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LEIBNIZ INSTITUTE *of* PHOTONIC TECHNOLOGY // ANNUAL REPORT 2018

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Thank you very much.

We would like to thank all our employees most cordially for their hard work and high level of commitment on a daily basis. We would also like to thank the Free State of Thuringia and the Federal Government, as well as all sponsors and partners from politics, science and industry, for their many years of close and trusting cooperation. We look forward to working successfully together in the future.

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Dear Readers,

» does the following scenario look familiar to you? You have a great idea. For example: You want to design and build the new bookshelf yourself, and then you are standing desperately in front of a loose wooden board, with a bleeding thumb and a hammer in your hand? The idea of the perfect solution for your book collection collapses – literally. Don't worry, you're not alone with this experience. Leonardo da Vinci seems to have been familiar with this phenomenon, for he concluded: "Ingenious people begin great works, diligent people complete them".

At Leibniz IPHT we research procedures for applications in the fields of medicine, health, environment and safety – from the idea to the final result. The fact that our claim "From Ideas to Instruments" is anything but trivial becomes clear when considering that for many people the construction of a bookshelf is already a seemingly insurmountable challenge. Da Vinci said that in order to start great works one needs "brilliant people" (a description that applies quite well to our scientists). But in order for the many ideas, which often have their roots in basic research, to actually become applications suitable for everyday use, diligence and a high degree of expertise are required. And teamwork. Research teams at Leibniz IPHT set an entire process chain in motion to achieve this. Some will come up with a good idea, others will contribute their technological expertise and the next one will convince partners of the feasibility of the application. Our research facility is characterized by this transfer concept. In this annual report, we will tell you how we succeed in working together successfully.

Enjoy reading!

Jürgen Popp
Scientific Director

Frank Sondermann
Administrative Director

Prof. Dr. Jürgen Popp © Sven Döring

Frank Sondermann © Sven Döring

PHOTONICS FOR LIFE
from Ideas to Instruments

Contents

News from Leibniz IPHT

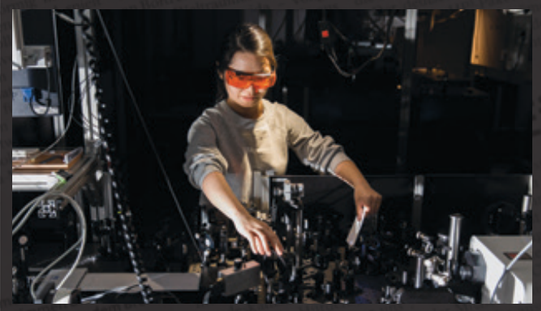
"Research that improves everyday life." Federal Minister Visits Leibniz IPHT

Scientific Director Jürgen Popp with Federal Minister Anja Karliczek. © Leibniz IPHT

"This is where research takes place that can improve people's everyday lives," said Anja Karliczek during her visit to the Beutenberg Campus in Jena. The Federal Minister of Education and Research visited the Leibniz IPHT in June 2018 to gather information about research activities in the field of optical health technologies.

Scientists and scholars explained how they use light to detect infectious pathogens and their resistances or to examine tissue for cancer diagnosis. In laboratories and in the fiber drawing plant, the Minister gained insight into spectroscopic imaging methods and technologies for the production of optical fibers. "The Beutenberg Campus is an example of how cutting-edge research can advance our country," summarized Anja Karliczek. "I am particularly pleased that the transfer of knowledge has such a high value for researchers," said the Minister, emphasizing one aspect that is central to Leibniz IPHT: the targeted implementation of research results in applicable solutions.

Detecting Diseases with Molecules: New European Network of Young Scientists



Ying Zhang investigates light-induced processes in molecules. © Sven Döring

Molecular logic switches are chemical compounds that function like electronic circuits in computers: They process information into a logical response. An international team of young scientists is investigating the properties of these molecules and whether they can be used to diagnose diseases in the future in the "Logic Lab – Molecular logic lab-on-a-vesicle for intracellular diagnostics" project coordinated by Leibniz IPHT. "Our goal is to adapt the molecular logic switches for applications in biological environments and cells," explains network coordinator Benjamin Dietzek. From April 2019 onwards, 14 PhD students will be working at nine universities, research institutions and companies in Germany, Ireland, the Netherlands, Poland and Slovakia in the Innovative Training Network (ITN). The European Union is funding "Logic Lab" with more than 3.5 million euros over the next four years.

www.logiclab-itn.eu

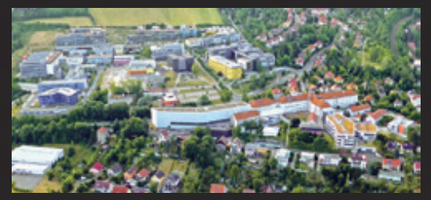
Progress in Medical Technology: New Innovation Center in Jena and Ilmenau

Planned innovation center ThIMEDOP in the CetraMed. © pbr

Thuringia's Minister of Science Wolfgang Tiefensee handed over the funding decision. © Leibniz IPHT

A new innovation centre for medical technology is being built in Thuringia. Teams of scientists from Leibniz IPHT, Jena University Hospital, and Ilmenau Technical University will work at the ThIMEDOP – short for "Thuringia Innovation Center for Medical Technology Solutions (Diagnosis, Therapy, Optimization through Optical Solutions)". There, they will focus on stem cells, ageing and oncology research, as well as research in biomedical technology and microscopy. The aim is to develop new optical, spectroscopic and biotechnological detection methods, to have them certified as medical devices as quickly as possible and to accelerate the overall translation of research results into economically viable processes and products. The centre, which is funded by the state of Thuringia, will be located in the CetraMed research building, which will be built on the premises of the University Hospital from 2019 on.

Excellent Research Partner in Spectroscopy and Imaging

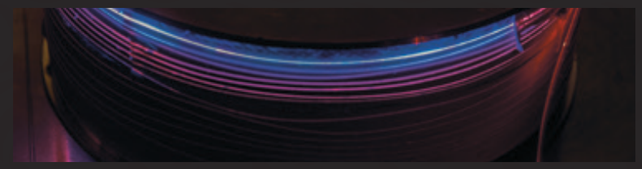


The Beutenberg Campus in Jena. © University Jena

The Jena research cluster "Balance of the Microverse", in which Leibniz IPHT also participates, is one of 57 selected alliances that will be funded in the Excellence Strategy of the German federal and state governments over the next seven years. The University of Jena cooperates with its hospital and eight non-university research institutions in the Cluster of Excellence. The aim of the research network is to explore the dynamic equilibrium of microbial communities from a holistic perspective. This has a stabilizing effect on living organisms and the environment, such as the health of humans, animals and plants, the fertility of soils or the quality of water bodies. Research teams are developing new technologies to maintain and restore these equilibria. Leibniz IPHT and its partners from life sciences and medicine are researching real-time imaging methods with the highest spatial resolution to answer biological and biomedical questions. For this purpose, a "Microverse Imaging Center" will be set up, where teams of scientists will develop innovative microscopic and spectroscopic methods. "We provide state-of-the-art and visionary microscopy platforms in biological security level 2 laboratories," explains Christian Eggeling, who heads the research department "Biophysical Imaging" at Leibniz IPHT. "To this end, we are accelerating the development of new biophotonic technologies in order to identify correlations between cause and effect."

www.microverse-cluster.de

For Future Technologies: European Team of Scientists Researches New Fiber Lasers

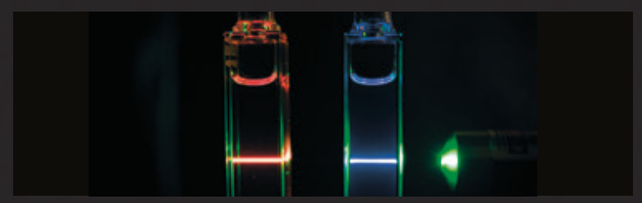


The EU project NCLas is developing fiber lasers with new wavelengths. © Leibniz IPHT

As the only network coordinated from Germany, a team of scientists from the Department of Fiber Photonics at the Leibniz IPHT has been awarded the funding for the top-class EU program "FET Open". In the interdisciplinary project "NCLas" scientists in Germany, Spain, Poland and Great Britain are researching novel fiber lasers. "We want to incorporate nanocrystallites into a fiber in order to provide fiber lasers with new wavelengths," explaines the head of the "Active Fiber Modules" working group, Matthias Jäger, who coordinates "NCLas".

The research teams want to develop numerous new application possibilities in medicine and telecommunications. With the "FET Open" programme, the European Union supports scientific and technological research with the potential to develop new ideas for future technologies. The EU will provide almost 3 million euros for "NCLas" over the next four years, 900,000 of which for the Leibniz IPHT.

Producing Energy Following Nature's Example

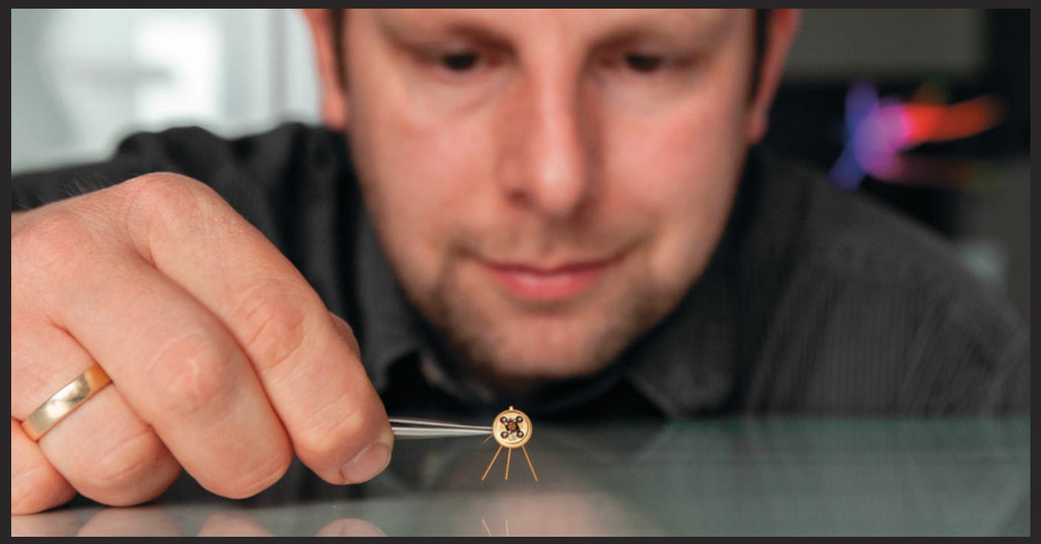


Rylene dyes, among others, are used as light collection units for photocatalytic water splitting. © Martin Schulz / FSU

The aim of the "CataLight" Sonderforschungsbereich (SFB, Collaborative Research Centre) is to research sustainable energy converters modelled on nature. Since July, Leibniz IPHT has been working on the project funded by the German Research Foundation (DFG) together with the Universities of Jena, Ulm and Vienna and the Max Planck Institute for Polymer Research in Mainz. Over the next four years, teams of scientists from the fields of chemistry, materials science and physics will work on using light to produce high-energy chemicals and new materials for sustainable energy conversion. Following the example of natural photosynthesis, they want to develop molecular catalyst systems for the light-controlled production of hydrogen and oxygen from water. The goal is to stabilize them. "We look at how nature does it and integrate the molecular components into soft matter," explains Benjamin Dietzek, head of the "Functional Interfaces" research department and deputy speaker of the Collaborative Research Centre (SFB). "We want to establish new concepts for photocatalytic water splitting."

www.catalight.eu

On a Space Mission: Sensors Explore the Secrets of the Planets



Frank Hänschke with the thermosensor TS-72. Six of the sensors developed at Leibniz IPHT are used on the Mars mission InSight. © Leibniz IPHT

The Hayabusa 2 spacecraft approaches the asteroid Ryugu. © DLR

Equipped for extreme conditions: the sensor for Mercury. © Leibniz IPHT

Measuring an asteroid, taking off for Mercury and landing on Mars: Three space missions in 2018 had sensors from Leibniz IPHT on board. The successful deployment on the near-earth asteroid Ryugu in October marked the beginning of the mission. The German-French measuring device "MASCOT" collected data on the temperature, magnetic properties and composition of Ryugu. Researchers want to track down the origins of the solar system and investigate whether the asteroid could pose a threat to Earth.

