Leibniz ipht
LEIBNIZ INSTITUTE of PHOTONIC TECHNOLOGY

reflexion

Biophotonics

Annual Report 2023

Precision
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Leibniz Association

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PHOTONICS FOR LIFE
from Ideas to Instruments

Dear Readers,

Prof. Dr. Jürgen Popp

Dr. Karina Weber

Welcome to a new issue of our magazine *reflexion*, the annual report of the Leibniz Institute of Photonic Technology, which this time focuses on biophotonics.

At Leibniz IPHT, we use the possibilities of light to research innovative solutions - for health and medicine, for safe food and clean water and for climate-friendly energy generation of the future. Our research is interdisciplinary and networked by nature. By collaborating with other institutions, universities and companies, we have the opportunity to expand our expertise and always align our research activities with the needs of society.

Optical health technologies play a central role in this. As we understand it, optical health technologies use photonic, biophotonic and quantum biophotonic approaches to develop medical solutions and applications for diagnosis, monitoring and therapy. They contribute to maintaining human health and can also be used to monitor and protect the environment.

This annual report is not only about our innovative technological solutions, but also about the stories behind these successes. They are the result of many years of work by dedicated teams, especially with clinical partners.

"Photonics for Life" is more than just a motto for us; it is an incentive to find creative solutions and to unleash the full potential of our research. Our goal goes beyond the mere publication of research results. We strive to translate our findings into applicable solutions and are committed to identifying the needs of society and adapting our research goals accordingly.

In this sense, our magazine is not simply a summary of the latest research advances. Rather, it offers a perspective on the potential for interdisciplinary synergies between science, medicine, and industry.

Best regards

Jürgen Popp
Scientific Director

Karina Weber
Administrative Director

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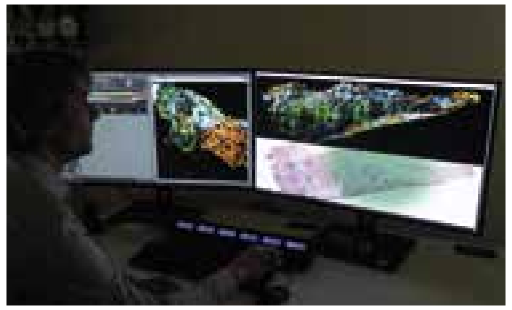
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Networked Visions

The Beginning of a Trilogy: How Biophotonics, Fiber Optics, and Photonic Detection Combine to Enable Innovation

In three issues, our magazine *reflexion* is dedicated to the program areas that are intertwined at Leibniz IPHT in order to research innovative light-based technologies for the life sciences: Biophotonics, Fiber Optics and Photonic Detection.

The research results, approaches and projects that are the subject of this magazine fit together like pieces of a puzzle to form a larger picture. It shows the networking and interdisciplinarity of our research departments under the umbrella of the three program areas Biophotonics, Fiber Optics and Photonic Detection. This and the two following issues of Reflections form a trilogy that highlights the innovative power of our research in these areas. The series begins with Biophotonics.

Biophotonics, with its focus on optical health technologies, is an integrative force. It combines the key technologies of Leibniz IPHT and technological research in Fiber Optics and Photonic Detection. These provide basic technologies and methods for biophotonic applications, enable new imaging and diagnostic methods and support precise measurements at the molecular level.

Marie-Luise Enghardt and Dr. Richard Grohs are working at Leibniz IPHT and the Leibniz Center for Photonics in Infection Research on the development of a laser-based rapid test. The test, which can be read on a portable microspectrometer, is intended to bring rapid infection diagnostics to patient care (page 38). © Sven Döring

Biophotonics builds bridges to the life and environmental sciences. It stands for the development of high-precision methods and tools to answer fundamental questions in medicine, health, security, the environment and energy.

The stories in this magazine illustrate the close collaboration between the research and technology teams. To develop the RamanBioAssay© rapid test for detecting infectious pathogens and their resistance (page 38), the team from the Spectroscopy / Imaging research department is working hand-in-hand with clinical partners, while the Photonic Data Science research department is developing the AI-assisted analysis (page 26). A portable Raman spectrometer – built by the Sensor Systems and System Integration Technology group – will bring the method to the point of care. The optical gratings that replace lenses and mirrors are manufactured in the institute's clean room by the team from the Competence Center of Micro- and Nanotechnologies.

Another example: Dr. Sindy Burgold-Voigt from the Optical-Molecular Diagnostics and Systems Technology research department is investigating the spread of resistance and disease by bacteriophages (page 50). She urgently needs new methods for rapid quality control in phage production and has therefore teamed up with the Microscopy and Biophysical Imaging research departments to develop suitable optical systems.

To conclude the trilogy, we offer a holistic view of the research results of Leibniz IPHT. It should become clear how the interweaving of the three program areas leads to new insights and technological developments that go far beyond what would be possible for individual groups – because the whole is more than the sum of its parts.

Artificial intelligence and photonics for more precise decisions in medicine: Prof. Dr. Thomas Bocklitz , Dr. Shuxia Guo and Elena Corbetta are using mathematics to make optical data useful for medicine (page 26). © Sven Döring

How bacteriophages spread resistance and disease: Dr. Sindy Burgold-Voigt and Prof. Dr. Ralf Ehricht are developing innovative diagnostic techniques to better understand infectious diseases and their spread (page 50). © Sven Döring

Open-minded Research: Embracing Diversity at Leibniz IPHT

More Than Half of the Researchers at Leibniz IPHT Come From Abroad

The international diversity at Leibniz IPHT is more than just a statistic – it is the cornerstone of our research and our success. More than 450 employees from 38 countries work together to develop groundbreaking solutions for global challenges.

Our success is built on the diversity of our minds, ideas and perspectives. We are committed to ensuring that our employees feel comfortable and are treated equally – no matter how old they are, where they come from, what they believe, how they live or define themselves, whether they are physically challenged or not.

Through our many international partnerships and projects, we help push the boundaries of knowledge and make a positive difference in the world. We are proud to be a place where people from all backgrounds come together to advance science.

charta der vielfalt

weltoffenes Thüringen

#ZUSAMMENLAND
VIELFALT MACHT UNS STARK!

Diversity Makes us Strong

We are part of the "Weltoffenes Thüringen" (Open Thuringia) initiative, the Diversity Charter and the "#Zusammenland – Vielfalt macht uns stark" (Together – diversity makes us strong) campaign of the major German media companies. Together with some 500 companies, foundations and associations, we are taking a stand against right-wing extremism and for freedom, diversity and a welcoming culture. We want a society characterized by openness, tolerance, and equal opportunity, in which everyone is accepted and welcomed in their diversity.

Our commitment to open-minded research not only reflects our deep convictions, but also represents a strategic course for a better future. We firmly believe that a society that values and promotes diversity not only stands on solid moral ground, but also provides a fertile environment for innovation and progress.

A Ray of Hope in the Fight Against Cancer

How Optical Technologies Can Advance the Diagnosis and Treatment of the Disease

Dr. Tobias Meyer-Zedler analyzes images of cancer tissue: on the bottom right is an H&E image with pathohistological analyses, on the left is the corresponding multimodal image. With its detailed and marker-free representation of both the tissue structure and its biochemical composition (see pages 12-18 and page 20), this light-based method offers a new, highly precise method of tumor detection. © Sven Döring

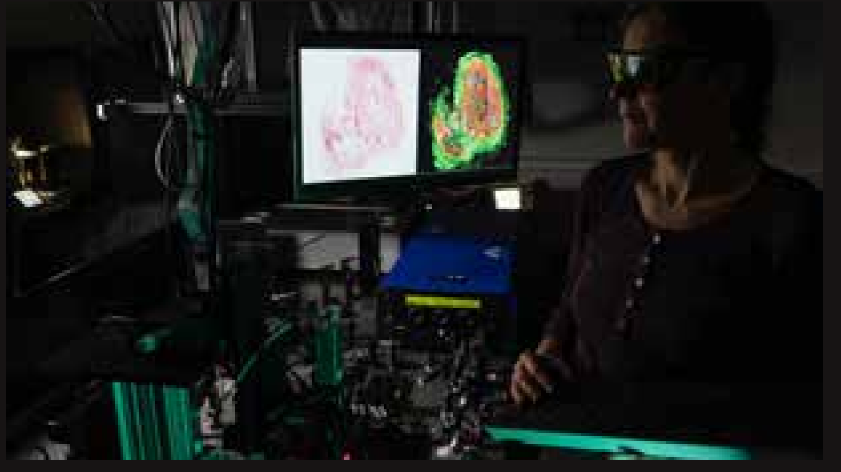
Light-based technologies can push the boundaries of what is possible in diagnosis and treatment of cancer. Researchers at Leibniz IPHT use light to gain fundamental insights into the ultra-fast processes of photodynamic therapy. They use it for the real-time analysis of tissue samples directly in the operating room. And they are developing a new type of probe that can precisely target and remove tumor tissue with laser light and remove it in a single step. Together with partners from medicine and industry, they are working on methods to improve the treatment of this disease, which statistically affects one in two Germans at some point in their lives.

This thematic focus highlights the innovative processes and instruments that are being developed at Leibniz IPHT – in close cooperation with researchers and users in Jena, Germany and around the world.

Special attention is paid to the implementation of these methods in clinical practice. Researcher Jürgen Popp and surgeon Orlando Guntinas-Lichius will provide insights into their long-standing collaboration and discuss the challenges and successes on the way to the cancer diagnostics and therapy of the future.

Insights Into the Cell

At a Glance: Methods for Label-free Optical Imaging



Dr. Astrid Tannert analyzes intestinal tissue using an intravital microscope. The tissue is examined microscopically and correlated with established histological stains. © Sven Döring

Using biophotonic technologies and artificial intelligence (AI), it is possible to obtain molecular and structural information from tissues in real time – without invasive procedures or markers. This enables deep insights into cells and tissues.

The Main Methods:

- **Hyperspectral imaging (HSI)** and **fluorescence imaging** including **fluorescence lifetime imaging (FLIM)** reveal biochemical composition.
- **Second and third harmonic generation (SHG and THG)** and **optical coherence tomography (OCT)** highlight molecular structures.
- **Photoacoustic Imaging (PAI)** combines optical and acoustic technologies for deep tissue penetration.
- **Vibrational spectroscopy** (infrared absorption (IR) and Raman scattering) and **Brillouin scattering** identify molecules and proteins by their specific vibrational patterns.

Contrast Mechanisms and Their Applications:

These methods use different contrast mechanisms to visualize biomolecules and proteins:

- **Infrared (IR) absorption and Raman scattering** identify molecules by their characteristic vibrations.
- **Absorption and emission:** Light interactions with chromophores such as hemoglobin or flavin allow their visualization by absorption or emission.
- **Protein structure and physical properties:** SHG visualizes specific proteins, while OCT and THG visualize structural changes through refractive index differences or material boundaries.

Raman Spectroscopy for Molecular Fingerprinting

Raman spectroscopy provides label-free detection of the molecular composition and morphology of complex samples. Raman spectroscopy is particularly valuable in histopathology because it provides a sensitive and specific "fingerprint" of the biochemical composition and structure of tissues. Pathological changes can be precisely identified in the Raman spectrum.

Despite its high molecular specificity and versatility, the low sensitivity of Raman spectroscopy limits its use in intraoperative imaging.

It is mainly used for targeted measurements on specific tissue samples, since the punctual scanning of a large area to obtain a detailed Raman image is very time-consuming – a consequence of the weak Raman signals of the samples.

Multimodal: CARS Microscopy

- To overcome these limitations, researchers at Leibniz IPHT use nonlinear coherent Raman methods such as **CARS microscopy**.

CARS significantly shortens measurement times and, in addition to point measurements, also enables the generation of image data, which, however, only show characteristic Raman-active vibrations. Due to its multimodal nature, CARS can detect not only Raman vibrations but also other nonlinear multiphoton effects such as two-photon fluorescence (TPEF) and second harmonic generation (SHG).

Light Through 10,000 Fibers

A Camera Probe for Gentle Diagnostics

Dr. Marko Rodewald develops image processing algorithms for multimodal imaging of head and neck cancer tissue. © Sven Döring

A team of researchers from Leibniz IPHT and the University Hospital Jena has developed a novel fiber probe for medical imaging in cooperation with the company Grintech. It provides highly accurate tissue images at the cellular level.

The technology could improve cancer diagnostics in dermatology, gastroenterology, neurosurgery, and head and neck surgery by precisely localizing tumor boundaries during surgery and reducing the need for invasive tissue sampling during biopsies.

The researchers are combining three nonlinear multimodal imaging techniques in one probe to examine tissue in real time with minimal invasiveness: coherent anti-Stokes Raman scattering (CARS), which is primarily used to visualize lipids; second harmonic generation (SHG), which observes collagen; and two-photon excited fluorescence (TPEF), which is used to image endogenous fluorophores.

This allows detailed, marker-free visualization of both tissue structure and biochemical composition. This is known as morphochemistry.

Using approximately 10,000 individual fibers, the probe projects laser light onto the tissue. Point scanning of the individual fibers allows imaging without moving elements. *Ex-vivo* tests on bulk tissue samples confirmed the probe's ability to perform precise morpho-chemical analyses and thus its applicability for *in-vivo* studies. "The camera probe is very simply constructed. This makes it much easier to use in a clinical setting," explains Dr. Tobias Meyer-Zedler, who developed the method with his Molecular Imaging group.

Multimodal Imaging

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combines different spectroscopic imaging techniques to provide a comprehensive picture of the morphological and chemical composition of tissue. These techniques allow detailed, marker-free analysis and provide valuable insights into living tissue.

Without moving or electrical parts in the probe head, the fiber probe could not easily be expanded into a therapy probe (see page 20). However, this not only lowers the barriers to use, but also promises greater mechanical stability and easier sterilization – important aspects for use in the operating room. Further research will focus on clinical applicability, in particular by improving image reconstruction and further customization and adaptation to clinical needs. "Our goal is to enable fast and gentle spectral histopathology at the patient's bedside or in the operating room," says Dr. Hyeonsoo Bae, who designed the microscope. This could reduce invasive diagnostic procedures and improve patient care.

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Publication:

Bae, H., Rodewald, M., Meyer-Zedler, T. et al. Feasibility studies of multimodal nonlinear endoscopy using multicore fiber bundles for remote scanning from tissue sections to bulk organs. Sci Rep 13, 13779 (2023). https://doi.org/10.1038/s41598-023-40944-6

Light-guided Precision in Surgery

A Conversation: Physical Chemist Jürgen Popp and Surgeon Orlando Guntinas-Lichius Discuss the Potential of Light-based Technologies and Their Joint Research for the Future of Cancer Care

Biophotonic technologies from Leibniz IPHT in the operating room: The invaScope makes cancer tissue visible using Raman spectroscopy and is currently being tested in a clinical study at the University Hospital of Jena. In the picture: Surgeon Prof. Dr. med. Orlando Guntinas-Lichius with the probe, in the background researchers Ayman Bali and Prof. Dr. Iwan Schie, whose Multimodal Instrumentation working group developed the invaScope. © UKJ

Prof. Guntinas-Lichius, from your perspective as a surgeon: Why are new imaging techniques needed for surgical removal of tumors?

Orlando Guntinas-Lichius (OGL): We need to be able to better identify the tumor margins to be more certain that we have completely removed the tumor. Complete removal is essential for the success of the operation, i.e. the patient's chances of survival.

Prof. Popp, what are the advantages of light-based technologies over conventional imaging methods in cancer diagnostics?

Jürgen Popp (JP): In contrast to conventional methods, our new light-based methods make it possible to analyze not only the structure but also the chemical composition of a tissue non-invasively and in real time. This means that we can obtain valuable information about the tumor during surgery, which I believe is the key advantage in the field of tumor diagnosis and therapy. The technology provides us with morphochemical information, i.e. data on both the shape and the chemical composition of the tissue.

Today's standard imaging modalities used to prepare for surgery – such as ultrasound, computed tomography, magnetic resonance imaging or endoscopy – can "only" visualize the pathological correlate of tumor disease, i.e. the physically tangible, measurable part of a tumor, its mass. They show its location and size, but cannot provide specific information about the type of tumor. Light-based approaches can fill this gap.

Another advantage is the use of artificial intelligence, which allows the images to be evaluated quickly and reliably. This provides surgeons with diagnostically relevant, tumor-specific information in real time. As Mr. Guntinas-Lichius said, this is crucial for targeted surgical interventions.

How do the biophotonic methods for cancer diagnostics that you and your team are researching work?

JP: Biophotonic techniques use complex interactions between light and matter to provide deep insight into tissue structure and function. When light strikes biological tissue, it is partly reflected at the surface and partly refracted into the tissue. Within the tissue, it can be absorbed, emitted, or scattered. These light-matter interactions provide the contrast for imaging morphochemical tissue phenomena.

Together with Mr. Guntinas-Lichius and his team, we have made significant progress in recent years. One key is multimodal imaging (see pages 13 and 20). Combined with automated imaging algorithms developed by Prof. Dr. Thomas Bocklitz's Photonic Data Science research department, it opens up new perspectives in the field of stain-free tissue diagnosis. They make it possible to precisely localize tumors during surgery: in a frozen section procedure (*ex-corpore in-vivo*) or potentially also *in-vivo*.

Prof. Dr. Jürgen Popp is Scientific Director of Leibniz IPHT and Professor of Physical Chemistry at the University of Jena. He heads the Spectroscopy/Imaging research department. © Sven Döring

"There is no point in researching a "cool" biophotonic method that is not clinically needed. Translational biophotonic research must always be driven by an unmet medical need. We have learned this from our many years of successful collaboration between researchers in technology and the clinic."

Jürgen Popp

How can these technologies be adapted for clinical use?

JP: In order to make these technologies clinically applicable, we have been working with our partners to develop compact, easy-to-use devices that transfer multimodal imaging to various endoscopic probes. This is a significant technological challenge that we have successfully overcome.

In order to exploit the full potential of this multimodal imaging technology, it would be a major step forward to introduce a procedure that works with extreme precision: femtosecond ablation, controlled by spectroscopic analysis – according to the principle of "detect and treat".

In the BMBF project TheraOptik, we have implemented a multimodal, nonlinear microendoscope that can treat tissue with very short laser pulses, so-called femtosecond lasers (see page 20). This instrument could enable surgeons to see and assess in real time during an operation whether the edge of the tissue removed is completely free of tumors. This could ensure that the operation is completed only after all tumor cells have been removed.

Powerful analysis of the data and images is crucial (see page 26). It is the basis for extracting meaningful diagnostic and therapeutic information from the data we obtain. For this reason, we began establishing our own research structures for AI-supported image and data analysis at Leibniz IPHT more than 15 years ago.

How exactly can the tumors detected by your multimodal imaging be removed?

JP: Our method uses femtosecond lasers, which emit light in extremely short flashes. This allows us to work very precisely and with minimal thermal stress to the surrounding healthy tissue. As a result, the ablated areas are very small and precise, typically in the micrometer range – about the thickness of a human hair. When the laser is set very precisely, as we do with our TheraOptik probe, for example, we can treat areas as small as a few micrometers. The more we increase the laser energy, the larger the area we can treat. We are currently researching how to optimize the energy of the laser to be as precise as possible without damaging the surrounding tissue.

Mr. Guntinas-Lichius, how could this procedure assist you during surgery?

OGL: Ideally, the result of the measurement would be displayed to me as a surgeon immediately during the operation, i.e. the tumor boundaries would be shown. I can then safely remove the tumor along the tumor boundaries.

Another device developed at Leibniz IPHT for the histopathological characterization of cancer tissue - the invaScope – is currently being tested in a clinical trial at the University Hospital of Jena. Can you already give a first assessment of how the technology works in practice?

OGL: The primary goal of this clinical trial is first of all to demonstrate its feasibility – in other words, to show that it is possible to examine patients during surgery with the invasCope, to show that this can be done safely without risk to the patients, and that it is possible to examine tumor tissue and surrounding normal tissue.

Prof. Dr. med. Orlando Guntinas-Lichius heads the Department of Otorhinolaryngology at the University Hospital in Jena. © Anna Schroll

"We need to be able to better identify the tumor margins to be more certain that we have completely removed the tumor. This is essential for the success of the operation and the patient's chances of survival."

Orlando Guntinas-Lichius

Even though the trial is still ongoing, we can be very optimistic: So far, it has been successful without any problems. Of course, we also want to show that the measurements can reliably distinguish between tumors and other tissue. It is still too early to say. More patients need to be examined.

Your joint project integrates not only optical sensors but also haptic sensors into a surgical robot. How does this technology help surgeons?

JP: In the "Sensory Surgery" breakthrough project funded by the Carl Zeiss Foundation and led by Mr. Guntinas-Lichius, we want to combine our biophotonic sensors with haptic sensors. This will enable surgeons to obtain not only visual but also tactile information about the tissue. The haptic sensors – researched by Prof. Dr. Hartmut Witte's team at the Technical University of Ilmenau – measure mechanical properties of the tissue, such as elasticity, and convert them into haptic signals.

Mr. Guntinas-Lichius, as a surgeon, what do you think of this sensory support during surgery?

OGL: It is the interaction of the technologies that provides the added value. The optical sensors provide information about the tissue, in particular where the tumor tissue is and where the tumor boundary is. The haptic sensors provide information about how the tissue feels. Surgeons work with their hands. Feeling the tissue is important for making decisions about where to cut. Finally, robotics enables a high degree of cutting precision. We can only really take advantage of this if we can also identify the tumor boundaries with high precision. Then we can safely remove the tumor while sparing healthy tissue.

How does the interdisciplinary collaboration between your teams affect the development of the technologies?

OGL: Only together, with the knowledge of the different disciplines, can the problem described be solved by developing an innovative technology. One discipline alone cannot do it.

JP: One of the most important lessons we have learned as technologists over the past 25 years is the need to involve the end user – the healthcare professional – in research from the very beginning. There is no point in researching a "cool" biophotonic method that is not needed clinically. Translational biophotonic research must always be driven by unmet medical needs and requires the successful interaction of technology and clinical researchers from the outset. I think the longstanding successful collaboration between Mr. Guntinas-Lichius and myself is a good example of this.

What are the challenges of moving from the research lab to the operating room?

OGL: It is a big leap: fast data processing must be implemented in the operating room to deliver information to the surgeon in real time. The information must be unambiguous and not misunderstood, so that the surgeon can incorporate it almost intuitively into his decision-making process for the next surgical step. And, of course, there are a number of regulatory requirements such as privacy, data security, hygiene, and more that need to be addressed.

JP: In addition to the technological challenges of biophotonics, which we typically address through an interdisciplinary research strategy – i. e., by involving various scientific disciplines – we are currently facing regulatory issues in particular. This is our biggest challenge. We have now reached the point where we can start clinical trials with our biophotonic approaches. But before we can start, we need to obtain regulatory approval. In terms of logistical and financial resources, this phase is usually far beyond what academic groups can handle. Because a new technology is usually considered very risky, it is not readily taken up by industry or commercial investors.

What are the hurdles?

JP: This is a general problem, i.e. the implementation of biophotonic research results faces major challenges, especially with regard to the EU Medical Device Regulation (MDR) for translational research. The regulation currently makes it very difficult to test biophotonic approaches on patients in the form of preclinical or clinical studies. Nevertheless, we have managed to document the above-mentioned Raman invaScope in an MDR-compliant manner so that it can be used for *in-vivo* studies. This was a big challenge, and we learned a lot that we can now use to document our nonlinear probes in an MDR-compliant manner.

What is your personal motivation to research and work in this field?

OGL: Leapfrog innovations, i.e. innovations that take patient care a big step forward, are the work of a large interdisciplinary team. It is a lot of fun to solve problems and remove barriers so that a technology can be used.

JP: I am driven by the motivation to take a promising research idea beyond publication, i. e. to translate it into a clinical device. I am always driven by the basic idea of further developing a successfully published and promising idea and translating it into a clinical procedure – translating it in the sense of the Leibniz IPHT motto: from ideas to instruments.

Together Against Cancer

Leibniz IPHT and its research partners in Jena and Europe focus on innovative light-based technologies. A selection of current projects:

CZS Breakthroughs

A team from Friedrich Schiller University, Jena University Hospital and Ilmenau Technical University is developing a sensor-based system that enables surgeons to detect and remove tumors more precisely. Funded by the Carl-Zeiss-Stiftung.

PHAST European Training Network

Research institutions, hospitals and industry partners from seven European countries are training young researchers to improve cancer prevention, diagnosis and treatment using photonics. Funded by the EU.

CRIMSON

Researchers, physicians and SMEs from four countries are working on a biophotonic tool for advanced imaging in cancer diagnostics to investigate the cellular causes of disease and support personalized therapies. Funded by the EU.

Quantum Optics in Search of Tumors
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Nonlinear interferometer
© Fraunhofer IOF / Walter Oppel

Imaging with marker-free infrared quantum microscopy could open up new ways of detecting tumors. In contrast to conventional methods in the infrared range, the detection principle here is based on so-called non-detected light, in which the samples interact with infrared light, but the detection is highly sensitive in the visible spectral range. The Quancer project is the first step to combine this technology with professional microscopy systems and to test it in clinical practice at the University Hospital Jena. Leibniz IPHT is involved in the project together with Friedrich Schiller University, Fraunhofer IOF, Rapp OptoElectronic GmbH and other renowned institutions. The goal: more precise and effective tumor diagnostics. With a budget of 6.7 million euros over a period of five years and funded by the BMBF as a lighthouse project, Quancer promises significant advances in medical imaging and could improve the early detection of cancer.

Chip for Rapid Blood Testing
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Researchers with microarray chips
© fzmb GmbH

Leibniz IPHT is part of the EU project SANGUINE, which is developing a new blood test for the early detection of cancers of the blood cells and bone marrow. Research partners from Europe and Israel are working to develop a cost-effective test for the early detection of such diseases, which have been difficult to diagnose in the past.

The HemaChip, developed by fzmb GmbH from Bad Langensalza as a partner of the InfectoGnostics Research Campus, uses microarray technology. Leibniz IPHT contributes significantly to the functionality of the chip by designing special DNA sequences.

Due to its high sensitivity and low cost the test is particularly suitable for routine use. It promises to be rapidly introduced into clinical practice to improve the diagnosis of blood cancer and enable early treatment.
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further information at
www.sanguine-project.eu

Yellow Fiber Lasers for Medicine
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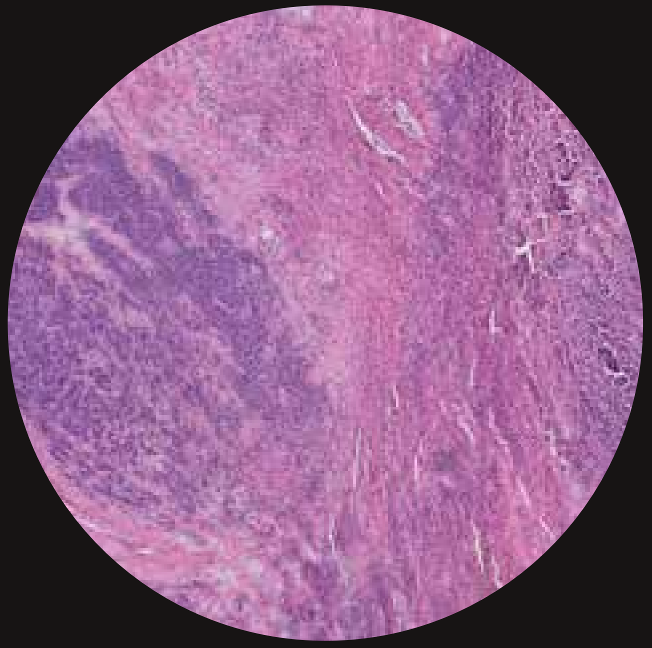
Fiber traction by the molten core method © Leibniz IPHT

The TAB research group Yellow is working on the development of yellow fiber lasers for biomedical diagnostics and therapy. The goal of the TAB research group is to overcome the disadvantages of lasers with blue and green wavelengths, such as higher phototoxicity. Yellow lasers promise gentler treatment options in ophthalmology and dermatology and offer potential applications in biophotonics, for example, to research new methods for cancer diagnostics.

