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Faszination **Forschung**

TUM Research Highlights

A New Window on the Universe

Machine Elements: Hugging the Road on Bends
Dermatology and Allergology: Tricking the Immune System
Organic Chemistry: Overcoming Antibiotic Resistance

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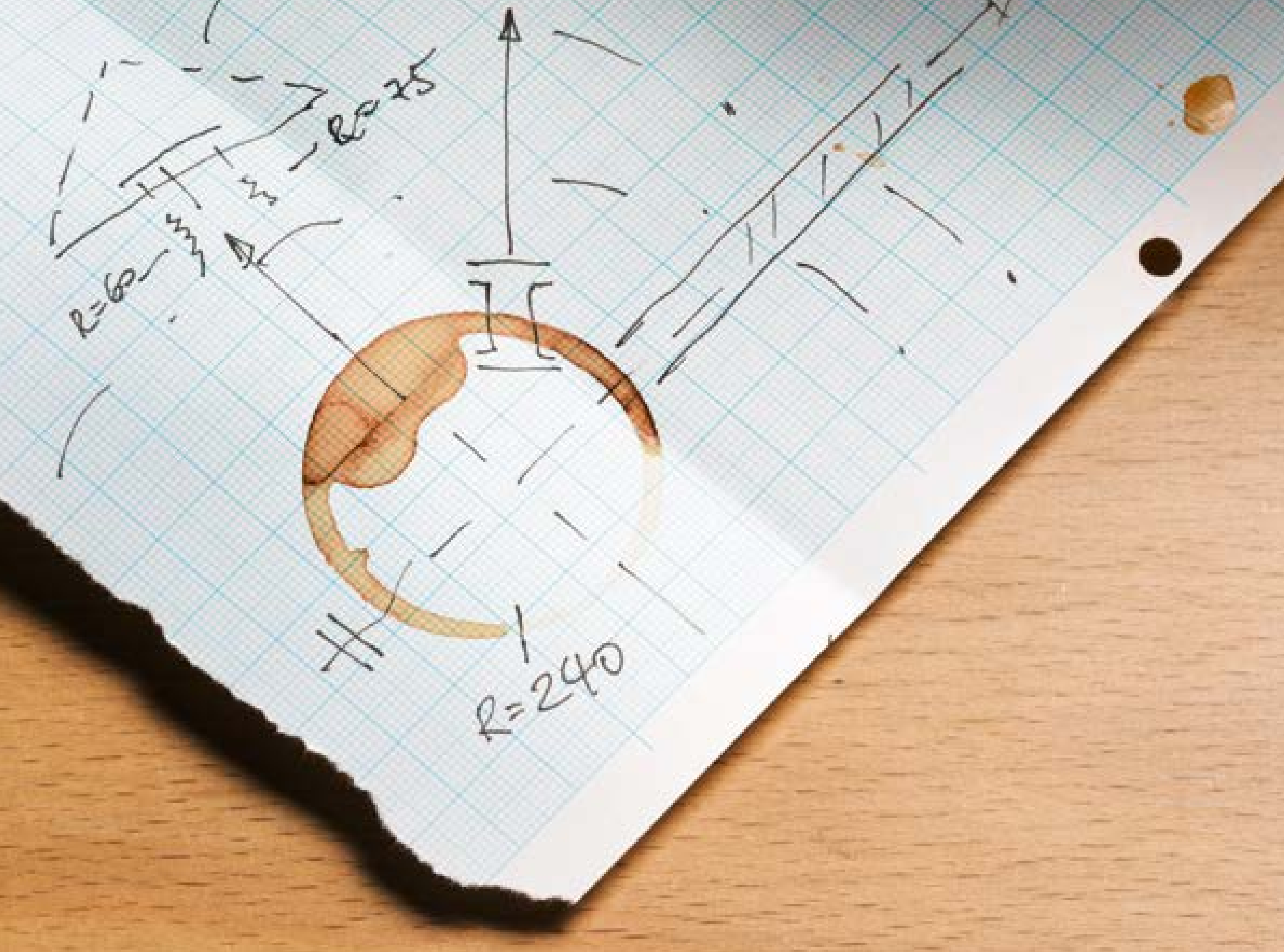
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Dear TUM friends and associates,

Here at TUM, our scientists are as varied and individual as the topics they research. Some of them, such as the physicians and chemists we introduce in this edition, work on topics that touch people's lives on a personal level. Our engineers, on the other hand, aim to advance society by improving technical infrastructure. And our astrophysicists explore fundamental questions about our existence in their search for neutrinos from distant regions of space. Depth and diversity are the hallmarks of our research efforts.

Deep below the Gran Sasso mountain in Italy lies the Borexino detector that has enabled Lothar Oberauer and Stefan Schönert to measure neutrinos generated by the fusion of hydrogen nuclei at the Sun's core. These are the first direct signals of the most fundamental reaction by which the Sun creates energy, thus sustaining life on Earth.
Meanwhile, Elisa Resconi has set her sights far beyond our solar system. Her team is involved in the IceCube Neutrino Observatory, embedded kilometers into the Antarctic ice at the South Pole, in an effort to detect highly energetic neutrinos from the depths of outer space. These may have arisen from cosmic catastrophes, such as the birth of a supernova, or from the vicinity of a black hole, and thus could offer a way to discover more about such phenomena.

Tilo Biedermann's research efforts literally "get under your skin." The allergist and immunologist is working to establish the immune system processes responsible for the exacerbation of atopic dermatitis when the skin is colonized by Staphylococcus aureus bacteria. His investigations not only pave the way for effective treatment options, they also reveal completely new findings about the mechanisms of our immune system.
At the same time, Stephan Sieber is exploring another, highly topical side of Staphylococcus aureus. These bacteria are becoming increasingly resistant to conventional antibiotics, posing a major challenge for our healthcare system. Searching nature's toolbox, the chemist has come up with substances to help render the bacteria harmless without triggering fresh resistance responses.

Fifty years after Gordon E. Moore first made his projections about the development of computer chips, his law is gradually reaching its limits. Now, Markus Becherer and his team of electrical engineers have come up with a radical new approach to further increase the density of switching elements on chips – circuits based on three-dimensional nanomagnetic logic.
As part of the Visio.M project, TUM is working with an industrial consortium to develop an economically attractive electric car with a good driving range. To this end, Karsten Stahl has devised a lightweight and compact torque vectoring drive system that opens up completely new opportunities for auto manufacturers when it comes to handling dynamics, stability and regenerative braking in electric vehicles.

We hope you enjoy this edition as it takes you on a voyage of discovery to the South Pole, an expedition deep below the Italian mountains, and a tour of our clinics, labs and workshops in Munich.

Prof. Wolfgang A. Herrmann

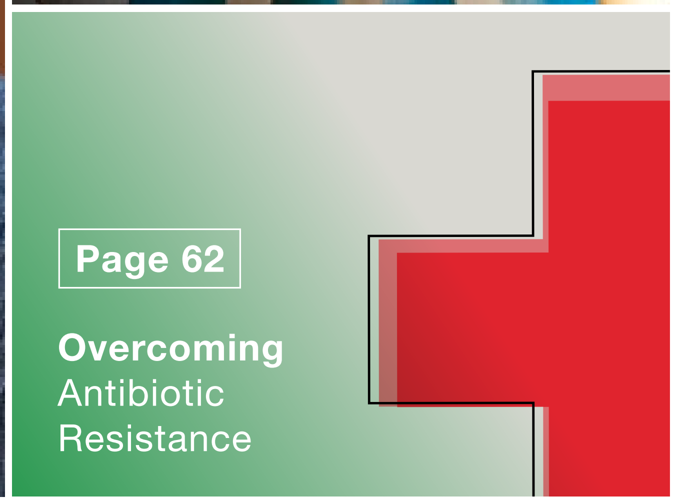
Picture credit: Eckert

Cover Story

"Trillions of neutrinos are passing through your body alone while you are reading this sentence."
Elisa Resconi

Research and Technology

Picture credits / illustrations: ediundsepp, Joss, Bauer, ediundsepp



In Every Issue

Hugging the Road **on Bends**

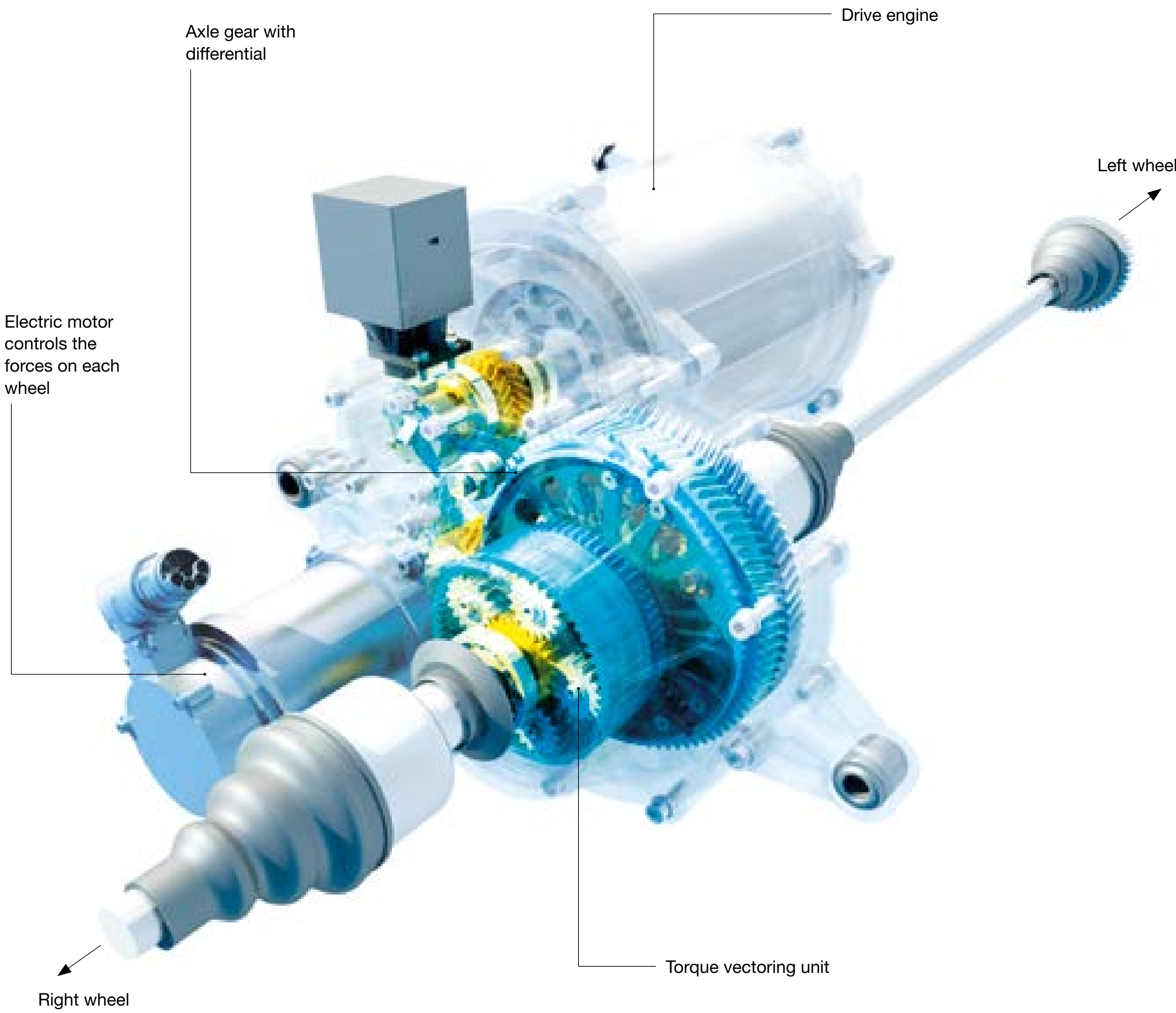
A new drive system developed by researchers from TUM is set to make electric vehicles a lot more attractive to drivers. The compact and lightweight drivetrain not only optimizes brake energy regeneration, it also increases stability on bends and makes for a more enjoyable ride.

Links
www.fzg.mw.tum.de www.visiom-automobile.de

Graphics: ediundsepp

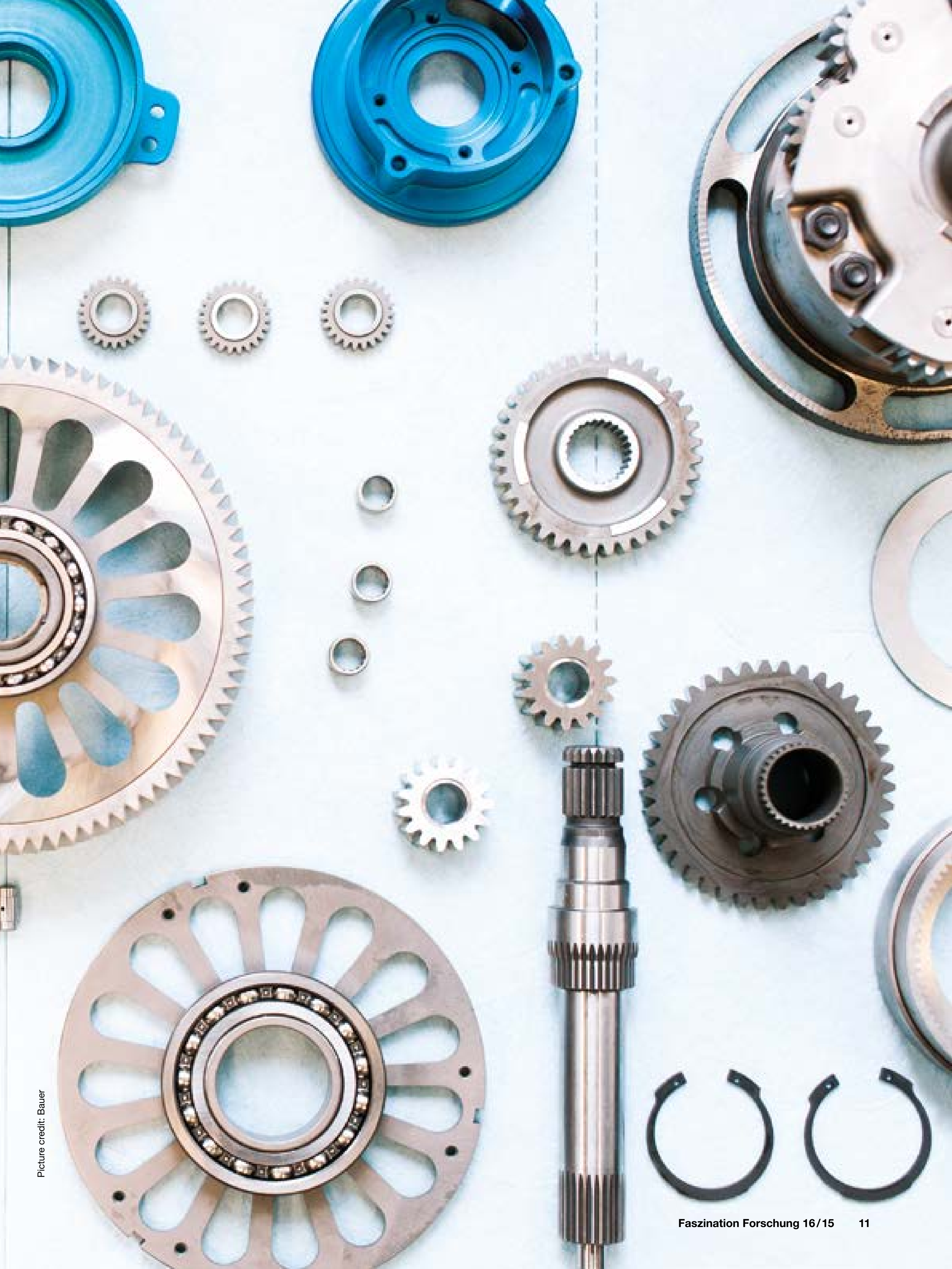
Picture credit: ediundsepp (source: TUM)

Visio.M is the result of a collaborative research effort to develop an electric vehicle that provides safety and comfort combined with a reasonable driving range at an affordable price. The car has a range of around 160 kilometers and space for two people and luggage. With only 15 kilowatts of engine power, the car achieves a top speed of 120 km/h (75 mph). Without its 85 kilogram battery Visio.M. weighs only 450 kilograms. An active torque vectoring differential distributes the force optimally between the two back wheels. This improves stability in curves and helps recover more brake energy.