Shortly afterwards, the next Jena sensor launched into space: with the BepiColombo space probe on Europe's first mission to Mercury. Armed against extreme conditions, the specially developed robust sensor will explore temperature fluctuations of up to 430 degrees Celsius during the day and down to minus 180 degrees Celsius at night. The spacecraft is scheduled to reach Mercury by the end of 2025.

"I'm here, I'm home", announced the Twitter account of InSight, the Mars lander, after grounding on the Red Planet at the end of November. Using a parachute, the thermoelectric sensors installed in a radiometer set off with InSight on Mars to measure the heat radiation on its surface. Researchers hope that the results will provide them with a key to exploring the planet: They want to find out whether Mars was created from the same material as the Earth and the Moon and better understand why it has developed differently from Earth over the past 4.5 billion years. "This is a highlight in my working life", said Frank Hänschke, head of the working group "Integrated Thermo-Electrical and Micromechanical Technologies" in a television report by the MDR about the sensors from Leibniz IPHT. Future joint space projects are already being prepared by scientists from Leibniz IPHT and the German Aerospace Center (Deutsches Zentrum für Luft- und Raumfahrt; DLR).

Engineer Henry John from the Sensor Systems group assembles the Raman2GO portable spectrometer.
A cross-departmental team from Leibniz IPHT joined forces to design the device: from clean room to product design. © Sven Döring

Crossing Borders

How Leibniz IPHT technologies interlock

» Using light as a tool to explore future solutions: This is the goal of Leibniz IPHT. In this annual report, we tell you how physicists and microfluidicists, technologists, engineers, programmers and device developers are exchanging knowledge and ideas.

The way we live has a lasting effect. Half the pack of the generously prescribed antibiotic against the mild infection ends up in the toilet instead of in the household waste. The meat for lunch is inexpensive because it comes from fattening farms, where thousands of animals are kept and given plenty of antibiotics. We are outsourcing the production of active ingredients to emerging markets. Tourists import multi-resistant pathogens from overseas trips. All this contributes to the fact that more and more people are becoming infected with germs against which available antibiotics are no longer effective. Resistant pathogens endanger people all over the world. Diseases that can still be easily treated today can become a fatal danger again in the near future.

Infectious diseases are already among the most frequent causes of death worldwide. On the other hand, people in industrialised countries are getting older and older. More and more of them have to be treated for cancer, cardiovascular diseases or diabetes. Longer hospital stays, in turn, increase their risk of becoming infected with resistant or even multi-resistant pathogens. This poses a major challenge for healthcare systems worldwide.

Scientists at Leibniz IPHT are researching methods for the social challenges of our time. They are researching photonic solutions for the diagnosis and treatment of illnesses, for pharmaceutics and process control as well as for food and environmental safety. For example, to prove how many drug residues pollute our aquatic environment and drinking water. Which pathogens have caused an infection and which antibiotic they are resistant to. Or whether a cancer patient receives the therapy to which the tumour responds best.

And just as the problems of our globalised society are not detached from each other, so the technologies at Leibniz IPHT interlock to move from basic research to application: From Ideas to Instruments. Scientists at Leibniz IPHT combine highly sensitive and specific photonic and biophotonic detection methods with technological expertise in fiber technology and microfluidics, in micro- and nanotechnologies, quantum and systems technology.

In the clean room of Leibniz IPHT, researchers produce tailor-made substrates for surface-enhanced vibrational spectroscopy in order to detect infectious pathogens. They combine highly specific optical detection methods with microfluidic sample preparation and artificial intelligence: for an analysis chip to identify drug residues in water, pollen in the air or cancer cells in the blood. And they use microstructured special fibers from the Institute's drawing plant to detect tiny amounts of antibiotics in patients' body fluids. They are researching innovative processes and integrated systems that are more than the sum of their parts.

© Sven Döring

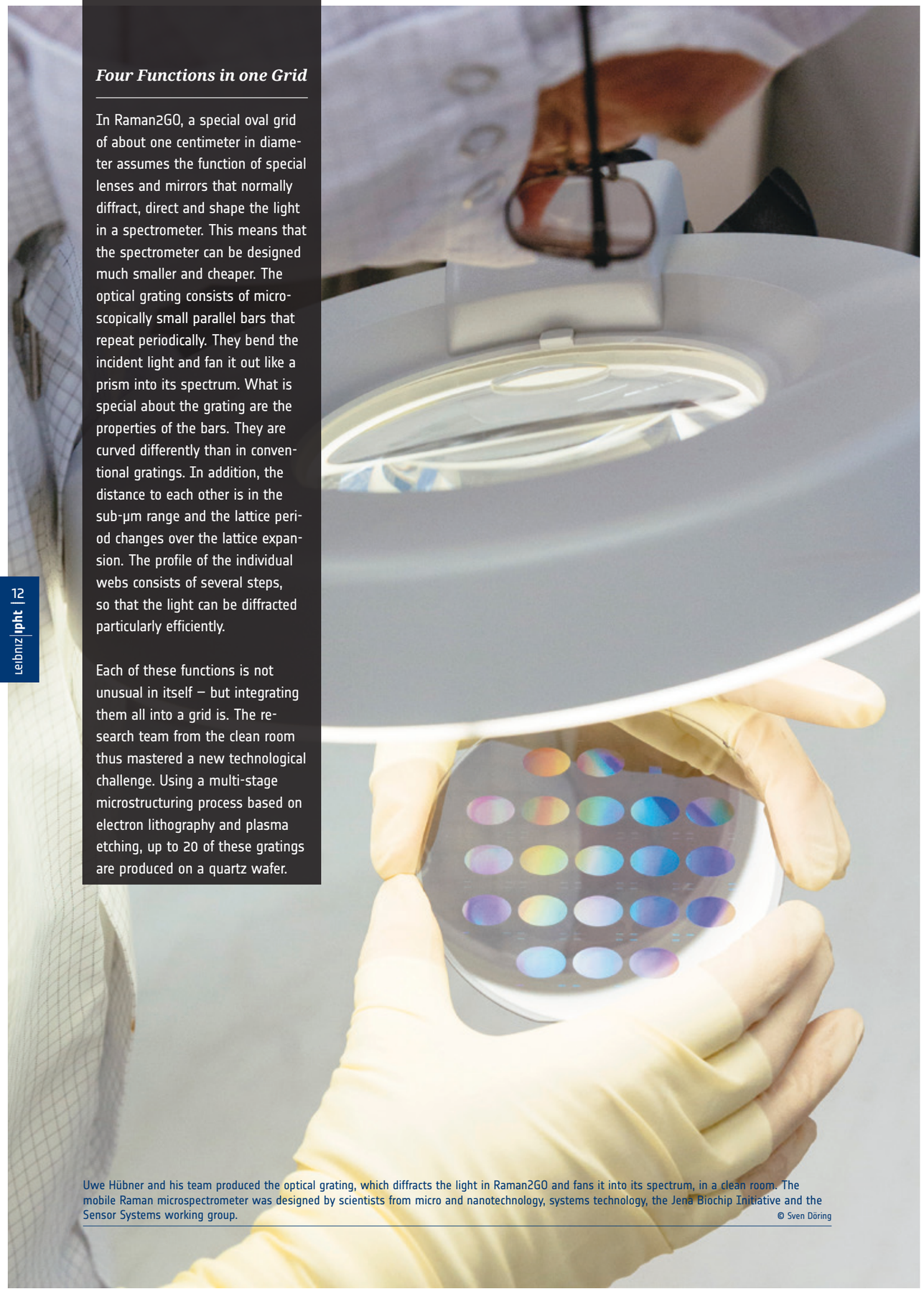
Reinforced: The Transfer from Research to Practice

It takes a long time for technological solutions from research to reach the patient: on average, it takes around 14 years for them to be applied in practice. One of Leibniz IPHT's main goals is to accelerate this process of translation from idea to product. A team headed by industrial researcher Ralf Ehricht is working on new bioinformatic methods for the diagnosis of infectious diseases and social health risks in the research department "Optical Molecular Diagnostics and System Technology", which was founded in December 2018. Ehricht, previously project manager at the Jena-based diagnostics company Abbott (Alere Technologies GmbH), wants to build a bridge to industrial partners: "To jointly implement innovative products for diagnostics and therapy".

Four Functions in one Grid

In Raman2GO, a special oval grid of about one centimeter in diameter assumes the function of special lenses and mirrors that normally diffract, direct and shape the light in a spectrometer. This means that the spectrometer can be designed much smaller and cheaper. The optical grating consists of microscopically small parallel bars that repeat periodically. They bend the incident light and fan it out like a prism into its spectrum. What is special about the grating are the properties of the bars. They are curved differently than in conventional gratings. In addition, the distance to each other is in the sub-µm range and the lattice period changes over the lattice expansion. The profile of the individual webs consists of several steps, so that the light can be diffracted particularly efficiently.

Each of these functions is not unusual in itself – but integrating them all into a grid is. The research team from the clean room thus mastered a new technological challenge. Using a multi-stage microstructuring process based on electron lithography and plasma etching, up to 20 of these gratings are produced on a quartz wafer.



Uwe Hübner and his team produced the optical grating, which diffracts the light in Raman2GO and fans it into its spectrum, in a clean room. The mobile Raman microspectrometer was designed by scientists from micro and nanotechnology, systems technology, the Jena Biochip Initiative and the Sensor Systems working group. © Sven Döring

A Portable Spectrometer

A cross-departmental team of scientists is researching an analytical laboratory that no longer needs a laboratory: the Raman2GO

» For seriously ill patients with infections, fast and effective treatment is essential for survival. Raman spectroscopic methods offer the opportunity to quickly identify pathogens and their resistances. However, they are not yet applicable where they are urgently needed: for the individual care of patients. The Raman2GO closes this gap. It could make a decisive contribution to on-site diagnostics.

Until a few decades ago, Raman spectroscopy systems were expensive and could only be found in well-equipped research laboratories. Since then, the technology has become more compact and even employees who are not specially trained can now perform routine tasks with Raman spectrometers. However, only in the laboratory: miniaturized and at the same time cost-effective Raman spectroscopy systems for patient-oriented diagnostics or on-site analysis in environmental analysis are not yet available.

Raman2GO closes this gap. A matt anthracite cube, compact and transportable, containing a complete Raman spectroscopy system. The system contains: the spectrometer and the light source for excitation, a detector, a universal sample holder as well as optical, optoelectronic and mechanical components. The result of this project is the "Development of a portable Raman spectroscopy system for point-of-care diagnostics in hospitals" (funded by the BMBF) from the InfectoGnostics research campus in Jena.

