3rd European Symposium on Ultrafast Laser driven Biophotonics

September 15 – 18
Volkshaus Jena // Germany

Organized by

Leibniz ipht Leibniz Institute of Photonic Technology

biophotonics 4 FUTURE

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Overview

SUNDAY // SEPTEMBER 15th // Volkshaus Jena	
18:00	**Welcome Reception** // Registration & Get-Together
MONDAY // SEPTEMBER 16th // Volkshaus Jena	
09:00	**Welcome Note** // Jürgen Popp & Peter Vogt / Christopher Dorman (EVP Lasers Business)
09:20	**Scientific Talks // Session I** // Chair: Ute Neugebauer
10:50	Coffee Break
11:30	**Scientific Talks // Session II** // Chair: Shuxia Guo
12:45	Lunch Break
13:45	**Scientific Talks // Session III //** Chair: Jer-Shing Huang
15:15	Coffee Break
15:45	**Scientific Talks // Session IV** // Chair: André Gomes
16:45	**Poster-Pitches** // each poster author presents his/her topic in 1 minute
17:15	**Poster Session** // with Beer & Pretzels
19:45	End
TUESDAY // SEPTEMBER 17th // Volkshaus Jena	
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10:30	Coffee Break
11:00	**Keynote Lecture** // Chair: Jürgen Popp
12:00	Lunch Break
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15:00	**Scientific Talks // Session VII** // Chair: Timea Frosch
19:00	**Conference Dinner** // Volksbad Jena // Knebelstr. 10
WEDNESDAY // SEPTEMBER 18th // Volkshaus Jena	
09:00	**Scientific Talks | Session VIII** // Chair: Anja Silge
10:30	Coffee Break
11:00	**Scientific Talks // Session IX** // Chair: Tomáš Čižmár
12:30	**Closing Remarks**
12:45	End

Welcome to ESULaB 2024

Conference Chairs

Juergen Popp
Leibniz IPHT

Peter Vogt
Coherent Europe BV

Dear Guests of ESULaB 2024,

The throughput and complexity of research work has steadily increased in recent years while maintaining the same level of quality. In terms of experimental setup and laboratory infrastructure, research results have been improved by applying new combinations of available hardware and software technologies.

Therefore, at this conference we would like to bring together scientists from different disciplines to share their experiences with new technologies and experimental setups. One common thread is the use of ultrafast lasers in biophotonics. The research field of biophotonics combines life sciences, environmental sciences and medicine with innovative optical technologies.

Biophotonics encompasses all optical methods for investigating the structural, functional, mechanical, biological and chemical properties of biological materials and systems. Biophotonics opens up great opportunities for basic research, biotechnology and medicine. With the help of biophotonics, for example, it is possible to better understand the causes of diseases in order to prevent them in the future or at least diagnose them earlier and more accurately and thus treat them more effectively.

In more than 20 scientific presentations by leading scientists in their field, this conference will report on the many new possibilities arising in biophotonics with ultrashort pulse lasers. The range of topics includes nonlinear imaging (e. g. SHG / THG microscopy, coherent Raman microscopy) for biomedical diagnostics, imaging of biological objects with highest spatial resolution using nonlinear phenomena as well as wavelengths in the EUV / X-ray range and ultrafast spectroscopy of biological systems.

We wish you a stimulating conference and a pleasant stay in Jena.
Juergen Popp & Peter Vogt

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Welcome to Jena – The City of Light

Jena's nickname "City of Light" is a synonym for everything that makes Jena so attractive across the region to this day: the flashes of inspiration of its bright minds, the light of enlightenment, the first-class research facilities that constantly bring the light of knowledge to people. And also the world-famous high-tech companies and the young, innovative companies for whom light is a key success factor.

With over 150 years of industrial history, Jena is considered the cradle of the optical industry in Europe and a recognized research center in the fields of optics and photonics. What began with the meeting of Carl Zeiss, Ernst Abbe and Otto Schott not only culminated in the scientifically sound construction of microscopes. It also laid the foundation for the internationally successful companies and consolidated one of Jena's most important traditions: the close integration of research and industry. Here, world-class interdisciplinary research and practical implementation go hand in hand.

Many of Jena's shining success stories describe holistic solutions using light. These make a significant contribution to tackling important future issues in the areas of health, energy, mobility, environmental protection, security, communications and information technology. Today, this close connection is reflected above all in the use of light-based technologies in the life sciences.

Organizer of ESULaB 2024

Leibniz Institute of Photonics Technology

At the Leibniz Institute of Photonic Technology (Leibniz IPHT) in Jena, researchers and technologists from a wide range of disciplines work together on light-based solutions for health and medicine, the environment, energy and safety. Under the motto “Photonics for Life”, they research light-based technologies that make our lives safer, healthier and cleaner. Especially in the field of optical health technologies, Leibniz IPHT, in cooperation with partners from research and industry, is specifically promoting translation: the transfer of research results into applicable solutions – *from Ideas to Instruments*.

www.leibniz-ipht.de

General Information

Conference Venue
Volkshaus Jena // Carl-Zeiß-Platz 15 // 07743 Jena

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Venue Conference Dinner
Volksbad Jena // Knebelstraße 10 // 07743 Jena

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WiFi at Volkshaus
SSID: Volkshaus-Kongress
Password: Vo#2022Kon!aus

–

Public Transportation
A single trip ticket is 2,70 €. Tickets can be purchased at the ticket machine at the bus stop or on the bus, as well as via the FAIRTIQ. Find more information on fairtiq.com and www.nahverkehr-jena.de.

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Organizing Team
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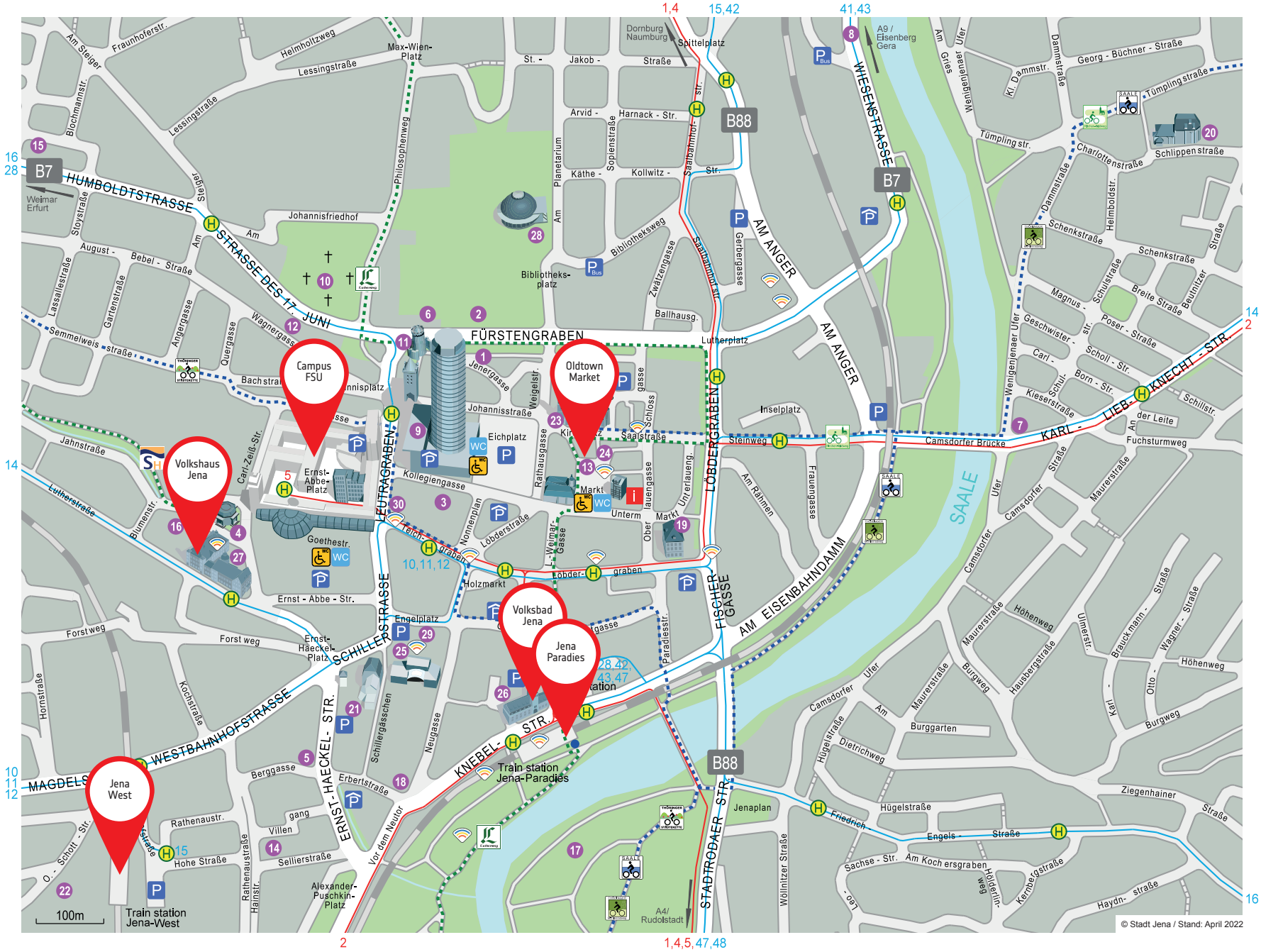
Map Jena City Center