The Visio.M project

Visio.M is a joint research project funded by the Federal Ministry of Education and Research and involving 14 TUM chairs, the Federal Highway Research Institute, TÜV and a number of partners from industry. The two-and-a-half-year project was completed last year. Its objective was to develop an efficient ultra-compact electric car for two occupants. The brief was that it should not only be safe and lightweight, but also prove that an electric car appealing to the mass market can achieve a lower total cost of ownership than comparable gasoline-powered cars. In October 2014, the Visio.M car was unveiled to the public. The total budget of the project was EUR 10.1 million.


Picture credit: Bauer

“With this small and lightweight torque vectoring drive, we are offering auto manufacturers a powerful component to integrate in electric car designs of the future.”

Karsten Stahl

Ab durch die Kurve

Dank eines neuen Autogetriebes mit Kunststoffgehäuse, das Forscher der TUM entwickelt haben, könnten Elektrofahrzeuge künftig deutlich attraktiver werden. Das kompakte und leichte Getriebe gewinnt nicht nur Bremsenergie optimal zurück, es erhöht auch die Stabilität bei Kurvenfahrten.

Elektrofahrzeuge sind leise und umweltfreundlich, sofern man sie mit regenerativ erzeugtem Strom betankt. Dennoch gibt es hierzulande erst rund 21.000 Stück, da diese Autos meist zu teuer sind und eine geringe Reichweite haben. In dem BMBF-Verbundprojekt Visio.M wurde deshalb in den vergangenen 2,5 Jahren ein Elektrokleinstfahrzeug entwickelt, das leicht und kostengünstig zu produzieren ist und eine attraktive Reichweite hat. An der Entwicklung des Autos war auch die Forschungsstelle für Zahnräder und Getriebebau (FZG) der TUM beteiligt, die für das Visio.M-Fahrzeug ein spezielles Getriebe gebaut hat. Es ist leicht, kompakt und trägt dazu bei, die Energie auch bei Kurvenfahrten optimal zurückzugewinnen – und so insgesamt die Reichweite des Autos zu erhöhen. Wie andere Elektro- oder Hybridfahrzeuge auch gewinnt der Visio.M Energie zurück, wenn er bremst (Rekuperation). Der Motor schaltet dann auf Generatorbetrieb. Die Räder drehen dabei den Motor wie einen Dynamo und werden so abgebremst.

Allerdings ist die Leistungsfähigkeit herkömmlicher Rekuperationssysteme bei Kurvenfahrten begrenzt. Bei normalen Autos wird der äußere Reifen höher belastet, weil das Fahrzeug stärker nach außen drückt. Dieser Reifen kann eine hohe Bremskraft auf die Straße bringen. Der innere Reifen jedoch wird entlastet und kann damit weniger zum Bremsen beitragen. Das an der TUM entwickelte Getriebe hingegen regelt die Kraft, das sogenannte Drehmoment, mit der ein Rad angetrieben oder bei der Rekuperation abgebremst wird, für jedes Antriebsrad individuell. Damit lässt sich bei Kurvenfahrten die Bremskraft eines jeden Rades optimal dosieren.

Zwar gibt es heute bereits derartige Getriebetypen – Experten sprechen von Torque-Vectoring-Getrieben – doch sind diese bisher viel zu groß, zu schwer und zu teuer für Elektroautos. Sie werden allenfalls in einigen wenigen edlen Sportwagen verbaut. Die Leistung der TUM Ingenieure besteht darin, ein besonders kompaktes, leichtes und stabiles Torque-Vectoring-Getriebe mit Kunststoffgehäuse erschaffen zu haben, mit dem die Torque-Vectoring-Technik erstmals auch in Elektroautos eingesetzt werden kann. *Tim Schröder*

Electric vehicles (EV) have a lot going for them. They move silently through busy city streets and don’t emit noxious fumes. There are even some good-looking models on the market now – a far cry from the no-go designs that first appeared ten or twenty years ago. The German federal government is encouraging commercialization of electric cars with measures such as tax incentives. Nevertheless, in 2014, only 21,000 electrically powered vehicles were being driven on German roads. A drop in the ocean compared to the number of conventional cars, which stands at 43 million. It is doubtful that the target of one million electric vehicles in Germany by the year 2020 will be achieved. The high price tag is one factor; another drawback is the limited range of vehicles powered by a battery.

Many engineers around the world are working on a solution to the EV range challenge. But it does not come down to just one technical detail. Rather, the developers will have to optimize the entire car. In November last year, the Visio.M consortium presented a possible answer. A team of developers from industry and various chairs of TUM produced a completely new electric vehicle model. Thanks to its cutting-edge efficiency, its estimated total cost of ownership, including initial investment and operating costs, will be lower than that of a comparable combustion engine car. Decisive for the exceptional energy efficiency of the Visio.M is its light weight. At the same time, the car fulfills all significant requirements of a normal mass market car, from passenger safety to infotainment and navigation assistance to climatization. With its smart design, the Visio.M attracted plenty of media attention when it was unveiled to the public last fall. ▷

Prof. Karsten Stahl heads TUM's Institute of Machine Elements, also called the “Gear Research Centre (FZG)”, today’s leading international research institute for gears and transmissions.

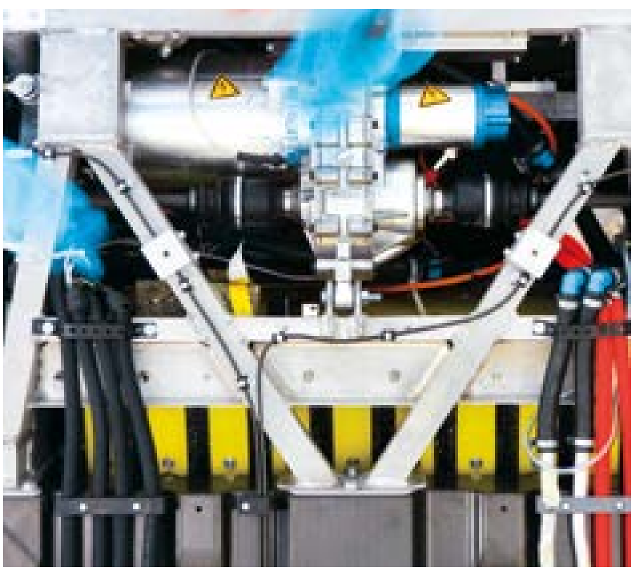
Picture credit: Bauer

“A torque vectoring drive not only offers better recuperation. Car makers can also use it to improve driving stability.” *Philipp Gwinner*

Picture credit: Bauer

TUM engineer Philipp Gwinner and his colleagues first realized a torque vectoring drive that fits into a compact aluminum housing. Then they went one step further and used lightweight glass fiber reinforced plastic to make the housing. Only the shaft bearings are mounted inside an aluminum structure, which is extrusion-coated with the liquid plastic.

Picture credits: Bauer



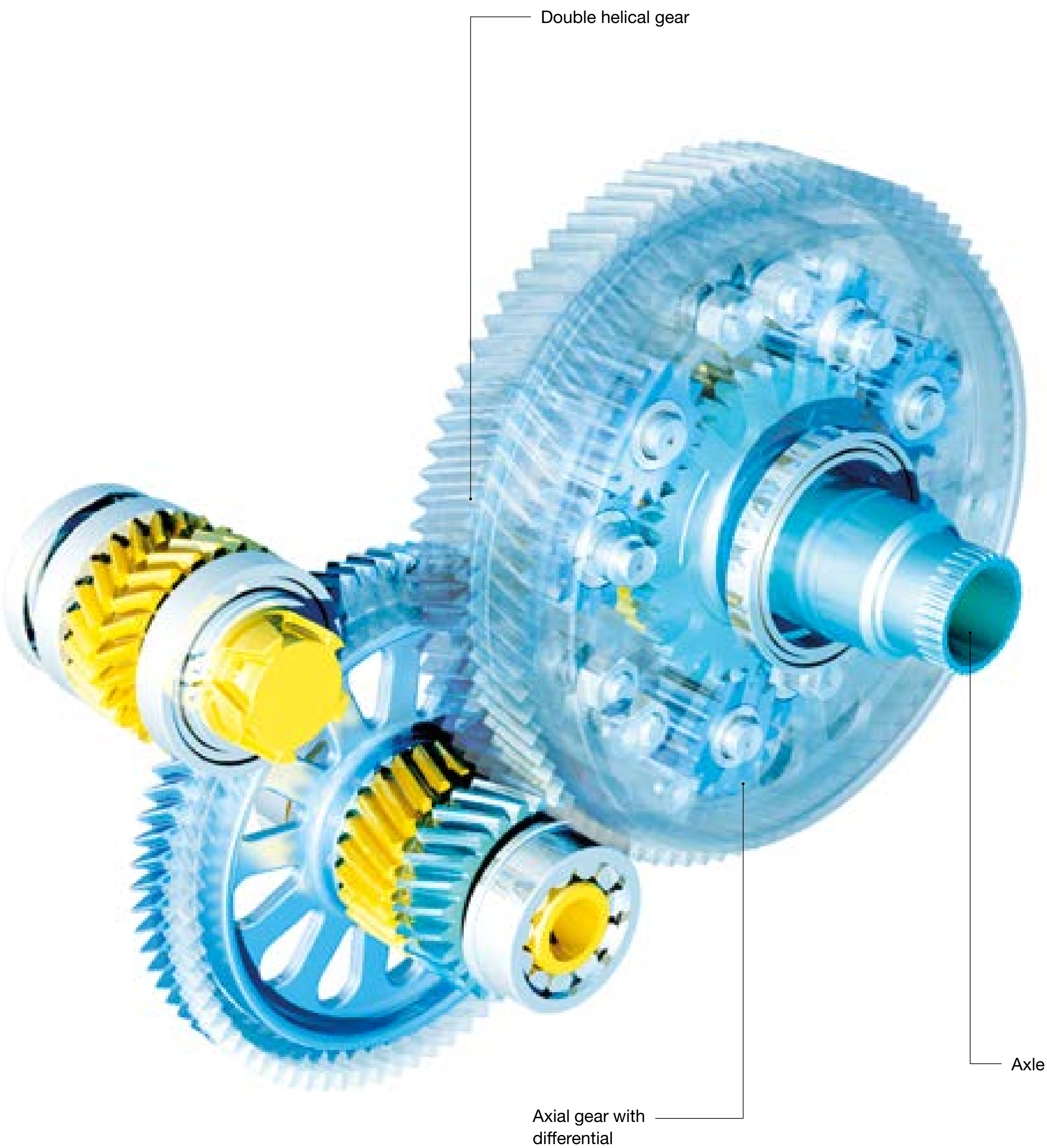
In the workshop of TUM's Institute of Automotive Technology: The torque vectoring drive installed in the Visio.M electric vehicle (left page). Philipp Gwinner connects one of the sensors (top) to the drive.

Regenerating brake energy

As is customary in electric or hybrid vehicles, the Visio.M recuperates energy when it brakes. When the driver brakes, the motor switches to generator mode. The wheels turn the motor like a dynamo and thus apply braking power. The efficiency of regenerative braking could be increased even further if the braking energy could also be recuperated when driving around bends. However, conventional regeneration systems are not very effective when it comes to handling curves. In standard cars, the left and right wheels of a driving axle exert different pressure on the road surface when going around a corner. There is more load on the outer wheel because the vehicle is veering more to the outside. This wheel can exert a strong braking force on the road. At the same time, there is less pressure on the inner wheel, so it is less effective in braking. Brake energy regeneration has basically not been very effective on bends up to now. In theory, this problem could already have been solved with a torque vectoring drive. Torque vectoring varies the power – or the torque – delivered to each wheel. The same applies to the braking power recuperated from each wheel. This means that just the right amount of braking power gets to each wheel during cornering. Up to now, however, torque vectoring systems were too heavy, too large and indeed too expensive to install in mass-produced electric vehicles. They are currently to be found in only a handful of models, mostly high-end sports cars.

But this is set to change. Researchers at TUM's Gear Research Centre (FZG) have developed a torque vectoring drive system that is sufficiently lightweight and compact for future EVs. Torque vectoring is a particular form of differential gear. A "differential" is located at the center of almost every vehicle's driving axle and is responsible for moving the latter together with the wheels. An ordinary differential gear drives the entire axle and therefore uniformly drives the left and right wheel. Torque vectoring gearboxes do this differently. Depending on the type of bend, more torque can be distributed to the left or right wheel. In conventionally driven axles, that would not be possible. With the new torque vectoring drive, TUM engineer Philipp Gwinner and his colleagues have realized their aim of a compact design. The gearwheels inside the gearbox have been designed and arranged with a view to fitting as much into as small a space as possible. They are closely linked to a small electric motor. This selectively increases the rotation of the left or right axle end, delivers more torque to the left or right, or in the case of cornering, applies the required braking power to individual wheels.

Some experts have long favored wheel hub motors as the future EV drive system of choice. With this concept, each wheel has its own motor that turns or brakes each wheel individually. The effect is therefore similar to that of a torque vectoring drive. With torque vectoring, however, you can get this effect with a single central drive, which is more economical and safer than individual wheel hub motors. A torque vectoring drive offers automakers a range of potential applications – not just better recuperation. "They could also use the drive to improve driving stability," maintains Philipp Gwinner. "If a car becomes unstable when cornering, the individual wheels will be decelerated so that the vehicle restabilizes." If the torque of the wheel at the outside of the bend is increased, ▷



Picture credits: Bauer; left: ediundsepp (source: TUM)

In order to realize a plastic housing for the torque vectoring unit, the TUM engineers had to find a way to reduce the forces of the gear system. They overcame this challenge by designing a double helical gear, in which the axial forces cancel each other out.

it pushes the car into the bend, so to speak. The new drive can also compensate for crosswinds or slippage on wet leaves and ice. “We have designed the torque vectoring drive to be economical, small and light enough for EVs like the Visio.M,” says Prof. Karsten Stahl, Director of the FZG. It took several development stages to achieve the end result. The first task was to arrange and design the gearwheels so that the gear system could fit inside a compact aluminum housing. Stahl and Gwinner then went one step further. They used lightweight glass fiber reinforced plastic to make the housing. Only the shaft bearings are mounted inside an aluminum structure, which is extrusion-coated with the liquid plastic. “With this small and lightweight torque vectoring drive, we are offering auto manufacturers a powerful component to integrate in electric car designs of the future,” proclaims Stahl.