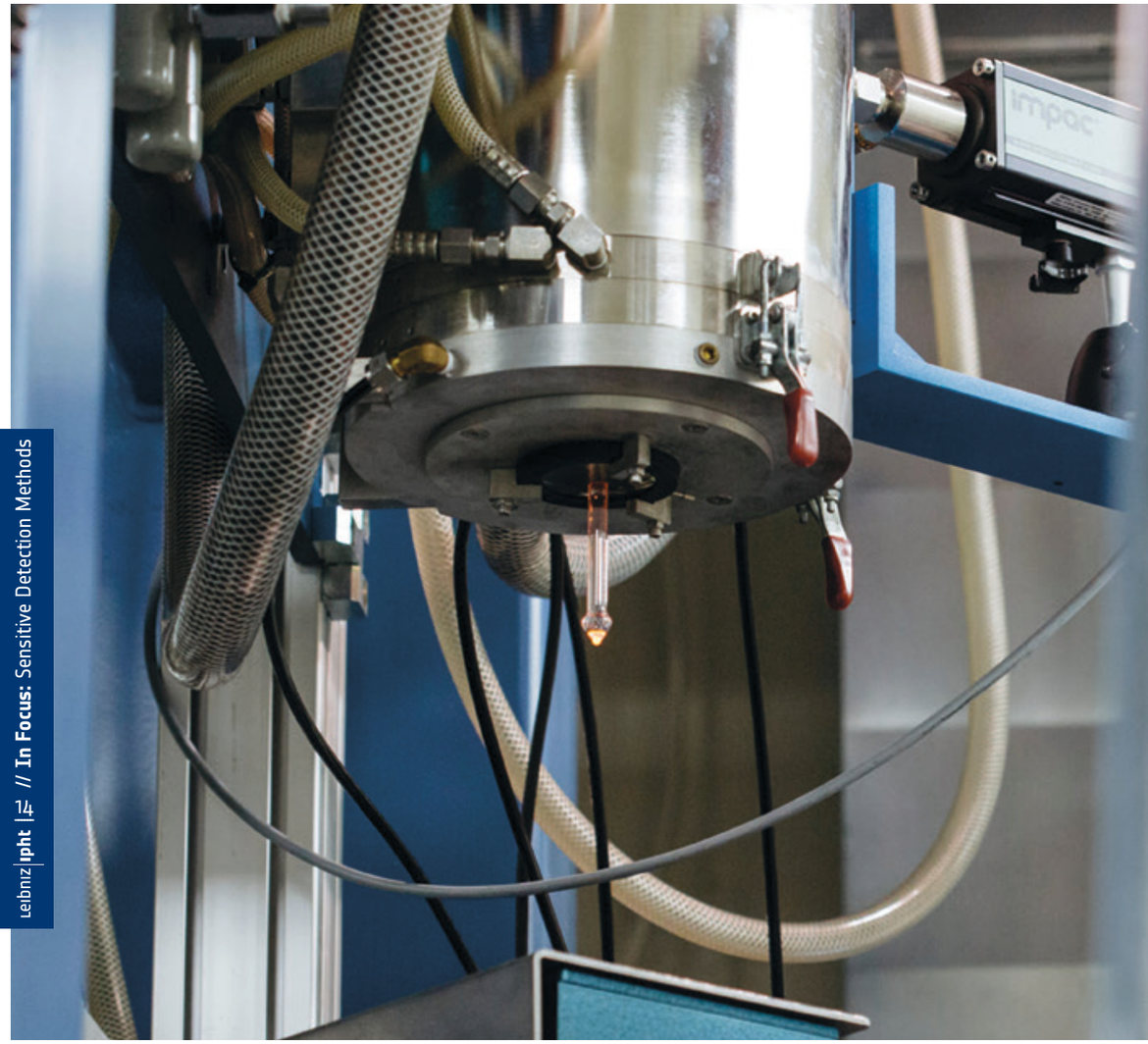
With Raman2GO, patient samples such as blood or urine will be analyzed directly in the clinic and quickly evaluated by automated data analysis. No samples have to be transported. in the household waste "For clinical application, the system must be economical. Therefore, we pay special attention to keeping the procurement and operating costs for Raman2GO as low as possible".

The mobile Raman microspectrometer is the result of years of research, technology development and experience. An optical grating manufactured by electron beam lithography in the clean room of the Leibniz IPHT replaces complex components such as lenses and mirrors. It is part of the researched spectrometer concept that makes Raman2GO compact. Other customized components come from the 3D printer. To produce an adapted miniaturized laser module, is planned with partners from the Ferdinand Braun Institute, with which Leibniz IPHT researches solutions for better medical care of patients in the Leibniz Health Technologies Research Network. The unit, in which the sample is excited with light, is to do without moving parts in order to save time-consuming adjustment.

"The new system for immediate clinical diagnostics should be able to be operated without special technical expertise," explains Karina Weber.

"Nevertheless, the quality of the results must be at least equivalent to conventional laboratory diagnostics." In order to characterize biological samples quickly and accurately, the Raman system must be specific and sensitive, and it is important that the data generated is reproducible and can be transferred to other devices. Together with partners from Jena University Hospital and the Integrated Research and Treatment Center for Sepsis and Sepsis Sequences (CSCC), the Leibniz IPHT research team is testing Raman2GO on samples from immunosuppressed patients. They are particularly susceptible to infections that can lead to pneumonia, for example. Successful treatment depends on doctors determining the pathogen and its resistances at an early stage. With Raman2GO, this could be possible in the future.

Compact and portable: Raman2GO contains a complete confocal Raman spectrometer. It was researched, designed and partly manufactured at Leibniz IPHT. © Leibniz IPHT



© Sven Döring

The fiber technologists Jörg Bierlich and Jens Kobelke draw thin-walled quartz glass capillaries in the fiber drawing plant. As one of only two institutes in Germany, Leibniz IPHT has the know-how to produce hollow core fibers with very complex structures. Together with an outstanding technology base in the fields of system technology, photonic detection, and micro- and nanotechnology, this forms the basis for research into the methods for clinical diagnostics and the investigation of samples of water presented on the following pages.

Trackers

Small quantities with big consequences: How research teams identify the lowest concentrations of biomolecules in our bodies and in our environment

» Does the seriously ill patient receive enough antibiotics? To what extent is the river contaminated with residues of drugs? And how can these questions be answered if the samples are difficult to examine and there is not enough time for a complex diagnostic procedure? Scientists at Leibniz IPHT are researching methods that use light to break down information.

The tiniest amounts of certain substances are enough to upset the ecosystem: such as drug residues that end up in rivers and lakes or even in our drinking water. In patients' body fluids, the concentration of active pharmaceutical ingredients and their metabolic products provides information on whether a treatment is successful. Biologically active molecules such as hormones, antibodies and enzymes in our blood, saliva or urine are indicators for diagnosing diseases.

In order to be able to analyse the tiny amounts in which these molecules are present sensitive detection methods are required which can quickly lead to an accurate result and ideally can be used directly on site. For example, physicians in hospitals could adjust the drug dose directly in order to better protect patients from life-threatening infections.

Precise and sensitive

The challenge: In order to detect the substances using spectroscopic methods, researchers must first isolate them from a complex biological matrix: from blood, saliva or urine samples. Expensive and time-consuming processes in which substances are broken down into their components or enriched and stained.

In contrast, scientists at Leibniz IPHT can use light-based methods such as Raman spectroscopy or absorption spectroscopy to identify the smallest amounts of substances quickly, non-staining and non-destructively. They are investigating chips that capture the bacteria from the sample. They design optical fibers with special properties. And they combine different in-house researched methods into a novel investigation method.

Torsten Frosch and Di Yan from the working group "Fiber Spectroscopic Sensor Technology" analyse the fiber-reinforced detection of antibiotics. © Leibniz IPHT

Tailor-made Treatment

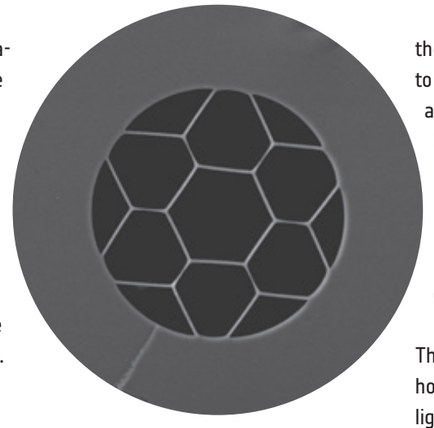
Novel fibers help to determine drug levels

» A network of ultrathin glass membranes surrounds the antibiotic solution in its hollow core with air holes: With the ingenious sensor fiber, even the smallest traces of antibiotics can be detected optically. A team of researchers developed it for patient-oriented diagnostics. In the future, physicians will be able to control which doses patients need.

Every hour that passes before a patient with an infection receives the antibiotic, the patient's risk of dying of sepsis increases. Up to now, it has been difficult to dose this antibiotic exactly as required by the patient. Dosage recommendations result from studies on healthy people or patients with mild infections and cannot be transferred to seriously ill patients.

Determining the drug level using conventional methods such as chromatography and electrophoresis is time-consuming and takes hours or even days. Time that is not there: In patients with sepsis, the way in which their body absorbs drugs can change within hours and cannot be predicted. A rapid procedure to monitor the concentration of antibiotics in the patient's body and adjust the dosage immediately is urgently needed.

Torsten Frosch and his team "Fiber Spectroscopic Sensors" at Leibniz IPHT are investigating a solution that could enable patient-oriented laboratory diagnostics in the future. In cooperation with Mathias Pletz, who is the head of the Institute for Infectious Medicine and Hospital Hygiene at the University Hospital of Jena, they designed a complex fiber sensor to detect the concentration of the antibiotic cefuroxime in urine with Raman spectroscopy.



Microscope image of a hollow core fiber © Leibniz IPHT

"The failure of antibiotic therapy has basically two causes. Either the pathogen is resistant or no effective antibiotic levels are reached at the site of infection because, for example, the dose is incorrect. The determination of antibiotic levels from urine at the point of care could, for example, help to identify the cause of treatment failure in urinary tract infections. The results are very promising and a great motivation for further work."

Prof. Mathias W. Pletz //
Head of the Institute for Infection Medicine and Hospital Hygiene at the University Hospital Jena

The scientists are investigating optical hollow fibers in order to amplify the weak Raman scattering of light at the antibiotic molecules.

They can also use the liquid-filled hollow core fiber, which guides the light with low loss, as a miniaturized sample container. Together with fiber technologists, they developed a new type of hollow core fiber step by step. "This sensor fiber far surpasses the previous possibilities," explains Torsten Frosch, who heads the working group "Fiber Spectroscopic Sensors": "Both in terms of its excellent optical properties, its efficiency and its broadband light guidance, which enables a wide range of wavelengths."

The research team had already shown that fiber-reinforced Raman spectroscopy can reliably detect very low concentrations of antibiotic active substances. The new fiber significantly improved the detection limit – and hereby the chance that the method could in future help patients with infections to receive individualised treatment.

Publications //
Yan et al. (2018), „Fiber-Enhanced Raman Sensing of Cefuroxime in Humane Urine", Analytical Chemistry, 90, 13243–13248, https://DOI: 10.1021/acs.analchem.8b01355 // Yan et al. (2018), „Fiber enhanced Raman Sensing of Levofloxacin by PCF Bandgap-shifting into the Visible Range", Analytical Methods, 10, 586, https://DOI: 10.1039/C7AY02398G

One research department provided the fibers, the other one the chemical expertise: Mona Nissen (left) with Dana Cialla-May. For her research project, Leibniz IPHT awarded Mona Nissen the prize for the best master's thesis. © Sven Döring

How Much Antibiotic is in the River?

Mona Nissen detects drug residues in water

» Drugs are essential to our health. Yet they are becoming a problem for our environment. More and more drug residues end up in our waters. Simple and cost-effective procedures are needed to control water quality. Physicist Mona Nissen combined technologies from Leibniz IPHT into a new method.

Antibiotics, antihypertensives and pain killers: In recent years, scientists have discovered more than 150 active pharmaceutical ingredients in German rivers, streams and lakes, occasionally even in drinking water. The residues, which sewage treatment plants cannot filter out, come from human excreta, from drug residues that are disposed of in drains and toilets or reach the fields via liquid dung and manure from treated farm animals. Even in low concentrations, they impair the fertility of fish or cause antibiotic resistance to pathogenic bacteria to spread further.