1. Archaeological Collection
2. Botanical Garden
3. Collegium Jenense
4. Ernst Abbe Monument
5. Ernst Haeckel House
6. Goethe Laboratorium (from summer 2024)
7. Grüne Tanne
8. Imaginata
9. JenTower / Observation platform
10. St. John's Cemetery and Church of Peace
11. St. John's Gate & Powder Tower
12. Johannes Church
13. Market square with Hanfried monument & the historical town hall
14. Mineralogical Collection
15. Museum 1806, Jena-Cospeda
16. German Optical Museum (closed until 2026)
17. Paradies / Volkspark Oberaue
18. Museum of Phylogenetics
19. Romanticists' house
20. Schiller Church
21. Schiller's Summer House
22. SCHOTT Villa
23. St. Michael Town Church
24. Jena Municipal Museum & Art Collection
25. Theatre House
26. Volksbad Jena
27. Volkshaus Jena
28. Zeiss Planetarium Jena
29. Carmelite Abbey
30. Anatomy Tower

- Lockers for bicycle tourists
- Saale Cycle Route
- Towns of Thuringia Cycle Route
- Thuringian Mills Route
- Churches Cycle Route
- Walking trail SaaleHorizontale
- Luther trail
- Jena Tourist Information
- Free WLAN via App MeinJena
- Bus
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Agenda

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18:00	**Welcome Reception** // Registration & Get-Together
MONDAY // SEPTEMBER 16th // Volkshaus Jena	
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09:20	**Scientific Talks // Session I** // Chair: Ute Neugebauer
Linda Zedler	Leibniz IPHT // Jena, Germany // 30 min ***Multiphoton Processes and Light-induced Multi-electron Charge-transfer in Covalent Polyoxometalate Dyads and Triads***
Michele Celebrano	Politecnico // Milano, Italy // 30 min ***Nonlinear Interferometry with Metasurfaces: Towards Light Routing and Sensing***
Mantas Butkus, Stephen Duffy	Coherent Scotland Ltd. // Glasgow, United Kingdom // 30 min ***Global Centre of Excellence in Ultrafast Technology in Glasgow and Innovations in Ultrafast Lasers for Nonlinear Microscopy***
10:50	Coffee Break
11:30	**Scientific Talks // Session II** // Chair: Shuxia Guo
Andreas Zumbusch	University Konstanz // Konstanz, Germany // 30 min ***Sensitive Imaging Without Labeling: SRS Microscopy***
Margherita Maiuri	Politecnico // Milano, Italy // 30 min ***Ultrafast Spectroscopy in Bio-molecules and Optical Nanostructures: Harnessing Light and Manipulating Matter***
François Sylla	Source LAB // Paris, France // 15 min ***KAIO-Beamline – A Modular High-repetition Rate Laser-plasma Electron Accelerator for a Broad Range of Applications***
12:45	Lunch Break
13:45	**Scientific Talks // Session III //** Chair: Jer-Shing Huang
Maria Chernysheva	Leibniz IPHT // Jena, Germany // 30 min ***Advances and Challenges of Shortwave- and Mid-infrared Ultrafast Fibre Lasers***
Karsten König	Saarland University // Saarbrücken, Germany // 30 min ***In Vivo Skin Imaging with Femtosecond Lasers***
Leonardo Sacconi	LENS – European Laboratory for Non-Linear Spectroscopy // Florence, Italy // 30 min ***Exploring Cardiac Electrophysiology Through Advanced Microscopy***
15:15	Coffee Break
15:45	**Scientific Talks // Session IV** // Chair: André Gomes
Helen Fielding	University College London // London, United Kingdom // 30 min ***Unravelling the Photodynamic of Biochromophores Using Transient Absorption Spectroscopy and Liquid-microjet Photoelectron Spectroscopy***
Christian Eggeling	Leibniz IPHT // Jena, Germany // 30 min ***Advanced Super-resolution Minflux and STED Microscopy for Studying Molecular Interactions***
16:45	**Poster-Pitches** // Each poster author presents his/her topic in 1 minute
17:15	**Poster Session** // with Beer & Pretzels
19:45	End

Agenda

TUESDAY // SEPTEMBER 17th // Volkshaus Jena	
09:00	**Scientific Talks // Session V** // Chair: Mantas Butkus
Dafne Suraci	LENS – European Laboratory for Non-Linear Spectroscopy // Florence, Italy // 30 min ***Autofluorescence Label-free High-contrast Imaging of Tumor Margins in Freshly Excised Gastro-intestinal Biopsies***
Eirini Papgiakoumou	Institut de la Vision // Paris, France // 30 min ***Scanless Two-photon Illumination for All-optical Neurophysiology***
Felix Grasbon	Grättinger · Möhring · von Poschinger Patentanwälte Partnerschaft mbB // Starnberg, Germany // 30 min ***Patent Trends and Patent Practice in the Field of Ultrafast Laser Driven Biophotonics***
10:30	Coffee Break
11:00	**Keynote Lecture** // Chair: Jürgen Popp
Mihaela Žigman	Max Planck Institute of Quantum Optics // Garching, Germany // 60 min ***Advancing Infrared Molecular Fingerprinting to Profile Health and Disease***
12:00	Lunch Break
13:00	**Scientific Talks // Session VI** // Chair: Wolfgang Paa
Alfred Leitenstorfer	University Konstanz // Konstanz, Germany // 30 min ***Applications of Ultrabroadband Femtosecond Fiber Lasers: from Single Electrons and Zero Photons to Biophotonics***
Markus Gräfe	Technische Universität Darmstadt // Darmstadt, Germany // 30 min ***Nonlinear Interferometers for Quantum Sensing with Undetected Lights***
Ingo Rimke	APE Angewandte Physik & Elektronik // Berlin, Germany // 15 min ***APE Multispectral SRS Imaging and Ultra-sensitive Detection for the Fingerprint Region and Raman Labels with New Picosecond Light Source***
Matteo Negro	Cambridge Raman Imaging Ltd. // Milano, Italy // 15 min ***Multiplexing Stimulated Raman Microscopy for Biomedical Imaging and Chemometric Histology***
14:30	Coffee Break
15:00	**Scientific Talks // Session VII** // Chair: Timea Frosch
Thomas Bocklitz	Leibniz IPHT // Jena, Germany // 30 min ***Photonic Data Science: Translating Linear and Non-linear Optical Data to Knowledge***
Christian Spielmann	Friedrich-Schiller-University // Jena, Germany // 30 min ***Lens-less Imaging of Biological Samples***
Gregor Knopp	Paul Scherrer Institute // Villigen, Switzerland // 30 min ***Resonant Nonlinear X-ray Four Wave Mixing in Atomic and Molecular Systems: A Tool Also for Chemical and Biological Samples?***
19:00	Conference Dinner // Volksbad Jena // Knebelstr. 10

Agenda

WEDNESDAY // SEPTEMBER 18th // Volkshaus Jena	
09:00	**Scientific Talks | Session VIII** // Chair: Mantas Butkus
Arseny Finkelstein	Tel Aviv University // Tel Aviv, Israel // 30 min ***Optical Mapping of Neural Interactions on Multiple Spatial Scales During Behavior***
Sophie Brasselet	IInstitut Fresenel // Marseille, France // 30 min ***Polarized Microscopy for Molecular-organization Imaging in Cells and Tissues***
Shuxia Guo	Leibniz IPHT // Jena, Germany // 30 min ***Long-term Setup Stability in Raman Spectroscopy***
10:30	Coffee Break
11:00	**Scientific Talks // Session IX** // Chair: Tomáš Čižmár
Brice Bathellier	Institut Pasteur // Paris, France // 30 min ***High-efficiency Single Pulse Two-photon Stimulation for in Vivo all-optical Interrogation of Neuronal Circuits with Acousto-optic Deflectors***
Amanda Foust	Imperial College London // London, United Kingdom // 30 min ***Enabling High-throughput, Scattering-mitigated, Volumetric Imaging Through Two-photon Informed Light-field Deep Learning***
Tobias Meyer-Zedler	Leibniz IPHT // Jena, Germany // 30 min ***Multimodal Nonlinear Endomicroscopy for Use in Clinics***
12:30	**Closing Remarks**
12:45	End

Conference Venue: Volkshaus Jena

Volkshaus Jenakultur (©Karoline Kramer)

The Volkshaus was built between 1901 and 1903 on the initiative of Ernst Abbe, largely with funds from the Carl Zeiss Foundation. Today, the building is owned by the Ernst Abbe Foundation and operated by JenaKultur. Since 2019, it has been converted into a modern cultural and congress center, which opened in 2022. The ESULaB is one of the first events to be held in the newly renovated Volkshaus after completion of the conversion work. In parallel, the Volkshaus is not only the playing and working place of the Jena Philharmonic Orchestra, but has also developed into a fixed cultural address beyond the city limits due to its versatile events and rentals.

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www.volkshaus-jena.de

Conference Dinner at Volksbad Jena

The historic Volksbad building was built between 1907 and 1909. It was designed by the architect Prof. Wilhelm Werdelmann. From 1900 onwards, bathing culture and sport became increasingly important for the general public. Many Jena citizens learned to swim in the 9 x 20 meter pool of the Volksbad.

However, the Volksbad was closed as a public swimming pool in 2001 and it initially remained unclear what would happen to the listed building.

In the 2003 / 2004 season, the theater building could not be used due to construction work. The theater ensemble at the time needed an alternative and "breathed new life into" the Volkshaus, which was temporarily used for a dance festival, an art market, concerts and readings. From then on, it was clear that the city would convert the Volksbad into a new event venue that would combine modern, contemporary facilities with the preservation of the historic ambience.

In 2007, the time had come and the Volksbad was reopened for its second life.

Enjoy a relaxed evening in the historic Volksbad Jena. The band "Bar Muppets" will provide the musical accompaniment, conjuring up a relaxed bar atmosphere for the audience with smooth jazz and laid-back Latin arrangements.

