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Max Planck RESEARCH

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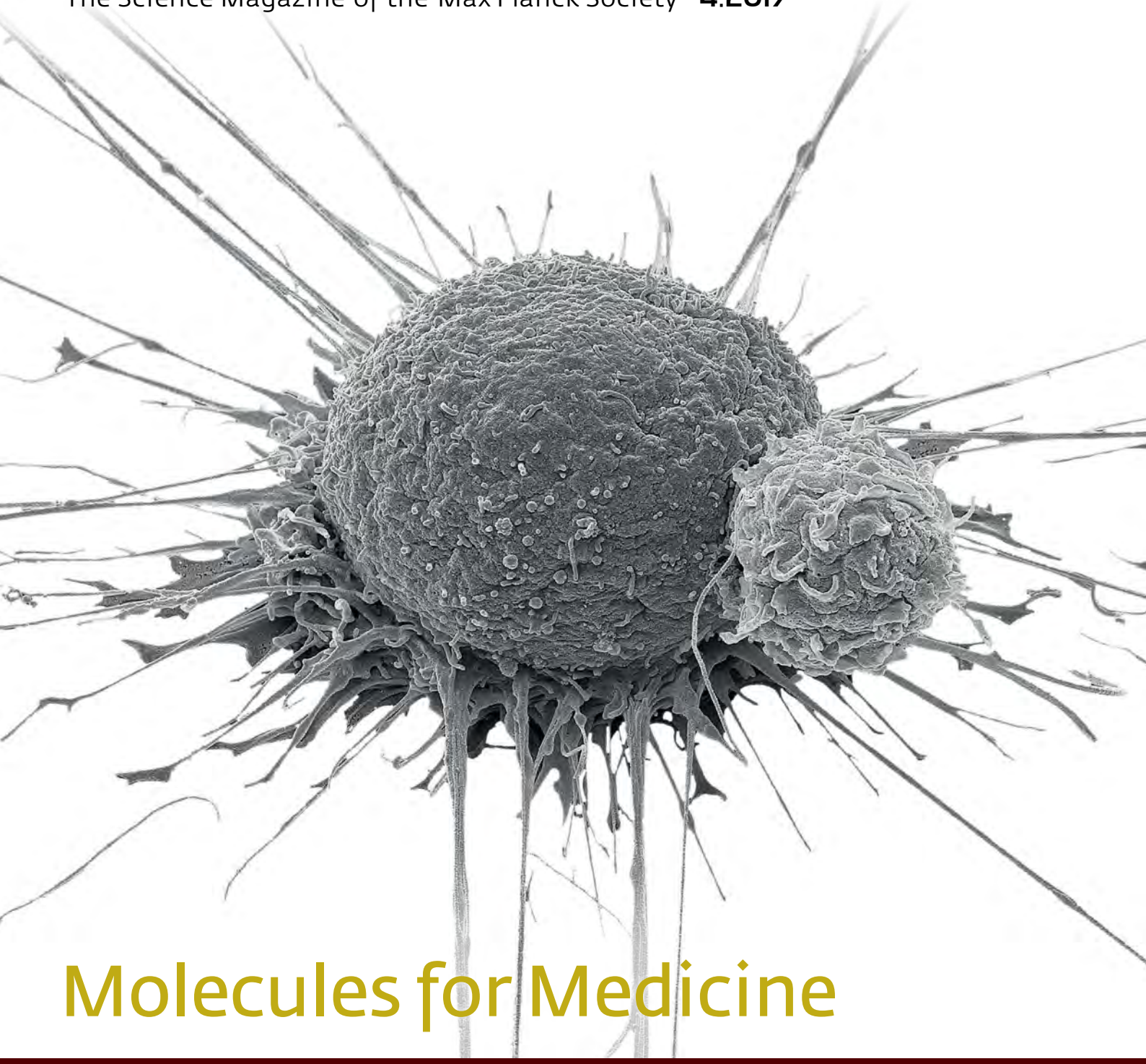


Molecules for Medicine

INNOVATION
The Digital Future Is at Stake

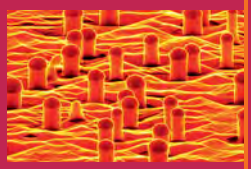
COSMOLOGY
The Big Bang Clock

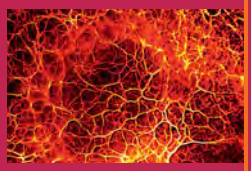
ECOLOGY
A Beetle Overcomes a Plant's Defenses

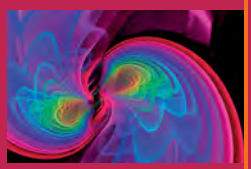
COLLECTIVE GOODS
Getting the Trolls Under Control

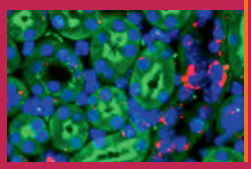
Max-Planck-**Innovation**

Connecting **Science and Business.**









Max Planck Innovation is responsible for the technology transfer of the Max Planck Society and, as such, the link between industry and basic research. With our inter-disciplinary team we advise and support scientists in evaluating their inventions, filing patents and founding companies. We offer industry a unique access to the innovations of the Max Planck Institutes. Thus we perform an important task: the transfer of basic research results into products, which contribute to the economic and social progress.

Connecting Science and Business

www.max-planck-innovation.de

Photo: MPI for Nuclear Physics/Christian Föhr

On the Racetrack

Most of the vast expanse of space is extremely cold and empty. Nevertheless, chemical reactions take place there, too. These result in the formation of ions (electrically charged particles), small and large molecules, and interstellar dust. The dust clouds, in turn, give rise to stars and planets. The chemistry of interstellar space is therefore one of the most active research fields in astronomy.

With the new Cryogenic Storage Ring (CSR), scientists at the Max Planck Institute for Nuclear Physics are bringing space into their lab. However, the level of technical complexity it requires is almost as extreme as the conditions in space: the temperature in the inner vacuum system of the CSR is just a few degrees above absolute zero, or minus 273 degrees Celsius; the pressure of less than 10^{-14} millibar is one hundred trillion times lower than normal air pressure. It is thus possible to keep even highly reactive, multiply charged molecular ions on the 35-meter circuit of the storage ring for several minutes – or sometimes even hours. As they circle at high speed, covering distances that correspond to many times the distance between the Earth and the moon, the ions cool down to temperatures that resemble those in interstellar clouds.

The ion beams are steered and focused by electric fields. The scientists can use these fields to bring about a reaction between the stored ions and electrons or neutral atoms, or to investigate them with laser beams. In this way, low-energy collisions, which are typical for the conditions in interstellar space, can be examined under controlled conditions in the laboratory.

Similar to a person who wears several layers of clothing to protect themselves against the cold, the cryogenic region of the storage ring has a number of shielding layers to insulate it against the ambient heat. Cooling down the apparatus takes more than three weeks – as does heating it up again after several months in measurement mode. The photo shows the storage ring when it was still open four months before it was cooled down for the first time.

18 MOLECULES FOR MEDICINE

ON THE COVER Substances that kill tumor cells, such as the prostate cancer cell shown here, while leaving healthy tissue largely unscathed are a challenge not only for biomedical specialists, but also for chemists.

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Photos: Frank Vinken, Anna Schroll, picture alliance/dpa Themendienst (from left to right)

With a Little Help from Apollo

The Max Planck Institute for Intelligent Systems opens its new building in Tübingen

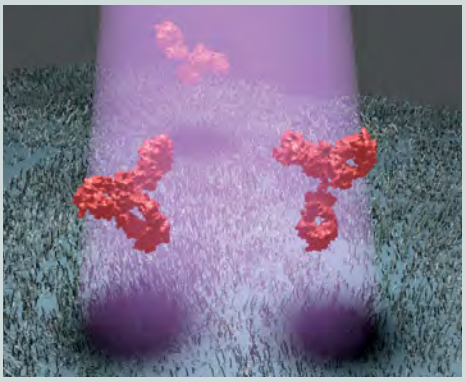
The opening ceremony saw genuine teamwork between man and machine: Apollo, the humanoid robot, held the red ribbon as it was cut by Minister President Winfried Kretschmann and Max Planck President Martin Stratmann. Science Minister Theresia Bauer and the Institute's Managing Director Stefan Schaal also helped cut the symbolic ribbon, thus officially opening the new building of the Max Planck Institute for Intelligent Systems following two years of construction work.

"With this Institute, the Max Planck Society has firmly anchored one of the most significant research fields for the digital revolution in Baden-Württemberg," said the Minister President at the opening ceremony held in late July. The Max Planck Institute, which also has a site in Stuttgart, was founded six years ago. Max Planck President Martin Stratmann spoke of his hope that the Institute's research would lead to major advances in cognitive robotics. The new building provides the perfect conditions for theoretical and experimental research. The generously dimensioned robotics lab, for instance, will provide a flexible training ground for robots. In the near future, the "Capture Hall" is set to become home to a globally unique 4D full-body scanner that can record the body and its movements through space and time in high definition.

Opening ceremony with distinguished guests (from left): Director Stefan Schaal, Science Minister Theresia Bauer, Apollo the robot, Max Planck President Martin Stratmann and Minister President Winfried Kretschmann after they jointly cut the ceremonial red ribbon.

Physics and Medicine for Patients

The Max Planck Society and the university and university hospital in Erlangen seal agreement on collaboration



Protein sensor: Max Planck researchers developed a method to identify unmarked biomolecules using their shadows. Such techniques could be used at the Center for Physics and Medicine.

The newly established Center for Physics and Medicine in Erlangen is putting an often-neglected factor in the development of diseases under the microscope: physics. The collaboration agreement was signed in late July. The Free State of Bavaria is supporting the project and the new premises with funding totaling 60 million euros. One of the Center's tasks will be to develop a better understanding of the mechanical, electrical and chemical processes in inflammations and tumor diseases so as to improve diagnosis and therapy. "We will use entirely new methods to measure and model living organisms' fundamental physical processes, such as the communication and forces between cells in diseased tissue," said Vahid Sandoghdar, Director at the Max Planck Institute for the Science of Light and one of the driving forces behind the Center. "We hope that the understanding we will gain of these processes will enable the development of novel treatments and drugs."

The precise focal points of the collaboration project will depend on the scientists appointed. The Center comprises a new department of the Max Planck Institute in Erlangen along with two new chairs for biophysics and mathematics in life sciences and the recently vacated chair for medical physics at the university, as well as five other research groups.

Photos: MPI for the Science of Light (bottom); Wolfram Scheible (top)

"Temperatures will continue to rise"

Thorsten Mauritsen of the Max Planck Institute for Meteorology is investigating how much time is left to achieve the Paris climate target

Thorsten Mauritsen

Earth's climate is in turmoil: Increasing levels of CO_2 collecting in the atmosphere have seen global temperatures rise by 0.8 degrees since the start of industrialization. According to a study conducted by Thorsten Mauritsen of the Max Planck Institute for Meteorology in Hamburg and Robert Pincus of the University of Colorado, even if all fossil fuel emissions were to cease immediately, the Earth would still become 0.3 degrees warmer. In an interview, Mauritsen explains why it will take millennia for the Earth to return to a state of equilibrium.

Mr. Mauritsen, what prompted you to conduct this study?
Thorsten Mauritsen: In 2015, I was a little confused as to why the 1.5-degree target was even being discussed in the Paris negotiations. I was certain that we had already passed that point, so I wanted to demonstrate in simple terms that this objective is no longer attainable. However, as I delved into the literature and carried out more calculations of my own, I came to realize that the scenario isn't entirely unrealistic – which is really something of a positive result.

You discovered that the Earth's temperature would rise by a total of 1.1 degrees Celsius even if fossil emissions suddenly stopped completely. How can that be?
The Earth system is out of balance: more energy flows into the system than is emitted. This excess energy is absorbed primarily by the oceans: water has considerable thermal capacity and therefore a long reaction time, so the oceans are currently cooling the air. Over time, however, the deep ocean layers will become warmer until eventually, after thousands of years, the climate system settles with the oceans and atmosphere at a higher average temperature. Without new emissions, at the end of this century, the temperature would be 1.1 degrees Celsius higher than before industrialization.

What factors do you think play a role in this?
In addition to CO_2, when we burn fossil fuels, we also emit aerosol particles into the atmosphere. These aerosol particles probably cool the Earth down a little – counteracting the CO_2, as it were. However, if we stopped burning coal and crude oil, these aerosols would disappear in a matter of weeks – but the CO_2 would remain in the atmosphere. As a result, temperatures would jump suddenly. Over a longer timeframe, though, the deep ocean layers absorb a portion of the CO_2. This reduces the predetermined warming at the end of the century by 0.2 to 0.3 degrees compared with the scenario where CO_2 remains constant. So that means nature is helping us out a bit.

What is the impact of other greenhouse gases such as methane and nitrous oxides?
These gases have a rather short lifespan of ten years at most. Of course, ten years is no short time at all until we consider these temperature increases over a period of a hundred years. These gas emissions contribute to the fact that the Earth is slightly warmer now. If these gases were to disappear from the atmosphere, the global temperature increase would be moderated somewhat.

How did you calculate the predetermined warming?
We actually only needed to know two things for this. First, we needed to find out how sensitive the Earth system is and how easily it reacts to the increase of CO_2 in the atmosphere over the course of a century – so-called transient climate sensitivity. We can estimate this using data from temperature increases to date as well as ocean temperatures. We also needed to know how strong the impact would be if aerosols, methane and nitrous oxides from fossil fuels were to disappear. This allowed us to estimate the temperature increase by the end of the century.

What is the difference between this and previous studies?
We used observation data to estimate sensitivity. Previous studies have been based on the results of climate models that involve many more assumptions, though our results do broadly support such model-based studies.

What can we learn from the results? Unfortunately, it's not possible to stop emissions with immediate effect.
We can see how far humanity is from climate goals like the Paris Agreement, which states that the Earth's temperature shouldn't rise by more than 1.5 to 2 degrees. According to our study, there is a 13 percent chance that we have already surpassed the 1.5-degree target. It also shows that, taking current emission levels as a basis, we still have 30 years until the probability of staying below the 1.5-degree level falls to 50 percent.

How do you explain the strong attention your study has gained?
We've clearly struck a chord. Surveys have shown that many people believe global warming would cease if greenhouse gas emissions stopped. Many people even think that temperatures will return to pre-industrial levels in a few decades. However, as climate researchers, we have known for a long time that this isn't the case. CO_2 has a much longer lifespan – it remains in the atmosphere for up to thousands of years. It is thus important to state it very clearly: temperatures will continue to rise even if emissions stop.

Interview: Ute Kehse

Photo: Private collection

Considering the Immune System as a Whole

Research Group created at Julius-Maximilians-Universität Würzburg

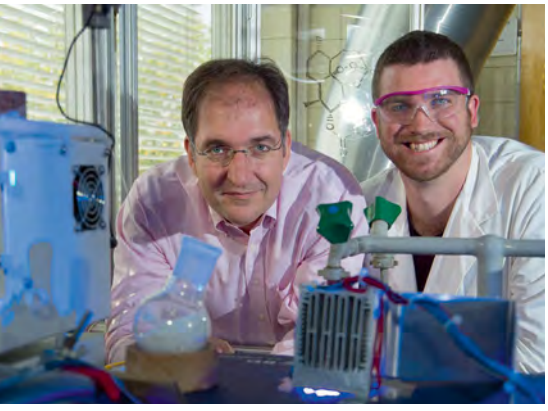
The new Max Planck Research Group for Systems Immunology at Julius-Maximilians-Universität Würzburg (JMU) has started work following the appointment of Georg Gasteiger. Its objective is to investigate the immune system and its interaction with the entire organism. This work isn't concentrated on protecting against pathogens or cancer cells alone: it is also focused on diseases caused by the immune system itself, such as multiple sclerosis or rheumatism. Financing was provided by the Free State of Bavaria, which contributed 25 million euros, and the Max Planck Society, with 2 million euros. An initial five-year term has been agreed.

Work began four years ago after the initial contract was signed. As Director, Gasteiger has led his team since June; at the same time, he holds the newly created Chair for Systems Immunology at the University. Wolfgang Kastenmüller has undertaken leadership of the second team as well as a further chair in the field. The appointment procedure for the third Director is currently ongoing. "We want to ensure that the Max Planck Society's research is closely linked with German universities," said Max Planck President Martin Stratmann in explaining the strategy for Max Planck Research Groups at universities. This applies particularly to fields that offer the prospect of significant new insights.

Campus location: The new Max Planck Research Group is housed in the building of the Institute of Pharmacology and Toxicology at JMU Würzburg.

Drugs for Developing Nations

Process for cost-effective production of pharmaceutical ingredients licensed



Promising development: Peter Seeberger (left) and Kerry Gilmore have created a new method to produce medications efficiently through their flow chemistry process.

The company Fluxpharm has obtained a license for a chemical process developed at the Max Planck Institute of Colloids and Interfaces in Potsdam. Using flow chemistry technology, a variety of standard ingredients can now be produced significantly more efficiently and cost-effectively than with conventional methods. Until now, pharmaceutical substances have often been produced using a so-called batch process, in which all requisite reagents are placed in a single vessel where they react with one another. However, this production method is time consuming and requires significant quantities of additional chemicals. The reaction in the flow chemistry process developed by Max Planck researchers, in contrast, takes place as the reagents flow through the pipes of a specially constructed reactor. This method enables much smaller quantities of substances to react more safely and efficiently.

Fluxpharm wants to develop the technology further and make it commercially available. Plans include advancing production of the pharmaceutical HIV drug Efavirenz in order to provide the drug to more people in poorer countries. The process is also suitable for other substances.

Photos: Ulrich Kleiner (bottom); Josef Wilhelm/Uni Würzburg (top)

Graduate Education with an International Profile

Pilot phase begins for three Max Planck Schools

The Max Planck Schools' stated aim is to bring together exceptional scientists from across Germany to attract the most talented junior scientists for doctoral study. Three selected schools will commence a five-year pilot phase in 2018: the Max Planck School of Cognition, the Max Planck School of Photonics and the Max Planck School on Physics, Chemistry and Construction of Life. The development was announced in Berlin in early September by German Federal Minister of Education and Research Johanna Wanka, Max Planck President Martin Stratmann, and President of the German Rectors' Conference Horst Hippler. The schools are composed of members of 21 universities and 31 institutes from non-university research organizations, including 22 Max Planck Institutes. The diverse nature of their composition underlines the initiative's inter-institutional character.

Future-oriented concept: Max Planck President Martin Stratmann and German Federal Minister Johanna Wanka publicly announce the new Max Planck Schools at a press conference in early September.

"As supra-regional research and education networks, the Max Planck Schools bring together the best minds from across Germany. This new method of concentrating scientific excellence in particularly innovative fields of research will allow us to compete in the international arena for the most creative talent," said Max Planck President Martin Stratmann. The three schools, whose concepts for implementation are to be further refined, will receive annual funding of 9 million euros from the German Federal Ministry for Research and Education during the pilot phase.

On the Net

Pioneer of Glycobiology
Peter Seeberger, who was awarded the 2017 Stifterverband Science Prize, discovered a method to develop novel vaccines, therapies and diagnostic agents using automated sugar synthesis. A video on our YouTube channel profiles the scientist and explains how his research is developing innovative treatment methods in the fight against multi-resistant hospital germs and malaria.
www.youtube.com/user/MaxPlanckSociety

A Scalpel for the Genome
The CRISPR/Cas9 method makes it possible to alter the genetic make-up of an array of organisms much faster and more easily than ever before. But how does this promising technique actually work? And what are its applications? Our subject portal on genome alteration sheds light on the system's background and discusses its ethical limitations. The portal features interviews, photos and videos as well as an overview of other genetic engineering techniques.
www.mpg.de/10729275/genome-editing

Picture This
Since August 2017, the Communications Department of the Max Planck Society has been running an Instagram account. Employees can share photos and videos from their institutes, of events and of the results of their research using the hashtag #MaxPlanckSociety. This social media presence, aimed at a younger audience, aims to convey an entertaining image of life and work in all 84 facilities.
www.instagram.com/maxplanckgesellschaft

Photo: BMBF/Hans-Joachim Rickel

Germany's Digital Future **Is at Stake**

The German economy is booming, with research and development seeing welcome growth in recent years. However, our author, Chair of the German government's Commission of Experts for Research and Innovation (EFI), warns that we shouldn't content ourselves with our achievements to date. Germany still has some catching up to do, particularly when it comes to digital infrastructure and the internet offerings of German public authorities and ministries. But higher education institutions and young, innovative businesses need support from the new federal government, as well.

TEXT **DIETMAR HARHOFF**

Germany has already achieved considerable successes in its research and innovation (R&I) policy. For example, there have been significant increases in public and private research and development spending since 2005. There have been improvements in the positioning of German universities and research institutions in terms of attractiveness and excellence, and in the modernization of the German economy. Germany has moved significantly closer to its aim of playing a leading role as a location for innovation. At the same time, the challenges the country faces have continued to grow over the past few years.

> We should be targeting a pioneering role in research and innovation

These challenges include, for instance, combating climate change and shaping the future of mobility and our energy supply, as well as dealing with demographic change and ensuring equitable participation in the fruits of innovation. On top of this, the digital transformation poses major problems for German politics.

Germany won't be able to respond to these problems adequately unless its science, research and innovation sectors are further strengthened. In addition to implementing specific measures, the Commission of Experts for Research and Innovation (EFI) has recommended that German research and innovation policy formulate clear objectives that can be used to measure and evaluate future progress.

According to the EFI, Germany should invest 3.5 percent of its gross domestic product (GDP) in research and development by 2025, and should aim

A decisive role: Expanding the digital infrastructure, especially high-speed broadband networks in both the countryside and in cities, is crucial to the future success of the German economy.

Photo: Stihl024/fotolia


WILLEN

to establish three of the country's universities among the top 30 in the world. Furthermore, venture capital as a share of gross domestic product should double within the same period. The federal government should strive to ensure that Germany

For years, Germany has suffered from a lack of venture capital for young companies

becomes one of the five leading nations in terms of digital infrastructure in the coming years, and that it takes a pioneering role in e-government. In addition, the government should double its funding in the field of digitalization.

Germany has achieved notable successes with its research and development spending in recent years. In 2002, the European Union set member states the goal of increasing research and development expenditure to 3 percent of gross domestic product by 2010; in 2005, Germany was a long way from reaching that goal, with a share of 2.5 percent. In 2015, the share spent on domestic research and development finally reached 3 percent.

As one of the world's leading economic powers, though, Germany should be setting its sights much higher. Investing 3.5 percent of gross domestic product in research and development by 2025 would demonstrate the country's willingness to develop its technological competitiveness on a long-term basis and to catch up with other innovation nations.

Introducing tax incentives for research and development would represent a key step on the road to the 3.5 percent target, and would effectively complement existing, proven project funding measures. It would make sense to initially limit such support to small and medium-sized enterprises, whose willingness to innovate has receded in recent years. Tax incentives with modest subsidy costs would have significant effects for this group of businesses, making this a relatively efficient use of funds.

For years now, the Commission of Experts has recommended raising the prominence and international profile of the German science system. Despite their methodological shortcomings, international university rankings are an important point of reference for internationally mobile researchers and students. Positioning German universities at the top of international rankings would visibly document successful science policy – but this requires further substantial improvements in the higher education sector.

Over the last ten years, the federal government has already introduced a package of measures that have strengthened Germany as a location for science. One of those measures was the Excellence Initiative. The agreement on an open-ended follow-up program to the Excellence Initiative – the Excellence Strategy – is a welcome development. This program comprises two funding lines: institutional funding for the highest-performing universities and support for exceptional research structures.

A central challenge in the coming years will be to substantially improve the basic funding German universities receive and further reinforce their ability to compete internationally. The majority of German higher education institutions remain structurally underfinanced, and it is primarily the federal states that are under obligation. However, the Commission of Experts recommends that the German government and the federal states together initiate a follow-up program to the Higher Education Pact. The German government should continue to support the federal states in funding teaching and overhead costs, but this must not result in the federal states reducing their university funding contributions in other ways. The German government must therefore attach verifiable conditions to its support.

It is also important to increase the number of permanent professorships while at the same time improving student-faculty ratios and reducing teaching commitments for professors. This would enhance the German science system's attractiveness

in the international arena – both for outstanding researchers and for particularly talented students – as well as improve the quality of teaching for all students. More permanent professorships would also benefit junior scientists, as such a change would improve the career opportunities of the rapidly growing number of young researchers. Against this backdrop, universities could then rely more heavily on the tenure-track process, which provides junior scientists greater clarity regarding their career path and professional requirements.

Besides improving basic staffing and physical facilities, universities' organization and leadership also need to be modernized. Higher education institutions require greater scope to set themselves apart and to experiment with new administration and management structures.

But research and innovation policy doesn't end at the universities' gates. The German government can also lay important foundations for businesses – particularly young, innovative companies – to build on. For years, Germany has suffered from a shortage of venture capital. Young, innovative enterprises simply can't create and market their innovative products and business models without venture capital.

An international comparison shows that the German venture capital market is considerably less developed than those in the US and other European countries. While Germany invested some 0.027 percent of gross domestic product in young, growing companies in 2015, the proportion of GDP invested in such businesses in the US was more than ten times higher. Even in a European comparison, Germany comes in, at best, in the middle of the pack.

To overcome the weakness of the German venture capital market and make the country an internationally competitive location for investment, the German government introduced an array of improvements for venture capital investments and government-financed funds in recent years. However, the Commission of Experts advises against providing additional public funds for this purpose, recommending instead that the government remove barriers and create incentives to make investment in venture capital funds and startups more attractive for private investors.

The Act on the Further Development of Tax Loss Carryforwards for Corporations, passed in late 2016, was an important step in facilitating venture capital investments. Previously, loss carryforwards were eliminated when an investor purchased a certain number of shares in a company. But innovative companies in particular incur considerable research and development expenses in their first years that are then adjusted into loss carryforwards. If these unused losses for research and development work can no longer be used following a takeover, such companies become less attractive to potential investors.

The new regulation introduced by the German government aims to ensure that loss carryforwards can still be used despite a change in shareholders. This is conditioned on the entity's business operations being

> The expansion of the digital infrastructure shouldn't be aimed at achieving average targets

maintained after the change of shareholders, and on the losses not being used in any other way. However, it is now important that this condition be applied flexibly, as startups often amend and adjust their business model, target customer groups and technology. These changes are determined by commercial factors and mustn't lead to a situation where these loss carryforwards can't be used.

There is still one considerable handicap to Germany as a location for investment, namely the fact that – in contrast to many other European countries – fund managers' administrative services are subject to value-added tax, which makes Germany a relatively unattractive location to build and maintain venture capital funds. >

Photo: Stihl024/fotolia

A further important component of support for innovation is the development of digital infrastructure, which is now a major determinant of growth for modern economies. Digitalization is placing ever-increasing demands on the availability and capacity of internet connections. In an international comparison, Germany lags behind in almost all indicators relating to broadband expansion with high-speed networks above 50 megabits per second. At the same time, it can be assumed that an internet infrastructure with bandwidths of 50 megabits per second will no longer be sufficient in the not too distant future.

Network operators are currently predicting that, by 2025, average private internet speed demands will reach 400 megabits per second for downloads and 200 megabits per second for uploads. The Commission of Experts thus considers the German government's existing plans to expand the country's broadband infrastructure to be far from adequate. Germany needs an ambitious expansion of its infrastructure – not one that is in line with the average values for OECD member states, but one that leads the way in terms of output and capacity for further expansion. The expansion targets must be dynamically adapted to the respective technical standards.

Germany also needs to catch up in terms of digital governmental and administrative processes – so-called e-government. The range of digital public-sector services remains limited and isn't very user friendly. What's more, government-managed datasets still haven't been made freely accessible as Open Government Data, and well-structured access modalities are lacking, too.