"In order to improve the quality of our waters we need highly sensitive methods that are inexpensive and easy to use," explains Mona Nissen, PhD student in the Department of Fiber Photonics at Leibniz IPHT. She looked at what other research teams at the institute were working on – and combined in-house developed technologies into a novel method for detecting drug residues in water. Using UV absorption spectroscopy, she examined water samples for traces of the antibiotic sulfamethoxazole, which is supposed to help against urinary tract infections, and for sodium salicylate, a precursor of the headache drug acetylsalicylic acid.

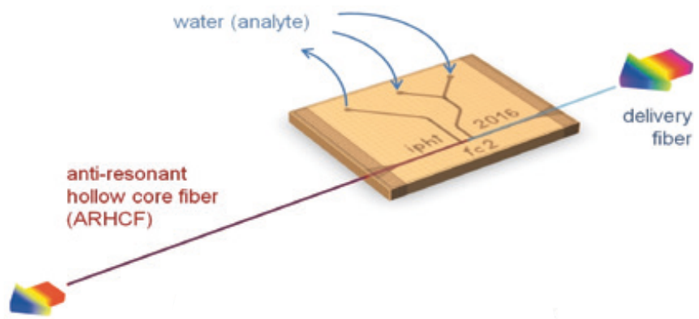
The spectroscopy method takes advantage of the absorption characteristics of many biological substances at wavelengths below 300 nm to determine the amount of a substance contained in a liquid. The highlight: Instead of the usual cuvette, Mona Nissen used a 1 meter long fiber in whose hollow core she filled the liquid. The effect: The distance on which light and matter interact is extended a hundredfold – which in principle makes it possible to detect substances at a hundred times lower concentrations.

"The recording of the UV Vis absorption spectra in a fiber is suitable for detecting impurities in water samples on site."

Dr. Dana Cialla-May //
leads the Jena Biochip Initiative

The solution for guiding the light inside the waveguide filled with water comes from Leibniz IPHT's fiber drawing plant: antiresonant hollow core fibers. They are easy to manufacture, have only a small optical loss and their transmission windows are distributed over a broad spectrum. In this case, they also cover part of the UV range. Because their core is relatively large at about 30 micrometers, the water samples can also be exchanged quickly and easily. But how can this be achieved while at the same time light is coupled into the fiber? – The researchers from the Department of Microfluidics contributed a tailor-made optofluidic chip. Liquid can be pumped into the fiber via the channels of the chip without impairing the light guidance.

Mona Nissen was able to detect the antibiotic sulfamethoxazole up to a concentration of 0.1 µM. This corresponds to ten granules of sugar in a litre of water – pharmaceuticals in our waters are up to ten times more concentrated. Her method is not yet ready for application, classifies the young scientist. However, it delivers accurate results quickly, requires neither time-consuming sample preparation nor bulky equipment – and is thus a building block for a future solution to control the quality of our waters.



UV spectroscopy with a water-filled antiresonant hollow fibre (red), a microfluidic chip and the delivery fiber (blue) into which the light is coupled. © Mona Nissen

Publications //
Nissen et al. (2018), „UV Absorption Spectroscopy in Water-Filled Antiresonant Hollow Core Fibers for Pharmaceutical Detection", Sensors, 18, 478, https://DOI: 10.3390/s18020478

In the clean room of Leibniz IPHT, employees produce tailor-made substrates for optical analysis. © Sven Döring

Well-prepared

How a research team optimizes chips for optical analysis

» In order for Raman spectroscopic methods to be used as rapid tests in hospitals and medical practices, simple strategies are required to prepare the samples. A research team from Leibniz IPHT found a new approach.

A patient's bodily fluids can reveal the type of infection he is suffering from. Susanne Pahlow can quickly and precisely identify the pathogens contained in saliva, blood or urine using Raman spectroscopy. In order to examine real samples with this method, the bacteria must first be isolated from the complex matrix of this sample. The chemist captures the bacteria on a chip whose surface she has previously equipped with special capture molecules. The bacteria are immobilised, the chip is placed under the spectrometer and the bacteria are characterised by Raman spectroscopy.

In the clean room of Leibniz IPHT, the silicon chips are coated with metals such as nickel or aluminium that do not interfere with the spectra of the bacterial cells. Susanne Pahlow has only been able to check whether the biomolecules used to capture the bacteria have actually been applied to them during the measurement. In order to be able to check the quality during the production process, a suitable procedure was lacking.

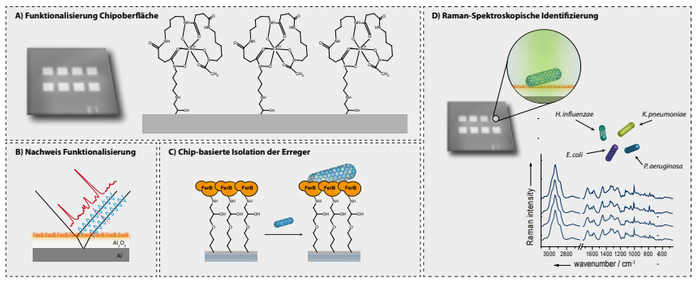
Until, while exchanging ideas with fellow scientist Thomas Mayerhöfer, the following solution came up: Why not use the same tool to monitor substrate production for the investigation? So far, this has failed due to the weak Raman signal of the biomolecules applied to the chip. In order to reinforce this, the research team used interference effects that occur when the smooth, highly reflective aluminium surface of the chip is modified. They prepared them with thin layers of aluminum oxide. The effect: The Raman signal of the molecules can be amplified or attenuated controllably.

For the first time, the scientists succeeded in using interference enhanced Raman scattering (IERS) to detect biomolecules whose signals would otherwise be too weak. To date, IERS has mainly been used for inorganic or organometallic materials.

Depending on the thickness of the aluminum oxide layer, the chips shimmer in different colors. © Sven Döring

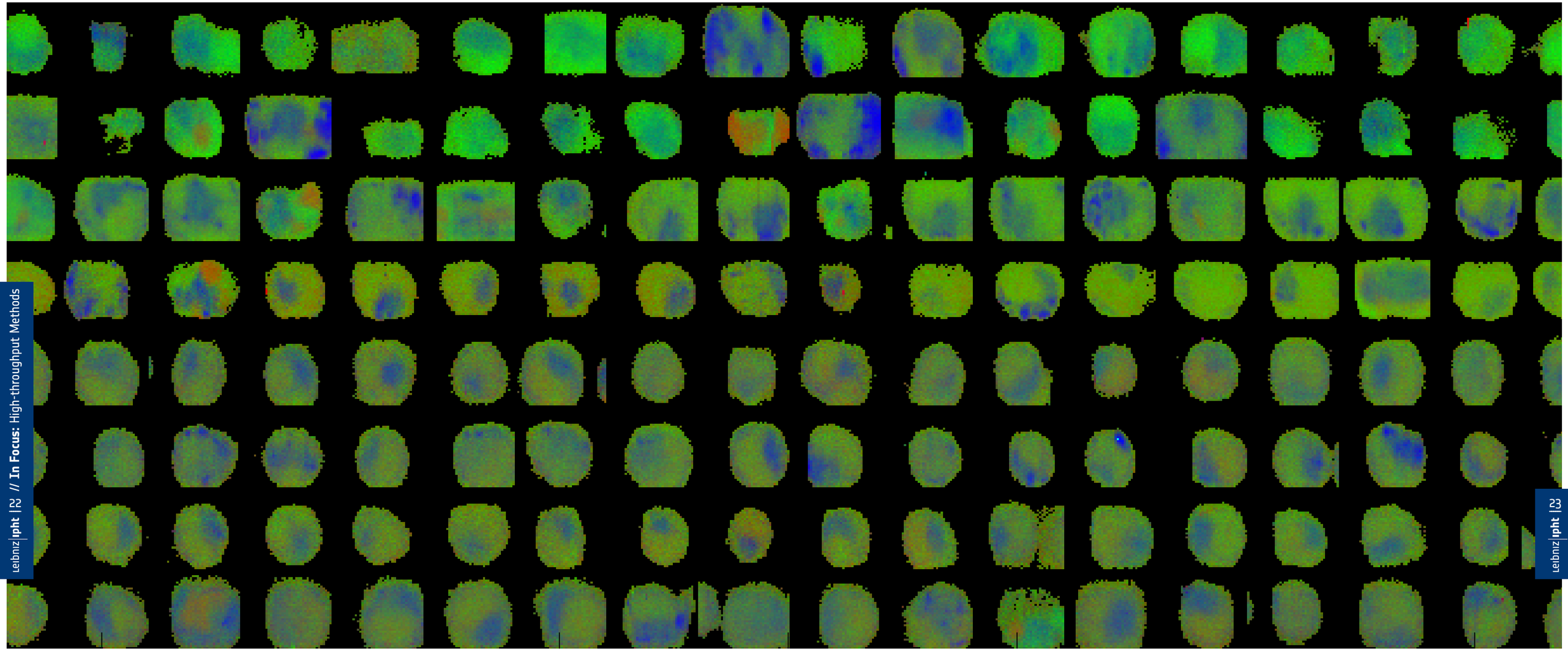
In contrast to surface-enhanced Raman spectroscopy (SERS) – the much more common technique – to amplify the weak Raman scattering – IERS substrates allow a homogeneous but less pronounced amplification of the signal over the entire surface. "One can compare the effect with the illumination by different light sources. While with SERS you can aim very bright lights at certain points just like with a flashlight, IERS provides a weaker but even illumination, i.e. rather like a street lamp", explains Thomas Mayerhöfer.

IERS substrates are easier to produce and remain stable for a long time. Susanne Pahlow believes that there is great potential to use this technology in the future for quality control in chip-based sample preparation for Raman spectroscopy. She is currently testing the method with other molecules and bacteria. "The results form a very good basis for our further research work".



Whether the capture molecules have been successfully applied to the chip (Figure A) can be checked using interference-enhanced Raman spectroscopy (B). The pathogens are then immobilised on the chip and characterised by Raman spectroscopy (C and D). © Susanne Pahlow

Publications //
Pahlow et al. (2018), „Interference-Enhanced Raman Spectroscopy as a Promising Tool for the Detection of Biomolecules on Raman-Compatible Surfaces", Analytical Chemistry, 90, 9025-9032, https://DOI: 10.1021/acs.analchem.8b01234



Molecular fingerprint information of cells, determined with Raman spectroscopic methods. The RGB-coded images show the macro-molecular distribution of proteins, nucleic acids and lipids. Some of the cells are treated with pharmacological substances and show significant changes.

Thousands at One Blow

Optical methods detect cells and pollen at high throughput rates

» The more doctors know about the state of health of their patients, the more individually they can respond to them in their treatment. This information must be precise and meaningful and the examination methods must be so sophisticated that they filter out what is important – even when it comes to detecting cells that are as rare as a needle in a haystack. In clinical routine, this is often impossible or can only be realized with great effort. Scientists at Leibniz IPHT are investigating solutions that can spare this time: with intelligent systems that open up high-throughput analysis for optical methods.

For physicians, precise observation has always been the basis for making a diagnosis. The more precise and the earlier doctors make their diagnoses, the more targeted their treatment can be. Body fluids contain information. They reveal, for example, whether a tumor has already metastasized or whether a cancer therapy is effective. Circulating tumour cells in the blood can be an indicator of this.

In this case, precise observation means: to record more quickly than laboratory staff can routinely detect. Circulating tumour cells, for example, are relatively rare in the blood. Previous methods yield too little, are not specific enough or destroy the cells.

Research teams at Leibniz IPHT are developing optical spectroscopic methods with which they can quickly and reliably analyse cells and bioparticles in high throughput.

A microfluidic chip takes over the function of a miniature laboratory, artificial neural networks automatically evaluate captured data, and chemometric methods extract the maximum amount of information from them.

Simple and accurate

With the RamanCellAssay® platform, Raman spectroscopy can be used for the first time for high-throughput analyses. This makes it possible to identify tens of thousands of cells using their molecular fingerprints, including circulating tumor cells.