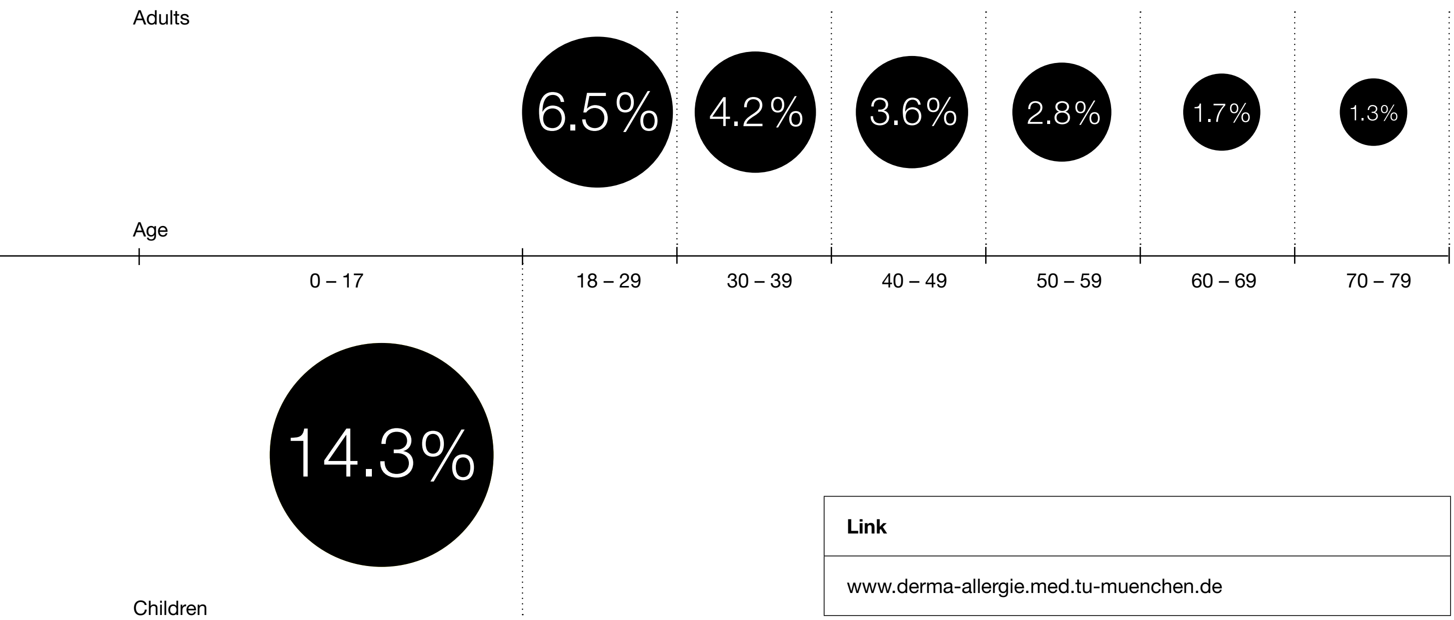
A lightweight gearbox housing made of plastic

Normally, though, plastic housings are scarcely able to withstand the strong forces of a gear system. This was another problem that Gwinner had to overcome. As a rule, the forces of the gearwheels under high load result in severe deformation of the plastic. This happens because

the gear teeth are usually arranged at an angle to reduce noise and increase the load-carrying capacity. A normal housing made of plastic is not able to withstand the forces that occur in helical gearing. That is why Philipp Gwinner uses a “double helical gear,” in which the axial forces of each half cancel each other out. This enables the use of plastic material for the automotive gearbox housing.

With a number of benefits incorporated into the new gear design, Stahl is optimistic: “We cannot wait to see how the automobile industry will respond to and eventually use what we have developed.” In any case, the team has proved that it is possible to design a small, lightweight and economical torque vectoring drive. Philipp Gwinner adds: “I firmly believe that this development has huge potential.” The drive is one of the features that make the Visio.M so efficient. The car requires just around a quarter of the energy equivalent consumed by a conventional small car. “It is of course possible to drive a car axle without torque vectoring and to do without the highly complex differential we have used,” admits Gwinner. But that would mean settling for much less functionality, less energy efficiency and less driving pleasure on bends. Above all, this innovative development will make electric vehicles of the future a much more attractive proposition for drivers. *Tim Schröder*

Picture credit: iStockphoto.com, aprott; graphics: ediundsepp (source: KiGGS and DGES studies, Germany, Bundesgesundheitsblatt 2014/2013)

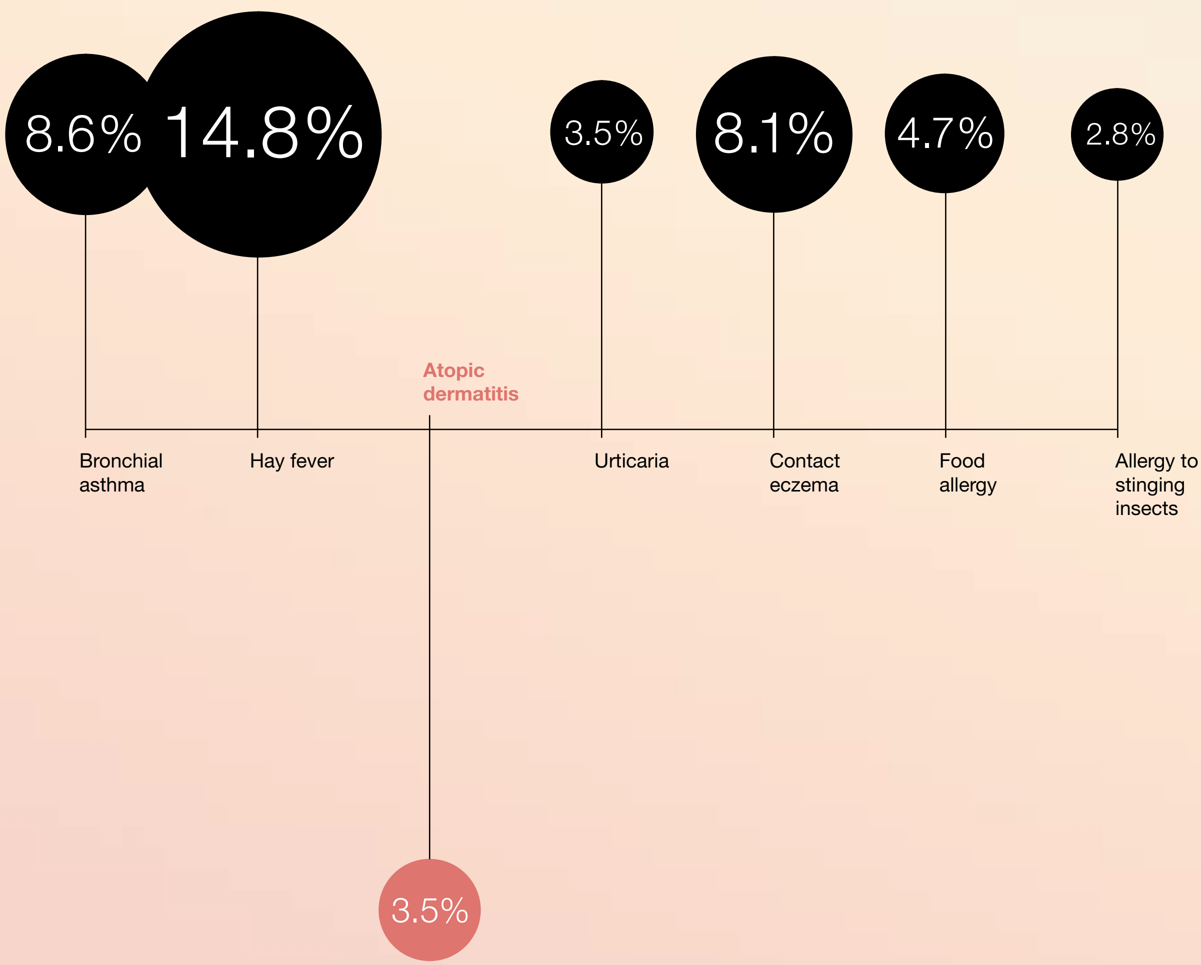


Link

www.derma-allergie.med.tu-muenchen.de

Tricking the Immune System

Particularly severe cases of atopic dermatitis, a common inflammatory skin condition, are accompanied by high levels of Staphylococcus aureus bacteria in the affected areas. Allergist and immunologist Prof. Tilo Biedermann has long been grappling with the way these infections aggravate this condition. He recently published some surprising findings in the scientific journal "Immunity." In this interview, Biedermann explains the trick bacteria use to sidestep the immune system in the presence of atopic dermatitis and discusses what is really new about these observations and how they impact his research.



Allergies on the rise: About 30 percent of all adults in Germany suffer or have suffered from an allergic disease. Atopic dermatitis and urticaria rank fifth after hay fever, bronchial asthma, contact eczema and food allergy. (source: DGES study conducted by Robert Koch Institut; Bundesgesundheitsblatt 2013)

Graphics: ediundsepp (source: KiGGS and DGES studies, Germany, Bundesgesundheitsblatt 2014/2013)
Picture credit: Jooss

Before taking over as Chair of Dermatology and Allergology at TUM's Klinikum rechts der Isar last year, Tilo Biedermann headed a research group at the University Hospital of Tübingen's Department of Dermatology. There, he was already investigating the molecular mechanisms that occur in inflamed skin following infection with Staphylococcus aureus.

Ausgetrickstes Immunsystem

Unter dem Mikroskop ist Staphylococcus aureus ein hübscher Bursche. Nicht zufällig bedeutet sein Name, der aus dem Lateinischen stammt, frei übersetzt so viel wie „goldene Traubenkügelchen". Der schöne Schein trügt jedoch. Denn bei dem Bakterium handelt es sich um einen höchst gefährlichen Keim, der hinter einer Vielzahl ernsthafter Krankheiten steckt, wie beispielsweise Wundinfektionen, Abszesse, Pneumonien, Nahrungsmittelintoxikationen und nicht zuletzt auch Neurodermitis. So fand man bei etwa 90 Prozent aller Patienten, die an dieser entzündlichen Hauterkrankung litten, eine Besiedelung der Haut mit Bakterien der Sorte Staphylococcus aureus vor. Nun ist es Wissenschaftlern um den Allergologen und Immunologen Prof. Tilo Biedermann gelungen, im Labor, und letztlich auch am Patienten, nachzuvollziehen, wie diese Infektionen die Krankheit zusätzlich verschlimmern. Demzufolge besitzt das Bakterium in seiner Zellwand Proteine, die gegenläufige Reaktionsmechanismen des Immunsystems triggern. „Dadurch wirkt das, was normalerweise als Bremse gedacht ist, plötzlich als Verstärker, der die Situation verschlimmert", erklärt Biedermann, der sich schon vor seinem Amtsantritt im April vergangenen Jahres als Leiter der Dermatologischen Klinik des Klinikums rechts der Isar mit seiner Forschungsgruppe an der Hautklinik der Universität Tübingen mit diesem Thema befasst hat. Wie sich bei den Experimenten im Reagenzglas und an Mäusen zeigte, wird ausgerechnet durch den Versuch, die Entzündung zu beenden, letztlich das Gegenteil erreicht. Interessant sind seine Ergebnisse nicht nur hinsichtlich der Behandlung von Neurodermitis, sondern auch aufgrund der neuen Erkenntnisse über die Mechanismen im angeborenen Immunsystem: Das Wissen, dass dort selbst vermeintlich starre Schlüsselmechanismen und Prozesse nicht zwangsläufig immer binär und linear ablaufen, stellt Wissenschaftler, die sich mit dem vergleichsweise jungen Forschungsgebiet unseres angeborenen Abwehrsystems befassen, vor ganz neue Herausforderungen des Denkens und Arbeitens. *Birgit Fenzel*

Prof. Biedermann, one of your main focuses as a doctor and a scientist is atopic dermatitis – an inflammatory skin disease that affects one in four children and is also very common in adults. So when someone comes to your clinic with eczema, itchy blisters or other typical symptoms of this condition, how do you proceed?

Essentially, in most cases, atopic dermatitis is diagnosed by clinical presentation, meaning that we do not always need further procedures to confirm the diagnosis itself. Obviously, though, when we are trying to identify the triggering factors exacerbating a patient's atopic dermatitis – finding out what has brought it on, what is making their condition worse – then we need to do more than just examine their skin. ▷

One such triggering factor is the bacterium Staphylococcus aureus (S. aureus), which is extremely prevalent on the skin of over 90 percent of atopic dermatitis patients. Along with your research groups, you have been making intensive efforts to determine the correlation between this bacterial load and aggravated inflammation for some time now, recently identifying processes that literally hold the key. But first, the most immediate question: how does S. aureus get onto the affected skin to start with?
Ultimately, up to 60 percent of people carry Staphylococcus aureus in the mucous membrane of their noses without necessarily falling ill. But in patients prone to atopic dermatitis, certain skin functions tend to be compromised – impairing the skin's ability to act as a barrier, for instance. And a weakened barrier makes it easier for bacteria to adhere to the skin in the first place, as well as to subdivide and form colonies.

So in this case, the bacteria itself does not cause the inflammation, but is piggy-backing on another condition. How does it aggravate the atopic dermatitis then?
To understand that, it is important to know a bit about the immune system. Today, we generally divide it into two main branches: innate (or natural) immunity and adaptive immunity. The natural immune system, which is present even in very simple organisms like insects, works by means of specific receptors that detect specific substances or pathogenic materials. These substances fit together with the receptor like a lock and key. So when a pathogen is on the skin, the innate immune system springs into action – switched on by the pathogen so to speak. In our case, toll-like receptors – TLR2, to be precise – sense certain bacterial substances from the surface membrane of the bacterial cells and initiate pathways of inflammation.

What usually happens then, in terms of immune response?
The skin's innate sentinel cells are then activated. They take in material from their environment and translate the signals derived from the innate sensing into biological information, which they transport to the lymph nodes and present to the immune system there. The immune system then determines whether it can mount an appropriate response. And this process in the lymph nodes involves the second branch of the immune system – adaptive immunity. Here, the lymph nodes can generate specific immune cells, for example, which then migrate back to the skin to combat the pathogen. ▷

"I always say that research is like stepping into the fog and trying to find a path that may or may not exist, because you are the first to explore that route."