These deficits are due mainly to Germany's federal structures, as administrative organization is largely the responsibility of the federal states. The lack of higher-level, legally binding specifications and the various federal actors' divergent interests in expanding e-government have led to disjointed and technologically heterogeneous provision in this area.

An important step toward overcoming this unsatisfactory situation was taken in late 2016, when the reform of federal and state financing relations was passed. As part of this reform, an amendment to the Basic Law gives the German government legislative power to structure access to the administrative services of the federal and state governments, including at the municipal level.

The complementary law passed by the Cabinet – known as the Online Access Improvement Act – requires the federal government, states and municipalities to provide their administrative services online and make them accessible via a network of federal and state administration portals within five years. This should make it possible for citizens and businesses to access all online-capable services easily and with no media discontinuity through an administration portal, and to use a single user account for all services.

> The government neglected to direct sufficient funding to information technologies

Fortunately, these changes have led to significant improvements in the basic conditions over the past few months. As a result, there is now an opportunity to create and develop effective digital portals for government and administration and thus raise the quality of e-government in Germany to international standards in the next few years. To achieve this objective, the German government must actively use its newly gained authority in the new legislative period and present workable solutions to expand e-government in Germany.

The digital transformation is progressing at an impressive pace and currently represents a major challenge for the German economy. The technologies and business models being used aren't among the core strengths of the German research and innovation system. Especially for Germany, the digital transformation represents a radical change in almost all areas and challenges the competitive and specialization advantages the country has earned over the years.

Research and innovation policy to date has paid far too little attention to the technological and eco-

Photo: Stihlo24/fotolia

nomic dynamics underlying this transformation. Government support for research and development in information and communication technologies remains underdeveloped, despite the welcome fact that the federal government significantly increased total spending for research and development – from 12.0 billion euros in 2009 to 15.8 billion euros in 2016. However, the distribution of these funds to individual funding areas has remained largely constant.

Between 2009 and 2015, the German government simply neglected to direct sufficient funding to information and communication technologies, which are crucial to managing the digital transformation. It wasn't until 2016 that the target funding amount suggested that this area was being assigned higher priority. In view of digitalization, Germany must develop new technological and economic strengths in the coming years, so this field of action should be a high priority in the new legislative period.

It is also important to more effectively focus the currently fragmented and sometimes even opposing activities of departments tasked with establishing digital policy. Above all, the new federal government must ensure that it quickly implements further measures to strengthen digital infrastructure and that it effectively supports research and innovation, particularly in small and medium-sized enterprises. Potential solutions include an innovation agency, which has already been discussed in the Bundestag; a coordination office in the Federal Chancellery; and the formation of a ministry for digital affairs with broad competence in such areas as infrastructure, promoting innovation and e-government. These organizational structures each entail various benefits and drawbacks – it is the Commission of Experts' opinion that no one of these options is clearly superior to the others.

In any case, political leaders must focus the competencies available to them more effectively than has been done to date, thus sustainably reducing complexity. Considering the challenges it faces, Germany can't afford long-winded decision-making and implementation processes – its politics, too, must become much more agile. ◀

Photo: David Ausserhofer/MPG

THE AUTHOR

Dietmar Harhoff, born in 1958, is a Director at the Max Planck Institute for Innovation and Competition and Chair of the German government's Commission of Experts for Research and Innovation (EFI). After completing a degree in mechanical engineering, he began his professional career as a research engineer in the United Kingdom and Germany. He then obtained a master's degree from Harvard University and earned his doctorate at Massachusetts Institute of Technology (MIT). In 1996, he qualified as an economics professor at the University of Mannheim and, two years later, was appointed to a position at Ludwig-Maximilians-Universität in Munich, where he headed the Institute for Innovation Research, Technology Management and Entrepreneurship from 1998 to 2013.

Science as a Profession, Not as a Hobby

Max Planck scientists cooperate with partners in more than 110 countries worldwide. Here they relate their personal experiences and impressions. Marcin Serafin studied sociology at the University of Warsaw. For his doctoral thesis, he chose to attend an International Max Planck Research School, where he enjoyed the opportunity to concentrate exclusively on his doctoral research – a stark contrast to the usual working conditions of doctoral students in Poland.

I had already become interested in the social aspects of economic phenomena when I was in high school, and this interest remained with me throughout my master's studies at the Institute of Sociology at the University of Warsaw. At the time, though, I wasn't aware that there was an entire sub-field dedicated to this topic: economic sociology. It wasn't until I spent time at the Max Planck Institute for the Study of Societies that I was able to discover the field and really pursue my interests.

For my doctoral thesis, I researched how various social aspects of the lives of taxi drivers affect their working time. Unlike people working in many other occupations, taxi drivers aren't employees who have fixed working hours. Instead, they are individual entrepreneurs who have the flexibility to decide when they want to work and for how long. As a result, unlike other workers whose working hours are governed by their employment contract, the time they spend working is influenced by a wide range of factors that are often neglected in standard economic models – such as their living conditions, gender and family situation.

Graphic: iStockphoto

Marcin Serafin, 31, studied sociology at the University of Warsaw from 2005 to 2010 before joining the Max Planck Institute for the Study of Societies through the International Max Planck Research School. He is currently an assistant professor at the Institute of Sociology and Philosophy at the Polish Academy of Sciences and has been Leader of the Max Planck Partner Group for the Sociology of Economic Life since April of this year.

Taxi drivers' working hours also reflect the fact that they don't see themselves as workers, but as sole proprietors who are in direct competition with each other. For this reason, it's difficult to mobilize them to act collectively and to motivate them to join a trade union that would represent their interests. Other occupational groups fight for better working conditions and the reduction of their working hours with the help of trade unions.

While doing my doctorate, I received a lot of support from my Institute and my International Max Planck Research School. It was wonderful to be able to focus completely on the task at hand and not have to concern myself with administrative or teaching responsibilities. This is very different from the typical working conditions of doctoral students in the social sciences in Poland. It's difficult to focus exclusively on your doctoral thesis there, as you usually have to take on other jobs to earn a living. As a result, the doctoral research often becomes more of a hobby or an investment in a non-academic career.

Of course, pursuing a career in science is difficult everywhere, particularly in the beginning when you start out as a Research Group Leader. My group being granted Max Planck Partner Group status made life considerably easier for me when I started in this role, and I really wish more people were aware of this possibility. I lead a small and creative team at the Polish Academy of Sciences, and we plan to commute to the Max Planck Institute for the Study of Societies in Cologne several times a year. Scientists there will also come to Warsaw, as our kickoff workshop will take place here next year. I think my team will really enjoy this collaboration with the Max Planck Institute.

My team is working on two research projects. The first studies how people's expectations about the future influence their current economic behavior. For example, the decision to take out a mortgage on a house is based on an expectation of how your life will unfold over the next 20 years – something that is very difficult to predict. We're also researching how digital platforms such as Airbnb and Uber are restructuring economic and social life – particularly the working conditions of the members of this new digital economy and their participation in trade unions and different forms of collective action.

Photo: Private collection

Nature **as a Pharmacy**

Bacteria, plants and animals are full of unknown substances that could be beneficial for humans. At the **Max Planck Institute of Molecular Physiology** in Dortmund, **Herbert Waldmann** tests natural products for their biological efficacy and tries to mimic their effects with simpler molecules.

TEXT **CATARINA PIETSCHMANN**

Evolution has endowed many species with substances that enable them to communicate, attract partners or deter enemies. Some of those substances have also proved to have powerful effects in humans. Taxol, a compound discovered in the bark of the Pacific yew, is one example. And Germanic tribes were already aware of the analgesic effect of salicylic acid obtained from willow bark.

Atropine, a substance from deadly nightshade that blocks nerve cell receptors; morphine from the opium poppy; and penicillin antibiotics from various fungi – the list of small molecules with potent effects is endless. "Almost a third of our drugs are still derived from natural products, and another third are proteins," says Herbert Waldmann, Director of the Department of Chemical Biology at the Max Planck Institute of Molecular Physiology.

In the 1990s, a scientific field known as combinatorial chemistry was used to synthesize a large number of chemical compounds. Hundreds of thousands of compounds were collected in substance libraries and screened in high-throughput tests for their pharmacological effects on cells.

TOO FEW NEEDLES IN THE HAYSTACK

The sobering conclusion was that just one in one hundred thousand compounds has a biological effect, corresponding to a hit rate of just 0.001 percent. Now, you might argue that, given one million candidate compounds, you would at least have ten hits. "Unfortunately, this calculation was not borne out," says Waldmann. "Continuously expanding the substance libraries isn't the solution." An ever-growing haystack doesn't automatically contain more needles.

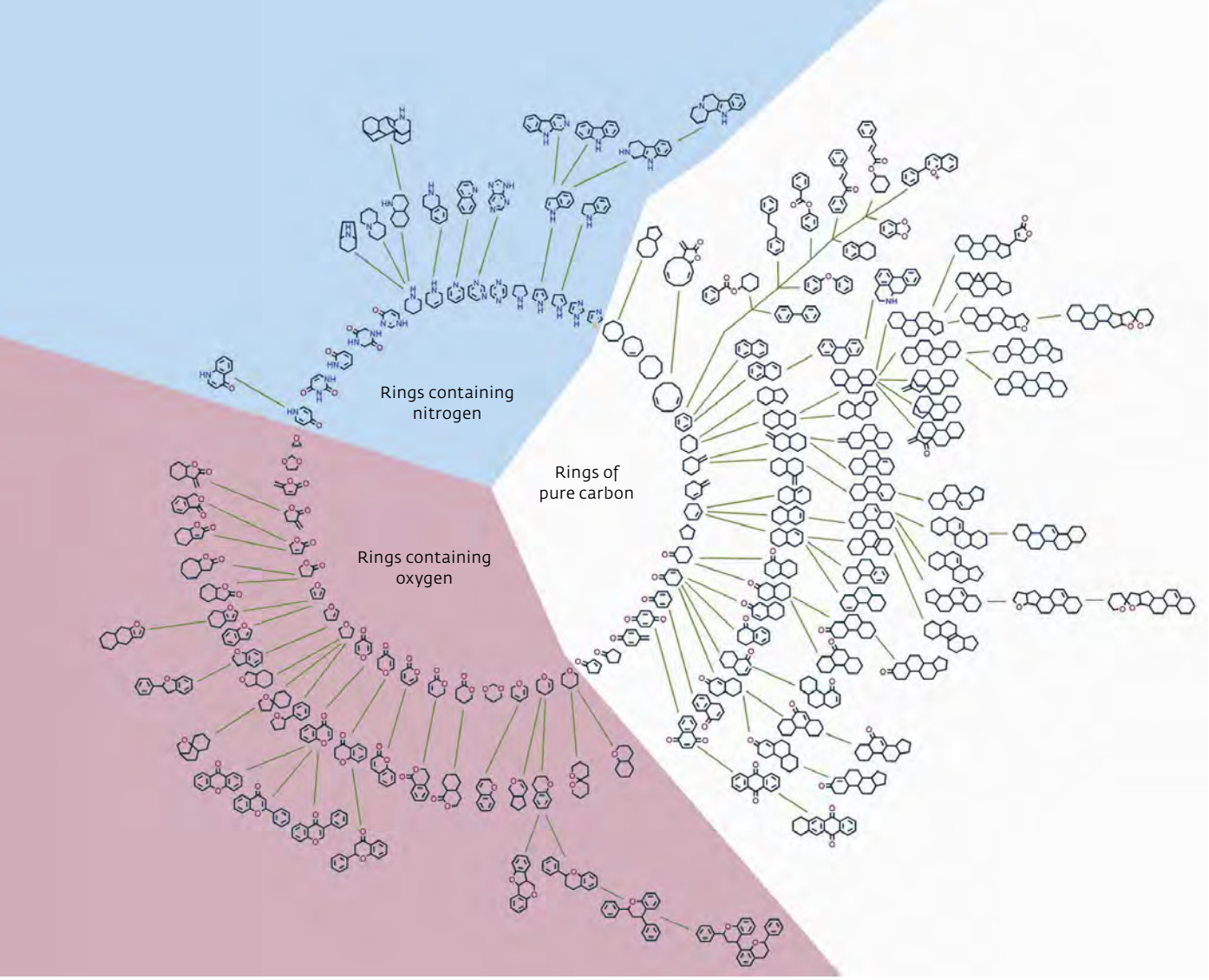
The synthesis of complex natural compounds is still an exciting challenge for chemists. It also marked the start of Waldmann's scientific career. "But this form of drug discovery is slow, and multi-stage chemical syntheses are often unsuitable for producing substances on a large scale for industry."

Waldmann therefore took a different approach. Instead of randomly synthesizing and screening chemical compounds, he let himself be guided by chemical structures that have already proved effective. "We are trying to understand what is essential in the structures of natural products and to use those findings to synthesize new compounds," Waldmann explains.

A drug works because its active substance binds to the active center of a protein, altering or completely block-

The pain-relieving and fever-reducing effects of an extract of willow bark were already known in antiquity. The effects are due to the presence of salicin, which the body converts into the active substance salicylic acid. It is the lead structure of the even more potent and safer compound acetylsalicylic acid (ASA), the active substance in aspirin.

Photo: Shutterstock



Molecular tree: The chemical structure of the natural substances at the twigs can be simplified in a step-by-step process. In this way, researchers can trace along a branch to a basic structure that still exhibits similar biological activity to the original compound but that can be more easily synthesized in the lab. The computer program Scaffold Hunter, which was developed in Waldmann's department, is based on this principle.

ing the protein's activity in the process. It is striking that nature uses only a modest number of proteins from all that are theoretically possible. In purely mathematical terms, 10^{390} proteins with a length of 300 amino acids could be synthesized from the 20 naturally occurring amino acids. Yet even the genomes of highly developed organisms contain the blueprints for no more than a hundred thousand proteins.

Nature is just as parsimonious when it comes to protein folding. "There are probably no more than several thousand folding types," Waldmann speculates. "This makes sense – after all, nature doesn't need to constantly reinvent the wheel." As a result, a substance from bacteria is effective in humans because it fits into the binding pocket of a protein that the common ancestor of bacteria and humans already largely possessed hundreds of millions of years ago.

The active molecules that occur in nature are likewise limited. They usually consist of up to nine interlinked ring systems, but most natural substances have only two to four rings. With this format, they evidently fit into the binding pockets of most proteins. Although the basic shape and size of the binding pockets thus vary within only a narrow range, their chemical "lining" is highly variable. "How selectively a drug binds depends on the side chains of the proteins and the functional groups of the natural substances."

Waldmann's strategy for discovering new drugs is to simplify the chemical scaffolding of the natural products to such an extent that a compound is just barely effective. He then approaches the effectiveness of the original by attaching functional groups to the molecule. In this way, he doesn't have to deal with large, complex molecules and can instead concentrate on smaller ones that are easier to synthesize. "What's the use of even the most effective natural substance if its complicated structure means that only a few crumbs can be produced? It might be the savior of humankind, but if 100 kilograms of it were needed, it would still be useless," Waldmann says.

First, he needed an overview of the diversity of the structures of natural substances – a Herculean task that would be impossible without the help of a computer. Waldmann's team wrote a software program and analyzed all 190,000 natural products

Graphic: Max Planck Institute of Molecular Physiology

Photo: Frank Vinken

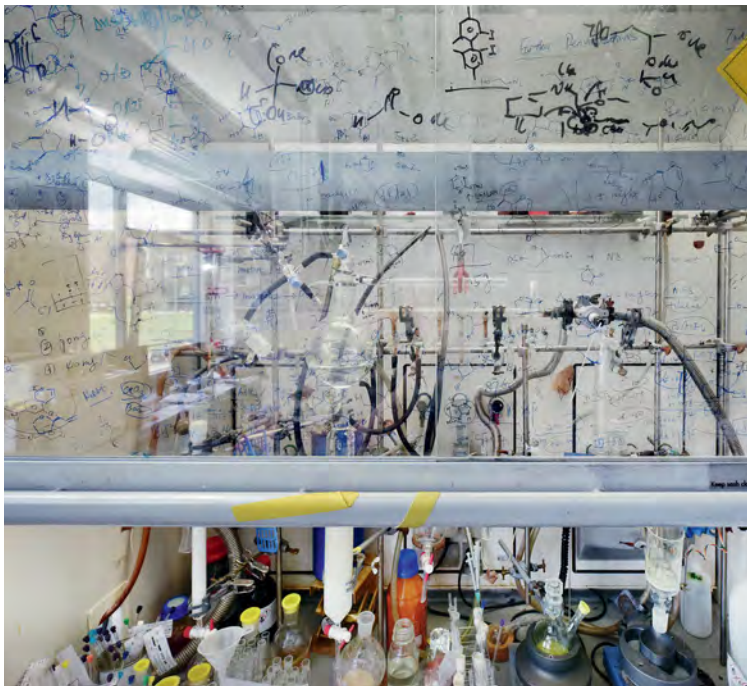
Tracking down new drugs: Taking nature as a model, Herbert Waldmann is utilizing naturally occurring molecules to develop new substances for medicine that are easier to synthesize and more effective than their natural counterparts.

known at the time. They then trimmed them back to their chemical backbone and sorted them according to complexity and structural kinship. The result was a tree-like structure. The most complex, but often most effective, nodes are located on the outermost branches. Toward the trunk, the structures become simpler and their biological activity weaker.

The trunk is formed by the simple molecular rings arranged by size and divided into sectors of pure carbon rings and oxygen- and nitrogen-containing rings.

FROM COMPLEX MOLECULES TO SIMPLE ONES

Scaffold Hunter, as Waldmann named the program, is available to scientists and pharmaceutical companies the world over free of charge. The software contains – if known – the biological activity of the natural products stored in it. If a researcher has found an active substance corresponding to a particular disease, he or she can trace the branch from the complex original structure toward the trunk to find a simple compound that can easily be synthesized and optimized. Because such a basic compound is simpler in structure than a natural product, it tends to be less selective and can bind to multiple proteins. The drug candidate then has to be tweaked so that it binds exclusively to the target protein. Otherwise, it could trigger severe side effects and would be useless as a drug. >



Left For screening purposes, a robotic dispenser applies solutions to test plates. Instead of a test liquid, an orange dye is applied from the device's supply tank to check the accuracy of the instrument, which can then be calibrated.

Right Glass extraction shafts in the labs prevent gaseous substances from escaping from the apparatus. The researchers sometimes scribble chemical formulas on the front panels of the extractors.

Waldmann's team has in fact had significantly greater success with this approach. Instead of 0.001 percent, their hit rate is now around 1 percent. "When we make 200 variants of a selected class of substances, an average of two turn out to be useful. After the second optimization round, we usually have 20 to 30 potent molecules," Waldmann says.

Things become especially interesting where there are gaps in the structural tree of natural products. For example, if a substance with four rings is biologically active and one with two rings is as well, it can be surmised that a compound with three rings will also be active. "We tested that premise and confirmed it in cell tests. The program is therefore able to predict the biological activity of substances," Waldmann explains.

Herbert Waldmann's research would hardly be possible without extensive cell tests, known as screenings. In creating the Compound Managing and Screening Center (COMAS) at the Max Planck Institute in Dortmund, the Max Planck Society merged its previously scattered substance libraries. The combined library now contains over 250,000 chemical compounds. Most of them were acquired from other suppliers, but 10 percent of them come from Max Planck laboratories. They don't exist anywhere else in the world. Every Max Planck scientist can use the Center and test substances for their effects.

SUBSTANCES FOR CANCER RESEARCH

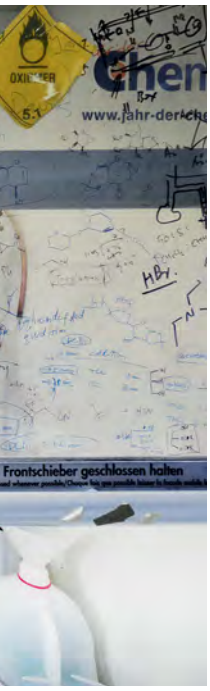
Some of the samples are from Waldmann's own department. His team has used Scaffold Hunter to synthesize its own library of substances based on natural products. The scientists use the program mainly to search for cancer drugs, taking a biological hypothesis as their starting point.

An example: "Cancer cells need large amounts of nutrients to grow. If we block the channel proteins in the cell membrane through which, for instance, sugar enters, we could starve the cancer cells. So we searched for an inhibitor of those membrane channels in our library – and our efforts paid off." The researchers then optimized the inhibitor and handed it over to the Lead Discovery Center next door.

The Lead Discovery Center was founded in 2008 on the initiative of the Max Planck Society to bridge the gap between basic research and industry. The Center's scientists test the efficacy, uptake and tolerance of promising drug candidates in animals and, if necessary, improve those properties. If the tests are satisfactory, a pharmaceutical company can purchase the license for the active substance and carry out the necessary clinical tests.

Very few candidates successfully make it past the Lead Discovery Center. Englerin, for example, a plant-derived natural substance that selectively kills renal cancer cells in cell tests, failed the

Photos: Frank Vinken (2)



Left The cells grow in the liquid-filled wells of the plates at a temperature similar to that of the human body. This allows researchers to directly test the effects of substances from the Center's library of compounds.

Right Sonja Sievers heads the Screening Unit of COMAS. Using a modern robotic system, she is able to screen a large number of chemical compounds for biochemical and cellular effects.

first experiments in animals. "The mice died within five minutes, because englerin blocks a calcium channel not only in cancer cells but also in lung tissue, resulting in massive edema," Waldmann says.

Substances that block the Ras signaling pathway in cancer cells have long been right at the top of Waldmann's agenda. They attracted his attention as early as the 1990s while he was still working in Bonn. A mutation leads to Ras proteins, which are anchored in cell membranes via their fatty acid residues, giving cancer cells a signal to undergo division. Mutated Ras proteins play a role in one third of all cancers.

Waldmann began to develop active anti-Ras substances and, in doing so, reached "the natural limit of chemists," as he puts it. "You've synthesized a molecule – and then what? You open the fridge door, put the substance in, close the door … and move on to the next project?" That wasn't enough for Waldmann. He searched around for someone who knew more and discovered Alfred Wittinghofer, who was then head of the Structural Biology Department at the Max Planck Institute in Dortmund. Wittinghofer was studying the mode of action of these signaling proteins together with cell biologist Philippe Bastiaens, now also Director at the Institute.

TRACKING RAS TOGETHER

"Wittinghofer was, so to speak, 'Mr. Ras'. And I thought to myself: you should call him," Waldmann recalls. This was the start of a highly successful collaboration between the two scientists. In 1999, Waldmann himself was appointed to the Max Planck Institute, where he now heads the Department of Chemical Biology, and Bastiaens came to Dortmund a few years later. From that point on, the three departments complemented each other. Wittinghofer and Bastiaens unraveled how Ras is transported in cells. What the researchers then needed was a molecule that blocks this transport process. That's where COMAS came into play. "Together with COMAS, we developed a cell test and combed through our library. We then further optimized the prime candidates in the lab."

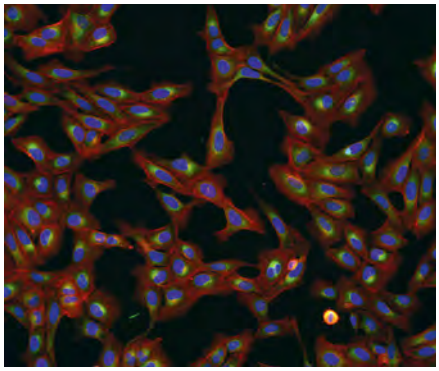
One of those candidates was deltarasin, which blocks Ras transport and therefore the signal pathway. Unfortunately, however, it also disrupts other processes, causing serious side effects. Other candidates, on the other hand, produced fewer side effects but weren't effective enough. Cancer cells even succeed in reversing the Ras blockade. Meanwhile, the Max Planck scientists are developing the fourth generation of blockers that dock so tightly to their target protein that cancer cells are unable to remove them.

Waldmann has high hopes for a technique known as cell painting. He plans to develop a cell test that will allow him to say right after the synthe-

Photos: Frank Vinken (2)

Below Cell painting is a technique for staining cellular organelles such as the nucleus (blue), the endoplasmic reticulum (green) and the cytoskeleton (red). If a substance acts on one of these organelles, it will produce an altered color pattern.

Right System operator Miriam Kunkel curates the COMAS substance library, which contains more than 250,000 compounds. Temperatures of around minus 20 degrees Celsius ensure that the molecules remain intact even after prolonged periods.



sis: "We don't know what the molecule can do yet – but we do know that it has potential!"

Next, Waldmann would like to go beyond what nature can do. "We know that the number of basic chemical structures in nature is limited. So far, we have only mimicked what nature has already achieved, so we only find the bioactivities of those natural products, never anything completely new." Waldmann therefore wants to break down the molecular structures found by Scaffold Hunter into smaller fragments. "Then we can reassemble them in ways that nature has never done!" This will create substances that look like natural compounds but aren't: pseudo-natural substances – "nature 2.0", as it were.

But will it work? Waldmann nods. They have already been successful on two occasions – not enough to be able to make a definitive statement, but the signs are good that his drug libraries will soon be enriched with new, promising substances. ◂

TO THE POINT

- **Using a software program, scientists are able to strip the chemical structure of a biologically active natural product down to its basic molecular scaffolding. Such products are easier to synthesize and, if necessary, optimize in the lab.**
- **By combining individual structural elements of natural products, scientists hope to create chemical compounds with completely new properties.**
- **A number of institutes have grown up around the Max Planck Institute of Molecular Physiology in Dortmund to explore potential new drugs and pave the way for their use in medicine.**

GLOSSARY

Cell Painting: A technique that involves labeling various signaling pathways or cell organelles with fluorescent dyes, resulting in a multicolored pattern. For drug screening, the colorful cells are distributed across multiple test samples and exposed to substances whose effects on cells are well known. These reference substances change the color patterns in a characteristic way. The effects of a new, unknown molecule can then be derived by comparing the color patterns.

COMAS: The aim of the Compound Management and Screening Center is to exploit scientific findings from basic research by the Max Planck Society for medical research and the development of new therapeutic applications. Each substance in the substance library, which currently holds 250,000 compounds, is stored in barcoded tubes at minus 20 degrees Celsius. Tiny amounts of substance – just a few billionths of a liter (nanoliters) – are sufficient for the screening tests. Substances that show promise in the tests at COMAS are passed on to the Lead Discovery Center, where they are refined for medical applications.