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www.volksbad-jena.de
www.barmuppets.de

Session I

Monday // September 16th // 09:20 – 10:50

Session Chair
Ute Neugebauer

Speakers

09:20 – 09:50
Linda Zedler // Leibniz IPHT // Jena, Germany
Multiphoton Processes and Light-induced Multi-electron Charge-transfer in Covalent Polyoxometalate Dyads and Triads
–
09:50 – 10:20
Michele Celebrano // Politecnico // Milano, Italy
Nonlinear Interferometry with Metasurfaces: Towards Light Routing and Sensing
–
10:20 – 10:50
Mantas Butkus, Stephen Duffy // Coherent, Scotland Ltd. //
Glasgow, United Kingdom
Global Centre of Excellence in Ultrafast Technology in Glasgow and Innovations in Ultrafast Lasers for Nonlinear Microscopy

Multiphoton Processes and Light-Induced Multi-Electron Charge-Transfer in Covalent Polyoxometalate Dyads and Triads

Linda Zedler // Leibniz IPHT; IPC // Jena, Germany

Artificial systems for solar energy conversion utilize multi-electron processes and charge separation by accumulation of reduced and oxidized species. Polyoxometallate (POM)-based systems are promising candidates for the generation of green fuels and combine structural variability with unique electron storage and electron transfer properties. By covalent functionalization of POMs with light-absorbing noble-metal free bodipy-quinone dyads and metal complexes like ferrocence as well as proton/electron donors, a wide range of dyads and triads with tuneable (photo)redox-properties can be realized in which both the light-absorption and the charge transfer properties to the POM can be independently optimized (Figure 1). This research focuses first on the investigation of this novel class of substances with respect to light-induced multi-electron and multi-proton processes and second on the iterative structural optimization. For characterization we use spectroscopic tools such as time-resolved spectroscopy and spectroelectrochemistry to analyze the light-induced formation and the properties of charge-separated states during multiple electron transfer from the peripheral groups to the POM.

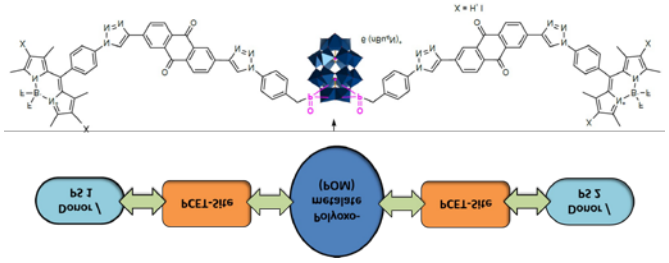

Figure 1. Schematic and molecular structure of bodipy-quinone POM triads.

To investigate multielectron charge transfer to the POM the charge separated state was mimicked by electrochemical methods and its structure analyzed by UV-Vis and rR spectroelectrochemistry. The observed spectral changes upon reduction of the POM prove delocalization of several charges across multiple metal centres.

Nonlinear Interferometry with Metasurfaces: Towards Light Routing and Sensing

Michele Celebrano // Politecnico di Milano // Milan, Italy

Metasurfaces have emerged as versatile, ultrathin platforms for light manipulation. Their rapidly evolving functionalities include precise control over light-wavefronts and the ability to perform light-by-light manipulation. Nonlinear optical processes are key mechanisms to realize light modulation by light. Leveraging the interference between degenerate nonlinear optical processes – specifically third-harmonic and sum-frequency generation (THG and SFG) – excited by dual beam illumination at ω and 2ω, we demonstrated all-optical routing of telecom photons upconverted to the visible range by an all-dielectric metasurface [1]. Light routing with attosecond control is enabled by the nonlinear parity conversion inherent to the SFG process, which converts two photons into one [2]. Expanding upon this paradigm, whereby the interference can be controlled with high speed and accuracy by the relative phase between the pump beams, we envision applications to optical sensing. Indeed, sensitivity can be boosted by implementing a homodyne amplification scheme, where an upconverted signal at 2ω interferes with a reference beam of identical wavelength, effectively mitigating the low conversion efficiency of third order processes in these nonlinear metasurfaces. In this regard, we recently realized a plasmonic metagrating [3] that, coupled to this concept, may allow enhanced nonlinear optical sensing. We could also leverage the common mode rejection naturally occurring among the diffraction orders to suppress intensity fluctuations. The all-optical routing demonstrated is not limited to intensity, but it also enables to modulate the polarization of the nonlinear light directed to the different diffraction orders of the metasurface. Notably, when circular polarization is produced in one diffraction spot, the opposite circular polarization is generated in the spot symmetrically positioned across the optical axis. This feature can be particularly appealing for chiral sensing applications,

[1] A. Di Francescantonio, A. Zilli, D. Rocco, L. Coudrat, F. Conti, P. Biagioni, L. Duò, A. Lemaître, C. De Angelis, G. Leo, M. Finazzi, and M. Celebrano, Nat. Nanotechnol. 19, 298 (2024).
[2] A. Zilli, D. Rocco, M. Finazzi, A. Di Francescantonio, L. Duò, C. Gigli, G. Marino, G. Leo, C. De Angelis, M. Celebrano, ACS Photonics 8, 1175 (2021)
[3] A. Verneuil, A. Di Francescantonio, A. Zilli, J. Proust, J. Béal, D. Petti, M. Finazzi, M. Celebrano, A.-L. Baudrion, Nanophotonics (2024). https://doi.org/10.1515/nanoph-2023-0842

Session I

Global Centre of Excellence in Ultrafast Technology in Glasgow / Innovations in Ultrafast Lasers for Nonlinear Microscopy

Stephen Duffy, Mantas Butkus // Coherent Scotland Ltd. // Glasgow, United Kingdom

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In this presentation we will discuss two key topics. In the first part we will review recently created global centre of excellence in ultrafast laser technology in Coherent's location in Glasgow, Scotland. Here, all R&D, manufacturing, and support activities were unified for all key Coherent femtosecond and picosecond laser product lines. We will discuss how the new approach and activities in this state-of-the-art volume production facility are shaping the next generation ultrafast laser products and what this means to our scientific and OEM customers.

In the second part of the presentation, we will look into multiphoton microscopy, which continues to find new applications across diverse fields such as neuroscience, cancer studies, and immunology. There is also a pursuit to leverage the benefits of multiphoton imaging for clinical and diagnostic applications, driven by both research advancements and commercial developments. Alongside this diverse range of applications, there is a growing array of probes, laser beam manipulation techniques, and optical delivery schemes that are aimed to expand the functionality of multiphoton microscopy. In turn, these advancements drive continuous progress in femtosecond laser sources, which are essential for driving nonlinear excitation processes in these imaging techniques. We will review novel developments in femtosecond lasers and their interplay with existing and emerging nonlinear imaging techniques.

Session II

Monday // September 16th // 11:30 – 12:45

Session Chair
Shuxia Guo

Speakers

11:30 – 12:00
Andreas Zumbusch // University Konstanz // Konstanz, Germany
Sensitive Imaging Without Labeling: SRS Microscopy
–
12:00 – 12:30
Margherita Maiuri // Politecnico // Milano, Italy
Ultrafast Spectroscopy in Bio-molecules and Optical Nanostructures: Harnessing Light and Manipulating Matter
–
12:30 – 12:45
François Sylla // Source LAB // Paris, France
KAIO-Beamline – A Modular High-repetition Rate Laser-plasma Electron Accelerator for a Broad Range of Application

Session II

Sensitive Imaging Without Labeling: SRS Microscopy

Andreas Zumbusch // University of Konstanz //
Konstanz, Germany

Label-free imaging techniques have recently met a lot of interest as a complement to fluorescence based imaging approaches. While imaging modalities such as second harmonic generation (SHG) and third harmonic generation (THG) microscopy allow contrast generation based on symmetry breaks in the samples, especially non-linear Raman microscopy has been pursued by many groups worldwide. The special advantage of these techniques is the possibility to generate contrast without the need for sample labelling. Instead, molecule specific contrast is generated based on the vibrational spectra of sample molecules. The two main approaches of this type are coherent anti-Stokes Raman scattering (CARS) microscopy and stimulated Raman scattering (SRS) microscopy. While the basic mechanism behind the two techniques is the same, the experimental setups required differ significantly, mainly with respect to the detection scheme. In this contribution, I will give an overview of the state of the art for the different nonlinear Raman microscopy techniques. Different experimental approaches will be shown and their virtues will be demonstrated with examples from cell biology, material science, and biomedicine. Special emphasis will be put on the discussion of recent efforts to increase the sensitivity of non-linear Raman microscopy techniques by exploiting electronic resonances. I will demonstrate that using this approach, the detection of vibrational spectra of single molecules is within reach.

Session II

Ultrafast Spectroscopy in Bio-molecules and Optical Nanostructures: Harnessing Light and Manipulating Matter

Margherita Maiuri // Politecnico di Milano // Milano, Italy

The advent of femtosecond light pulses has enabled the real-time visualization of dynamic processes at the nano- and molecular scale. Ultrafast transient absorption (TA) spectroscopy has provided an enormous amount of information on photoinduced dynamical processes in (bio)-molecules, nanostructures and solids1. Furthermore, these experiments have generally contributed to deepening our understanding of nonlinear light-matter interactions. In recent years. the ultrafast manipulation of light-matter interactions in photonic nano-architectures has unlocked unprecedented opportunities in the field of nanophotonics, ranging from high-speed signal processing to the control of photophysical material functionalities. One of the most promising approaches to actively drive and dynamically reconfigure nanostructures at ultrafast speed, is indeed to use femtosecond optical pulses. In this context, I will discuss our contribution to design and experimentally demonstrate the control and the functionality of ultrafast metasurfaces (ultrathin planar sub-wavelength arrangements of resonant nano-antennas) in different scenarios [1-4]. First, I will show how ultrafast hot carrier spatial inhomogeneities at the nanoscale can manifest and even dominate the transient transmission of photonic metasurfaces. We theoretically predict and experimentally observe by femtosecond transient absorption spectroscopy that spatiotemporal dynamics of hot electrons can promote and control an ultrafast photoinduced anisotropy in plasmonic metasurfaces, enabling active reconfiguration of the nanostructure nonlinear response. Then, I will report on our observation of a giant all-optical modulations of dichroism in an anisotropic AlGaAs metasurface. Finally, I will introduce a new platform for controlling physico-chemical processes to tailor molecular dynamics on demand. By exploiting optical nanostructures, ultrashort laser light pulses and strong light-matter interactions, we aim at manipulating in real-time molecular reactions, with applications ranging from photovoltaics to photocatalysis.

