

RESEARCH NEWS – SPECIAL ISSUE

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Profiles of the awards

Research prizes are awarded at the annual meeting of the Fraunhofer-Gesellschaft's General Assembly, which this time takes place in Hannover. Four Fraunhofer prizes will be awarded this year – one in the special category of Human-Centered Technology – and three Hugo Geiger prizes.

1 Plasma in a bag

Plastic bags coated by plasma at atmospheric pressure serve as a GMP laboratory for the cultivation of adherent cells. The plasma is used to modify the internal surface of the bag specifically, so that different cell types can grow on it.

2 Programming model for supercomputers of the future

The demand for even faster, more effective, and also energy-saving computer clusters is growing in every sector. The new asynchronous programming model GPI might become a key building block towards realizing the next generation of supercomputers.

3 3D Magnetic field measurement

Magnetic field sensors are a contact- and wear-free means of measuring the position of machine parts and products. A new generation of Hall sensors is now making the process even more precise and free of interference.

4 Automated plant factory for the production of vaccines

Molecular farming is an easy, fast, and safe method for producing vaccines and therapeutic proteins in plants. Now a team of Fraunhofer researchers from the USA has built up a Good Manufacturing Practices (GMP) compliant plant factory.

5 Prize for outstanding research theses

Three young researchers have been recognized for producing final dissertations that demonstrate scientific excellence. Their findings include new methods of naturally preserving fresh foods with hops extracts, an ultra-compact microscope that makes it possible to examine hundreds of prepared samples simultaneously, and the use of protein-protein interaction analysis to nip fungal pathogens in the bud.

The prizes

Joseph von Fraunhofer prize – research for practical applications

This prize has been awarded by the Fraunhofer-Gesellschaft every year since 1978, in recognition of outstanding scientific work by members of its staff leading to the solution of application-oriented problems. To date, more than 200 researchers have received this honor. This year, four prizes each worth 50,000 euros will be awarded. The prize-winners also receive a silver lapel pin bearing the face of the man for whom the award is named, as illustrated in the logo included in topics 2, 3 and 4.

The award for Human-Centered Technology is funded by former Executive Board members and institute directors of the Fraunhofer-Gesellschaft and outside sponsors associated with them. This prize is awarded every two years – alternating with the Donors' Association Prize – to those employees whose research and development work makes a significant contribution to improving people's quality of life and maintaining their active participation in daily life into old age (topic 1). The prize of 50,000 euros will be awarded on June 10 at the Fraunhofer-Gesellschaft's annual conference in Hannover.

Hugo Geiger prize – promoting young researchers

The Bavarian state government instituted this award in 1999 to mark the 50th anniversary of the Fraunhofer-Gesellschaft. It is named for former Bavarian secretary of state Hugo Geiger, who led the inaugural assembly of the Fraunhofer-Gesellschaft on March 26, 1949. This prize is awarded in recognition of outstanding and application-oriented theses for Bachelor, Master's and Doctorate degrees from all research fields within the Fraunhofer-Gesellschaft. The prizewinning papers are selected on the basis of scientific quality, economic relevance, uniqueness and interdisciplinary approach. The work must be closely related to or have been developed in a Fraunhofer institute. The first-prize winner receives 5,000 euros in prize money, the second 3,000 euros and the third 2,000 euros (topic 5).

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Plasma in a bag

It sounds like one of those puzzles where you have to change a matchstick figure into something else without adding or taking away any matches: How do you alter the inside of a closed bag without opening it? Impossible, I hear you say. But that is precisely what a team of researchers under Dr. Kristina Lachmann and Dr. Michael Thomas at the Fraunhofer Institute for Surface Engineering and Thin Films IST in Braunschweig have managed to do. They use plasma to activate the inner surfaces of plastic bags. The plasma acts as a disinfectant while also transforming the surface of the bag so that cells want and are able to grow on it.