Photos: MPI of Molecular Physiology (left); Frank Vinken (right)

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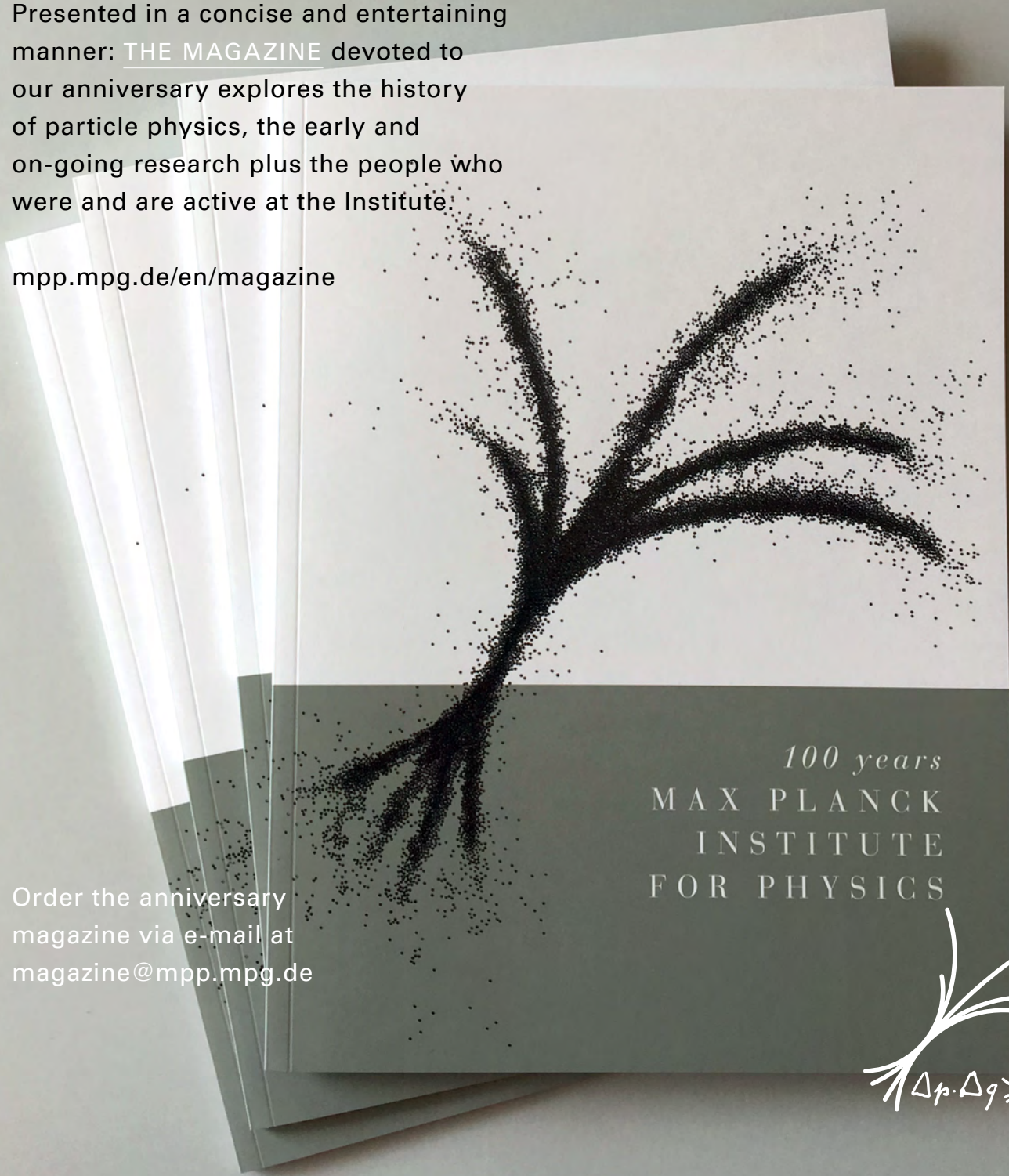

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Transporting Toxins to Tumors

Developing drugs that eliminate cancer cells effectively and have few or no side effects – this is one important aim of the Research Group led by **Tanja Weil**, Director at the **Max Planck Institute for Polymer Research** in Mainz. Weil and her team of chemists convert proteins into traceable drug transporters for nanomedicine with the help of miniscule diamonds.

TEXT **PETER HERGERSBERG**

You could be forgiven for thinking you had misheard her at first: "I always found polymers to be a bit suspicious," says Tanja Weil, who completed her doctorate at the Max Planck Institute for Polymer Research and is now Director there. Polymers are long, often net-like molecules composed of numerous small chemical subunits that are repeated many times. The highly versatile and durable synthetic materials that have become indispensable to our everyday lives consist of these chains of molecules.

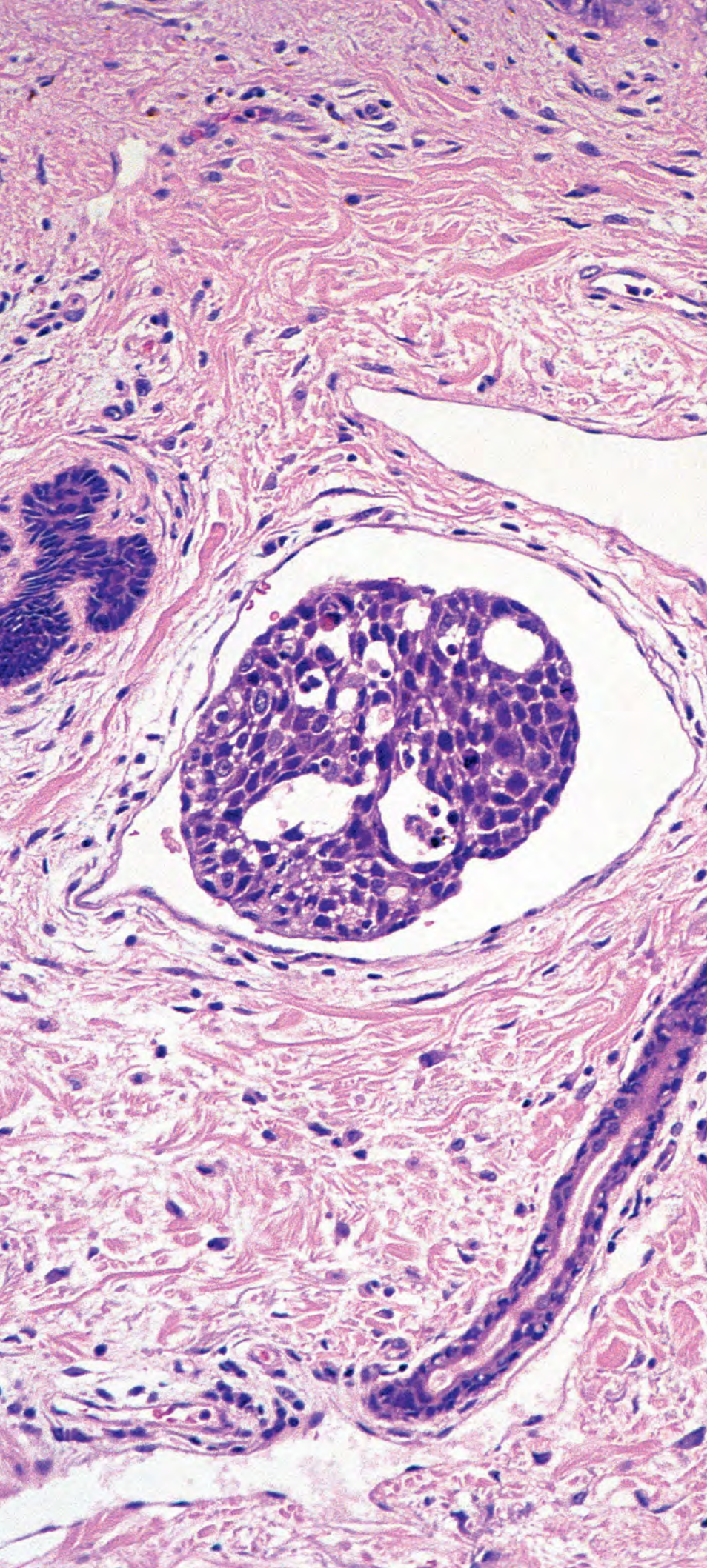
The fact that Tanja Weil was nevertheless initially wary of polymers owes not least to aesthetic factors: "I felt that the beauty and precision of organic chemistry had been left by the wayside here." The scientist, who switched to the MPI in Mainz from the University of Ulm in 2016, explains it in very simple terms: "In classical polymer chemistry, when you mix the monomers and press the start button, the reaction comes to an end at some point and that's it." In most cases, the product of such reactions is a more or less diverse mixture of chain molecules of varying lengths. Unsurprisingly, for her doctoral research, Weil also worked on one of the few polymer classes with a precisely defined structure: dendrimers – symmetrical tree-like molecules whose branches are assembled in a controlled fashion from the same basic chemical components.

POLYMERS AS VEHICLES FOR SUBSTANCES

The often uncontrolled growth that dominated in the test tubes of polymer chemists seemed less than optimal for the applications that Tanja Weil had set her sights on for polymers. She wanted to use the chain molecules as transporters for medical substances, for example to precisely maneuver cytotoxins to a tumor. The aim of this form of nanomedicine would be to wreak as much havoc as possible within cancer cells while causing no damage to the rest of the body. However, when chain molecules differ in length, they could also be loaded with different amounts of active substances. "But promising new approaches are now available that implement structural precision in polymer synthesis and make it possible to change this," says Tanja Weil. As she explains, it is essential that the polymers used in medicine be able to be loaded with an active substance in a controlled and reproducible fashion: "Patients would like their daily pills to contain the same dosage every day."

Leukemia patients, for example, could benefit from a treatment that specifically targets cancer cells: "With the standard treatment that has been used for acute forms of leukemia since the 1960s and 1970s, we ride roughshod over all blood-forming cells," explains Michaela Feuring-Buske, who is a professor at the Department of Internal Medicine III and at the Institute for Experimental Cancer Research of Ulm University Hospital and works on the development of new therapeutic ap-

Photo: Science Photo Library/Biophoto Associates



proaches for the treatment of leukemia. She has been working with Tanja Weil since her time as a professor in Ulm. The scattergun approach aimed at all rapidly dividing cells also affects healthy cells – with corresponding side effects: hair loss, nausea, a reduced white cell count and even damage to the cardiac muscle and the central nervous system, to name just a few. "So the development of a more targeted approach to cancer treatment is timely and a very attractive prospect," says the Ulm-based physician.

Tanja Weil's motivation for developing transporters for pharmaceutical substances probably originates from the time she spent working for pharmaceutical company Merz. She managed various positions there while also carrying out independent research at the Max Planck Institute for Polymer Research. Although nanocarriers that transport drugs to the exact location in the body where they are needed don't currently feature in the standard repertoire of pharmaceutical concerns, Tanja Weil has been working on their development with her colleagues since she returned to full-time academic research.

The list of requirements for a targeted drug transporter is long: it not only needs a protected loading space for the active ingredient, but it must also have a kind of address label so it can identify its destination. In addition, the drug carrier must be able to disguise itself to

Target of the nanoattack: Max Planck researchers in Mainz aim to use protein carriers to infiltrate cytotoxins into cancer cells, including breast cancer tumor cells (purple).

evade the vigilance of the immune system. It would also be nice if it had markers on it that would make it possible to track the active ingredient's progress through the body. And of course all of this must be tolerated by the body. There are very few materials that can fulfill these requirements.

PROTEINS AS PRECISION POLYMERS

For this reason, Tanja Weil and her colleagues came up with a new idea. They asked themselves whether the precision biopolymers, such as proteins, can be used as classical polymers. Proteins occur in different spatial forms in the body, but most of them tend to be stubby with bulges and dents. This specific spatial structure and the surface chemical properties mean that every protein molecule is a specialist. Some of them adhere to other proteins so they can carry out tasks together; others convert smaller molecules into substances the organism needs at a given time, or transport these molecules to a specific site.

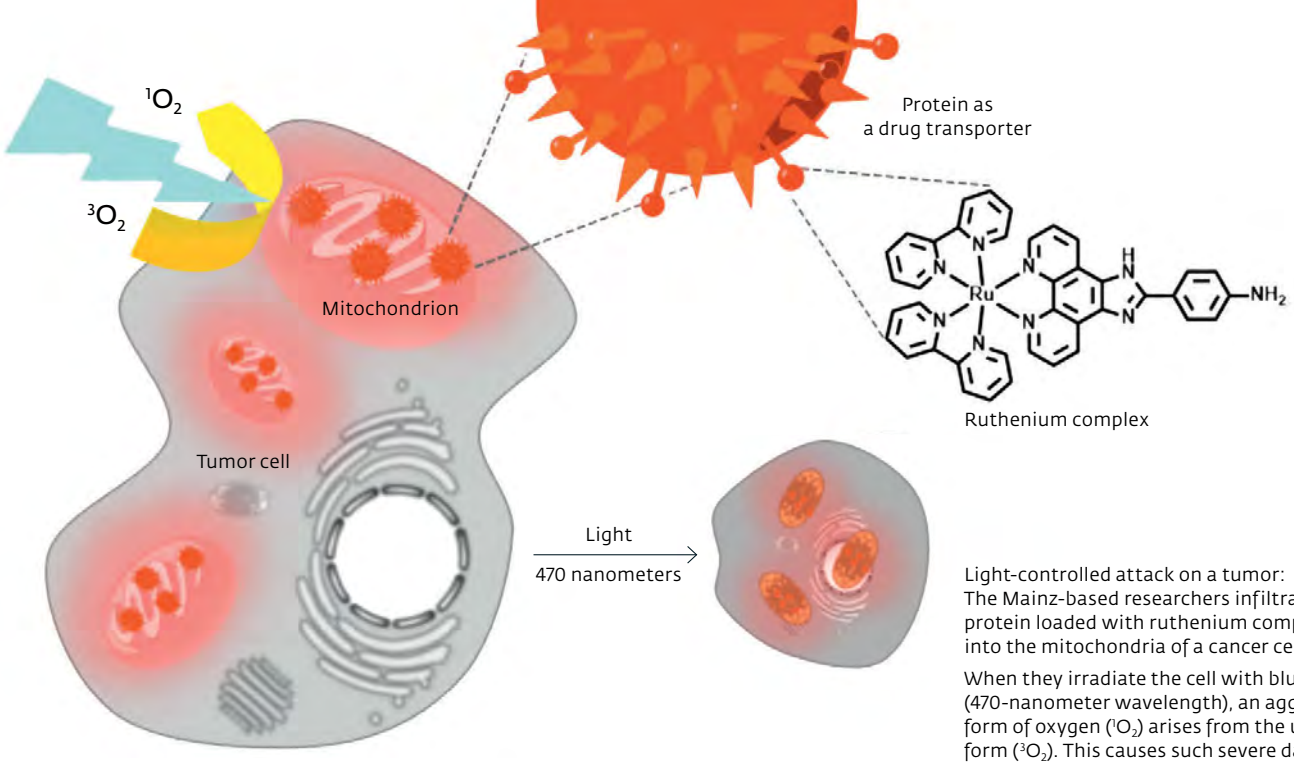
When untangled, however, a protein is always a chain molecule with a precise length and composed of a defined sequence of 21 different amino acid components. Absolute precision is required here, as a specific chain of amino acids is essential for the protein to be able to fold itself into the form that does the job assigned to it within the organism.

The properties of the amino acids are determined by characteristic molecular groups – functions, as chemists call them. Some of them work like chemical hooks to which other molecules, such as active drug molecules, can attach themselves. This is precisely what Tanja Weil and her colleagues do. They have developed some promising candidates for animal studies, in which potential drugs are now being tested. And it is very much a team effort, as Tanja Weil emphasizes. Indeed, the most ingenious solutions for a particular problem often arise only when a group gets together for a chat over coffee in her office.

This was also the case when Weil's group faced its first hurdle in the process of developing protein carriers for medical substances. To enable proteins to be used as polymeric materials, the entangled amino acid chains first had to be unraveled. This involved dissolving the bonds between links in the chain molecule located far away from each other and folding the protein into its biologically active form. To prevent the polymer from being entirely dismantled, however, the stronger chemical bonds between the individual links in the amino acid chain had to remain intact. This process, which biochemists refer to as denaturation, is simply what happens when you fry an egg: the heat breaks down the bonds that give the protein molecule its three-dimensional structure. The unfolded proteins coagulate, and the egg white solidifies. This renders the proteins useless for any other application except being served on a plate: "You can never get them back into solution," says Yuzhou Wu, a Research Group Leader in Weil's Department and now also a professor at Huazhong University of Science and Technology in Wuhan, China.

Orchestrating the team effort: When Tanja Weil and her colleagues work on converting proteins into nanotransporters for drugs, she often formulates the problems to which solutions are found during the team's discussions.

Photo: Thomas Hartmann



Light-controlled attack on a tumor: The Mainz-based researchers infiltrate a protein loaded with ruthenium complexes into the mitochondria of a cancer cell.

When they irradiate the cell with blue light (470-nanometer wavelength), an aggressive form of oxygen ($^1O_2$) arises from the usual form ($^3O_2$). This causes such severe damage to the cell that it dies.

Primarily through the tests that Yuzhou Wu carried out when she worked with Tanja Weil at the University of Singapore, the group found a way to denature proteins without causing them to coagulate. "Before or shortly after we unfold them, we graft water-soluble components, such as polyethylene glycol, to certain amino acids," explains Yuzhou Wu. "In this way, we keep the denatured proteins in solution."

Polyethylene glycol, known as PEG, not only makes the protein water-soluble, it also enrobes it in a cloak of invisibility. The appeal of the protein transporter lies in the fact that it is biodegradable, but this process shouldn't begin until the drug carrier has reached its destination – so the fact that the PEG attachments can hoodwink the immune cells is very helpful. The body's law enforcement units don't initially identify the unfolded protein, which means that it can circulate in the bloodstream for a longer period and its inevitable destruction as a foreign body is delayed.

Yuzhou and other members of Tanja Weil's group have already packed drugs in such cunningly disguised nanotransporters, such as Doxorubicin – a drug used in the treatment of acute myeloid leukemia, which affects mainly older people. Because this cytotoxin has strong side effects, the Max Planck chemists wanted to use a protein to transport it directly to the tumor cells. In this case, they used human serum albumin (HSA) from human blood. "We load HSA with Doxorubicin at the stage we can control most precisely, which is directly after denaturation," says Yuzhou Wu.

DRUG TRANSPORT INTO THE CELL ORGANELLES

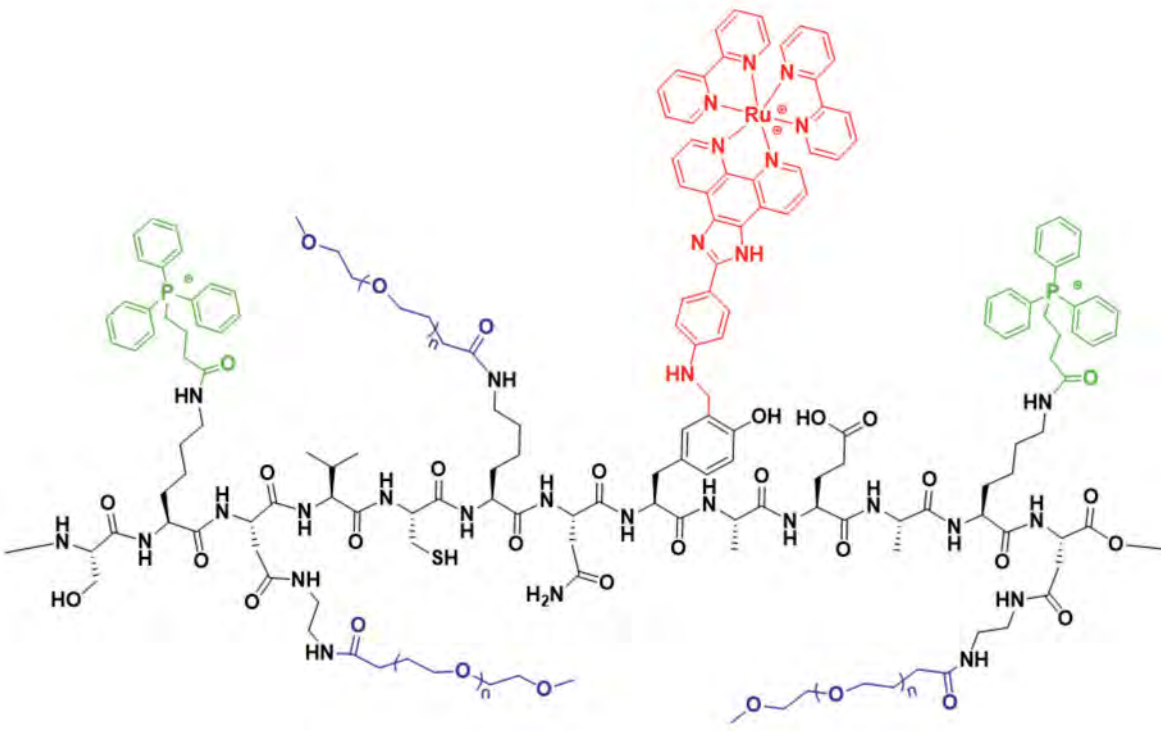
The researchers attach the drug molecules to thiol groups of the amino acid cysteine. "And because all HSA molecules have the same number of accessible thiol groups, each protein molecule carries around 27 molecules of the active ingredient," says Yuzhou Wu. Deviations occur only when no drug molecule finds its way to a thiol group in the reaction mixture.

And, as initial tests have shown, the concentrated loading of the drug on the protein is effective: a comparatively small volume of Doxorubicin-loaded biopoloymers succeeded in killing half of the cancerous cells in cultures containing different leukemia cells. The effect was also confirmed in a study carried out over a period of 12 weeks in which mice were initially injected with differently treated cancer cells. While mice with leukemia cells that had been treated only with Doxorubicin survived on average for 69 days, all of the animals whose cancer cells had been targeted by protein carriers loaded with the cytotoxin were still alive at the end of the entire study period.

Tanja Weil's group is now investigating an approach for optimizing the effectiveness of the transport of the toxin to tumor cells. The idea for this arose when a project wasn't as successful as the scientists had initially hoped. Sabyasachi Chakrabortty, a postdoc working in Weil's group, had packed an HSA carrier with around ten ruthenium complexes. The application of light energy to this precious metal produces an aggressive form of oxygen. In addition, the researchers equipped the ruthenium complex with a human hormone that bonds specifically with receptors on tumor cells.

"We then observed in cell cultures that the nanotransporters actually go into tumor cells and their toxicity increases when we irradiate them with light," explains the chemist. "The combination with the hormone also made them specific to cancer cells." However, compared with treatment with a pure ruthenium complex, the nanotransporter that targeted the tumor cells worked only slightly better. "We were very disappointed with this result," admits Sabyasachi Chakrabortty. However, the Max Planck chemists refused to simply accept it and asked themselves why it was that their targeted freight wasn't more effective and how they might be able to improve it.

Graphic: Journal of The American Chemical Society, ACS, Jan 2017



Graphic: Tanja Weil

Again, a crucial suggestion arose during a team meeting: they should try to transport the drug specifically to certain organelles in the cell instead of simply infiltrating it into a tumor cell and leaving it to its own devices. The chemists quickly identified the mitochondrion, the power plant of the cell, as a promising target for such an attack. They suspected that this organelle would respond particularly sensitively to the aggressive form of the oxygen. So Sabyasachi Chakrabortty programmed the transporters to head for mitochondria – he found a suitable molecular address label in a sort of catalogue that biochemists had already compiled for targeted navigation to the different cell organelles.

When the researchers applied the transporter to the mitochondria of the cancer cells, the effect was resounding: the cytotoxin was 200 times more effective than when the pure active ingredient was infiltrated using a nanotransporter. For each of the ten drug complexes on the carrier, this meant a 20-fold increase in toxicity. "That was really great," says Tanja Weil. The fact that even very small volumes of drugs can fight tumor cells effectively if they can reach the right site in the cancer cell could represent a major advance in oncology. University of Ulm professor of medicine Michaela Feuring-Buske, too, hopes to significantly reduce the side effects of cancer drugs in this way. It is also possible that this principle will apply not only to the substance that gets to work on the curative destruction of malignant cells when exposed to light, but also to other drugs.

The fact that a drug doesn't switch on until a button is pressed – that is, when it is illuminated at its target – is practical in the research context, but less so in medical use. The light that releases the aggressive oxygen doesn't penetrate deep into the body, and the cancer cells in the bone marrow that flood the body with useless blood cells can't be fought in this way.

However, working in collaboration with doctors at the Ulm University Medical Center, the team has found a potential application for this approach: following initial chemotherapy, patients with myeloid leukemia may be given a stem cell transplant to consolidate the treatment. If a suitable donor can't be found, the stem cells are taken from the patients themselves and the light-controlled therapy would offer a suitable method for liberating the stem cells from the cancer cells. For this method to succeed, the drug must cause greater damage to the malignant cells than to the healthy ones.

When the scientists from Mainz and Ulm were investigating this, they discovered something surprising: "We observed a trend indicating that the protein-linked ruthenium drug showed a preference for damaging cancer cells," says Tanja Weil – and it did this without the researchers having to target it directly at the cancer cells using complicated address labels. "We were unable to explain this at first and the doctors had no answer either," she admits. The idea that put the researchers on the right track arose, again, at a team meeting. They are currently pursuing this and may discover a new approach for targeted cancer therapy in the process.

DIAMONDS AS BIOLOGICAL NANOSENSORS

This prospect could also arise from another project on which Weil's group is currently working intensively: together with physicists at the University of Ulm, the scientists aim to use diamonds as biological nanosensors. "I always found diamonds rather boring as a functional material," says Tanja Weil. "They are very hard and beautiful as decorative stones, but not very interesting from the perspective of materials chemistry, as it is difficult to control their functionalization and morphology." That was until

Left Tanja Weil's team developed a serum albumin protein (black) into a versatile nanotransporter. The protein, of which only a part can be seen here, occurs in human blood. The researchers loaded it with different attachments to it: Polyethylene glycol (blue) makes the protein water soluble and protects it from rapid degradation in the body. The ruthenium complex (red) generates an aggressive form of oxygen that acts as a cytotoxin when exposed to light. The triphenylphosphine groups (green) navigate the drug carrier into the mitochondria, where the cytotoxin is particularly effective.

Right Christiane Seidler, Wenhui Dong and Tanja Weil (from left) examine solutions of protein-coated nanodiamonds. Due to targeted impurities with foreign atoms, the diamonds shine in different colors and enable the scientists to track the progress of the drug transport in cell cultures.

two physicists from Ulm, Fedor Jelezko and Martin Plenio, visited Weil's office one day and the three scientists had a conversation about what diamonds are capable of. Due to defects – minute flaws at which other atoms such as nitrogen sit in the carbon lattice – they can be used, among other things, as nanosensors for structural elucidation, for example in particularly sensitive magnetic fields. "I found the wide-ranging possibilities offered by this use of diamonds very exciting after all," says Weil.

A SYNERGY GRANT WORTH NEARLY TEN MILLION EUROS

The three scientists thus joined forces to carry out research on the diamond nanosensors. "Firstly, we liked each other, and secondly, we were convinced that we could make a scientific difference with our interdisciplinary knowledge and skills," says Tanja Weil. For her, this difference consisted above all in the fact that it would enable diamond sensors to track the progress of drug-loaded biopolymers in the body and possibly even in a cell. "It would be interesting to be able to observe in an MRI scanner whether the biopolymers we equipped with nanodiamonds actually go where we want them to," explains the researcher.

The enthusiasm with which Weil reports on this project wasn't initially shared by the research sponsors. The answer she received to the funding applications she submitted with her partners was always the same: it was far too uncertain whether it would actually be possible to implement the project. The scientists were deeply frustrated with this response. They eventually decided to make one last attempt to obtain funding and applied for a Synergy Grant from the European Research Council ERC – and were one of the 11 projects out of more than 700 submitted to be awarded a grant worth nearly ten million euros for their project. The researchers from Mainz and Ulm are therefore now working on transporters for nanomedicine that not only maneuver drugs directly to a tumor, but also can be observed in detail every step of the way. ◂

TO THE POINT

- **As biopolymers, proteins can be loaded with medical active ingredients that provide a precisely defined length and composition and are directed specifically at tumor cells.**
- **The effectiveness of cancer treatment could be increased significantly if such nanotransporters were able to infiltrate cytotoxins into cell organelles such as the mitochondria.**
- **The researchers expect that nanodiamonds will be suitable for use as detectable drug transporters whose path through the body can be traced right up to the target cells.**

GLOSSARY

Biopolymer: A chain molecule that is synthesized by an organism. In addition to proteins, biopolymers include polysaccharides and DNA.

Chemical function: The part of a molecule that determines its properties and behavior in chemical reactions.

Nanomedicine: The application of nanotechnology in medicine.

Photo: Thomas Hartmann

Widespread in cancer diagnostics: Positron emission tomography enables tumors to be identified, like this one in a lung, because the glucose in it, for instance, accumulates fluorine-18. On the images, diseased tissue is clearly recognizable as a bright area.