[1] M. Maiuri, A. Schirato, G. Cerullo, G. Della Valle, “PERSPECTIVE: Ultrafast All-Optical Metasurfaces: Challenges and New Frontiers” – ACS Photonics -accepted
[2] A. Schirato, M. Maiuri, G. Cerullo, G. Della Valle, “Ultrafast hot electron dynamics in plasmonic nanostructures: experiments, modelling, design”, Nanophot. 12, 1 (2023).
[3] A. Schirato, M. Maiuri, et al. “Transient optical symmetry breaking for ultrafast broadband dichroism in plasmonic metasurfaces” Nature Photonics 14, 723-727 (2020).
[4] A. Schirato, A. Toma, R. Proietti Zaccaria, A. Alabastri, G. Cerullo, G. Della Valle, M. Maiuri, “All-Optical Reconfiguration of Ultrafast Dichroism in Gold Metasurfaces”, Adv. Opt. Mater. 10, 2102549 (2022).

We acknowledge the ULYSSES project (no. 101077181) funded by the EU ERC-Stg-Programme

Session II

KAIO-Beamline – A Modular High-repetition Rate Laser-plasma Electron Accelerator for a Broad Range of Applications

François Sylla // Source LAB // Paris, France

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The KAIO-Beamline was designed to address scientific applications of laser-plasma accelerators such as complex parametric studies in radiobiology [1]. Its modular design incorporates (i) a commercial ultrafast laser driver, (ii) a temporal post-compression stage based on multi-pass cell technology [2] to reach optimal electron acceleration conditions in the few-cycle regime [3], and (iii) a compact plug & play electron accelerator module.

Here we will present the first implementation of KAIO-Beamline [4], using an ASTRELLA USP Ti:Sapphire laser driver (Coherent Inc.), delivering 7 mJ 40 fs pulses at 1 kHz repetition rate. The laser pulses are comprehensively characterized with the novel spatio-temporal metrology techniques INSIGHT [5] and TIPTOE [6].

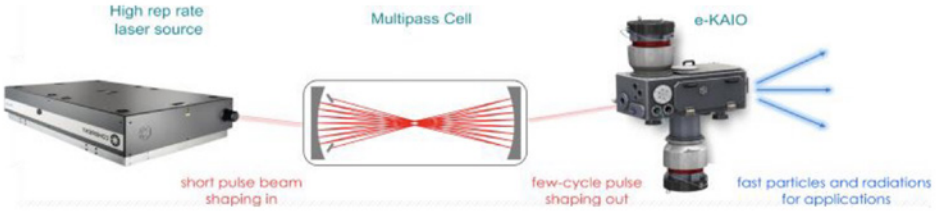

Figure 1: The KAIO-Beamline: the industrial laser system (e.g. ASTRELLA) is compressed to produce few-cycle pulses and sent into the compact table-top e-KAIO source for electron and radiation generation.

[1] M. Cavallone et al., Appl. Phys. B 127 (2021)
[2] L. Daniault et al., Opt. Lett. 46, 5264 (2021)
[3] D. Guénot et al., Nat. Phot. 11, 293-297 (2017)
[4] C. Greb et al., Instruments 8, 40 (2024)
[5] A. Borot and F. Quéré, Opt. Exp. 26, 26444 (2018)
[6] W. Cho et al., Sci Rep 9, 16067 (2019)

Session III

Monday // September 16th // 14:00 – 15:30

Session Chair
Jer-Shing Huang

Speakers

14:00 – 14:30
Maria Chernysheva // Leibniz IPHT // Jena, Germany
Advances and Challenges of Shortwave- and Mid-infrared Ultrafast Fibre Lasers
–
14:30 – 15:00
Karsten König // Saarland University // Saarbrücken, Germany
In Vivo Skin Imaging with Femtosecond Lasers
–
15:00 – 15:30
Leonardo Sacconi // LENS – European Laboratory for Non-Linear Spectroscopy // Florence, Italy
Exploring Cardiac Electrophysiology Through Advanced Microscopy

Session III

Advances and Challenges of Shortwave- and Mid-infrared Ultrafast Fibre Lasers

Maria Chernysheva // Leibniz IPHT // Jena, Germany

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Once considered a solution for various technological challenges, lasers have become essential for creating the next generation of innovative light source technologies. Exceptionally compact, highly stable, cost-effective and maintenance-free ultrafast lasers based on optical fibres have become a workhorse for the increased diversity of applications. Particularly, ultrashort pulse fibre lasers at short-wavelength infrared (SWIR) and mid-infrared (1.7-12 μm) spectral ranges have sparked high interest as a key instrument for various existing and emerging vital applications in areas ranging from environmental monitoring and non-invasive biological scanning technology to materials micro- and nanomachining and surgery. The potential of these ultrafast fibre lasers is immense, yet they have not reached the maturity level required for widespread and industrial use, despite a substantial research effort over several decades. In this presentation, I will discuss the challenges associated with the future development of ultrafast fibre lasers operating at longer wavelength ranges and provide an outlook on how to enhance generation performance.

Session III

In Vivo Skin Imaging with Femtosecond Lasers

Karsten König // Saarland University // Saarbrücken, Germany

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The first ultrashort laser scanning microscope was built in Jena in 1988 by ZEISS and the Friedrich Schiller University (FSU) using a picosecond dye laser and time-resolved single photon counting (TCSPC). We performed FLIM microscopy on porphyrins in living cells and live mice with that unique microscope. Shortly later, Denk, Strickler, and Webb introduced two-photon microscopy using a sub-picosecond dye laser. With the support of Coherent, we built the very first two-photon microscope in Europe based on a modified LSM310 and the femtosecond laser Vitesse in the Institute of Anatomy II in Jena. Starting in 2000, a medical two-photon microscope termed “Multiphoton tomograph DermaInspect” was developed in Jena and tested at the FSU-Department of Dermatology. In 2003, the DermaInspect became the very first two-photon medical device. The tomograph provides high-resolution virtual skin biopsies and is used to detect skin cancer and to test anti-ageing cosmetics and pharmaceutical products. 10 years later, the second-generation-tomograph MPTflex based on the 80 MHz fs lasers Chameleon and MaiTai has been introduced. The MPTflex was upgraded with a CARS module for fast Raman imaging.

I report on the development and application of the third-generation multiphoton tomograph MPTcompact based on an ultracompact 80 MHz femtosecond fiber lasers at 780 nm with a laser head dimension of 18x9x3.5 cm3 integrated in the 360° measurement head. An optical arm and a water chiller are no longer required resulting in 50% weight reduction and 75% reduced power consumption (235 W). The novel PRISM AWARD 2024 winning tomograph can run on batteries and recharged with flexible solar panels. The multimodal tomograph provides label-free high-resolution (300nm) virtual biopsies based on horizontal and vertical sectioning down to the upper dermis in 0.2 mm tissue depth. Images include (i) confocal reflectance microscopy images, (ii) two-photon autofluorescence (AF) images of NADH and flavin coenzymes, keratin, melanin, and elastin, (iii) second harmonic images of the collagen network, (iv) autofluorescence lifetime images (FLIM) by TCSPC with 200 picosecond temporal resolution for optical metabolic imaging (OMI), an (v) white light images for dermoscopy. The tomograph has been tested in multicenter studies on patients diagnosed with malignant melanoma as well as in the French and Japanese cosmetic industry. The tomograph has been used at the MGH in Boston to optimize skin treatment. Here we provide results of an OMI-FLIM study during oxygen inhalation. Specific single intratissue cells could be traced and checked for AF modifications with subcellular resolution for a period of four hours.

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K. König. Medical femtosecond laser. J. Eur. Opt. Society-Rapid 19 (36) (2023) 1-9.
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Journal of Optics and Photonics Research. 1(2024)51-58.

Session III

Exploring Cardiac Electrophysiology Through Advanced Microscopy

Leonardo Sacconi // University of Freiburg // Freiburg, Germany

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Action potentials, via the T-tubular system (TT), synchronously trigger uniform calcium release throughout the cardiomyocyte. Remodeling processes, associated with genetic and non-genetic cardiac diseases, introduce TT structural remodeling, leading to asynchronous calcium release across the myocyte and contributing to contractile dysfunction. In our laboratory, we developed an imaging method to simultaneously assess TT electrical activity and local calcium release. We documented the presence of TT elements that failed to propagate action potentials, generating slower calcium transients compared with regions with electrically coupled elements. It is concluded that TATS electrical remodeling is a major determinant of altered kinetics, amplitude, and homogeneity of calcium release in diseased hearts. Recently, the system has been implemented to probe and manipulate the electrical dynamics of subcellular membrane domains in optogenetically modified cardiomyocytes. We demonstrated that TT is intrinsically excitable and reveals distinct characteristics of self-generated T-tubular action potentials.

