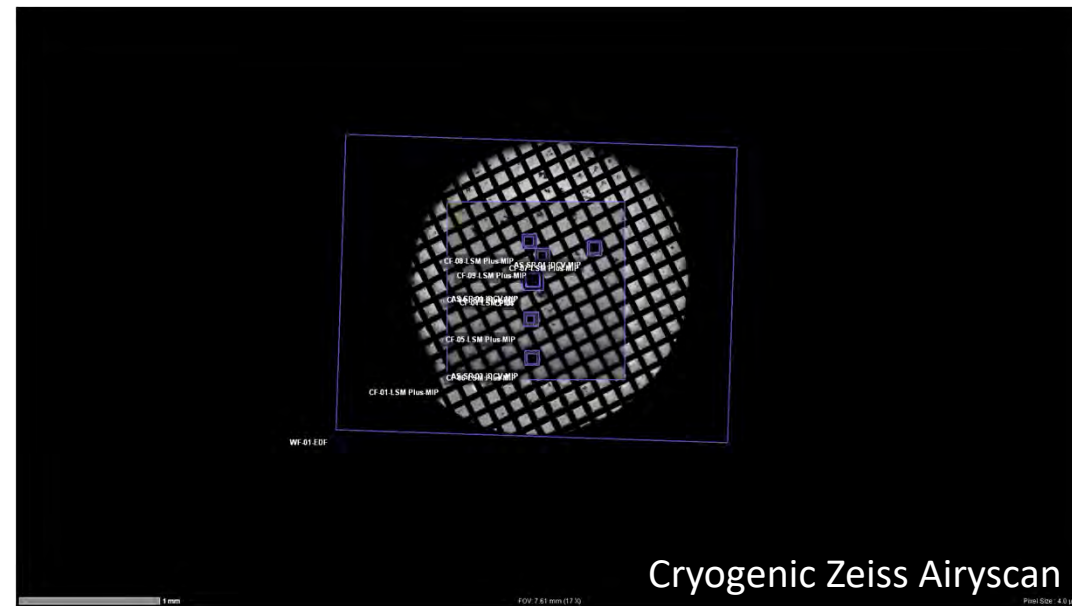
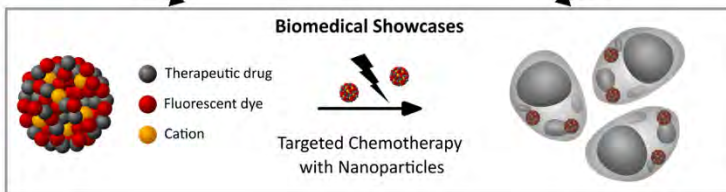
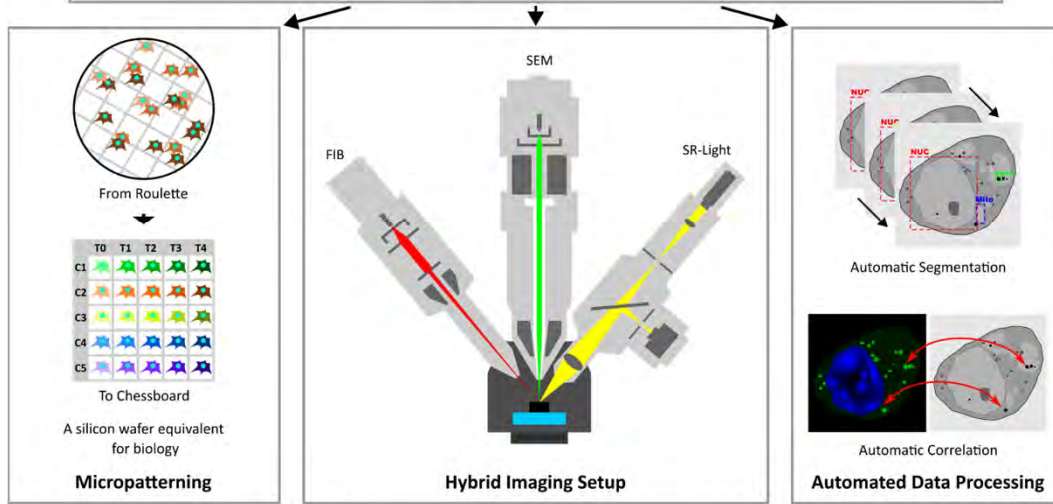
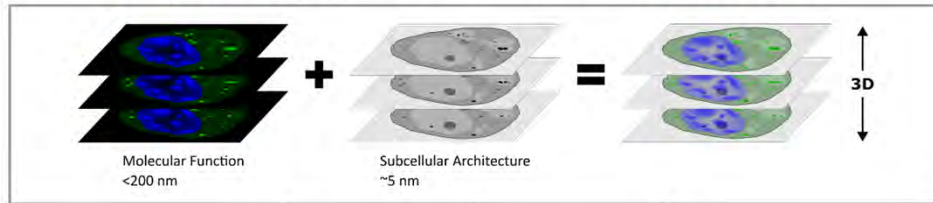