Tilo Biedermann

Picture credits: Jooss

Picture credit: Jooss; graphics: ediundsepp (source: TUM)

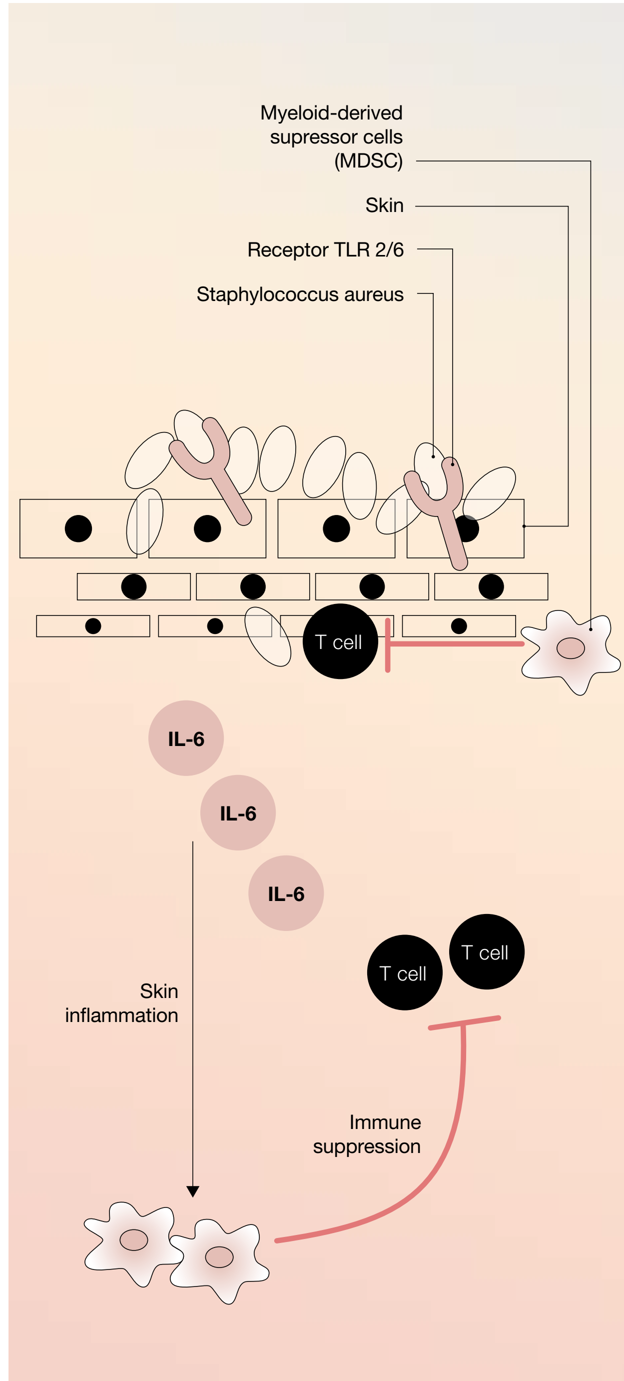
And to start with, when the skin is infected with Staphylococcus aureus, everything takes its normal course. The substances in the bacterial cell membrane fit into the lock of the TLR2 and so the immune system mounts a resistance against the microbes. Yet somehow, the bacteria are still able to continue proliferating on the skin, aggravating the inflammation. What is going wrong?
That is because another process is triggered simultaneously – with exactly the opposite effect. Not only does Staphylococcus prompt a simple immune response via TLR2, it is evidently able to trigger a cascade of reactions at the same time, resulting in increased formation of myeloid-derived suppressor cells (MDSCs).

Those cells that are actually there to suppress or stop the immune reaction?
Exactly. Because, of course, every inflammatory response needs to end sometime. Inflammation does not just draw to an automatic close, like a wave washing up on the shore, but would simply continue to advance if the immune system did not actively shut it off again at some point.

And how do the bacteria take advantage of this mechanism?
The mass formation of MDSCs also leads to a reduction in the skin's antibacterial immune response. This allows the bacterial population to increase, and their growing numbers exacerbate the inflammatory process further. Unfortunately, it just keeps escalating. The more severe someone's condition, the worse affected they are by this mechanism.

What are the therapeutic implications of these findings?
What we have established here is relevant for patients whose condition is severe, with large areas of skin affected. Our findings confirm the risk and underline the danger these patients are in. We simply need to admit these patients for more intensive therapy, including systemic treatment with antibiotics where appropriate, to reduce the concentration of bacteria.
Antibiotic-resistant Staphylococcus is a major problem. The important thing is not to treat the skin with antibiotics, to which the bacteria can develop a specific resistance, but with antiseptic agents, to which the bacteria cannot develop resistance. Many decades ago, we regularly used antiseptic dyes in dermatology. Then they were frowned upon, and now they are making a comeback.

What was the most exciting result for you as a scientist?
We actually drew two interesting conclusions. First, we were surprised to find that colonization of the skin with ▷



How Staphylococcus aureus bacteria sidestep the immune system in the presence of atopic dermatitis: The natural immune system identifies the bacteria on the skin surface via toll-like receptors (TLR/6). The adaptive immune system produces immune cells (T cells), which migrate to the skin and combat the pathogen. However, S. aureus also triggers the production of interleukin 6 (IL-6), which regulates the inflammatory response. The immune system produces myeloid-derived supressor cells (MDSC), which block the activation and the effect of the T cells. As a consequence, the bacterial population increases and the inflammation is exacerbated further.

"The important thing is not to treat the skin with antibiotics, to which the bacteria can develop a specific resistance, but with antiseptic agents, to which the bacteria cannot develop resistance."

Tilo Biedermann

S. aureus is in itself sufficient to trigger these mechanisms. In sepsis cases, we know that a very similar mechanism of the innate immune system plays a major role in making patients so critically ill. There, too, a great deal is determined by a specific receptor for a specific sub-species of bacteria – the latter going on to spread in the blood. In sepsis, though, the receptor is TLR4, rather than TLR2 as in atopic dermatitis.
What is really striking in this case is our observation that it clearly suffices if the skin is infected, without the microbes penetrating further into the body (or our model). Both cases lead to massive up-regulation of the pro-inflammatory messenger interleukin 6. In atopic dermatitis, this results in accumulation of MDSC production, in turn triggering the whole counter-reaction and increasingly vicious circle.

And the second lightbulb moment?
That was the realization that, although innate immunity is a relatively rigid system in itself, the same receptor can be used both to suppress and to amplify it. The receptor is the lock, so to speak, and the ligand the molecular key. And when the key fits into the lock, that sets the alarm. But, as we have seen here, the same key can have a completely different impact on the immune system. So it is not the case that we can only turn it either on or off – obviously both at once is possible, too. For me, that is the most exciting finding from these efforts over the past few years – that we need to think in much more complex terms to grasp that not every model that appears to be binary actually works that way.

Is that not sometimes exasperating though?
It can be. I always say that research is like stepping into the fog and trying to find a path that may or may not exist, because you are the first to explore that route. So you do sometimes feel you have lost your way. On the other hand, if your curiosity and inner drive are strong enough, that is exactly what keeps you going forward despite it all.

So going forward in this case means widening the focus?
The innate immune system has always been investigated in very linear terms to date. You take a receptor and a ligand – a lock and a key – and A happens, and then maybe B. But we now know it doesn't work that way. Innate immunity is highly complex and integrates a large amount of data at once, which can lead to totally conflicting output. It depends what information about the immune system's environment is available at the point when the key is placed in the lock – inflammation levels, for instance, or other input signals that affect the immune system. In the end, it's a combination of data that influences the end result. And that's biology. It is actually quite logical, but you do have to get there.

The interview was conducted by Birgit Fenzel

Picture credit: Jooss

Particles That Fly Straight through Matter: **Neutrino Research at TUM**

Neutrinos travel through our universe nearly unaffected by interactions with matter. They thus provide pristine information about their various origins and offer completely new insights into our solar system and the universe. Astroparticle physicists at TUM participate in large international experiments that detect neutrinos from different origins. The Excellence Cluster Universe in Garching is a hub for all these activities. As one of the world's leading research centers in the field, it links the physics faculties of TUM and LMU and brings them together with partners from several Max Planck institutes and the European Southern Observatory.

Neutrinos I

A New Window on the Universe

Prof. Elisa Resconi and her team participate in the IceCube Neutrino Observatory at the South Pole, where she is searching for high-energy neutrinos from outer space.

Neutrinos II

Signals from Deep inside the Sun

Prof. Stefan Schönert (above) and Prof. Lothar Oberauer (below) are deeply involved in the Borexino experiment under the Gran Sasso mountain in Italy. Their focus lies on neutrinos with particularly low energies, which originate from the core of the Sun.

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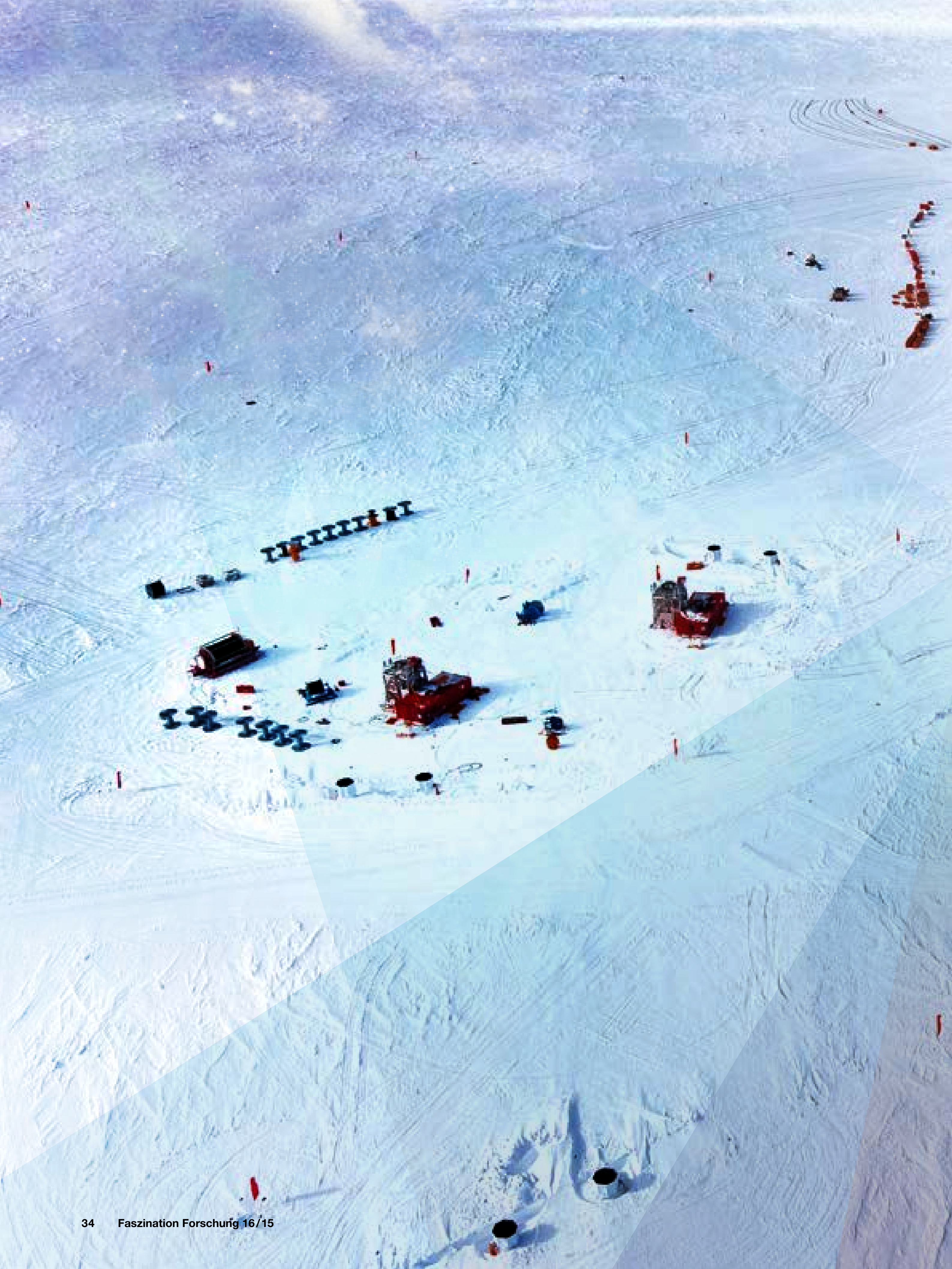
Neutrinos I

A New Window **on the Universe**

Energy-laden neutrinos making their way to us from outer space must have originated in cosmic catastrophes that were more powerful than anything we could ever imagine here on Earth. As part of the IceCube project, TUM physicists are investigating various phenomena including the sources of such cataclysmic events in the heavens.

Links
www.cosmic-particles.ph.tum.de www.icecube.wisc.edu

Picture credit: IceCube Collaboration; graphics: ediundsepp



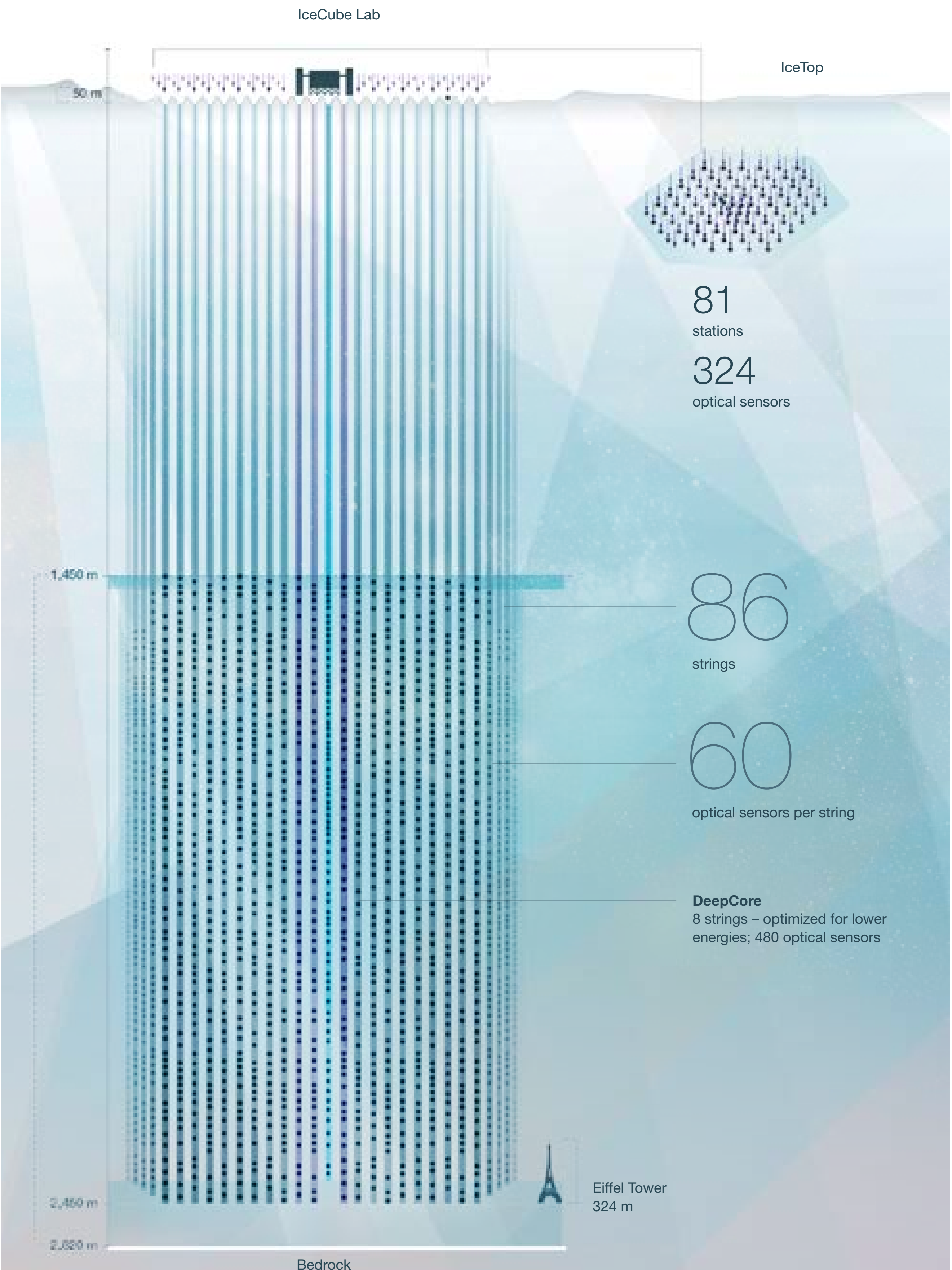
An aerial view of the IceCube Lab. To the left of the lab are drilling hoses, towers and equipment, to the back right is the seasonal equipment site. The lab covers a surface of 1 square kilometer.