The Stuff of **Enlightening Diagnoses**

Doctors today already frequently rely on positron emission tomography – PET for short – in cancer diagnostics. However, in order to use this method for other diseases, too, they need suitable tracer substances containing radioactive fluorine-18 – a challenge for **Tobias Ritter** and his team at the **Max Planck Institut für Kohlenforschung** in Mülheim an der Ruhr. The chemists are searching for ways to label diverse molecules with fluorine-18 and thus expand the range of possibilities for medical specialists.

TEXT **KARL HÜBNER**

Every couple of days, early in the morning, a messenger pulls up to Kaiser-Wilhelm-Platz 1 in southern Mülheim to deliver a small, rather unspectacular stainless-steel box. Each time, two employees of the Max Planck Institut für Kohlenforschung are already waiting at the entrance to the building to accept the delivery. A couple of signatures, then straight to the lab they go with the box. The heavy security door and the sign with the familiar international radiation symbol make it quite clear: radioactive substances are used in this lab.

The box that was just delivered also contains such a substance: fluorine-18. Unlike natural fluorine, which has a mass number of 19, fluorine-18 is synthetically produced and is highly unstable. Its half-life is 110 minutes, then it decays into oxygen-18. When that happens, high-energy radiation is released, which is why the chemists in Mülheim use a special lab when they work with fluorine-18. And they have to work fast: after 110 minutes, half of the fluorine atoms have already disappeared; after 220 minutes, three-quarters of them; and so on.

MOLECULES FOR INNOVATIVE DIAGNOSTIC APPLICATIONS

The researchers are pursuing a specific goal with their work against the clock. "We are looking for ways to incorpo-

Photo: Science Photo Library/LIVING ART ENTERPRISES, LLC

rate fluorine-18 into molecules that permit novel diagnostic applications of positron emission tomography," explains Tobias Ritter. A chemist, he has been Director of the Organic Synthesis department at the Max Planck Institute in Mülheim since 2015. Fluorine chemistry and especially the short-lived fluorine-18 are key topics of interest for his group. Positron emission tomography, a well-established method for tumor diagnostics, relies on radioactive substances that release positrons. The special radiochemical laboratory was set up a year ago specifically for the purpose of conducting synthesis experiments with these positron suppliers.

HOW EASY IS IT TO FLUORINATE SUBSTANCES?

At the heart of the lab are two chambers surrounded by lead walls and a thick leaded glass window. In technical jargon, shielded chambers like these are called hot cells. It is into just such a chamber that the researchers in Mülheim now place the metallic cylinder they liberated from the freshly delivered stainless steel box. It's barely larger than a normal tin can, but it weighs 15 kilograms. "Solid lead," explains Matthew Tredwell, who heads the radiochemical lab in Ritter's department. Only when the hot cell has been completely sealed off again does one of his colleagues remove the cylinder's lid. This requires highly focused concentration as she operates the external controls that steer the steel gripper arms protruding into the sealed chamber.

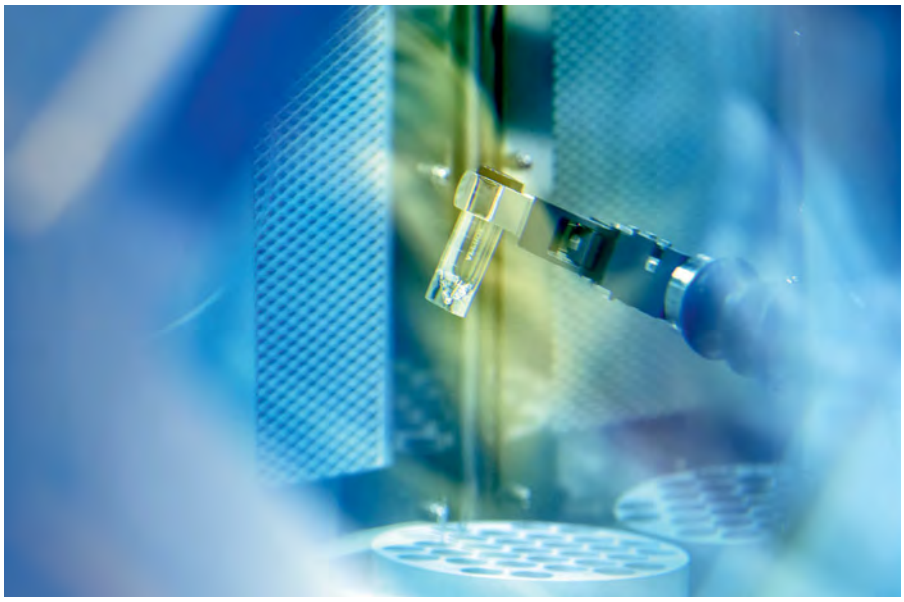
Then she removes the cargo's key component: a small vial containing a clear liquid. "It's simply water in which fluoride-18 ions have been dissolved," Tredwell explains. And as if the few milliliters of liquid didn't already appear tiny enough given their 15-kilogram packaging, the chemist adds that the amount of fluorine in the liquid is just over one picogram – one trillionth of a gram.

Despite being an inconceivably small amount, it is plenty for the experiments the scientists have planned for this day. They want to test how easily they can fluorinate other substances – that is, incorporate a fluorine atom into them. The working group already produced the necessary synthesis components previously, and they are now waiting in small vials in the hot cell. The rest happens automatically: a sort of hollow needle goes to each vial, withdraws a precisely determined quantity and combines the desired reactants. To be able to then immediately examine whether and in what amount and purity the desired products were formed, the radiochemical lab also contains analytical equipment. These devices have recently repeatedly shown that the researchers are on the right track.

THE METHOD HAS GREAT POTENTIAL

Verena Ruhlmann, a physician, finds it very interesting, too. She was in attendance when the Max Planck Institute presented its special laboratory to the residents of Mülheim in late 2016. In fact, she was invited to be a speak-

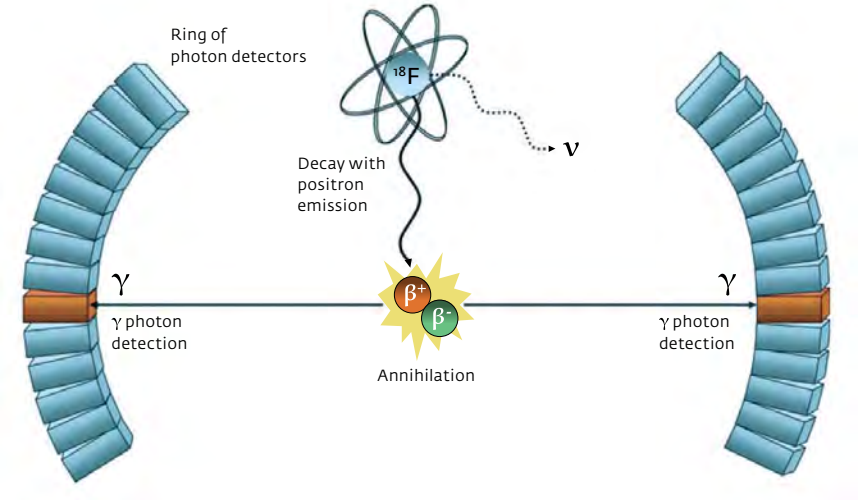
Photo: Frank Vinken



Secure access: In a special lab, Marta Brambilla (left) controls a gripper arm that protrudes into a chamber for radiochemical experiments. This hot cell has lead walls and leaded glass windows to shield the radioactive radiation. The chemists place all the components for their planned reactions in there in small vials (right) – including substances that contain radioactive fluorine-18. A robot then mixes the source materials for the reactions together.

er that day. This is surprising at first, since Ruhlmann has no connection with the Max Planck Institute – her workplace is actually several kilometers away to the east. In the neighboring city of Essen, she is a senior physician in the Essen University Hospital Clinic for Nuclear Medicine. That evening, she spoke about what positron emission tomography is used for at her clinic. One area is tumor diagnosis, where PET is used, for example, to distinguish between benign and malignant growths. Or to visualize changes in lymph nodes. Or to show whether and how well a treatment is working. And also whether a tumor may have returned after an initial successful treatment. Ruhlmann raved about what an "outstanding method" it is. Her department already uses PET to examine around 25 patients every day. But the physician also emphasized that she sees even greater potential for PET in the future, both in tumor diagnostics and for other diseases, such as Alzheimer's, Parkinson's and cardiovascular disorders.

It is this vision that unites facilities like Essen University Hospital and the Max Planck Institut für Kohlenforschung. After all, the new substances that Ritter's team is attempting to manufacture in the radiochemical lab could one day also be of interest to nuclear medicine specialists like Verena Ruhlmann. >



Indirect detection: Beta decay of fluorine-18 releases a positron (β+), the antiparticle of the electron, and a neutrino (ν). The positron immediately annihilates with an electron (β-), emitting two γ-photons in precisely opposing directions. These are then detected, making it possible to reconstruct where the fluorine-18 decayed.

Photo: Frank Vinken; graphic: Angew. Chem. Int. Ed. 2008, 47, 8998 – 9033

As she explains, “For every PET scan we perform, we need, of course, a substance that releases positrons.” Fluorine-18 is by far the most important isotope for PET tracers – what experts call the substances whose path in the body can be traced during a scan.

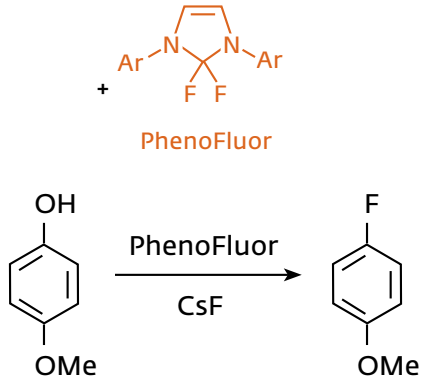
For most PET scans, however, simply administering fluorine-18 in the form of a fluoride salt would be pointless. At most, it would accumulate in the bones, but not where it is needed for most diagnostic tasks. For that reason, chemists are attempting to incorporate the fluorine into molecules that are suitable for use as tracers. These are molecules that accumulate as selectively as possible – that is, exclusively – at the sites in the body that are relevant for the diagnosis. Those sites then become visible from outside the body.

TRACERS THAT DOCK ONTO PLAQUE IN THE BRAIN

Currently, the most important such molecule is a fluorodeoxyglucose. This substance is similar to normal glucose; the only difference is that one carbon atom carries a fluorine atom – a fluorine-18. Despite this modification, in the body, the fluorinated sugar behaves almost like glucose. Therefore, once it is injected into the bloodstream, this substance goes wherever

Pioneering new PET applications: Tobias Ritter and his team develop tools in order to produce new tracer substances for diagnosing such things as tumors and cardiovascular diseases.

Photo: Frank Vinken



Key reaction: Tobias Ritter found a substance – PhenoFluor – that can be used to specifically replace OH groups with fluorine atoms.

there is a demand for sugar. Demand is particularly high in most tumor cells. Fluorodeoxyglucose thus makes tumors easily visible in a PET scan.

At Essen University Hospital, Verena Ruhlmann also has access to a radiochemical lab; there, this substance is manufactured fresh every day because the radioactive isotope decays too quickly to be stored for long periods. For patients, though, the particularly short lifespan of the PET tracers is an advantage, as it means that the already low radioactivity in their body completely subsides relatively quickly. Contributing to this is the fact that fluorine-18, like other tracer substances, is transformed exclusively into stable isotopes and leaves no radioactive derivatives behind.

If the PET visions are to become reality, then many other PET tracer molecules besides the fluorinated sugar will be needed. Molecules, for instance, that dock onto the brain plaque that is characteristic for certain forms of dementia – an initial Alzheimer's tracer is already on the market. Or molecules that, in tumor diagnostics, would enable predictions as to which cancer drug is best for an individual patient.

FLUORINE IS EXTREMELY REACTIVE

In order for them to reach their targets in the body, the molecules must have a suitable chemical structure. However, to function as tracers, they must also include, for example, fluorine-18. And that's precisely where the problem – and the work of the chemists in Mülheim – begins.

Incorporating fluorine into a more complex organic molecule isn't always as easy as synthesizing fluorodeoxyglucose, which can be done with a simple fluoride solution. Normally, considerable thought must be given as to how to source even natural fluorine-19. "Elemental fluorine is generally out of the question, as it is much too reactive," explains Tobias Ritter. Fluorine is more reactive than any other element, so if pure fluorine were used for fluorination, it would, in most cases, affect multiple locations in the molecule rather than selectively affect just the one desired location.

On top of this, elemental fluorine is extremely difficult to handle in the lab. In compounds, on the other hand, it is often bound so stably that it requires an enormous amount of energy to activate it. This property played no small part in helping fluorochlorocarbons and also Teflon®, a fluorochemical, make it big. >

Checking the result: Matthew Tredwell uses high-performance liquid chromatography, or HPLC, to analyze whether a reaction produced the desired products.

Photo: Frank Vinken

Radiation-proof construction: Steel plates on which lead slabs rest are mounted on stable beams in the ceiling of the special radiochemical lab (top). The walls are built from radiation-protection bricks; their dark coloring is due to the large amounts of iron oxide they contain (bottom left). Iron oxide particles are added to the mortar (bottom right).

In the case of fluorine-18, its short lifespan is an additional complicating factor, forcing Tobias Ritter and his colleagues to completely rethink their approach. "In the case of complex target molecules, a chemist would normally try to incorporate the fluorine in as early a reaction step as possible," Ritter explains, "because the molecule becomes ever more complex with each additional step. This, in turn, increases the risk that the fluorination will no longer be selective, but will occur at various sites in the molecule."

With volatile fluorine-18, however, it isn't possible to fluorinate in an early stage of synthesis. A complex molecule is frequently constructed over the course of ten or even more steps, each of which takes some time. If the radioactive fluorine were to be incorporated in an early phase, there would be hardly any of it left in the finished molecule. "So with fluorine-18, we have to find a way to incorporate it only in the last or perhaps next to last reaction step," says Ritter, and immediately adds: "That's precisely what is so difficult."

OH GROUPS CAN BE SPECIFICALLY REPLACED

In 2011, though, the scientific community sat up and took notice. In a scientific journal, Ritter, who at the time was still conducting research at Harvard University in Cambridge, Massachusetts, and two of his colleagues published a method by which OH groups can be specifically replaced by fluorine atoms in a certain class of molecules. At the heart of the method was a reagent that was later given the commercial name PhenoFluor. The researchers found that it could be used to fluorinate a number of even quite complex organic molecules with good yields. There was just one requirement: the initial substance had to carry an OH group at the site where the fluorine was to end up. A milestone.

But there was one thing that didn't work even with PhenoFluor: the incorporation of fluorine-18. The problem

Photos: M. Teske

» We expanded the set of chemical building blocks with which we can produce fluorine tracers for PET.

was that PhenoFluor contains two fluorine atoms that are so homogeneous that it isn't possible to control which of the two ultimately carries out the actual fluorination step. "We would have needed to create a PhenoFluor with two F-18 atoms, but that isn't possible for technical reasons because fluorine-18 is always contaminated with fluorine-19," explains Tobias Ritter. They therefore needed a different reagent.

Another five years passed before the researchers solved this problem. Their trick was to first use a reagent that has a similar structure to PhenoFluor but that contains, in place of the two fluorine atoms, two atoms of chlorine, a chemical relative. This substance allows a similar reaction to be carried out as with PhenoFluor, but the chemists intervene again before its final step. "In that moment, one of the chlorine atoms is present as a chloride ion, which we then replace with a fluoride-18 ion using a common technique," says Ritter. This ensures that the OH group is exchanged for the fluorine-18.

"With this reaction, we expanded the set of chemical building blocks with which we can produce fluorine tracers for PET," says Ritter. But that won't happen overnight. In many cases, it isn't yet known exactly which molecules medical diagnostics will ultimately really need. To more closely align the chemical tools with medical demand, Ritter's department is collaborating with clinical facilities such as Essen University Hospital and also Massachusetts General Hospital in Boston. Their goal is to identify suitable molecules for very specific fields of application and to develop feasible methods for synthesizing them. Then, in the second step, fluorine-18 has to be integrated into these molecules in order for them to function as PET tracers.

It isn't yet possible to say whether the existing fluorination tools will suffice for this, as it depends on the individual target molecule. In any case, the researchers are working in their radiochemical lab to create more tools for syntheses with fluorine-18. After all, they want to expand the spectrum of fluorinatable molecule classes. So the messenger will continue to make regular trips to Kaiser-Wilhelm-Platz to unload the 15-kilogram metal case with the trillionth of a gram of fluorine-18. ◂

TO THE POINT

- **Positron emission tomography requires tracer molecules with radioactive atoms, such as fluorine-18. However, it is difficult to synthesize such molecules due to the short lifespan of these atoms.**
- **Chemists working with Max Planck Director Tobias Ritter are developing methods to specifically attach fluorine-18 to desired sites in a molecule. They conduct the corresponding experiments in a special radiochemical lab.**
- **Initial success: a synthesis method that replaces OH groups with fluorine-18 in many organic molecules, including in complex ones. In the future, the Max Planck researchers hope to further optimize this method and extend it to even more complex molecule classes.**

GLOSSARY

Half-life: The time after which the amount of a radioactive isotope has been halved. Every radioactive isotope has a constant rate of decay – and thus a fixed and unambiguous half-life.

Isotope: Chemical elements can occur in different atomic versions due to a difference in the number of neutrons in the atomic nucleus. The different versions of one and the same element are known as isotopes.

Positron: An elementary particle that is also considered to be an antiparticle. It is the same size and weight as an electron, but has the opposite electrical charge – that is, a positive one. A positron annihilates with an electron, releasing energy in the form of two gamma quanta. Since all matter contains electrons, the annihilation occurs practically immediately, so positrons always exist only briefly.

Positron emission tomography (PET): An imaging technique that, like magnetic resonance tomography (MRT) or computer tomography (CT), is capable of producing sectional images of individual layers inside the body. The method requires substances containing the radioactive elements fluorine-18 or gallium-68, which accumulate for instance in tumors and emit positrons as they decay. These elementary particles immediately annihilate with an electron – essentially at the site where they come into existence – releasing two radiation pulses in precisely opposing directions. If detectors register these pulses outside the body, it is possible to calculate the precise location where the fluorine atom decayed.

Wolves Understand Cause and Effect Better than Dogs

Men's best friends seem to have lost some cognitive abilities when they were domesticated

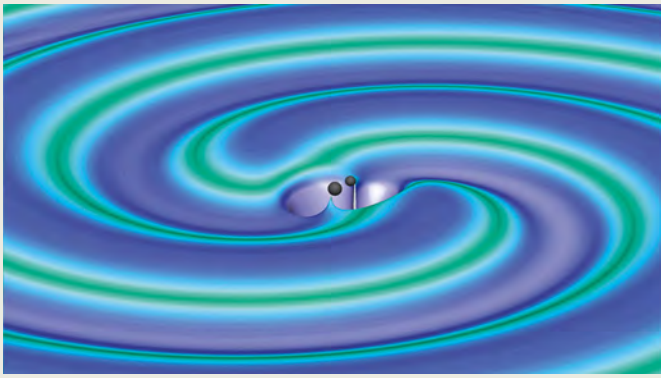
Children learn the principle of cause and effect early on: if you touch a hot stove, you'll get burned. But animals such as wolves understand causal relationships, too – and as a study has shown, they are even better at it than dogs. A research team that includes Juliane Bräuer from the Max Planck Institute for the Science of Human History investigated the behavior of dogs and of wolves that are used to people. To do this, the researchers hid food and tested whether the animals understood cues indicating the food's location. Both dogs and wolves understood communicative signals such as eye movements, pointing fingers and nodding, as well as gestures directed toward the location in question. When the animals were expected to recognize that a can containing food makes a noise when shaken, while an empty can doesn't, only the wolves reached the correct conclusion. "This suggests that domestication affected the cognitive abilities of today's pet dogs," says Bräuer. "However, it can't be ruled out that the differences could be due to wolves being more persistent in exploring than dogs. Dogs are conditioned to receive food from us, whereas wolves have to find food themselves in nature". (www.mpg.de/11477998)

A telling glance: Wolves can interpret human eye movements and gestures correctly when it comes to finding hidden food.

All Good Things Come in Threes

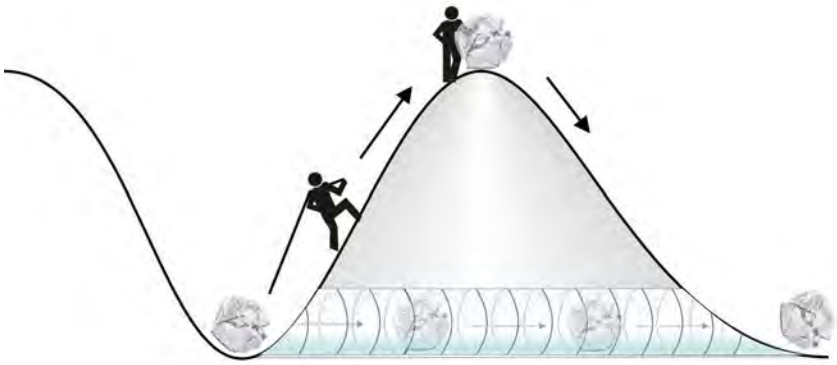
Gravitational waves from two black holes caught also by Italian Virgo detector

The observation of gravitational waves is gradually becoming a routine occurrence: once again, researchers have recorded the space-time ripples that Albert Einstein predicted a hundred years ago. This time, however, in addition to the two Advanced LIGO observatories in the US that detected all three gravitational waves recorded thus far, the Italian Virgo detector was also involved. On August 14, all three detectors observed the GW170814 signal produced by the merger of two black holes. These cosmic monsters measured 31 and 25 solar masses. The signal reached the LIGO detector in Livingston around 8 milliseconds before it reached Hanford and about 14 milliseconds before it reached Virgo in Tuscany. The direction to the source could be inferred by combining these differences in arrival time. In this way, GW170814 could be localized to an area of 60 square degrees between the Eridanus and Horologium constellations in the southern celestial hemisphere. Comparing the measured waveform with predictions from the general theory of relativity, in turn, yielded a distance of about 1.8 billion light-years. This time, scientists from the Max Planck Institute for Gravitational Physics in Potsdam and Hannover were also involved in the discovery and data analysis. (www.mpg.de/11492342)



Signal from space: Two black holes with 31 and 25 solar masses merge and emit gravitational waves. The colors characterize the strength of the field.

Photo: Shutterstock; numerical relativity simulation: S. Ossokine, A. Buonanno (MPI for Gravitational Physics); Simulating eXtreme Spacetimes Project; scientific visualization: T. Dietrich (MPI for Gravitational Physics), R. Haas (NCSA)



Over the energy wall or through it? Classical particles can overcome energy barriers only if energy is expended to lift them above it. Quantum particles, however, have the possibility to cross the wall even if they don't actually have sufficient energy: they can tunnel through the obstacle.

Measuring Time in a Tunnel

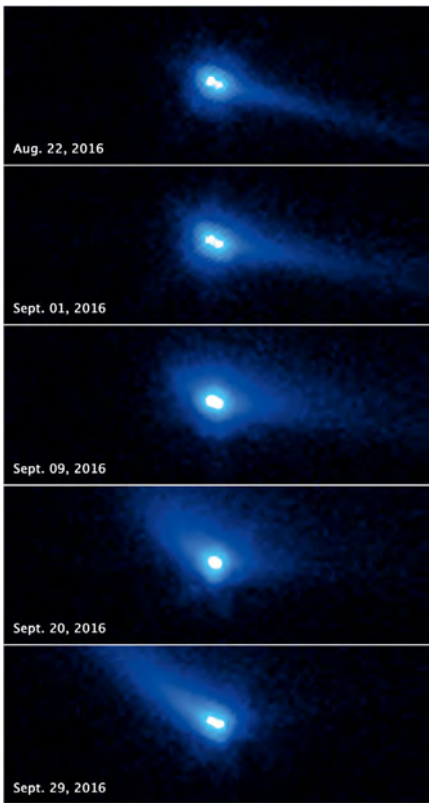
In the quantum tunneling effect, particles overcome an energy barrier in a few attoseconds

Harry Potter can do a lot of things that we can't, including walking through walls: to reach platform 9 ¾ where the train to Hogwarts School of Witchcraft and Wizardry stops, he and his classmates slip through a wall between platforms nine and ten. Impossible in real life, this feat is normal in the crazy world of quantum physics. Particles such as electrons are able to penetrate energy barriers that are actually insuperable. Physicists call this the quantum tunneling effect. Now researchers at the Max Planck Institute for Nuclear Physics in Heidelberg have shown for the first time that it takes electrons a finite amount of time to tunnel. To investigate this, the researchers used the electromagnetic field of a laser to rotate the potential well, which forms the electrical field of an atom and confines its electrons. Then they observed an electron as it tunneled out of the potential well. Due to the rotation, the particle's trajectory was shifted slightly, indicating that the electron had spent a few attoseconds – billionths of a billionth of a second – in the quantum tunnel. Although the tunnel effect has been known for nearly a hundred years, it was previously unclear whether a particle tunnels through a barrier in a finite amount of time or whether it instantaneously appears at the tunnel exit. (www.mpg.de/11419700)

The Double Asteroid

An object with the name 288P is the only known active binary planetoid

Body 288P, which orbits the Sun in the asteroid belt between the orbits of Mars and Jupiter, is unique. For one thing, it belongs to the group of unusual asteroids that discharge dust and gas into space – thus behaving more like comets, which traverse the solar system as lone wolves. For another, Hubble Space Telescope data analyzed by a team of scientists under the leadership of the Max Planck Institute for Solar System Research suggests that it also comprises two separate components rotating about a common center of gravity. This makes 288P the first known active binary asteroid. It probably broke into two pieces under the force of its own rotation no more than 5,000 years ago. These two pieces each have a diameter of about one kilometer. Simulations show that they circle each other at a distance of around 100 kilometers on a highly elliptical orbit. Similar to a comet, the asteroid always becomes active when its orbit approaches the Sun. This is apparently due to gases that are then exposed and sublime. (www.mpg.de/11481624)

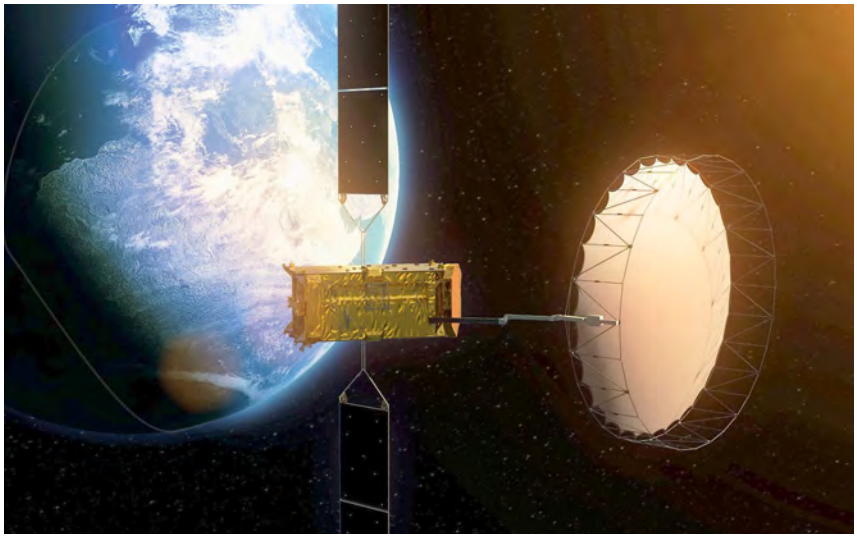


Not one, but two: This series of images from the Hubble Space Telescope show that the binary asteroid 288P comprises two parts that orbit each other and exhibit comet-like features. These include the coma – a thin gas envelope – and the long tail of dust.

Graphic: MPI of Quantum Optics; photos: NASA, ESA and J. Agarwal (MPI for Solar System Research)

Quantum Communication with a Satellite

Transmitting information from orbit will enable secure global data exchange



A versatile satellite: A part of the Alphasat I-XL was actually developed to demonstrate data transmission between Earth observation satellites and the Earth, but it is also suitable for transmitting quantum states.