In parallel, alterations can occur in the electrical conduction at the organ level. Current models employed to predict functional alterations caused by structural remodeling commonly do not draw upon comprehensive functional and structural data and furthermore are often based on low-resolution and non-integrated information. In our laboratory, we recently developed a correlative imaging approach to quantify and integrate electrical function with 3D micro-scale structural reconstructions of intact ventricles in an arrhythmogenic cardiomyopathy mouse model, to characterize the dynamics of conduction wavefronts traveling through fibrotic lesion.

Session IV

Monday // September 16th // 16:00 – 17:30

Session Chair
André Gomes

Speakers

16:00 – 16:30
Helen Fielding // University College London // London, United Kingdom
Unravelling the Photodynamic of Biochromophores Using Transient Absorption Spectroscopy and Liquid-microjet Photoelectron Spectroscopy
–
16:30 – 17:00
Christian Eggeling // Leibniz IPHT // Jena, Germany
Advanced Super-resolution Minflux and STED Microscopy for Studying Molecular Interactions
–
17:00 – 17:30
Poster-Pitches

Session IV

Unravelling the Photodynamic of Biochromophores Using Transient Absorption Spectroscopy and Liquid-microjet Photoelectron Spectroscopy

Helen Fielding // University College London // London, United Kingdom

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Photooxidation is observed in many biological systems following excitation with ultraviolet (UV) light. Even though it is a driving force for numerous important photochemical reactions, for example in photocycles of fluorescent proteins, it can also have deleterious effects, such as in photodamage of DNA. We will present the results of femtosecond transient absorption spectroscopy experiments, complemented by liquid-microjet photoelectron spectroscopy measurements and quantum chemistry calculations, that probe the photochemical dynamics of UV photooxidation in biochromophores.

Session IV

Advanced super-resolution Minflux and STED microscopy for studying molecular interactions

Christian Eggeling // Leibniz IPHT // Jena, Germany

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Molecular interactions are key in cellular signalling. They are usually ruled by the organization and mobility of the involved molecules. For example, the direct and non-invasive observation of the interactions in the living cell membrane is often impeded by principle limitations of conventional far-field optical microscopes, for example with respect to limited spatio-temporal resolution and information content. Here, we present an advanced optical microscopy study involving tools such super-resolution STED microscopy in combination with spectral imaging and fluorescence correlation spectroscopy (FCS) or single-molecule tracking on a MINFLUX microscope. We highlight how these approaches can reveal novel aspects of membrane bioactivity such as of the existence and function of potential lipid rafts and during pathogen invasion, but also reveal limitations.

Session V

Tuesday // September 17th // 09:00 – 10:30

Session Chair
Mantas Butkus

Speakers

09:00 – 09:30
Dafne Suraci // LENS - European Laboratory for Non-Linear Spectroscopy // Florence, Italy
Autofluorescence Label-free High-contrast Imaging of Tumor Margins in Freshly Excised Gastro-intestinal Biopsies
–
09:30 – 10:00
Eirini Papgiakoumou // Institut de la Vision // Paris, France
Scanless Two-photon Illumination for All-optical Neurophysiology
–
10:00 – 10:30
Felix Grasbon // Grättinger · Möhring · von Poschinger Patentanwälte Partnerschaft mbB // Starnberg, Germany
Patent Trends and Patent Practice in the Field of Ultrafast Laser Driven Biophotonics

Session V

Autofluorescence Label-free High-contrast Imaging of Tumor Margins in Freshly Excised Gastro-intestinal Biopsies

Dafne Suraci // LENS – European Laboratory for Non-Linear Spectroscopy // Florence, Italy

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Liver cancer is a global health challenge and its incidence is growing worldwide, with more than 1 million cases per year by 2025. While hepatocellular carcinoma (HCC) is the most common form of liver cancer, hepatic metastases of colorectal carcinoma (CRC) are the natural disease evolution in almost 50% of patients with CRC. For both HCC and CRC liver metastases, surgical resection represents the only chance of long-term survival. In this context, a label-free optical diagnostic and/or surgical guidance tool would be highly suitable to reduce possible positive margin and improve the patient disease outcome. In this study, we used a custom-made autofluorescence lifetime fiber-based imaging instrumentation[1] to provide real-time discrimination of tumor from perilesional tissues in freshly excised liver samples. The proposed approach allowed discriminating tumor from perilesional tissue, reporting the fluorescence lifetime decay of cellular metabolic markers, i.e. NADH and FAD(H). In particular, we reported about the characterization and delineation of tumor against healthy margin in different clinical cases of gastrointestinal tissues[2], demonstrating the capability of our method. The approach was further validated on a larger statistic by examining around 30 surgical specimens of both HCC and CRC hepatic metastases, demonstrating that this approach is a powerful method for delineating tumor borders as well as for differentiating HCC from CRC metastases to the liver. The obtained results, together with the capability to acquire and process images in real time under bright background enables our methodology to be translated into surgical and clinical instrumentation for label-free tissue diagnostics and surgical guidance.

References
[1] J. L. Lagarto, V. Shcheslavskiy, F. S. Pavone, and R. Cicchi, "Real-time fiber-based fluorescence lifetime imaging with synchronous external illumination: A new path for clinical translation," J. Biophotonics, vol. 13, no. 3, Mar. 2020.
[2] D. Suraci, E. Baria, L. Tirloni, J.L. Lagarto, S. Buccianti, C. Agostini, S. Pillozzi, L. Antonuzzo, A. Taddei, and R. Cicchi, "Time-resolved autofluorescence imaging of freshly excised liver biopsies using an optical fiber probe", Proc. SPIE, 12846-22

Session V

Scanless Two-photon Illumination for All-optical Neurophysiology

Eirini Papagiakoumou // Sorbonne Université // Paris, France

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Light interaction with neurons offers a sensitive non-invasive approach of probing and mimicking brain activity. Recent advances in what is now called neurophotonics have opened the route for simultaneously recording information from cell populations, with pure optical methods: light is used to target neurons that have been previously genetically modified to express fluorescent sensors indicating their activity (via calcium or voltage imaging), or light-sensitive ion channels or pumps that control their activity (via optogenetics).
Here, I will present optical techniques developed in our group that optimize the excitation volume inside the sample for efficient multi-neuronal photoactivation and functional imaging. Specifically, I will present methods for three-dimensional light patterning of the excitation laser beam, based on the modulation of beam's optical wavefront through liquid crystal spatial light modulators [1]. The methods presented can be used for one- and multi-photon excitation. Particularly for the non-linear regime, controlling the volume of the excitation patterns in the axial direction can be achieved by simultaneous temporal focusing of the laser pulses [2,3]. Applications of these methods to functional imaging with voltage sensors [4], and neuronal optogenetic activation [5,6] will be shown.

References

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2) Papagiakoumou, E., de Sars, V., Oron, D. & Emiliani, V. Patterned two-photon illumination by spatiotemporal shaping of ultrashort pulses. Opt. Express 16, 22039–22047 (2008).
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5) Chen, I.-W. et al. In Vivo Submillisecond Two-Photon Optogenetics with Temporally Focused Patterned Light. Journal of Neuroscience 39, 3484–3497 (2019).
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Session V

Patent Trends and Patent Practice in the Field of Ultrafast Laser Driven Biophotonics

Felix Grasbon // Grättinger · Möhring · von Poschinger Patentanwälte Partnerschaft mbB // Starnberg, Germany

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We illustrate the global patent landscape and its development with a special focus on patenting in Ultrafast Laser driven biophotonics. We look at regions, companies, and key technologies, as well as changes in recent years. For example, China's IP activity should prompt all European players – companies, universities and research institutions – to raise their IP awareness.

As Europe increasingly recognizes the importance of IP protection in an innovative international world, we want to motivate the implementation of an IP strategy at all stages. To this end, we summarize fundamental knowledge on patents (IP-IQ) and provide insights into exemplary patents.

Keynote Lecture

Tuesday // September 17th // 11:00 – 12:00

Session Chair
Jürgen Popp

Speaker

11:00 – 12:00
Mihaela Žigman // Max Planck Institute of Quantum Optics //
Garching, Germany
Advancing Infrared Molecular Fingerprinting to Profile Health and Disease

Keynote Lecture

Advancing Infrared Molecular Fingerprinting to Profile Health and Disease

Mihaela Žigman // Ludwig Maximilian University of Munich (LMU), Garching, Germany; Max Planck Institute of Quantum Optics (MPQ), Garching, Germany; Center for Molecular Fingerprinting (CMF), Budapest, Hungary.

Recent advances in optical spectroscopy have unveiled new opportunities for probing living systems at a molecular level. Our primary objective is to advance and assess vibrational spectroscopy as an analytical framework for comprehensive cross-molecular profiling of systemic human biofluids and to evaluate the feasibility of employing infrared fingerprinting for high-throughput in vitro biomedical diagnostics. More specifically, we are investigating its viability for the analysis of human blood serum and plasma within the context of clinical diagnostics.

By combining vibrational fingerprinting of liquid blood plasma and serum with the integration of data analyses using machine learning, the results based of various studies[1,2,3,4] will be discussed. On a smaller scale, we have uncovered a remarkable degree of stability in the infrared molecular fingerprints within individuals over time[1], laying a crucial foundation for potential health screening applications.

In large scale case-control clinical study, we have gathered evidence indicating that the spectral information of plasma and serum contains distinct signatures for four types of cancer[2]. The effectiveness of disease detection is linked to the stage of cancer progression. We underscore the potential for early cancer diagnostics, highlight possible applications forging primary cancer diagnostics and provide evidence for distinguishing between different cancer entities. Yet, blood-based vibrational fingerprints are not able to detect only very severe health phenotypes like cancer. Infrared spectra also carry the capacity to just as well detect common chronic health deviations[5]. Interestingly,

in a large-scale population scenario with its inherent heterogeneity, we identified further potential of infrared fingerprinting to distinguish between various co-occurring conditions, opening up the possibility of screening for a variety of conditions and enhancing risk stratification.