Picture credit: Ben Tibbets, IceCube/NSF, © 2012

Ein neues Fenster zum All

Am Südpol befindet sich das außergewöhnlichste Teleskop der Welt: Es heißt IceCube und soll die kleinsten Teilchen des Universums, sogenannte Neutrinos, aufspüren. 44 Organisationen aus zwölf Ländern beteiligen sich an der Kooperation, darunter auch ein zwölfköpfiges Team der TUM unter der Leitung von Prof. Elisa Resconi.

Die Anlage, die aus 5.160 optischen Sensoren besteht, wurde 2.000 Meter tief ins antarktische Eis versenkt und umfasst ein Volumen von rund einem Kubikkilometer. IceCube registriert Zusammenstöße von Neutrinos mit Eismolekülen, die Teilchenschauer auslösen und letztlich zu einem blau-ultravioletten Tscherenkow-Blitz führen. Durch die große Ausdehnung des Experiments lassen sich sowohl die Energie als auch die Einfallsrichtung der Teilchen messen. Eines der Hauptziele von IceCube ist es, hochenergetische Neutrinos aufzuspüren, die aus katastrophalen Ereignissen im Weltall stammen. Sie sollen sowohl helfen, die Prozesse bei ihrer Entstehung zu verstehen, als auch die Quellen derartiger kosmischer Ereignisse zu finden. Bis Anfang 2015 konnten die IceCube Forscher bereits 53 derartige Neutrinos aufspüren. Je nachdem, welches Bild sich in den kommenden Jahren aus der Durchmusterung des Himmels ergibt, könnten sie alternativ auch Hinweise auf dunkle Materie im All sein. Ein weiterer wichtiger Forschungszweig, an dem die TUM Wissenschaftler beteiligt sind, ist die Erforschung der Natur des Neutrinos. Durch die Untersuchung von atmosphärischen Neutrinos, von denen weit über 100 täglich in IceCube registriert werden, möchte man Näheres über die Oszillation dieser Teilchen erfahren. Bisher weiß man nur, dass sie aus drei verschiedenen Zuständen bestehen, die ineinander übergehen können. Welche Masse diese Zustände jeweils haben und wie sie physikalisch erklärt werden können, ist heute noch nicht bekannt. Zur Klärung der Lage soll ein neuer Detektor namens PINGU beitragen, der im Zentrum von IceCube geplant ist. Die Forscher hoffen, dafür finanzielle Mittel zu bekommen. *Brigitte Röthlein*



Picture credit: ediundsepp (source: IceCube Collaboration)

The IceCube Neutrino Observatory is the world's largest neutrino detector. Located at the South Pole, IceCube is buried inside the ice masses of Antarctica, reaching a depth of about 2,500 meters. In total, it encompasses a cubic kilometer of ice. IceCube is made up of 5,160 light sensors attached to 86 vertical strings spaced at intervals of 125 meters. The sensors collect light emitted by particles that are produced during interactions between neutrinos and ice molecules.

The Sun never sets – it circles the horizon, always at the same height, and night is just as bright as day. Dr. Martin Jurkovic from TUM experienced this spectacle when he spent a month at the South Pole in December to work on the yearly inspection of the IceCube neutrino telescope. "It was a fantastic experience," says the physicist, "and a completely foreign world to me. While there, I worked on the IT system and I spent a lot of time outside digging snow, as we need to measure the snow accumulation on the surface detectors."

IceCube is a large-scale international project intended to detect neutrinos – particles that have the special property that they can pass through matter without difficulty. They fly straight through stars as well as the Earth without impact.

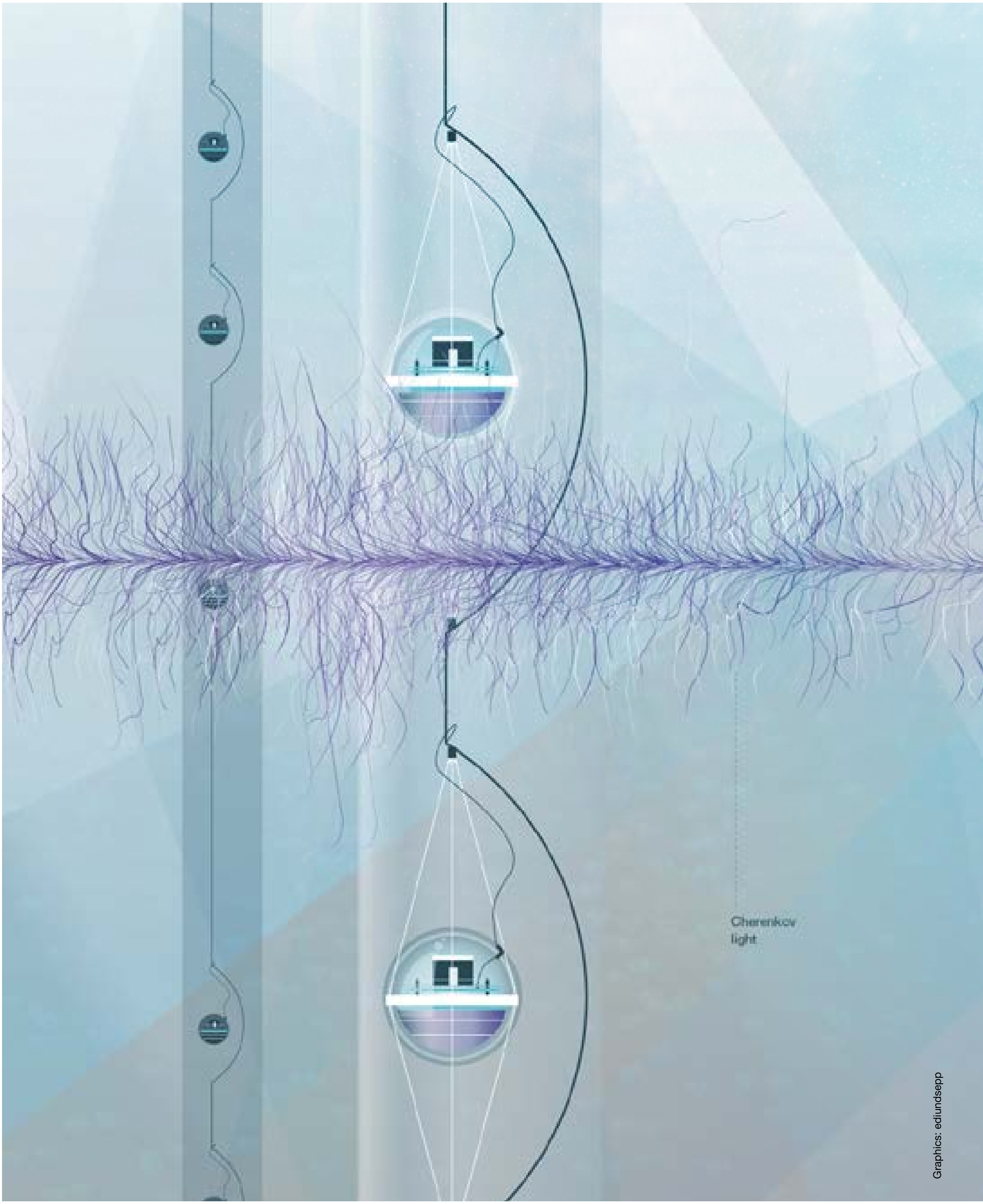
As a result, neutrinos are difficult to detect, although countless numbers of them are continuously racing through the galaxy and the solar system. "Trillions of neutrinos are passing through your body alone while you are reading this sentence," claims Prof. Elisa Resconi, Head of TUM's research team at IceCube, "but probably only once in your life does one remain inside you." One of the objectives of the experiment is to detect extremely energetic neutrinos arriving from outer space. In November 2013, the IceCube Collaboration announced the first detection of such neutrinos. These may have arisen during the birth of a supernova, or they could have been ejected from the vicinity of a black hole. Neutrinos could offer a means of receiving signals directly from these objects that until now have been regarded as mysterious. This is not possible with light, radio or X-ray radiation because their photons are hindered by intergalactic clouds or other obstructions. IceCube is continuously searching the skies for such neutrinos, thus opening up a completely new window on the universe.

A three-kilometer-thick layer of high-quality ice

The neutrino detector was sunk deep into the Antarctic ice, where it occupies a volume of about one cubic kilometer. It has 5,160 optical sensors, each the size of a basketball, which were deployed into the ice in vertical lines (strings) in groups of 60 to depths between 1,450 and 2,450 meters. Power supply and signal cables are integrated in the strings. The reason to choose such a harsh environment – the South Pole – for the high-tech observatory is due to the huge volume and the quality of the ice there. It is three kilometers thick, highly transparent, and the adjacent US Amundsen-Scott Station provides the necessary infrastructure. It is located at an altitude of 2,835 meters on the inland ice, only a few hundred meters from the geographic South Pole. ▷

"Trillions of neutrinos are passing through your body alone while you are reading this sentence, but probably only once in your life does one remain inside you."

Elisa Resconi



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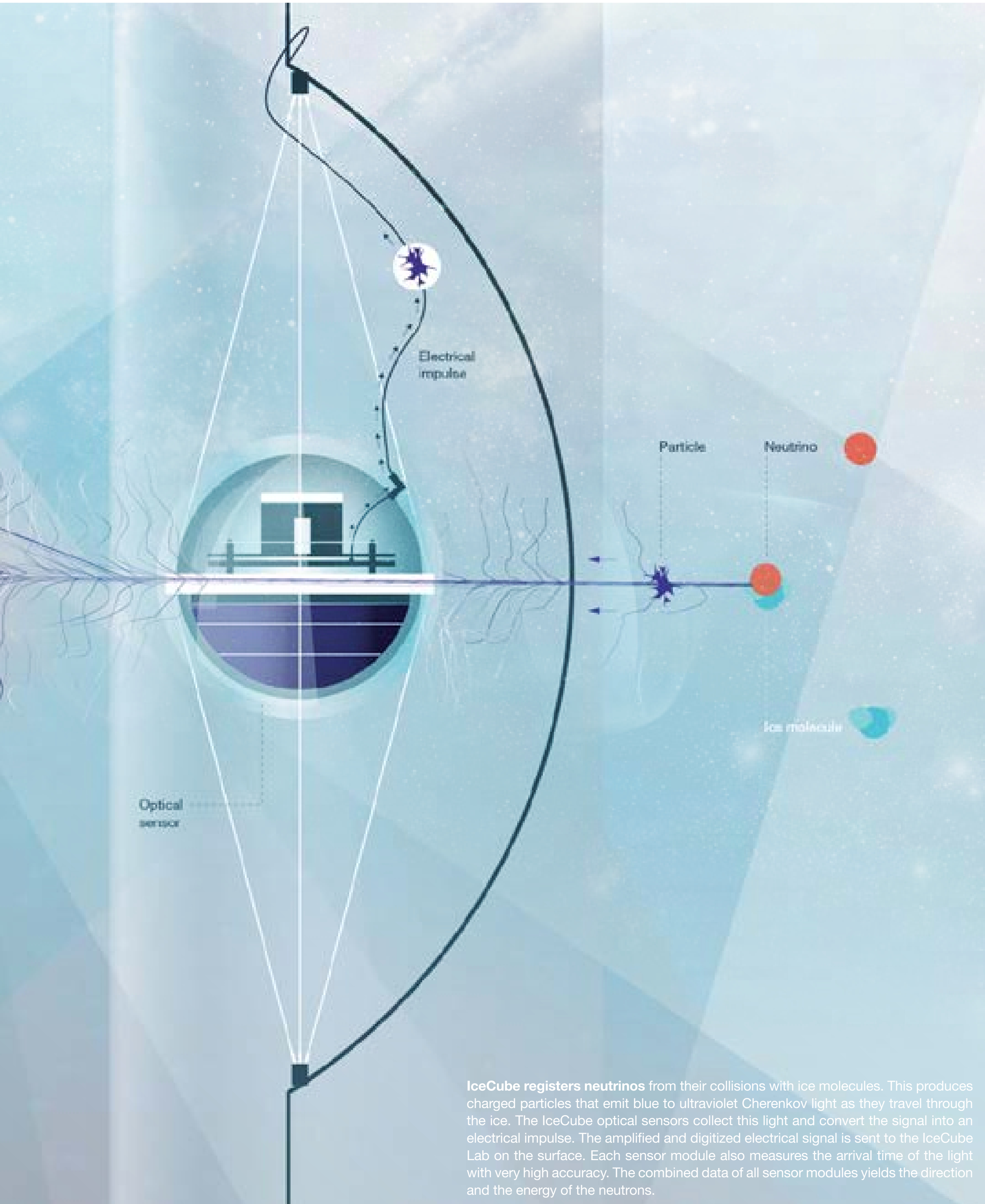


IceCube registers neutrinos from their collisions with ice molecules. This produces charged particles that emit blue to ultraviolet Cherenkov light as they travel through the ice. The IceCube optical sensors collect this light and convert the signal into an electrical impulse. The amplified and digitized electrical signal is sent to the IceCube Lab on the surface. Each sensor module also measures the arrival time of the light with very high accuracy. The combined data of all sensor modules yields the direction and the energy of the neutrons.

There are 44 universities and organizations from 12 countries, the so-called IceCube Collaboration, participating in this mammoth project. The experiment is led by the University of Wisconsin-Madison in the USA. About half of the participating institutions are European, nine of them located in Germany. The 12-person TUM team is primarily involved in software development for analyzing data searching for signatures of energy-rich, so-called cosmic neutrinos. This is an extremely demanding task, as the required results have to be filtered out of the terabytes of data recorded every day by the experiment. The group is also involved in the design and sensor development of the next-generation IceCube detector, an even larger neutrino telescope.

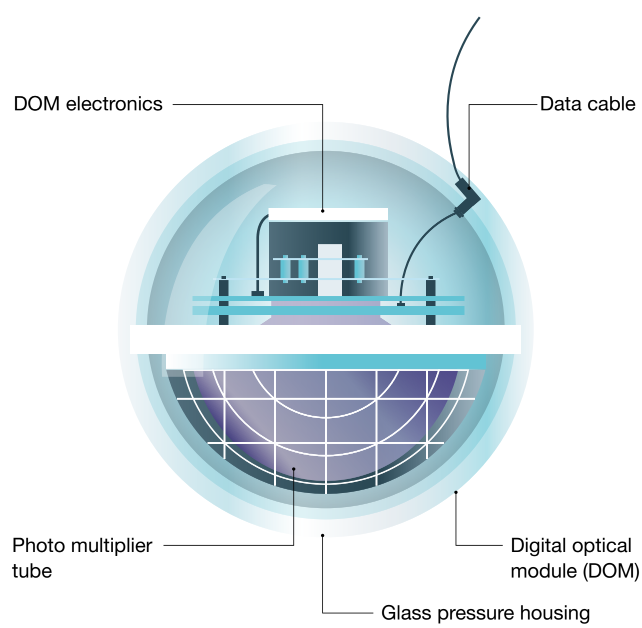
"More data and a larger detector will provide a clue about the origin of these incredible neutrinos in the coming years."