Towards Advanced CLEM: Control H8N8 cancer cells without nanoparticles using FIBSEM

FIBSEM at room temperature (Zeiss Crossbeam)

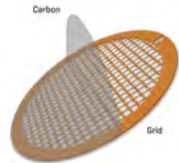


High throughput 3D Light & Electron Microscopy under native/cryogenic conditions below the diffraction limit



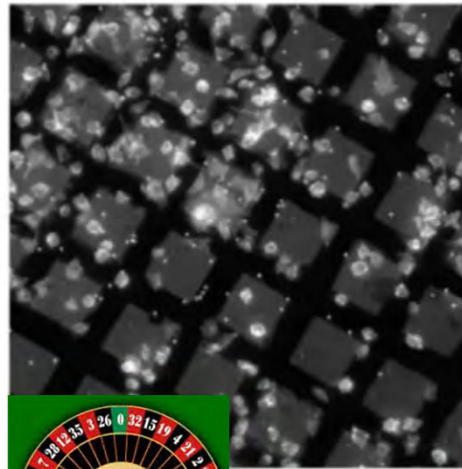
Cryogenic Zeiss Airyscan

Towards Automation: Micropatterning

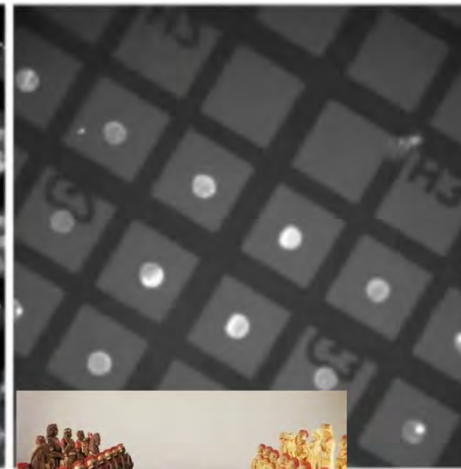


Growing Cells on EM grids

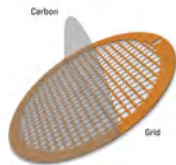
Conventional



Micropatterning

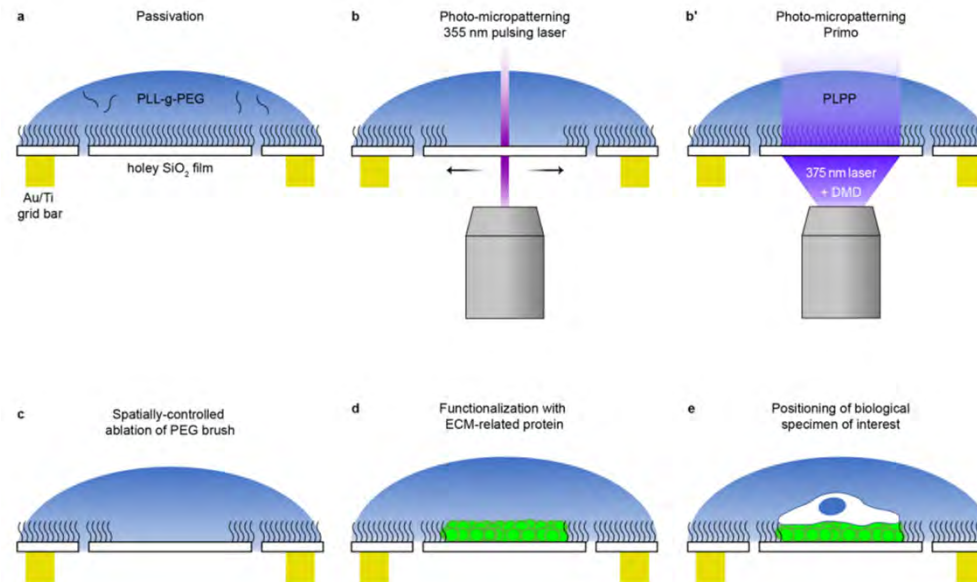