Quantum cryptography: What started out as exotic research in physics laboratories could soon change global communication of sensitive data. The most recent work in this field, which a team headed by Christoph Marquardt and Gerd Leuchs at the Max Planck Institute for the Science of Light in Erlangen has now presented, is set to further heighten the rapidly growing interest in this technology, and not just on the part of telecommunications companies, banks and governmental institutions. In collaboration with the company Tesat-Spacecom and the German Aerospace Center, the physicists have now created one of the conditions for using quantum cryptography to communicate even over great distances without any risk of interception. They measured the quantum states of light signals that were transmitted from a geostationary communication satellite 38,000 kilometers away from Earth. The physicists are therefore confident that a global interception-proof communications network based on established satellite technology could be set up within no more than a few years. (www.mpg.de/11389946)

Parasites and an Early Warning System

Dodder helps host plants inform other plants about hungry insects

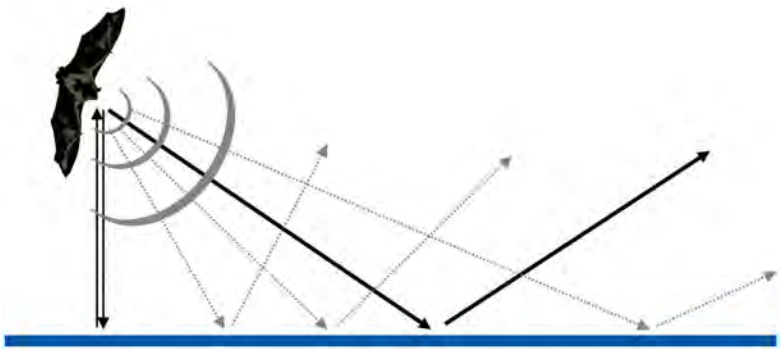
Plants can communicate with each other by means of gaseous substances and underground fungal networks. A team of scientists from the Kunming Institute of Botany in China and the Max Planck Institute for Chemical Ecology in Jena has discovered that parasites, too, can function as mediators. Dodder, a parasitic vine, transmits information between its host plants about infestations of other parasites. This plant of the genus Cuscuta has no roots of its own. Instead, it forms haustoria with which it can extract nutrients from its hosts. Dodder attacks multiple plants simultaneously and creates a network between them. The scientists analyzed all the active genes in the leaves of the dodder-connected plants and determined that insect-infested plants transmit signals via dodder bridges to neighboring plants – even to different plant species. This enables the recipients to boost the production of defense genes and arm themselves against an attack. Further studies are planned to determine whether dodder is acting completely altruistically in this mediator role. (www.mpg.de/11410164)

Dodder causes considerable economic damage in pasture farming with alfalfa, clover and soybeans.

Photos: ESA (top), Jingxiong Zhang, Kunming Institute of Botany, Chinese Academy of Sciences (bottom)

Glass Facades Are Traps for Bats

Bats rely largely on their echolocation calls to orient themselves in the dark. However, if their calls strike smooth horizontal surfaces – such as water – at an oblique angle, they are reflected away from the bats. The surfaces of lakes, ponds and rivers thus act like acoustic mirrors to them, from which they receive hardly any echo signals. Artificial smooth horizontal surfaces have the same effect: the animals mistake them for water. A similar thing occurs with smooth vertical surfaces – sometimes with fatal consequences: scientists at the Max Planck Institute for Ornithology in Seewiesen found that bats usually don't recognize a smooth vertical surface until it's too late, initially perceiving it as a hole to fly through. Such surfaces are inaudible for the animals and thus essentially invisible. The scientists used infrared cameras and microphones to analyze the flight and echolocation behavior of greater mouse-eared bats (*Myotis myotis*). In a darkened flight room, 19 out of the 21 animals involved collided with a smooth panel on the wall within a short time. When the researchers put the panel on the floor, there wasn't a single collision, but 13 animals tried to drink from it. The researchers are now calling for measures to prevent collisions of bats with glass facades. (www.mpg.de/11465022)



When a bat flies toward a smooth surface, its echolocation calls are initially reflected away from it. Only when it is directly next to the smooth surface (image) are echoes reflected back to it.

Extra Years at No Extra Cost

People who don't smoke, aren't obese and consume alcohol moderately can expect to live seven years longer than the average population. In addition, they can expect to spend most of those extra years in good health. These were the findings of a study conducted by Mikko Myrskylä, Director at the Max Planck Institute for Demographic Research, and Neil Mehta from the University of Michigan. The researchers analyzed data from more than 14,000 US citizens and found that people who have smoked a total of no more than 100 cigarettes and have a body mass index of less than 30 live four to five years longer than the average population and with far fewer physical impairments. The results of their analysis also showed that people with moderate alcohol consumption live, on average, seven years longer than the general population, surpassing even the average life expectancy in Japan, a country whose inhabitants are generally considered to have particularly long lifespans. (www.mpg.de/11407661)

Graphic: MPI for Ornithology/S. Greif; photo: Stadtarchäologie Augsburg

Surprising origins: Researchers found numerous women from distant regions in Bavarian graves from the Bronze Age. They were buried just like the native population.

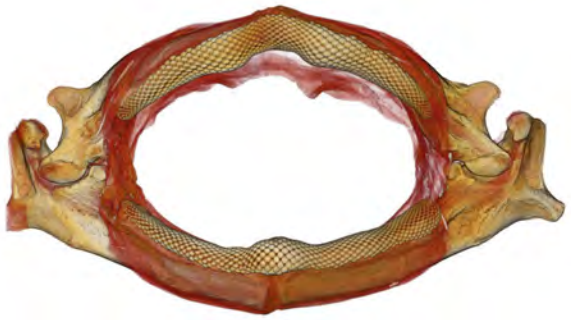
Women from Far Away

Four thousand years ago, many brides came to the Lech Valley from Bohemia and Central Germany

At the end of the Stone Age and in the early Bronze Age, families were established in a surprising manner in the Lech Valley south of Augsburg, Germany: many women came from outside the area, probably from Bohemia or Central Germany, while men were usually from the region. And this wasn't a temporary phenomenon, but persisted over a period of 800 years. These findings are the result of archaeological analyses conducted in a research collaboration in which Johannes Krause from the Max Planck Institute for the Science of Human History is involved. The researchers examined the human remains of 84 individuals using genetic and isotope analyses in conjunction with archaeological evaluations. The individuals were buried between 2500 and 1650 BCE in burial grounds that belonged to individual homesteads. Genetic and dental analyses showed that the majority of the women did not originate from the region. However, they were buried just like the native population, indicating that they were integrated into the local community. (www.mpg.de/11463384)

Deceptive Teeth

Although the jaws of the wedgefish are designed only to crush shellfish, it also eats stingrays



A sharp aftertaste: A CT scan of the jaw of a wedgefish provides unmistakable evidence of previously unknown feeding behavior: it clearly shows stingray spines in the jaw of this cartilaginous fish.

Some animals have a different diet than the shape of their teeth would suggest, as shown by a recent study on the jaw of the wedgefish conducted by a team headed by Mason Dean, a scientist at the Max Planck Institute of Colloids and Interfaces in Potsdam-Golm. Although these rays have wide teeth and normally eat mussels and shrimps, fragments of tail spines in their jaws reveal that they also hunt stingrays. Previously, zoologists and paleontologists based their work on the principle of "show me your teeth and I'll tell you what you eat." As the current findings show, they should begin looking harder for evidence of animals' dietary and living habits that aren't immediately apparent. For the researchers in Potsdam, another reason the results of the jaw analysis were surprising was because the wedgefish had enveloped the spine tip fragments in bone tissue, which is very rare in cartilaginous fish, a group of which rays are a member. (www.mpg.de/11478384)

Intestinal Flora Can Trigger Multiple Sclerosis

Microorganisms from the intestines of MS patients set off encephalitis in genetically modified mice

Escherichia coli is one of around 1,000 types of bacteria in the human intestine.

Mice can contract an MS-like encephalitis when they receive the intestinal flora of patients with multiple sclerosis. This is the result of a study conducted by an international research team including scientists from the Max Planck Institutes of Neurobiology, Biochemistry, and Immunobiology and Epigenetics. In the study, the scientists inoculated genetically modified mice that had no intestinal flora of their own with microorganisms from the intestines of MS patients. With their findings, the researchers confirmed for the first time that components of the human gut flora play an active role in activating errant T-cells in the immune system. The researchers further analyzed how the microorganisms differ in the intestines of diseased and healthy humans. Pairs of twins in which only one twin had developed multiple sclerosis are particularly well suited for this because, as monozygotic twins are genetically identical, any differences can't be explained by genes. The researchers recruited more than 50 such pairs of twins and found some subtle differences in the intestinal flora of diseased and healthy siblings. It isn't yet possible to say whether these findings will one day lead to new diagnostic procedures or treatments. (www.mpg.de/11471726)

Oil as a Source of Energy for Marine Animals

In the Gulf of Mexico, at a depth of around 3,000 meters, oil and asphalt seep out of the ocean floor and form bizarre structures reminiscent of cooled lava. They are known as asphalt volcanoes, and a thriving biological community of various organisms has formed there. Today, 15 years after this community was discovered, it still holds many surprises, as researchers at the Max Planck Institute in Bremen have now shown. Since higher organisms such as sponges and mussels can't eat asphalt and oil, and since there is hardly any other source of food in the deep sea, some of them have joined forces with bacteria: the researchers have discovered mussels and sponges that live in a symbiotic relationship with bacteria at these volcanoes. The microorganisms can extract both energy and vital carbon from the oil. The microbes have specialized in the oil's easily degradable compounds – so-called short-chain alkanes such as butane, ethane and propane – and are members of the group of free-living, oil-degrading bacteria that play a key role in degrading oil in the oceans. Unlike their free-living relatives, those that live inside sponges and mussels are unable to utilize the persistent oil compounds, so-called polycyclic aromatic hydrocarbons. (www.mpg.de/11353055)

Photos: Mason Dean/MPI of Colloids and Interfaces (top), Eric Erbe, public domain

Creating 3-D Animation with a Simple Camera

Smartphone or webcam images can be used to reconstruct the movements of a person in a three-dimensional model

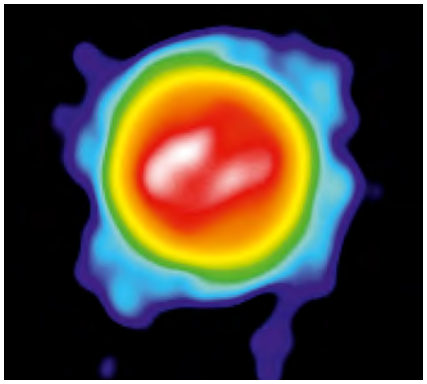
Portraying people and their movements three-dimensionally in virtual reality in real-time is set to become much easier. Researchers at the Max Planck Institute for Informatics in Saarbrücken have developed a method called VNect that creates digital 3-D models using only images from simple cameras like those in a smartphone. Demand is constantly growing for these kinds of models of people and their movements, for applications ranging from the animation of virtual figures in computer games to movement analysis in sports to medical examinations. The researchers in Saarbrücken used machine learning to translate human poses into a digital model in real-time: they trained a neural network, which imitates the function of the human brain, to recognize any pose by feeding it more than 10,000 images of various body postures taken with simple cameras. Previously, this was possible only with expensive camera systems. (www.mpg.de/11386365)

Srinath Sridhar demonstrates how well VNect calculates a three-dimensional model of the researcher's body poses in real-time based on images captured with an inexpensive webcam.

A Star's Turbulent Twilight Years

Researchers map the atmosphere of Antares, a red supergiant

On a clear summer night in central European latitudes, Antares, in the Scorpius constellation, shines brightly above the southern horizon. Astrophysicists know that this enormous star – which is almost 700 times larger than our Sun and, in the Sun's position, would extend past the orbit of Mars – is nearing the end of its life. Located nearly 600 light-years from Earth, Antares has expended much of its fuel, has reached the red supergiant stage and is gradually losing matter. An international team that includes scientists from the Max Planck Institute for Radio Astronomy in Bonn is investigating what exactly is taking place. To this end, the astrophysicists captured a snapshot of the turbulent motions in Antares' atmosphere. They measured both the radiation intensity, which is a measure of the gas distribution, and the gas velocity across its entire surface. This is the first time researchers have succeeded in obtaining such measurements for a star other than the Sun. To compile the surface map, the researchers had to combine no fewer than three telescopes at the European Southern Observatory ESO to create an interferometer. (www.mpg.de/11456828)



Zooming in on Antares: The first relatively detailed image of the red supergiant star shows the stellar disk (yellow) with two brighter regions (white) and the star's extended atmosphere (green and blue). Its irregular shape with several bulges and the variable distribution of gas indicate that the star is losing matter in turbulent currents, but only in some regions.

Photos: Oliver Dietze (top); K. Ohnaka et al. 2017, Nature (bottom)

The **Big Bang Clock**

It's the question of all scientific questions: How did the universe come into being? **Jean-Luc Lehners** at the **Max Planck Institute for Gravitational Physics** in Potsdam-Golm is addressing the question using state-of-the-art mathematical tools. In the process, he is also investigating the possibility that there was a precursor universe.

TEXT **THOMAS BÜHRKE**

In the beginning was the Big Bang. This foundation of our cosmic world view is as fundamental as it is incomprehensible. How can it have been possible for such an enormous quantity of matter – all the stars and planets, gas and dust nebulae – to be compressed into a single point? That suddenly exploded, creating space and time? It's an unimaginable scenario.

It is thus somehow immediately calming when even an established expert like Jean-Luc Lehners of the Max Planck Institute for Gravitational Physics (Albert Einstein Institute) finds the birth of the universe "extremely mysterious." But this is precisely why he has spent years studying it. "The question of where everything originates has always fascinated me," says Lehners, whose paper-strewn desk looks like it has recently experienced a miniature Big Bang …

The circumstantial evidence in the case of the Big Bang is clear. In the 1920s, Georges Lemaître and Edwin Hubble discovered the expansion of the universe: it can be seen in the fact that almost all galaxies are moving away from us – and the further away a galaxy is, the faster it is moving. Cosmologists interpret this galactic flight in the context of Einstein's general theory of relativity. Accordingly, the universe – that is, space – is expanding and the galaxies are moving further away from each other – similar to raisins in a rising yeast dough.

THERE WAS NO TIME TO EXCHANGE INFORMATION

In his mind, Belgian mathematician and abbot Lemaître reversed this expansion and, in 1927, postulated the "birth of the universe from a primeval atom." Simple and logical. "However, we've known for a long time that it can't have been that simple," says Lehners. "Instead, the Big Bang occurred in numerous places simultaneously." This doesn't make the idea any easier, but Lehners can explain.

If we calculate the beginning of the expanding infant universe using Einstein's equations, we find that many regions couldn't have been in causal contact. There wasn't enough time for information to be exchanged between these regions, which is fundamentally limited to the speed of light. Yet the universe was astonishingly homogeneous.

This is demonstrated by the oldest tidings from this young universe that we are able to receive in the microwave range: cosmic background radiation. It reflects the temperature and density of the primeval gas 380,000 years after the Big Bang. Visible deviations from a mean value reach no more than hundredths of a part per thousand. But how could the universe be so uniform if numerous regions weren't in contact? Jean-Luc Lehners associates each of these regions with a Big Bang – the emergence of space and time from a quantum fluctuation. The remaining question is then: What coordinated these "Big Bangs"?

Lehners visualized the problem in the auditorium during a presentation at a Falling Walls conference. Ten members of the audience found a small bowl and a stick beneath their seats. Lehners then asked one of them to use these to make a sound. The gong represented a

Everything started with the Big Bang. According to cosmologists' theories, the universe originated in a single point. This singularity, however, is extremely mysterious even for experts.

» The inflationary universe theory states that, prior to the Big Bang, there was a state in which all particles were in mutual contact.

metaphorical Big Bang. Then the other nine observers were also asked to bang the bowl simultaneously. This functioned precisely only when Lehners dictated the rhythm. But who dictated the rhythm for the Big Bang?

There are two proposals on the table. The best known one was developed more than 30 years ago: the theory of the inflationary universe claims that prior to the Big Bang there was a state in which all particles were in mutual contact. This was then followed by a brief phase in which space expanded faster than the speed of light. This means that regions were separated to such an extent that they were no longer in contact. When this phase ended, the inflation energy transformed into radiation and matter – this moment is regarded as the Big Bang.

But there is a second possibility – one to which Lehners has devoted intensive research. It states that the Big Bang may have been a transition stage. Before that, there existed a different universe that eventually contracted and then expanded again in the Big Bang. "If we analyze such a contraction phase, we find that it probably occurred very slowly. This could have had the effect that the successor universe was homogeneous and isotropic," explains the Max Planck researcher. Here, the Big Bang corresponds to the swing from the contraction to the expansion phase, again producing radiation and matter.

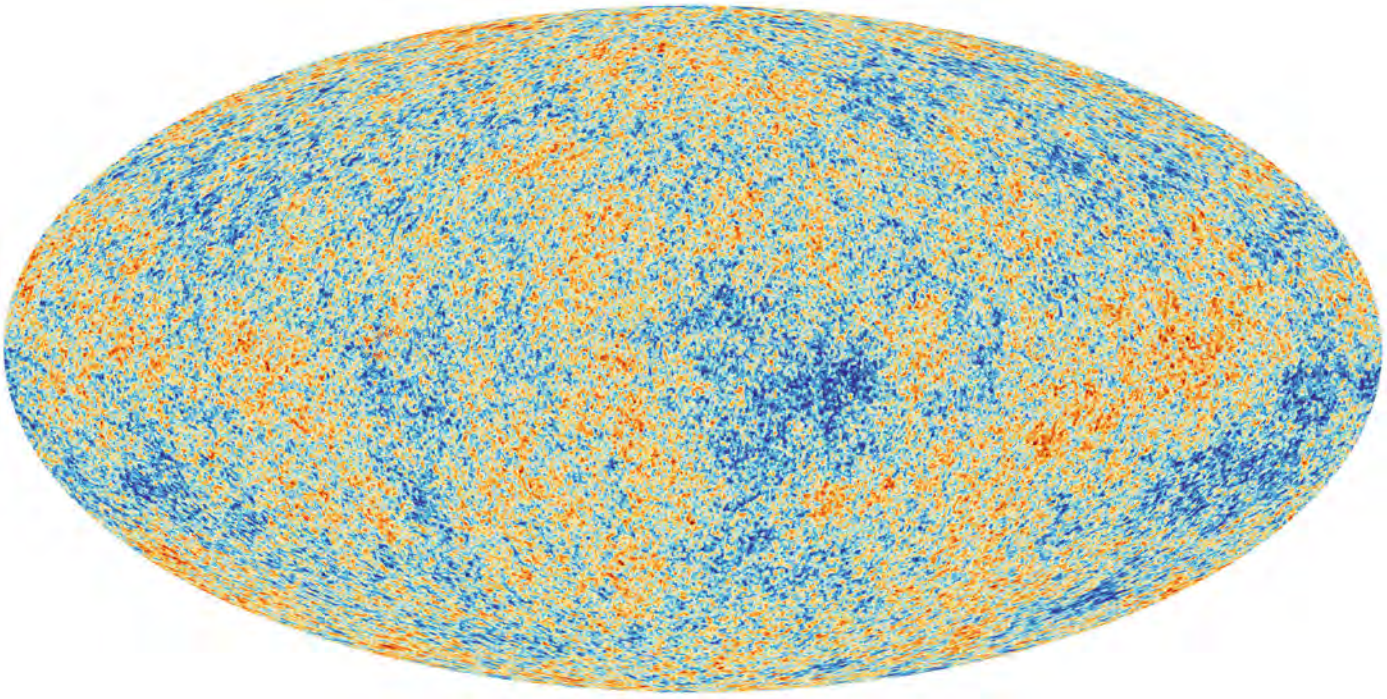
EXISTING MATTER DOESN'T ADMIT OF A REBOUND

The concept of such a cyclic universe seems appealing, echoing ancient Hindu and Buddhist myths. But does this scenario really reflect reality? Jean-Luc Lehners tackled this question – with the sobering result that the matter existing in the universe today doesn't admit of such a rebound. There would have to have been an unknown energy field that caused matter to swing. Could the recently discovered Higgs particle have played a role here?

As is common in quantum physics, the Higgs particle is associated with a

A view into the distance: This section from the Hubble Ultra Deep Field shows galaxies at the edge of space and time. Because of cosmic expansion, all of these galaxies appear to be moving away from us – the further away they are, the faster they are receding from us.

Photo: NASA, ESA, R. Ellis (Caltech) and the HUDF 2012 Team



A baby picture of space: Around 380,000 years after the Big Bang, the universe became transparent to radiation. The *Planck* satellite recorded this microwave background with great precision. The map shows minute temperature fluctuations in regions of slightly differing density, from which stars and galaxies emerged.

Photo: ESA and Planck Collaboration

space-filling field. However, the currently known strength of this field would be insufficient to initiate a matter rebound. "I investigated whether, at extremely high densities, the Higgs or a similar field could have had different properties than in today's universe, but with little success," says Lehners. So things aren't looking too good for the concept of a cyclic universe.

However, the scientist doesn't intend to give up on this idea that easily. He is currently investigating a different approach that was already proposed back in the 1920s but that wasn't pursued intensively. It's based on the fact that specific particles, such as electrons, twist the space around them slightly. This is caused by what is referred to as their spin, which can be imagined as similar to the rotation of a spinning top. The rotation in space caused by the spin is so small that it is completely irrelevant under normal conditions.

But this idea suggested that perhaps, under the extreme conditions before the rebound, this twisted space developed a force that protected the compacting matter from total collapse and reversed the compression to expansion. We can perhaps imagine this as resembling twisted rubber bands that, in trying to untangle, exercise an outward-directed force.

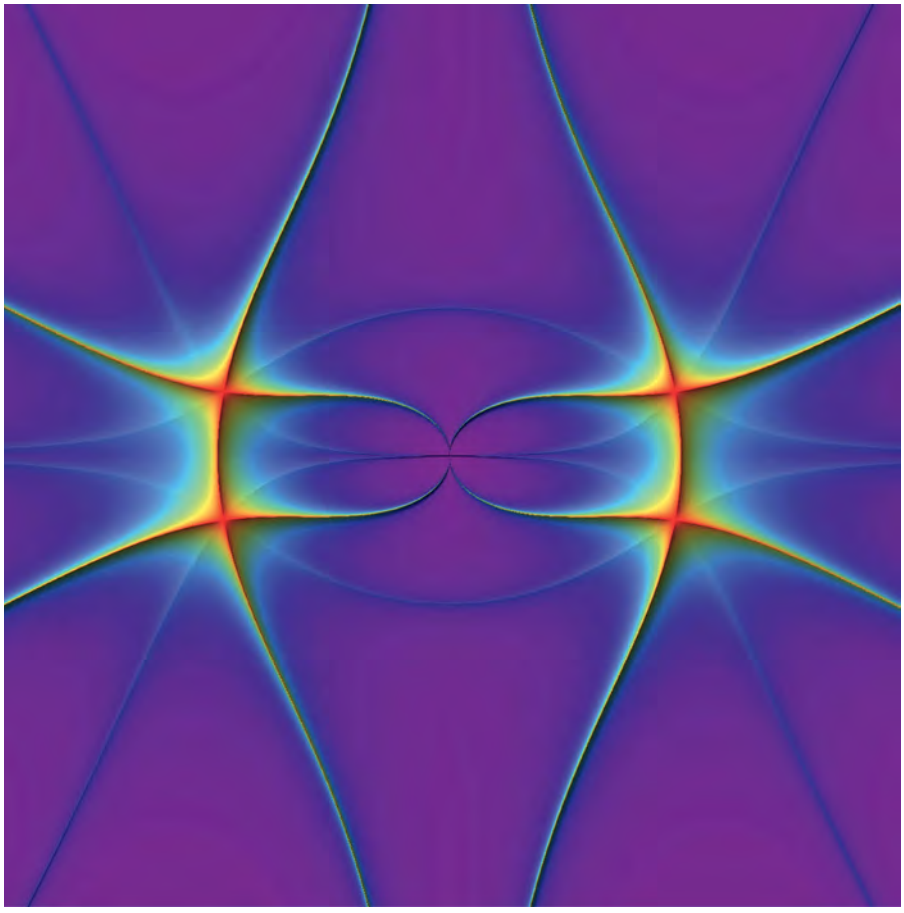
This kind of theoretical research requires an amalgamation of the general theory of relativity, which describes the physics of space and time in variables, and quantum physics, which is responsible for the particle microcosmos. For decades, the aim has been to unify the two fields in an overarching theory of quantum gravity. It may then be possible to understand and describe extreme states – such as the Big Bang or the inner workings of black holes.

Until this aim has been achieved, theoreticians must apply insights from the one theory to the other and determine the effects. It approximates a "theory of everything," although it is never quite clear how closely one has approached the truth. This could perhaps be compared to an attempt to completely dissolve oil in water, and because that doesn't work, one instead studies what happens if a drop of oil (a particle) falls into water (space and time). Analyses like this require not only excellent knowledge of the two fundamental pillars of physics, but also strong familiarity with mathematical methods that would drive most physicists to despair.

SUPERGRAVITY AS A DOCTORAL THESIS TOPIC

Native Luxembourger Jean-Luc Lehners acquired these skills in world-class institutions. Leading up to his doctoral degree, he alternated between Imperial College London and Stephen Hawking's group at Cambridge University. In his doctoral thesis, Lehners studied the topic of supergravity, which is an attempt to transfer a certain symmetry from particle physics to the theory of relativity.

Lehners has a simple answer to the question of why he ultimately ventured into this difficult territory: "I thought, if I don't learn the theory now, I never will." He then went to Princeton University, Einstein's former academic home, and after a short stopover at the Perimeter Institute in Can-



Complex mathematics: This image symbolizes the response of the integral over time if a quantum theory is developed about the scale factor of the universe (that is, about its size). This integral must be regarded as a sum across possible universes that all require different times to advance to today's state. In a quantum theory of the cosmos, the time required by the universe to arrive at today from the time of creation isn't predetermined. In this model, the most probable evolutionary paths of the universe occur at the points in the image where the lines meet.

ada, moved to the Max Planck Institute in Potsdam-Golm where he has led the Theoretical Cosmology Research Group since 2010.

The approximation methods employed by quantum cosmology often lead to a multitude of possible solutions. It is only when certain assumptions that appear physically plausible are brought into play that this diversity is limited to such an extent that, ideally, only a few solutions remain. "But what is plausible when it comes to the Big Bang, anyway?" Lehners remarks, highlighting the limitations of the method. Ultimately, astronomical observations must decide whether a possible solution accurately describes nature.

Cosmologists now find themselves in the unique situation of being able to look into the past. The reason is the very fast, but nonetheless finite, speed of light. For example, the radiation from galaxies that can be observed today had to travel for approximately 13 billion years before reaching our telescopes. Astronomers thus see these star systems in a stage of development as they were 13 billion years ago, or 800 million years after the Big Bang.