[1] Huber M, Kepesidis KV, et al. Stability of person-specific blood-based infrared molecular fingerprints opens up prospects for health monitoring. Nature Communications 2021 Mar;12(1). https://doi.org/10.1038/s41467-021-21668-5.
[2] Huber M, et al. Infrared molecular fingerprinting of blood-based liquid biopsies for the detection of cancer. eLife 2021 Oct;10. https://doi.org/10.7554/elife.68758.
[3] Kepesidis KV, et al. Breast-cancer detection using blood-based infrared molecular fingerprints. BMC Cancer 2021 Dec;21(1). https://doi.org/10.1186/s12885-021-09017-7.
[4] Eissa T, et al. Limits and prospects of molecular fingerprinting for phenotyping biological systems revealed through in silico modeling. Analytical Chemistry. 2023 Apr 25;95(16):6523-6532. https://doi.org/10.1021/acs.analchem.2c04711.
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Session VI

Tuesday // September 17th // 13:00 – 14:30

Session Chair
Wolfgang Paa

Speakers

13:00 – 13:30
Alfred Leitenstorfer // University Konstanz // Konstanz, Germany
Applications of Ultrabroadband Femtosecond Fiber Lasers: From Single Electrons and Zero Photons to Biophotonics
–
13:30 – 14:00
Markus Gräfe // Technische Universität Darmstadt // Darmstadt, Germany
Nonlinear Interferometers for Quantum Sensing with Undetected Lights
–
14:00 – 14:15
Ingo Rimke // APE Angewandte Physik & Elektronik // Berlin, Germany
APE Multispectral SRS Imaging and Ultra-sensitive Detection for the Fingerprint Region and Raman Labels with New Picosecond Light Source
–
14:15 – 14:30
Matteo Negro // Cambridge Raman Imaging Ltd. // Milano, Italy
Multiplexing Stimulated Raman Microscopy for Biomedical Imaging and Chemometric Histology

Session VI

Applications of Ultrabroadband Femtosecond Fiber Lasers: From Single Electrons and Zero Photons to Biophotonics

Alfred Leitenstorfer // University Konstanz // Konstanz, Germany

Based on optical telecom technology, femtosecond fiber lasers represent compact and versatile tools for nanoscience and microscopy [1,2]. Owing to the long carrier wavelength centered around 1.55 µm, both Ge doping and waveguide dispersion of highly nonlinear germanosilicate fibers may be exploited to form precisely tailored supercontinua. This aspect underlies generation of pulse trains with either an ultrabroad spectral tuning range or single-cycle temporal duration [3], passive phase locking [4] and ultranarrow linewidths of free-running frequency combs [5]. All these features are central for our studies on e.g. electron transport at the atomic spatio-temporal scale [6], few-fermion dynamics in individual semiconductor quantum dots [7] or time-domain quantum electrodynamics [8]. After briefly featuring these core activities, the talk will focus on biophotonics applications which have emerged in close collaboration with Prof. Elisa Ferrando-May in the Department of Biology at University of Konstanz who now works at the German Cancer Research Center. Here, we exploit the high peak intensities of femtosecond laser pulses focused tightly into the nuclei of live cells to induce localized DNA lesions. This work is aiming to advance our knowledge about photon- and electron-mediated mechanisms of DNA damage and the cellular DNA repair response. It turns out that femtosecond irradiation in the visible range induces UV photoproducts via two-photon absorption while intense infrared pulses excite hot electrons by interband tunneling in H2O, thus mimicking DNA strand break induction after exposure to ionizing radiation [9].

[1] D. Brida et al., Laser Photonics Rev. 8, 409 (2014)
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[3] G. Krauss et al., Nature Photon. 4, 33 (2010)
[4] D. Fehrenbacher et al., Optica 2, 917 (2015)
[5] S. R. Hutter et al., Laser Photonics Rev. 17, 2200907 (2023)
[6] M. Ludwig et al., Nature Phys. 16, 341 (2020)
[7] P. Henzler et al., Phys. Rev. Lett. 126, 067402 (2021)
[8] S. Onoe et al., Phys. Rev. D 105, 056023 (2022)
[9] M. Schmalz et al., PNAS 120, e2220132120 (2023)

Session VI

Nonlinear Interferometers for Quantum Sensing with Undetected Light

Markus Gräfe // Technical University of Darmstadt, Fraunhofer IOF // Darmstadt, Jena, Germany

Exploiting nonclassical states of light allows new imaging and sensing approaches. In particular, nonlinear interferometers enable quantum sensing with undetected light. Here, based on the effect of induced coherence, samples can be probed with light that is not detected at all. Instead, its quantum-correlated partner light is recorded and yields the information of the sample, although it never interacted with it. The talk will outline the fundamental concept, recent progress, limits, and perspectives for biomedical applications of nonlinear interferometers.

Session VI

Multispectral SRS Imaging and Ultra-sensitive Detection for the Fingerprint Region and Raman Labels with New Picosecond Light Source

Ingo Rimke // APE Angewandte Physik und Elektronik GmbH // Berlin, Germany

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Here we present a new picosecond light source for ultra-sensitive SRS imaging of Raman labels as well as in the fingerprint region.

Fast tuning with settle times of about one second over the whole wavelength range enables easy multispectral SRS imaging. We achieved a signal to noise improvement of one order of magnitude compared to the previous version of the light source. This was achieved by reducing the repetition rate by a factor of two combined it with other measures. Its shot noise limited characteristics allow for SRS imaging of compounds in biological relevant concentrations. Several hundreds of mW output power with a spectral bandwidth of about 10 cm-1 and pulse length of 2 ps in Pump and Stokes give access to 210 - 5450 cm-1. This does address all relevant vibrational bands with the spectral bandwidth necessary to resolve them.

The light source is fully hands-free, and combines Pump and Stokes in space and time to ensure perfect overlap at the sample site.

We will present comparative measurements to show the sensitivity and speed improvements as well as fast multispectral SRS imaging of biological samples in the fingerprint region as well as imaging of Raman labels.

Session VI

Multiplexing Stimulated Raman Microscopy for Biomedical Imaging and Chemometric Histology

Matteo Negro // Cambridge Raman Imaging Ltd. // Milano, Italy

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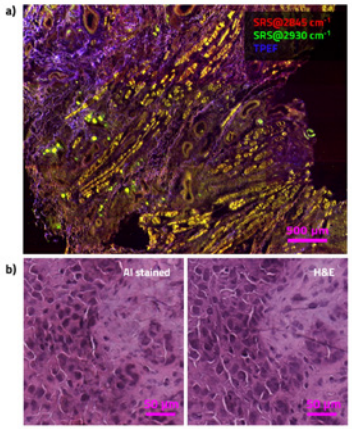
In the realm of label-free imaging techniques, coherent Raman imaging (CRI) emerges as a powerful tool, offering sub-cellular spatial resolution, molecular-specific contrast, and addressing the unmet need in life sciences for label-free chemically specific imaging by detecting the intrinsic vibrational fingerprints of cells and tissues.

Multiplex stimulated Raman scattering (SRS) microscopy, combining single-shot detection of broad vibrational spectra and high spectral resolution, fully exploits the innovative potential of CRI tools. State of the art implementations of multiplex SRS systems are based on custom and complex solutions, rendering them completely inaccessible to non-specialists in the field.

Here, we present a fully engineered Broadband Coherent Raman Platform (CORAL) designed to achieve state-of-the-art performance in multiplex SRS with unprecedented ease of use and long-term reproducibility. CORAL comprises an all-fiber dual-wavelength self-synchronized laser and a detection unit based on a compact multichannel lock-in amplifier, ensuring shot-noise-limited SRS performance over the entire CH spectrum (2800-3100 cm^{-1}), parallelizing detection across 38 spectral channels in 2 µs. Additionally, the system is equipped with an epi-detection module for TPEF and SHG signals.



Moreover, CORAL combines a broadband label-free approach for chemometric analysis of biological specimens with artificial intelligence tools, enabling users to unleash the full power of hyperspectral data. Such a system finds broad application in biomedical sectors where traditional exogenous labelling is a limiting factor, such as in live cell imaging, metabolomics, and histopathology.

Figure 1: a) Image of human head and neck tumour tissue obtained combining SRS signal @2845 cm-1 (red), SRS signal @2931 cm-1(green) and two-photon excitation fluorescence (TPEF) signal (blue). b) Comparison of AI-generated H&E-like image from SRS data with the very same tissue area H&E stained

Session VII

Tuesday // September 17th // 15:00 – 16:30

Session Chair
Timea Frosch

Speakers

15:00 – 15:30
Thomas Bocklitz // Leibniz IPHT // Jena, Germany
Photonic Data Science: Translating Linear and Non-linear Optical Data to Knowledge
–
15:30 – 16:00
Christian Spielmann // Friedrich-Schiller-University // Jena, Germany
Lens-less Imaging of Biological Samples
–
16:00 – 16:30
Gregor Knopp // Paul Scherrer Institute // Villigen, Switzerland
Resonant Nonlinear X-ray Four Wave Mixing in Atomic and Molecular Systems: A Tool Also for Chemical and Biological Samples?

Session VII

Photonic Data Science: Translating Linear and Non-linear Optical Data to Knowledge

Thomas Bocklitz // Leibniz IPHT // Jena, Germany
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Raman spectroscopy and non-linear Raman spectroscopic techniques are increasingly employed across various disciplines, including chemical analytics, life sciences, and medicine. The applications in these fields rely on artificial intelligence (AI)-based methods to translate measured data into high-level information and knowledge within the application domain. The high-level information depends on the specific task and sample characteristics, such as disease types, tissue types, and other properties like constituent concentrations.