Towards Automation: Micropatterning



Growing Cells on EM grids

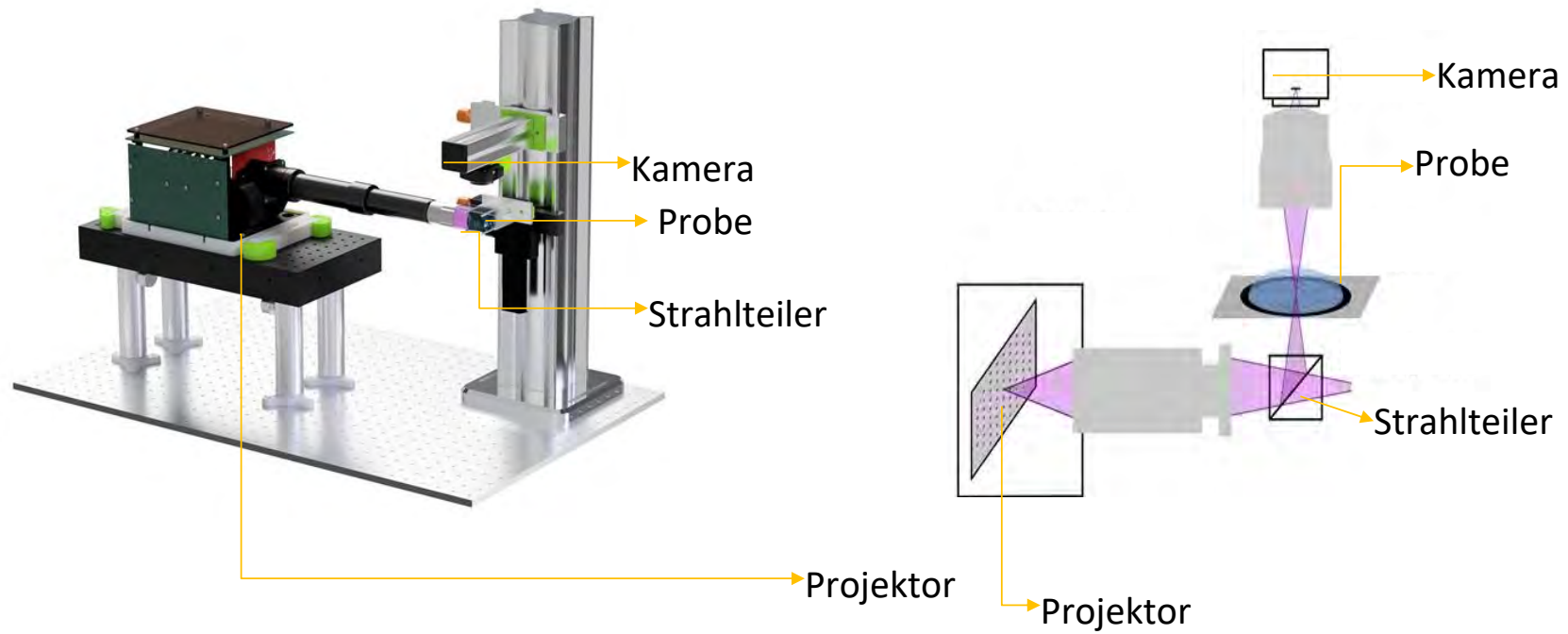
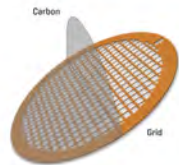
- Plasma cleanen EM – Grids
- Zugabe PLL-g-PEG
 - Passivierung
- Entfernen von PLL-g-PEG an bestimmten Stellen
 - Gepulster Laser
 - Photoaktivator
- Abwaschen von PLPP
- Erstellen zelladhäsiver Bereiche
 - Zugabe von Fibronectin
- Zugabe von Zellen



Supplementary information, Toro-Nahuelpan, Zagoriy, Tailoring cryo-electron microscopy grids by photo-micropatterning for in-cell structural studies, p. 2