The challenge in generating yellow laser light is the difficulty in finding laser materials and diodes for this spectral range. The Spectroscopy/Imaging and Fiber Photonics research departments are working with the Competence Center for Specialty Optical Fibers to develop new fiber materials and technologies to create efficient, cost-effective yellow fiber lasers suitable for clinical use. These will be optimized for use in Raman spectroscopy. The industry-oriented research group is funded by the Thüringer Aufbaubank.



Histopathological tissue section from a patient with a head and neck tumor at the University Hospital of Jena, Germany, stained with hematoxylin and eosin (H&E). This staining technique is considered the gold standard in pathology for the evaluation and diagnosis of various diseases.

Multimodal nonlinear image of the same tissue section. Three nonlinear modalities (see page 12) were used: CARS (red), TPEF (green) and SHG (blue). The combination allows a comprehensive morphochemical analysis of the sample.

Precision Tool

Innovative Probe Detects and Removes Tumor Tissue in Real Time

Whether a cancer operation was successful or not can currently only be determined after the fact. Only after pathological examination of the removed tissue can surgeons be sure that all cancer cells have been removed. In the future, a new type of probe could bring pathology analysis directly into the operating room – detecting and removing tumor tissue in a single step.

When removing tumors, surgeons rely primarily on their experience and intuition to decide which tissue to cut away. Final confirmation that the tumor has been completely removed during surgery often comes days or weeks later, after extensive pathological examination of the removed tissue. The waiting period carries the risk that remaining cancer cells will continue to grow.

Researchers at Leibniz IPHT, together with partners in the BMBF project TheraOptik, have developed an endoscopic probe that could significantly improve this situation for patients in the future. The probe combines diagnostics and therapy in a single instrument. Using laser light, it enables the precise identification and immediate removal of tumor tissue. The light-based technology makes it possible to detect tumor boundaries down to the micrometer range, enabling removal at the subcellular level. By integrating this precision into robotic surgical systems, the previously untapped cutting accuracy of surgical robots can be fully exploited for the first time.

In head and neck surgery in particular, it is crucial to precisely determine tumor boundaries. "This requires new imaging technologies that provide detailed images of the inside of the body during surgery and allow the tumor to be precisely localized. This is because the targeted detection of malignant tissue during curative surgery is the most important prerequisite for the complete removal of a tumor," explains surgeon Prof. Dr. Orlando Guntinas-Lichius from the University Hospital Jena (UKJ). He is working with researchers from Leibniz IPHT, Friedrich Schiller University Jena (FSU) and the company Grintech to develop the procedure.

"The probe combines three different imaging techniques with artificial intelligence-supported software. This enables it to distinguish tumor cells from healthy tissue at the molecular level in real time. Based on this detection, it is able to immediately remove the tumor using femtosecond laser ablation," explains Dr. Tobias Meyer-Zedler from Leibniz IPHT. His team from the Molecular Imaging working group has been researching the further development of the method for many years in numerous collaborative projects. The TheraOptik project, funded by the German Federal Ministry of Education and Research, was successfully completed in 2023. In addition to the Jena-based companies Grintech and Active Fiber Systems, the medical technology manufacturers Karl Storz and Diaspective Vision were also involved.

The team is currently working on transferring the procedure from tissue preparation to the operating room and is planning a preclinical study with around 200 patients to validate the effectiveness of the technology.

In the future, this optical diagnostic method could reduce the need for biopsies and help avoid repeated surgeries or stressful therapies.

In addition to improving people's chances of recovery, the technology could result in significant cost savings for the healthcare system. "Every minute spent in the operating room is one of the most costly in the hospital," says Orlando Guntinas-Lichius. In head and neck surgery, where cancer cells are found in nearly one in ten operations, this new method could represent a significant advance.

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Publications:

Lai, C., Calvarese, M., Reichwald, K., Bae, H., Vafaeinezhad, M., Meyer-Zedler, T., Hoffmann, F., Mühlig, A., Eidam, T., Stutzki, F., Messerschmidt, B., Gross, H., Schmitt, M., Guntinas-Lichius, O., & Popp, J. (2023). Design and test of a rigid endomicroscopic system for multimodal imaging and femtosecond laser ablation. Journal of biomedical optics, 28(6), 066004. https://doi.org/10.1117/1.JBO.28.6.066004

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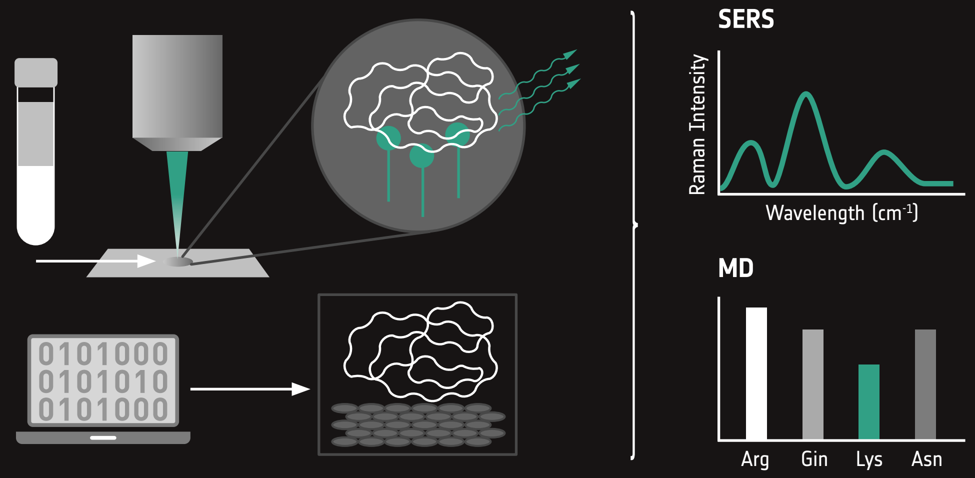
Calvarese, M. & Meyer, T. & Schmitt, M. & Guntinas-Lichius, O. & Popp, J.. (2023). Recent developments and advances of femtosecond laser ablation: Towards image-guided microsurgery probes. TrAC Trends in Analytical Chemistry. 167. 117250. https://doi.org/10.1016/j.trac.2023.117250.

On the Road to Early Detection

Can a Saliva Test Detect Cancer?

From Florence to Jena: Edoardo Farnesi examines body fluids for cancer markers. © Sven Döring



SERS uses metallic nanoparticles to amplify the weak Raman signals of biomarkers; MD simulations visualize how these molecules dock onto the nanoparticles.

New diagnostic methods play a crucial role in the fight against cancer. Edoardo Farnesi came to Jena from Florence to develop methods for the efficient and non-invasive detection of tumor markers in body fluids.

"Our goal is to enable precise diagnosis with just a few drops of saliva or, in the future, blood serum," explains Edoardo Farnesi. He is working on the development of SERS (surface-enhanced Raman spectroscopy)-based methods to identify cancer indicators directly in body fluids.

Farnesi combines surface-enhanced Raman spectroscopy (SERS) and molecular dynamics (MD) simulations to detect markers in saliva that indicate diseases such as throat cancer and oral infections. SERS uses metallic nanoparticles to amplify the weak Raman signals of biomarkers, while MD simulations visualize how these molecules dock onto the nanoparticles.

With SERS, researchers can analyze the biochemical composition of body fluids and characterize changes caused by cancer. When combined with MD simulations, the cancer-related changes observed in the SERS spectrum can be interpreted at the molecular level. This approach opens up the possibility of simple point-of-care diagnostics of molecular cancer signatures at an early stage.

Edoardo Farnesi moved from Florence to the Friedrich Schiller University Jena and Leibniz IPHT in 2021 as a young scientist in the European training network PHAST (Photonics for Healthcare: multiscAle cancer diagnosis and Therapy). In the PHAST program, renowned research institutions such as the ICFO in Barcelona and the Medical University of Vienna are working together with Leibniz IPHT, the Friedrich Schiller University Jena and the University Hospital Jena as well as other hospitals and industrial partners in Europe to research new diagnostic tools for the early detection and treatment of cancer.

Surface-enhanced Raman Spectroscopy (SERS)

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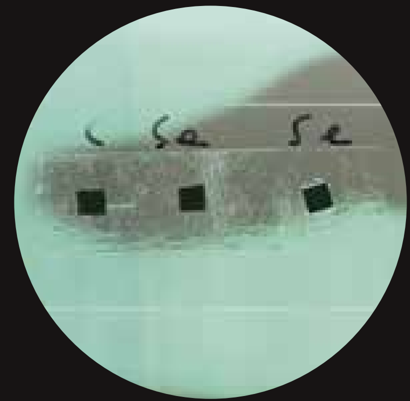
uses metals such as silver and gold to dramatically enhance molecularly sensitive Raman signals, enabling the detection of individual molecules. This technique provides detailed insight into molecular structures and is widely used in chemistry, environmental analysis and biomedicine, particularly for the highly sensitive detection of biomarkers.



SERS-active sensor surfaces for the detection of biomarkers in body fluids © Sven Döring

Using a simple saliva test, the method developed by Edoardo Farnesi and his team could lead to rapid, non-invasive diagnoses directly at the patient's bedside and enable tailored therapies. "We are still at the beginning of our research," he stresses. Further studies are needed to optimize and validate the technology for clinical practice and to standardize the procedure.

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Publications:

Farnesi, E.; Rinaldi, S.; Liu, C.; Ballmaier, J.; Guntinas-Lichius, O.; Schmitt, M.; Cialla-May, D.; Popp, J. Label-Free SERS and MD Analysis of Biomarkers for Rapid Point-of-Care Sensors Detecting Head and Neck Cancer and Infections. Sensors 2023, 23, 8915. https://doi.org/10.3390/s23218915

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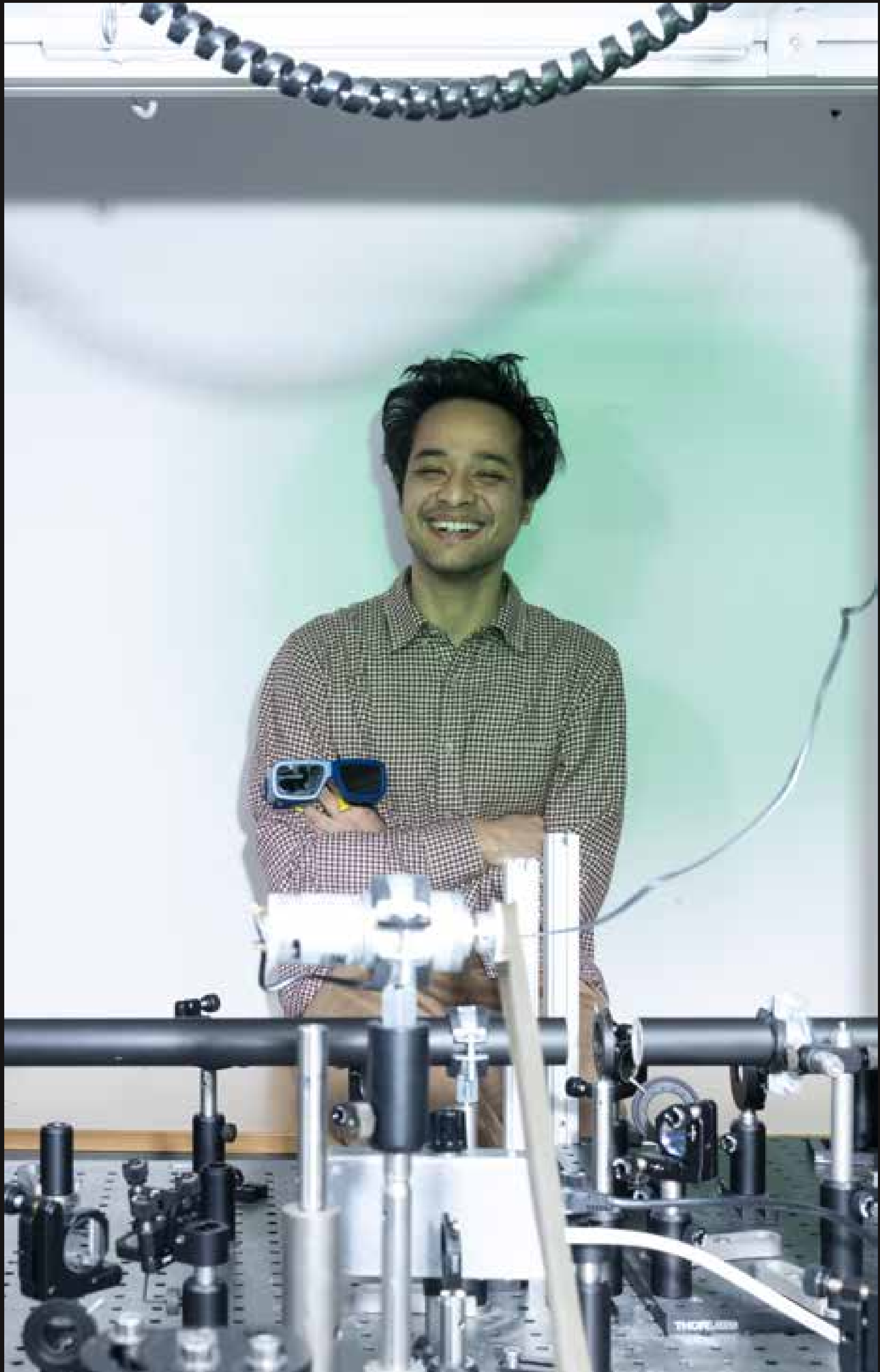
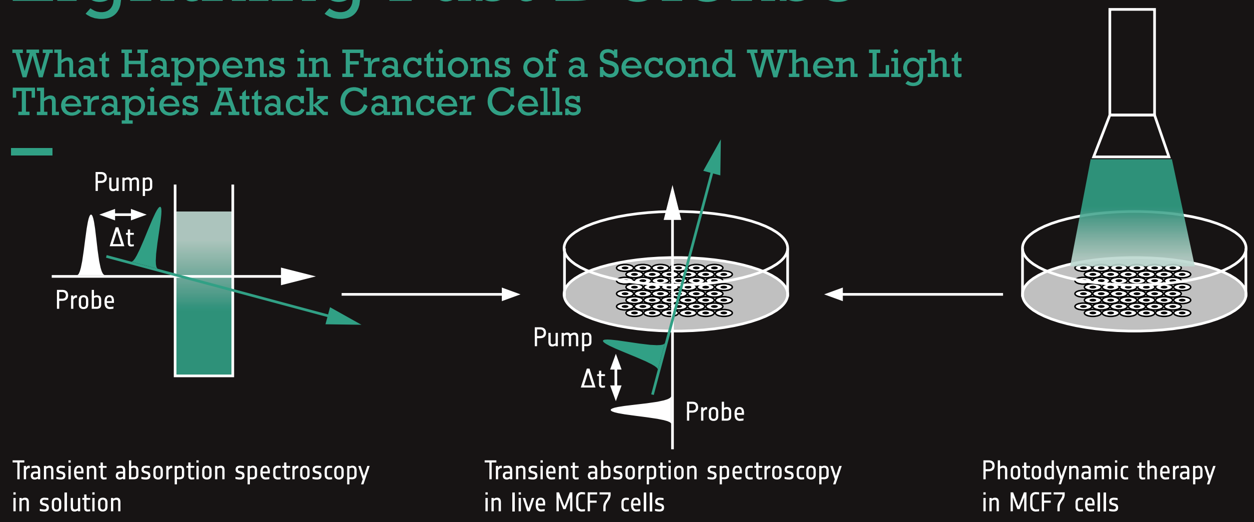
Issatayeva, A., Farnesi, E., Cialla-May, D., Schmitt, M., Rizzi, F. M. A., Milanese, D., Selleri, S., & Cucinotta, A. (2024). SERS-based methods for the detection of genomic biomarkers of cancer. Talanta, 267, 125198. https://doi.org/10.1016/j.talanta.2023.125198



Dr. Avinash Chettri uses transient absorption spectroscopy (TA) and microscopy to observe the ultrafast processes that take place in cancer cells during photodynamic therapy.

Lightning Fast Defense

What Happens in Fractions of a Second When Light Therapies Attack Cancer Cells



The innovative research method allows the activation of photosensitizers by light and their action in living cells to be observed: The image on the left shows how light activates photosensitizers in a liquid. One beam of light (the "pump") is used to activate the molecules, while a second beam of light (the "probe") then measures how the molecules behave. The middle image shows how the behavior of the photosensitizers is observed inside living cells. On the right, you can see how these activated molecules can be used in photodynamic therapy to destroy cancer cells.

Photodynamic therapy uses light to target cancer cells. Avinash Chettri investigates what happens in a tiny fraction of a second inside a cancer cell when a flash of light activates therapeutic compounds.

TLD1433 targets cancer cells. The photosensitizer, currently in clinical trials for bladder cancer, is used in photodynamic therapy (PDT) to target cancer cells. This light-sensitive substance is introduced "inactive" into the cancer cells and activated by light irradiation. There it produces highly reactive forms of oxygen, known as singlet oxygen, which can destroy cancer cells from the inside out. The special feature is the selective photoactivation of the photosensitizer TLD1433, which is absorbed by both cancerous and healthy cells, but only activated in the cancerous areas through targeted irradiation. This makes it possible to effectively target cancer cells while leaving the surrounding healthy tissue largely unharmed.

Although PDT using photosensitizers has been researched and applied since the 1970s, many of its properties are still undiscovered. Avinash Chettri, in a team with the Functional Interfaces research department, developed an experimental methodology based on transient absorption spectroscopy (TA) and microscopy. This allowed the researchers to observe the ultrafast processes that take place in the cells after light activation of the photosensitizer.

Time-Resolved Spectroscopy

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makes it possible to record and analyze extremely fast processes on the time scale of femtoseconds – a quadrillionth of a second. It provides insight into the dynamics of atoms and molecules, as well as the study of chemical reactions, physical changes in materials, and biological processes, providing a window into the fundamental processes of life and matter.

These methods make it possible to study the processes in cancer cells, especially in the breast cancer cell line MCF7, in real time. Their study contributes to the fundamental understanding of the photophysics and excited state dynamics of photosensitizers in living cells. More research is needed before photosensitizers can be developed to target different types of cancer. A deeper understanding of the complex influences on photosensitizers is an important step toward more effective treatments.

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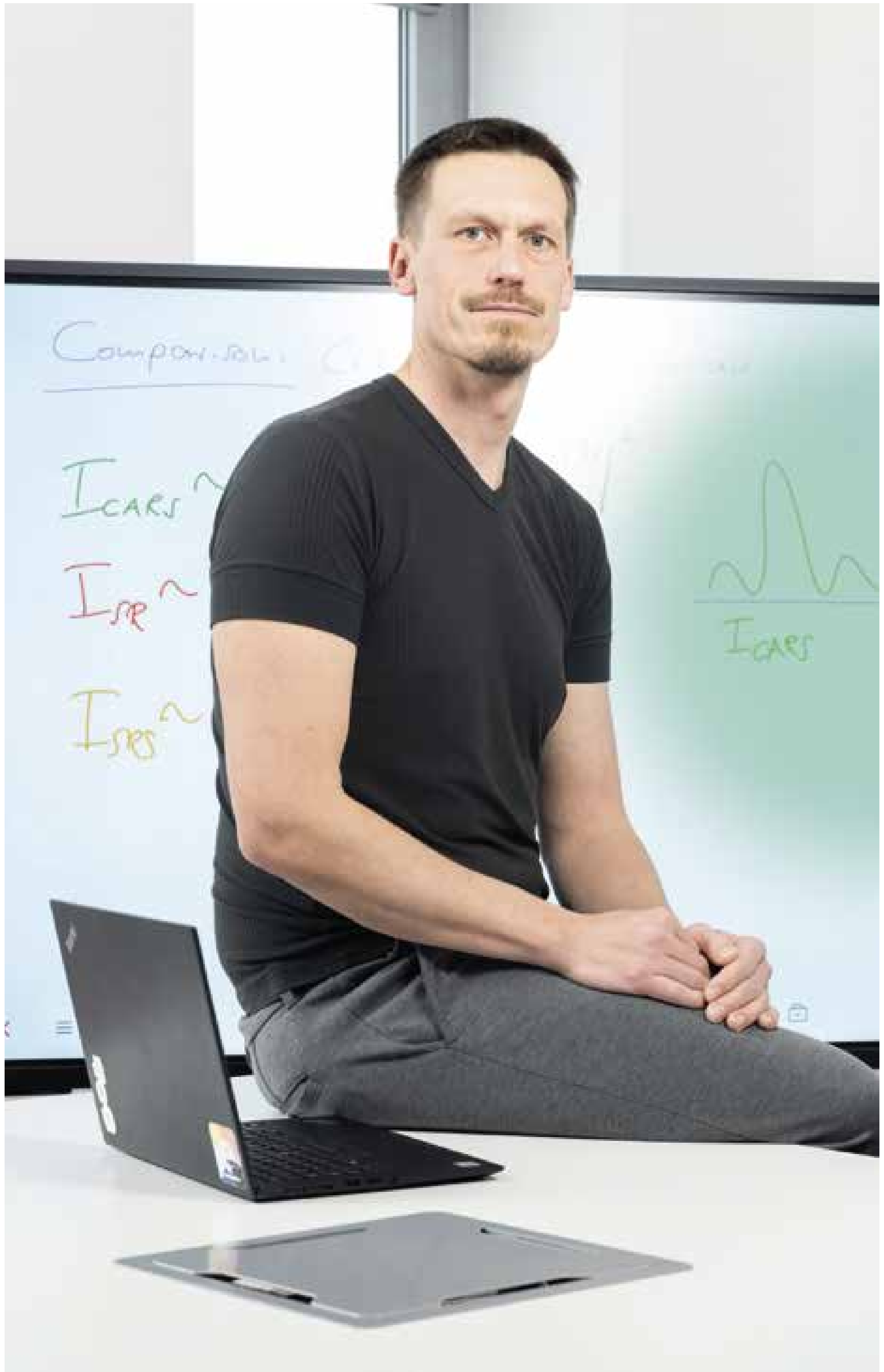
Publication:

A. Chettri, T. Yang, H. D. Cole, G. Shi, C. G. Cameron, S. A. McFarland, B. Dietzek-Ivanšic, Angew. Chem. Int. Ed. 2023, 62, e202301452; Angew. Chem. 2023, 135, e202301452. https://doi.org/10.1002/anie.202301452



Prof. Dr. Thomas Bocklitz and his team use mathematics to make optical data useful for medicine. © Sven Döring

Of Light and Data: New Paths in Diagnostics

Using Artificial Intelligence and Photonics to Make More Precise Decisions in Medicine

Which antibiotic does a patient with a life-threatening infection need? What organic chemicals are polluting a body of water? And how can the images from a fiber probe be improved so that doctors can clearly see the boundaries of a tumor in real time during surgery? To answer these questions, researchers at Leibniz IPHT are using a combination of optical methods and artificial intelligence (AI).

Photonic methods use light to analyze biological materials and processes, while AI algorithms help to extract meaningful information from the large amounts of data generated. For example, AI is behind the flexible camera probe that enables rapid tumor diagnosis during surgery (see page 13 of this magazine). This miniaturized endoscope provides high-precision images that may one day enable surgeons to distinguish between healthy and tumor tissue. The spectroscopic data is automatically analyzed and translated into classic standard diagnostic images with a resolution comparable to that of high-end microscopes.

Thomas Bocklitz and his team in the Photonic Data Science research department have spent years developing the algorithms that make this precise diagnosis possible. The starting point was a computer-assisted process for a compact microscope for rapid cancer diagnosis in the Medicars project. "We trained AI algorithms together with pathologists," explains Thomas Bocklitz. By taking multimodal images of a tissue sample, which is then classically stained and examined under a microscope by a pathologist, the algorithm learns to distinguish between healthy and diseased areas. The accuracy of this method is greater than 90 percent.

Appointed

In early 2024, Thomas Bocklitz has been appointed W3 Professor for Data Science in Photonics at the Friedrich Schiller University Jena. He heads the Photonic Data Science research department at Leibniz IPHT.

From Pixel to Detail

Designing the camera probe was particularly challenging: Although the probe's flexibility allows it to capture detailed images of the inside of the body, the image quality was initially poor. To solve this problem, Dr. Marko Rodewald and Thomas Bocklitz developed a method to reconstruct the images so that they accurately represent the morphochemical structure of the tissue. These corrected images are then converted into computer-generated H&E images, a standard procedure in pathology, which show the tissue structure in detail.

Awarded the ERC Consolidator Grant

In September 2023, Bocklitz received the prestigious ERC Consolidator Grant to expand this pioneering approach and prove its feasibility. In the STAIN-IT project, the team is developing a digital staining method for cancer diagnostics based on multimodal imaging. Deep learning models will be used to mimic immunohistochemical staining methods commonly used for differential diagnosis and therapy decisions. STAIN-IT promises to be a fast and cost-effective alternative to conventional methods that can be directly integrated into everyday clinical practice and provides clear insights into tissue changes.

The ERC Consolidator Grant of approximately 2 million euros recognizes not only the scientific excellence of Thomas Bocklitz, but also the supportive research environment at Leibniz IPHT, the Friedrich Schiller University and the University of Freiburg, as well as the University Hospitals of Jena, Bayreuth and Erlangen. In this project, researchers from various disciplines are working together to improve diagnostic reliability and gain new insights into disease mechanisms.

Thomas Bocklitz has been working at Leibniz IPHT since 2016 and has been head of the Photonic Data Science research department since 2019. In spring 2023, he was offered and accepted a professorship at the University of Bayreuth. Jena then launched its own appointment procedure – with success. A decisive factor for this appointment was the close interdisciplinary cooperation within Leibniz IPHT and its Jena network in research and clinics, from which Bocklitz was able to obtain the experimental spectroscopic data for the development of new AI methods. Thomas Bocklitz has accepted a W3 professorship for Data Science in Photonics at FSU Jena at the beginning of 2024. "I am very much looking forward to a fruitful collaboration with my team and the Jena cooperation network."

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Publications:

R. Houhou, E. Quansah, T. Meyer-Zedler, M. Schmitt, F. Hoffmann, O. Guntinas-Lichius, J. Popp, and T. Bocklitz, "Comparison of denoising tools for the reconstruction of nonlinear multimodal images," Biomed. Opt. Express 14, 3259-3278 (2023) https://doi.org/10.1364/BOE.477384

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Contreras, J. ; Bocklitz, T.: Agnostic eXplainable Artificial Intelligence (XAI) Method Based on Volterra Series. In: Proceedings of the 12th International Conference on Pattern Recognition Applications and Methods. - Sétubal : SciTePress , 2023 . - S. 597-606, ISBN 978-989-758-626-2, https://doi.org/10.5220/00118 89700003411

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Escobar Díaz Guerrero, R. & Gupta, Y. & Bocklitz, T. & Oliveira, J.. (2023). A Multimodal Image Registration System for Histology Images. 17-22. https://doi.org/10.1109/CBMS58004.2023.00185.