“Our goal was to realize a closed system in which cells grow undisturbed and without the risk of contamination,” says Dr. Henk Garritsen from Braunschweig Municipal Hospital (Städtisches Klinikum Braunschweig). “Coating the bags with plasma enables us to use them as a GMP laboratory.” The background to these endeavors is stem cell research and the idea of treating illnesses with stem cells that come from the patient’s own body. Until now researchers have mostly used Petri dishes, bottles, and bioreactors in a sterile environment for cultivating stem cells. However, these systems have to be opened in order to refill culture media or extract cells. This leads time and again to contamination, and the painstakingly cultivated cells become unusable.

Plasma coatings for different cell types

At the Helmholtz Centre for Infection Research in Braunschweig, Dr. Werner Lindenmaier and Dr. Kurt Dittmar were already working on bags for cultivating stem cells, but without making the breakthrough they were looking for. The geographical proximity and the expertise of Fraunhofer IST researchers in plasma coating brought the two teams together. Initial tests showed that the cells grow on plasma-coated films. A joint project sponsored by the German Federal Ministry of Economics and Technology BMWi set out to investigate the closed bag system and cell growth in greater detail.

The key part of the method is coating with plasma. To achieve this, ordinary bags such as those used for infusions are filled with a noble gas and voltage is applied. “This produces plasma inside the bag for a short period – a luminous, ionized gas that chemically alters and at the same time disinfects the surface of the plastic,” explains Dr. Kristina Lachmann from Fraunhofer IST. Bags were coated in a pilot plant at Fraunhofer IST, and then tests were carried out at the Helmholtz Centre for Infection Research and Braunschweig Municipal Hospital to determine which coating is best suited for which type of cell. “We work with stem cells for bones, cartilage, fat, and nerves – the coating can be optimized for each of these cell types,” says Dr. Kurt Dittmar.

The pilot plant at Fraunhofer IST has now been optimized to the extent that the individual coating steps are automated. This makes it possible to manufacture standar-

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dized and reproducibly modified bags for cell cultivation. “We use medically approved bags for the coating,” says Dr. Michael Thomas. “Nevertheless, the plasma treatment must be demonstrated to be innocuous before being approved for clinical use.”

For their work in developing plasma in bags for cell cultivation in closed systems, Dr. Kristina Lachmann, Dr. Michael Thomas, Dr. Henk Garritsen, Dr. Werner Lindenmaier, and Dr. Kurt E.J. Dittmar are receiving the Fraunhofer prize for human-centered technology.



The prize-winning team presents a bag whose inner surface is modified using plasma – Henk Garritsen, Werner Lindenmaier, Michael Thomas, Kristina Lachmann, Kurt Dittmar (from left to right). (© Dirk Mahler/Fraunhofer) | Picture in color and printing quality: www.fraunhofer.de/press

Programming model for supercomputers of the future

The demand for even faster, more effective, and also energy-saving computer clusters is growing in every sector. The new asynchronous programming model GPI from Fraunhofer ITWM might become a key building block towards realizing the next generation of supercomputers.

High-performance computing is one of the key technologies for numerous applications that we have come to take for granted – everything from Google searches to weather forecasting and climate simulation to bioinformatics requires an ever increasing amount of computing resources. Big data analysis additionally is driving the demand for even faster, more effective, and also energy-saving computer clusters. The number of processors per system has now reached the millions and looks set to grow even faster in the future. Yet something has remained largely unchanged over the past 20 years and that is the programming model for these supercomputers. The Message Passing Interface (MPI) ensures that the microprocessors in the distributed systems can communicate. For some time now, however, it has been reaching the limits of its capability.

“I was trying to solve a calculation and simulation problem related to seismic data,” says Dr. Carsten Lojewski from the Fraunhofer Institute for Industrial Mathematics ITWM. “But existing methods weren’t working. The problems were a lack of scalability, the restriction to bulk-synchronous, two-sided communication, and the lack of fault tolerance. So out of my own curiosity I began to develop a new programming model.” This development work ultimately resulted in the Global Address Space Programming Interface – or GPI – which uses the parallel architecture of high-performance computers with maximum efficiency.

GPI is based on a completely new approach: an asynchronous communication model, which is based on remote completion. With this approach, each processor can directly access all data – regardless of which memory it is on and without affecting other parallel processes. Together with Rui Machado, also from Fraunhofer ITWM, and Dr. Christian Simmendinger from T-Systems Solutions for Research, Dr. Carsten Lojewski is receiving a Joseph von Fraunhofer prize this year.