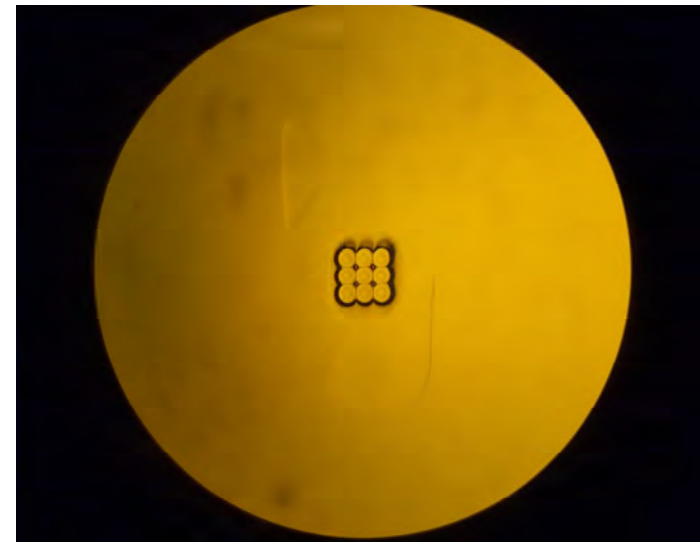
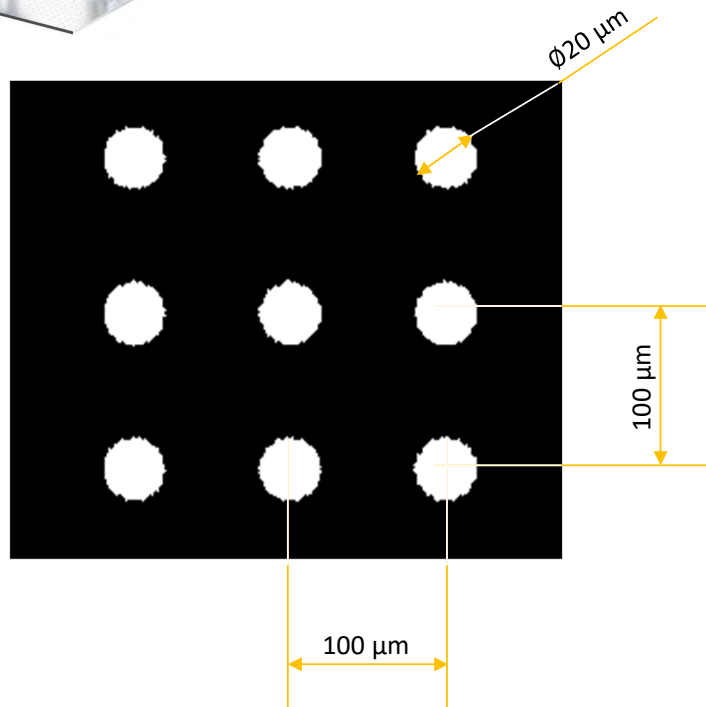
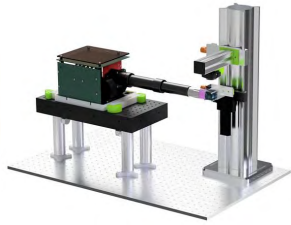
Towards Automation: Micropatterning

Own Setup: Growing Cells on EM grids



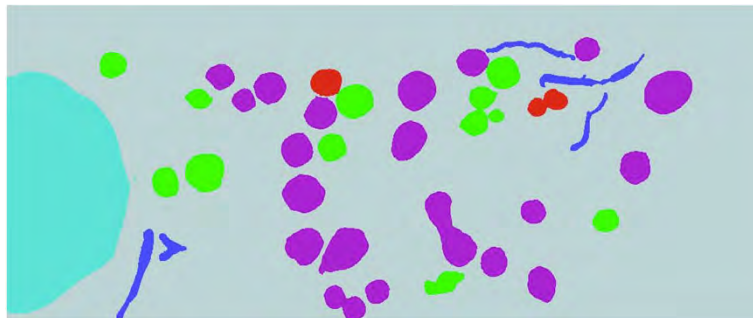
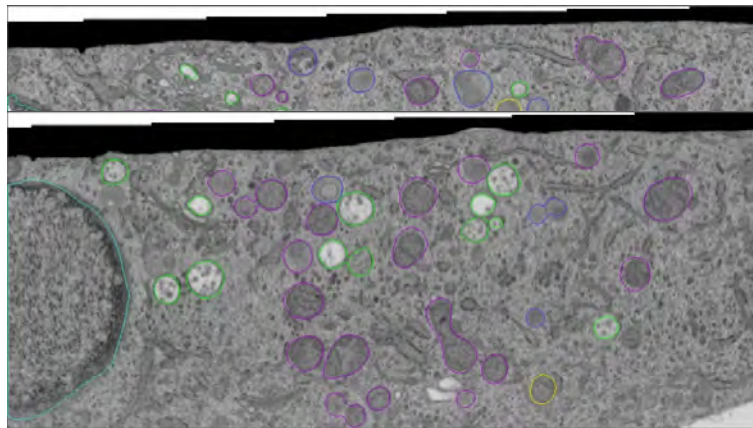
Towards Automation: Micropatterning