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R. Luo, T. Bocklitz, A systematic study of transfer learning for colorectal cancer detection, Informatics in Medicine Unlocked, Volume 40, 2023, 101292, ISSN 2352-9148, https://doi.org/10.1016/j.imu.2023.101292.

Photonic Data Science at the Federal Digital Summit

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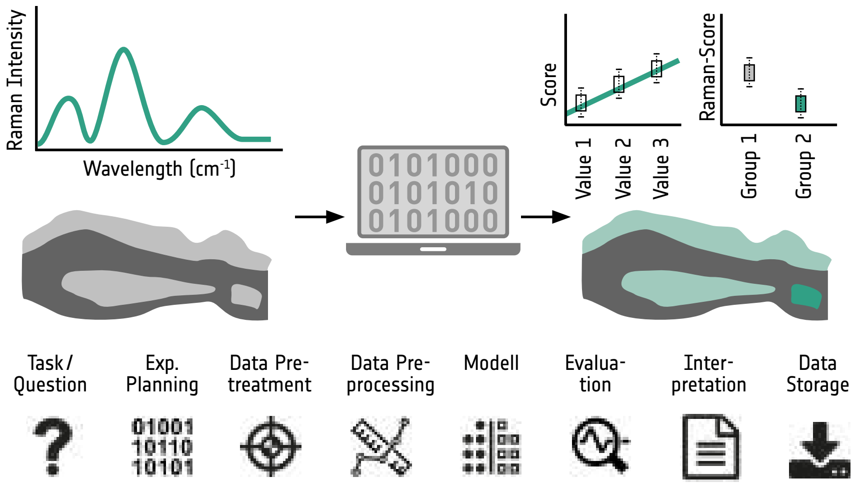
Prof. Dr. Thomas Bocklitz and Dr. Sophie Thamm present their research results in the market of digital opportunities at the Digital Summit.

By developing AI methods for rapid, light-based diagnostics, Thomas Bocklitz and his team are making a significant contribution to the technological equipment of the Leibniz Center for Photonics in Infection Research (LPI). They presented their solution for the evaluation of optical data at the Digital Summit of the German government in Jena in November 2023.



Workflow in the field of photonic data science, illustrated with the example of Raman spectroscopy

A Look Through the Keyhole

Researchers Use Machine Learning to Develop Gentle, High-resolution and Dynamic Microscopy Imaging

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Optical microscopy makes it possible to observe biological structures in living cells and their dynamics.

In particular, super-resolved microscopy methods such as STED microscopy make it possible to observe structures beyond the conventional optical resolution limit with a resolution of less than 50 nanometres – a dimension that is thousands of times smaller than the thickness of a human hair. This allows researchers to observe how virus particles interact with the cells they infect, for example.

One challenge, however, is that the necessary intensive illumination can cause damage to the cells. Together with a team from the College of Optics and Photonics at the University of Florida and the Max Planck Institute for Multidisciplinary Natural Sciences in Göttingen, the team from the research department Biophysical Imaging has developed and applied a method to circumvent this limitation by using deep learning techniques and to enable fast, gentle STED microscopy.

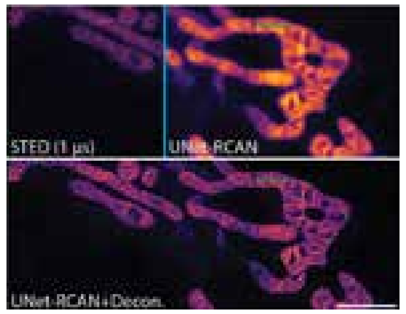
Insights into Living Cells

Prof. Dr. Christian Eggeling and Dr. Pablo Carravilla - now a postdoc at the Karolinska Institutet in Stockholm - and their partners have found a solution to the limitations of STED microscopy. Their approach of cross-modal image restoration quickly but gently transforms noisy images into high-resolution STED images without damaging cells.

"Using these techniques, we can reconstruct high-resolution images from less perfect, i.e. rough images that were taken with less light," explains Christian Eggeling. "This enables faster imaging and longer observation times without damaging the sample." By succeeding in significantly reducing the pixel time, the researchers minimize photobleaching and phototoxicity effects and achieve gentler imaging.

The AI models learn from a large amount of data what such images normally look like and can then reconstruct the best possible image from the available data.

To this end, the researchers developed a special algorithm that is driven by a two-stage prediction architecture. This architecture combines a U-network, which is responsible for the recovery of comprehensive context information, with a Residual Channel Attention Network (RCAN), which reconstructs the super-resolved final images.



Improved STED imaging with UNet-RCAN reduces photobleaching and damage. Shown here: Detailed structures of mitochondrial cristae in COS-7 cells. The image shows dynamics over 300 consecutive images.

The algorithm was trained using image pairs that had both low and high signal-to-noise ratios (SNR) to improve its effectiveness in image reconstruction.

Machine Learning: The Key to Better Images

This approach significantly expands the possibilities of STED microscopy in the direction of faster imaging and longer observation times. This allows researchers to observe living cells and their dynamic processes over longer periods of time with great clarity and detail. They gain insights into the movement of molecules and changes in cell structures during important cellular processes such as cell division, signaling and gene expression. These advances offer new perspectives for understanding fundamental biological mechanisms and could significantly contribute to the development of innovative therapeutic approaches.

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Publication:

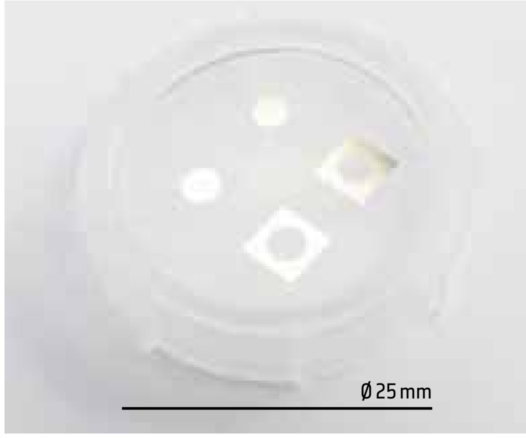
Ebrahimi, V., Stephan, T., Kim, J., Carravilla, P, Eggeling, C. et al. Deep learning enables fast, gentle STED microscopy. Commun Biol 6, 674 (2023). https://doi.org/10.1038/s42003-023-05054-z

See More With Less Light

Better Than a Lens? Researchers Develop a Creative Technique for High-resolution Images

Two separate images become one: Dr. Uwe Hübner (left in the mirror) and Prof. Dr. Rainer Heintzmann illustrate the trick of their research approach in this photo. Uwe Hübner fabricated the small elliptical mirror that Rainer Heintzmann and his microscopy team used to split the light passing through the microscope's lens and recombine it.
© Sven Döring

For centuries, researchers have used optical lenses to create detailed images of micro- to macrocosms, from distant galaxies to tiny molecules. Now, a team led by Jan Becker and Prof. Dr. Rainer Heintzmann presents an innovative approach that pushes the limits of traditional optical imaging without placing additional strain on the sample.



The researchers used this tiny mirror from the micro- and nanotechnology team to divide the pupil of the detection lens in the microscope. They placed the mirror at a precise angle to divide the pupil into two areas and create two separate images, which were then merged with the help of a computer. © Sven Döring

Instead of improving the signal-to-noise ratio (SNR) by increasing the amount of light – a process that can damage the sample – the team in Rainer Heintzmann's Microscopy research department came up with a creative solution: they split the pupil of the objective into two parts – or more precisely, they split the light that passes through the objective using a specially designed mirror.

This creates two separate images, which are then combined by computer to create a high-quality overall image. This method reduces noise and improves the signal-to-noise ratio. It makes it possible to see finer details without exposing the sample to more light. The small elliptical mirror was fabricated by Dr. Uwe Hübner and his micro- and nanotechnology team in the clean room at Leibniz IPHT.

By subsequently combining the images, the researchers can achieve image quality that would not be possible with conventional images that pass entirely through the lens. The technology offers significant advantages for biomedical research and medical diagnostics, enabling high-resolution imaging – for example of tissues – with a minimized risk of phototoxic damage. It also opens new horizons in live-cell research by enabling more detailed three-dimensional imaging.

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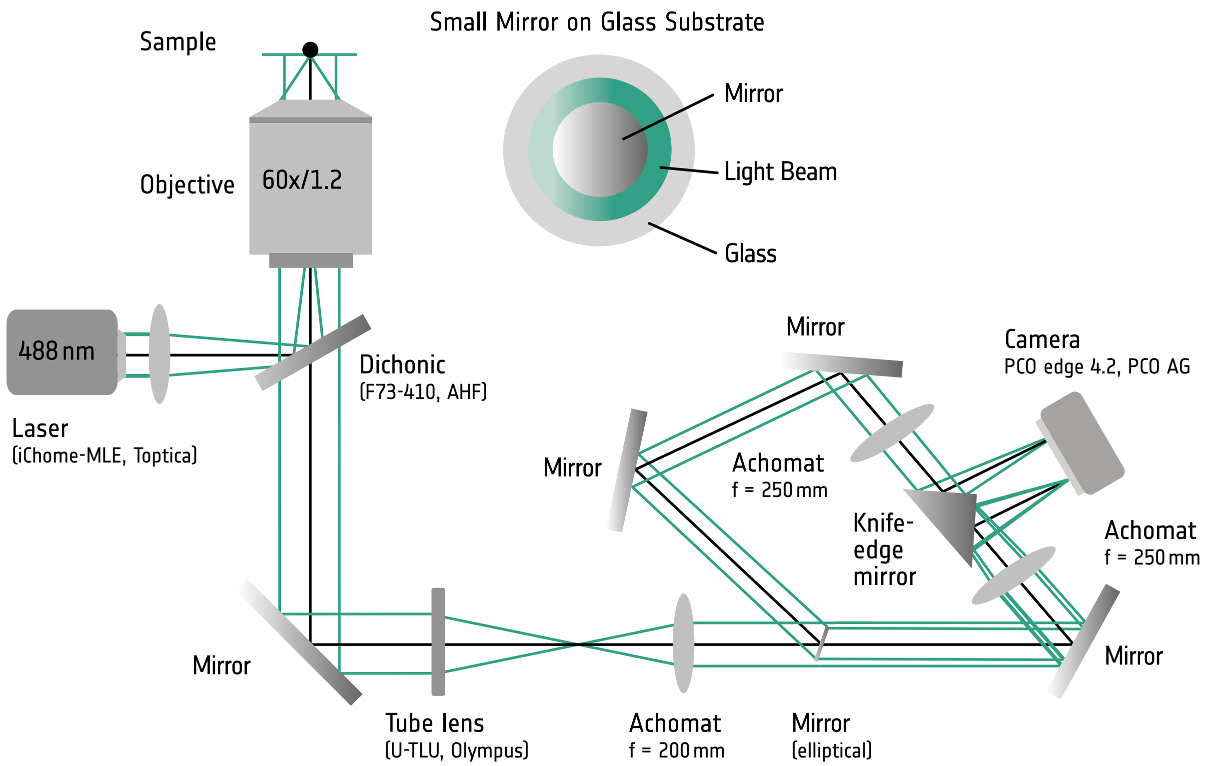
Publication:

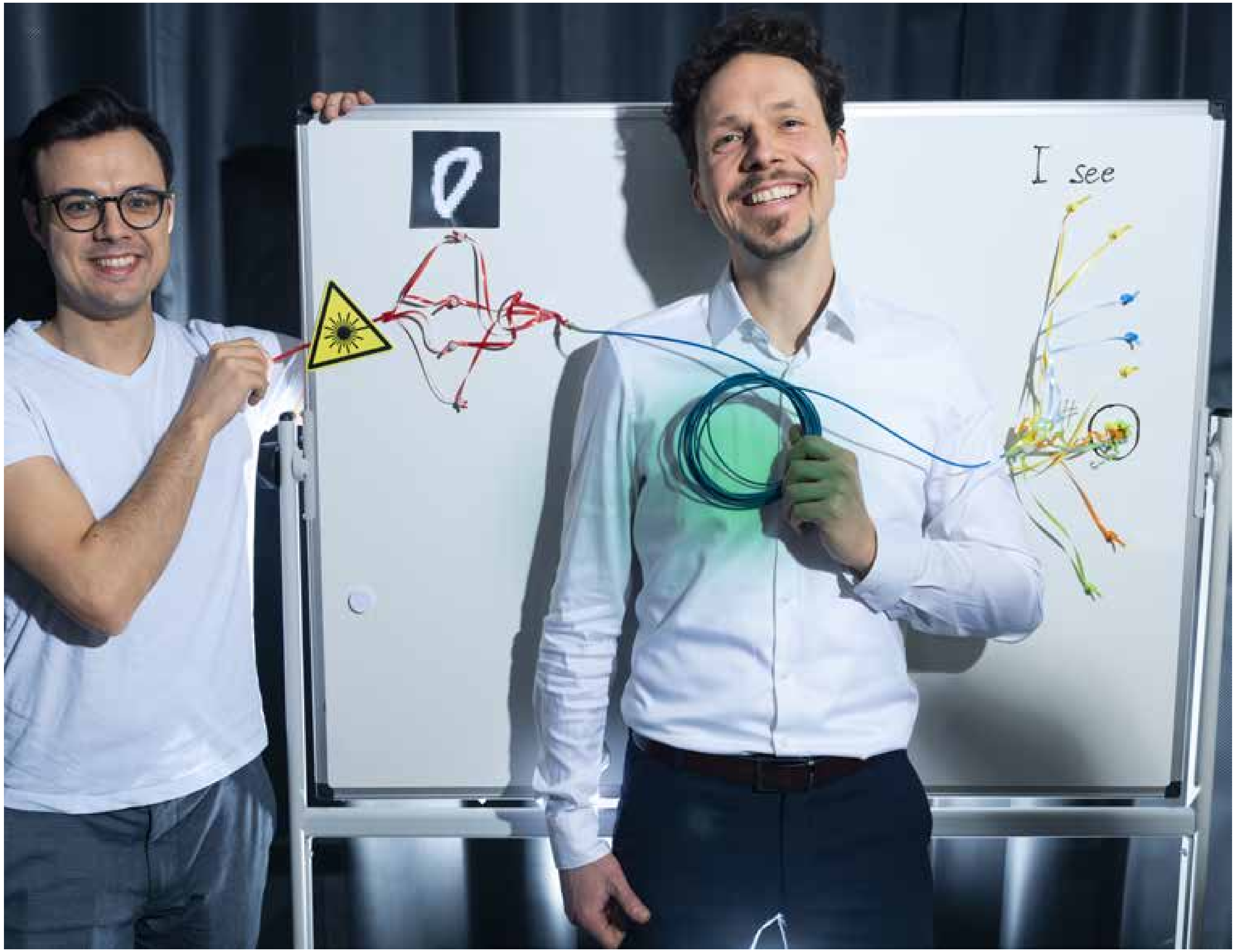
Jan Becker, Takahiro Deguchi, Alexander Jügler, Ronny Förster, Uwe Hübner, Jonas Ries, and Rainer Heintzmann, "Better than a lens? Increasing the signal-to-noise ratio through pupil splitting," Optica 10, 308-315 (2023) https://doi.org/10.1364/OPTICA.474947



The way to split an image in two: an ingenious arrangement of additional lenses and a small mirror in the microscope. The researchers cleverly split the light coming through the microscope lens to capture two different views of an object simultaneously on the same camera.

Neural Networks Made of Light

AI From Fiber Optics: Energy-efficient Computing With Optical Neural Networks



Dr. Bennet Fischer and Prof. Dr. Mario Chemnitz (from left) explore the possibilities of nonlinear optics. Their goal: to develop intelligent sensor systems and microscopes without computers, as well as methods for green computing.

Appointed

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Mario Chemnitz has been appointed as Junior Professor for Intelligent Photonic Systems at the Friedrich Schiller University Jena. He heads the Smart Photonics junior research group at Leibniz IPHT.

Together with an international team, researchers from the Smart Photonics junior research group have developed a technology that could significantly reduce the high energy consumption of AI systems in the future.

The process uses light for neural computing and is based on the neural networks of the human brain. As a result, data processing is not only more efficient, but also many times faster and uses significantly less energy than conventional systems.

Artificial intelligence is a key enabler of advances in biotechnology and medicine, from cancer diagnostics to the development of new antibiotics. However, the environmental footprint of large AI systems is significant. Prof. Dr. Mario Chemnitz and Dr. Bennet Fischer from Leibniz IPHT, together with international partners, have found a way to make potentially energy-efficient computing systems more sustainable, without the need for extensive electronic infrastructure. They use the unique interactions of light waves in optical fibers to create an advanced artificial learning system.

A Single Fiber Instead of Thousands of Components

At the heart of the technology is an optical fiber that replaces traditional computer chips and performs the functions of neural networks at the speed of light. "We use a single optical fiber to generate the computing power of a large number of neural networks," explains Mario Chemnitz, head of the Smart Photonics junior research group. These optical fibers use the unique physical properties of light to efficiently process data.

The technology is based on the principle of imprinting information on the color channels of ultrashort light pulses and passing them through the fiber. The light pulses are combined and modified along the fiber, ultimately resulting in new color combinations and insight into the processed data. One application is the classification of handwritten numbers, where the team modifies the light signals according to the data, creating a fingerprint for each digit.

System Recognizes COVID-19 From Voice Samples

The researchers have also successfully used their technology to diagnose COVID-19 using voice samples, surpassing the accuracy of existing digital systems. "We are the first to show that such a colorful interplay of light waves enables the direct classification of complex information," Chemnitz emphasizes.

By developing this technology, the researchers are not only opening up new avenues for more environmentally friendly AI applications, but also for innovative diagnostic procedures and intelligent microscopy that do not require traditional computer technology.

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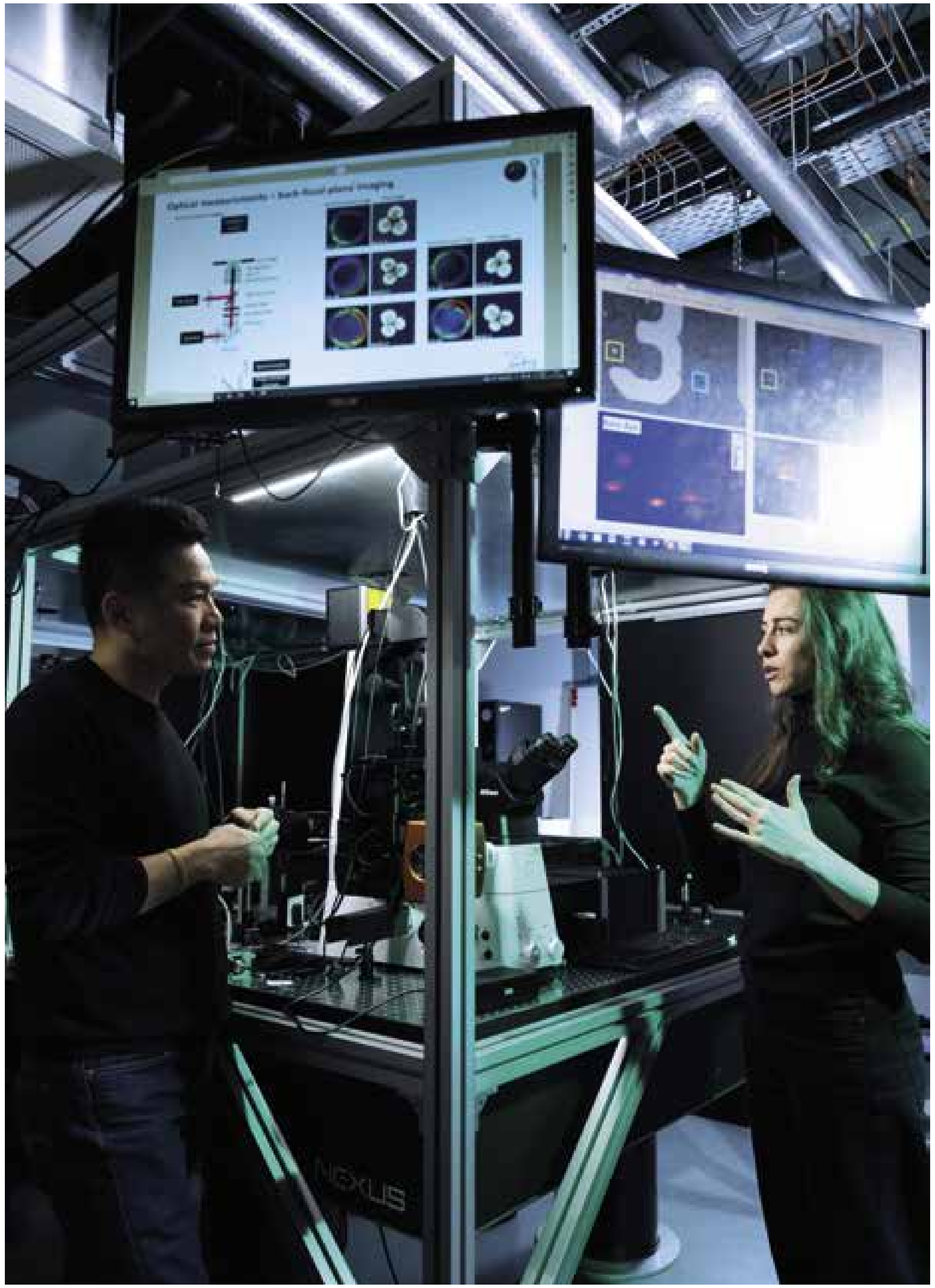
Publication:

B. Fischer, M. Chemnitz, Y. Zhu, N. Perron, P. Roztocki, B. MacLellan, L. Di Lauro, A. Aadhi, C. Rimoldi, T. H. Falk, R. Morandotti, Neuromorphic Computing via Fission-based Broadband Frequency Generation. Adv. Sci. 2023, 10, 2303835. https://doi.org/10.1002/advs.202303835

Light Control Through DNA Origami

Cleverly Folded Nanostructures for the Wireless Optical Communication of the Future



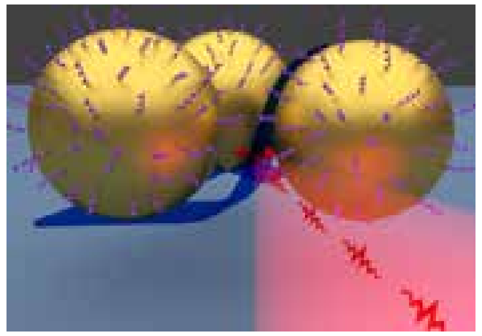
PD Dr. Jer-Shing Huang, Head of the Nanooptics research department, in the laboratory together with Ayşe Tuğça Mina Yeşilyurt, PhD student and first author of the paper © Sven Döring

A research team at Leibniz IPHT has succeeded in developing optical hybrid nanostructures that can specifically direct and control the light emission of individual quantum emitters. This achievement paves the way for the development of efficient photonic circuit components that can be used, for example, in wireless optical communication.

The researchers use DNA origami technology to create functional and nanoscopic structures with defined properties. They fold scaffolds of DNA into a suitable three-dimensional template to place a single dye molecule and metallic nanoparticles in the desired spatial configuration. These hybrid nanostructures can serve as directional single-photon light sources in photonic nanocircuits that use light for signal processing. The specific design allows to control the direction of propagation of the emitted photons.

In their current work, the researchers present an extremely compact meta-emitter that is less than 150 nanometers in size. It consists of three 60 nanometer large, spherical gold nanoparticles that are held together by a triangular DNA origami. A fluorescent dye molecule is cleverly placed in the center of the gap between two gold nanoparticles. This nanoantenna has the special property of directing the emitted light in a specific direction.

What is DNA Origami?



The researchers used DNA origami to precisely arrange three gold nanospheres and a dye molecule into a unidirectional meta-emitter © Leibniz IPHT

DNA origami is an advanced molecular technology that uses biomolecular self-organization to create precise one- to three-dimensional DNA scaffolds for various applications. Folding of DNA scaffolds into customized nanostructures enables the formation of a variety of complex geometric templates, including nanotubes, nanocages and diamond-like 3D networks, which can be used as key components in photonics and nanoelectronics. Researchers at Leibniz IPHT are using DNA origami to create hybrid structures that serve as unidirectional single photon sources. Recent breakthroughs, such as the development of ultra-compact meta-emitters, demonstrate the ability of this technology to precisely control the photon emission of a single quantum emitter while reducing the physical size of nanostructures.

DNA origami is a powerful tool for developing nanoscale devices with customized properties and functionalities.

The method enables unidirectional light emission, which is of great interest for applications in quantum communication and wireless optical nanocircuits. Experimental studies have shown that the plasmonic nanoantenna design can increase the emission by a factor of 23 while reducing the size by at least a factor of 5 compared to the previously realized Yagi-Uda nanoantennas. This lays the foundation for increasing the efficiency of wireless optical communications.

The original idea for this work arose during the traditional doctoral seminar in Dornburg in 2017 between the research departments Nanooptics and Nanobiophotonics at Leibniz IPHT. In collaboration with the group of Prof. Guillermo Acuna at the University of Fribourg, Switzerland, the researchers jointly published their results in the journal ACS Nano.