Like the programming model of MPI, GPI was not developed as a parallel programming language, but as a parallel programming interface, which means it can be used universally. The demand for such a scalable, flexible, and fault-tolerant interface is large and growing, especially given the exponential growth in the number of processors in supercomputers.

Initial sample implementations of GPI have worked very successfully: “High-performance computing has become a universal tool in science and business, a fixed part of the design process in fields such as automotive and aircraft manufacturing,” says Dr.

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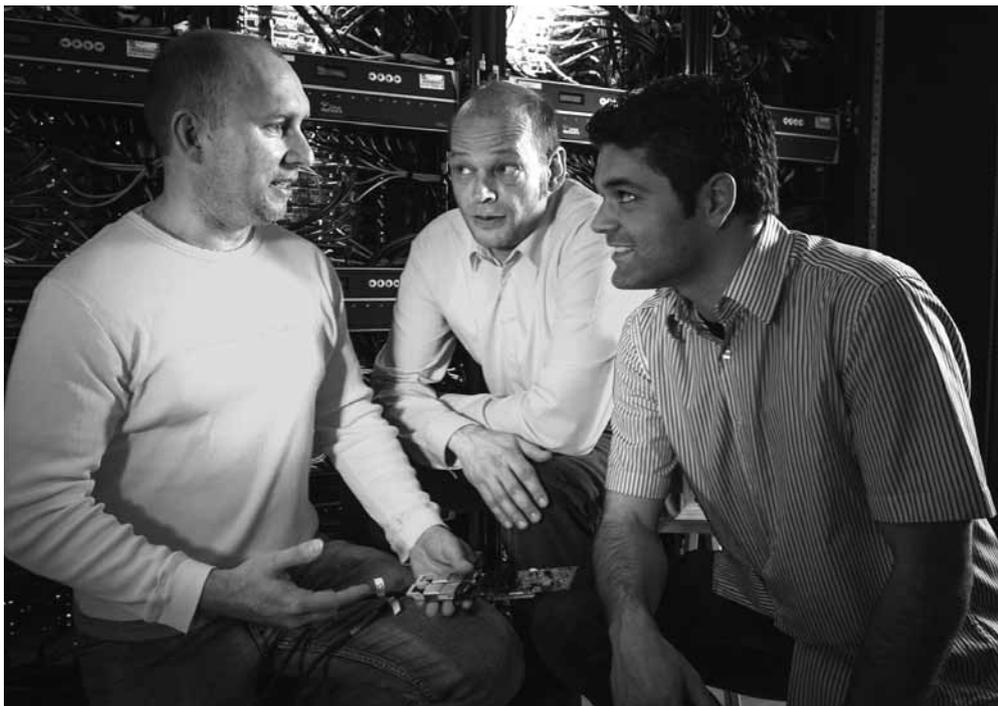
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Christian Simmendinger. "Take the example of aerodynamics: one of the simulation cornerstones in the European aerospace sector, the software TAU, was ported to the GPI platform in a project with the German Aerospace Center (DLR). GPI allowed us to significantly increase parallel efficiency."

Even though GPI is a tool for specialists, it has the potential to revolutionize algorithmic development for high-performance software. It is considered a key component in enabling the next generation of supercomputers – exascale computers, which are 1,000 times faster than the mainframes of today.



Dr. Carsten Lojewski, Dr. Christian Simmendinger, Rui Machado (from left to right) developed a programming model that uses high- performance computers as efficiently as possible.

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3D Magnetic field measurement

Magnetic field sensors are used to measure the position of machine parts and products with zero contact and zero wear – in a modern car, around 100 of such sensors are busy monitoring safety belt buckles and door locks, registering pedal positions, or are used for ABS, EPS, and engine control. They are cost-effective and robust, however, these conventional sensors generally measure only the magnitude of the magnetic field perpendicular to the chip surface. Good enough in many ways, magnetic field measurement remains imprecise and susceptible to interference. Michael Hackner, Dr.-Ing. Hans-Peter Hohe, and Dr.-Ing. Markus Stahl-Offergeld from the Fraunhofer Institute for Integrated Circuits IIS were not satisfied with these limitations. They wanted precise position measurement with the advantages of magnetic field sensors, and so they set about developing a 3D Hall sensor.