THE CONTRACTION OF SPACE WAS A SEDATE AFFAIR

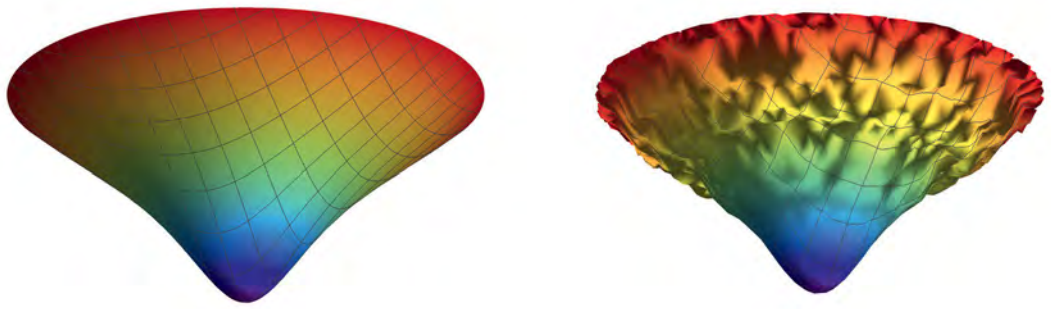
However, the researchers can't look back to just any distance they want. The oldest tidings are those of the cosmic background radiation mentioned above. It originated when the hot primeval gas became transparent, which happened around 380,000 years after the Big Bang – a relatively short period on the cosmic timescale. This radiation field thus also contains information on the Big Bang and the postulated inflationary phase. It is said to have given rise to strong gravitational waves – fluctuations that compress and stretch space in waves. We can picture this as being similar to ripples on the surface of a pond.

These gravitational waves are thought to have "blueprinted" themselves in a certain pattern onto the cosmic background radiation. Physicists say the radiation is polarized in a very characteristic way, meaning that it oscillates predominantly in one plane. In the cyclic universe theory, no – or only very weak – gravitational waves were generated, because the contraction of the precursor universe was more sedate, and space-time not as strongly agitated as assumed.

Observing polarization in the cosmic background radiation thus affords the great opportunity of differentiating between the inflationary and cyclic universe theories. However, the signal was probably extremely weak and overlain by other effects.

It therefore caused a sensation when, in spring 2014, a team of researchers from the Harvard-Smithsonian Center for Astrophysics claimed they had identified precisely this polarization pattern using the BICEP2 telescope operating at the South Pole. Some cos-

Graphic: Jean-Luc Lehners/MPI for Gravitational Physics



The wrong way out: Stephen Hawking (photo below) and James Hartle's no-boundary proposal avoids the singularity of the Big Bang. The quantum fluctuation from which the universe arose was finite (blue) and was subjected to inflationary expansion from there (cone expansion). However, the no-boundary proposal didn't pass a stress test: quantum fluctuations, which become stronger with time (right), prevent a stable universe such as ours.

mologists could already see the Nobel Prize within reach.

Following an analysis of the observational data recorded by the European Planck space telescope, the sobering conclusion was that the researchers had missed something: the polarization pattern didn't originate from gravitational waves, but from dust within our Milky Way, through which the background radiation had passed on its way to us. Nothing more than a misinterpretation, then! Because of the enormous importance of this observation for cosmology, background radiation measurements are now being carried out with greater sensitivity.

Discovering the polarization signal would be something akin to finding the Holy Grail of cosmology. But for theoreticians such as Lehners, even after this success, the question would remain: How can we understand and describe the singularity of the Big Bang, with its physically senseless, infinitely high density and temperature? Thirty-five years ago, Stephen Hawking and his then-colleague James Hartle caused a stir by proposing a possible solution, which they named the no-boundary hypothesis.

The idea is based on several assumptions about how to unite quantum physics and the general theory of relativity in a single Big Bang model and avoid the singularity. One of the most critical steps was that Hawking and Hartle described time as a complex variable. Time, now imaginary, thus formally becomes a fourth spatial coordinate, and space and time have become indistinguishable.

AN ELEGANT HYPOTHESIS – BUT UNFORTUNATELY WRONG

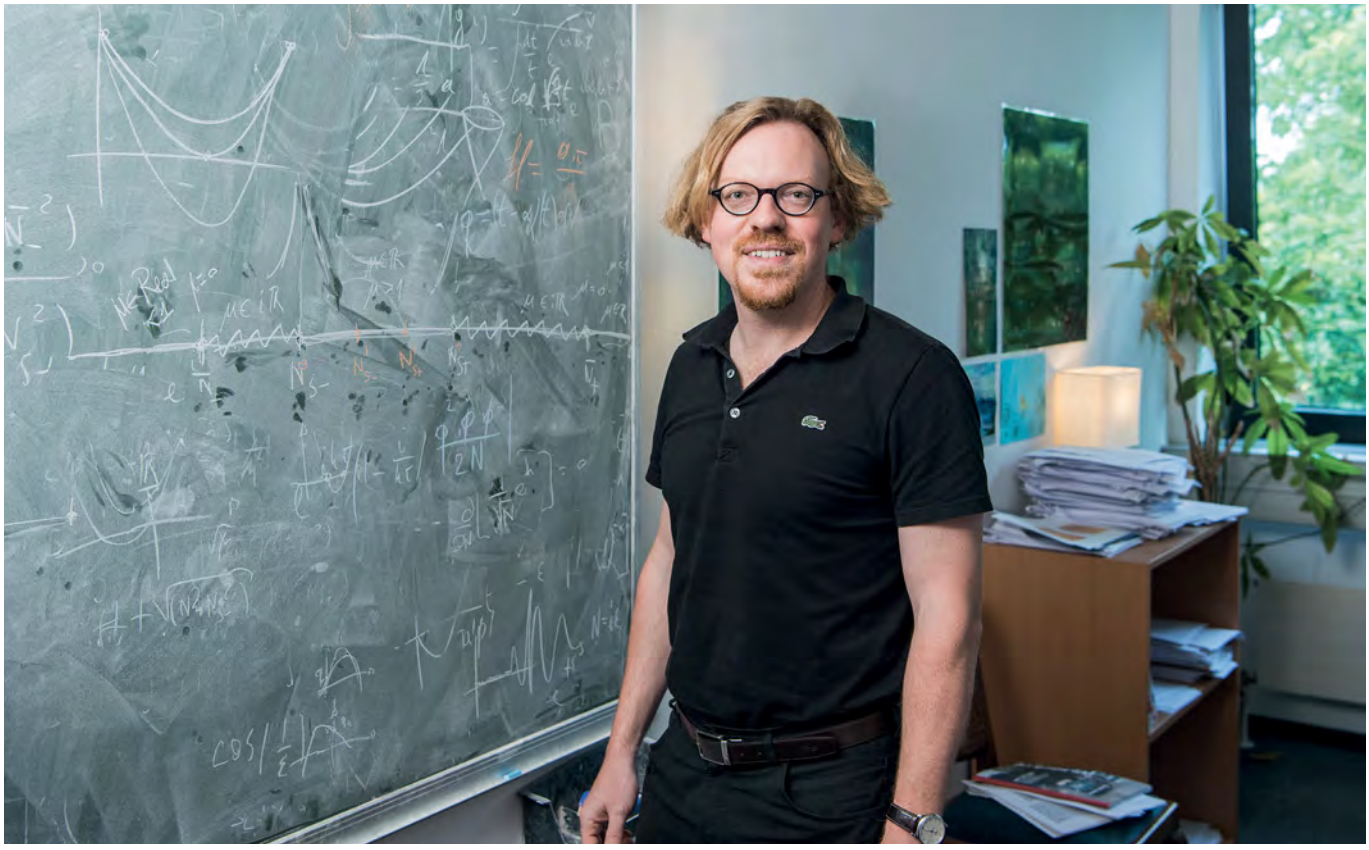
"One can no longer truly speak of space and time. Rather, the universe is now a quantum state or a quantum fluctuation," says Jean-Luc Lehners. In this description, the universe may have been self-contained, like a sphere. It thus had no edge, but was unbounded, similar to how, in principle, one can circumnavigate the Earth without encountering an edge or a boundary. Nor did it possess a singularity – a location with physically senseless variables.

In the Big Bang, this boundaryless quantum state expanded, and space and time as we know them today were created. Interestingly, this scenario requires an energy field for the initial no-boundary state – just as the theory of inflationary expansion does. "An inflationary universe would therefore automatically develop from the initial state," says Lehners. An elegant hypothesis, then, and it would have solved two problems at once: the initial singularity of the Big Bang would have been avoided and the cause of inflation identified.

But even Hawking had pointed out that the no-boundary hypothesis was merely a proposal and couldn't be derived from any underlying principle. In particular, due to the mathematical difficulties, this scenario was always analyzed using extreme simplifications, and nobody knew how realistic they were.

Jean-Luc Lehners, together with his colleagues Job Feldbrugge and Neil Turok from the Perimeter Institute in Canada, recently subjected Hawking's model to a stress test using improved

Graphic: Jean-Luc Lehners/MPI for Gravitational Physics; photo: Mike Hutchings/Reuters



Search for the answer: How was the universe created? This question has occupied humanity for millennia. At the Max Planck Institute for Gravitational Physics in Potsdam-Golm, Jean-Luc Lehners is addressing this problem using state-of-the-art mathematical tools.

mathematical methods – with an interesting result: it didn't work! The theoreticians investigated the stability of the initial quantum fluctuation and discovered that, the greater the fluctuation, the more chaotic it is. If we regard them as oscillations in spacetime, this means that the oscillations become stronger and stronger and prevent a stable universe such as ours from developing. And the greater the fluctuation is, the greater is the probability of its occurrence.

"There is no upper limit," says Lehners. That is, the probability that a sufficiently small quantum fluctuation occurred from which our universe could develop is zero. "We were amazed that the effects we had identified practically turned the Hawking and Hartle model on its head," says Lehners: "It didn't yield any sensible solutions."

The researcher doesn't consider this unpleasant result to be negative by any means. Rather, it shows him the path along which he wants to continue. "Today, we have better mathematical methods to continue questioning," he says. Right now, nobody knows when or whether this path will even lead to a final result. Ultimately, though, this is the greatest question that humans can ask: How was our world created? ◂

TO THE POINT

- **The birth of the universe in the Big Bang is undisputed among cosmologists. What is less clear, however, is what exactly happened at time zero.**
- **The most popular hypothesis assumes an inflationary, faster-than-light expansion of the infant universe. However, the possibility of a gentler transition from a precursor universe has not been ruled out.**
- **Recently, Jean-Luc Lehners and two colleagues brought down the no-boundary hypothesis with which Stephen Hawking and James Hartle had tried to avoid the initial singularity.**

GLOSSARY

Expansion of the universe: After Belgian Georges Lemaître had discovered the expansion of the universe in theory in 1927, US astronomer Edwin Hubble confirmed it in practice in 1929. Hubble observed the flight of the galaxies, which appeared as a redshift in the spectral lines of galactic systems. This galactic redshift, in turn, had already been found by American researcher Vesto Slipher in 1912.

Planck space telescope: This European space probe, launched in 2009, produced the most precise cosmic background radiation map to date before the mission ended in 2013. With the aid of the satellite, the researchers determined that the universe was 13.82 billion years old. In addition, they derived its composition very accurately: today it comprises 68.3 percent dark energy, 26.8 percent dark matter and 4.9 percent baryonic matter (atoms).

Photo: Andreas FranzXaver Süß

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Spring!

GEFÖRDERT VOM

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Fertile Research

Egg and sperm cells are highly sensitive during their development. When, for example, there is an error in the way the genetic material is divided between the individual gametes, the resulting embryo will often either be nonviable or suffer from severe birth defects. **Melina Schuh** from the **Max Planck Institute for Biophysical Chemistry** in Göttingen wants to find out why egg maturation is so error-prone. The results of her research could one day help couples who are unable to have children.

TEXT **CATARINA PIETSCHMANN**

At long last, a warm, dry summer evening in historic downtown Göttingen. Out on the terrace of the restaurant where we arranged to meet, Melina Schuh is waiting for us, already studying the menu. She has the night off from the kids, with her husband on childcare duty. She puts her phone where she can see it, "Just in case there are any problems at home," she says with a smile.

Schuh's professional interest is in a little understood process without which none of us would be here: meiosis. Whether fruit flies or humans – without meiosis, sexual reproduction would be impossible. While other cells in our bodies have two sets of chromosomes, egg cells and sperm must have only one. "Otherwise, when the egg and sperm cells fuse, the number of chromosomes would double – instead of two sets of chromosomes, the new cell would have four," explains Schuh. "That's why, during meiosis, one of the two sets of chromosomes is eliminated from the egg cell."

This first meiotic cell division occurs while the egg cell is still in the ovary. Unlike frogs, mice and most other animals, in humans, meiosis sometimes goes wrong. As a result, the desire to start a family remains unfulfilled, with miscarriages or an embryo that contains too many or too few chromosomes.

HALF A SET OF CHROMOSOMES

In meiosis, before cell division takes place, the cell doubles the amount of its genetic material. The meiotic spindle then arranges the chromosomes of each pair in such a way that they lie opposite one another in the egg cell. The protein fibers in the meiotic spindle then each pull one of the chromosomes in each pair to the spindle poles situated at opposite ends of the egg cell. At the end of this process, the two sets of chromosomes have been separated. In the second meiotic division, the same process is used to separate the copies that were produced when the amount of genetic material was doubled. In males, this results in the production of four sperm cells. In females, in contrast, only one egg cell is produced, along with two tiny polar bodies that contain the extra chromosomes.

Errors can occur during meiotic spindle formation, and also during chromosome separation. "If, for example, the egg cell ends up with two copies of chromosome 21, fertilization produces an embryo with trisomy 21, or Down syndrome," explains Schuh. Other chromosome number abnormalities also impact embryonic development. "In most cases, an embryo with an abnormal number of chromosomes will have such severe defects that it won't even be able to implant into the uterus. Often, women might not even be aware that fertilization has taken place."

An embryo with too many X chromosomes, however, is viable. "It's estimated that around one in a thousand women have three X chromosomes instead of the normal two, and they are usually unaware of it." So how do these errors – which become increasingly common as women enter their late 30s

Photo: Frank Vinken

At the moment, Melina Schuh's workplace is still a construction site: In late 2017, her department will move into the new premises designed especially for the study of live egg cells. The new site will allow them to accommodate high-resolution microscopes with which living, developing egg cells can be observed for long periods.

and early 40s – occur? At present, we really have a very limited understanding of the underlying mechanisms. Melina Schuh wants to change this.

In mammals, egg cells are produced early in embryonic development. These very small cells are enclosed in a thin layer of somatic cells, known as follicle cells, and are already present in the ovaries at birth. They remain inactive until puberty, after which two to three cells mature during each menstrual cycle. The follicle cells are connected with the immature egg and feed it via fine channels. The follicle cells divide and form a cocoon around the egg cell. Of the initially two to three follicles – that is, the eggs cells with the surrounding follicle cells – only one reaches full size, in the middle of the menstrual cycle. The others die off.

At this point, the pituitary gland secretes a hormone that initiates ovulation. Meiosis commences, and the follicle cell layer on the outside begins to loosen. Once chromosome segregation is complete, the egg cell slides out of its cocoon, exits the ovary and moves into the fallopian tube, ready for fertilization by a sperm.

"When a 40-year-old woman wants to get pregnant, both her egg cells and the chromosomes inside them are also 40 years old," says Melina Schuh. Chromosome pairs are held together by ring-shaped protein complexes, which act like a kind of glue. Normally, enzymes ensure that the protein complexes that hold the chromosome pairs together aren't severed until meiosis has commenced. "We have discovered, however, that chromosome pairs aren't as well bound together starting as early as age 25. Some chromosome pairs literally fall apart." Under the microscope, we observe that this results in chromosomes that are incompletely paired, chromosomes that turn during separation, or premature separation of chromosome pairs. "This means that the spindle fibers can't grasp and separate the chromosomes properly." As a result, depending on age, between 10 and 50 percent of egg cells are no longer viable.

GOOD EGGS AND BAD EGGS

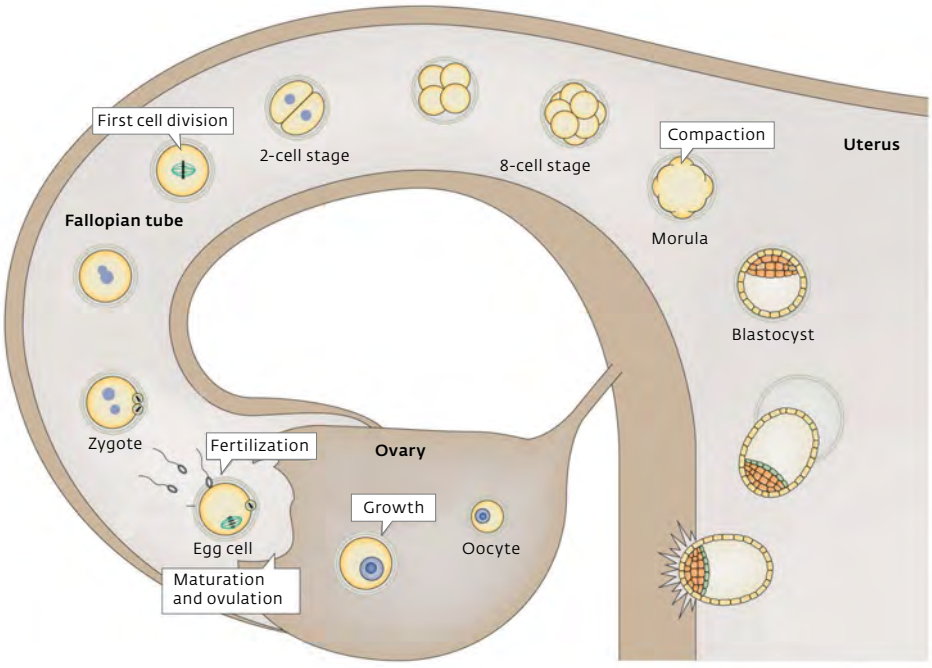
The drop in quality of immature egg cells is one of the reasons why the risk of chromosome anomalies and miscarriages increases with age. "But the good news is that, even if some egg cells are no longer good, other eggs may still be fine," notes Schuh. So, if nothing has happened after the first few months, don't give up! A good egg might come along with the very next ovulation.

Before she came to Göttingen, Melina Schuh worked at the MRC Laboratory of Molecular Biology (LMB) in Cambridge, England. There, she mostly worked on mouse egg cells, but she also conducted some research on human eggs. Even after her move to Göttingen, her laboratory maintains close links with Cambridge. She has a small laboratory at the Bourn Hall Fertility Clinic, where she researches how human egg cells develop. Bourn Hall Fertility Clinic is no ordinary clinic: it was the world's first in-vitro fertilization (IVF) clinic and was founded by IVF pioneers Sir Robert Edwards and Patrick Steptoe. In 1978, their pioneering work led to the birth of the very first "test tube baby," Louise Brown, paving the way for millions more IVF babies.

"When you collect egg cells for in-vitro fertilization, they are generally at different stages of development. If a cell hasn't yet undergone meiotic division, it can't be used for IVF. In that case, if the patient consents, we can use these extra, unfertilized cells – which would otherwise be discarded – for research."

Schuh comes from Bad Pyrmont, where she grew up with three younger siblings. As a child, she did a lot of sports, including swimming, athletics, volleyball and badminton. She also had

Photo: Frank Vinken



Left Katarina Harasimov (left) and Melina Schuh use a special microscope to inject RNA molecules into egg cells. This enables the researchers to visualize specific structures within the cells.

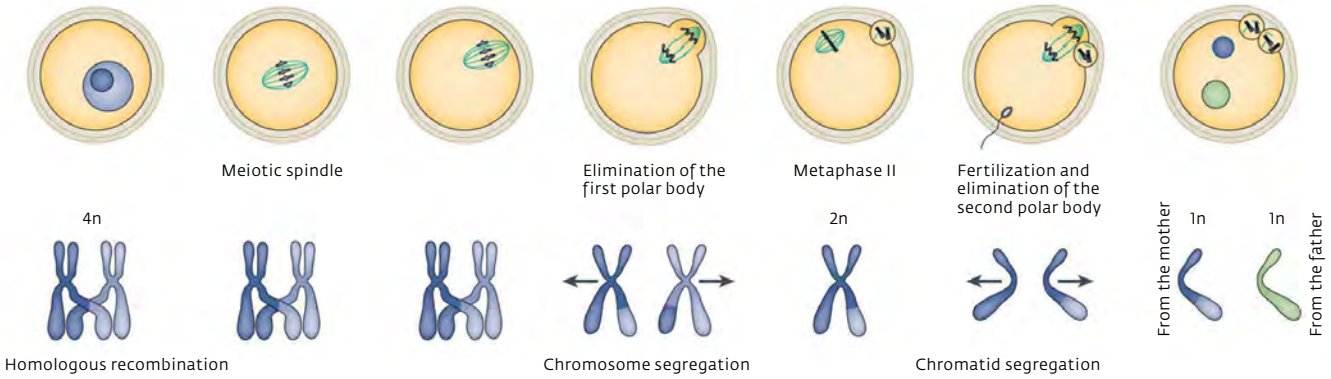
Right During human embryonic development, immature egg cells (oocytes) are stored in the ovaries. These egg cells are activated during puberty. In the middle of the menstrual cycle, one egg cell matures by undergoing the first meiotic division. It is then released into the fallopian tubes, ready to be fertilized. If fertilization takes place, it divides until it forms a compact ball of 32 cells known as a morula. After further cell division, the morula forms a fluid-filled cavity. At this stage, the embryo, now called a blastocyst, sheds its protein shell and implants into the uterus.

diverse musical interests: she sang in a choir and played several instruments, including piano and flute.

She majored in German and biology in high school before going to Bayreuth to study biochemistry. "Every time I walked out of a lecture, I felt like I understood a little more about the world around me." For her dissertation, she studied cell division in fruit fly embryos, completed her degree with distinction and then started her PhD at the European Molecular Biology Laboratory (EMBL) in Heidelberg. Jan Ellenberg, a specialist in cell division and microscopy, offered her the opportunity to work with starfish egg cells. She spent the first summer of her doctorate at the renowned Marine Biological Laboratory in Woods Hole, Massachusetts, which has been conducting research on reproduction in marine animals for more than a century.

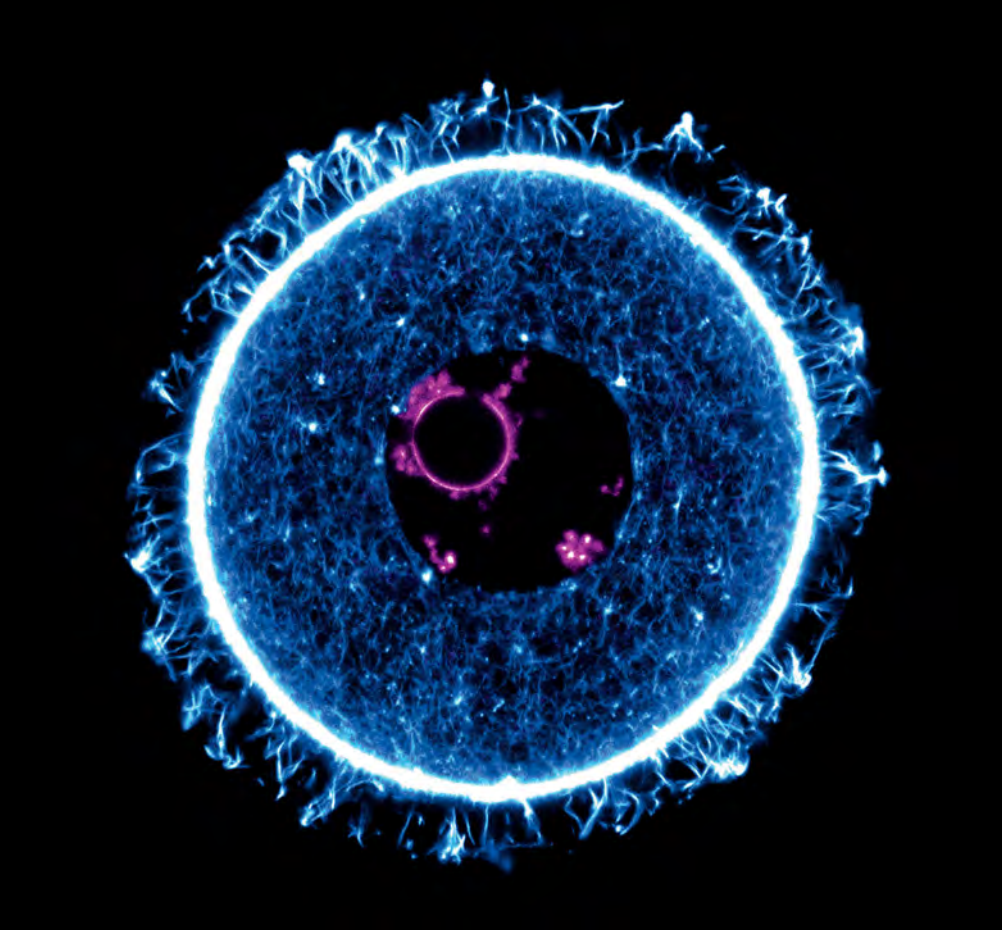
"Starfish egg cells are relatively large, and they can be harvested in fairly large quantities, making them great for use in biochemical experiments. Starfish eggs are also transparent, so they are easy to observe under the microscope." But what Melina was really interested in were the processes happening in human egg cells, so in Heidelberg, she started to develop techniques for high-resolution microscopy of mouse egg cells, which are much more similar to human egg cells.

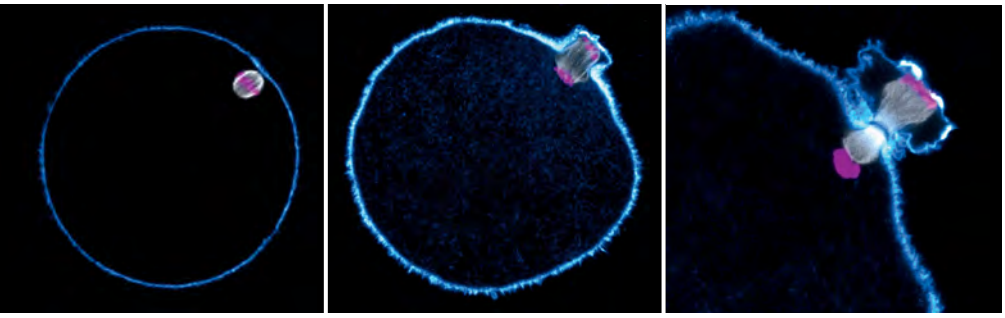
It was while writing her doctorate that she received an inquiry from Cambridge. She was encouraged to apply for a group leader position at the LMB. "I had just a week to put together a research plan," Melina Schuh re-



The phases of egg cell maturation: After the nuclear envelope has broken down, the newly formed meiotic spindle migrates to the surface of the cell and segregates the (previously doubled) chromosome pairs. After forming a second spindle, the cell remains in metaphase II until fertilization. If a sperm cell fuses with the egg cell, the spindle segregates the two copies of each chromosome. This second step thus halves the number of chromosomes. The extra chromosomes are eliminated from the cell into polar bodies. The fertilized egg cell (zygote) now contains two pronuclei, each containing a single set of chromosomes from either the mother (blue circle) or father (green).

Graphic: Nature Reviews, Molecular Cell Biology Vol.14, Sept. 2013





Above Mouse egg cells in prophase. Viewed under a fluorescence microscope, the network of actin fibers glows blue and the chromosomes in the interior of the cell nucleus (black circle) glow magenta. In this phase of meiosis, the chromosomes condense and the spindle forms.

Below Human egg cells during the first meiotic division. During the metaphase, the spindle (gray: microtubules; magenta: chromosomes) is anchored to the cell surface (left; blue: actin fibers). The chromosomes are separated from each other (center). One half remains in the egg cell while the other is eliminated from it. The first polar body is formed (right).

members. But the timing was perfect: "My husband had just successfully applied to the MBA program at the London Business School, so we decided he would go to London and I would go to Cambridge." In the beginning, they did a lot of commuting, then they bought and renovated a house in Cambridge. Their son was born just as the house was finished, followed two years later by a daughter.

"Cambridge is a small university city, perfect for bringing up children. There are lots of green spaces between the colleges, great playgrounds, cows right in the middle of the city – it's very idyllic."

Distances are short and most journeys can be made by bicycle – with the kids in a bike trailer. In England, childcare and working hours are designed to meet the needs of two working parents. The only time things got a little tricky was if she had to go to a conference and her husband, a management consultant, was away on business. When that happened, Melina's parents came over from Germany to spend some time with their grandchildren.