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Publication:

T. M. Yesilyurt, M. Sanz-Paz, F. Zhu, X. Wu, K. Suma Sunil, G. P. Acuna, J.-S. Huang, Unidirectional Meta-Emitters Based on the Kerker Condition Assembled by DNA Origami, ACS Nano (2023), https://doi.org/10.1021/acsnano.3c05649

New Opportunities in the Fight Against Infectious Diseases

How Light-based Technologies Can Give Us a Head Start in the Race Against Resistance

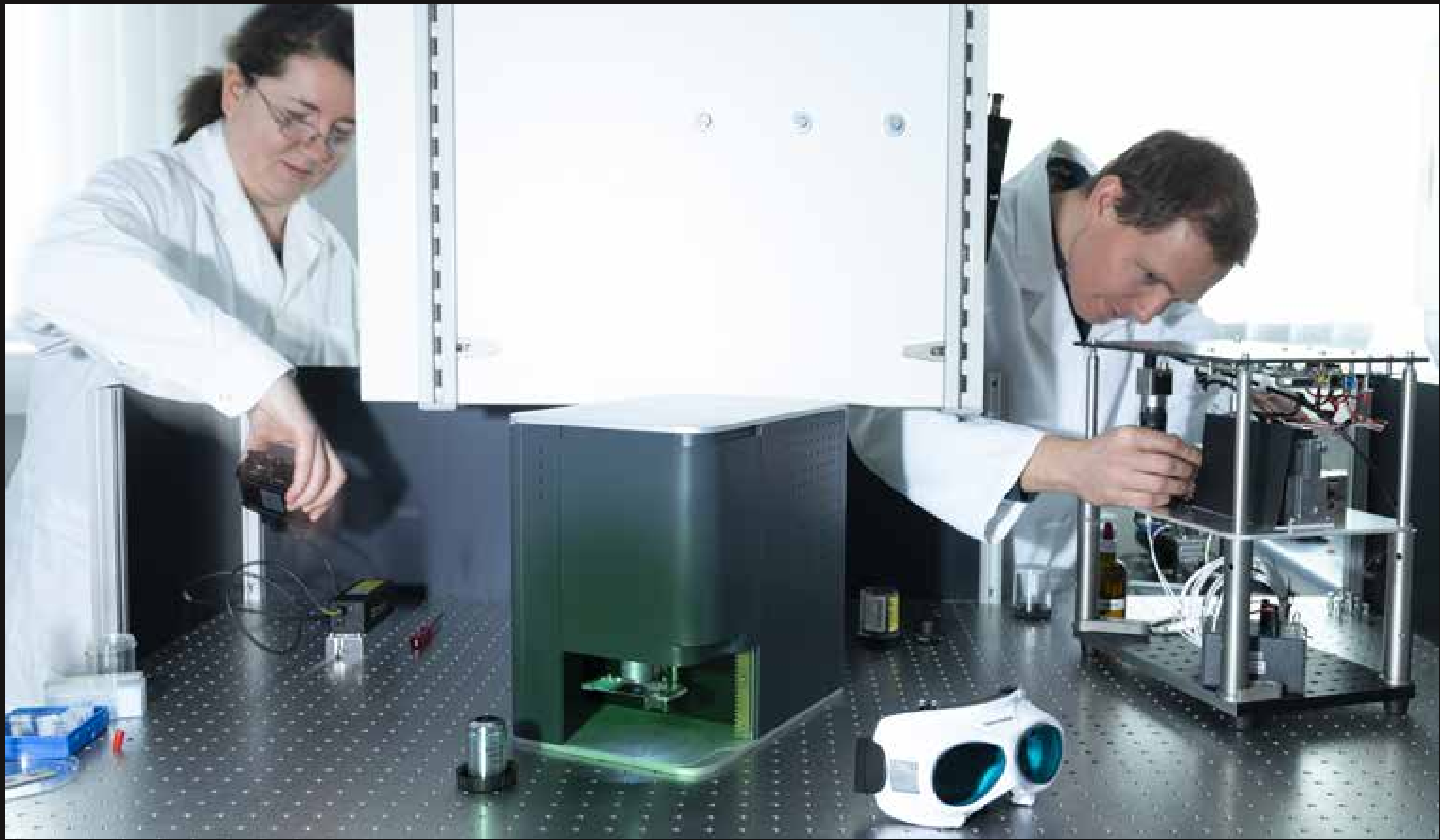
Marie-Luise Enghardt and Dr. Richard Grohs are working at Leibniz IPHT and the Leibniz Center for Photonics in Infection Research on the development of a laser-based rapid test. The test can be read on a portable microspectrometer, and is intended to bring rapid infection diagnostics to patient care.

Light-based technologies could mark a turning point in the diagnosis of infectious diseases. They are fast, sensitive, and non-contact. Combined with artificial intelligence, they offer a decisive time advantage in the treatment of life-threatening infections and in the race against increasing antibiotic resistance.

This feature highlights how biophotonic technologies are helping to push the boundaries of traditional methods. They enable rapid and accurate diagnosis and open up new therapeutic approaches. In doing so, they are helping to find medical answers to one of the greatest health challenges of our time.

On the Move

From Vision to Application: How Researchers at Leibniz IPHT Are Working Together on a Breakthrough in the Diagnosis of Life-threatening Infections



Dr. Izabella Jolan Jahn and engineer Henry John work in the Sensor Systems and System Integration group on the further development of the mobile Raman spectrometer Raman2Go, the POCT-Raman, which is being researched at the institute.
© Sven Döring

A laser-based rapid test from Leibniz IPHT could be a game-changer in the fight against resistant germs. The technology works – now the researchers face the challenge of implementing the method in medical practice.

When Dr. Walter Hauswald's systems technology team visited Dr. Anja Silge, Dr. Richard Grohs and Dr. Cornelia Reuter in the microbiology laboratory in December 2023 with the portable miniature spectrometer, they simply gave it a try. They placed the newly developed chip under the laser in the small gray box, filled the 40 small wells with bacterial samples and antibiotics, connected the rainbow-colored cables – and sure enough, it worked. "To the great delight of everyone involved, we were able to measure real bacteria with the new chip in the newly developed spectrometer," reports Anja Silge, deputy head of the Spectroscopy and Imaging research department at Leibniz IPHT. "For us, it was like a new rocket really landing on the moon.

A Chip That Could Save Lives

The gray box and the quartz glass chip with the colorful cables contain more than two decades of research work by various teams and groups at Leibniz IPHT and the University Hospital Jena. Technologists and chemists, data scientists and microbiologists, physicians and physicists have worked together to develop an optical method that could revolutionize the diagnosis of infectious diseases: the RamanBioAssay®, a laser-based rapid test that identifies pathogens and the appropriate antibiotic from a single sample – in less than three hours. Current microbiology methods take up to three days. This could be life-saving in cases of serious infections that can develop into sepsis. In the case of aggressive, resistant pathogens, a patient's chance of survival decreases by several percent every hour. Instead of prescribing a broad-spectrum antibiotic on suspicion, physicians could use antibiotics in a targeted manner – and thus make a decisive contribution to combating the growing number of resistant germs.

From Idea to Instrument

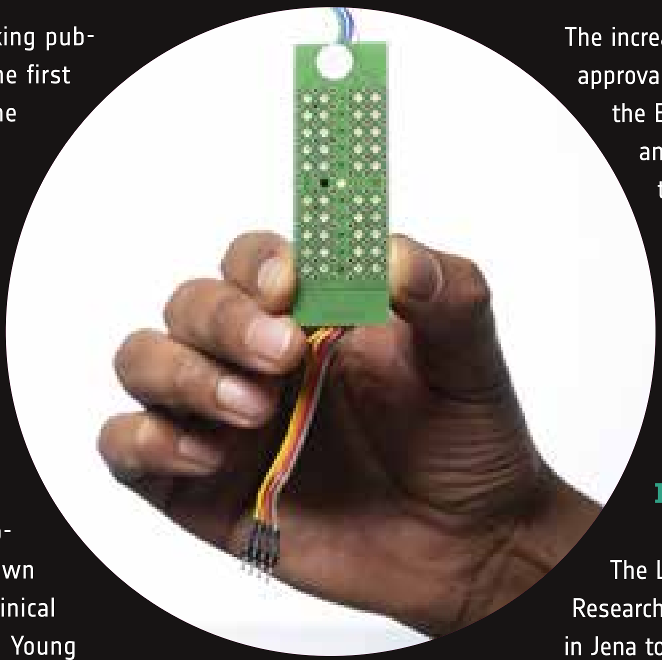
The gray box is a miniaturized Raman spectrometer for point-of-care diagnostics, fully functional with light source and detector - a handy mobile device that can be used in the future where there is no specialized laboratory nearby, for example in doctors' offices in structurally weak rural regions. Instead of lenses and mirrors, a cleverly structured optical grating the size of a fingernail directs the light. It was developed and manufactured by the micro- and nanotechnology team in the clean room of Leibniz IPHT.

Teamwork Is the Key to Success

The second generation of the mobile spectrometer – the successor to the Raman2Go – and the latest version of the RamanBioAssay® chip were developed by interdisciplinary research teams at the newly established Leibniz Center for Photonics in Infection Research (LPI). The latest chip, which is about the length of a stick of chewing gum, can now test twelve instead of four different antibiotics at the same time - in different concentrations, so that doctors can immediately see how high the correct dose of the drug needs to be. This allows multiple samples to be tested three times faster, one after the other. The bacteria from a patient sample – blood or urine – are sealed behind laser-transparent quartz glass, sterile and hygienically covered.

When Prof. Dr. Jürgen Popp first came to the Friedrich Schiller University in Jena in 2002 and then to Leibniz IPHT as scientific director in 2006, he brought with him the idea of using Raman spectroscopy to study bacteria in order to make their molecular fingerprints visible. With the help of laser technology, researchers are now able to detect differences between different bacteria. Since the first BMBF-funded research project, research teams have been working on the implementation of a portable device for the rapid detection of infectious pathogens using Raman spectroscopy. Since 2010, they have been investigating how bacteria react to antibiotics;

four years later, high-ranking publications followed, then the first patents and a spin-off. The method has received numerous awards, including the Thuringian Research Prize and the Berthold Leibinger Innovation Prize. Prof. Dr. Ute Neugebauer, who did her doctorate on this topic under Jürgen Popp, is now deputy scientific director of the Leibniz IPHT and heads her own research department of clinical spectroscopic diagnostics. Young researcher Dr. Johanna Kirchhoff received the German Academic Award for one of the most important dissertations in Germany for her work on the method.



RamanBioAssay® for laser-based rapid testing of bacteria and drug resistance © Sven Döring

Artificial Intelligence Speeds Up the Process

As the mobile spectrometer became more compact, the team grew larger. "We have left our laboratory and are continuing to develop the method and the devices together with our partners in clinical microbiology," says Jürgen Popp. Leibniz IPHT has established its own group for system technology and instrument development. Over the past 15 years, the institute has increasingly focused on the evaluation of spectroscopic data, which is the key to the speed and accuracy of the method. Since 2019, an entire research department for photonic data science, headed by Prof. Dr. Thomas Bocklitz, has been working on the further development of AI-based methods. In total, Popp estimates that more than 40 people are working on the research and development of the method.

The Challenge: Regulatory Hurdles

The project is now facing its biggest challenge: the transfer to clinical practice. Proof of concept has been achieved. "We have provided extensive evidence that the technology works," says Popp. Now it's all about marketing – specifically technical and regulatory issues. Feasibility studies for clinical validation are underway with the University Hospital of Jena. Leibniz IPHT is initiating a cooperation with the University of California Davis to further develop the technology for the American market.

At the same time, the teams at Leibniz IPHT are working on automating the procedure to make it easier for doctors to use. The devices must also be cost-effective to compete with existing diagnostic methods. "A test should not cost more than three or four euros," explains Jürgen Popp.

The increased requirements for the approval of medical devices under the EU Medical Device Directive and the associated documentation pose a challenge, especially since the handy miniature Raman device works with self-learning AI algorithms to quickly evaluate the pathogens.

Looking to the Future: The LPI

The Leibniz Center for Infection Research (LPI) is being established in Jena to exploit the potential of light-based technology for diagnostics (see page 41). The further development of the RamanBioAssay® with a compact Raman spectrometer for use directly at the point of care is being funded as the basic technology for the LPI. The unique translational infrastructure will bring together researchers with a proven concept and experts from industry on the way to market. "It is intended to become a one-stop agency for light-based infection research," explains Popp. "So that good ideas from the laboratory reach people faster."

Top Research Center in the Fight Against Infections

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BMBF State Secretary Prof. Dr. Sabine Döring and Thuringia's Minister of Economics Wolfgang Tiefensee visit the LPI in November 2023
© Michael Szabó / UKJ

The Leibniz Center for Photonics in Infection Research (LPI) in Jena is a globally unique research center for the development of light-based technologies to combat infectious diseases. The German Federal Ministry of Education and Research (BMBF) is funding the LPI with the aim of translating research results into marketable products more quickly, thereby significantly shortening the development times for new drugs and therapies. Thuringia's Minister of Economic Affairs, Wolfgang Tiefensee, assured the LPI of the state's full support during a visit with BMBF State Secretary Prof. Dr. Sabine Döring in November 2023. The center contributes to "Germany's technological sovereignty," he said.

The LPI combines research, technology development and clinical practice in order to improve the transfer of knowledge from research to society and to pave the way for better preventive measures and therapies. The LPI is initiated by Leibniz IPHT, Leibniz-HKI for Natural Product Research and Infection Biology, the Friedrich Schiller University, and the University Hospital Jena.

Prepare for the Next Pandemic

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PD Dr. Stefanie Deinhardt-Emmer and Prof. Dr. Volker Deckert © Sven Döring

A research team from Leibniz IPHT and the University Hospital Jena is working on an innovative method for the rapid and direct identification of viruses, in particular the SARS-CoV-2 pathogen. By precisely determining the size and morphology of the virus particles, the approach enables diagnosis without the need for knowledge of antibodies or gene sequences. The method is based on the correlation of fluorescent markers of RNA and spike proteins with scanning probe microscopy (AFM) data. After an initial detailed analysis of virus characteristics, such as their height, the AFM technique allows viruses to be identified with a high degree of confidence based on their size alone.

"This method is particularly valuable in the early stages of an epidemic, when no specific antibodies or gene sequences are available for identification," explains Prof. Dr. Volker Deckert, head of the Nanoscopy research department at Leibniz IPHT, who is involved in the research together with Prof. Dr. Christian Eggeling and his Biophysical Imaging team.

The team's approach aims to identify virus particles on the basis of their physical properties without the need for complex preliminary work such as staining the samples.

The method provides an important tool for early detection and can help reduce the spread of viruses through timely protective measures and faster development of rapid tests.

The research, led by PD Dr. Stefanie Deinhardt-Emmer from the Institute of Medical Microbiology at the University Hospital in Jena, is part of the BMBF-funded SARSCoV2Dx collaborative project. The aim is to develop methods for the early detection of viral epidemics. These technologies will be integrated into the newly established Leibniz Center for Photonics in Infection Research (see above) in order to be better prepared for future pandemics.

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Publication:

Deckert-Gaudig T, Yao X, Darussalam E, Hornung F, Carravilla P, Zhao Z, et al. Identification of RNA-containing virus particles using a triple correlative morphological and microscopic approach. ChemRxiv. 2023; (Preprint) https://doi:10.26434/chemrxiv-2023-b9mr1

Technology Meets Medicine

Anja Silge and Stefanie Deinhardt-Emmer Are Jointly Researching New Ways of Diagnosing Infectious Diseases

The physical chemist Dr. Anja Silge and the physician Dr. Stefanie Deinhardt- Emmer work in interdisciplinary teams to develop innovative approaches to combat infectious diseases. Their goal: to make the possibilities of Raman spectroscopy usable for medical diagnostics. In this interview, they talk about how their different perspectives enrich each other and how they and their teams manage to find a common language.

Do you remember the first time you met? Were there any reservations about the other discipline that you have since been able to overcome?

Anja Silge (AS): We quickly realized that the first hurdle was mutual understanding. Both sides must be prepared to understand the basic concepts and perspectives of the other discipline. For example, 'sensitivity' in the medical context means the ability of diagnostic tests to detect a particular disease. In spectroscopy, 'sensitivity' refers to how well one can detect the small amount of Raman-scattered light from a specific analysis target.

What are you currently working on together?

AS: Raman spectroscopy enables us to characterize intact immune cells without markers and non-destructively. We track the hypothesis that their spectral fingerprint could be used in diagnostics in the future. In view of the complexity of Raman spectroscopy and the particularities of biological samples, researchers are collaborating intensively across disciplines: from microbiology and immunology to spectroscopy and data science.

Why is interdisciplinarity so crucial for your project?

Stefanie Deinhardt-Emmer (SDE): The direct exchange with our colleagues from physics is essential for understanding the methods and technologies. The potential applications are primarily defined on the clinical side, while our colleagues from spectroscopy show us the possibilities of the technology. In this interdisciplinary dialogue, we work together to find approaches to improve patient care.

How does Raman spectroscopy compare to traditional diagnostic methods?

AS: Raman spectroscopy enables non-invasive and rapid determination of the molecular fingerprint of

Dr. Anja Silge (left) and Dr. med. Stefanie Deinhardt-Emmer are jointly researching new methods for the diagnosis of infectious diseases, including technologies for the new Leibniz Center for Photonics in Infection Research (LPI).

cells. In particular, the detection of biochemical changes in immune cells that are characteristic of a particular infection is our central diagnostic concept. In order to analyze large numbers of samples efficiently, we use specially adapted sample preparations, specific sample management, automatic image recognition of target particles and advanced illumination methods for laser Raman spectroscopy.

What are the key findings and how did the interdisciplinary collaboration contribute to these findings?

AS: Our results suggest that patients with systemic infections could benefit from a phenotypic study of their immune cell profile or status. High-throughput Raman spectroscopy provides an innovative method to directly detect changes in the composition and phenotype of white blood cells without damaging the cells.

SDE: We have found that neutrophils – a type of white blood cell that plays an important role in the immune system - produce certain substances when they come into contact with the coronavirus (SARS-CoV-2): the signaling molecules IP-10 and IL-6. These substances are important indicators of widespread infection in the body.

AS: Using high-throughput Raman spectroscopy, we were able to detect a characteristic phenotypic change in neutrophil granulocytes in response to pre-stimulation and SARS-CoV-2 infection. Raman spectroscopy has proven to be an effective method to study the phenotype of immune cells, especially because of its strong correlation with proinflammatory cytokines. The interdisciplinary collaboration allowed us to structure the experiments in a meaningful way and to perform them with appropriate positive controls and reference measurements to further develop Raman spectroscopic phenotyping.

Anja Silge und Stefanie Deinhardt-Emmer

© Sven Döring

Interdisciplinary Work for us Means …

… combining knowledge to solve complex practical problems.
Anja Silge

… translating basic research into clinical practice to improve patient care.
Stefanie Deinhardt-Emmer

How do you overcome the challenges of interdisciplinary research teams?

SDE: It takes time to find a common language. That's why informal meetings are so valuable, where we tackle things directly and practically. We invite colleagues to our lab to show them how and what we are working on. Conversely, I also enjoy visiting colleagues and having their equipment and methods explained to me. In this way, our understanding of each other's needs and challenges grows as we work together.

Can you give examples of the importance of constructive exchange?

AS: It is crucial that all parties clearly articulate their expectations. It is not enough to hand over a biological sample at the entrance of the laboratory and simply wait for a measured spectrum in return. As Stefanie pointed out, it is important to develop an understanding of each other's way of working: for the physicians to see how we work with cells under the Raman microscope, what solutions or fixatives we use, and how long a measurement takes. We show them which parts of the spectrum can be attributed to the instrument and which information is actually coming from the sample, so they understand what information is reflected in the spectrum and what is not. Conversely, our technology teams learn from the physicians how to handle biological materials, which properties and structures are most important, and which time periods need to be observed. This mutual learning and explanation helps to avoid misunderstandings.

Did your training prepare you to work in interdisciplinary teams?

SDE: I am a physician and was trained to work with patients. Maybe that helps me to interact with other people and find out what their interests and problems are.

AS: Leibniz IPHT is an interdisciplinary research institute, so cooperation between different disciplines is essential. This includes close cooperation with the medical community, which we involve from the very beginning: Unmet medical needs are the driving force behind our research.

What motivates you to look beyond the boundaries of your own discipline?

AS: The major challenges of our time, such as globalization, climate change, the rise of infectious diseases and increasing antibiotic resistance, are complex problems that we can only solve together. I look forward to contributing to the development of solutions to these pressing issues. This is the motivation for my scientific work.

Is the German scientific system well equipped for interdisciplinary research?

SDE: In international comparison, I have experienced it differently and still see potential for improvement. In Germany, people often work too much in isolation. We could benefit from systems that specifically promote and reward interdisciplinary work.

What can we learn from other countries?

SDE: Universities in the U.S. use interdisciplinary programs to encourage students to explore topics that cross traditional disciplinary boundaries. Such approaches could also enrich the research landscape in this country, where the academic system has traditionally been more structured and discipline-specific than in the US.

How do you promote networking in clinical research?

SDE: We are initiating networks such as ClinSciNet to bring together clinical and basic researchers. There is great potential to attract young clinical researchers to translational medicine and to promote interdisciplinarity. We are forging links with basic research in order to form joint networks at an early stage.

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The interview was conducted by Christian Nehls and Gregor Kalinkat for the Leibniz PostDoc Network. The unabridged English version can be read online: https://leibniz-postdoc.de/interdisciplinarity-interview-3-raman-spectroscopy-as-a-diagnostic-tool-a-stimulus-for-interdisciplinary-collaboration/

The Team

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Dr. Anja Silge is a researcher in the Applied Biospectroscopy & Bioassays group and deputy head of the Spectroscopy and Imaging research department at Leibniz IPHT.

With a background in the life sciences, she works on methods for the application of Raman spectroscopy for the investigation of cells in infection research.

PD Dr. Stefanie Deinhardt-Emmer is head of the Translational Microbiology research group at the Institute of Medical Microbiology at the University Hospital Jena. As a specialist in microbiology and virology, she works as a senior physician on the development of approaches for translational medicine.

Excellence in Interdisciplinarity: Their Role Model

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Prof. Katarina Svanberg, Associate Professor of Oncology at Lund University Hospital. Her research focuses on the use of fluorescence-based tumor imaging and photodynamic therapy.
Prof. Katarina Svanberg

When Light Meets Nanoparticles

How Researchers Are Using Localized Surface Plasmons to Decode the Genetic Signatures of Bacteria and Uncover Antibiotic Resistance

Dr. Anne Kathrin Dietel and Dr. Stephan Kastner use the optical properties of nanoparticles to decode the genetic structures of bacteria.

The increasing spread of antibiotic resistance poses a global threat to human health, rendering our most important weapons against bacterial infections ineffective and making it more difficult to treat otherwise curable diseases. A research team at Leibniz IPHT has developed a new sensor based on localized surface plasmon resonance (LSPR) to monitor the spread of antibiotic resistance. This cheap and simple method allows the identification of genes that make bacteria immune to common antibiotics.

Researchers use light and nanoparticles to decode the genetic signatures of specific bacteria.

Anne-Kathrin Dietel, Florian Seier and Stephan Kastner from the Department of Nanobiophotonics exploit the special optical properties of tiny metal structures called nanoparticles. These nanoparticles interact with light in a special way known as localized surface plasmon resonance. In this phenomenon, the free electrons of the nanoparticles oscillate in unison with the incident light waves, creating a clearly visible color resonance.

Customized Nanoparticles

The researchers are developing metal nanoparticles with precisely defined optical properties. They combine these customized particles with biomolecules, such as DNA, to create functional nanostructures. Using this approach, they have developed an optical sensor that can detect bacterial resistance genes with a high degree of accuracy. In particular, they focused on the *bla*SHV gene, which makes bacteria resistant to a broad spectrum of antibiotics.

The *bla*SHV Gene: A Carrier of Resistance

"This antibiotic resistance gene can render beta-lactam antibiotics, one of the most commonly used classes of antibiotics, ineffective," explains Anne-Kathrin Dietel. "The fact that these genes are transmitted by horizontal gene transfer between different bacterial species significantly accelerates the spread of antibiotic resistance."

"A key advantage of our method is that it does not require the usual markers or dyes and can be extremely miniaturized," explains Stephan Kastner. "This aspect makes the test simpler, faster and cheaper." The researchers demonstrated the efficiency of the sensor by detecting

Localized Surface Plasmon Resonance (LSPR) device for measuring the binding kinetics of antibiotic resistance genes. Photonic methods are used to identify the smallest genetic changes.

even single point mutations of the *bla*SHV gene, which are crucial for selecting the appropriate resistance gene inhibitor during treatment.

The research results could facilitate the selection of the right treatment for infections in clinical diagnostics and improve the monitoring of the spread of antibiotic resistance.

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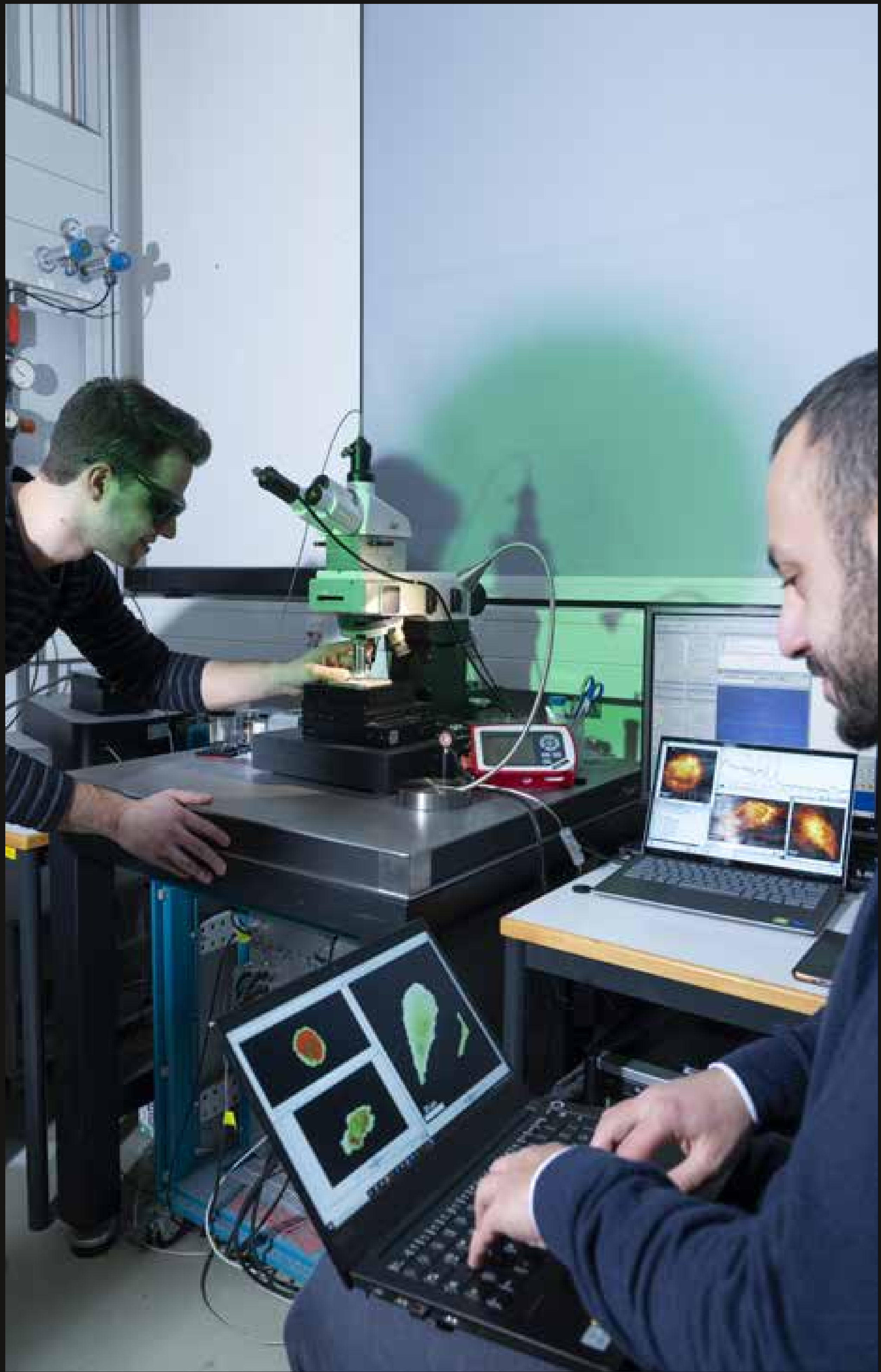
Publication:

S. Kastner, A.-K. Dietel, F. Seier, S. Ghosh, D. Weiß, O. Makarewicz, A. Csáki, W. Fritzsche, LSPR-Based Biosensing Enables the Detection of Antimicrobial Resistance Genes. Small 2023, 19, 2207953. https://doi.org/10.1002/smll.202207953



Max Naumann (left) and Rustam Guliev use spectroscopy to study macrophages and distinguish between different types of these immune cells: those that actively fight infections and those that support the healing process.