Manufactured using standard processes

“First we connected up several sensors on a chip in order to improve the measuring accuracy of the individual sensors,” says Markus Stahl-Offergeld. “Next we arranged several of these sensors to measure the three-dimensional magnetic field at one point. The result was our pixel cells.” And so a new generation of 3D Hall sensors was born, capable of measuring all three spatial axes of a magnetic field and calculating the exact position of an object. The sensor chip contains a designated sensor for each of the three magnetic axes. These sensors are placed together in the pixel cell and attain a resolution of just a few microteslas depending on the measurement speed. Tesla is the unit for magnetic flux density. Also integrated directly on the chip are the evaluation circuit and a coil, which enable self-testing and calibration. “In spite of its complexity, the HallinOne® magnetic sensor can be manufactured using standard processes of semiconductor technology – and that makes it cost-effective,” explains Dr.-Ing. Hans-Peter Hohe. For this global technological breakthrough, the three Fraunhofer IIS developers have been awarded a Joseph von Fraunhofer prize this year.

Long-term partnership

One of the first companies to exploit the potential of HallinOne® was Seuffer GmbH from Calw in southern Germany. As far back as 2006, it launched a sensor that prevents washing machines from wobbling and creeping across the floor during spin cycles. A magnet is attached to the tub and the sensor to a fixed, unmoving part of the washing machine. Depending on how much washing is in the drum and how it is distributed during a spin cycle, the tub moves and therefore the magnet, too. The sensor measures this movement, evaluates the data, and transmits it to the washing machine. If the drum is wobbling, it is stopped briefly and shaken around a bit in order to distribute the washing more evenly. Fraunhofer IIS and Seuffer are currently developing a wireless window sentinel, which detects whether a window is open or closed

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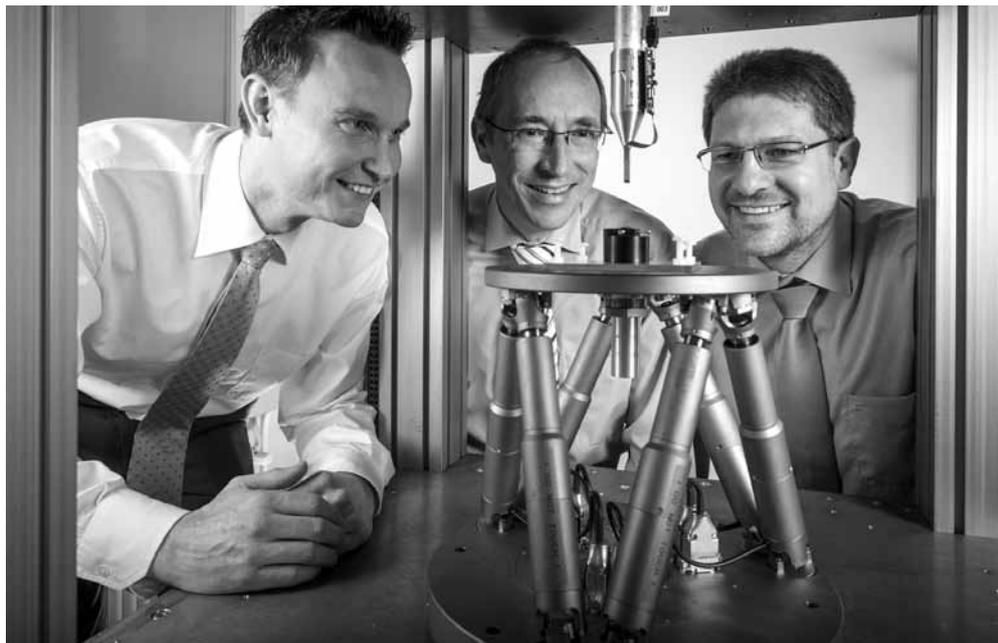
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and transmits this information via a wireless sensor network combined with energy harvesting.