Nevertheless, when she received an offer from the Max Planck Society to become Director at the Max Planck Institute for Biophysical Chemistry in Göttingen, Melina didn't have to think twice. "We have the perfect conditions for our research here, and it's close to my hometown!"

Does she miss anything about England? "Friends of course, and sometimes the British politeness. Shops open on Sundays. And healthy convenience foods!" she adds with a laugh. "All in all, I could have stayed there forever." But in Cambridge she had only a small research group. "Eventually, our ideas outgrew our capabilities. It's great that I can now pursue longer-term and higher-risk projects at the Max Planck Society."

Research, work trips, family, even meeting journalists like this – it all has to be organized. Since early 2016, the 37-year-old biochemist has been head of the Meiosis Department at the Max Planck Institute in Göttingen. She now has a secretary and lab manager to take care of most of the organization and planning – and for that she is very grateful: "When you have young kids, there are never enough hours in the day. I'd much rather spend my time at the Institute doing actual research, rather than administration."

Seven years as a researcher in Cambridge have also left their mark on her research style. "In Cambridge I experienced a largely non-hierarchical, friendly and collaborative way of working. I try to put a lot of what I learned at the EMBL and subsequently in Cambridge into practice here in my department." She now has a group of 15 PhD students and postdocs, "a good number," she says, for people to be able to bounce ideas off each other and develop a vision. "I want to give my staff as much freedom as possible and support them in tackling ambitious research projects."

Photos: Zuzana Holubcova and Melina Schuh, MRC Laboratory of Molecular Biology

As very few human egg cells are available for research, the researchers are in need of other model systems. Mouse egg cells, however, in addition to being smaller than human egg cells, also have a meiotic spindle with a different structure. In her search for suitable alternatives that more closely resemble the processes happening in human eggs, Melina Schuh stumbled upon pigs. Pig egg cells are easy to procure from slaughterhouses and they are easily isolated.

NEW SPINDLE PROTEIN DISCOVERED

Her team recently succeeded in showing that actin, a protein that, among other things, plays a crucial role in the shape and migration of cells, is present in the spindle in mice, sheep, pigs and humans. Without this protein, chromosome segregation in mammalian egg cells runs into problems. "If there's not enough actin, the chromosomes don't align correctly in the center of the cell prior to cell division. In addition, chromosome segregation is often slower, and the egg cell ends up with too many or too few chromosomes," explains Schuh. Actin is therefore thought to be required for spindle fiber assembly.

Why meiosis is less error-prone in other species – such as mice – remains a mystery. "You can argue, from an evolutionary point of view, that having lots of offspring is important for the survival of mice as a species." Mice are able to produce a litter of five to ten pups every few weeks. "If, say, one quarter of the embryos failed to develop, it would be an enormous waste of resources." Humans have always had relatively few offspring. "In humans, even if a quarter of egg cells are defective, this may not have much of a negative effect on reproduction. Most defective embryos are unable to implant into the uterus and the mother can become pregnant during her next menstrual cycle. Perhaps egg cells in humans just don't need to be as reliable as in other species," suggests Schuh.

Understanding all the details of meiosis, finding ways of distinguishing between egg cells with the right and wrong number of chromosomes before they are fertilized, and perhaps even helping them develop properly is a big goal. Melina Schuh's research could also help generate insights to improve fertility treatments. Her research thus also has implications beyond pure basic research. By the time Schuh first became pregnant, she already knew plenty about the subject and was well aware of the potential risks. "Before my first child was born, I could hardly believe that everything could turn out okay – there are so many developmental stages that have to go right before a child is born." Today, Melina and her husband have three healthy children.

Without doubt, Melina Schuh's life is very busy and there are hardly enough hours in a day. That there are not enough women in leadership positions in science is a recurring complaint. "There are programs for the advancement of women, quotas for women and many other initiatives, but the sticking point is still the compatibility of a research career with family life," stresses Schuh.

Particularly in research, it is very difficult for women and men to stay at home for long after having a child. Science today advances so quickly that a year of parental leave can mean that projects have already become outdated. There are very few childcare facilities with enough staff for children under the age of one. "It's never easy leaving your children in the care of others, so it's very important to know that they're happy and they're going to be well looked after. In my view, high-quality childcare options are important for combining research work with family life." The fact that the nursery on the Max Planck campus is open to children of ages 6 months and older – something that is normal in England – is due in part to her committed efforts.

A good 30 years of research lie ahead of Melina. Was it helpful to be made Director at such a young age? "Definitely. It means you can set yourself really big goals. I'm very much looking forward to seeing what the future has in store!"

Research and family? For Melina Schuh at least, it works well. In principle, it's just like meiosis: it's all a question of organization. ◂

GLOSSARY

Set of chromosomes: With the exception of the gametes, the cells of most vertebrates generally have two sets of chromosomes – that is, they contain two copies of each chromosome. Human embryos that have the wrong number of chromosomes usually die before implantation in the uterus. Only rarely are such embryos viable, for example embryos with three copies of chromosome 21, which results in Down syndrome.

Spindle: During cell division, this ensures that the chromosomes are arranged in pairs in the equatorial plane and are pulled away from each other in opposite directions. The spindle is constructed from protein fibers known as microtubules. These consist of an array of tubulin proteins and attach to a special protein complex on the chromosome, called kinetochore. Recent research has shown that, in addition to microtubule and kinetochore proteins, correct chromosome segregation by the spindle also requires actin. This protein also forms long fibers and enables muscle cells to contract, for example.

A Beetle
Overcomes a Plant's Defenses

Every cabbage plant conceals a bomb – a mustard oil bomb. For many insects, this makes the plant unpalatable. **Franziska Beran** from the **Max Planck Institute for Chemical Ecology** in Jena now knows, however, how insects can avert this danger: flea beetles, for example, outsmart the plants' defensive weapon and even commandeer it for their own protection.

Flea beetles are dreaded pests. When they are attracted in large numbers to rapeseed fields by pheromones released by other beetles of the same species, they can wreak havoc, leaving the foliage riddled with holes.

Nigel Cattlin/Holt Studios/OKAPIA (large photo); Marko Baum/processor: Veit Grabe (small photo)

» To produce their mustard oil bombs, the beetles use components they produce themselves as well as substances they take up from plants on which they feed.

TEXT **KLAUS WILHELM**

Franziska Beran heard about the mustard oil bomb for the first time while studying biology at Humboldt-Universität zu Berlin. "It's a highly effective defense system that plants activate only when they are being eaten – a truly ingenious invention of nature," says Beran, who leads the Sequestration and Detoxification in Insects Research Group in Jena. Only plants in the crucifer family (Brassicaceae) are armed with this chemical defense system. The Brassicaceae include important sources of vegetables, spices and oils, such as white cabbage, broccoli, cauliflower, brussels sprouts, kohlrabi, mustard, oilseed rape, radishes and cress.

The mustard oil bomb is conceived as a two-component system. Component 1: mustard oil glycosides (glucosinolates), which are completely harmless. Component 2: the enzyme myrosinase. When a plant is attacked by, say, a beetle, the enzyme degrades the mustard oil glycosides to form spicy toxic substances. In the intact state, the plant stores the two components neatly separated so they don't come into contact with each other – so the bomb doesn't go off inadvertently. However, if the plant is injured, this separation breaks down and the mustard oil bomb is triggered.

The substances formed include mustard oils, or isothiocyanates, which give mustard its characteristic sharp taste. But isothiocyanates also interfere with the insects' digestion, so the mustard oil bomb can have a toxic effect. "This deters most natural enemies of cruciferous plants," Beran explains. This includes mainly insects, but isothiocyanates can also protect the plants against pathogenic fungi and bacteria.

Yet the mustard oil bomb doesn't work against all predators: some insects have, over the course of evolution, developed strategies to defuse the bomb. For instance, the voracious caterpillars of the cabbage white butterfly are unable to prevent the breakdown of mustard oil glycosides, but they accumulate a protein in their gut that interacts with the myrosinase to produce much less toxic nitriles instead of mustard oils.

Another group of insects that are not impressed by the mustard oil bomb are the flea beetles – beetles that jump like fleas. It is this trait that gave them their name, which is as apt as it is misleading, as they are not related to fleas. In some parts of the world, flea beetles are dreaded pests that result in substantial crop losses. In Canada, for example, they attack rapeseed fields in hordes, leaving the plant leaves riddled with holes.

A PEST IN ASIA

The infestation of crops by these pests has increased considerably in recent years, especially in Southeast Asia. During an internship at the World Vegetable Center in Taiwan, the Max Planck researcher observed first-hand how flea beetles can wreak havoc on valuable cruciferous crops. The biggest culprit is the striped flea beetle, *Phyllotreta striolata*. "When we planted bok choy or radish seedlings on Friday, the plants were already devoured by Monday."

On closer inspection, the rearmost of the three pairs of legs of flea beetles appear to be much thicker than the others. Inside is a kind of spring that

Theresa Sporer collects the beetles once a week from mustard plants and provides them with fresh plants (top). Because the beetles are powerful jumpers and are thus difficult to catch, Sporer uses a small handheld, battery-operated vacuum apparatus to capture them (bottom).

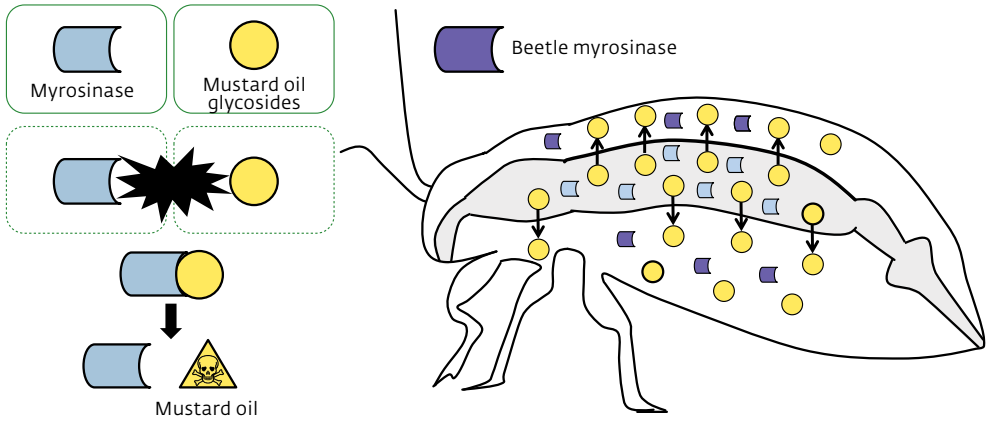
Photos: Anna Schroll (2)

the beetles can use to catapult themselves into the air to evade enemies. Beran's colleague Theresa Sporer, who cultivates the native horseradish flea beetle (*Phyllotreta armoraciae*) in the basement of the Max Planck Institute, is often treated to stunning athletic feats: the tiny insects, which measure only about three millimeters in length, achieve leaps of half a meter with ease. Once, a beetle escaped from the breeding room despite extensive security measures, and sated itself on the experimental plants of other colleagues in the Institute's greenhouse. "These colleagues were understandably not very pleased about this," says Sporer. Measures to prevent such breakouts have since been tightened.

A COMFORTABLE LIFE IN THE LAB

But why on earth would the little beetles want to escape? After all, they lead a very good life in their cozy basement. They have warmth and light and can chomp on mustard leaves to their heart's content. A few weeks after hatching, they lay eggs from which larvae develop. The larvae feed inside leaf stalks and finally pupate in the soil. Thanks to the lab's breeding program, "fresh" beetles are available daily for research. In the wild, in contrast, the horseradish flea beetle breeds just once a year. The striped flea beetle manages to do so up to nine times a year, thanks to the tropical climate in Asia.

Before turning her attention to the mustard oil bomb, Franziska Beran studied how striped flea beetles suddenly congregate on cabbages in hordes for



The principle of the mustard oil bomb: As long as the enzyme myrosinase and mustard oil glycosides are stored in separate cells, the substances are harmless. Only when they encounter each other, for example when the cells are injured, are toxic mustard oils formed. Flea beetles use components of various origins to produce their mustard oil bombs: the mustard oil glycosides are derived from the plants they feed on. They are absorbed through the gut and accumulate in the insects' body. The myrosinase contained in the plant, in contrast, remains unused and is synthesized by the beetles themselves.

a shared meal – despite only a few beetles having initially discovered the food source. The invasion is simply too fast and overwhelming for the plants' protection mechanism to be effective: the plants are consumed before they can mount a defense.

Beran, who is a native of Berlin, discovered that flea beetles are drawn to the feast by a pheromone. When a beetle finds a new food source, it emits a pheromone to attract fellow beetles, which can detect the scent over great distances. "Aggregation pheromones act in a similar way to sex pheromones, but in this case, they are released by the males and attract both sexes," Beran explains.

At first glance, it would appear to be counterproductive for a flea beetle to inform its fellow beetles when it has discovered food. After all, this seemingly selfless act attracts competitors to the scene. Nevertheless, it is beneficial for the beetles to beckon others, because together they can penetrate the hard outer layer of a leaf more quickly. The leaf layers that the beetles relish are only found under the waxy surface of many cruciferous plants. Studies have shown that each beetle can consume larger amounts of plant food when many animals eat together.

INVITATION TO THE FEAST

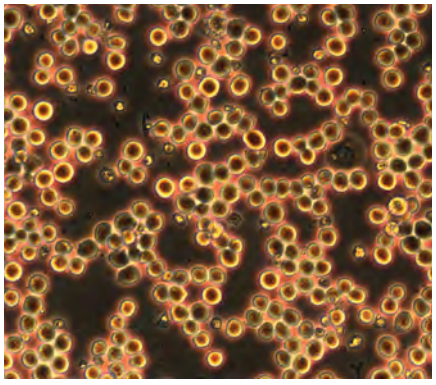
The male beetles don't release the pheromone signal until they have begun to munch on the plant. With their antennas, their fellow beetles can sense one millionth of a gram of pheromone and then follow the scent trail to its source.

Chemically, these pheromones are so-called terpenes, or more precisely, sesquiterpenes – a widely distributed group of secondary metabolic products that occur in fungi, bacteria and plants. These substances are responsible, for example, for the typical resinous odor of conifers. The biologist has shown that male *Phyllotreta striolata* beetles produce a terpene blend consisting of eight structurally related bicyclic sesquiterpenes. Franziska Beran has not yet been able to test the attractant power of the complete mixture, since not all the components are available. "Actually, it wasn't even necessary, because a mixture of just two terpenes reliably attracts the beetles."

Most insects don't produce terpenes. *Phyllotreta striolata* is an exception: according to studies Beran has carried out, the beetle possesses specific enzymes called terpene synthases. The researcher analyzed the genes that code for the enzymes and discovered that the beetles' enzymes differ from those found in bacteria and plants. This means that beetles have, so to speak, reinvented the production of terpenes: instead of using the terpenes of the plants they feed on or exploiting symbiotic bacteria that produce the substances, they synthesize the terpenes themselves.

Of course, these results raise the question of whether the terpenes can be used to the detriment of flea beetles, for example in the form of pheromone traps that selectively attract them. For Beran, however, this is a long way off. "We still know too little about how the beetles use their messenger substances to communicate," she says. She tested the effectiveness of pheromones in a field experiment and found that, although the artificial scents attract the beetles, they

Graphic: Franziska Beran/MPI for Chemical Ecology



Franziska Beran observes cultured insect cells under the microscope. The cells are genetically modified to produce the myrosinase of the striped flea beetle *Phyllotreta striolata* (bottom). Beran isolates the enzyme from the cells to investigate its properties.

Photo: Anna Schroll (top), Yannick Pauchet/MPI for Chemical Ecology (bottom)

are far less potent than the originals and are too weak to prevent the insects from feeding on crops. "Either all eight terpenes are needed, or other as-yet unknown substances play a role in the mass gatherings of the insects."

But back to the mustard oil bomb. Thanks to the findings of the researchers in Jena, we now know that flea beetles take up certain mustard oil glycosides from their food plants and accumulate them in their body. In fact, mustard oil glycosides make up nearly 2 percent of the beetles' body weight. The scientists now want to find out how the beetles prevent the mustard oil bomb from going off while they are feeding on the plants. After all, injury to the plant is supposed to cause myrosinase to break down the mustard oil glycosides into toxic mustard oils.

In fact, the beetles don't appear to be completely immune to the mustard oil bombs of cruciferae. Plants with very high myrosinase activity and a correspondingly high isothiocyanate content are better protected against the pests. "This means that the beetles are unable to completely disarm the plants' defense system," says Beran.

But what do the beetles do with the stored mustard oil glycosides? Is it possible that they have their own mustard oil bomb? In that case, the necessary enzyme would also have to be present. In fact, an analysis of the genome of flea beetles has revealed that they have the blueprint for producing myrosinase in their genes. "The beetles developed, independently of the plants, their own enzyme that breaks down mustard oil glycosides to form isothiocyanates. The

Below Sticky trap in a cabbage field in Taiwan. The trap is baited with an artificially produced beetle pheromone. The wind carries the scent into the surroundings and attracts the pests so that they become stuck in the trap.

Right During an internship, Franziska Beran observed first-hand the damage flea beetles can wreak on economically important cabbage varieties in Asia. Her research has since revealed a few secrets of the tiny insects. She hopes that her findings will help farmers combat the pests both selectively and in an environmentally friendly manner.

mustard oil bomb of the cabbage flea beetle is therefore based on myrosinase that it produces itself and mustard oil glycosides obtained from food plants," Beran explains.

It is conceivable that the beetles' real enemies aren't other animals – after all, their powerful legs enable them to deftly leap away – but rather pathogens such as bacteria and fungi. Or the mustard oil bomb may protect the beetle larvae, which feed on roots in the soil, where they are exposed to numerous enemies, including bacteria.

Flea beetles have therefore not only learned to render the defenses of their feed plants harmless; they also appropriate them for their own protection. Scientists can thus learn a great deal about the interrelationships between plants and insects from the tiny long-jumpers – knowledge that may one day be used to protect agricultural crops. ◂

TO THE POINT

- **Cruciferous plants convert mustard oil glycosides into toxic isothiocyanates with the help of the enzyme myrosinase. Only when the plants are being eaten does this enzyme come into contact with the glycosides to form toxins.**
- **Flea beetles can at least partially prevent the breakdown of mustard oil glycosides by myrosinase, thus circumventing the plants' defense system. They store some of the mustard oil glycosides in their body and use them together with self-produced myrosinase for their own protection.**
- **Flea beetles release a mixture of terpenes to attract fellow beetles to food plants. Together, the beetles are better able to penetrate the hard leaves of the plants.**

GLOSSARY

Flea beetles: These beetles measure about one and a half to three millimeters in size and are dark blue to black or yellow striped. They overwinter in the soil, and the females lay their eggs in young plants in the spring. The inconspicuous white larvae of flea beetles feed on plant roots or burrow into leaf stalks without causing significant economic damage. The young beetles appear in summer. They feed on leaves, boring round holes in them. Flea beetles can transmit plant pathogens such as radish mosaic virus. Fine-meshed insect netting can prevent the beetles from reaching the plants on which they feed.

Photos: Franziska Beran (left), Anna Schroll (right)

Getting the Trolls **Under Control**

Whether it's security, environmental protection, infrastructure or the internet – everybody has to play by the rules if we are to reap the benefits of collective goods. **Fabian Winter** of the **Max Planck Institute for Research on Collective Goods** in Bonn is studying the conditions needed for this to happen, and also providing surprising support for political intervention in social media.

TEXT **MARTIN TSCHECHNE**

Three men are standing on a platform waiting for a train. One finishes his coffee and carelessly throws his paper cup on the ground. How does the second man react? Sociologist Fabian Winter staged the entire scene. The man who throws the cup away is actually a member of his team, and Winter changes actors each time the scene is played out – sometimes his outward appearance is much like a typical German from Cologne or Bad Godesberg, sometimes he has a rather dark complexion and dark hair and looks like he could be Turkish or Syrian. A third man mingles among the other people waiting for trains and notes what happens – his job is to observe who reacts to this violation of the rules and how.

The sociologist, a Max Planck Research Group Leader at the Max Planck Institute for Research on Collective Goods in Bonn, has gone through a lot of tossed coffee cups. He was surprised to find that roughly one out of ten locals pounce on someone who breaks the rules when he looks like one of their kind, but about twice that number react when the person who litters looks like a foreigner. Conversely, only a very small number of people from southern Europe or the Middle East will let their displeasure be known to a blond and fair-skinned rule breaker, although they will be stricter with someone they perceive to also be a foreigner living in Germany.

GERMAN APPEARANCE PROTECTS FROM REPROACH

"I'm greatly interested in social norms," says Winter. "Under what circumstances do they change? When do they remain the same? That's what I'm investigating." The sociologist has many possible interpretations to offer for these highly varied reactions to a discarded coffee cup: the need to defend one's environs against foreigners; the fear of arguing in a language of which one might have only a limited command; the worry that an aberration in someone's own ethnic group could damage his or her own reputation; the concern that misbehavior from fellow countrymen could tarnish one's own reputation; a well-bred sense of respect; or a sense of responsibility that also extends to one's countrymen when abroad.

Although Winter's findings are easily confirmed and have been time and time again, every now and then the researcher still has doubts about his seemingly simple field study. "I feel there is a very sensitive subject that underlies all this," Winter explains, referring to the popular belief that ethnic diversity increases problems in social interaction. People don't look out for each other as much, their sense of responsibility dwindles, and norms and rules lose their binding character. Winter's empirical data tells a different tale: "It's generally Germans who escape unscathed. When foreigners commit a transgression, they're accosted more frequently, both by locals and by people of their own kind. If one aim is to punish as many violations of norms as possible – that is, to promote awareness in every-

Photo: picture alliance/dpa Themendienst

Protected by anonymity: People are often less restrained when expressing themselves on social media than they are in public. Sociologists are investigating what general conditions stimulate or curb hate and agitation on the internet.

Social control under the microscope: Fabian Winter (in the background) observes how bystanders in a train station react when a member of his team tosses an empty coffee cup to the ground. What's striking in his study is that perpetrators who appear to be foreign are reprimanded much more often.

day life – then society ought to be more heterogeneous than it already is."

That's the problematic nature of collective goods, whether climate, water and infrastructure, networks, free trade or domestic security – anyone can partake of them, but not everyone has to contribute. Street lights light the way also for people who don't pay taxes. Fabian Winter brings up the notion of non-excludability, and recommends a quick skim through any newspaper – the argument over climate protection and the plight of refugees, the continually mounting attacks of the likes of Donald Trump against the Western system of economy and values, Poland, Hungary, Brexit, Turkey – the list is endless. The summit of G20 industrial nations in Hamburg sparked a long-running debate on what kinds of objects, people and neighborhoods were legitimate targets of violence – parked cars, the police or the elegant district of Pöseldorf. Winter grew up in Hamburg and has some say in the matter. And in Berlin, neighbors hung small pieces of paper on trees and in hallways to make their thoughts on neighborhood life known – but given signs like "Hey! We're planning a home childbirth here. Could be a little loud" and "Go hang yourselves, you damn Swabians," no one could quite tell where sleepless despair ended and derisive joke began. Some people just enjoy causing trouble.

GLOBALIZATION CREATES MORE COLLECTIVE GOODS

The researcher sums it up thus: "Everybody benefits, but not everybody has to take part." For two years, he's taken great pleasure in getting together with his Institute colleagues every Monday. They spend the entire day in an old villa on the banks of the Rhine – economists, legal experts, psychologists, computer scientists and political scientists, sometimes with guests – and stake out a small symposium in which their areas of knowledge and expertise overlap and complement one another. Whoever has something to report on gives a talk. As already put forth by Elinor Ostrom, a political scientist who was awarded the Nobel Prize in Economics in 2009, knowledge, too, can be a collective good: it increases through sharing.

Of course, differences in academic opinions can also surface at these Monday meetings. How far does community extend? And how free is participation in it? From an economist's standpoint, as sociologist Winter explains, the Hartz IV unemployment and welfare benefits program, for instance, would count as a collective good: everyone contributes to the program by paying taxes, and it's available to practically anyone in case of emergency. He himself sees things a little differently and feels that anyone who takes advantage of Hartz IV will find themselves moved to the margins of society and stigmatized. "These are issues that tend to be addressed more in sociological debates."

Such contradictions are what attracts him: the fringes and points of transition where the terrain becomes uncertain and conflicts arise – and by no means just those between academic disciplines. While an agitated public at the G20 summit in Hamburg argued vociferously over such issues as how many emergency personnel it takes to protect parked cars from the black bloc, many more-significant problems got lost in the noise – once again. Why is it so difficult to unite industrial countries in the fight against CO_2 and global warming? How can a deal be drafted that will benefit everyone? What does it mean when public

Photo: Thomas Hartmann

hospitals, or even water companies or sections of highway, become privatized? "This creates not only wealth," concludes Fabian Winter "but increasingly also inequality."

Actual planning has long since caught up with what was, one or two generations ago, still a utopian idea. Exchanges are taking place at all levels – local, regional, national, continental and global – and in real-time. And even when goals still have to be defined retroactively, when setbacks, power struggles and corruption frequently complicate the process, the concepts are there, and often the means and the institutions are, too. Despite all the creaking and groaning, Europe is a reality. Even the declared opponents of globalization are proving themselves to be astonishingly cosmopolitan. They flocked to Hamburg in July for the G20 summit from as far away as Greece and Spain. They'll also journey to the next summit, more or less ready to resort to violence, in order to demonstrate their dissent. The range of collective goods is enormous and expanding, so what is causing the problems?

Fabian Winter is getting closer to an answer by following the trail of verifiable facts. His colleagues from the field of economics, at the time still in Jena, taught him, through their empirical studies and simulations, how to look at things from the viewpoint of economics. The researcher calls this experimental sociology, and he is also aware of earlier forerunners from social psychology. It's simply a fact: knowledge increases through sharing.

"I give you ten euros," says Winter, describing the basic form of a behavioral economics game in which he makes wealth and fairness the subject of negotiations, "under the condition that you give some of that amount to another player. If they accept your offer, you both get to keep the money; if they don't accept it, nobody gets anything."

Sense of community as a determining factor: Fabian Winter allowed test subjects sitting at a computer to choose how they would share ten euros with another person. Just a photo of their virtual opponent caused participants to act more generously.

How much of a loss will an opponent accept to ruin an unfair deal proposed by the donor? Offering just one euro would be risky, but who's going to be humble enough, generous enough or stupid enough to propose a straight 50-50 split with the money already in hand? Winter and others have varied this experiment in many ways – with people who were looking each other in the eye and with players who knew nothing about each other, with men

Photo: Thomas Hartmann

and women, students, children and senior citizens, with and without the possibility of telling the other person one's opinion afterwards. Of course the results confirmed again and again that community must first exist in order for the concept of collective goods to be recognized and seized upon as an opportunity. And if the money dispensed was still too moderate, all it took was a photo of one's opponent to make the person with the cash a little more cooperative in the unfair deal.

And then we have the World Wide Web, where anyone can confront anyone else and remain entirely unknown in the process – where every attack is met with applause and no one is ever accountable, where agitators, mobs and stalkers freely spread threats and slander, and where terrorists plan plots and finally give the signal to attack – a collective good that challenges the limits of comprehensibility and thus nullifies any kind of responsibility. "It's not exactly like that," Winter interjects, explaining that many forums and blogs establish conditions under which they grant access to users and punish cases in which these aren't followed. Facebook, Twitter, YouTube and Xing, a career portal, make sure their rules are followed and ban users who tolerate defamatory statements and slander, disseminate pornography and openly incite violence.