Guardians Of the Immune System

Spectroscopic Approach Allows Differentiation of Macrophages Without Disturbing Their Natural Environment

Macrophages are essential players in our immune system. They recognize, engulf and destroy pathogens and play a crucial role in repairing cell damage and healing tissue. A young research team at Leibniz IPHT is using Raman spectroscopy to differentiate different types of these immune cells non-invasively and without the use of labeling substances.

"We were particularly interested in better understanding the intracellular differences between pro-inflammatory M1 macrophages and pro-healing M2 macrophages," explains Max Naumann. "While the former actively fight infections, the latter support the healing process. The specific characterization of these cells can not only provide information on disease states, but also serve as an indicator of the course and severity of a disease. Max Naumann and Natalie Arend planned the study together with Prof. Ute Neugebauer in her department of Clinical Spectroscopic Diagnostics and carried out the measurements. Max Naumann is a PhD student at the Leibniz IPHT and the Center for Sepsis Control and Care at the University Hospital of Jena, while Natalie Arend has taken up a position in industry after successfully completing her doctorate.

Light As the Key to Cell Analysis

The team used Raman spectroscopy, a technique based on the scattering of light by molecules. This makes it possible to study cells in their natural state without damaging them. By analyzing macrophages derived from human blood monocytes, the researchers identified significant differences in the spectral signatures of different macrophage types.

Indicator of Disease

"The spectral signatures are crucial for distinguishing the states of macrophages. They give us a new understanding of their role in various disease processes," says Rustam Guliev, an expert in imaging and data analysis. The mathematician and computer scientist came to Jena from the Russian Academy of Sciences in Moscow via the European training network IMAGE-IN with Marie Skłodowska-Curie funding from the EU. The young researchers in the IMAGE-IN network are working on advanced imaging and data analysis methods for infection research.

From The Laboratory to the Clinic

The study shows that Raman imaging is a precise tool for rapid characterization of immune cell types. "Our results demonstrate the potential of Raman imaging as a powerful tool in immune cell research," summarizes Ute Neugebauer. However, before the method can be integrated into clinical practice, further research is needed, particularly with regard to its application in complex organ systems and perhaps later in living organisms.

Combining this advanced spectroscopic technique with biological knowledge could expand our understanding of the immune system and significantly advance the development of new treatment strategies for a variety of diseases, including inflammatory and autoimmune diseases and cancer.

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Publication:

Naumann, M.; Arend, N.; Guliev, R.R.; Kretzer, C.; Rubio, I.; Werz, O.; Neugebauer, U. Label-Free Characterization of Macrophage Polarization Using Raman Spectroscopy . Int. J. Mol. Sci. 2023, 24,824. https://doi.org/10.3390/ ijms24010824

Dr. Sindy Burgold-Voigt and Prof. Dr. Ralf Ehricht are developing innovative diagnostic techniques to gain more precise insights into infectious diseases and their spread.

On the Map of Invisible Vectors

How Bacteriophages Spread Resistance and Disease

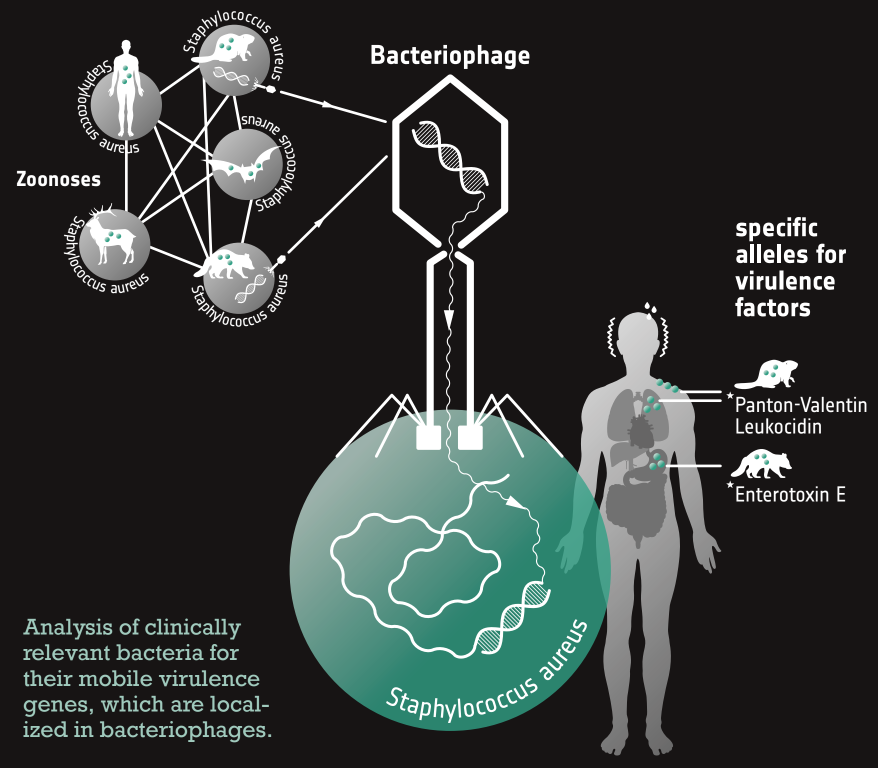
When the first patient in Germany was infected with a previously unknown virus in January 2020, Sindy Burgold-Voigt, Ralf Ehricht and their entire team were already in the lab researching a tool to combat the new infectious disease. As the coronavirus spread rapidly across the globe, the researchers worked with partners in Germany and China to develop a test in record time to help detect, understand, and better contain the emerging pandemic. Two months after the first infection was reported in Germany, Leibniz IPHT and the Weimar-based diagnostics company Senova were able to present an antibody test for the novel virus: ready to use and available on the market.

"It was an incredibly exciting experience to be right in the middle of it as a researcher," says Sindy Burgold-Voigt. She developed the test with the entire Optical Molecular Diagnostics and Systems Technology team and collaborators. They used microarray technology to test different antigens and select the most appropriate one. This method makes it possible to analyze the immune system's response to a large number of viruses simultaneously. Using a blood sample, the lateral flow test can determine which specific antibodies to the SARS-CoV-2 virus are present – an indicator of whether someone is currently infected or has already survived an infection. As the pandemic progressed, the microarray proved useful in demonstrating whether vaccination had successfully established immune protection.

"We did our research at a time when there was no vaccine against Covid-19," she says. "At first it was a challenge to find positive samples – later it became almost impossible to get samples without antibodies." Her work on the microarray-based test also became the subject of her doctoral thesis at Leibniz IPHT, which she successfully defended in December 2023.

In addition to her work on Covid-19, Sindy Burgold-Voigt focused on bacteriophages – viruses that infect bacteria. She studied how these phages transfer genes that make bacteria more resistant to antibiotics or increase their pathogenicity. By combining DNA microarray technology with state-of-the-art sequencing methods, she was able to achieve a comprehensive characterization of bacteria and their phages.

One focus of the research unit is to create an "epidemiological map" to track the spread of resistance and pathogen genes. "Of particular interest are the bacteriophages that serve as vectors for these genes. Identifying them will help us better understand the spread of resistant and pathogenic bacterial strains."



Analysis of clinically relevant bacteria for their mobile virulence genes, which are localized in bacteriophages.

Using the example of a Staphylococcus aureus strain isolated from a European badger, Sindy Burgold-Voigt demonstrated the adaptability of this bacterium to different host species. This strain carried a rare gene that made it particularly interesting. "Wild and domestic animals serve as a reservoir for bacteria and their genes. This is important for the transfer of antibiotic resistance and virulence genes by bacteriophages," she explains. Her research, which is in line with the WHO's One Health initiative, aims to deepen the understanding of the link between human and animal habitats and to minimize the resulting risks of disease transmission. "This knowledge is critical to controlling the spread of infectious diseases and developing new approaches to combat antimicrobial resistance."

To further advance this project, Sindy Burgold-Voigt is collaborating with researchers from the Microscopy and Biophysical Imaging departments at Leibniz IPHT. Together, they want to develop optical systems that enable efficient quality control in phage production. The approaches are part of the development of innovative molecular and biochemical assays for rapid diagnostics for the new Leibniz Center for Photonics in Infection Research. "Transmission electron microscopy is currently the only method for visualizing phages. We urgently need simpler methods for rapid quality control.

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Publication:

Burgold-Voigt, S.; Monecke, S.; Busch, A.; Bocklisch, H.; Braun, S.D.; Diezel, C.; Hotzel, H.; Liebler-Tenorio, E.M.; Müller, E.; Reinicke, M.; et al. Characterisation of a Staphylococcus aureus Isolate Carrying Phage-Borne Enterotoxin E from a European Badger (Meles meles). Pathogens 2023, 12, 704. https://doi.org/10.3390/pathogens12050704

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Dissertation:

Burgold-Voigt, Sindy. 2023, Optimized multiparameter methods for epidemiological studies and diagnostic purposes, Prof. Ehricht

Open Source: New Bioinformatics Tools for Molecular Analysis

Researchers from Leibniz IPHT and the InfectoGnostics Research Campus, together with other partners, have developed new bioinformatics tools whose open source code is now freely available.

The importance of bacteriophages, also known as phages, has increased significantly in recent years, particularly in the case of antibiotic-resistant pathogens. However, their impact on the microbiome in the environment and in the human body remains largely unexplored. The new software "What the Phage" enables the detection of phages, while "ConsensusPrime" supports the development of various molecular tests. The tools were developed by researchers at the University Hospital Jena, the start-up company nanozoo and the research department Optical Molecular Diagnostics and Systems Technology at Leibniz IPHT.

"What the Phage uses advanced algorithms and machine learning to detect phages and predict new variants from sequence data. Its modular, open-source structure allows for continuous improvement and an efficient workflow.

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Publication:

Mike Marquet et. al, GigaScience, Volume 11, giac110, 2022, https://doi.org/10.1093/gigascience/giac110

"ConsensusPrime" facilitates the design of oligonucleotides for molecular assays, such as PCR primers, making the process much faster and more efficient. The tool helps researchers design specific and robust primers for more accurate detection of different pathogen strains. PCR, or polymerase chain reaction, is considered the gold standard for molecular laboratory testing in infectious diseases.

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Publication:

Maximilian Collatz et. al, BioMedInformatics 2, no. 4: 637-642, 2022, https://doi.org/10.3390/biomedinformatics2040041

Spread of *Staphylococcus aureus* Strains Discovered in the Caribbean

Cultivation of *S. aureus* © Leibniz IPHT

The frequently (multi-)resistant bacterium *Staphylococcus (S.) aureus* causes the majority of hospital infections worldwide. Approximately 30 % of all people have nasal colonization. On the Caribbean islands of Trinidad, Tobago and Jamaica, the team from the Optical Molecular Diagnostics and Systems Technology research department successfully performed molecular characterization of *S. aureus* strains to gain an up-to-date understanding of its distribution and epidemiology. Using DNA sequencing and microarray-based assays, the researchers identified and characterized *S. aureus* and *S. argenteus* strains with respect to antibiotic resistance, virulence factors and toxin production. The results were published in the journal Antibiotics and presented at the 2023 Congress on Infectious Diseases and Tropical Medicine in Leipzig, Germany. The study was conducted as part of the InfectoGnostics research projects, which focus on the development of detection systems for *S. aureus* and are part of the Leibniz Center for Photonics in Infection Research. The InfectoGnostics Research Campus Jena, supported by the German Federal Ministry of Education and Research (BMBF) and the Free State of Thuringia, is driving innovation in the on-site diagnosis of infections.

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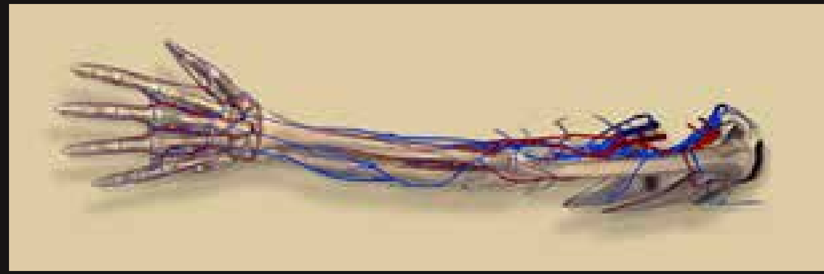
Publication:

Monecke S, Akpaka PE, Smith MR, Unakal CG, Thoms Rodriguez C-A, Ashraph K, Müller E, Braun SD, Diezel C, Reinicke M, et al. Clonal Complexes Distribution of *Staphylococcus aureus* Isolates from Clinical Samples from the Caribbean Islands, Antibiotics, 2023, 12(6):1050, https://doi.org/10.3390/antibiotics12061050

An Innovative Blood Vessel for Home Dialysis



The artificial blood vessel is designed to allow patients with chronic kidney failure to receive dialysis at home. © Adobe Stock

The Photonic Data Science research department and the Systems Integration Team are working with an international team to develop an artificial blood vessel for patients with chronic kidney disease. The EU project, TeleGraft, aims to enable these people to receive the dialysis treatment they need at home, without having to undergo regular surgical procedures.

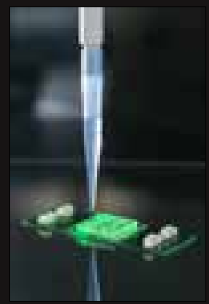
Dialysis is a life-saving treatment for people whose kidneys stop working properly. The blood is cleaned outside the body. This often requires access to the bloodstream through an artificial blood vessel called an arteriovenous graft. However, these grafts have a high failure rate - up to 70 % fail in the first year after implantation, mainly due to blood clots, scarring and infection.

The TeleGraft project aims to develop an "intelligent" arteriovenous graft that minimizes the risk of blood clots and infections through biomimetics – the imitation of nature's models – and drug delivery. It will also enable monitoring of blood flow and early detection of inflammation and infection.

Leibniz IPHT contributes its expertise in photonic data modeling to detect inflammation and infection using optical sensors and Raman spectroscopy. This technology enables continuous monitoring, allowing timely intervention to prevent serious complications. The collected data will be analyzed by AI-based learning models and presented on a dashboard that can be used intuitively by medical staff.

Eleven partners from seven European countries, including leading universities, research institutes and companies, are working together on the TeleGraft project, which has a budget of €5.3 million. The goal is to help people who do not have direct access to dialysis infrastructure.

Raman Spectroscopy in the Spotlight of Nature Photonics



International pioneers in the field of label-free optical imaging will give an overview of the application potential of these innovative methods for medical diagnostics in the renowned journal "Nature Photonics" in November 2023. Among the four authors is the scientific director of Leibniz IPHT, Prof. Dr. Jürgen Popp. Leibniz IPHT is one of the leading international research institutions in the field of optical health technologies. The focus is on optical imaging techniques for high-resolution imaging of tissue structures and chemical properties without external markers. The review is an important step in making label-free imaging more accessible to researchers and physicians and in promoting greater interdisciplinary collaboration.

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Publication:

Shaked, N. T., Boppart, S. A., Wang, L. V., Popp, J. Label-free biomedical optical imaging. Nat. Photon. 17, 1031–1041 (2023). https://doi.org/10.1038/s41566-023-01299-6

Prof. Dr. Ralf Ehricht and Prof. Dr. Christian Eggeling are pooling the expertise of their teams to investigate, together with other Leibniz partners, how antibiotics can be made more effective. © Sven Döring

New Strategies in the Race Against Resistant Bacteria

Leibniz IPHT and Partners Research Ways to Improve the Effectiveness of Antibiotics

Infections with antibiotic-resistant bacteria are on the rise worldwide and pose a major threat to healthcare systems. The World Health Organization (WHO) estimates that 1.27 million people die each year because antibiotics no longer work properly. To meet this challenge, research teams at Leibniz IPHT are joining forces with other Leibniz institutes to improve the effectiveness of antibacterial therapies.

For successful treatment with antibiotics, it is crucial that the drugs reach their target molecules inside the bacteria. However, the cell walls of bacteria are a difficult barrier for many antibiotics to overcome. In particular, infections caused by Gram-negative bacteria, which have a double-walled cell envelope, are becoming increasingly difficult to treat and are increasingly resistant to conventional antibiotics.

What structural changes in the cell membrane prevent active substances from passing through it, and how can this uptake be improved in order to optimize the effectiveness of antibiotics? These questions are the focus of the research project "Investigation of synergistic effects of membrane-active peptides and classical antibiotics" (AMPel), which will start in mid-2024. The Leibniz IPHT researchers are working together with teams from the Research Center Borstel, the Leibniz Lung Center (FZB), the Leibniz Institute of Virology (LIV) and the Friedrich-Alexander University Erlangen-Nuremberg. The goal is to understand the function of membrane-active peptides that can influence the cell membrane and thus contribute to the formation of pores.

Breaking Through Bacterial Defenses

The exact mechanism of action of these peptides and the development of resistance is not yet fully understood. However, their use in combination with classical antibiotics could significantly increase treatment efficiency and pave the way for innovative therapies. Over the next three years, an analysis platform will be developed to investigate the interaction between peptides and bacterial membranes using highly sensitive microscopic, electrophysiological and spectroscopic methods as well as modeling. The Leibniz Association is supporting the project with 950,000 euros.

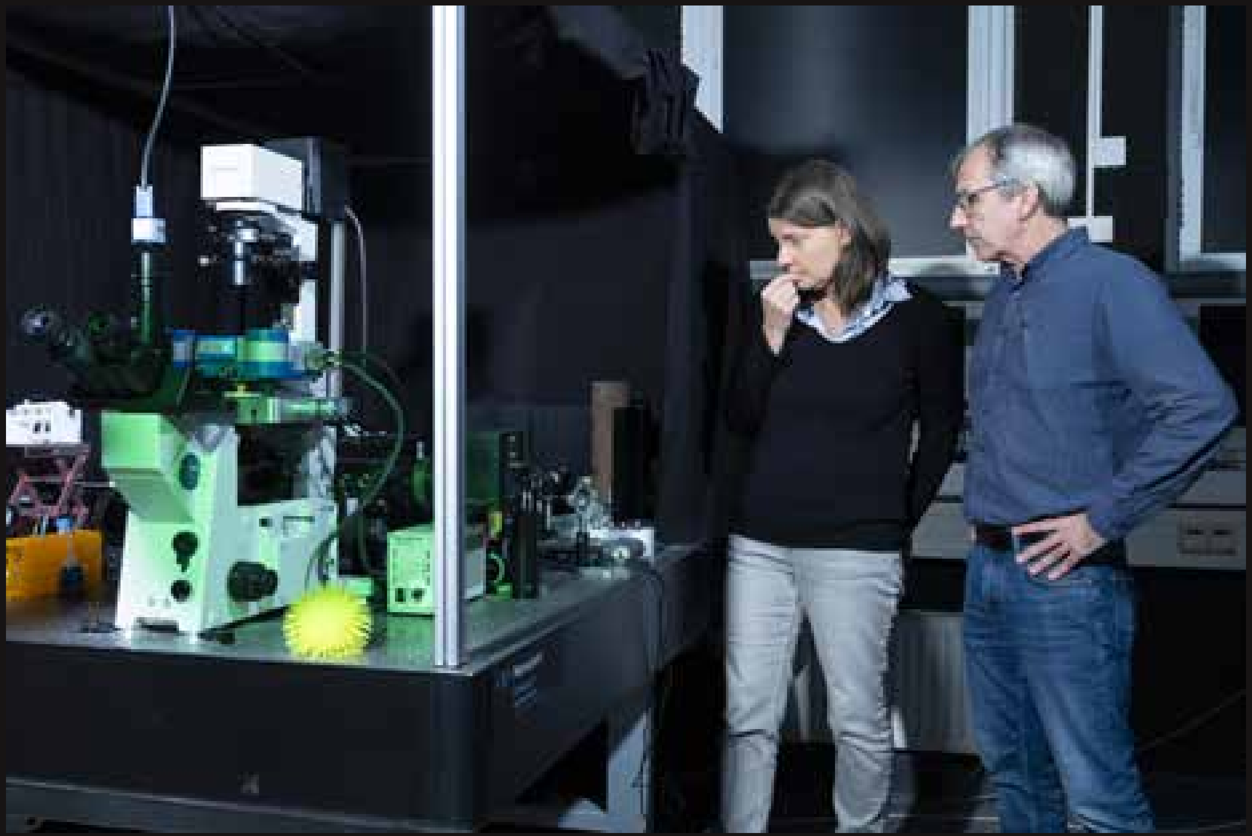
How Molecules Interact

"Our research focuses on how antimicrobial peptides (AMPs), cell-penetrating peptides (CPPs) and small antibiotic compounds interact," explain Christian Eggeling and Ralf Ehricht. AMPs, which are part of our immune system, attack the outer protective shells of microbes, while CPPs allow drugs to pass through the cell barrier and enter the cell directly. Antibiotics, on the other hand, fight bacteria by interfering with vital internal processes. The researchers want to understand how these three players work together synergistically to develop new and effective treatments against resistant bacteria. They are studying both the genetic and physical properties of the bacteria.

The potential of this strategy lies in the almost infinite possibilities offered by peptides. Each peptide is a "string of pearls" made up of up to 21 different natural amino acids. Even a chain of just 10 amino acids theoretically opens up 21^10, or over 10 trillion possible sequences. This immense variety of combinations represents an almost inexhaustible reservoir of potential new active ingredients, all of which are biocompatible because they are based on building blocks that occur in nature and have been tested in the course of evolution.

Microscopic Helpers

Researchers At the University of Jena Are Developing Nanoparticles That Deliver Drugs Directly to the Source of the Disease



Dr. Christiane Höppener and Prof. Dr. Volker Deckert analyze micelles with TERS and AFM. © Sven Döring

Drugs usually have side effects because they have to be administered in high doses to get the active ingredient to where it is needed. In the SFB Polytarget at the Friedrich Schiller University in Jena, Germany, researchers are looking for alternative carrier materials for the treatment of inflammatory diseases. They are developing tailor-made polymer nanoparticles in which drugs can be packaged and targeted to their site of action in the body.

Dr. Christiane Höppener and Prof. Dr. Volker Deckert, head of the Nanoscopy research department at Leibniz IPHT, are investigating which factors influence the effectiveness of chemical reactions within these nanoparticles. In particular, Höppener is investigating micelles, tiny structures made of amphiphilic block copolymers. These can self-assemble into a core-shell structure, in which the core is water-repellent and the shell is water-attracting – ideal for the transport and targeted release of drugs in the body.

"We want to understand which properties influence the chemical cross-linking reaction and how reversible cross-linking can be used for drug release," explains Christiane Höppener. Using TERS and atomic force microscopy (AFM), she analyzes the chemical and nanomechanical properties of the micelles with high spatial resolution.

The results provide deep insights into the reaction mechanisms on the nanoscale and illustrate how crucial it is to control the properties of the interface for the performance of the nanoparticles.

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Publication:

C. Höppener, J. K. Elter, F. H. Schacher, V. Deckert, Inside Block Copolymer Micelles—Tracing Interfacial Influences on Crosslinking Efficiency in Nanoscale Confined Spaces. Small 2023, 19, 2206451. https://doi.org/10.1002/smll.202206451

IR Biospectroscopy for Diagnostics and Medical Research

How Invisible Light Is Opening Up New Horizons in Healthcare Technology

PD. Dr. Christoph Krafft researches the use of Raman and infrared spectroscopy and imaging to characterize cells and tissue and to detect drugs and metabolites. © Sven Döring

By expanding its research activities in the field of infrared (IR) biospectroscopy, Leibniz IPHT underscores its pioneering role in the field of optical health technologies. The combination of technologies already established at the institute with IR spectroscopic methods opens up new horizons in the analysis and typing of body fluids, cells and tissues – without the need for markers.

Prof. Dr. Jürgen Popp, Scientific Director of Leibniz IPHT, explains the significance of this innovation: "The addition of IR biospectroscopy to our research portfolio is a milestone in our efforts to advance optical health technologies. With this method, we want to provide insights at the molecular level that were previously unimaginable".

IR biospectroscopy not only supplements Raman spectroscopy, which is already established at the institute, but the physical complementarity of the two methods now makes it possible to carry out tailor-made investigations at the highest level. IR biospectroscopy enables label-free quantitative analysis, which is invaluable for research and development in the fields of diagnostics, environmental monitoring and quality control.

With an additional budget of about 3.7 million Euros per year from a small strategic special budget (STB), the Leibniz IPHT is able to establish a specialized research department for IR biospectroscopy. The research department to be established will consist of two working groups: One will focus on research and implementation of new IR technologies, while the other will be dedicated to application-oriented basic research.

In addition, the institute is strengthening its expertise in photonic data science by establishing an additional working group focused on artificial intelligence (AI) in IR biospectroscopy. This approach includes the establishment of a FAIR data management and SmartLab system for IR data for AI-assisted evaluation of research data.

With the establishment of IR biospectroscopy for optical health technologies, Leibniz IPHT is tapping into a further unique selling point within the Leibniz Association and, thanks to invisible light, is strengthening its position in the international research landscape.

Light Into the Darkness of Cells

New Research Group for Field-Resolved Spectroscopy

Prof. Dr. Ioachim Pupeza in the laboratory of his research group for field-resolved spectroscopy © Sven Döring

Appointed

Ioachim Pupeza has been appointed W3 Professor at the University of Technology Kaiserslautern-Landau, Germany, where he will hold the Chair of Optical Quantum Metrology in conjunction with the working group of the same name at the Fraunhofer Institute for Industrial Mathematics (ITWM). He will also continue to lead his group at Leibniz IPHT. The three research groups are synergetically united in the Laboratory for Lightwave Metrology (lightwavelab.de).

Leibniz IPHT expands its research portfolio with a new working group in the field of field-resolved spectroscopic measurement methods under the leadership of Prof. Dr. Ioachim Pupeza.

At Leibniz IPHT, Ioachim Pupeza plans to further improve his technology and develop new applications, such as label-free cell detection and high-speed cell sorting. Field-resolved spectroscopy can make an important contribution to diagnostics and monitoring, especially in infection research. In his ERC Consolidator Grant-funded project "LIVE – Laser-Based Infrared Vibrational Electric-Field Fingerprinting", the scientist is working on the development of novel light sources and an innovative approach for the detection of optical electric fields. The aim is to exploit the full potential of vibrational spectroscopy in terms of sensitivity, specificity and throughput. Ioachim Pupeza is also involved in the Balance of the Microverse Cluster of Excellence and the Leibniz Center for Photonics in Infection Research.

A Ray of Hope in Brain Research: New Ultrathin Endomicroscope

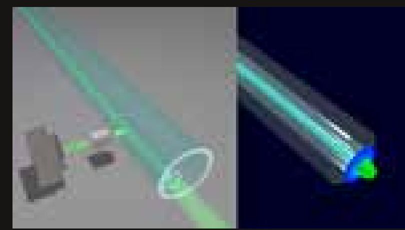
Fiberendoscope for Neuroscience © Tomáš Čižmár

Minimally invasive technologies are crucial for the study of neuronal activity and the interaction of nerve cells. A new hair-thin endomicroscope, developed jointly by Tomáš Čižmár's team at the Fiber Research and Technology research department and researchers at the Institute of Scientific Instruments of the Czech Academy of Sciences in Brno, Czech Republic, promises unprecedentedly gentle in-depth observations. It opens up the possibility of examining areas of the brain in detail and developing new strategies to combat neuronal diseases. The endoscope, which is only 110 micrometers thin, achieves sub-micrometer resolution (~800 nm) that is unaffected by the use of longer probes, allowing researchers to explore the brain at the subcellular level to a previously unattainable depth. As a result, deep brain structures and neuronal connectivity can be precisely studied. The use of an ultra-thin optical fiber as a probe enables high-resolution, distortion-free images, making it the least invasive technique for visualizing sensitive brain regions. This technology offers hope in the fight against neurological diseases such as autism, epilepsy, Alzheimer's and Parkinson's by providing deep insights into the functioning of the brain. The work was funded by the ERC grant LIFEGATE. The researchers have published their findings in the journal Nature Communications.