Growing Cells on EM grids: Illumination Mask

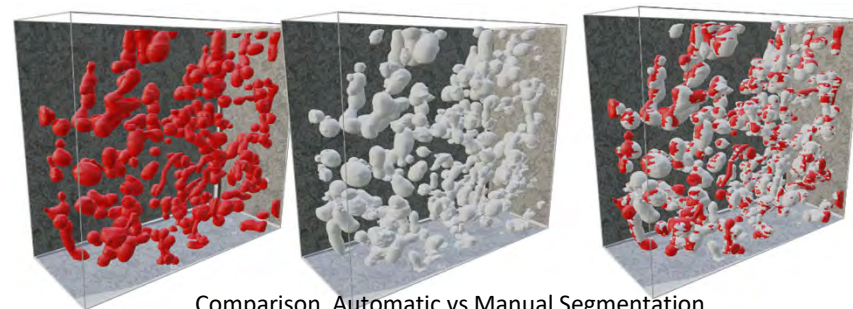
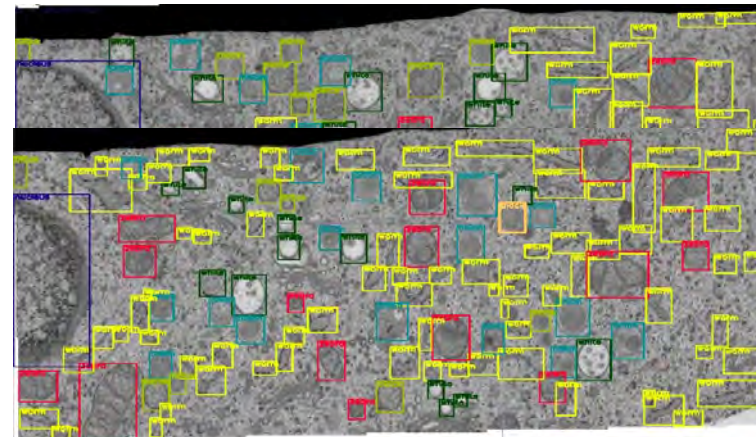


Towards Automation: Automatic segmentation of cellular components using neural networks (YOLO)