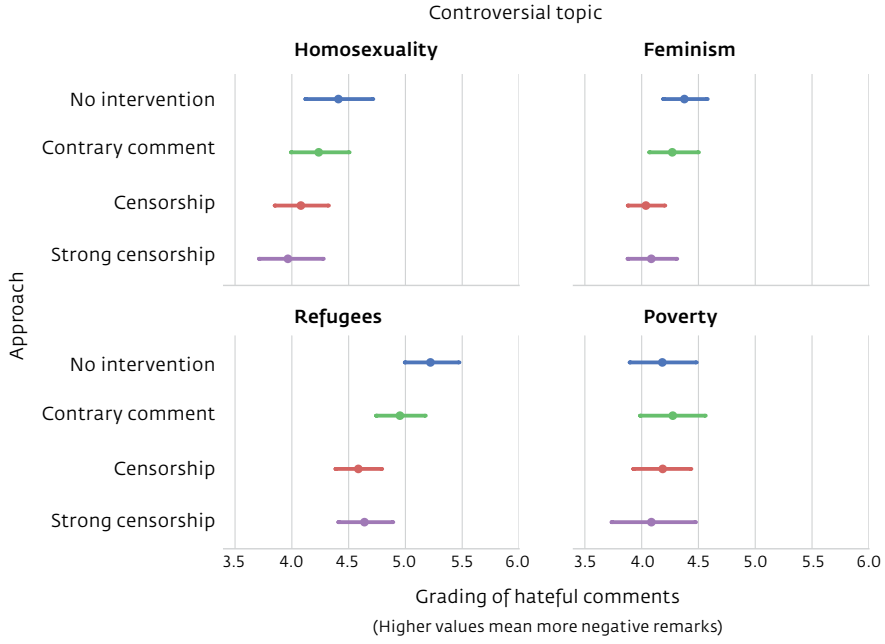
HATE AND AGITATION CAN BE CONTAINED

Winter used experimental sociology methods to examine the impact of control on the internet, which makes him a pioneer in the field of the sociological examination of hate and agitation on social media. How do members of a forum react to a photo showing a man carrying a child on his back and kissing another man? How do they react to images of violence, suffering refugees or political protest? And how do they react after someone else has already expressed their opinion on the same platform?

Winter sees social norms as a bundle of rules and conventions that are developed and consolidated through agreement with others. As a result, it's important for one to have experienced other people in at least similar situations, and to find such observations confirmed. But does that which appears to be self-evident in every marketplace apply in the anonymous, unprecedented expanse of the internet? The sociologist recalls a report by politician Renate Künast, who wanted to find out what kinds of living circumstances and personalities lie behind the abuse and threats she repeatedly found in her e-mail inbox. In the fall of 2016, the former chairperson of the Green party and parliamentary fraction set off to knock on the doors of some of these so-called trolls. She was surprised, she later confessed, at how well-to-do these trolls were and how reserved and even courteous many of the dreaded angry citizens were in their personal dealings.

"It's quite likely they didn't mean Ms. Künast personally at all," suspects Fabian Winter, "but just wanted to articulate some vague resentment of the distant elite and their own unmanageable and perhaps unfair conditions. It's also quite likely that they didn't have any inkling of how public their actions were."

But where did their anger come from, and what transformed these townhouse residents into vicious hellcats? In a series of independent experiments, the researcher varied the environment in which posts regarding internet debates are formulated, as well



Intervention helps: Unfiltered communication (blue) in internet debates often leads to hate and agitation rising further. Even contrary comments (green) can heat up the controversy. Deleting extreme comments (red), in contrast, helps bring the discussion to a more objective level. However, fundamental censorship (violet) can have the opposite effect.

Graphic: MPI for Research on Collective Goods

"Ugh!!!," "Unacceptable!!!!!," "Embarrassing!!!!!!"

"Just seeing her!"

"We'll soon be bringing politicians like you to trial!"

"As dumb as a stump!"

"Poor Germany!"

"Traitor!"

Equipped with a sense of humor: Green Party politician Renate Künast regularly receives abuse and threats on the internet. As a result, she posted ironic instructions for hateful comments on her Facebook profile, quoting abuse she commonly receives. Künast does, however, also defend herself through legal action.

as the way in which they're controlled. In an internet forum set up specifically for that purpose, he presented the participants in his series of studies with a wide range of comments on photos of gay couples or long lines of migrants. These comments were presented to a first group unfiltered, and then the replies to the comments were also included in the comments presented to a second group – as is common in chatrooms. He prompted participants to "Add your voice to the debate! Let us know what you think about this!" In a third list, statements that were especially hostile were deleted by members of the research team, and a fourth list included only decidedly positive comments on the controversial themes of the photographs. The researcher's goal was to find out how strongly a person's opinion is influenced by the climate of his or her social environment.

The results apparently surprised the researcher himself a little: deletion helps. Contrary comments seldom diminish the controversy, nor do they decrease the frequency of extremely hateful comments. In addition, fundamental censorship that allows only harmless words into further debates appears to have engendered angry reactance in some participants. However, removing – as a matter of precaution – comments that were openly racist, abusive or sexist helped keep the flow and content in the forum to more objective lines of discussion. Fabian Winter shrugs his shoulders and quotes an old internet community adage: "Don't feed the trolls. There are people out there who simply enjoy escalation. You shouldn't give them a free opening."

Renate Künast filed charges every time she found a hateful comment to be too personal and threatening. It didn't help much – most proceedings were dropped. It's like tilting at windmills. Fabian Winter realizes that the bypass methods of using complicated encryption processes or a server located in some remote tundra makes it extremely difficult to trace fake news and criminal agitation. With the act passed this summer on improving law enforcement in social networks (NetzDG for short), the German Minister of Justice seeks to have the responsibility for such issues be placed on network operators themselves. Facebook has already stepped up the self-control of its content. However, critics up to and including the United Nations fear for freedom of expression and information, and warn against totalitarian censorship.

Winter's data suggests that, in the collective good of the internet, it's necessary to implement regulations and curb momentum before it can build up. The corresponding forms and authorities must still be negotiated and established. The discussion moves on to the next round. ◂

TO THE POINT

- **Sociologists are examining how rules of social interaction can be maintained when social contacts increasingly take place in the virtual world.**
- **In personal face-to-face encounters, such as those on a railway platform, whether a violation of rules is admonished depends on one's assessment of the offending party.**
- **The more anonymous the environment, the more severely people who are normally polite and reserved will violate fundamental rules of propriety.**
- **It's very easy for hate and agitation to build up on the internet. A debate can often be made more objective only by deleting extreme comments.**

Photo: picture alliance/Geisler-Fotopress

Metal for the Military

The **Kaiser Wilhelm Institute for Iron Research** was founded in 1917, in the midst of the First World War. It was intended to become an innovation laboratory for the German steel industry but morphed into a knowledge center for military technology. Its history illustrates the risk associated with application-oriented basic research in times of economic and political crisis.

TEXT **SUSANNE KIEWITZ**

Spring 1917. The telegrams are stacking up on Fritz Wüst's desk in the Steel Institute at Aachen University. The chemist, who specializes in alloys, is very busy. Germany is at war, and military officials consider Wüst's advice on how to improve heavy guns, rifle barrels and grenades to be crucial to the war effort. Given the bitter realization that the armaments being supplied to German soldiers are inferior to those of the enemy, the euphoria of anticipated victory that had prevailed in August 1914 has disappeared. The armed hardware battles being fought on the western front require supplies to be replenished rapidly, but German steel is more difficult to work with than French. On top of this, shipyards and submarine manufacturers, too, are "hungry for iron." This unforeseen industrial dimension of the war demands every last ounce of effort from the German coal and steel industry.

Fritz Wüst has been working on a memorandum for the establishment of a special institute for metal, alloy and iron research and has the full support of Friedrich Schmidt-Ott at the Ministry of Education and Research in Berlin. The steel industry as well, represented by the powerful Association of German Steel Manufacturers (VDEh), has long been demanding an industry-wide research institution and applauds Wüst's proposals. The new institute is to explore the entire iron smelting production chain in order to gain new theoretical and practical knowledge about iron ore and about iron production, processing and alloying.

The VDEh had been aware of the poor quality for some time, but the war had now turned it into a massive problem. Since the industrial revolution, German engineers had been looking to England, the pioneer in the development of metallurgical methods. Spurred on by the enthusiasm to found new companies, the steel barons on the Rhine and Ruhr Rivers had been cranking up mass production since 1871, but they had neglected the quality. The modest amount of industrial research that was being done was a company secret and provided no impetus for the industry as a whole to innovate, and the universities could offer little help.

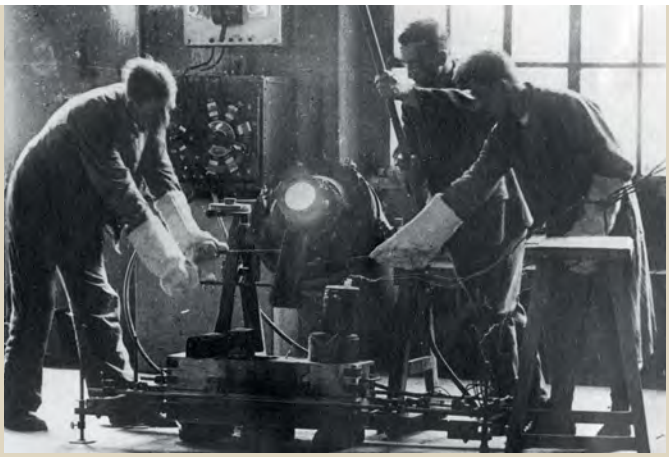
The chemical industry had shown that things could be done differently. Not only was its discipline included in university curricula, but it also had research laboratories that were strong on innovation. Moreover, since 1912 it had had an institution whose knowledge was available to the industry as a whole: the Kaiser Wilhelm Institute for Physical Chemistry and Electrochemistry in Berlin. The steel industry, whose main problem was the low iron content of local ores, wanted to have something similar. More knowledge about the chemical and physical properties of these ores would help to exploit them more efficiently and to develop new alloys that could be processed at lower cost and with less material.

Laying the foundation stone: Albert Vögler, steel industry representative and later President of the Kaiser Wilhelm Society, gives his talk at the celebrations in Düsseldorf on June 3, 1934.

However, the Ministry of Education also considered the closeness to industry to be a risk and involved the Kaiser Wilhelm Society (KWG) in the negotiations as a guarantor of scientific quality and autonomy. The Society had been founded in 1911 and tasked with promoting non-university research. It was agreed to align the statutes of the new institute with those of the KWG, funded by the VDEh via a special levy to be paid by the industry. The plan was successful, as the hefty profits that entrepreneurs such as Krupp, Thyssen and Stinnes had posted during the war meant that two pfennigs of the profit gained per ton of pig iron were deemed to be a good investment.

In June 1917 "at half-past four in the afternoon in Stahlhof, Düsseldorf" the Association of German Steel Manufacturers passed a resolution to establish the Kaiser Wilhelm Institute for Iron Research. The chairperson, Albert Vögler, emphasized that the institute was "devoted exclusively to peaceful purposes." This echoed the sentiments of those in the industry who were already thinking about the time after the war with great concern and were preparing to convert their production to a peacetime economy.

Photo: Archives of the Max Planck Society



Hard work: Staff in the metallurgy department working at the high-frequency furnace. The photo was taken around 1920.

The contentious question of the location was postponed, and would keep Fritz Wüst, who was appointed Director, busy during the upcoming months. Vögler had at least managed to convince the ministry to establish the new institute in the industrial region of Rhineland-Westphalia and not in the research mecca of Berlin-Dahlem. Subject to these conditions, work began on April 1, 1918 on the premises of Wüst's university institute in Aachen. In 1920, the growing number of staff relocated to an engineering works in Düsseldorf – the Rheinische Metallwaren- und Maschinenfabrik.

Although long-drawn out negotiations had finally resulted in the city of Düsseldorf promising to provide a site at a central location in "a worthy neighborhood," which meant that none of Wüst's wishes were left unfulfilled, construction was delayed until 1934. Since the institute was directly dependent on the income generated by the industry, the economic crises of the post-war years had a direct effect as well. The Treaty of Versailles had put the main blame for the war on Germany and demanded hefty reparations, a share of which this industry, too, had to pay. In 1923, the Weimar Republic experienced its first big economic disaster in the form of inflation. And when French troops occupied the Ruhr Valley, this paralyzed scientific work for several months. In protest against the occupying forces, the German workers boycotted factories and conveyor systems, including the Rheinische Metallwaren- und Maschinenfabrik, and with it, the institute as its tenant.

Berliner Tageblatt of May 13, 1934

» Three million marks for "pure research!" For the spacious building for the new institute of iron research in Düsseldorf, for desk work and work at the microscope. But those doing hands-on work in industry are well aware that this "long-term bill" will eventually pay for itself many times over. […]

It wasn't until 1925 that the situation temporarily improved. Research efforts expanded under Friedrich Körber, who had succeeded Wüst as Director in 1922. The five departments were dedicated to metallurgy, chemistry, physics, mechanical testing and metallography. As planned, the focus was on how the low-grade German iron ores could be enriched. These were the most important source of raw materials for the steel industry after the mines in Lorraine and their richer ores had been lost when the region reverted to France in 1919. From 1926 onward, the scientists – marked as most Germans were by the humiliating experience of national defeat – secretly worked for the German army as well.

The appointment of Adolf Hitler as Reich Chancellor in 1933 put an end to the first German democracy, whose weak powers couldn't defend it against a dominating nationalistic and conservative majority. The powerful industry in the Ruhr valley had also provided massive financial support for Hitler. Almost immediately after seizing power, the National Socialist state started a massive rearmament program – in part as a job creation scheme, but also to prepare for the next war.

Funds for the Kaiser Wilhelm Institute for Iron Research were now pouring in, enabling the institute to realize its long-delayed building plans. The foundation stone was laid in summer 1934, and the opening ceremony followed soon after, in November 1935. At both events, the institute management – most of whom were members of the NSDAP – and their staff demonstrated their firm National Socialist convictions. The press reports conveyed how impressed it was with the event, which was a highly pretentious ceremony typical of the National Socialists. The "ringing of cast steel bells" by three members of the Hitler Youth was followed by the ritual hammer blows, struck by Minister of Science and Research Bernhard Rust representing the National Socialist state, KWG President Max Planck representing science, and Albert Vögler representing the industry.

Although the speakers differed significantly in their political pitch, they all praised the collaboration between science and industry for the national good. The musical accompaniment for the celebration was provided by the city orchestra, which played two of Adolf Hitler's favorite pieces: the overtures to the operas *Rienzi* and *Die Meistersinger von Nürnberg*. The celebration ended with the Horst Wessel Song, the party hymn of the NSDAP, and the German national anthem as a political avowal, before the invited guests sat down to a hearty stew.

A different spirit emanated from the building itself, however, as the architects Heinrich Blecken and Paul Bonatz had designed the cube-like clinker brick building in the style of the Bauhaus, which had already been closed down at this time as a result of pressure from the National Socialists. The designers chose steel for the offices as well – tubular steel furniture that avant-garde artists Marcel Breuer and Ludwig Mies van der Rohe had designed in the mid-1920s – thus demonstrating how versatile, flexible and modern steel was as a material.

Although the scientists continued to work on various aspects of metallurgical materials research at the institute, whose outstanding equipment made it one of the most modern of its kind anywhere in the world, most of what they did was for military purposes. As part of the war economy, the institute was placed under the command of the German Army Ordnance Office in 1940 and tasked with improving weapons, rifle barrels and tank tracks. It had already been advising the Ministry of Aviation since 1933.

After the building was hit by a bomb, research gradually relocated to the academy of mining (Bergakademie) in Clausthal starting in 1943. After the end of the war, the Americans imposed a work ban; it was lifted in 1947 and the reconstruction began – starting in 1948 under the umbrella of the newly founded Max Planck Society. This ultimately ensured the long-term research autonomy and political independence that had been deemed to be essential when it was founded.

Photo: Archives of the Max Planck Society

Dr. Jekyll and Mr. Hyde

Hans Clevers delivers the Harnack Lecture on the pros and cons of stem cells

In late October, Dutch immunologist and molecular geneticist Hans Clevers delivered this year's Harnack Lecture, pithily titled "Dr. Jekyll and Mr. Hyde." He spoke before 180 guests in the Goethe Auditorium on the subject of stem cells.

After the initial euphoria, the hype surrounding stem cell research has quieted somewhat in recent years. Now, not least since this research began to focus increasingly on stem cells that are found in various organs throughout a person's life, the enormous potential of adult stem cells is gradually returning to the forefront of scientific consciousness.

Clevers has significantly advanced this development. An expert in adult stem cells, he identified a gene that is active in these cells, and this enabled him to demonstrate the presence of stem cells in organs such as the intestines, lungs, liver and pancreas. Clevers even succeeded in cultivating these stem cells in laboratories to create miniature versions of human organs. These so-called organoids now make it easier for researchers to examine biological processes; in the future, they could even render organ transplants unnecessary.

However, the role these cells play in forming and regenerating organs is only one side of the coin: cells that retain their ability to divide throughout an organism's life can easily get out of control and become cancer cells. Clevers was able to show that some processes in stem cells and cancer cells are identical. He titled his Harnack Lecture, to which renowned scientists have been invited each year since the reopening of the Max Planck Society's conference center in Berlin-Dahlem, "Dr. Jekyll and Mr. Hyde" to reflect the ambivalent nature of these cells.

Hans Clevers was born in Eindhoven and studied at Utrecht University, to which he returned as a professor following a research residency at Harvard University in the early 1990s. For two years now, he has also served as Director of Research at the Princess Máxima Center for Pediatric Oncology.

A video of the lecture:
https://www.youtube.com/watch?v=TJ4TRD2BWXg

Expert in adult stem cell research: Hans Clevers delivering his lecture in a packed Goethe Hall in the Harnack House.

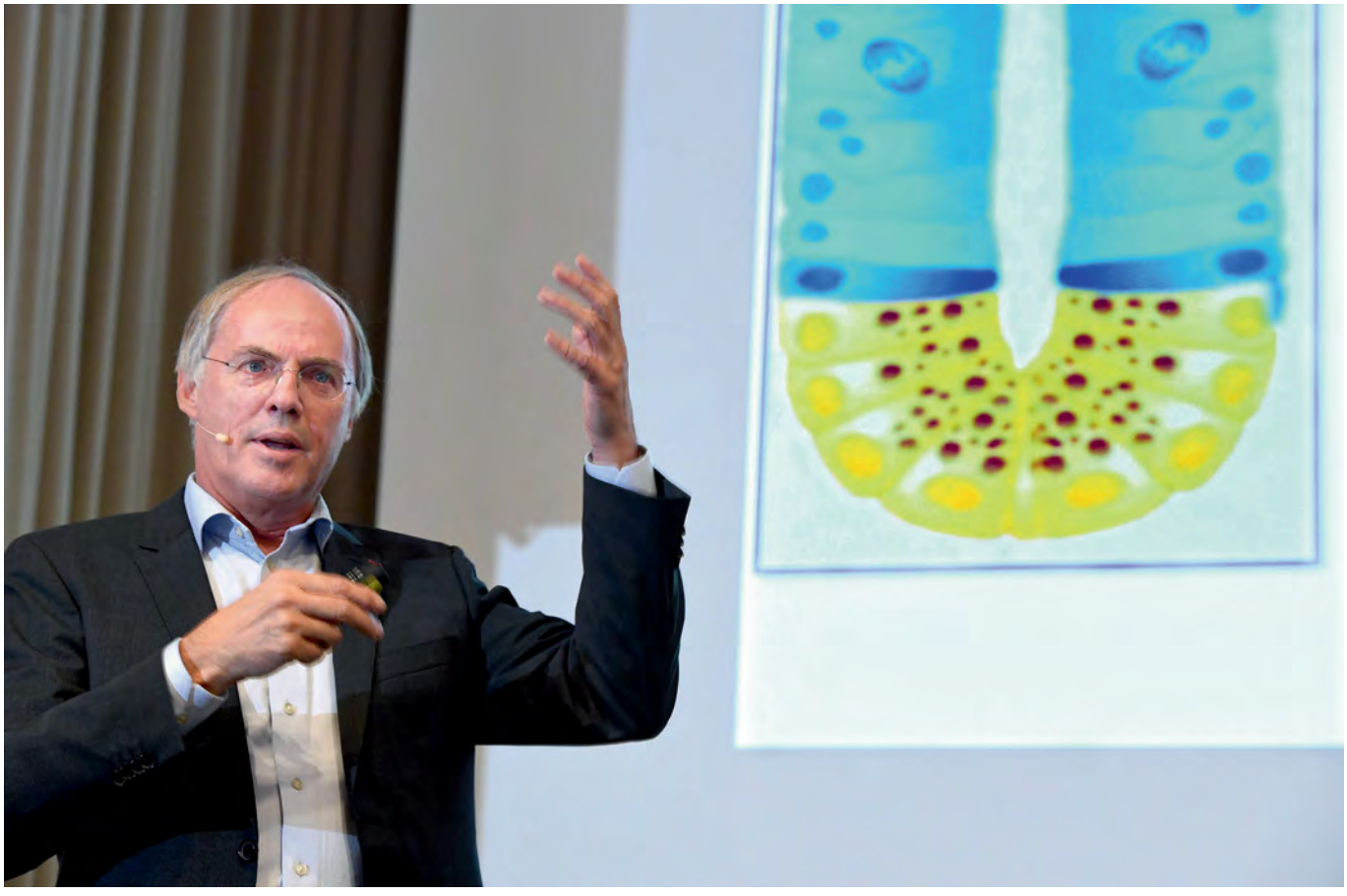


Photo: David Ausserhofer / MPG

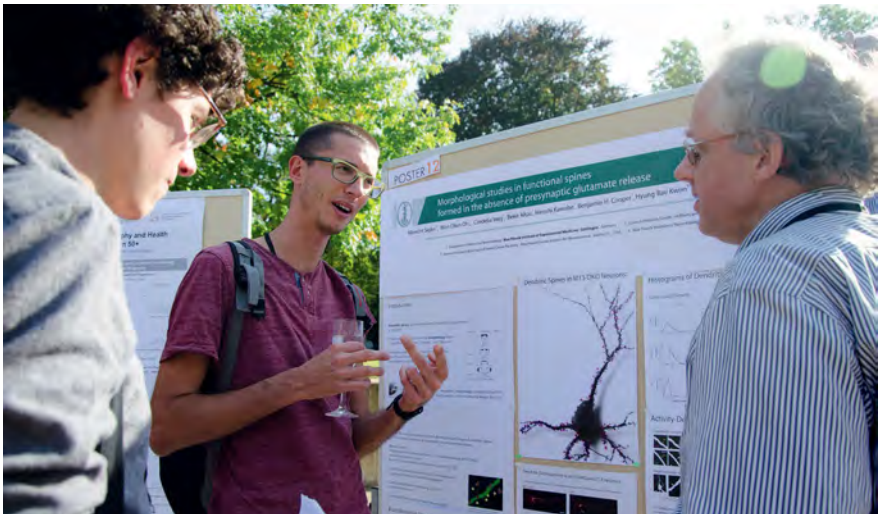
Communication, Collaboration, Inspiration

Varied program addresses trends in research and provides career advice

The "Visions in Science" conference and the "Max Planck Career Fair" – both aimed at bringing together inquisitive, forward-thinking minds – were held simultaneously for the third time. Once again, this year's conference in late September was well attended, with 80 participants each day enjoying the diverse program that ranged from inspiring talks by renowned scientists to a science slam contest and a poster session.

On the first day of the conference, the Harnack House provided the perfect venue for the Career Fair's 13 exhibitors and 215 visitors to hold individual discussions and network with new contacts. Facilitating the exchange between speakers and junior scientists was a key priority throughout the three-day conference, which is organized each year by members of Max Planck PhDnet.

"The panel discussions in particular were a great success," said Beniamino Abis, doctoral student at the Max Planck Institute for Meteorology and head of the organizational team. "Both our speakers and the audience contributed to this with a lot of questions and comments. Afterwards, the presenters and participants mingled during dinner and into the evening, providing the opportunity for discussion and conversation in smaller groups."



Specialist topics were also discussed in the poster session at the "Visions in Science" conference at Harnack House.

Photos: Beniamino Apis (2)

Application Round for Dioscuri Centers

The first call for applications for the establishment of up to three Centers of Scientific Excellence in Poland is underway

In connection with the Max Planck Society's new program for boosting cutting-edge research in Central and Eastern Europe, the first call for applications for Poland is now open. Until February 12, 2018, scientists may apply as Principal Investigator (PI) for one of up to three Dioscuri Centers of Scientific Excellence to be established at Polish universities or research centers with appropriate infrastructure. More than 50 institutions have already signaled their interest. The PIs and their research groups will each receive 300,000 euros over a five-year period. The Dioscuri program aims to strengthen and expand scientific excellence in Central and Eastern Europe and is now entering its first implementation phase in Poland. The financing is shared equally between the German Federal Ministry of Education and Research and the Polish government.

Moved by Nobel Prize for Gravitational Waves

Max Planck researchers congratulate and celebrate with their American colleagues

Rainer Weiss, Kip Thorne and Barry Barish were awarded this year's Nobel Prize for Physics for their groundbreaking evidence of Einstein's "ripples in spacetime." Max Planck researchers celebrated with their US colleagues, especially since they played a role in the discovery that is transforming astronomy.

There was excitement in the air at the Max Planck Institute for Gravitational Physics in Hannover and Potsdam on October 3. Around 120 guests in Hannover, including the Lower Saxony Minister for Science, Gabriele Heinen-Kljajić, and an additional 50 in Potsdam followed the livestream from Stockholm. Though the Nobel Prize was not awarded to Karsten Danzmann, as one local newspaper prematurely announced online, the mood among the Max Planck researchers remained positive.

"We wholeheartedly congratulate our colleagues and are delighted by this award for three pioneers of gravitational wave research. They never lost sight of their objective and have inspired generations of young scientists," said Max Planck Director Alessandra Buonanno and her colleagues Karsten Danzmann and Bruce Allen. They added: "We are proud to be part of an international collaboration that discovered the first gravitational wave some two years ago."

Expert in demand: Alessandra Buonanno gave TV interviews at the Max Planck Institute for Gravitational Physics in Potsdam following the awards ceremony.

Karsten Danzmann's team at the GEO600 facility near Hannover actually developed almost all of the technologies deployed in the major detectors, such as LIGO and Virgo. The Institute in Hannover is also home to the Atlas Computing Cluster, where researchers in Bruce Allen's department work on programs that make it possible to search for and analyze the gravitational wave signals in the first place, and in Potsdam, Alessandra Buonanno and her staff created the models that would help to better understand and simulate the waves. This alone shows how the success of this collaboration rests on the shoulders of more than 1,000 participating researchers.

"Adventures in Archaeological Science"

A colouring book for archaeologists in training

The Max Planck Institute for the Science of Human History has recently completed a special outreach venture. Primarily directed at children, it is bound to appeal to archaeologists of any age: the *Adventures in Archaeological Science* coloring book. Produced for the 2017 "Long Night of Science", the booklet is the final project of a scientific illustration training workshop taught by Max Planck researchers Christina Warinner and Jessica Hendy in the summer of 2017.

Each page is hand-drawn by a scientist at the Max Planck Institute for the Science of Human History and features real research and archaeological projects. It also provides brief explanations not only on the work of archaeologists in the field and the lab, but also on topics such as human origins, ancient diets and ancestral microbiomes. The book is edited by Christina Warinner and Jessica Hendy, with special contributions by: Zandra Fagernäs, Jessica Hendy, Allison Mann, Åshild Vågane, Ke Wang, and Christina Warinner, and is currently available in English and German.

http://christinawarinner.com/2017/11/25/adventures-in-archaeological-science-coloring-book-now-available/

Photo: M. Mohring / Milde Marketing

Research Establishments

- Institute / research center
- Sub-institute / external branch
- Other research establishments
- Associated research organizations

The Netherlands
- Nijmegen

Italy
- Rome
- Florence

USA
- Jupiter, Florida

Brazil
- Manaus

Luxembourg
- Luxembourg

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