Publication:

M. Stiburek, P. Ondráčková, T. Tucková, S. Turtaev, M. Šiler, T. Pikálek, P. Jákl, A. Gomes, J. Krejčí, P. Kolbábková, H. Uhlířová & T. Čižmár, 110 µm thin endo-microscope for deep-brain *in-vivo* observations of neuronal connectivity, activity and blood flow dynamics, Nature Communications 14, 1897 (2023), https://doi.org/10.1038/s41467-023-36889-z

Observing Nanoparticles with Unprecedented Precision



Complex nanostructures in optical fibers ensure the formation of the new light mode (left) and the detection of even the smallest particles (right) © Leibniz IPHT

The team from the Fiber Photonics research department has succeeded in contributing to significant progress in deciphering tiny nano-objects: using special optical fibers, they identified a new optical mode that enables uniform illumination along the entire length of the fiber and determined the resolution limit of individual objects that could previously be measured with fibers. This lays the foundation for studying nanoparticles with unsurpassed precision.

Fiber-assisted nanoparticle tracking analysis (FaNTA) enables the precise observation and sizing of individual nano-objects trapped in microchannels of optical fibers. The researchers are thus contributing to the optimization of the FaNTA process for the detection of the smallest nano-objects. The findings can be used in a variety of ways, for example for the precise determination of rapidly diffusing particles in the life sciences or to study the mechanisms of action of drugs. Potential applications extend to fields such as pharmaceuticals, bioanalytics, materials science and the semiconductor industry, opening up previously inaccessible nanoscale processes and improving the monitoring of nanoparticles and drug quality. The research results have been published in the journals OPTICA and Nature Communications.

Publications:

F. Gui, S. Jiang, T. Wieduwilt, R. Scheibinger, J. Hofmann, R. Foerster, M. A. Schmidt, Light strands: exploring flat-field modes in optofluidic fibers for tracking single nano-objects, OPTICA, Vol. 10, No. 6, June 2023, https://doi.org/10.1364/OPTICA.486144

T. Wieduwilt, R. Förster, M. Nissen, J. Kobelke, M. A. Schmidt, Characterization of diffusing sub-10 nm nano-objects using single anti-resonant element optical fibers, Nature Communications, 14, 3247 (2023), https://doi.org/10.1038/s41467-023-39021-3

Photonic Technologies for a Green Future

How Researchers Are Developing Innovative Processes for Clean Water

Dr. Dana Cialla-May heads the Raman and IR Spectroscopic Analysis group and researches methods for environmental analysis, such as clean water.

© Sven Döring

Innovative Sensors for Clean Water

Together with European research institutions and companies, Leibniz IPHT is working on the European research project IBAIA to develop innovative sensor modules to improve the monitoring of water quality. The sensors are based on photonic and electrochemical technologies and are designed to measure water quality and detect microplastics, salinity, organic chemicals, nutrient salts and heavy metals in water in real time.

Prof. Dr. Thomas Bocklitz, head of the Photonic Data Science research department, is contributing his expertise in photonic data acquisition, processing and fusion to optimize the sensor technology. The modules to be combined in the IBAIA system include photonic sensors that can detect microplastics and salinity in the visible to near-infrared spectrum, as well as mid-infrared sensors specifically designed to detect organic chemicals.

The EU is funding the project, coordinated by the French National Center for Scientific Research (CNRS), with 4.7 million euros. The IBAIA project brings together experts in materials science, microfluidics, data processing and integration technology. Its goal is to make water quality monitoring more efficient, cost-effective and environmentally friendly. Finally, the IBAIA system will be tested under real conditions.

Spectroscopic Detection of Pollutants in Water

© Leibniz-IPHT

In the MIKA project, researchers from Leibniz IPHT, the Friedrich Schiller University Jena and other regional partners are developing a new method for the detection of micropollutants in water. Although these contaminants, including drug residues, hormones and chemicals, are present in low concentrations, they have the potential to significantly affect water quality and aquatic life.

MIKA uses a combination of plasmonic multiplex assays and fingerprint analysis. It uses tiny noble metal particles coated with specific DNA strands called aptamers. These aptamers can selectively recognize and bind target molecules such as carbamazepine, diclofenac or benzotriazole. This binding leads to a spectral modulation of the optical properties of the nanoparticle sensor spots. This so-called spectral shift is detected by an innovative detector unit using imaging spectroscopy in the visible spectrum.

Surface-enhanced Raman spectroscopy (SERS) increases the accuracy of detection by capturing the specific "fingerprints" of the molecules. The combination of the two methods enables rapid, label-free analysis of water samples directly in the field, providing comprehensive information about the contaminants present. "Thanks to the use of metallic nanostructures in both spectroscopic methods, we achieve high sensitivity in the detection of extremely low concentrations of pollutants," explains Dana Cialla-May, head of the Raman and IR Spectroscopic Analysis working group.

MIKA is part of the Thuringian Water Innovation Cluster (ThWIC).

Nature as a Role Model

Thuringian Research Prize for Fundamental Findings for Artificial Photosynthesis

Awarded: Prof. Dr. Benjamin Dietzek-Ivanšić and Dr. Linda Zedler during their research work © Leibniz IPHT

Making the previously invisible visible – a research team from Friedrich Schiller University Jena and Leibniz IPHT is making this a reality: Innovative methods of time-resolved and in operando absorption spectroscopy make it possible to observe the processes of photocatalysis with unprecedented resolution and accuracy. Prof. Dr. Benjamin Dietzek-Ivanšić, Dr. Linda Zedler and Dr. Carolin Müller were awarded the 25,000 euro Thuringian Research Prize in the Applied Research category on April 19, 2023.

Their research focuses on the development of innovative processes for the environmentally friendly production and storage of renewable energy. Photocatalysts inspired by nature play a central role in this by absorbing light energy and converting it into chemical energy, similar to how plants do photosynthesis.

To investigate these processes, the team has developed two experimental methods: Time-resolved absorption spectroelectrochemistry combines electrochemistry and optical spectroscopy to make the molecules accessible for analysis in a stable state. At the same time, in operando absorption spectroscopy enables the observation of the chemically unstable photocatalysts during the reaction, allowing precise tracking of the short-lived intermediates and the progress of photocatalytic reactions.

The Thuringian Research Award recognizes the team's methodological innovations, which were made possible by years of research and close collaboration. The optical measurement methods help to identify new ways of tackling global challenges in the field of renewable energies. This enables, for example, a deeper understanding of the mechanisms of water splitting by sunlight, which can make a significant contribution to the development of solar energy as a future energy source.

Leibniz IPHT is actively involved in the DFG-funded Collaborative Research Center / Transregio CataLight, in which light-driven molecular catalysts in hierarchically structured materials are being investigated.

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Further information at
www.catalight.uni-jena.de

Appointed

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© Sven Döring

Prof. Dr. Carolin Müller has been appointed Junior Professor for the Theory of Electronically Excited States at the Department of Chemistry and Pharmacy at Friedrich-Alexander-Universität Erlangen-Nürnberg since November 2023.

Potential for Improved Solar Cells

Research Team Develops New Process for the Production of Customized Semiconductor Thin Films

Dr. Sarah Jasmin Finkelmeyer and PD Dr. habil Martin Presselt at the setup, which can be used to produce thin films with specific properties that are used, for example, in the production of improved flexible solar cells. © Katrin Uhlig

A German-American research team led by Leibniz IPHT has developed a new process for the automated production of semiconductor thin films with customized electronic properties. These thin films open up new possibilities for the development of state-of-the-art optoelectronic components for use in areas such as photovoltaics, sensor technology and microelectronics.

The process is based on the Rolling Transferred Langmuir Layer technique, a further development of the Langmuir-Blodgett technique. In this process, organic semiconductor molecules are transferred to a solid substrate at air-water interfaces. PD Dr. habil. Martin Presselt, head of the Organic Thin Films and Interfaces working group at Leibniz IPHT, explains: "Our process enables the automated production of crystalline films with minimal surface defects. Both monolayers and multiple thin-film layers with individual properties can be produced precisely, uniformly and scalably with high quality."

Two parameters are crucial for the production of these tailor-made films: the packing density of the molecules within a layer and the number of overlapping molecule layers.

Dr. Sarah Jasmin Finkelmeyer, co-developer of the method, points out: "By systematically varying these parameters, we can reproducibly create semiconducting thin films with targeted interactions between molecules and specific energy layers."

The technological approach developed by the researchers lays the foundation for the fabrication of novel (opto-) electronic components with optimized properties based on thin films. For example, organic photovoltaic modules that efficiently generate electrical energy from sunlight can be further developed, as can thin films that convert sunlight into chemical energy.

The scientists published their findings in the journal Advanced Materials.

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Publication:

S. J. Finkelmeyer, E. J. Askins, J. Eichhorn, S. Ghosh, C. Siegmund, E. Täuscher, A. Dellith, M. L. Hupfer, J. Dellith, U. Ritter, J. Strzalka, K. Glusac, F. H. Schacher, M. Presselt, Tailoring the weight of surface and intralayer edge states to control LUMO energies, Advanced Materials (2023), https://doi.org/10.1002/adma.202305006

Highlights

Microscopy for All

Dr. Benedict Diederich led a summer school in Nigeria © Leibniz IPHT

Benedict Diederich wants to make microscopes a standard tool for everyone and promote scientific exchange not only for researchers in well-equipped institutes. With this vision in mind, he and his team have developed an open-source microscopy toolbox and founded the startup openUC2 from Leibniz IPHT. Supported by the Chan-Zuckerberg Initiative, the head of the Open-Source Instrumentation Group is committed to making microscopy technologies available in underprivileged regions of the world. During a summer school at Yobe University in Nigeria, he and 40 researchers built brightfield microscopes using the openUC2 kit and taught modern imaging techniques. "The collaboration was a great experience," says Diederich, who is eager to continue. "There is enormous power in sharing knowledge where resources are limited but curiosity and enthusiasm are boundless."

Light Meets Matter: DFG Strengthens Jena

Experiments on non-linear optical effects © Jens Meyer / Uni Jena

The German Research Foundation (Deutsche Forschungsgemeinschaft - DFG) is extending funding for the Collaborative Research Center (CRC) "NOA - Nonlinear Optics on Atomic Scales" at Friedrich Schiller University Jena, in which Leibniz IPHT is also conducting research with other interdisciplinary partners, for a further four years from July 1, 2023. Around eleven million euros will be used to continue research on light-matter interactions, especially on atomic and nanostructures. The aim is to explore non-linear optical processes down to the atomic level and to develop new applications. Possibilities range from nanolasers to real-time observation of chemical reactions between individual molecules, which would not be possible with linear optical systems.

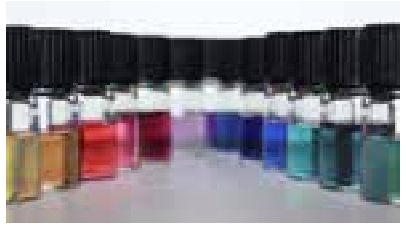
More information about the SFB *NOA*:
www.noa.uni-jena.de

Collaborative Creativity

Dr. Linda Zedler and Dr. Tobias Meyer-Zedler © Katrin Uhlig

The innovation projects at Leibniz IPHT fund joint project proposals from at least two research departments or junior research groups with a total of 50,000 euros each year. This enables professional exchange, cooperative collaboration and the generation of new research findings across the boundaries of research departments, regardless of third-party funding. In 2023, two projects were funded: "Ultrafast transient two-photon-absorption spectroscopy and microscopy" by Dr. Linda Zedler and Dr. Tobias Meyer-Zedler and "Fluorescence correlation spectroscopy meets meta-fibers - an innovative platform for characterizing single nano-objects" by Prof. Dr. Markus Schmidt and Prof. Dr. Christian Eggeling, each with 25,000 euros in support from Leibniz IPHT.

Nano World Visits Jena



Variety of colors of plasmonic nanoparticles © Stefanie Hentschel

From May 11 to 13, 2023, Leibniz IPHT hosted the Molecular Plasmonics conference, which brought together over 110 nanotechnology experts from all over the world in Jena. The conference offered lectures and poster sessions that provided an insight into current research work in the field of metallic nanostructures, which are particularly suitable for bioanalytics. A varied supporting program with historical insights into the life of Otto Schott and excursions into Jena's nature provided space for an exchange of ideas and impulses as well as in-depth discussions. Molecular Plasmonics 2023 was organized by Prof. Dr. Wolfgang Fritzsche, Head of the Nanobiophotonics research department and Prof. Dr. Thomas Pertsch from the University of Jena in collaboration with the Collaborative Research Centre "NOA – Nonlinear Optics down to Atomic Scales".

Connecting Jena and Innsbruck

Researchers from Leibniz IPHT visit Innsbruck © Leibniz IPHT

Prof. Dr. Jürgen Popp and Prof. Dr. Christian Huck, Head of the Institute of Analytical Chemistry and Radiochemistry at the University of Innsbruck, have intensified their collaboration in order to establish spectroscopic and imaging technologies of Leibniz IPHT at the University of Innsbruck and to advance the joint research field of biophotonics, in particular NIR / IR and Raman spectroscopy. During Jürgen Popp's guest professorship, many synergies arose with Christian Huck, including a joint book project on the topic of "Novel Vibrational Spectroscopy Empowered by Artificial Intelligence". Scientific exchange is also promoted through joint workshops. For example, a group of researchers from Leibniz IPHT visited the University of Innsbruck to discuss imaging methods for investigating tissue and metabolic processes.

From Addis Ababa to Jena

Menbere Mekonnen Researches Sensors for Environmental and Food Safety

Menbere Mekonnen synthesizing nanoparticles © Lavinia Meier-Ewert

As a research fellow from Ethiopia, Dr. Menbere Mekonnen brings his expertise to Leibniz IPHT to develop sensors for food safety and environmental issues.

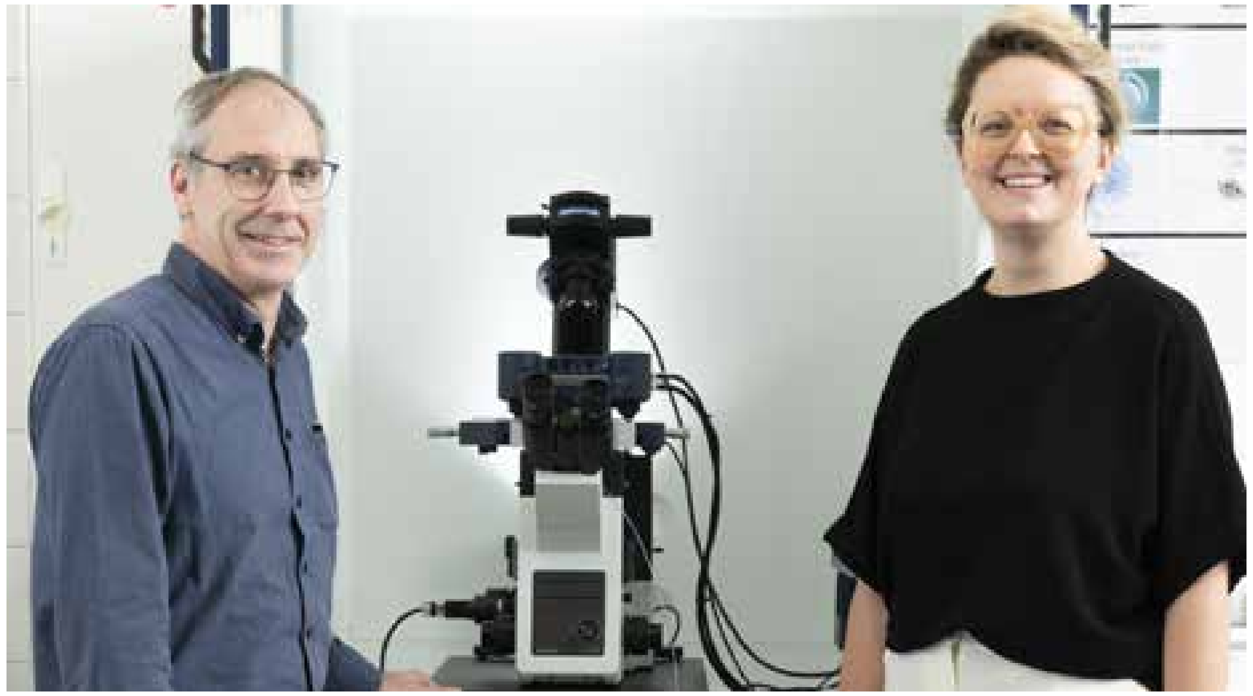
His research focuses on improving the stability and functionality of gold and silver nanoparticles through an ultra-thin silica shell. He strives to increase the applicability of these nanoparticles in the detection of medically and environmentally relevant molecules, in particular by obtaining the effect of localized surface plasmon resonance (LSPR).

Menbere Mekonnen is an Associate Professor at Addis Ababa Science and Technology University and holds a PhD from the National Taiwan University of Science & Technology. His interest in research at Leibniz IPHT was aroused during his participation in the International Conference on Raman Spectroscopy in Korea. Having successfully applied for the Georg Forster Research Fellowship of the Alexander von Humboldt Foundation, he is now working for two years in the Nanobiophotonics research department under the supervision of Prof. Dr. Wolfgang Fritzsche.

After his return to Ethiopia, Menbere Mekonnen plans to help establish the Nanotechnology Center of Excellence in order to transfer knowledge, train young researchers and tackle urgent local problems. The cooperation between the scientist and Leibniz IPHT opens up the possibility of expanding the field of bioanalytics in Ethiopia through the use of metallic nanostructures with a plasmonic effect. In the long term, Leibniz IPHT plans to promote the exchange of students, strengthen research capacities in Ethiopia and develop customized solutions for local challenges.

A Forward-Looking Signal for the Region

Research Landscape in Jena Strengthened by Multi-Million Investment



PD Dr. med. Stefanie Deinhardt-Emmer from the University Hospital in Jena and Prof. Dr. Volker Deckert from Leibniz IPHT and FSU and their teams are involved in numerous joint research projects (see page 41) – including this newly acquired microscope. It combines fluorescence microscopy with a special atomic force microscope (AFM), which can be used, among other things, for the targeted manipulation of nanoparticles and the labeling of individual cells. The researchers plan to use this technique primarily to study cell infections in detail, an approach that is important for understanding and researching diseases. The new microscope was financed by EFRE funds in 2023. © Sven Döring

An initiative between the Friedrich Schiller University Jena (FSU) and Leibniz IPHT to expand research-related infrastructure by 2023 has succeeded in further intensifying cooperation for the sustainable expansion of joint research priorities.

With the support of the Free State of Thuringia, research-related infrastructure was acquired with funds from the European Regional Development Fund (Europäischer Fonds für regionale Entwicklung – EFRE) amounting to more than ten million euros. This infrastructure will be used jointly by FSU and Leibniz IPHT. This is also intended to intensify cooperation between the jointly appointed professors. The focus will be on the development of biophotonic and microscopic processes for applications in medicine and pharmacy as well as in the life and environmental sciences. The implementation took place from March to October 2023, including the procurement and installation of various devices, such as IT infrastructure, spectroscopic and microscopic instruments, a 3D nanoprinter, as well as devices for the expansion of reference methods for optical molecular diagnostics and freeze-drying systems for samples. Institute director Prof. Dr. Jürgen Popp praised the rapid implementation of the project, which was made possible by the committed cooperation of the FSU administration, the purchasing department of Leibniz IPHT and the Thuringian Ministry for Economy, Science and Digital Society. The highly visible sign at the main entrance of the institute that reads "EFRE moves Thuringia" is a symbol of the progress that the partnership between FSU and Leibniz-IPHT is driving in the region. The investments will not only advance scientific knowledge, but also promote the development of innovative technologies and the training of talented researchers.

From Jena to Hollywood? Gold for Green Screen Technology

Prof. Dr. Rainer Heintzmann developed an award-winning method for better film images © Jens Dahlems/PATON-PTH

Prof. Dr. Rainer Heintzmann from Leibniz IPHT and Ryan Ketterer from the Friedrich Schiller University Jena have been awarded the gold medal at the international inventors' fair iENA in Nuremberg for an innovative optical method to improve green screen technology. Their method, which was developed in the Microscopy research department, makes it possible to create green-screen videos without reflections and semi-transparent objects, which often have to be laboriously removed in post-production.

Green-screen technology is a standard tool for showing people or objects against changing backgrounds – from weather reports to scenes from fantasy worlds. However, it is not uncommon for artifacts to appear, such as a greenish tint to hair or the temporary disappearance of fine details, that break the illusion. Even in fully produced blockbuster movies, a thin strand of hair may disappear and reappear in some frames due to the green-screen technique.

Heintzmann and Ketterer's approach, a confocal masking technique, captures these problem areas with high precision, resulting in higher quality and more accurate green screen images. This patent-pending method opens new possibilities for the film and television industry as well as for camera technology providers.

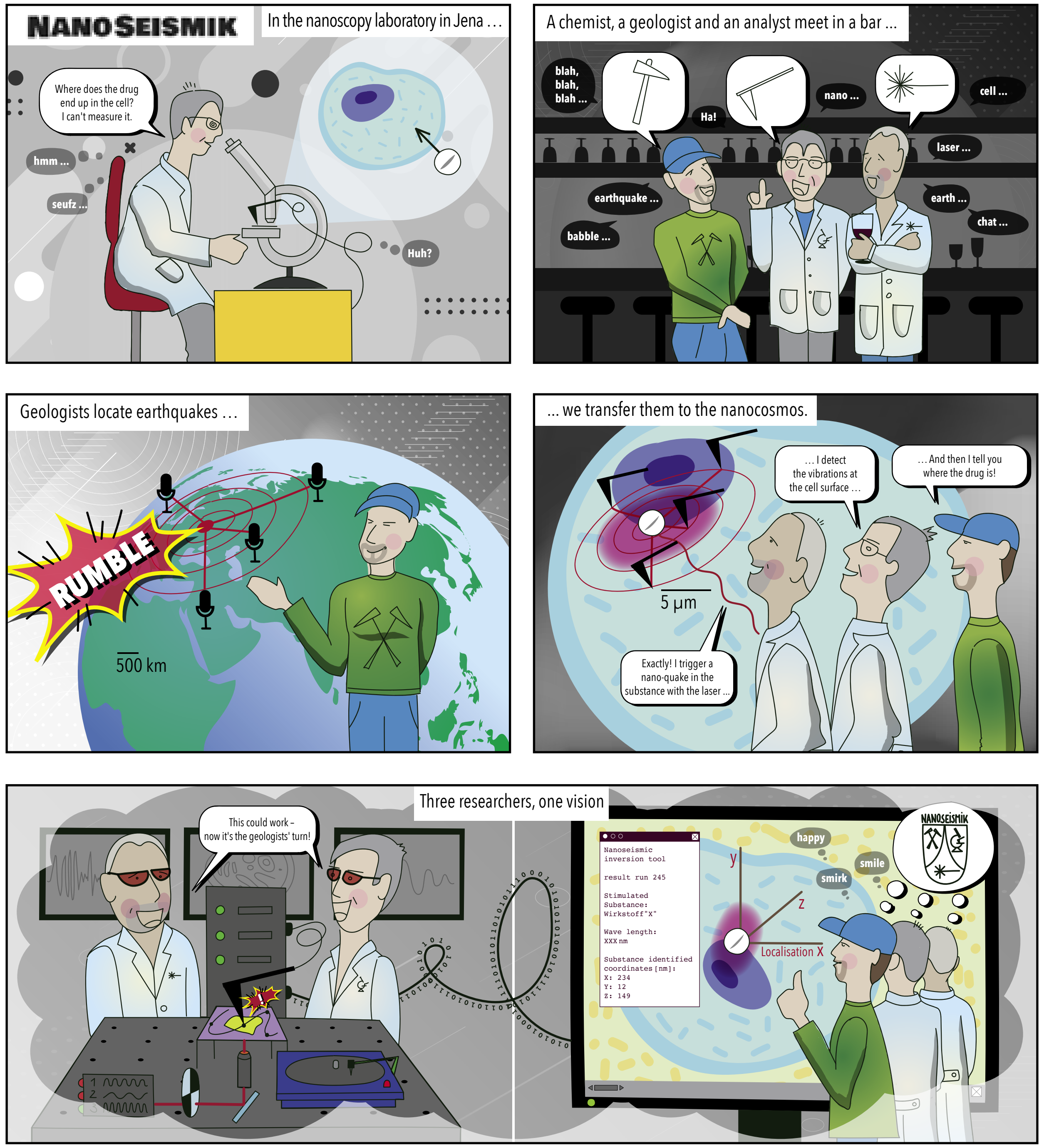
As an expert in modern microscopy methods and computer-aided image reconstruction, Rainer Heintzmann develops and optimizes light microscopy techniques at Leibniz IPHT to visualize biomedical processes down to the smallest detail. These techniques provide new insights into the structure and function of cells, thus expanding our understanding of fundamental life processes.

Earthquake in the Living Cell

Research trio Boris Mizaikoff, Hagen and Volker Deckert © Leibniz IPHT

The idea with which Prof. Dr. Volker Deckert hopes to gain insights into the molecular structure of living cells sounds audacious: the nanoscopy expert wants to trigger miniature earthquakes in living cells. The Carl Zeiss Foundation considers the project, which is coordinated by Jena University, to be radically new and particularly daring, and is supporting Deckert's interdisciplinary research team with 750,000 euros in the "CZS Wildcard" program to test the feasibility of their idea. Deckert and his team plan to fire pulses of infrared light into the cell to induce molecule-specific nano-quakes without damaging the cell. By measuring these earthquake waves, the researchers plan to use mathematical methods to create a 3D analysis of the inside of the cell, just like a "real" earthquake.

"If all goes well, we could use a cell sample to study where a virus docks inside the cell.



For the "Wildcard" grant from the Carl Zeiss Foundation, the three researchers explained their project in a comic – realized by Katrin Uhlig from Leibniz IPHT. © Katrin Uhlig

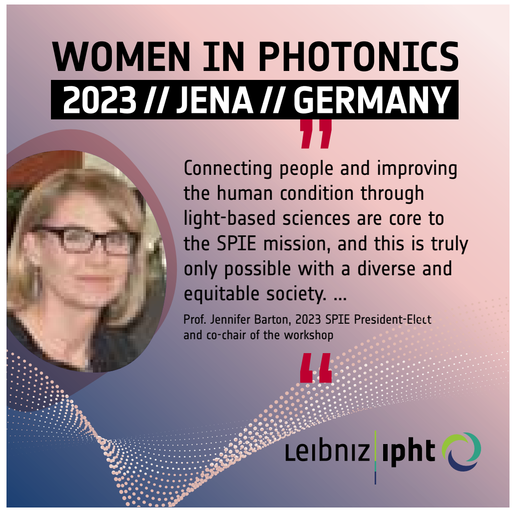
Or it would be possible to determine exactly where a drug unfolds its effect," says Volker Deckert, professor at FSU Jena and head of the Nanoscopy research department at Leibniz IPHT.