*Usually cell organelles are manually segmented: Easily
3 months for PhD*

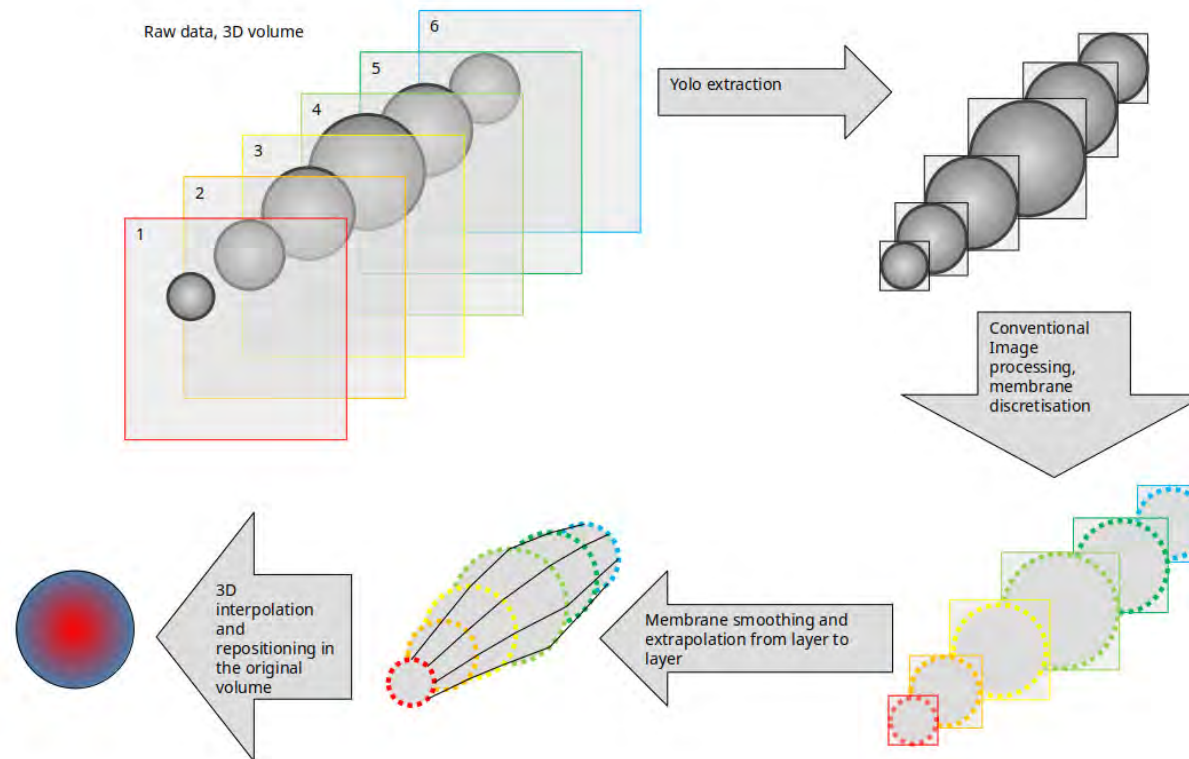


Using deep learning: Automation of process



Comparison, Automatic vs Manual Segmentation

Towards Automation: Automatic segmentation of cellular components using neural networks (YOLO)



Towards Automation: Automatic segmentation of cellular components using neural networks (YOLO)

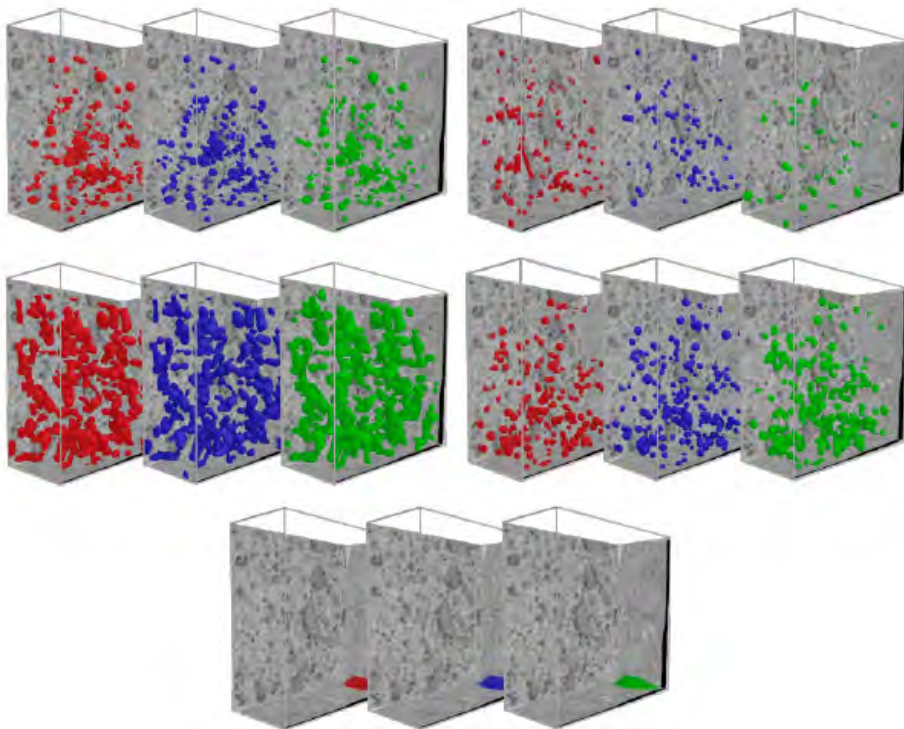


Figure 2: FIBSEM final visualization - Early Endosomes (top left) - Late Endosomes (top right) - Mitochondria (middle left) - Lysosomes (middle right) - Nucleus (bottom) - M1(red) - M2(blue) - Automatic(green)

Table 2: Precision, Recall, Jaccard index and F1 scores of the automatically segmented data by FAMOUS compared to M1 - FIBSEM