“Our next goal is to develop a sensor for 5-axis position measurement,” says Michael Hackner. “This will allow us to detect more mechanical degrees of freedom simultaneously, including translatory and rotary movements by the magnet in all directions. It already works in laboratory tests, but the system still needs some adjustments before it is ready for real-life applications.” Such applications could include use in the control systems of computers, construction machines, robots and airplanes.



A 3D Hall sensor developed by Dr.-Ing. Markus Stahl-Offergeld, Dr.-Ing. Hans-Peter Hohe and Michael Hackner (from left to right) can measure position exactly.

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Automated plant factory for the production of vaccines

The vaccine shortage during the swine flu pandemic in 2009 showed that although chicken-egg production is a reliable method, in a global emergency, it takes too long and does not yield enough vaccine. What is required are alternative methods with shorter production times and larger capacity, such as the production of vaccines and therapeutic agents in plants for example. Molecular farming, as this method is known in the trade, is easy, fast, and safe: the genetic information needed for target protein production is introduced into the plant via virus vectors that are harmless to humans. Moreover, plants have protein synthesis machinery similar to that of humans and can accommodate complex proteins.

“We use tobacco plants because they multiply and maintain our virus vectors very well. In addition, they grow fast yielding, large quantities of biomass in a short period of time,” says Vidadi Yusibov from the Fraunhofer Center for Molecular Biotechnology (CMB). It has already been demonstrated in the laboratory that the method works well. But can this approach be scaled for mass production? The researchers have already cleared the first hurdles: they have developed a fully integrated, automated, GMP facility – a fundamental prerequisite for the production of biopharmaceuticals. In recognition of this achievement, one of this year’s Joseph von Fraunhofer prizes is being awarded to two Fraunhofer researchers from the United States: Prof. Dr. Andre Sharon from the Fraunhofer Center for Manufacturing Innovation (partner institute of the Fraunhofer Institute for Production Technology IPT) and Prof. Dr. Vidadi Yusibov from the Fraunhofer Center for Molecular Biotechnology (partner institute of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME).

Plants with predictable quality – any time, any place

The decisive moment was receiving a contract from the U.S. government’s Defense Advanced Research Projects Agency (DARPA), which was looking for vaccine production alternatives. “Once some initial difficulties in understanding each other were overcome, our teams of biologists and engineers succeeded in building up our automated plant-based vaccine production factory. Now we have plants that consistently grow and make proteins to the same predictable quality, time after time whenever and wherever we like – crazy as that might sound!” says Andre Sharon from Fraunhofer CMI and Professor of Engineering at Boston University.

The plants grow in trays with hydroponic cultures of mineral wool as opposed to soil, in specially designed growth modules. Light, water, and nutrients are precisely dosed and distributed. Specially developed robots bring the plants from station to station to carry out the various steps – from inserting the tiny seeds and vacuum infiltration, to harvesting and extraction.

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The plants grow for four weeks before the vector is introduced by means of vacuum infiltration. This process goes as follows: A robot picks up a tray with plants, turns it upside down, and submerges the tobacco plants headfirst into water. "This water holds the vector (biological carrier) containing the genetic information that tells the plants which protein they should produce. Then a vacuum is applied by drawing the air from the water and the plants. As soon as we switch off the vacuum, the plants suck in the water together with the vector. This takes just a few seconds," explains Sharon. Then the plants are put back in the growth module to grow further. In about a week they have produced the proteins. Once harvested, the leaves are cut into small pieces and homogenized in fully automated processes. This produces a liquid, from which the proteins are extracted. The end product is a clear liquid.

The pilot facility is capable of producing up to 300 kilograms of biomass a month, which roughly corresponds to 2.5 million units of vaccine.



Professor Vidadi Yusibov and Professor Andre Sharon (from left to right) in the fully automated plant factory. (© Dirk Mahler/Fraunhofer) | Picture in color and printing quality: www.fraunhofer.de/press

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Prize for outstanding research theses

Three talented young scientists have been awarded the Hugo Geiger Prize for their outstanding research findings: First place has gone to Andrea Hickisch, who has come up with new ways of naturally preserving fresh foods with hops extracts. René Berlich's ultra-compact microscope has made it possible to examine hundreds of prepared samples simultaneously. Thanks to the microscope's integrated lighting, even non-transparent specimens are easily studied. Third prize has been awarded to Yannick Bantel, whose research has nipped fungal pathogens in the bud: his protein-protein interaction analysis provides an important basis for the development of potential remedies.