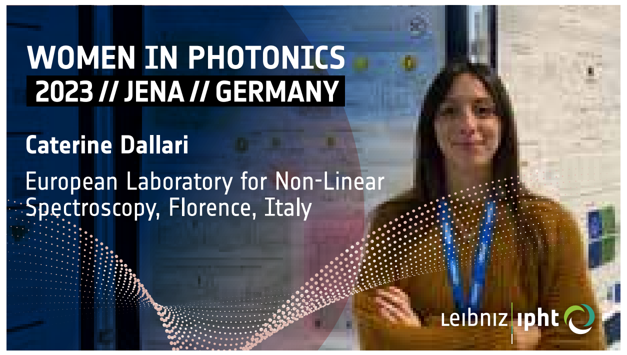
The creative approach, which the three researchers presented in the form of a comic strip, is based on an interdisciplinary vision par excellence: Deckert hatched it together with his brother, Dr. Hagen Deckert, a geologist at the University of Mainz. The third member of the team is the chemist Prof. Dr. Boris Mizaikoff from the University of Ulm.

They now have two years to test whether their idea can be used to create precise 3D analyses of the inside of cells. If it works, this could provide detailed information about disease-causing processes at the molecular level and thus enable advances in the treatment of diseases in the future.

Women in Photonics

How Leibniz IPHT Promotes Women in Science





With strategic measures and innovative programs, Leibniz IPHT establishes effective tools for career advancement and creates an inspiring environment for female researchers who want to explore new horizons in photonics.

"At Leibniz IPHT, we are passionate about pursuing the goal of equal opportunities not only as a formal principle, but as a lived reality," emphasizes Prof. Dr. Jürgen Popp, scientific director of the institute. "For us, the implementation of gender equality guidelines is not a compulsory exercise, but a central component of the institute's strategy. From workshops that raise awareness of gender equality to targeted mentoring and programs that facilitate the transition to management positions, the institute spans an arc that strengthens and makes visible women in science.

A new and central component of these efforts is the "Women4Photonics" seed fund program, which will support young scientists starting in 2024. Designed by Leibniz IPHT, the program's three complementary lines of funding are aimed specifically at female postdocs to help them acquire third-party funding, establish their own research groups and host visiting scientists. The special feature of this program is its holistic support, ranging from start-up projects to professional writing and leadership training to financial support.

Women4Photonics Support Program

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SEED FUND

For postdocs up to 3 years after PhD. Funds one-year projects in preparation for external funding applications with up to 12,000 euros for support staff, materials, and travel expenses. Includes professional writing and management training.

SEED FUND+

For female postdocs up to 6 years after their PhD, supports the establishment of their own junior research groups. Projects may be funded up to 25,000 for personnel and equipment, with the goal of applying for external funding within two years. Also offers writing and leadership training.

SEED FUND++

Supports female guest researchers up to 6 years after their doctorate in the preparation of applications for external funding with and at the Leibniz IPHT to promote the internationalization of research. Grants a monthly stipend of 1,500 euros for a stay at the Leibniz IPHT of up to three months, including a travel allowance and access to writing and leadership training.

The "Women in Photonics" event series, which last took place in December 2023, is another flagship project of Leibniz IPHT. It provides a platform for young female researchers to present their work, network and learn from the experiences of established female scientists and company representatives. The fourth edition of this international career workshop was extremely successful and provided a stimulating platform for 73 participants from more than 18 countries on 5 continents. Meetings with inspiring personalities such as Jennifer Barton, President of SPIE, and Ulrike Fuchs from asphericon GmbH opened new horizons and motivated the participants to find their own way in photonics.

Leibniz IPHT's commitment shows how important it is to establish a culture that values diversity and promotes equality. By specifically promoting female scientists, the institute is helping to change the landscape of optical technologies in the long term. The aim is not just to promote individual female researchers, but to create an environment in which everyone can develop their potential equally.

Leibniz IPHT's initiatives are designed to help lay the foundations for a more equal future in science through targeted funding and an inclusive research culture. Diversity and equal opportunities are not just goals for the institute, but an ongoing journey – a journey towards a fairer and more diverse scientific community.

Research and Family Life

Leibniz IPHT Sets New Standards in Work-Life Balance

Family friendliness is a top priority at Leibniz IPHT: Research group leader Dr. Benedict Diederich and his son experimenting together in front of the institute. © Sven Döring

Family friendliness is firmly anchored at Leibniz IPHT: the balance between work and family is a reality for our more than 450 employees. With a comprehensive range of measures and an open organizational culture, the institute has created an atmosphere in which employees can reconcile professional and personal demands. The goal is to give employees the opportunity to find fulfillment in their work while also being able to meet their family obligations.

Andrea Borowsky, Prof. Dr. Ute Neugebauer and Ute Hoffman at the 25th award ceremony on June 13, 2023 in Berlin

> I think it is a very important step that Leibniz IPHT is now a member of the berufundfamilie network. The individual advice, the training and above all the opportunity to share the experience of other certificate holders is a great chance to find suitable solutions for our institute.
>
> Prof. Dr. Ute Neugebauer, Deputy Scientific Director at Leibniz IPHT

Representatives of Leibniz IPHT received the audit berufundfamilie certificate in Berlin on June 13, 2023. Prof. Dr. Ute Neugebauer, deputy scientific director, Ute Hoffmann, head of the human resources team, and Andrea Borowsky, head of communications with a focus on internal communications, accepted the award. The significance of the certificate lies not only in the recognition of the work already done, but also in the ongoing commitment to promoting the compatibility of work, family and private life.

The berufundfamilie audit is a strategic instrument with which Leibniz IPHT implements a sustainable human resources policy that takes into account family and life phases. The cooperation with berufundfamilie Service GmbH gives the institute access to a broad network of companies and institutions that are also committed to these goals. The audit is conducted in a multi-stage process that ensures that measures to improve compatibility are regularly reviewed and adjusted.

An important step in the audit process was the identification of opportunities for improvement through a facilitated strategy workshop attended by representatives from all departments. This participatory approach enabled the formulation of concrete objectives to initiate new measures, develop existing approaches and maintain good standards. Particular attention is paid to supporting new employees and continuously raising managers' awareness of the importance of a family-friendly work environment.

Certification by the berufundfamilie audit underscores Leibniz IPHT's commitment to creating a work culture that focuses on the needs of employees. By offering flexible working hours, support with childcare and care for family members, and open communication about professional and private matters, the institute contributes to a work culture that provides room for personal development and family responsibility.

Leibniz IPHT regards the compatibility of work, family and private life as a key aspect of being an attractive employer. After the scientific excellence of our institute, the family-friendly environment is one of the most important arguments in favor of Leibniz IPHT.

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Further information on the *certificate*

Awards and Honors 2023


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Honorary Doctorate from the University at Albany

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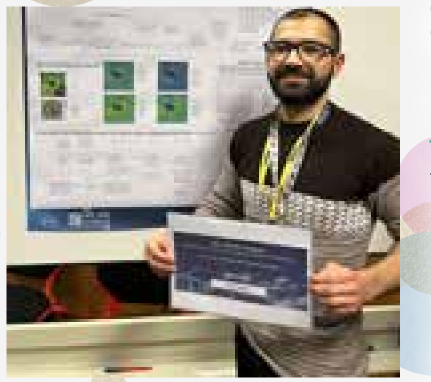
to **Prof. Dr. Jürgen Popp** for his merits and pioneering research achievements in the field of optical health technologies and biophotonics for improved diagnostics and therapy.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Poster Prices of the Winter Seminar "Biophysical Chemistry, Molecular Biology and Cybernetics of Cell Functions"

–

to **Sobhi Saeed** and **Haoran Wang** from the Microscopy research department. Sobhi Saeed is researching the use of small detectors in ptychography arrangements, a special type of microscopic imaging. Haoran Wang impressed the jury with his work on a high-resolution microscope based on the openUC2 optics kit with structured illumination (SIM) and image scanning (ISM) processes.

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ANAKON Poster Prices

–

to **Julian Plitzko** and **Markus Salbreiter** from the Spectroscopy / Imaging research department. Julian Plitzko is researching biophotonic methods for the controlled release of drugs from polymer-based nanoparticles in the body in order to target their effect on diseased tissue. Markus Salbreiter characterizes bacteria of the species Bacillus and Clostridium using Raman spectroscopic methods in order to help identify their antibiotic resistance.


© Katrin Uhlig

Klaus Tschira Boost Funds

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a grant from the German Scholars Organization e. V. (GSO) and the Klaus Tschira Foundation was awarded to **Dr. Bennet Fischer**, which will allow him to intensify his research in the field of 3D nanoprinting of novel optical lenses that are applied to the end surfaces of glass fibers. His goal is to develop new designs of these nanostructures or metal lenses that enable optical signal processing directly during light propagation.


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Poster Price of the International Conference on Advanced Vibrational Spectroscopy

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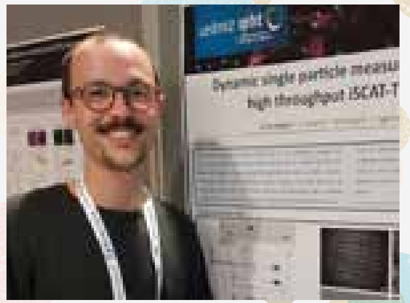
to **Dr. Timea Frosch** from the Spectroscopy / Imaging research department. Her research work shows how the monitoring of drugs, for example for the individualized treatment of diseases or for improved quality control, can be made even more successful with the help of Raman spectroscopic approaches.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Poster Price at the Conference of the European Biophysical Society Association

–

to **Giovanni De Angelis** from the Biophysical Imaging research department. His presented setup combines interferometric scattering microscopy with internal total reflection fluorescence microscopy to generate images of single molecules with uniform contrast and high localization accuracy over the entire field of view.


© Thomas Müller

Pitch Winners at the Investor Days Thuringia and at HANNOVER MESSE

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in 2023 are **openUC2** with their open-source optical construction kit, twice in fact: at the 8th Thuringian Investor Days, the start-up won a pitch award from 20 participating companies for the presentation of its business idea. The openUC2 team was also recognized at HANNOVER MESSE for the best pitch of the day on the Industrial Start-up Stage.


© Science4Life

The Winner of the Science4Life e. V. Venture Cup

–

is the start-up **DeepEn** in all three rounds of the competition. With their cutting-edge endoscopy technology developed at the institute, the spin-off enables better examination of sensitive brain structures and thus contributes to future research into the causes of diseases such as Parkinson's or Alzheimer's.


© Prof.-Glen-Jackson_SciX-Conference

Charles Mann Award

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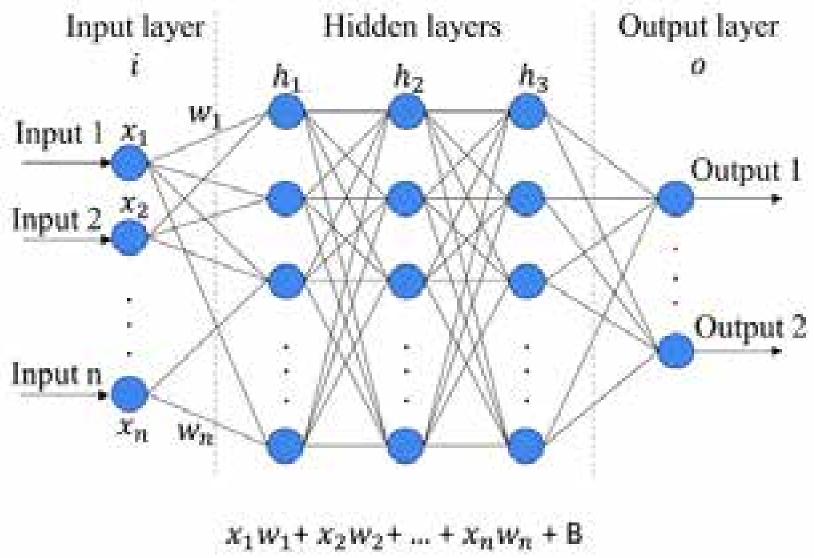
presented to **Prof. Dr. Jürgen Popp** in recognition of his outstanding contributions in the field of spectroscopy. The American Federation of Analytical Chemistry and Spectroscopy Societies honored his contribution to the application of research ideas and his long-standing commitment to enhanced disease diagnostics.

Publication Highlights 2023

Molecules



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Exploring the Steps of Infrared (IR) Spectral Analysis: Pre-Processing, (Classical) Data Modelling, and Deep Learning

Azadeh Mokari, Thomas Bocklitz, Shuxia Guo

This publication deals with the analysis of infrared spectra. Infrared spectroscopy is an important method for studying the chemical composition of materials. In this paper, the researchers describe various steps that are important for the analysis of infrared spectra. These include preprocessing of the measurement data to remove noise and improve the quality of the spectra, as well as classical statistical methods that can be used to infer chemical composition. In addition, the researchers show how modern AI methods, such as deep neural networks, can be used to analyze infrared spectra. The novelty of this work is that it provides a comprehensive overview of the entire process of infrared spectral analysis - from data preprocessing to modern AI methods. This should facilitate the application of this important analytical method. The research results are relevant to all scientists and engineers who use infrared spectroscopy in their work, such as in materials science, chemistry, or biology. The publication provides valuable information to improve and streamline the analysis of infrared spectra. Infrared spectroscopy is a powerful analytical technique used in many areas of science and industry. It allows the chemical composition of materials to be studied without extensive sample preparation. However, the interpretation of infrared spectra can be complex and often requires specialized expertise. This publication provides a comprehensive overview of the various steps involved in infrared spectroscopy and shows how modern methods such as deep learning can help to simplify and accelerate the analysis.

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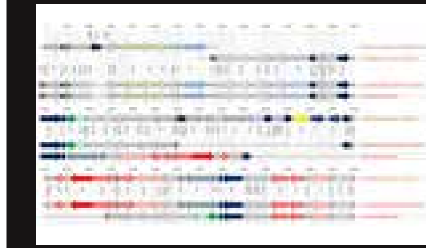
Antibiotics



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Clonal Complexes Distribution of *Staphylococcus aureus* Isolates from Clinical Samples from the Caribbean Islands

Stefan Monecke, Patrick Eberechi Akpaka, Margaret R Smith, Chandrashekhar G Unakal, Camille-Ann Thoms Rodriguez, Khalil Ashraph, Elke Müller, Sascha D Braun, Celia Diezel, Martin Reinicke, Ralf Ehricht

This publication examines the distribution of different strains of the opportunistic bacterium *Staphylococcus aureus* on the Caribbean islands. *Staphylococcus aureus* is a widespread pathogen that frequently causes infections in humans and is often resistant to common antibiotics. The researchers collected and analyzed samples of *Staphylococcus aureus* isolates from clinical samples on the Caribbean islands. They examined and compared the genetic properties of the bacterial strains in order to characterize the distribution of different strains in this region. The novelty of this study is that it provides the first detailed overview of the distribution of different *Staphylococcus aureus* strains in the Caribbean region. Previous data on this topic in this region were very limited. The research results show that there is a great diversity of *Staphylococcus aureus* strains in the Caribbean islands. Some of these strains are capable of producing a specific toxin (Panton-Valentine leukocidin, PVL). This toxin can lead to more serious infections as it impairs the body's immune defenses. In addition, the researchers found that many of the PVL-producing strains are still sensitive to common antibiotics. While this makes treatment easier compared to resistant strains, it also increases the risk of severe and recurrent infections. The findings of this study are relevant for doctors and health authorities in the Caribbean but also worldwide, as they enable a better understanding of the *Staphylococcus aureus* strains occurring there. This knowledge can help to take appropriate measures to combat infections with this bacterium and improve treatment in the region.

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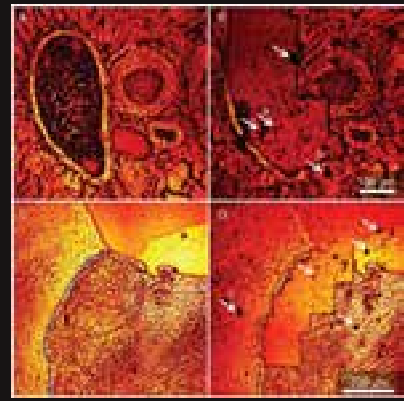
Analytical Chemistry



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Recent developments and advances of femtosecond laser ablation: Towards image-guided microsurgery probes

Matteo Calvarese, Tobias Meyer, Michael Schmitt, Orlando Guntinas-Lichius, Jürgen Popp

This review article summarizes the latest developments and advances in the research field of ablation of biological materials using femtosecond lasers. Femtosecond lasers are extremely short pulses of light that last only a billionth of a second. These lasers can ablate tissue precisely and gently without damaging surrounding tissue. This makes them interesting for use in medicine, especially in microsurgery. Femtosecond lasers are already being used in eye surgery. The article starts with a brief review of fundamental work dealing with the physical processes involved in laser ablation with femtosecond pulses. This fundamental work is important because it helps to make microsurgery safer and more precise, as it leads to a better understanding of the interaction between laser and tissue. By using femtosecond lasers, procedures can be performed more gently for the patient as only the necessary tissue is removed. This can speed up healing and reduce complications. However, the actual focus of the review article is on the use of femtosecond laser ablation as part of image-guided microsurgery. The review article therefore summarizes the latest studies on how these femtosecond lasers can be used in image-guided surgery. This includes the development of probes that combine laser ablation with imaging methods such as ultrasound, optical coherence tomography or the latest biophotonic imaging methods such as coherent Raman imaging. These imaging methods can be used to precisely visualize pathological tissue changes, which can then be specifically ablated using femtosecond laser ablation according to the principle of "see and treat". Overall, this review article shows how modern laser technology can advance medicine. The development of image-guided microsurgery probes is an important step towards further improving the precision and safety of operations.

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Publication Highlights 2023

Nature Communications

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110 µm thin endo-microscope for deep-brain *in-vivo* observations of neuronal connectivity, activity and blood flow dynamics

Miroslav Stibůrek, Petra Ondráčková, Tereza Tučková, Sergey Turtaev, Martin Šiler, Tomáš Pikálek, Petr Jákl, André Gomes, Jana Krejčí, Petra Kolbábková, Hana Uhlířová, Tomáš Čižmár

This research project is about the development of a new, tiny microscope that can observe processes deep inside the brain of living beings in real time.

What makes this microscope special is that it is extremely thin and small – only 110 micrometers thick. Yet it can provide high-resolution images of nerve cells, their activity, and even blood flow in the brain.

Researchers developed this tiny microscope to get a better look at the complex processes in the brain. Using conventional methods, it is very difficult to examine structures deep in the brain without causing damage. The new microscope is so small and thin that it can be inserted into the brain with virtually no damage. For the first time, researchers will be able to make detailed observations of neuronal activity, neuronal connectivity and blood flow in deep brain regions.

The novelty of this research is that a new type of miniaturized microscope has been developed that allows the real-time study of areas of the brain that were previously difficult to access. These findings are highly relevant to the neurosciences. They contribute to a deeper understanding of the complex processes in the brain, from the activity of individual neurons to blood flow and connectivity. This in turn can help to better understand brain diseases and develop new treatments.

For example, the new microscope could be used to study how diseases such as Alzheimer's or Parkinson's affect the activity and connectivity of nerve cells. Or it could be used to observe how the brain changes and adapts after injury or stroke. Overall, this release represents a major technological advance that will allow scientists to study the workings of the brain in greater detail than ever before. This opens up exciting possibilities for neuroscience and medicine.

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Nature Photonics

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Label-free biomedical optical imaging

Natan T. Shaked, Stephen A. Boppart, Lihong V. Wang, Jürgen Popp

This review article deals with the presentation of recent developments in the important field of novel label-free optical imaging methods for biomedical diagnostics / analytics.

Label-free methods do not require dyes or other markers and use the natural optical properties of cells and tissue to visualize their morphology and chemical composition (morphochemistry). This has several advantages: most importantly, the samples are not altered by dyes or other markers, which is essential for medical diagnostic applications, for example, as the use of markers entails cost-intensive approval studies.

In their review article, the authors report on various novel marker-free optical technologies such as phase-contrast microscopy, linear and non-linear Raman approaches, optical coherence tomography and photoacoustic imaging, to name but a few. The characteristics of these methods based on their underlying light-matter interactions are compared and illustrative examples for the visualization of the morphochemistry of biomedical samples are shown.

One example of the application of these label-free approaches is cancer diagnostics, where the methods presented can significantly improve intraoperative tumor diagnostics. However, these approaches also offer promising possibilities for other areas such as basic biomedical research, e.g. for research into pathophysiological processes.

Overall, this review article offers end users such as clinicians, clinical researchers or biologists who urgently need new methods of label-free imaging a good overview of which method is best suited to their research question.

An important component of this review article are the research results of the "Spectroscopy and Imaging" research department headed by Prof. Dr. Juergen Popp, who is the author of this review article alongside three other internationally well-known experts in this field.

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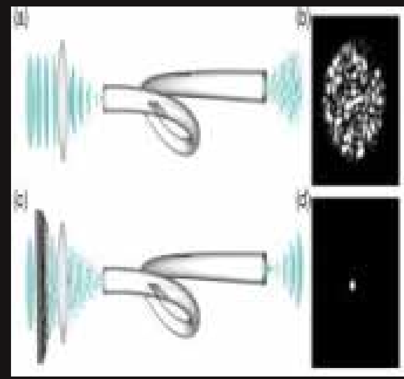
Advances in Optics and Photonics



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Controlling light propagation in multimode fibers for imaging, spectroscopy, and beyond

Hui Cao, Tomáš Čižmár, Sergey Turtaev, Tomáš Tyc, and Stefan Rotter

This publication is about the control and manipulation of light behavior in so-called multimode fibers.

Multimode fibers are special optical fibers that are capable of transmitting light in multiple different forms, the so-called modes. This makes them very versatile, for example in medical imaging, spectroscopy, or optical communication. The challenge, however, is that the light in these multimode fibers often experiences undesirable interactions, which can impair the performance of the applications. This is where the research comes in - the scientists have developed methods to better control and manipulate the propagation of light in multimode fibers. The innovation of this work is that the researchers present new techniques with which the behavior of light in multimode fibers can be precisely manipulated. This allows the fibers to be optimized for a variety of applications. These research results are relevant for scientists and engineers working on the development of innovative optical systems. The improved control over light behavior in multimode fibers can contribute to significantly increasing the performance and functionality of such systems. For example, the technology could be used to improve medical imaging techniques or increase data transmission rates in optical communication. New possibilities in sensing also open up through the better control of light behavior in multimode fibers. Overall, this publication provides important insights that can be used for the further development of many optical technologies. The new methods for controlling light in multimode fibers are an important step in improving the performance of such systems.

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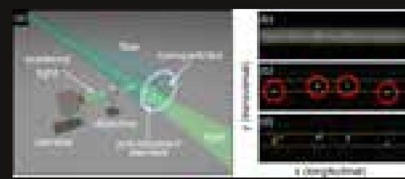
Nature Communications



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Characterization of diffusing sub-10 nm nano-objects using single anti-resonant element optical fibers

Torsten Wieduwilt, Ronny Förster, Mona Nissen, Jens Kobelke, Markus A. Schmidt

Publication Highlights 2023

This publication focuses on characterizing nano-objects smaller than 10 nanometers. The researchers have developed a new method based on so-called "single anti-resonant element optical fibers".

The innovation of this method is that it allows extremely small nano-objects to be precisely studied and characterised. Until now, it has been very difficult to analyse objects of this size, as conventional optical methods have reached their limits.

The research is relevant because nano-objects of this size play an important role in many fields, including medicine, materials science and electronics. For example, they can be used as sensors, in medicines or in new types of electronic components. To further develop these applications, it is important to understand the properties and behavior of these nano-objects.

In their study, the researchers showed that their new method principally makes it possible to precisely characterize individual nano-objects such as proteins, viruses or synthetic nanoparticles. This includes information about the size, shape and motion of the objects. The method is based on the nano-objects being inserted into a special glass fiber in which they scatter light sideways so that individual particles can be tracked. The properties of the objects can then be determined based on this light interaction.

Compared to other optical methods, this technique has the advantage of being very sensitive and capable of detecting individual nano-objects. It is also relatively easy to handle and can be used in a variety of applications. The researchers therefore see great potential for this method in the research and application of nano-objects.

Overall, this research makes an important contribution to the characterization of nano-objects in the sub-10 nanometer range. The newly developed method makes it possible to precisely examine these extremely small structures and thus opens up new possibilities for applications in medicine, materials science and nanotechnology.

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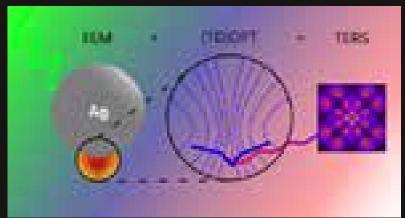
American Chemical Society



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A Full Quantum Mechanical Approach Assessing the Chemical and Electromagnetic Effect in TERS

Kevin Fiederling, Mostafa Abasifar, Martin Richter, Volker Deckert, Stephan Kupfer, Stefanie Gräfe

In this publication, the focus is on how scientists can utilize quantum mechanics to better understand the chemical and electromagnetic effects of the so-called Tip-enhanced Raman spectroscopy (TERS). TERS is a method for the chemical analysis of surfaces on the nanometer scale. In their study, the researchers combine the interaction of strong laser fields (electromagnetic effect) with the chemical interaction between the tip of the TERS device and the sample. Through this combination, they can simulate and understand the Raman signals more accurately.

The novelty of this research lies in the simultaneous investigation of both effects, leading to a better understanding of the fundamentals of the TERS method. The results contribute to pushing the resolution limits in the analysis of molecules on surfaces into ever smaller dimensions. This could help in the future to investigate even submolecular structures at room temperature and also in liquids, thereby gaining new insights for nanotechnology and materials science.

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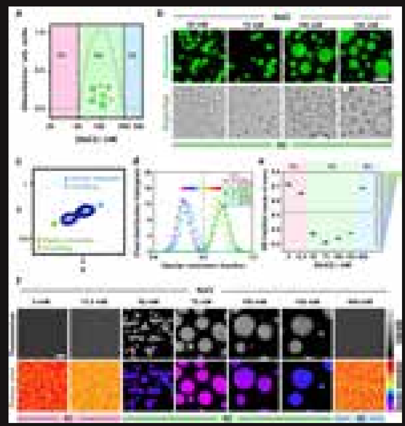
Nature Communications



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Biomolecular condensates modulate membrane lipid packing and hydration

Agustin Mangiarotti, Macarena Siri, Nicky W. Tam, Ziliang Zhao, Leonel Malacrida, Rumiana Dimova

This research focuses on how wetting of biomolecular condensates affects lipid membrane properties.

Biomolecular condensates are droplet-like compartments of proteins and other biomolecules that reside in cells, also recognized as membraneless organelles. Until now, it has been unclear how these condensates affect the properties of cell membranes.

The researchers have now discovered that biomolecular condensates can indeed alter the packing density and hydration level of lipids in artificial membranes.

Specifically, they have shown that the condensates influence the arrangement and water content of lipid molecules in the membrane. This affects important membrane functions such as mass transport and signaling.

These findings are important because cell membranes play a central role in all life processes. They act as a barrier, but also as a communication interface between cells and their environment.

If biomolecular condensates change membrane properties due to the wetting behavior, this has far-reaching effects on cellular functions. The researchers were able to show that the condensates-membrane interaction can even influence the secondary structure of proteins.