Elisa Resconi

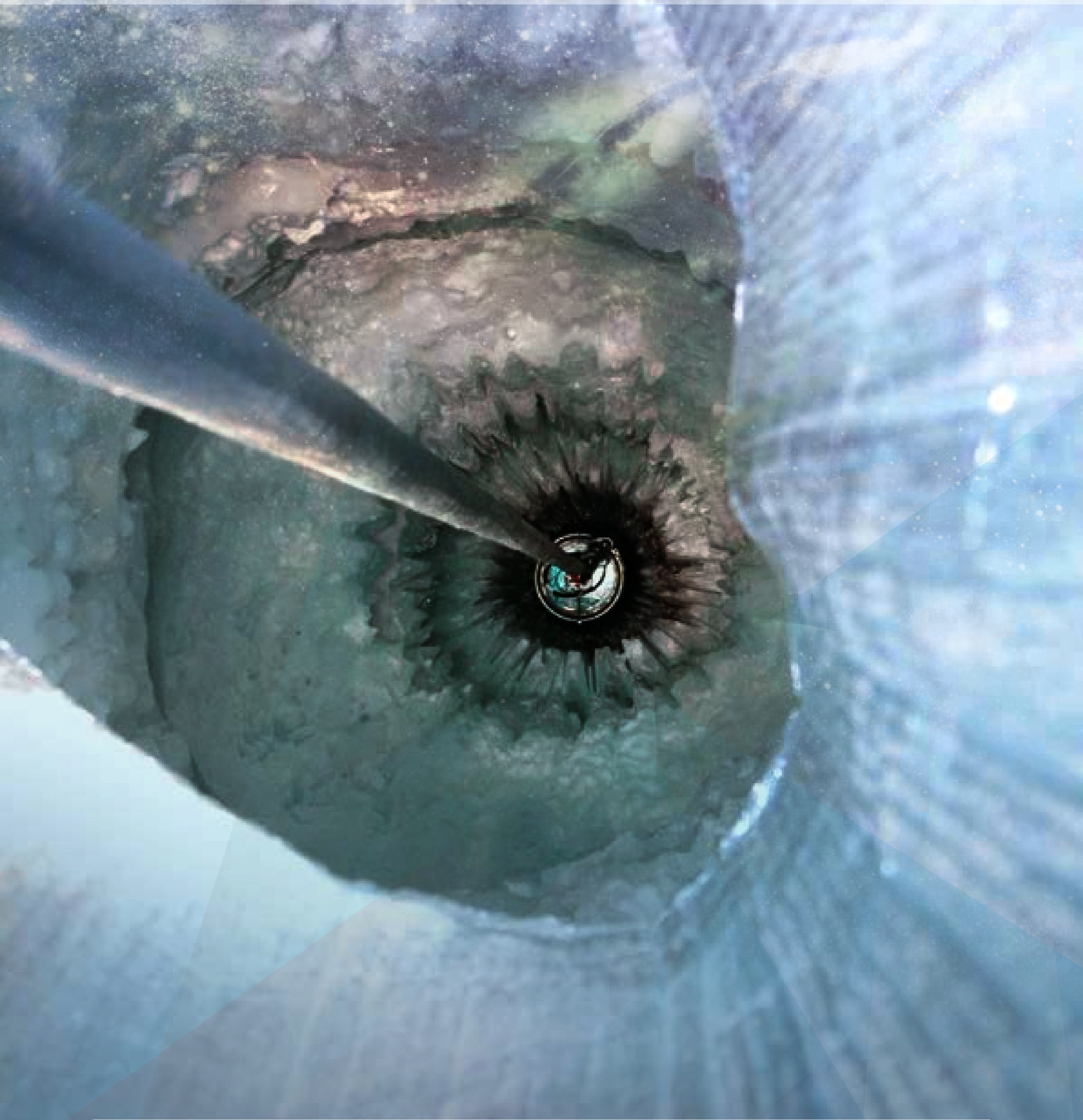
Collisions between neutrinos and ice molecules

IceCube registers collisions between neutrinos and ice molecules. This results in charged particles that radiate a shock wave of blue to ultraviolet Cherenkov radiation in the ice. The optical sensors of the IceCube detector are so sensitive that they react to a single photon. Each light signal is amplified, converted to an electrical pulse and then to a digital signal while still in the detector. Each module has its own mini-computer and a high-precision clock to accurately measure the arrival time of photons to within 5 nanoseconds. The digitized signals then run through kilometers of cables to the data center near the South Pole Station, from where they are finally transmitted to researchers in different centers throughout the world for further analysis. Despite the shielding afforded by the kilometer-thick ice layer, many other particles can still interfere with the measurements. Using a host of clever tricks, the researchers are able to distinguish these particles from the neutrinos. Moreover, it is vital to separate particularly energetic neutrinos from the depths of outer space from neutrinos that occur due to the effects of cosmic radioactivity in the Earth's atmosphere – i.e., directly on our doorstep. These are admittedly also objects of interest for research, but for completely different purposes, as we will explain later in this article. Scientists involved in IceCube discovered, in 2012, two of the sought-after neutrinos with an incredibly high energy level of more than one peta electron volt (PeV), which they named Ernie and Bert. "One PeV corresponds to roughly the energy of a tennis ball moving at hundreds of kilometers per hour," estimates Resconi. This is an unfathomably high value for a particle that is even smaller than an electron. "The neutrinos we detect at IceCube come from all directions and therefore ▷

IceCube comprises 5,160 light sensors called digital optical modules. Each sensor is made up of a glass sphere containg a photomultiplier tube and electronics for time measurement and signal processing. The sensors are so sensitive that they react to a single photon.



Graphics: ediundsepp; picture credit left: Jooss; right: IceCube/NSF

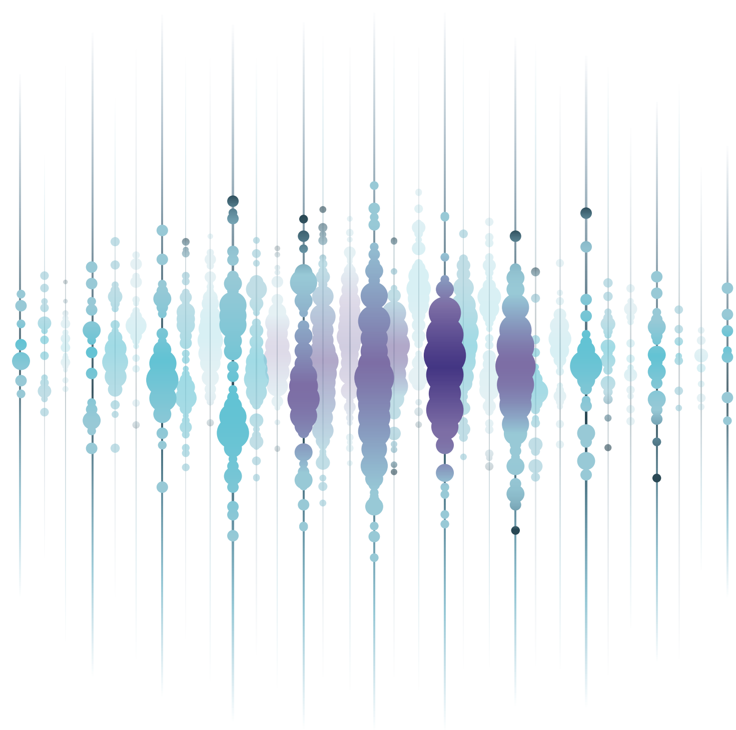


Hot-water drilling

It was no easy task to position the optical detectors precisely in their designated locations at depths of between 1,450 and 2,450 meters. Although ice can be easily melted with a hot-water drill, the technical challenge lies in transporting the hot water to such great depths. The tube made of reinforced aramid rubber specially developed for the task was 2.5 kilometers long and weighed more than 11 tons when empty. "This is a really high-tech device," explains system engineer Jeff Cherwinka. "It was the critical part of the project and we could find only one manufacturer to produce it."

The first hole was drilled and the observatory tested in January 2005. Another eight holes were drilled the following year. The holes around the sensors freeze over immediately.

A further 14 holes were bored in each of the subsequent years until the system was completed in 2010. John Wiley, former Chancellor of the University of Wisconsin-Madison, even compared the gigantic project, in terms of its scale and difficulty, to the construction of the Egyptian pyramids.



A neutrino observed in IceCube: The colored spheres indicate optical sensors that detected light. The color corresponds to the arrival time of the light signal. Red marks the beginning, light blue the end of the event, which typically lasts a few microseconds. The size of the colored spheres corresponds to the amount of detected light.

Powers of ten and their syntax

kilo-	k or K	10^3
mega-	M	10^6
giga-	G	10^9
tera-	T	10^{12}
peta-	P	10^{15}

most of them have passed through Earth. Hence we are using our planet to filter out particles that are not neutrinos. We did so for our first searches, but in 2013 we showed that we can significantly increase measurement accuracy if we consider only the interior volume of our experiment. This relatively simple observation was a major step in the search for the cosmic neutrinos," says the physicist. "Think of it as an onion. Most particles get caught in the outer layer, while we look only at the inner parts." When using the method to again search through the data that had already been collected up to that point for slightly lower energy levels, another 26 high-energy candidates of between 30 and 2,000 TeV were found. By the beginning of 2015 the count had already reached 54 particles.

Where do the neutrinos come from?

The direction of entry of the neutrinos measured by IceCube can be used to trace them back to their origin. With a thousand times more energy than can be generated with a terrestrial particle accelerator, astrophysicists conclude that these neutrinos can only derive from cataclysmic events in outer space, and that they could supply information regarding the genesis of these events. So far, arrival directions of the observed high-energy neutrinos are distributed regularly across the entire globe. However, the greater the number of particles, the more complete the picture. It could be the case that there are particular sources that transmit significantly large numbers of these neutrinos. Resconi illustrates this with an image: "It is like the situation on a cloudy day: We can't see the Sun as the light is diffuse in all directions. We cannot say that the light is emitted by the Sun until we have taken more measurements over time. In analogy, we think that individual objects emit these high-energy neutrinos. Currently we cannot yet resolve these objects, but more data and a larger detector will provide a clue about the origin of these incredible neutrinos in the coming years." The researchers could then draw their conclusions about the properties of these sources. Should ▷

Graphics: ediundsepp (source: IceCube); Picture credit: Jooss

Physicist Elisa Resconi is a Heisenberg Professor at TUM and leader of the research field “Experimental Physics with Cosmic Particles.” She heads the 12-person IceCube research group at TUM’s Excellence Cluster Universe.

“Our goal is to significantly progress in the understanding of the nature of neutrinos, and in doing that, provide a clue about the still many unknowns in particle physics.” *Elisa Resconi*

the neutrinos remain not associated to point sources, then they could only come from dark matter. “We shall attempt in the coming years to associate the detected neutrinos with the universe as we know it from explorations with high-energy photons and gamma rays,” says Resconi. “If we are unsuccessful, it could be that the neutrinos provide us with a completely different insight into the dark universe. This would then suddenly no longer be so dark anymore.”

The nature of the neutrinos themselves

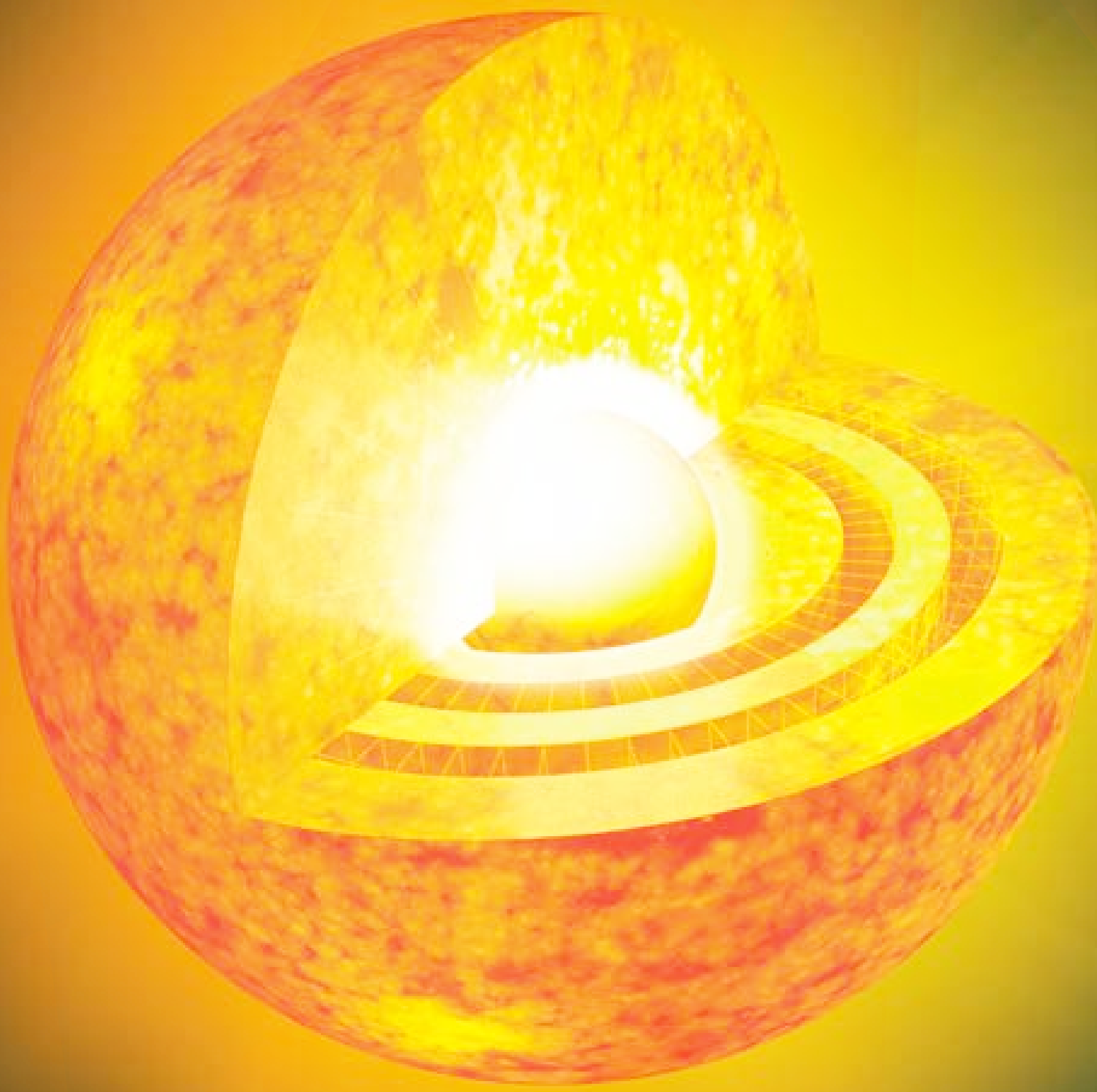
An even more ambitious undertaking for the future is that Resconi and her team want to investigate the nature of the neutrinos themselves, which remains a mystery to this day. We know that they have to have mass, even if extremely low, and that they comprise three different states that can change from one to another in a phenomenon called oscillation. However, different theories have different predictions for which of these states is heavier or lighter, and whether perhaps completely different types of neutrinos exist. Resconi and her team want to make a substantial contribution in this regard. “The atmospheric neutrinos are particularly suitable for analyses of this kind. Hundreds of these are registered every day,” explains the professor. “For this reason, we are working on a new detector for IceCube – we call it PINGU, an acronym for Precision IceCube Next Generation Upgrade, which we could use to carry out precision measurements. It would be located at the center of the current IceCube. At the moment, we are looking for national and international funding. Just five years ago, nobody believed that we would be able to observe the oscillation of atmospheric neutrinos in IceCube. But now, after the first results, we are being taken very seriously. Our goal is to significantly progress in the understanding of the nature of neutrinos, and in doing that, provide a clue about the still many unknowns in particle physics.” *Brigitte Röthlein*

The IceCube research team at TUM is one of nine German members of the IceCube Collaboration. The scientists develop software for analyzing the extreme amounts of data collected by the IceCube detector. The TUM team is also involved in the design and sensor development for a next-generation IceCube detector, an even larger neutrino telescope.