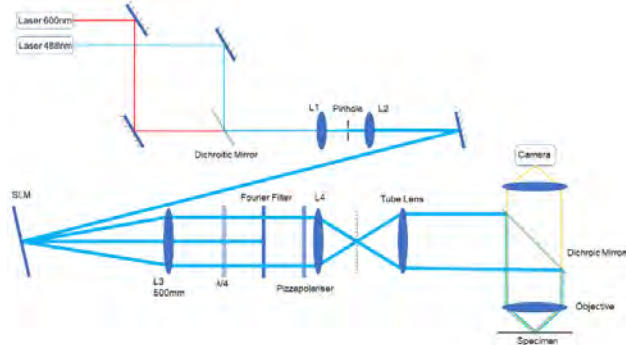
Class	Precision	Recall	Jaccard Index	F1 Score
Early Endosomes	84.02%	79.33%	68.93%	81.61%
Late Endosomes	37.50%	14.29%	11.54%	20.69%
Mitochondria	84.43%	92.27%	78.85%	88.18%
Lysosomes	72.83%	82.72%	63.21%	77.46%
Nucleus	100.00%	100.00%	100.00%	100.00%

Table 3: Precision, Recall, Jaccard index and F1 scores of the automatically segmented data by FAMOUS compared to M2 - FIBSEM

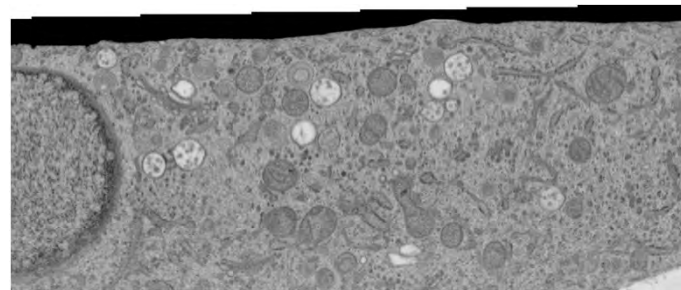
Class	Precision	Recall	Jaccard Index	F1 Score
Early Endosomes	82.42%	66.67%	58.37%	73.71%
Late Endosomes	17.50%	11.29%	7.37%	13.73%
Mitochondria	88.57%	92.81%	82.89%	90.64%
Lysosomes	74.19%	75.00%	59.48%	74.59%
Nucleus	100.00%	100.00%	100.00%	100.00%

- Arbeitsgruppe Andreas Walter: Biophotonik

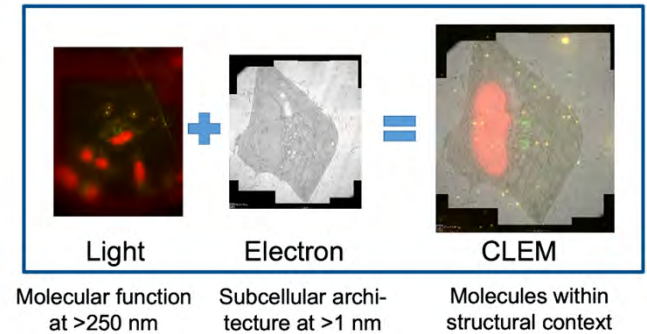
Kryogene Super-Resolution Mikroskopie



Elektronenmikroskopie



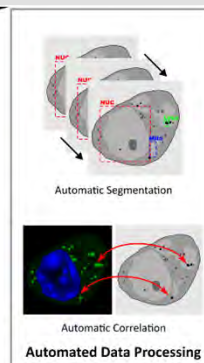
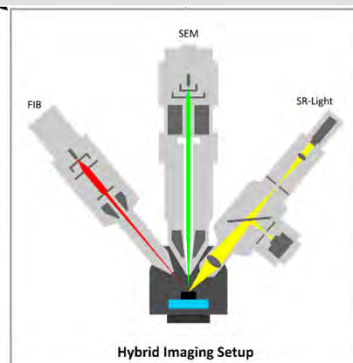
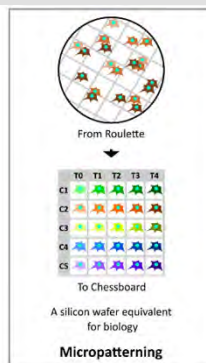
Korrelative Licht- und Elektronenmikroskopie