Another example: a microfluidic chip automatically identifies thousands of pollen in one go. This takes only a few seconds. For comparison: For pollen flight predictions, pollen is currently captured on adhesive foils and counted under the microscope.

The optical detection methods do not require time-consuming sample preparation. That makes them fast. Automated and digitized approaches make them efficient and also help to avoid sources of error and routine errors and at the same time reduce costs.

This is where the pollen buzz: Scientist Andreas Kleiber explains to Klaudia Remus from the German Bee Museum in Weimar how he can determine several thousand pollen at once with the microfluidic chip under his experimental setup. © Sven Döring

There's Something in the Air

Microfluidics meets Artificial Intelligence: Andreas Kleiber analyses pollen at high speed

» Birch, hazel or alder: As soon as the first pollen fly, people with allergies suffer. To protect themselves, they need to know what invisible pollen particles they are dealing with. Andreas Kleiber can answer this question: He uses a chip to capture several thousand pollen particles in high-resolution microscopic images. Neuronal networks process the images and classify the particles – a few seconds later, the result is there.

The grass under the apple tree glitters in the late summer sun. All around, wild flowers sprout, from which it quietly hums. In the garden of the German Bee Museum in Weimar, bees find plenty of food. The carefully inscribed labels read: wild mallow and marigolds, columbine, chamomile and lavender. Which of these end up in honey is unknown to Klaudia Remus. When the beekeeper wants to find out what her honey consists of, she counts pollen under the microscope. When Andreas Kleiber wants to find out which flowers provided the nectar for Mrs. Remus' honey, he puts a stamp-sized chip in front of a camera with a microscope lens and opens his laptop. A few moments later – and the scientist knows what kind of pollen his sample contains. Andreas Kleiber is a doctoral student at Leibniz IPHT and has designed a chip that works like a miniature laboratory. It enables high-resolution microscopic images of several thousand pollen particles in just a few seconds. Neural networks identify which species they belong to. The hit rate: almost 100 percent.

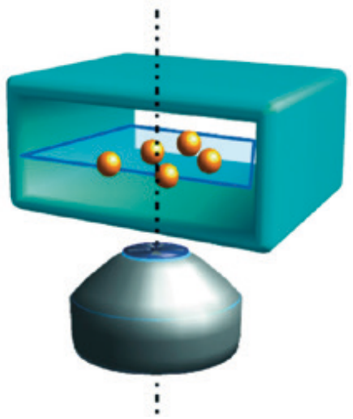
With this technology, Andreas Kleiber can automatically analyse large quantities of bioparticles in the shortest possible time. Up to 100 pollen per second flow past a viewing window on his chip in a narrow channel. Each of the tiny granules is captured by a digital camera through a microscope lens. In order to obtain sharp images for data processing, Andreas Kleiber and the Leibniz IPHT research team mastered a technological challenge. The particles must flow through the liquid channel exactly in the focal plane of the objective. Which is not even a hundredth of a millimeter narrow.

A chip as a miniature laboratory

The solution: an ingenious design that Leibniz IPHT has already patented. "As with a nozzle, we compress the particle flow with two liquid streams from the sides to form a vertical lamella and rotate it 90 degrees into a plane," explains the scientist. The research team can precisely control how thick this layer is and where it runs. They can arrange the particles in such a way that they cross the image field of the camera in a row – and let them rotate in a controlled manner. This provides 3D image information about the outer shape and structure of the pollen grain and makes identification more reliable. To evaluate the images, Andreas Kleiber uses programs for particle tracking and feature selection. A neural network, which he has trained beforehand, assigns the images to the respective pollen species based on the extracted data – and is correct in more than 98 percent of cases.

Andreas Kleiber tested his method on highly allergenic pollen species. This provides beekeepers with an instrument for quality control and is a ray of hope for pollen allergy sufferers. They can avoid allergic reactions if they know what is in the air. They are currently learning this from pollen flight forecasts, the result of a lengthy evaluation of pollen captured on adhesive foils.

But even this is just one of many applications, because the chip design is flexible. "Basically," says Andreas Kleiber, "we can use it to analyze anything smaller than 40 micrometers." For example, white blood cells – which Andreas Kleiber is already researching with the "Clinical Spectroscopic Diagnostics" team at Leibniz IPHT.



The special arrangement of the microfluidic channels makes it possible to align all particles in the focal plane. © Thomas Henkel

Patent //
T. Henkel: Fluid rotation apparatus and method, DE 10 2015 115 343 B4 (26.10.2017), WO/2017/041785 A1

Iwan Schie and his team are researching new optical devices to diagnose diseases. © Sven Döring

One Device for Several Applications

Tens of thousands of cells are automatically analyzed for the first time

» Raman spectroscopic techniques reveal the molecular fingerprints of cells. They are fast, precise and label-free – but have so far failed high-throughput analyses for clinical use. The RamanCellAssay® is changing this: machine and deep learning techniques interpret the results and provide evidence to track down diseases.

For cancer patients, it is crucial that they receive the treatment that helps them best. Circulating tumour cells provide information on how the disease progresses and how a therapy works. They spread in the bloodstream and can develop into metastases. New methods for reliably identifying circulating tumour cells are therefore urgently needed in order to better understand cancer and increase patients' chances of survival.

The RamanCellAssay® platform of the Leibniz IPHT team enables the characterization of thousands of cells in a very short time and thus sets new standards for the high-throughput application of Raman spectroscopy. © Leibniz-IPHT

A team of scientists from Leibniz IPHT has now researched a system with which tens of thousands of cells can be characterised quickly, easily, and label-free using their molecular fingerprints – tested on circulating tumour cells in the blood, among other things. The RamanCellAssay® platform makes it possible for the first time to use Raman spectroscopic methods for high-throughput analyses of living cells as well as for mixed cell populations. The system can be combined with common Raman devices and could thus contribute to the spectroscopy method becoming a standard tool in clinical diagnostics and cell research.

It offers decisive advantages over methods that currently represent the gold standard. Hidden infections or undiagnosed diseases are usually detected using fluorescence-based approaches. The time-consuming sample preparation, however, costs valuable time and the fluorescent labels can damage cells and tissue. However, it is particularly important for tumour cells to remain cultivable and still be available for subsequent examinations, for example to detect mutations. Current methods for identifying the rare cells, are only approved for a few types of cancer, provide a low yield or too little specific information.

Raman spectroscopy, on the other hand, can be used to classify cells using the chemical information from their spectra. One limitation was that experiments and analyses required a lot of time and qualified personnel – but real applications require the reliable statistical evaluation of a large amount of data and the measurement of many thousands of cells.

The RamanCellAssay® overcomes this obstacle. The platform combines automated microscopic imaging methods with Raman spectroscopy. In this way, entire series of experiments can be carried out in a short time without personnel having to intervene. In detail: The RamanCellAssay® records the spectra of more than 100,000 individual cells and enables fully automated sampling of 1,000 individual cells in less than 20 minutes. The spectra are evaluated, assigned, and the results can be read.

The RamanCellAssay® provides a platform for high-throughput cell analysis – without preparation and for a variety of label-free diagnostic applications: to identify tumor cells or stem cells, to demonstrate the effect of drugs, to non-destructively analyze artificially cultured tissue or for differential blood imaging. A clinical study in sepsis patients as part of the European research project "Hemospec", which aims to develop a device for sepsis diagnosis, as well as other applications, have already achieved positive results.

Publications //
Schie et al. (2018), „High-Throughput Screening Raman Spectroscopy Platform for Label-Free Cellomics", Analytical Chemistry, 90, 3, https://DOI: 10.1021/acs.analchem.7b04127 // Rüger et al. (2018), Markierungsfreies Hochdurchsatz-screening mit Raman-Spektroskopie", BIOspektrum, 05.18, 24. Jg., https://DOI: 10.1007/s12268-018-0952-3

Maria Chernysheva establishes the junior research group for ultra-short pulse fiber lasers at Leibniz IPHT. © Sven Döring

“Be Persistent in What You Want”

Maria Chernysheva is one of the few women to research ultrafast fiber lasers. She does not believe that it is therefore necessary to protect her like an endangered animal species though.

» It is two days ago, that the head of the new junior research group for ultrafast fiber lasers started at Leibniz IPHT – “10 time zones away from the beginning of my studies,” says Maria Chernysheva and laughs. That was in Khabarovsk, in the far east of Russia, not far from China. Her next stations: Moscow and Birmingham. The last experiments at Aston University she is still managing via Skype conference. She has already found an apartment in her new home and a place at the International School in Weimar for her four-year-old daughter. At Leibniz IPHT, Maria Chernysheva plans to investigate novel ultrafast fiber lasers that will be used in infrared spectroscopy for cancer diagnostics. Would she like to tell us how she makes her career as a young scientist? Sure. Which version, “the scary one or the softened one”?

Mrs. Chernysheva, only one in ten in the photonics industry in Europe is a woman. Are you passed around a lot as a role model?

Quite, yes (laughs). I am always one of those invited to conferences and workshops by women's associations to tell how stony her career path was.

How stony was it?

In fact, I have mixed feelings about this gender issue. Every woman who chooses an engineering science knows what she is getting into. She knows that she will be in the minority – but also that there are advantages to being a woman. It is not that you have to worry about us like you do about an endangered species.

How was it with you?

I always wanted to do something with technology. Shortly before my diploma as telecommunications engineer I went to Moscow, to the Research Center for Fiber Optics of the Russian Academy of Sciences, first for an internship, then for my diploma project. Thereupon I was offered the opportunity to start my thesis there. But when I wanted to start, I was told: “We'll take you – but only on one condition: you'll work with a man”.

I beg your pardon? They didn't want to hire you alone?

No. Ten years ago they still thought it risky to employ women because they didn't believe that they would complete their doctorate. They could go on parental leave and not come back. I was only the second doctoral student at that time.

And did you find a colleague?

Fortunately, someone from my course also wanted to go to Moscow, yes. In the end, I even surpassed my goal and they hired two men: One of them later decided that science was not for him and dropped out. The other completed his doctorate and embarked on a scientific career.

Just like you. So what happened next?

During my doctorate in laser physics I took part in a scientific conference and learned what it's all about: gaining experience and networking. And I thought: I want to try it out. I looked for the conference with the next deadline, that was another two days. I wrote a proposal, got the OK from my supervisor, applied – and travelled to the USA for the first time in my life.

After graduating, you went to England.

Yes, I had an invitation for an internship in the USA, but by the time I had the money, the deadlines had passed. At that time, my future professor at Aston University invited me to continue my research there. I first worked as a research assistant, then with a Marie Curie fellowship from the EU Commission and then with a fellowship from the Royal Academy of Engineers. From there I moved here to the Leibniz IPHT.

... which you got to know at the international workshop "Women in Photonics" ...

... yes exactly. I have never been in a workshop with so many women (laughs).

A good experience?

The workshop was useful, in any case. But as I said, for me the topic of gender justice is double-edged. I know that women have to fight prejudices, that they are paid less according to statistics and that they sometimes have a harder time progressing with their careers than men. On the other hand, every woman knows what possibilities she has: that she gets more attention at conferences, that the organising committees are looking for a balance between women and men. There are many possibilities: Scholarships especially for women and those for a better work-life balance. Thanks to the support of institutions such as the European Commission, there are more opportunities than disadvantages.

What kind of tips do you give pupils and students?

Networking. All my possibilities only arose because I took part in conferences, talked to people, asked them about possibilities at their institutes. Equally important: family support. I moved to England with my husband Sergey. He gave up his doctorate in Russia and started all over again in England – because my career was just developing. Unfortunately, he then moved to Scotland, and I stayed in England with our one-year-old daughter. Sergey always supported me and he encouraged me to apply for scholarships. This brings me to my third tip: you have to be persistent in what you want.

Also in organizing research and family time. How do you manage that?