Picture credit: Jooss

Picture credit: Freija Descamps, IceCube/NSF

Pulling cables to connect the deployed sensors to the IceCube Lab in the detector's center. The 86 strings holding the sensors are distributed over an area of about one square kilometer. The lab houses data processing and storage and sends about 100 gigabytes of data by satellite every day.



Sun

Links
www.e15.ph.tum.de borex.lngs.infn.it

Neutrinos II

Signals from Deep **inside the Sun**

With the Borexino experiment, physicists at TUM have been able to gain direct insight into the core of the Sun for the first time and explore how it generates energy. This success was enabled by a custom-built experimental set-up with the lowest levels of radioactivity on Earth.

Graphics: ediundsepp

Signale aus dem Innersten der Sonne

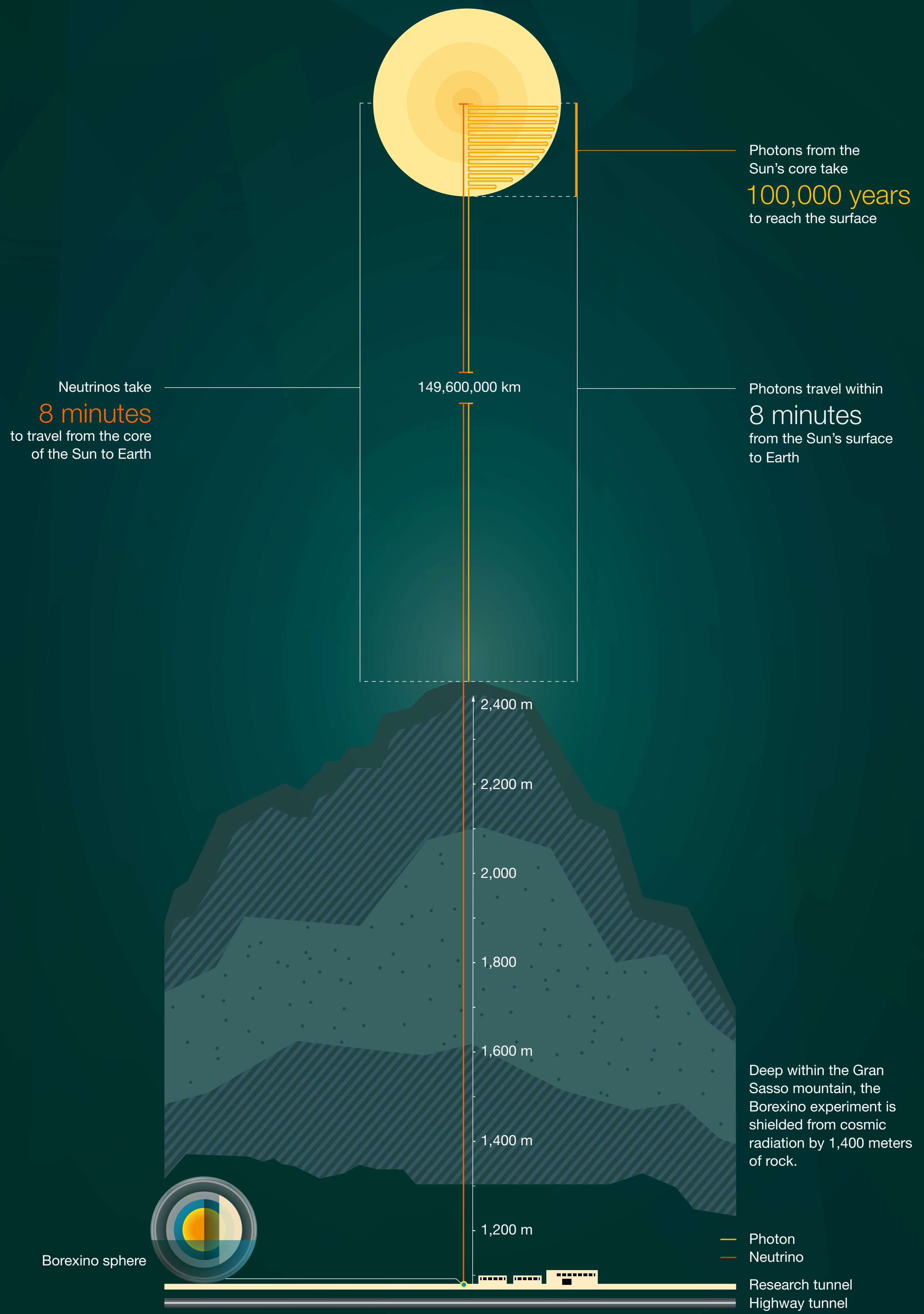
Im Gran-Sasso-Untergrundlabor ist es Forschern der TUM mit dem Experiment Borexino im Rahmen einer internationalen Kollaboration gelungen, Neutrinos nachzuweisen, die direkt bei der Verschmelzung von Protonen im Inneren der Sonne zu Helium entstanden sind. „Damit konnten wir zum ersten Mal wirklich zusehen, wie die Sonne ihre Energie gewinnt. Das ist die fundamentalste Reaktion, die Ursprungsreaktion, alles andere baut darauf auf, auch das Leben auf der Erde“, sagt Prof. Lothar Oberauer, der zusammen mit Prof. Stefan Schönert und Prof. Franz von Feilitzsch das Borexino-Experiment von deutscher Seite initiiert hat.
Bisherige Analysen der Sonnenenergie beruhten auf Messungen der Sonnenstrahlung. Im Durchschnitt braucht diese jedoch über 100.000 Jahre, um aus dem dichten Sonneninneren an die Oberfläche zu gelangen. Das bedeutet, dass die errechneten Werte der Energie entsprechen, die über 100.000 Jahre zuvor im Inneren der Sonne freigesetzt wurde. Ganz anders verhalten sich Neutrinos: Weil diese als elektrisch neutrale Elementarteilchen mit anderer Materie kaum in Wechselwirkung treten und sich deshalb frei bewegen können, verlassen sie auch das Sonneninnere wenige Sekunden nach ihrer Erzeugung und erreichen bereits nach gut acht Minuten, also quasi mit Lichtgeschwindigkeit, die Erde.
Mit diesem Erfolg, der 2014 in „Nature“ veröffentlicht wurde, vervollständigten die Wissenschaftler am Borexino-Experiment eine ganze Reihe von Messungen, bei denen schon in den vergangenen Jahren Neutrinos aus unterschiedlichen Fusionsschritten in der Sonne nachgewiesen wurden. Da die Neutrinos aus der Proton-Proton-Reaktion zwar am häufigsten sind, aber gleichzeitig eine besonders niedrige Energie aufweisen, war es vorher nirgendwo auf der Welt gelungen, sie direkt in Echtzeit nachzuweisen. Borexino konnte aufgrund seines einzigartigen Aufbaus, der von radioaktiven Einflüssen fast vollständig frei gehalten wurde, den störenden Untergrund bei den Messungen unterdrücken und eine fünfprozentige Messgenauigkeit erzielen. *Brigitte Röthlein*

One does not have to look billions of light-years into space to find exciting astrophysical events – sometimes a glance in the immediate vicinity is sufficient. Although the Sun is just eight light-minutes removed from us, it only recently became possible to observe fundamental processes within its core in real time. The reason for this is that the Sun – a gas ball with a temperature of 15 million degrees Celsius – is so dense that photons can escape from the center to the outside only with great difficulty. It takes about 100,000 years on average for a light particle to reach us from the Sun. A photon experiences so much in this time that is does not provide information on how it was formed.

Neutrinos: messengers from the Sun

However, there are other elementary particles that pass through the Sun relatively unimpeded. As a result, they can provide us with information from the heart of the Sun. Neutrinos have no electric charge and are therefore subject to only the forces of gravity and weak interaction. The latter is what now gives researchers the opportunity to prove their existence in an experiment.
Rutherford, Walton and Cockcroft were the first to observe the nuclear reactions of light elements as early as 1932. They showed that a lithium nucleus, after capturing a ▷

The Gran Sasso laboratory lies deep underground in a tunnel in the Abruzzo region, around 120 kilometers northeast of Rome. It is shielded from unwanted radioactivity by 1,400 meters of rock. Solar neutrinos not only pass through all the layers of the Sun, but also through the rock more or less unhindered. Photons, on the other hand, need to travel for 100,000 years or so until they reach the edge of the Sun.



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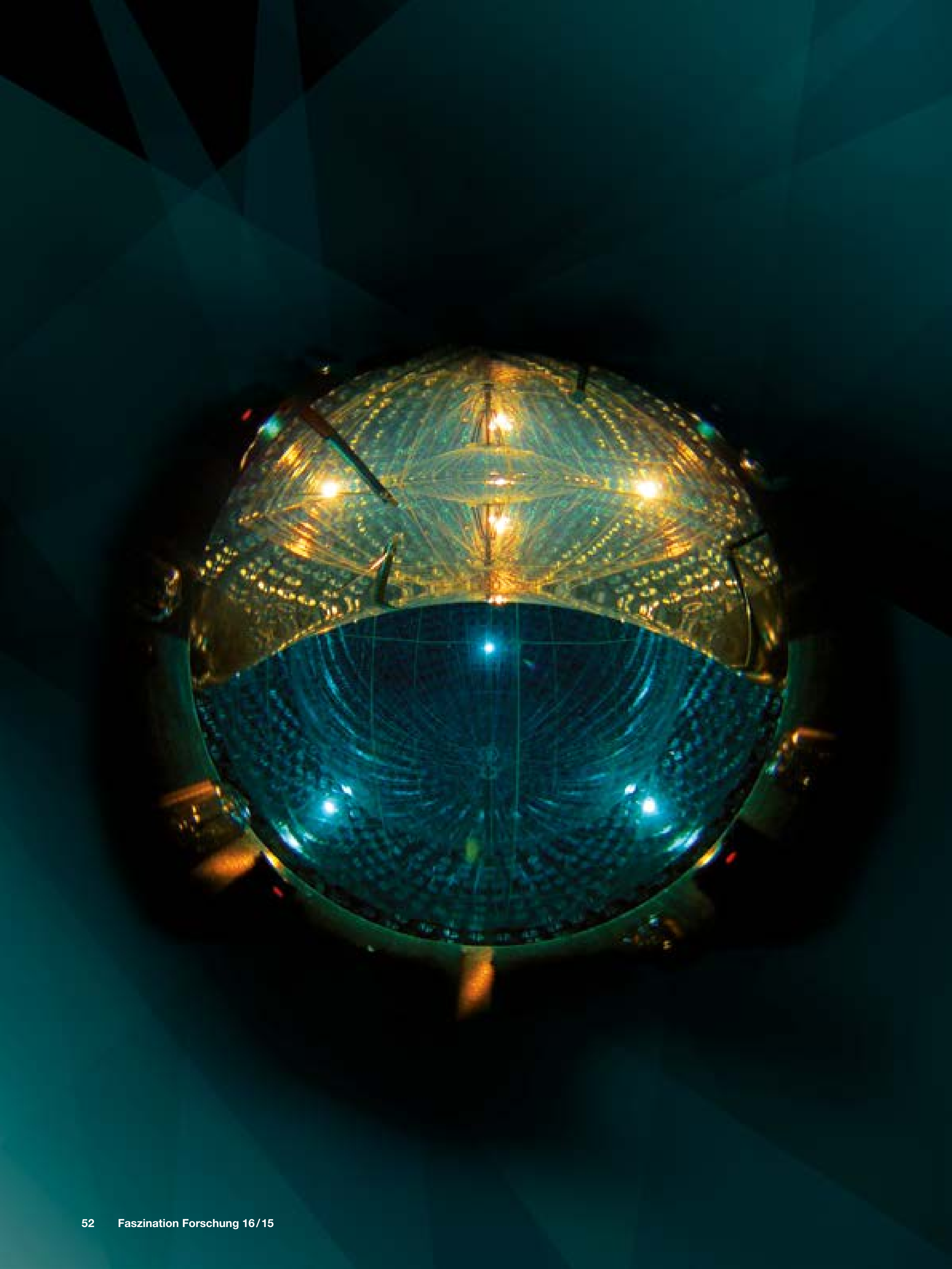


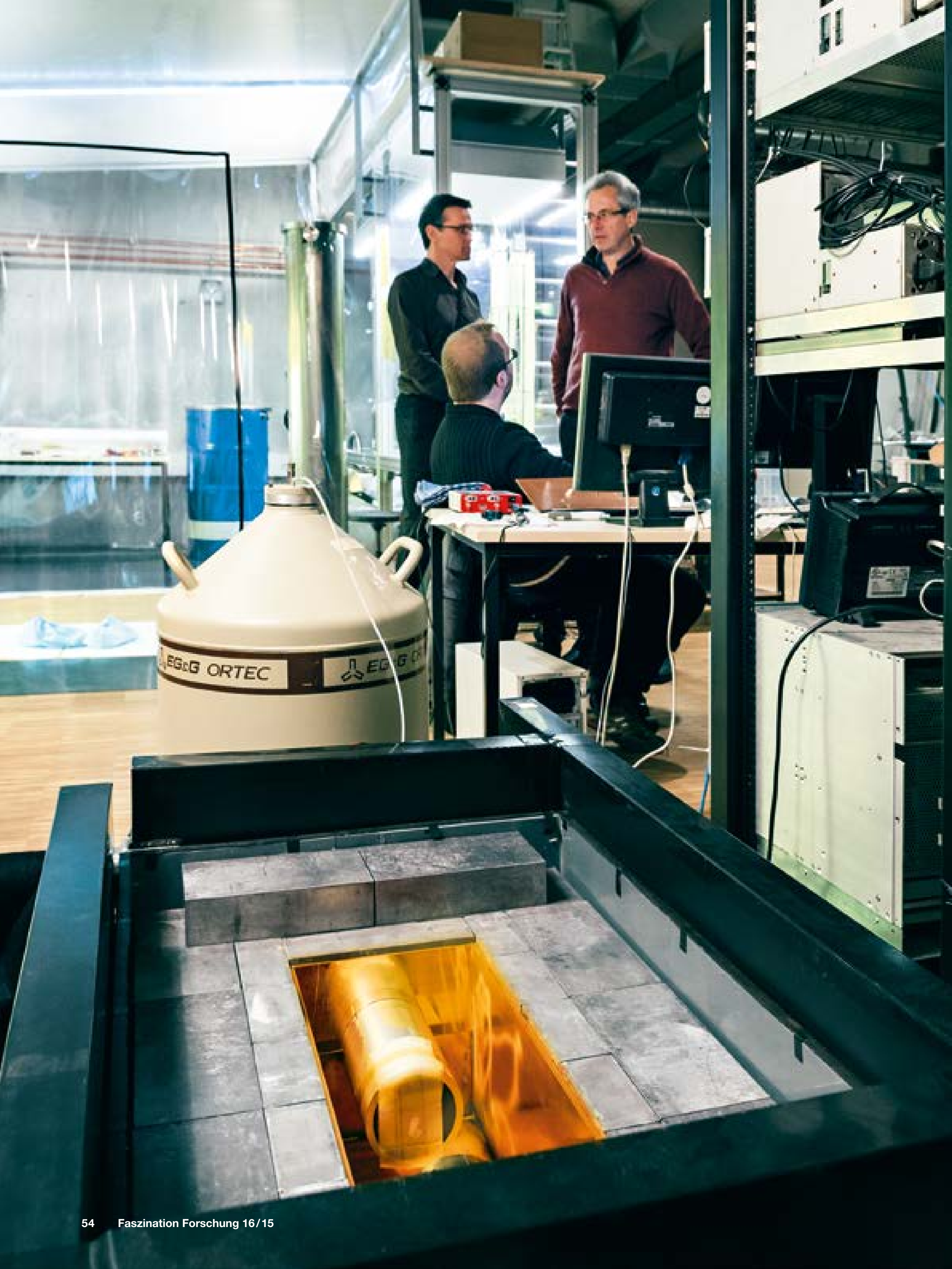
300

tons of organic liquid scintillator

Picture credit: Borexino Collaboration

“We were able to really see for the first time where the Sun get its energy from. This is the most fundamental reaction – the first ever reaction – everything else derives from it, including life on Earth.”