Hops extracts as a natural preservative

From colorful salads to bite-sized pieces of fruit: while fresh ready-to-eat foods are healthy and in high demand, they also spoil easily. In the course of her diploma thesis, Andrea Hickisch of the Fraunhofer Institute for Process Engineering and Packaging IVV exploited the antibacterial effect of hops extracts to make fresh foods "naturally" preservable and safe.

Our nutrition is important to us: on lunch breaks, we like to eat fruits, vegetables, or meals that have been prepared in a healthy manner. The food industry has responded to this trend by offering ready-to-eat foods at every supermarket, such as sliced fruits, salads or meals with fish or meat. But such fresh and minimally processed products present a problem: they spoil easily. And since consumers tend to eat these foods raw or briefly heated, they can pose a health risk.

A young researcher at the Fraunhofer Institute for Process Engineering and Packaging IVV has now found a way to significantly minimize the microbiological risk in the production of fresh and minimally processed foods. As she describes in her diploma thesis, natural hops extracts are a promising alternative to conventional preservatives.

In Europe, we have known that hops preserve beverages since the Middle Ages, and the substance is still used in beer production today. But as Andrea Hickisch has proven, hops are capable of a great deal more. She examined the effects of natural hops extracts on the bacteria and pathogens that spoil different foods.

The results of her research showed that hops open up new ways of providing consumers with naturally preserved fresh foods. Whether they are added to packaging or placed directly on products, hops have an antibacterial effect. The experiments of Andrea Hickisch are likely to have far-reaching consequences for the food industry. After all, consumers of healthy foods are generally critical of synthetic preservatives.

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Ultra-compact fluorescence microscope

While insect eyes may appear strange to us because of their small size, insects see a great deal, and their vision is truly multifaceted. In technical terms, an insect's eye is equipped with several lenses arranged next to each other. Each of these lenses transmits individual parts of an image. Taken together, they make up a full view. Thanks to their compact build, micro-optical systems based on this idea provide fascinating new possibilities and insights.

For his master's thesis, René Berlich (M. Sc.) of the Fraunhofer Institute for Applied Optics and Precision Engineering IOF not only developed an integrated illumination module for this microscope, which fits comfortably into any trouser pocket. He also enhanced the existing systems: thanks to his work, the microscope's resolution improved, and even smaller structures are now visible. For the first time, it can be used to examine fluorescence signals.

Compared with conventional fluorescence microscopes, which have only one imaging objective, the wide visual field makes it possible to investigate several samples at the same time without the need for sequential scanning. Examining hundreds of prepared samples simultaneously also saves time and money. This marks a significant step toward automating biomedical laboratory experiments.

Berlich's system offers a unique combination: cost-efficient manufacturing, a large image field, and an ultra flat design. With a distance of just 7 mm between the object and detector, the system is ideal for application in mobile medical analysis devices, for instance.

New paths for biotechnology

Pathogenic fungi are well adapted to attack and colonize the human body. This ability is partly based on their protein repertoire and the interactions between these proteins.

Candida albicans is a well-known fungal agent. Each year, it causes more than 10,000 deaths in Germany alone. While many of the fungus' proteins are well known, until now very little was known about their interactions. But Yannick Bantel of the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB has taken the analysis of protein-protein interaction a significant step further with his diploma thesis.

In his research, Bantel applied the concept of the expanded genetic code: he added an unnatural amino acid to the genetic code of *Candida albicans*. Hereby customized proteins can be created that do not exist naturally. With this method, the young scientist could not only detect protein-protein interactions *in vivo*. He also identified interactions that were previously unknown, and did this with a high level of specificity and efficiency. His analyses provide an important basis for the development of possible therapeutic substances. They also demonstrate the potential of the expanded genetic code for medical and industrial biotechnology.



The Hugo -Geiger prize winners: Andrea Hickisch, René Berlich and Yannick Bantel. (© privat | Picture in color and printing quality: www.fraunhofer.de/press)

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