When my daughter was nine months old, she went to the nursery. I wanted to get back to work again. When she was asleep, I was writing – papers, reviews, scholarship applications. Friday to Sunday Sergey was at home, these were my laboratory days. When he then followed Tomáš Čižmár to Jena, it became more complicated, of course. He could only come every two weeks. But our daughter was already older. She is now four and is a great helper. Now that we live together again, it gets easier again.

What convinced you as a researcher to apply for Leibniz IPHT?

I'm working on ultrafast fiber lasers. Leibniz IPHT gives me the opportunity to research such fiber lasers and also apply them, for example in diagnostics. I'm very interested in that. The institute covers all stages of technology: from the production of fiber preforms to the research of lasers and other photonic technologies and their application. This last step into the application has been missing at my previous institutes. The combination distinguishes Leibniz IPHT from others.

What do you want to achieve with your research?

That the lasers I develop will actually be used, for example in the spectroscopic diagnosis of cancer or in surgery. I don't have one specific application in mind. If you think of research as a bowl of water in which every researcher adds a drop: Then I would like to be an important drop in this bowl.

More about the work of Maria Chernysheva's junior research group can be found at **www.leibniz-ipht.de/en/research-units/junior-research-groups/ultrafast-fiber-lasers/overview.html**

© Leibniz IPHT

Female Experts for Photonics

Young women researchers established relationships with Jena

» The photonics industry is growing and is a focal point in the European research landscape. More and more graduates come from universities – but are still underrepresented at the management level of research institutes and high-tech corporations. To change this, Leibniz IPHT launched the international career workshop "Women in Photonics".

Jena radiates: Young female scientists from four continents accepted Leibniz IPHT's invitation to the first international career workshop "Women in Photonics" from April 17 to 19, 2018. The institute thus gave excellent female photonics researchers an impulse to network better – among themselves and with executives from research institutions and companies.

"I am convinced that the young women scientists will use the experiences from this workshop for their careers. They learned a lot here for their professional and private lives."

Prof. Katarina Svanberg //
Lund University & former President of SPIE

A mentoring program in three days: "The participants exchanged ideas with experienced colleagues and were able to jointly develop strategies for a successful career," reports Ute Neugebauer. The professor herself started as a junior researcher at Leibniz IPHT. Today, she is a vice scientific director and belongs to the leadership team.

"Our goal is to involve young female researchers more closely in the scientific community," emphasizes Jürgen Popp, scientific director of the institute. Jena as an international research and industrial center for optics and photonics is proving to be an ideal location. The 40 participants with doctorates from Europe, Brazil, the USA, Canada and Australia exchanged about personal career paths with female researchers and female executives from Carl Zeiss, Jenoptik and Asphericon. The workshop was supported by Friedrich Schiller University, the Fraunhofer Institute for Optics and Precision Engineering, many regional companies, and "The Optical Society of America" (OSA) and "The International Society for Optics and Photonics" (SPIE).

The female scientists used this opportunity not least to present their own research. Their topics ranged from research into ultrafast fiber lasers and fluorescence lifetime microscopy to light-based therapies against cancer. "By enabling excellent female scientists to establish their own research topic, we can make an academic career or an industrial perspective more attractive for them," said Jürgen Popp. Although more and more well-educated female scientists come from universities, they are still underrepresented at the management level in research and high-tech industry. For Jürgen Popp, promoting the careers of women is therefore a clear goal.

Jan Rüger, Eliana Cordero Bautista, Eric Boateng and Wei Yang are doctoral students at Leibniz IPHT. © Sven Döring

From the World to the Beutenberg

How Leibniz IPHT is living Welcome Culture

» The world of science is international – and so is Leibniz IPHT. Researchers from China, India, the Czech Republic or Ghana come to Jena and enrich the scientific cooperation at the institute. To make them feel at home, Leibniz IPHT staff members try to make their start easier with a variety of measures – which of course also apply to newcomers from Castrop-Rauxel or Wuppertal.

Selamat datang di institut – ¡Bienvenido al instituto! – Üdvözöljük az intézetben – Bienvenue à l'institut – Willkommen am Institut – Welcome to the institute! That was: Indonesian, Spanish, Hungarian, French, German and English. Or also: only a small selection of the languages spoken by the staff at Leibniz IPHT. From from 32 nations came the people who were permanently employed at the institute in 2018 as doctoral students and guest researchers.

There are also guests from all over the world. Leibniz IPHT is committed to creating an international environment characterized by openness, tolerance, responsibility, solidarity and diversity. The foundation for this is laid by an living welcome culture.

"I immediately felt welcome at the institute – especially because of my colleagues. We exchange a lot of ideas among ourselves. That makes it easy for me to integrate."

Eliana Cordero Bautista //
comes from Colombia and is doing her doctorate in the research department Spectroscopy / Imaging

This starts with the lingua franca: In addition to German, English is also spoken at the Institute as a matter of course. All important documents are bilingual; a simultaneous interpreter translates at the staff meeting. And if you are new, you will be provided with Welcome Guides.

They know where which laboratory is, how to handle complicated forms and how to find a parking space on the Beutenberg Campus and an apartment in Jena.

Outstanding Personnel

3rd Prize of the Berthold Leibinger Innovation Award for Applied Laser Technology
for the Rapid Determination of Resistances, RamanBioAssay®
to Ute Neugebauer and Jürgen Popp

Kaiser Friedrich Prize
for Optical Rapid Method for the Diagnosis of Cancerous Tissue
to Jürgen Popp, Thomas Bocklitz, Tobias Meyer, Orlando Guntinas-Lichius, Andreas Tünnermann, Jens Limpert, Thomas Gottschall, Michael Schmitt

Raman Award for the Best Junior Researcher
for Outstanding Research in the Field of Raman Spectroscopy
to Marie Richard-Lacroix

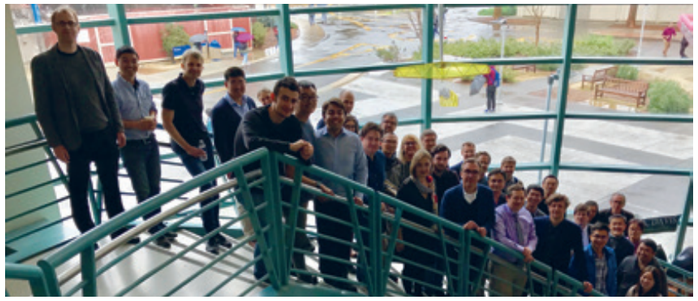
Ioannes Marcus Marci Medal
for Outstanding Contributions in the Field of Spectroscopy
to Jürgen Popp

Forcheurs Jean-Marie Lehn
for Outstanding Collaboration in the Field of Artificial Photosynthesis
to Benjamin Dietzek and Vincent Artero

Exchange of Ideas Across the Atlantic

JeDis Alliance explores new approaches for the diagnosis of cancer and infectious diseases

» Light as a research topic brings together scientists from clinics and technology development on both sides of the Atlantic. Teams from Leibniz IPHT and the University of California, Davis, are working together to advance the development of new biophotonic technologies and processes. The basis for this is provided by an excellent training and exchange programme and a joint research laboratory.



Jena research team visited UC Davis in March 2019 © Leibniz IPHT

"JeDis offered me an ideal environment to explore a field of regenerative medicine: Artificial tissue cultivation using fluorescence lifetime microscopy. I learned from experts and expanded my focus. I am very grateful for that."

Abdullah Saif Mondol //
does his PhD in the research department "Spectroscopy / Imaging" and stayed for one month at UC Davis

"In order to solve global problems in medicine and the life sciences, we urgently need to exchange ideas," says Laura Marcu: "about innovations in biophotonics". The professor teaches at the North American University of California, Davis (UC Davis), and coordinates the transatlantic consortium JeDis together with Jürgen Popp. In the Jena Davis Alliance of Excellence in Biophotonics, scientists from Leibniz IPHT, Friedrich Schiller University, Jena, and UC Davis have been networking since January 2018. Together, research teams from hospitals and technology development want to push the development of new biophotonic technologies and processes.

"One focus of our research is the spectroscopic diagnosis of cancer," explains Jürgen Popp. "We are combining UC Davis' expertise in fluorescence lifetime imaging with Leibniz IPHT's expertise in Raman spectroscopy to create new tools for tumor edge detection and tumor classification.

In order to expand the competence in Raman spectroscopy for clinical diagnostics, a joint research laboratory will be established at UC Davis: the "Biomedical Engineering and Comprehensive Cancer Center".

JeDis offers young scientists a top-class training and exchange program to promote long-term cooperation. This will lay the foundation for a future international graduate school in which 15 doctoral students from Jena and Davis will research biophotonic issues.

One step towards this goal was the first JeDis Summer School in September 2018 in Jena with 20 PhD students from Jena and Davis. The second edition will take place in Davis in 2019. JeDis is funded over three years within the framework of the Transatlantic Programme of the Federal Republic of Germany.

The cubes of the optical construction kit, which René Richter (left) and Benedict Diederich are investigating, can be playfully combined – whether to a telescope, a chemical workbench, a pen holder or to observe living cells in an incubator. © Sven Döring

You can find out more about the project at: **useetoo.org**, the sources for the construction kit at: **github.com/bionanoimaging/UC2-GIT.**

"Anyone Can Build a Microscopy System"

Benedict Diederich and René Richter researched a construction kit with which researchers and hobbyists can design creative optical solutions.

» The cubes can be magnetically clicked together and combined as desired: with lenses, mirrors or displays – to form a magnifying glass, a telescope or a microscope. UC2 – You see, too – is what Benedict Diederich and René Richter from Leibniz IPHT and their doctoral colleague Swen Carlstedt from Jena University Hospital call their optical construction kit. And they want to say: Everyone can see. Hobbyists can use it to build a fully automatic fluorescence microscope for less than 250 euros. For example. Technophile "makers" assemble the cubes from the 3D printer into ever new structures. A pupil uses them to write his school-leaving thesis on microscopy. In addition, the scientists work together with the University Hospital and Jena schools. The idea is spreading – and this is exactly the plan behind UC2: the more there are, the more new ideas.

Mr. Diederich and Mr. Richter, with your system you can turn a mobile phone into a high-performance microscope. How does it work?

We have developed a modular optical construction kit from a small craft project – which can be connected to the camera of a smartphone, for example. We use image-processing algorithms to achieve good results with inexpensive components such as lenses from the student construction kit or simple video projectors as lighting units. We implement some of these algorithms on mobile phones, thus compensating for the inadequacies of the components. We have also experimented with lighting techniques and built an intelligent lighting system that optimally enhances the contrast of the sample. To do this, we analyze the image data of the samples live on the mobile phone using machine learning techniques and then project a new pattern into the rear focal plane of the imaging optics using a projector.

What microscopy methods are possible?

You can start with a 2D telescope setup. If you bring the 3rd dimension into play, you can easily build a transmission or fluorescence microscope. A few clicks and you get a light sheet microscope. All is connected and can be transferred into each other. This is the highlight of the modular system. We have developed algorithms for mobile phones that enable a variety of methods and techniques in computer-based microscopy.

To what else can I combine the building blocks?

Basically, to everything. The form is fixed, but size and material are not. In this way, the system can be scaled and adapted to one's own wishes. Whether for microscopes, telescopes, pen holders, chemical workbenches or Raman spectroscopy.

Is the system already used for other research projects at Leibniz IPHT?

For system integration, we are investigating a device that can image E. coli bacteria with a simple structure. In addition, the expertise in optics and device development complement each other. The first prototypes to observe the morphology of bacteria on an electrophoresis chip have already been developed with the UC2 system. UC2 is also used in the incubator to measure living cells over a period of up to one week. It is ideally suited for biolabs with special hygiene regulations: Instead of having the device cleaned in a time-consuming process, it can simply be disposed of after the experiment.

However, they are not only aimed at scientists ...