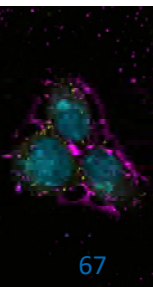
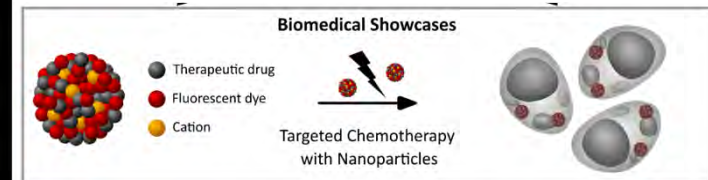
Entwicklung und Anwendung biomedizinischer Bildgebung
 (1 Postdoc, 1 Doktorand, typ.: 3-5 Duale Master, 3-5 Abschlussarbeiten)

Automatisierung
 (Präparation,
 Aufnahme, Daten
 & KI)

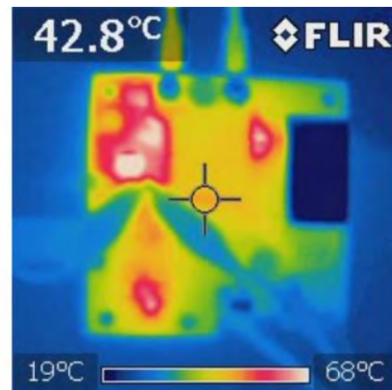
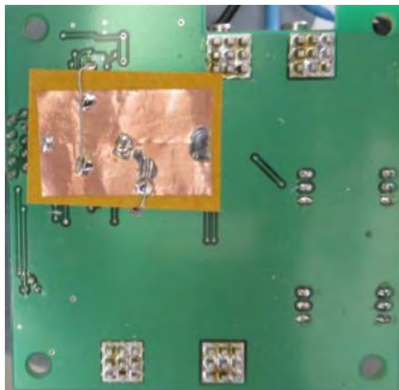
17.02.2024



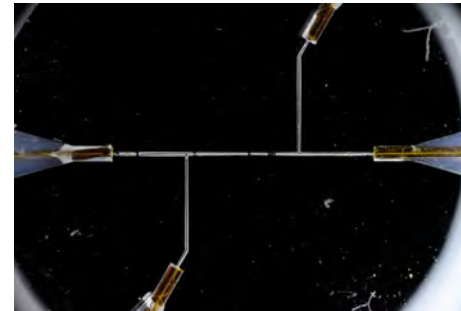
Biomedizinische Fragestellungen



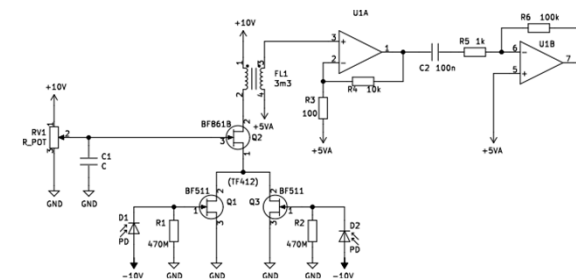
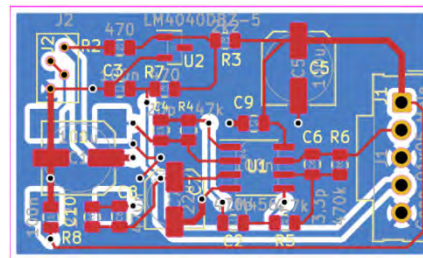
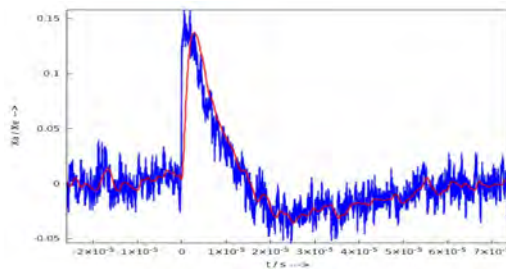
- Arbeitsgruppe Peter Zipfl: Optoelektronik



- Instrumentelle Entwicklung und Anwendung mehrdimensionaler elektromigrativer Trenntechniken
- (DFG-Projekt 507290570 in Kooperation mit Uni Tübingen)



Anwendungen der Elektronik in Detektion und Erzeugung optischer Strahlung, Signalverarbeitung und elektrischer Messtechnik



Vielen Dank für Ihre Aufmerksamkeit!