To achieve this translation, specialized data pipelines must be constructed for each measurement modality, comprising experimental design, sample size planning, data pre-treatment, data pre-processing, chemometric and machine learning-based data modeling, model transfer methods, and transfer learning. Almost every step in the data pipeline can be optimized using AI-based methods, including machine learning and deep learning.

This talk will highlight common pitfalls encountered when generating data pipelines for linear and non-linear Raman spectroscopic measurement techniques and discuss strategies to avoid them.

Lens-less Imaging of Biological Samples

Christian Spielmann // Institute of Optics and Quantum Electronics // Jena, Germany

Microscopy using extreme ultraviolet (XUV) radiation is crucial for achieving higher resolution due to the short wavelength or for conducting element-specific measurements. However, organic samples, for example, are at significant risk of being quickly damaged or even destroyed by the intense, short-wavelength radiation. Although methods utilizing powerful X-ray lasers can collect essential information before the samples are harmed, these techniques are highly complex and resource intensive.

In ghost imaging (GI), object information is obtained non-locally through the correlation of two beams. One beam interacts with the object and is measured by a single-pixel detector, while the other beam, which does not interact with the object, is recorded by a spatially resolved array detector. The first GI experiments utilized quantum-entangled photons generated through spontaneous parametric down-conversion. Later, GI was also demonstrated with thermal and pseudothermal light sources using randomly generated intensity patterns with low exposure dose. In computational GI (CGI), illumination is modulated with a spatial light modulator or a digital micromirror device, simplifying the GI setup to a single-pixel detector by computationally generating the illumination pattern.

The CGI image is reconstructed by correlating the intensity signals with the calculated sequential random speckle patterns. Through detailed study, we identified the most suitable speckle patterns to achieve higher quality and resolution images with fewer iterations. Additionally, we utilized deep learning technology to enhance the quality of blurred ghost images, transforming them into high-quality outputs.

These significant findings can be directly applied to the XUV range. However, achieving CGI in the XUV domain required addressing the challenges of finding a suitable modulator and light source. A femtosecond laser-driven high harmonic generation (HHG) source provides XUV radiation with the necessary flux and beam quality. The patterns are generated using transmission masks mounted on a translation stage. Since these masks need to be prefabricated, it is crucial to precisely define their shape in advance. With this setup, we recently demonstrated CGI using a tabletop XUV source for the first time.

With further advancements in our setup and reconstruction algorithms, we anticipate obtaining detailed information about biological samples, with enhanced resolution sufficient to achieve sub-micrometer precision.

Resonant Nonlinear X-ray Four Wave Mixing in Atomic and Molecular Systems: A Tool Also for Chemical and Biological Samples?

Gregor Knopp // Paul Scherrer Institute // Villigen, Switzerland

Ultra-fast inner-shell electron dynamics and electron correlations are fundamental to characterize atomic and molecular states, their structure and dynamics, which are at the heart of chemical reactions and biochemical processes. Nonlinear wave mixing in the X-ray range can provide valuable insights into the structural and electron dynamics of atomic and molecular systems on ultrafast time scales, with state- and site-selectivity and atomic resolution. In particular, resonant X-ray four-wave mixing (XFWM) can deliver information about coherence, complex orbital relaxations and electron dynamics, being locally initiated near a specific atom. We will discuss the successful realization of a XFWM process at the Swiss free electron laser (SwissFEL), at which we have measured background-free XFWM signals from Neon with all interacting photons in the X-ray regime [1,2]. This first all-X-ray four-wave-mixing approach represents a major breakthrough towards coherent multidimensional X-ray spectroscopy and the general application of nonlinear X-ray wave-mixing. However, many chemical reactions and almost all biological chemistry occur in liquid solutions necessitating the investigation of solvent and solvation dynamics. To the best of our knowledge, no hard X-ray-FWM experiment has been realized in a liquid sample so far. We will additionally discuss preliminary results from a mixed X-ray/optical FWM measurement in pure water and in Ferrioxalate aquaeous solution in a micro-meter liquid jet [3] and give a perspective to more complex biological systems.

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Session VIII

Wednesday // September 18th // 09:00 – 10:30

Session Chair
Anja Silge

Speakers

09:00 – 09:30
Arseny Finkelstein // Tel Aviv University // Tel Aviv, Israel
Optical Mapping of Neural Interactions on Multiple Spatial Scales During Behavior
–
09:30 – 10:00
Sophie Brasselet // IInstitut Fresenel // Marseille, France
Polarized Microscopy for Molecular-organization Imaging in Cells and Tissues
–
10:00 – 10:30
Shuxia Guo // Leibniz IPHT // Jena, Germany
Long-term Setup Stability in Raman Spectroscopy

Session VIII

Optical Mapping of Neural Interactions on Multiple Spatial Scales During Behavior

Arseny Finkelstein // Tel Aviv University // Tel Aviv, Israel

–

Studying neural interactions in the living brain at cellular resolution is a major challenge in neuroscience. In the first part, I will present a novel 'all-optical' method for mapping neural connectivity in vivo. This method, involving 2-photon volumetric calcium imaging of neural activity and targeted 2-photon optogenetic perturbations, allows large-scale and rapid mapping of neuronal interactions in the living brain (500,000 neuronal pairs in 30 mins). Combining connectivity mapping with a novel naturalistic behavior in mice revealed functional connectivity motifs underlying a cognitive map for reward positions and outcomes in the frontal cortex. In the second part, I will show that analyses of interactions between 1,000,000 neurons, that we imaged simultaneously across multiple cortical areas during the same behavior, revealed an intricate organization of cortical population dynamics and inter-areal communication patterns during action-selection. These results, which are based on recent advances in brain imaging technology, pave the way to study how neuronal interactions on different spatial scales give rise to behavior.

Polarized Microscopy for Molecular-organization Imaging in Cells and Tissues

Sophie Brasselet // IInstitut Fresenel // Marseille, France

Fluorescence imaging and nonlinear coherent optical microscopy can reveal important spatial properties in cells and biological tissues from fixed situations to in vivo dynamics. While microscopy can guide interpretation through morphological observations at the sub-micrometric scale, optical imaging cannot directly access the way molecules are organized with given orientations in 3D at the nanoscale. This property, which is important in many processes in biology, from immunology to development biology and mechanobiology, is today most often studied using methods that are not compatible with real time imaging.

We will show that reporting molecular orientational organization down to the nanoscale is made possible using polarization resolved optical microscopy, which takes advantage of the orientation-sensitive coupling between optical excitation fields and molecular transition dipole moments. Remarkably, the non-paraxial fields propagation allowed in high numerical aperture (NA) microscopy permits to access 3D orientation information that is otherwise delicate to access from pure transverse optics. We will describe how high NA optical polarized imaging can provide information on the way molecules are oriented in 3D, including information on their orientational fluctuations. We will describe in particular polarization sensitive approaches in fluorescent single molecule localization microscopy to reveal actin filaments' organization in dense regions of the cell cytoskeleton, which is generally challenging to image in super resolution imaging. We will describe possible methods to perform polarized microscopy calibration and optical fields-assessment in 3D (i.e. 3D nanoscale polarimetry), and finally discuss the transposition of 3D polarized methodologies to scanning nonlinear optical microscopy for structural imaging in tissues.

Long-term Setup Stability in Raman Spectroscopy

Shuxia Guo // Leibniz IPHT, IPC // Jena, Germany

By indirectly detecting molecular vibrations, Raman spectroscopy provides the unique fingerprints of molecular components under measurement and is playing an increasing role in biological investigations [1]. Its capability is further enhanced by machine learning techniques, in which the spectral fingerprints are translated effectively into interpretable knowledge. To push the technology into clinical applications, however, remains challenging due to the substantial variations between different devices and the overtime drifts within one device [2, 3]. The device-relevant spectral variations often disable a machine learning model to be applied on data from a different device or the same device but measured at a different time as the training data.

In this study, we measured 13 substances as quality control references weekly over 10 months on one Raman setup to investigate the instrumental stability and the time-dependence of the variations. The 13 substances were selected to be stable and span a broad range of solvents, lipids, and carbohydrates. 50 Raman spectra were acquired from each substance every measurement day. All spectra were preprocessed to remove spikes and fluorescence baselines. After investigating the performance of calibrating the wavenumber axis with different standards [4], we characterized the overtime spectral variations of each substance based on the intensity and correlation analysis. The clustering properties were explored across measurement days. With this, we aim to discover and characterize the overtime stability of the Raman setup, which is important to find a better way of spectral standardization in Raman spectroscopy to push it forward in real clinical applications.