Exactly, our goal is to get more people interested in optics, even those beyond the well-equipped laboratories. That's why we're lowering the hurdles: with optical components you can afford. Following the example of the microprocessor unit Arduino or the simple computer Raspberry Pi, we disclose sources and documentation and hope that our system will spread as quickly as possible within the open source community. This would enable everyone in the world to build a microscopy system using simple means – including developers, hobbyists and researchers from other disciplines. This would generate completely new ideas: The more people participate, the greater the opportunities.

Publications //
Diederich et al. (2018), „Using Machine-learning to Optimize Phase Contrast in a Low-cost Cellphone Microscope", PLoS ONE 13(3): e0192937, https://DOI:10.1371/journal.pone.0192937 // Diederich et al. (2018), „cellSTORM – Cost-effective Super-resolution on a Cellphone Using dSTORM", PLoS ONE 14(1): e0209827, https://DOI:10.1371/journal.pone.0209827

Publications with Special Impact in 2018

Three-dimensional holographic optical manipulation through a high-numerical-aperture soft-glass multimode fiber

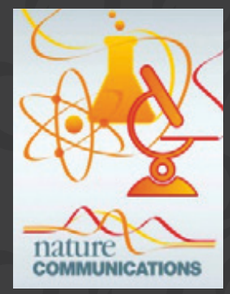
I. T. Leite // S. Turtaev // X. Jiang // M. Šiler // A. Cuschieri // P. St. J. Russell // T. Čižmár

Nature Photonics 12 (1), 33 (2018)

Thermodynamic control of soliton dynamics in liquid-core fibers

M. Chemnitz // R. Scheibinger // Ch. Gaida // M. Gebhardt // F. Stutzki // S. Pumpe // J. Kobelke // A. Tünnermann // J. Limpert // M. A. Schmidt

Optica 5 (6), 695 (2018)



Analytic mode normalization for the Kerr nonlinearity parameter: Prediction of nonlinear gain for leaky modes

I. Allayarov // S. Upendar // M. A. Schmidt // T. Weiss

Physical Review Letters 121 (21), 213905 (2018)

Robustness of Light-Transport Processes to Bending Deformations in Graded-Index Multimode Waveguides

D. E. Boonzajer Flaes // J. Stopka // S. Turtaev // J. F. De Boer // T. Tyc // T. Čižmár

Physical Review Letters 120 (23), 233901 (2018)

Controlling Intermolecular Interactions at Interfaces: Case of Supramolecular Tuning of Fullerene's Electronic Structure

S. K. Das // J. Plentz // U. Brückner // M. von der Lühe // O. Eckhard // H. Schacher // E. Täuscher // U. Ritter // G. Andrä // B. Dietzek // M. Presselt

Advanced Energy Materials 8 (32), 1801737 (2018)

Lateral heterostructures of two-dimensional materials by electron-beam induced stitching

A. Winter // A. George // Ch. Neumann // Z. Tang // M. J. Mohn // J. Biskupek // N. Masurkar // A. Leela // M. Reddy // T. Weimann // U. Hübner // U. Kaise // A. Turchanin

Carbon 128, 106 (2018)

PHYSICAL REVIEW LETTERS

Magnetically induced transparency of a quantum metamaterial composed of twin flux qubits

K. Shulga // E. I'lichev // I. S. Besedin // S. Butz // O. Astafiev, // U. Hübner // A. V. Usitnov

Nature Communications 9, 150-1 (2018)

Electron transfer in a covalent dye–cobalt catalyst assembly – a transient absorption spectro-electrochemistry perspective

S. Bold // L. Zedler // Y. Zhang // J. Massin // V. Artero // M. Chavarot-Kerlidou // B. Dietzek

Chemical Communications 54, 10594 (2018)

Simple ciprofloxacin resistance test and determination of minimal inhibitory concentration (MIC) within two hours using Raman spectroscopy

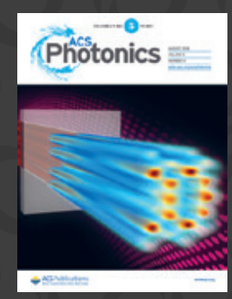
J. Kirchhoff // U. Glaser // J. A. Bohnert // M. W. Pletz // J. Popp // U. Neugebauer

Analytical Chemistry 90 (3), 1811 (2018)

High Throughput Screening Raman Spectroscopy Platform for Label Free Cellomics

I. W. Schie // J. Rüger // A. S. Mondol // A. Ramoji, // U. Neugebauer // Ch. Krafft // J. Popp

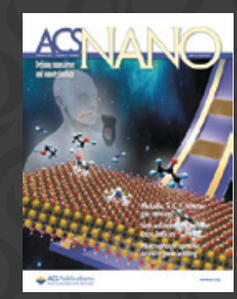
Analytical Chemistry 90 (3), 2023 (2018)



Slit-Enhanced Chiral- and Broadband Infrared Ultra-Sensing

R. Knipper // T. G. Mayerhöfer // V. Kopecký, Jr. // U. Hübner // J. Popp

ACS Photonics 5 (8), 3238 (2018)



Protein Handshake on the Nanoscale: How Albumin and Hemoglobin Self-Assemble into Nanohybrid Fibers

Ch. Helbing // T. Deckert-Gaudig // I. Firkowska-Boden // G. Wei // V. Deckert // K. D. Jandt

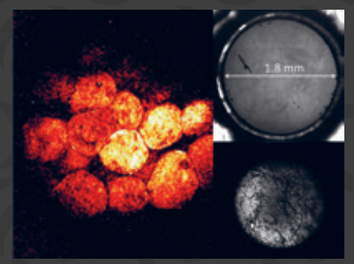
ACS Nano 12 (2), 1211 (2018)

Scientific Articles in the App

Biophotonics

» *The research focus Biophotonics researches and implements innovative photonic methods and tools for molecular spectroscopy and hyperspectral imaging, high-resolution light microscopy as well as fiber-, chip- and nanoparticle-based analytics and diagnostics with the highest specificity, sensitivity and resolution, integrating technology research in fiber optics and photonic detection.*

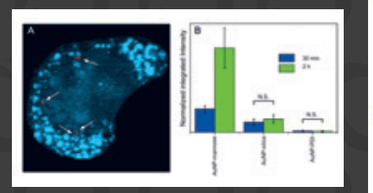
CARS Endoscope Used for Imaging in Medicine



Left: Adipocytes. Top right: GRIN lens. Lower left: CARS image of brain tissue at 2850 cm^{-1}.
© Leibniz IPHT

P. Zirak // G. Matz // B. Messerschmidt // T. Meyer // M. Schmitt // J. Popp // O. Uckermann // R. Galli // M. Kirsch // M. J. Winterhalder // A. Zumbusch

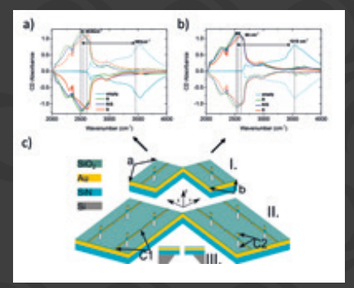
Towards SERS-based Detection of Dangerous Atherosclerotic Plaques



1A. False color Raman image of the distribution of SERS tags within the macrophage cell; 1B. A semi-quantitative estimate of the uptake of three types of SERS tags by macrophages: bare gold nanoparticles carrying only PDI (AuNP-PDI), silica coated SERS tags (AuNP silica), and mannose functionalized SERS tags (AuNP mannose). © Leibniz IPHT

D. Cialla-May // V. Dugandzic

Substrates for Plasmon-enhanced VCD Spectroscopy



Substrates for the plasmonic amplification of chiral effects a) spectra of substrates filled with analyte with a smaller slit turned to the left b) ditto, but with the slit turned to the right c) structure of substrates. © Leibniz IPHT

T. Mayerhoefer // R. Knipper

Coherent Anti-Stokes Raman and Spontaneous Raman Microscopy Investigate Microalgal Carotenoid Content

C. Krafft // M. Schmitt // J. Rüger // F. B. Legesse // T. Meyer // J. Popp

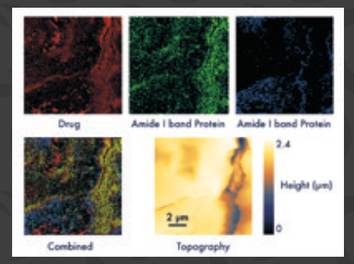
Identification of Exacerbation-relevant Fungal Spores in Chronic Respiratory Diseases using UV-Raman Spectroscopy

K. Weber // O. Zukovskaja

Degradation of Model Pollutants in Gas Phase by Plasmonic Catalysis on Gold Nanoparticles

A. Csaki // L. Stolle // A. Stolle // F. Garwe // T. Krech // B. Oberleiter // T. Rainer // W. Fritzsche

Nanochemical Imaging for Supporting Theranostics



PiFM investigation of liver tissue using three different IR excitation frequencies. Top row: PiFM contrasts obtained at a frequency characteristic for the drug (red), and at two frequencies related to amide I bands of a protein (green and blue). Bottom: (right) the three contrasts combined into one image and (left) topography. © Leibniz IPHT

D. Täuber

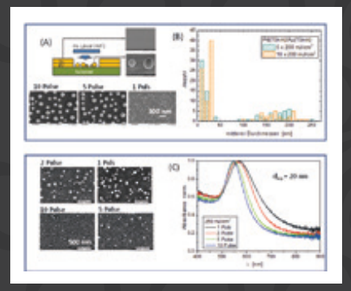
Biophysical Imaging with High Spatial and Temporal Resolution

C. Eggeling

Plasmonic Biosensing

O. Stranik // D. Zopf // W. Fritzsche // A. Csaki

Self-assembled Spherical Metal Particles by Pulsed UV Laser Treatment of Thin Films



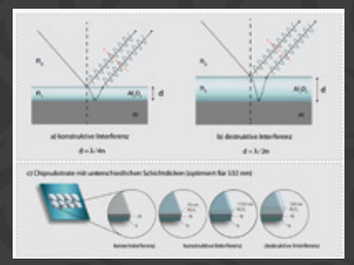
(A) Schematic representation of the laser-induced process; (B) particle size distributions of Pd/Au mixed particles (200 mJ/cm^2, 1-10 laser pulses); (C) extinction spectra of gold particles.
© Leibniz IPHT

G. Schmidl // G. Jia // J. Dellith // A. Gawlik // Z.-H. Lin // Yi-Ju Chen // J.-S. Huang // J. Plentz

Better than a Lens – A Novel Concept to Overcome the SNR-limit Given by the Fermat Principle

J. Becker // R. Förster // R. Heintzmann

Interference-enhanced Raman Spectroscopy for the Detection of Surface Functionalization



Schematic representation of the principle of a) amplification and b) attenuation of light intensity by means of interference. c) Structure of the chip substrates used. © Leibniz IPHT

K. Weber // S. Pahlow

Hybrid Protein Nanofibers – An Analysis on the Nanoscale

T. Deckert-Gaudig // V. Deckert

Spectroscopic Charakterization of Innovative, Light-activatable Complexes for the Intracellular Administration of Carbon Monoxide

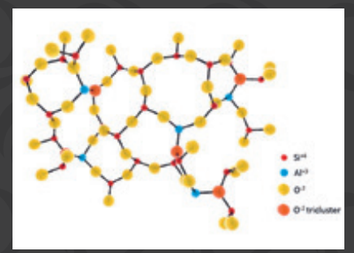
P. Hoffmann // J. Popp // U. Neugebauer

Scientific Articles in the App

Fiber Optics

» The research focus Fiber Optics is dedicated to the propagation properties and the efficient and flexible control of fiber- and planar-guided light. This includes technology and basic research for the understanding of light propagation in fiber waveguide systems and for the realization of novel fiber modules and systems. The focus is on novel microstructured and functionalized fibers for sensory applications in biophotonics as well as nonlinear and laser-based fiber light sources.