The innovation of this study is that it demonstrates for the first time the direct influence of biomolecular condensates on the physical properties of lipid membranes. This relationship was previously unknown.

These findings are relevant to the understanding of fundamental life processes at the cellular level. They contribute to a better understanding of the complexity of cells and could also have long-term implications for medicine, for example in the development of new therapeutic approaches.

Overall, this research provides important new insights into the interactions between biomolecular condensates and cell membranes. It expands our understanding of how cells work and could pave the way for further advances in biology and medicine.

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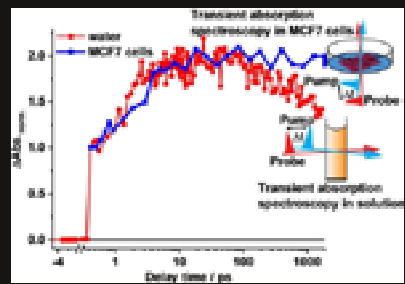
Angewandte Chemie



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Using Biological Photophysics to Map the Excited-State Topology of Molecular Photosensitizers for Photodynamic Therapy

Avinash Chettri, Tingxiang Yang, Houston D. Cole, Ge Shi, Dr. Colin G. Cameron, Prof. Dr. Sherri A. McFarland, Prof. Dr. Benjamin Dietzek-Ivanšić

The purpose of this research is to investigate the properties of photosensitizers used in photodynamic therapy (PDT).

Photosensitizers are molecules that can generate reactive oxygen species when exposed to light. These oxygen molecules can then damage cancer cells or other target structures and be used to treat diseases such as cancer.

The researchers focused specifically on the photosensitizer TLD1433, which is already in clinical trials for the treatment of cancer. They wanted to find out how the properties of this molecule behave in the complex environment of cancer cells.

They used state-of-the-art photophysical methods to study the dynamics of the photosensitizer's excited states in cancer cells. For the first time, they were able to observe in detail how TLD1433 absorbs light energy and converts it into reactive oxygen species.

The novelty of this study is that it has developed a methodology to analyze the photophysics of photosensitizers directly in living cancer cells. Until now, it has been very difficult to study these processes in the complex biological environment.

The research is important because it contributes to a better understanding of how photosensitizers work in photodynamic therapy. The more we know about the light excitation and energy conversion of these molecules, the more targeted they can be used to treat cancer.

In addition, the study provides important methodological insights that can be used to study other

Publication Highlights 2023

photosensitizers or similar agents in cells. This will help advance the development of new, more effective phototherapies.

Overall, this research demonstrates how modern biophysical methods can contribute to a better understanding of the fundamentals of photodynamic therapy and thus improve the treatment of diseases such as cancer.

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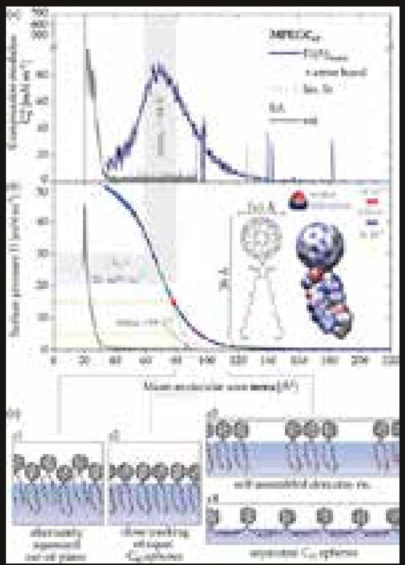
Advanced Materials



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Tailoring the Weight of Surface and Intralayer Edge States to Control LUMO Energies

Sarah Jasmin Finkelmeyer, Erik J. Askins, Jonas Eichhorn, Soumik Ghosh, Carmen Siegmund, Eric Täuscher, Andrea Dellith, Maximilian L. Hupfer, Jan Dellith, Uwe Ritter, Joseph Strzalka, Ksenija Glusac, Felix H. Schacher, Martin Presselt

This publication deals with the development of a new method to specifically control the electronic properties of semiconductor materials.

The key to this is to influence the so-called surface states in the semiconductor layers. These states at the surfaces and interfaces play a decisive role in the electronic properties of the material.

The researchers have discovered that they can control the weight of these surface states as compared to the total number of states in the material by changing the layer structure. This allows the energy levels of the conduction bands (LUMO) in the semiconductors to be precisely adjusted.

This is important because the conduction band energy largely determines the electronic and optical properties of a semiconductor. Depending on the application, these properties must be precisely matched to the requirements - be it for solar cells, light-emitting diodes or electronic components.

With the new method, the researchers can now control the conduction band energy much more precisely than before. They can virtually "tailor" the semiconductor layers to achieve the desired properties.

This opens up many possibilities: On the one hand, semiconductor materials can be optimized for special applications. On the other hand, completely new functionalities can also be developed by specifically adjusting the conduction band energy.

The research results are relevant as they make an important contribution to the further development of semiconductor technologies. Semiconductors are the basis for almost all modern electronic devices - from smartphones and solar cells to computers. The more precisely their properties can be adjusted, the more powerful and efficient these devices can become.

Overall, this work shows how a deeper understanding of material structure and composition can help to optimize semiconductor layers specifically for a wide range of applications. The ability to precisely adjust conduction band levels is an important step towards customized semiconductor materials of the future.

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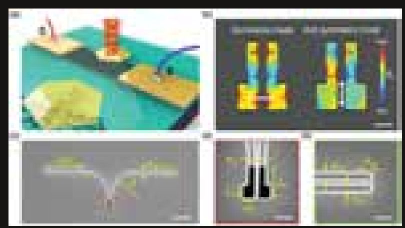
Advanced Science



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Near-Field Photodetection in Direction Tunable Surface Plasmon Polaritons Waveguides Embedded with Graphene

Chia-Hung Wu, Chih-Jen Ku, Min-Wen Yu, Jhen-Hong Yang, Pei-Yuan Wu, Chen-Bin Huang, Tien-Chang Lu, Jer-Shing Huang, Satoshi Ishii, Kuo-Ping Chen

In this paper, the researchers investigate how graphene can be integrated into plasmonic photodetectors.

Plasmonic photodetectors can detect special light waves called surface plasmon polaritons (SPPs) by converting the optical near field into electrical signals via an atomically thin graphene layer. The advantage of SPPs is that they can confine and transport optical energy at a scale much smaller than the wavelength of the light itself.

The novelty of this research is that the scientists embed graphene, an atomically thin 2D material with special electronic and optical properties, into the SPP waveguides. By incorporating graphene, they can directly and electrically detect the optical near field of the guided SPPs. The direct and electrical detection of SPPs greatly relaxes the need of complex output nanoantennas to convert the optical near field of SPPs to propagating photons that can be detected by typical photon detectors. This enables the realization of highly sensitive electric near-field optical detectors for surface plasmons.

The research results are relevant to various applications that require precise and compact near-field photodetectors, such as optical communications, sensing, or imaging. The possibility of electronically detecting optical near fields opens new perspectives for the development of high-performance optoelectronic devices.

In conclusion, this study presents an innovative approach to improve the performance of plasmonic photodetectors using graphene. The results contribute to the understanding and further development of this promising technology.

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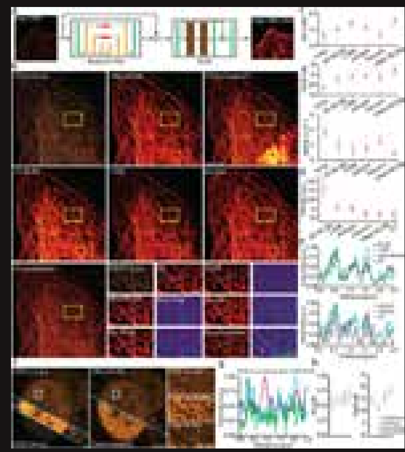
Communications Biology



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Deep learning enables fast, gentle STED microscopy

Vahid Ebrahimi, Till Stephan, Jiah Kim, Pablo Carravilla, Christian Eggeling, Stefan Jakobs, Kyu Young Han

In this study, the researchers present an innovative approach to improve the performance of super-resolution optical stimulated emission depletion (STED) microscopy. STED microscopy is a technique that allows scientists to image structures within cells at a resolution well below the conventional diffraction limit of light microscopy.

The novelty of this research is that the scientists have developed a deep learning method to improve STED microscopy images. Typically, STED microscopy requires high light intensity, which may damage the sample and cause the fluorescent dyes to fade quickly. By using deep learning, the researchers now significantly reduce the exposure time without losing resolution or image quality. Specifically, the scientists have developed a two-step deep learning model that first restores image information at a large scale and then generates the final super-resolution. This allows them to capture STED microscopy images with a an up to 32 times shorter acquisition time without compromising resolution. Consequently, the time resolution for recording cellular dynamics like virus infection events is significantly improved and at the same time light-induced damage to the sample reduced.

The research is relevant to many fluorescence microscopy applications that require high-resolution imaging of sensitive biological samples. These include the study of cell structures, the observation of dynamic processes in cells over long periods of time, and the analysis of tissues. The researchers' approach makes it possible to use STED microscopy more gently and efficiently, which could greatly facilitate the use of this technology in the life sciences.

In summary, this study presents a promising deep learning-based approach to improve the performance of super-resolution STED microscopy while reducing the exposure of samples to light. The results help to further explore the limits of optical microscopy and open up new possibilities for high-resolution imaging in the life sciences.

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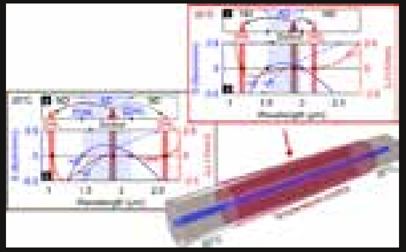
Publication Highlights 2023

Laser & Photonics Reviews



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Temperature-Sensitive Dual Dispersive Wave Generation of Higher-Order Modes in Liquid-Core Fibers

Ramona Scheibinger, Johannes Hofmann, Kay Schaarschmidt, Mario Chemnitz, Markus A. Schmidt

This research deals with the generation of special light signals, called "dispersive waves", in certain optical fibers. Dispersive waves are generated by nonlinear effects in fibers and can be used for various applications. The special feature of the fibers studied is that they are filled with a liquid. The researchers discovered that the generation of dispersive waves in these liquid-filled fibers is very sensitive to temperature changes. By slightly heating the fiber, two different dispersive waves can even be generated simultaneously. This is an important innovation because it has not been possible to generate two different dispersive waves in a fiber in such a simple way. This discovery is important for research because it opens up new possibilities for the development of temperature-sensitive optical sensors and wavelength-adjustable light sources. Such light sources could be used in medical technology or biophotonics, for example, to chemically excite and read cells and biomarkers. In addition, the findings from this work contribute to a deeper understanding of the complex nonlinear effects in optical fibers. The researchers were able to show how temperature changes affect the propagation and interaction of light signals in the fiber. Overall, the publication makes important contributions to the field of nonlinear fiber optics research. The results show ways to develop new types of optical components and sensors that are very sensitive to temperature changes.

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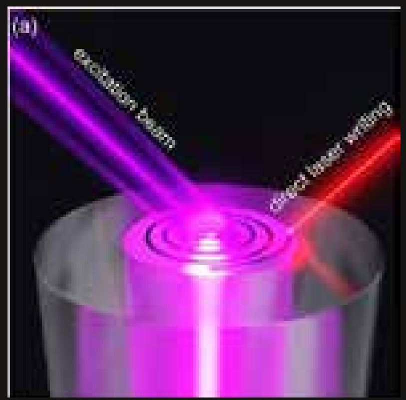
Applied Physics Reviews



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Advanced fiber in-coupling through nanoprinted axially symmetric structures

Oleh Yermakov, Matthias Zeisberger, Henrik Schneidewind, Jisoo Kim, Andrey Bogdanov, Yuri Kivshar, Markus A. Schmidt

This paper describes a novel method for more efficient coupling of light into optical fibers. Optical fibers are thin glass strands that are used today in many areas of telecommunications, sensing, and data transmission. One of the challenges is to couple light from a light source into the fiber with as little loss as possible. Typically, light is coupled into fibers by lenses or mirrors that focus the light onto the face of the fiber. However, some of the light is lost because not all the light power is directed into the acceptance angle of the fiber. This acceptance angle is limited and depends on the optical properties of the fiber. The researchers in this study have now developed a new method to improve the incoupling. They have designed special nanostructured elements that are attached to the end face of the fiber. These elements have an axially symmetric shape and direct the light so that it is optimally coupled into the fiber. The main advantage of this method is that the coupling efficiency can be significantly increased. These research results are relevant to a variety of applications where optical fibers are used. These include high-speed data transmission in telecommunications networks, fiber optic sensors in industrial and medical applications, and laser-based materials processing and metrology. Improved coupling can increase the performance and efficiency of such systems, leading to cost savings and new applications. Overall, this study demonstrates an innovative approach to optimizing fiber coupling and thus improving the performance of fiber optic systems. The results are relevant to many areas of photonics and optoelectronics and can contribute to the advancement of various technologies.

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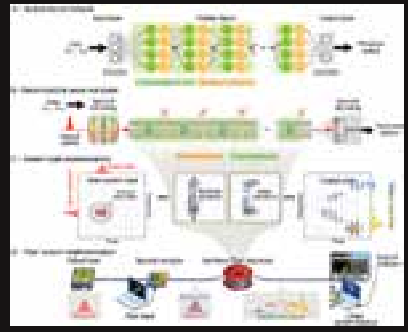
Advanced Science



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Neuromorphic Computing via Fission-based Broadband Frequency Generation

Bennet Fischer, Mario Chemnitz, Yi Zhu, Nicolas Perron, Piotr Roztocki, Benjamin MacLellan, Luigi Di Lauro, A. Aadhi, Cristina Rimoldi, Tiago H. Falk, Roberto Morandotti

This publication is about a new method called Neuromorphic Wave Computing, which is inspired by the way the human brain works. Instead of conventional computers, it uses optical solutions that are potentially more energy efficient and faster. Researchers have developed an innovative technique that uses light to process complex information in a similar way to the brain.

The innovation is that data is no longer processed with electrical current, but in the form of ultrashort pulses in optical fibers. The optical information is mixed and networked in the fiber in a special way, similar to the way neural networks work. The transformed mixed signals at the fiber output then allow intelligent prediction of the type of data to be received. Experimentally, for example, COVID-19 patients could be diagnosed with about 78% accuracy using audio recordings. The research shows how this new technology can contribute to the development of more powerful artificial neural networks. In the future, these could be used in areas such as image and speech recognition to solve tasks faster and more energy-efficiently.

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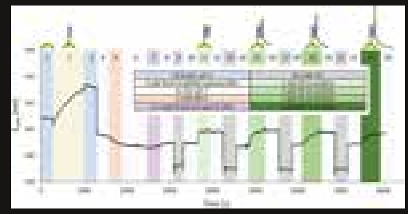
Nano – Micro – Small



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LSPR-Based Biosensing Enables the Detection of Antimicrobial Resistance Genes

Stephan Kastner, Anne-Kathrin Dietel, Florian Seier, Shaunak Ghosh, Daniel Weiß, Oliwia Makarewicz, Andrea Csáki, Wolfgang Fritzsche

This publication describes the development of a novel method for the rapid and reliable detection of antibiotic resistance genes. The key is the use of localized surface plasmon resonance (LSPR). LSPR uses tiny metal particles to detect the presence of specific DNA sequences. The research team developed LSPR sensors to detect the blaSHV resistance gene. This gene confers resistance to a number of beta-lactam antibiotics. The advantage of the LSPR method is that it is very sensitive and fast. The researchers were able to reliably detect short DNA sequences with only 23 building blocks. The technique is capable of detecting single mutations in genes. This is important because such mutations determine whether an antibiotic is still effective against an infection or not. Doctors can thus quickly select the right treatment and save patients' lives.

Conventional methods for detecting resistance genes are often time-consuming and require the use of dyes or other markers. LSPR sensors, on the other hand, are label-free and provide real-time results. This makes them much more efficient and cost-effective.

With antibiotic resistance on the rise around the world and the associated threat to public health, rapid and accurate diagnostics are essential to detect resistance early and initiate appropriate treatment. The LSPR-based biosensors could therefore help curb the spread of antibiotic resistance. In addition, the technology can be transferred to other applications such as cancer diagnostics.

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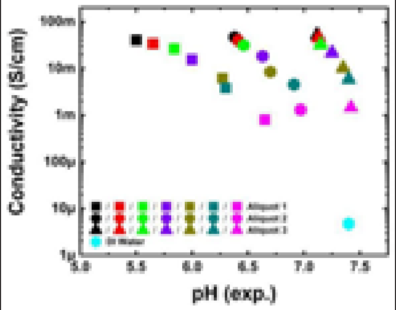
Publication Highlights 2023

Biosensors



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A Novel Approach to Monitor the Concentration of Phosphate Buffers in the Range of 1 M to 0.1 M Using a Silicon-Based Impedance Sensor

Bhat, Vinayak J., Daniel Blaschke,
Elke Müller, Ralf Ehricht,
Heidemarie Schmidt

The goal of this research project is to develop a novel impedance sensor that can accurately measure the concentration of phosphate buffers in liquids using impedance.

Phosphate buffers are chemical solutions used in many areas of science and technology, such as biological experiments or medical technology. They are used to keep the pH of a liquid constant. It is therefore important to be able to measure the exact concentration of these buffers. The researchers have developed a special sensor based on silicon technology. This sensor can analyze very small amounts of liquid, just a few microliters, and measure the concentration of phosphate buffers in a wide range from 0.1 to 1 mole per liter. This means that the sensor in question measures the concentration of phosphate buffers much more accurately and sensitively than previous methods. It is also very compact and can be easily integrated into various applications.

These research results are relevant for researchers and engineers working with phosphate buffers. The new sensor can help to conduct and control biological, chemical or medical experiments more accurately. The sensor could also be used in industry, for example in food production, to monitor and optimize production processes. The work also shows how modern silicon technology can be used to develop highly sensitive sensors.

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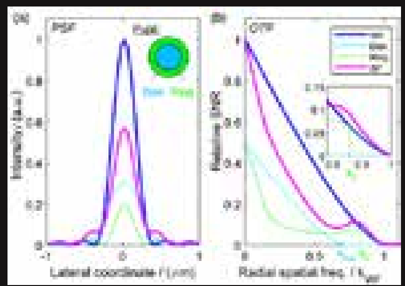
OPTICA



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Better than a lens? Increasing the signal-to-noise ratio through pupil splitting

Jan Becker, Takahiro Deguchi, Alexander Jügler, Ronny Förster,
Uwe Hübner, Jonas Ries,
Rainer Heintzmann

This paper discusses an innovative method in optical imaging that aims to improve the signal-to-noise ratio (SNR). SNR is a measure of how much of the "useful" signal is present in an image or signal compared to the "useless" noise. A higher SNR means that the image or signal is clearer and easier to interpret.

Traditionally, it has been assumed that using a full pupil (the part of an optical system that transmits light) without modification provides the maximum achievable SNR in incoherent imaging. Incoherent imaging refers to a process in which the light is radiated back or emitted by an object is out of phase, which is typical of most everyday imaging situations, such as taking a photo with a camera.

The novelty of this research is that it splits the pupil rather than using it in its entirety. This approach represents a departure from the traditional assumption and shows that by dividing the pupil, SNR can be improved. This is similar to the idea that instead of looking through one large window, you look through two smaller windows strategically placed to get a clearer picture of what is outside.

The relevance of this research lies in its potential applications in various areas of optical imaging. Improving SNR can lead to clearer and more accurate images, which is particularly important in areas such as medical imaging, astronomy, and microscopy.

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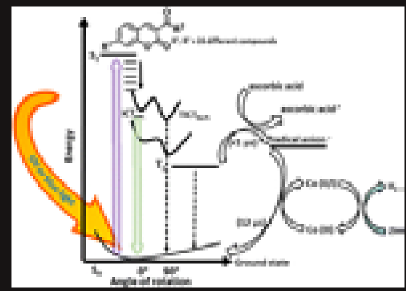
Journal of Materials Chemistry A



© Journal of Materials Chemistry A _open access

Unlocking the potential of ketocoumarins: efficient photosensitizers for sustainable light driven hydrogen evolution

Gergely Knorr, Konrad Hotzel, Avinash Chettri, Artem Skabeev, Maria Wächtler, Benjamin Dietzek-Ivanšić, Kalina Peneva

This paper deals with the development of a new method for the production of hydrogen from sunlight based on ketocoumarins. Ketocoumarins are chemical compounds that can absorb light and are used as photosensitizers in this research. A photosensitizer is a substance that absorbs light energy and then uses that energy to drive chemical reactions - in this case, the production of hydrogen from water.

The research team proposes ketocoumarins as an efficient and viable alternative to the heavy metal-based photosensitizers commonly used to date. The researchers have synthesized a series of new ketocoumarins and optimized the reaction conditions to achieve remarkably high conversion rates. This means that a large amount of hydrogen can be produced with these new photosensitizers before their effectiveness diminishes. They also showed that by increasing the concentration of a specific catalyst (cobaloxime), photodegradation of the photosensitizers can be prevented and hydrogen production can be maintained for up to 22 days.

The research results are significant for several reasons. The use of ketocoumarins offers a sustainable and more environmentally friendly alternative to heavy metal-based photosensitizers. The high efficiency of the new ketocoumarins in hydrogen production could help to improve the use of sunlight as an energy source for hydrogen production. The simple synthesis and the ability to obtain the photosensitizers without complex purification steps also make the method practical and potentially scalable for industrial applications.

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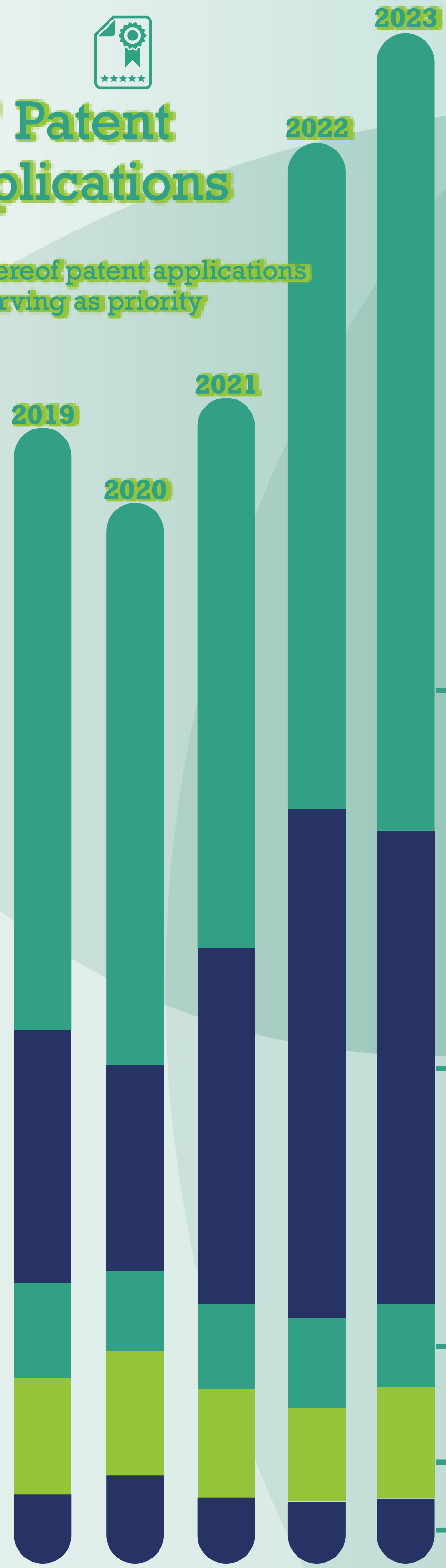
Key Figures of 2023*

6 Patent applications

5 thereof patent applications serving as priority



19 Patents granted

4 thereof national

15 thereof international

21,876,881 €
Institutional funding

10,867,143 €
National projects, 3,941,908 € thereof for Leibniz Center for Photonics in Infection Research (LPI)

2,195,999 €
DFG funding

3,142,851 €
Industrial projects

1,755,782 €
EU third-party funding

39,838,656 €
Total budget
=45.09 % Third-party funding

456 Employees

54 % Proportion of international researchers and doctoral students

Employees from **38** countries

29 EU financed projects

9 of which coordinated by Leibniz IPHT

22 Doctorates

7 thereof women

1 EU co-financed project (ERA-Net, Eurostars etc.)

201 Publications in peer-reviewed journals

6 Trademark registrations

1 thereof national

5 thereof international

134 PhD students

*In December 2023, Leibniz IPHT was the target of a cyber attack. Due to the ongoing recovery of our systems, the figures systems, the figures presented in this report should be considered preliminary.

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Institute Personnel 2023*

	Institutional Funding (Full-time Equivalents)	Third-Party Funding (Full-time Equivalents)	Professors (Full-time Equivalents)	Total	Persons
Scientists	29.19	77.10	9.00	115.9	127
Visiting Scientists[2]	–	–	–	–	46
External Funded Scientists[1]	–	–	–	–	21
External Funded Employees[1]	–	–	–	–	2
External Funded Doctoral Students[1]	–	–	–	–	62
Doctoral Students	7.30	36.70	–	44.00	72
Technical Staff	35.12	39.35	–	74.47	81
Administration	13.20	8.96	–	22.16	24
Scientific Coordination	3.81	6.75	–	10.56	11
PR and Research Marketing	2.88	3.50	–	6.38	7
Executive Committee	1.00	–	0.50	1.50	2
Trainees	1.00	–	–	1.00	1
Total Personnel	**93.50**	**172.36**	**9.50**	**275.36**	**456**

[1] Employees, not financed from Leibniz IPHT payroll or employees financed by another institution (e.g. University Jena), who have their main working place at Leibniz IPHT.

[2] Scientists, who worked in the legal year 2023 longer than one week at Leibniz IPHT and who are financed by another institution. Key date regulation December 31st, 2023 does not apply.

*In December 2023, Leibniz IPHT was the target of a cyber attack. Due to the ongoing recovery of our systems, the figures systems, the figures presented in this report should be considered preliminary.

Budget of the Institute 2023*

	spending in T Euro
Institutional Funding: Use	
Free State of Thuringia, Federal	21,876.9
Third-Party Funding	17,961.8
total	**39,838.7**

Institutional Funding: Use

Staff	9,136.1
Materials	4,826.9
Investments	7,913.9
total	**21,876.9**

Third-Party Funding

Federal Ministries of which 307.1 T€ for projects financed by the Leibniz Association of which 3,941.9 T€ for Leibniz Center for Photonics in Infection Research (LPI)	8,903.2
DFG Additionally Leibniz IPHT scientists at the University Jena used DFG-funds of 1,289.4 T€	2,196.0
Free State of Thuringia of which for restructuring in the frame of EFRE 964.2 T€	1,311.8
EU	1,755.8
Assignments from Public Institutions	180.4
Other Contributions	652.1
Subcontracting in Joint Projects	81.4
R&D Contract incl. Scientific-Technical Activities	2,881.1
total	**17,961.8**

*In December 2023, Leibniz IPHT was the target of a cyber attack. Due to the ongoing recovery of our systems, the figures systems, the figures presented in this report should be considered preliminary.

Thanks for the Financial Support

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EFRE – Europa für Thüringen
STIFT – Stiftung für Technologie, Innovation und Forschung Thüringen
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Publisher: Leibniz Institute of Photonic Technology

Location: Albert-Einstein-Str. 9, 07745 Jena

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