Acknowledgements
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Session IX

Wednesday // September 18th // 11:00 – 12:30

Session Chair
Tomáš Čižmár

Speakers

11:00 – 11:30
Brice Bathellier // Institut Pasteur // Paris, France
High-efficiency Single Pulse Two-photon Stimulation for in Vivo All-optical Interrogation of Neuronal Circuits with Acousto-optic Deflectors
–
11:30 – 12:00
Amanda Foust // Imperial College London // London, United Kingdom
Enabling High-throughput, Scattering-mitigated, Volumetric Imaging Through Two-photon Informed Light-field Deep Learning
–
12:00 – 12:30
Tobias Meyer-Zedler // Leibniz IPHT // Jena, Germany
Multimodal Nonlinear Endomicroscopy for Use in Clinics

Session IX

High-efficiency Single Pulse Two-photon Stimulation for in Vivo All-optical Interrogation of Neuronal Circuits with Acousto-optic Deflectors

Brice Bathellier // Institut Pasteur // Paris, France

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Combining two-photon (2P) calcium imaging and digital holography is now the state-of-the-art approach to image and perturb neuronal circuits in vivo simultaneously. This all-optical approach, however, is limited, on the photostimulation side, by digital holography, in terms of speed and throughput. Employing acousto-optic deflectors (AOD)-based 2P approaches ("ULoVE", Villette et al. 2019; "3D-CASH" Akemann et al. 2022) we could overcome such limitations, combining simultaneous recording and perturbation of neuronal circuits in awake head-fixed mice across single planes and three-dimensional volumes with tens of microseconds temporal resolution. These techniques enhance indicator excitation and opsin activation efficiency within a minimal dwell time, by sequential sampling the target neurons with extended volumes. For neuronal manipulation, this implies it could be possible to manipulate with single-cell precision the activity of multiple neurons by performing random access ultrafast local scanning, without compromising the photon budget. First, we validated stimulation of ChRmine-expressing neurons using ULoVE, which resulted in robust responses to as brief as 70µs illumination periods. This encouraging result led us to try designing the minimal photostimulation possible, using 3D-CASH. By phase locking AODs modulation to the laser repetition rate (40kHz), we could deliver high-energy single femtosecond laser pulses to different target locations, every 25µs. Single-pulse stimulation was successful, allowing for example co-activation of 50 neurons in just 1.25ms. Such a precise and efficient perturbative approach is compatible with in vivo 2P voltage imaging, paving the way to unprecedented all-optical electrophysiological dissection of neuronal circuits in the intact brain.

Enabling High-throughput, Scattering-mitigated, Volumetric Imaging Through Two-photon Informed Light-field Deep Learning

Amanda Foust // Imperial College London // London, United Kingdom

Multiphoton excitation enables optically sectioned fluorescence imaging in scattering media. However, small cross sections and scanning limit multiphoton imaging's bandwidth and application to high-throughput functional imaging. In contrast, light-field microscopy (LFM) enables high-throughput volumetric imaging but is corrupted by scattering, limiting its use in biomedical contexts. To address the competing requirements of bandwidth and scattering mitigation, we developed a bimodal imaging and processing strategy that integrates two-photon laser scanning with one-photon light-field imaging. We imaged calcium transients in mouse brain slices co-expressing the soma-targeted fast calcium indicator jGCaMP8f and the static structural label tdTomato in layer 2/3 excitatory neurons. We trained a deep neural network (DNN) with matched one-photon light fields (LFs) and scattering-robust scanned two-photon volume stacks. The DNN reconstructs scattering-mitigated neuronal volumes from scattering-corrupted LFs faster and with higher accuracy than conventional model-based LF processing methods. A second DNN, based on the LFM wave-optics forward model, calculates the LF footprint for each segmented neuron, enabling rapid spatio-temporal factorization of jGCaMP8f time series from LFs acquired at 100 Hz. Our strategy volumetrically resolved putative spikes in 60 neurons distributed throughout a 530 x 530 x 100 micron volume, up to 100 microns deep in live brain slices. The DNN approach reduced signal crosstalk between neighboring neurons compared to 8-iteraton Richardson-Lucy deconvolution of LF videos. Putative spikes fired at up to 10 Hz were resolved with high signal-to-noise ratio enabling volumetric mapping of correlated neuronal ensembles. This optically and computationally efficient LFM strategy based on two-photon informed DNNs advances the goal of high-throughput and scattering-robust volumetric imaging.

Multimodal Nonlinear Endomicroscopy for Use in Clinics

Tobias Meyer-Zedler // Leibniz IPHT // Jena, Germany

The combination of nonlinear imaging techniques such as Coherent Raman Scattering (CRS), two photon excited fluorescence and second harmonic generation enable the rapid investigation of large specimen for disease diagnostics, i.e., to identify disease specific marker molecules or to localize compositional changes. For complex diagnostic tasks, e.g., tumor margin detection, grading and staging of tumors or the recognition of infectious diseases at an early stage, multimodal nonlinear imaging and specifically imaging of a broader part of the vibrational spectrum is advantageous.

In this contribution, we will present our latest research results on multimodal nonlinear imaging focusing on the implementation into endoscopes for clinical application. We cover also the combination of diagnosis and treatment by combining imaging and fs-laser ablation. In addition, laser concepts and application for broadband CARS (BCARS) and broadband SRS which enable the acquisition of parts or the full vibrational spectrum within time frames as short as an individual laser pulse are presented. By simultaneously probing a significant part of the spectrum, broadband CRS is ideally suited for fast composition diagnostics on complex tissue and cell samples, but broadband laser sources are crucial. To identify small disease induced changes machine learning and AI based data analysis algorithms are crucial and need to be used.

Acknowledgements
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Poster Session

P-01 Sven Breitkopf // Active Fiber Systems GmbH // Jena, Germany
Fiber-laser Driven Spectroscopy & Imaging from the MIR to the XUV

P-02 Jer-Shing Huang // Leibniz IPHT // Jena, Germany
Surface Enhanced Coherent Anti-Stokes Raman Scattering on Plasmonic Gratings

P-03 Katerina Prohaska // Biotech Campus Tulln, FH Wiener Neustadt // Tulln, Austria
Biomarker Detection: Implementation of Raman Fingerprint Profiles in OMICs Data Analysis

P-04 Uliana Finaeva // Czech Technical University in Prague // Prague, Czech Republic
Effect of Lung Degradation on its Optical Properties and Agar-based Optical Phantom Fabrication

P-05 Sarka Nemcova // Czech Technical University in Prague // Prague, Czech Republic
Ophthalmic Edoscope

P-06 Olga Szewczyk // Wrocław University of Science and Technology // Wrocław, Poland
Widely Tunable Laser Source with Spectrally-compressed Linewidth for Long-wavelength Optical Coherence Tomography at 1700 nm

P-07 Katarzyna Kunio // Wrocław University of Science and Technology // Wrocław, Poland
Enhancing Multiphoton Microscopy with Picosecond Pulses

P-08 Istvan Csarnovics // University of Debrecen // Debrecen, Hungary
Peculiarities of Using Different Nanostructures for Surface-enhanced Raman Scattering for Future Biophotonics Applications

P-09 Ruqyyah Mushtaq // The University of Naples Federico II // Pozzuoli, Italy
Effect of Chain Length on Skeletonema Pseudocostatum as Probed by THZ Spectroscopy

P-10 Luisa Hofmann Hehl // Toptica Photonics AG // Graefelfing, Germany
Femtosecond Fiber Delivery at 920 and 1050 nm for Two-photon Microscopy

P-11 Sonal Saxena // University of Exeter // Exeter, United Kingdom
Limitations of Effective Medium Models for Water Content Estimation in the THz Frequency Range

P-12 Krystyna Herasymenko // CNRS-IPCMS // Strasbourg, France
Changes in the Excited State Dynamics of ArchaeRhodopsin-3 via Site-Specific Mutations

P-13 Sinuhe Perea // King's College London / Max Planck Institute // London, United Kingdom
Imaging in Lossy Media via Complex Wavevectors

P-14 Gerald Auböck // Slicon Austria Labs GmbH // Villach, Austria
Spectro-temporal Mapping in Broadband Sum-frequency Generation Infrared Spectroscopy

P-15 Jakub Bogusławski // Wrocław University of Science and Technology // Wrocław, Poland
Multiphoton Frequency-domain fluorescence Lifetime Imaging Microscopy Using Digital Homodyning

P-16 Christian Maibohm // International Iberian Nanotechnology Laboratory INL // Braga, Portugal
Few-cycle Ultra-broadband Laser Microscopy for Bioimaging

P-17 Chang Liu // Helmholtz Institute Jena // Jena, Germany
Nanoscale Structure and Compositional Imaging of Bacteria with Tabletop EUV Ptychography

P-18 Carolyn Moll // University of Amsterdam // Amsterdam, The Netherlands
IR-DOSY (Infrared- Diffusion Ordered Spectroscopy): Adding the Size Dimension to Spectroscopy

P-19 Tomas Martan // Czech Technical University in Prague // Prague, Czech Republic
Fiber Optic Tapers for Local Biological Detection

P-20 Bhawna Bhawna // Institut national de la recherche scientifique (INRS)-EMT // Montreal, Canada
Exploratory Study of the Evolution of Collagen in Mouse Mammary Gland Using Second Harmonic Generation Microscopy

P-21 Mohammad Sadegh Vafaeinezhad // Leibniz IPHT // Jena, Germany
High Energy Semi Stable Supercontinuum Generation for CARS Spectroscopy

P-22 Julian Plitzko // Leibniz IPHT // Jena, Germany
Illuminating Drug Delivery: Localization and Characterization of Polymer-based Nanoparticles in Fibrotic Liver Cells.

P-23 Behjat Sadat Kariman // Politecnico Milano // Milan, Italy
Fabrication of high-NA Microlenses using 2PP for Linear and Non-linear Excitation Bio-imaging

P-24 Tobias Gäbler // Fraunhofer IOF // Jena, Germany
Fluorescence Lifetime Spectroscopy using Entangled Photons from a Continuous-Wave Source

P-25 André Weber // Leibniz Institute for Neurobiology LIN // Magdeburg, Germany
LINCam: Principle, Applications and Perspectives of Wide-field Time Correlated Single Photon Counting

P-26 Stefan Richter // Leibniz Institute for Neurobiology LIN // Magdeburg, Germany
Imaging of a Trapped Ion Crystal via Intensity Interferometry

P-27 Brian Molesky, Erin McCole Dlugosz // Coherent // Glasgow, United Kingdom
Ultrafast Oscillators and Amplifiers for Physics and Chemistry

P-28 Jan Ornik // Leibniz IPHT // Jena, Germany
High Throughput Infrared Field-Resolved Spectroscopy of Particles in Flow

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