Up to Boson Peak – Towards Enhanced Homogeneity in Optical Aluminosilicate Glasses



Drawing of the network topology in a binary aluminosilicate glass under the assumption that all cations are fourfold coordinated and a certain proportion of oxygen triclusters is present. © Ando et al. 2018

K. Wondraczek // V. Reichel // J. Bierlich

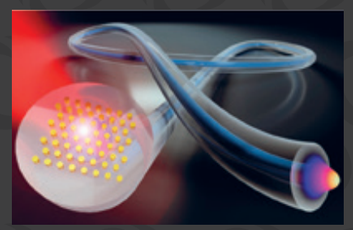
Far Above the Norm – Development of Anomalous Photonic Crystal Fibers

J. Bierlich // K. Wondraczek // A. Lorenz

UV Spectroscopy in Water-filled Anti-resonant Hollow Core Fibers

M. Nissen

Functional Nanostructure-enhanced Optical Fiber Probes for Light Collection



Nanostructured fibers to increase light collection efficiency: The incident light (red area on the left side) is diffracted by the nanostructure (array of yellow dots), which enables efficient coupling into the fiber. © Leibniz IPHT

N. Wang // M. A. Schmidt

Absorption Spectroscopy with Nanobore Fibers

S. Jiang // K. Schaarschmidt // S. Weidlich // M. A. Schmidt

Sharp Images with Flexible Fibers

T. Čižmar // D. Boonzajer Flaes

First Flexible Tweezers from Light

T. Čižmar // I. Leite

Diffusion-Reduced Large-Mode-Area Yb Fiber for High-Performance Amplifiers with Excellent Beam Quality

Concept of the tapered fiber amplifier © Leibniz IPHT

M. Leich // Y. Zhu // M. Lorenz // T. Eschrich // A. Schwuchow // J. Kobelke // H. Bartelt // M. Jäger

Dispersion Analysis in a Tunable Fiber Laser

T. Tiess, // A. Hartung // M. Becker // C. Chojetzki // M. Rothhardt // T. Tieß // M. Jäger

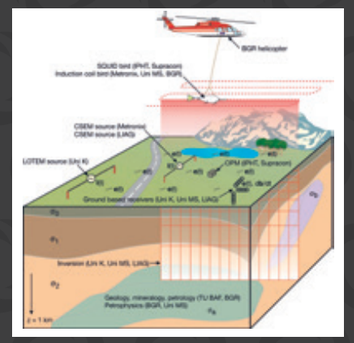
Photonic Detection

» The research focus Photonic Detection researches and uses light-matter interactions to realize innovative sensor and detector concepts of highest sensitivity, precision and specificity. This includes technology research in the field of micro- and nanotechnologies, sensor-related assembly and interconnection technologies as well as multiplex and readout circuits and the integration of the investigated molecular and solid state components into spectroscopic and imaging photonic instruments.

Biomagnetic Imaging with Optically Pumped Magnetometers

U. Graichen // R. Eichardt // G. Oelsner // F. Wittkämpfer // T. Scholtes // R. Stolz // R. Ijsselsteijn // J. Haueisen // Ch. B. Schmidt // V. Schulze

Search for Deep-lying Raw Material Sources with Novel Magnetic Field Sensors



ystem sketch of the semi-airborne exploration process in DESMEX © Uwe Meyer, BGR Hannover

R. Stolz // V. Zakosarenko // M. Schmelz // M. Schiffler // T. Schönau // V. Schultze // G. Oelsner // R. IJsselsteijn // F. Wittkämper

Microwave Readout of Quantum Detectors

M. Schmelz

Charged Particle Beam Monitor for Future Basic Research Facilities

M. Schmelz // R. Stolz // V. Zakosarenko

Ultrathin Niobium Nitride Films Enable Basic Quantum Experiments and New Quantum Devices

S. Linzen // E. Ilichev // M. Ziegler // U. Hübner // L. Fritzsch // S. Goerke // H.-G. Meyer // R. Stolz // H. Schmidt

Thermal Radiation Sensors for Space Travel – An Overview

F. Hänschke // A. Ihring // G. Zieger

Electro-architected Porous Platinum for Optimization of Infrared Sensors

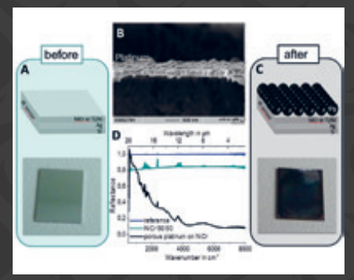


Figure 1. Optical properties of the electrochemically constructed porous platinum thin layer. (A) The schematic representation (up) and the photograph (down) of the IR sensor component (nanolayers of Si / Ag / NiCr) before electrochemical deposition of porous platinum; (B) Lateral view SEM image of the porous platinum thin layer partially detached from the substrate [2]; (C) the schematic representation (up) and the photograph (down) of the IR sensor component after electrochemical deposition of porous platinum; (D) FTIR reflectance spectra in the region 400-8000 cm^{-1} of the 1 cm x 1 cm chip before (green) and after (black) electrochemical deposition of porous platinum [3]. Silver mirror was used for reference spectrum. © Leibniz IPHT

S. Stanca

Key Figures of 2018

11 Eu-co-financed projects (ERA-Net, Eurostars, JPI etc.)

3 thereof coordinated by Leibniz IPHT

15 EU-funded projects,

5 thereof coordinated by Leibniz IPHT

5 Trademark registrations

16 Patent applications,

7 thereof with cause for the right to priority

8 with patent grants

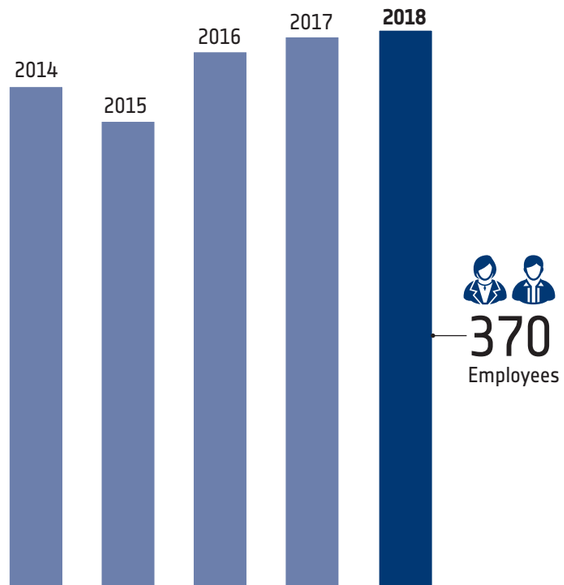
20 Doctorates,

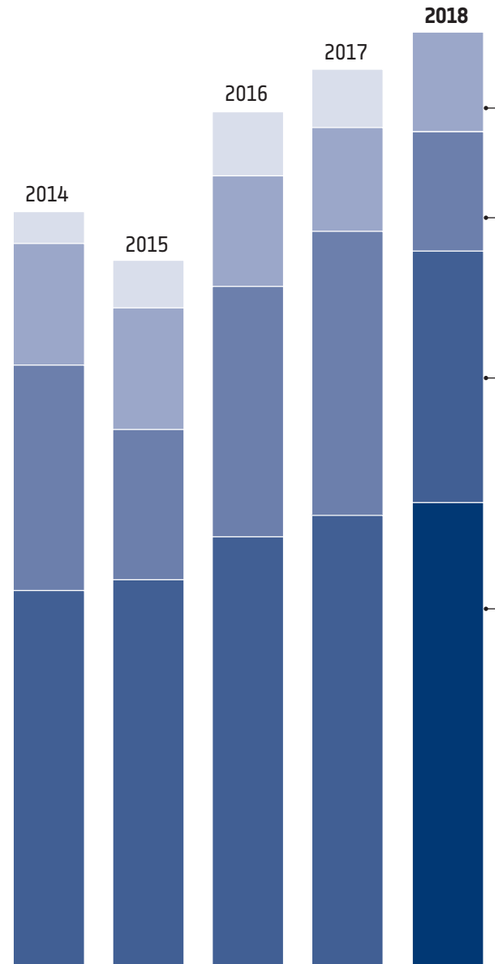
6 thereof women

185 Talks or posters,

83 thereof invited talks / keynotes / plenary talks

197 Published articles in peer-reviewed journals





2.097.982 € EU third-party funding,
1.005.305 € thereof from ERA-Net / ERA-NetPlus, JPI etc.

3.319.041 € Industrial projects

7.457.818 € National projects,
1.672.397 € thereof from DFG funding

12.248.839 € Institutional funding

25.123.680 € Total budget
= 51,25 % Third-party funding

Organizational Chart *(as of March 2019)*

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Prof. Dr. Benjamin Dietzek //
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Dr. Karina Weber // Consultant to the Executive Committee

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Personal Consultant
to the Scientific Director

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Mario Ziegler //
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Gabriele Hamm //
Internationalization

Research Units *(as of March 2019)*

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Quantum Detection
Prof. Dr. Heidemarie Schmidt

Functional Interfaces
Prof. Dr. Benjamin Dietzek

Optical and Molecular Diagnostics and System Technology
Prof. Dr. Ralf Ehricht

Fiber Research and Technology
Prof. Dr. Tomáš Čižmár

Nanobiophotonics
apl. Prof. Dr. Wolfgang Fritzsche

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Biophysical Imaging
Prof. Dr. Christian Eggeling

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Magnetometry
Dr. Ronny Stolz

Nanooptics
Dr. habil. Jer-Shing Huang

Junior Group

Ultrafast Fiber Lasers
Dr. Maria Chernysheva

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Frank Sondermann // Leibniz Institute of Photonic Technology e. V., Jena

Prof. Dr. Herbert Stafast // Jena

Budget of the Institute 2018

	in T Euro
Institutional Funding (Free State of Thuringia, Federal)	12.248,8
Third-Party Funding	12.874,8
	25.123,6

Institutional Funding: Use

Staff	8.173,3
Materials	3.482,7
Investments	592,8
	12.248,8

Third-Party Funding

Federal Ministries of which for projects funded by Leibniz Accociation 685,7 T€	3.778,1
DFG Additionally IPHT-scientists at the Universtiy Jena used DFG-funds of 542,3 T€	1.672,4
Free State of Thuringia of which for restructuring in the frame of EFRE 833,9 T€	1.877,7
EU of which for EU-Initiatives such as ERA-Net / ERA-NetPlus, Joint Programming Initiatives and more: 1.005,3 T€	2.098,0
Assignments from Public Institutions	161,4
Other Contributions	129,6
Subcontracting in Joint Projects	256,5
R & D Contracts incl. Scientific-Technical Activities	2.901,1
	12.874,8

Institute Personnel 2018

	Full-time Equivalents				
	Institutional Funding	*Third-Party Funding*	*Professors*	*Total*	*Persons*
Scientists	39,18	60,76	8,00	107,94	119
*Visiting Scientists***	-	-	-	-	20
*External funded Scientists**	-	-	-	-	16
*External funded Employees**	-	-	-	-	2
*External funded Doctoral Students**	-	-	-	-	39
Doctoral Students	8,10	29,48	-	37,58	64
Technical Staff	32,56	37,86	-	70,42	76
Administration	15,16	2,63	-	17,79	19
Scientific Coordination	3,00	2,88	-	5,88	6
PR and Research Marketing	4,26	2,37	-	6,63	7
Executive Committee	1,00	0,00	0,50	1,50	2
Trainees	0,00	0,00	-	0,00	0
Total Personnel	**103,26**	**135,98**	**8,50**	**247,74**	**370**

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

**Scientist, who worked in the legal year 2017 longer than one month and who are financed by another institution. Key date regulation 31.12.2018 does not apply.

Imprint

Publisher:
Leibniz Institute of Photonic Technology e.V.

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from Ideas to Instruments

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