Lothar Oberauer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The scientists commute between their institutes and the Gran Sasso facility. A lot of detailed work and preliminary investigations, as well as data analysis and theoretical discussion, also happen outside of the Borexino lab. At TUM's underground laboratory in Garching, the scientists test the radioactive purity of their detector materials for Borexino using a germanium detector.

proton, splits into two helium nuclei and releases energy in the process. The knowledge gained from this event and from later experiments prompted theoretical physicists to examine fusion processes more closely to see where the Sun gets its energy. Today we know in what processes neutrinos are created inside the Sun: first, in the fusion of two hydrogen nuclei (or protons, p) to form heavy hydrogen (deuterium, D); then in lateral lines during radioactive decays of the beryllium isotope with an atomic weight of 7 (^{7}Be) and of the boron isotope ^{8}B. At the same time, there is the Bethe-Weizsäcker cycle – another cascade of fusion reactions named after its discoverers – in which neutrinos are also created. All neutrinos have very different but in some cases characteristic energy distributions; these allow us to identify the process that created the corresponding neutrinos. They fly out of the interior of the Sun in all directions. Even on Earth, 150 million kilometers from the Sun, almost 70 billion solar neutrinos pass through each square centimeter every second.

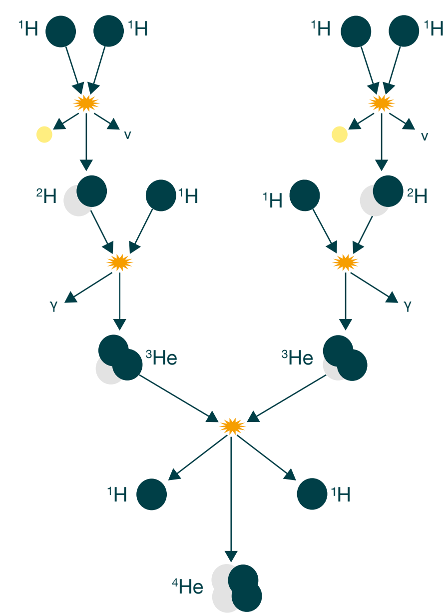
Solar research in a tunnel

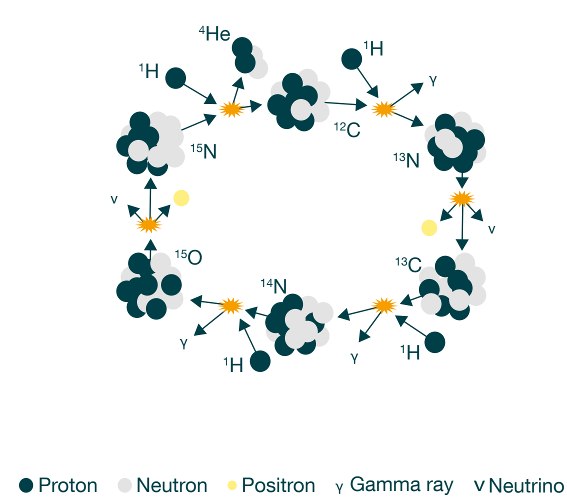
What is paradoxical here is that these particles are being measured at a location where there is absolutely no evidence of the Sun – in a tunnel deep underneath the Gran Sasso mountain in Italy. The tunnel houses Borexino, which contains an 8.5 m large, transparent sphere made of nylon foil and filled with 300 tons of exotic liquid scintillator. Using this sphere, researchers collaborate across borders to unravel the solar fusion processes by measuring solar neutrinos. The experiment began in 2007 and a large number of exciting results have been published since. For example, scientists there were able to detect and measure a wide range of neutrinos derived from different fusion steps: ^{7}Be neutrinos in 2007, ^{8}B neutrinos in 2009, and so-called pep neutrinos in 2012. "These neutrinos occur during very rare three-body processes in the Sun, in which two protons and an electron come together at the same time and fuse with each other," explains Prof. Lothar Oberauer, who initiated Borexino together with ▷

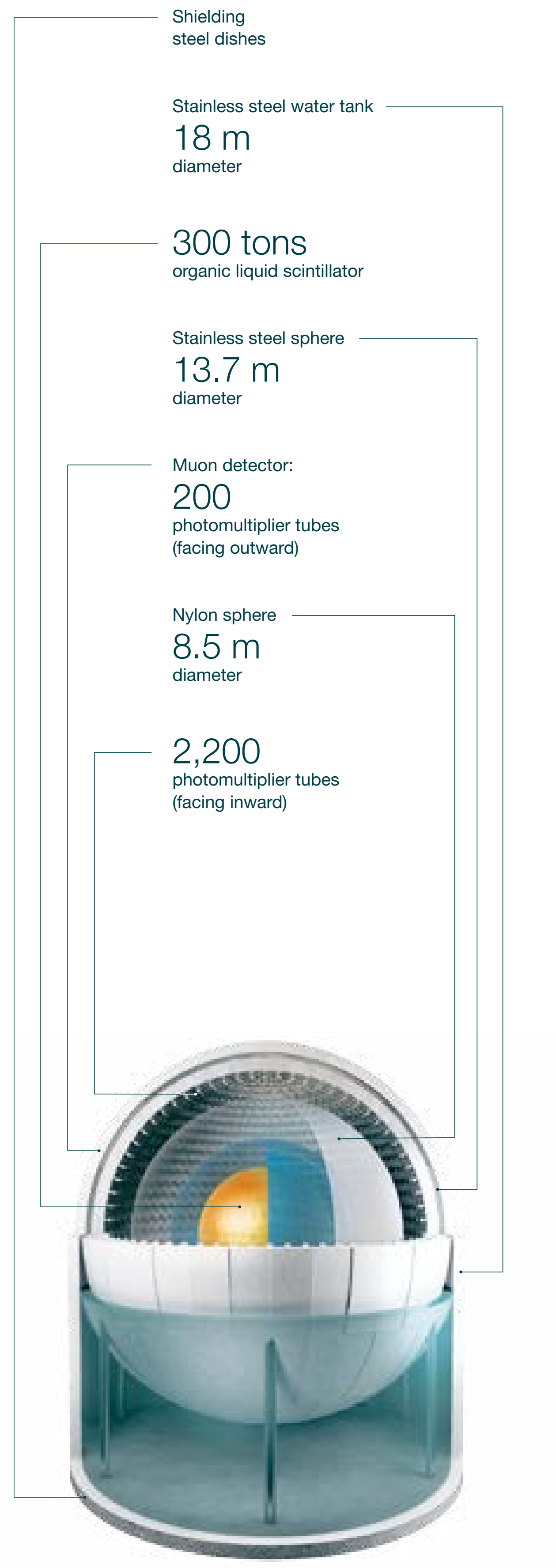
Picture credit: Eckert; graphics: ediundsepp

Fusion reactions inside the Sun

In principle, the Sun gets its energy from the fusion of hydrogen nuclei into helium. This involves a number of stages that produce heavy hydrogen (deuterium, D) and an isotope of helium with one neutron (helium-3) (top diagram) as intermediate products. At the same time, there is the Bethe-Weizsäcker cycle or CNO (carbon-nitrogen-oxygen) cycle, in which the elements act as a catalyst (bottom diagram). With all of these fusion processes, energy is released and a range of elementary particles are formed, including the neutrinos.







The actual Borexino detector is the innermost sphere (yellow), where incoming neutrinos create tiny flashes of light. This core is surrounded by a number of layers of shielding intended to intercept all disturbances from external radioactivity or decay processes. Photomultiplier tubes around the sphere amplify and record the strength and direction of the light flashes.

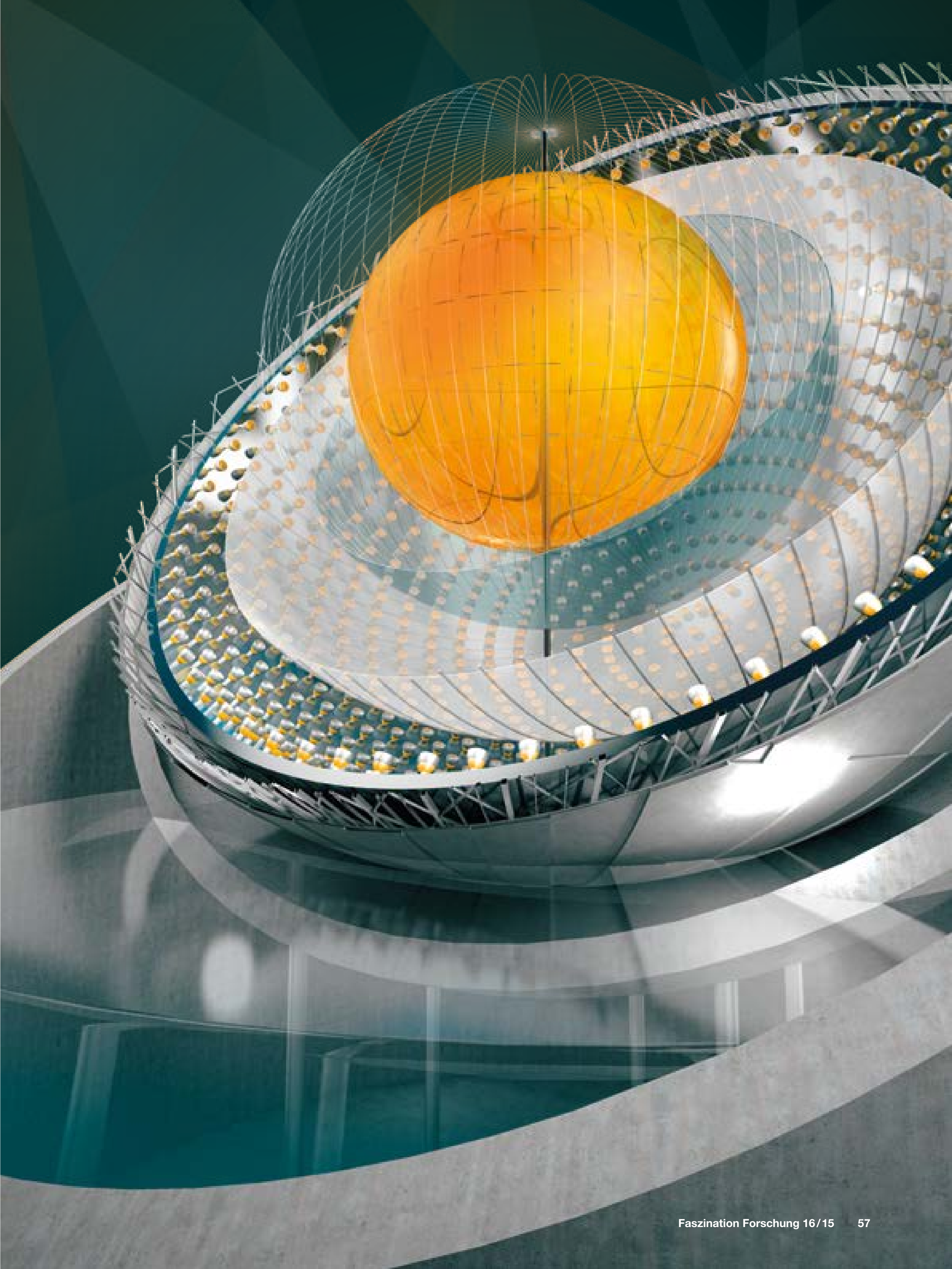
Graphics: ediundsepp

his colleagues Prof. Stefan Schönert and Prof. Franz von Feilitzsch. "In doing so, heavy hydrogen – a deuteron – and an electron neutrino are formed. These events are so rare that the radioactive background in the experiment plays a major role. At Borexino, we were the first in the world to prove the existence of these neutrinos."

A dream come true for the physics community

2014 marked a new highlight: at long last, the researchers in the underground laboratory were able to prove the existence of neutrinos from the core of the Sun that were the result of the very fundamental fusion of proton with proton. In this way, they could practically directly observe how hydrogen nuclei fuse together inside the Sun to produce energy – the fulfillment of an ancient physics dream. The generated pp neutrinos have very little energy and can therefore be detected only in extremely sensitive systems, since the lower the energy, the more difficult it is to distinguish the flash of light from the background for absolute proof. "We were very pleased that we were able to verify their existence with the required level of certainty after such a long time, because we have come to know our detector very well," says Oberauer. "We were able to really see for the first time where the Sun gets its energy from. This is the most fundamental reaction – the first ever reaction – everything else derives from it, including life on Earth."

The measurements taken benefited from the fact that the researchers constructed Borexino with particular care and attention. "We were able to measure in real time neutrinos with particularly low energies and thus provide quantitative information on the processes taking place within the core of the Sun. This was impossible with previous experiments," Stefan Schönert emphasizes. "The measurements were successful only because Borexino is the most sensitive detector on Earth and because we were able to massively reduce disturbances due to radioactivity and other cosmic particles." This was attributable to the care that was taken when setting up the experiment to ensure ▷



that all sources of radioactivity were diminished as much as technically possible. No normal materials were used, as these always contain some natural radioactivity. Instead, each component had to be composed of extremely pure material; the further into the system, the purer the material.

Incredible standards of cleanliness

The reason for these precautionary measures is that the Borexino detectors cannot, in principle, distinguish a natural decaying process from a neutrino event. "This means, however, that we have to be very careful and develop an incredible level of cleanliness. Materials cannot be purchased and transported as pure as we need them. Instead, we have to develop ways of purifying them," explains Oberauer. And that is what was done, using chemical and physical methods. For example, the liquid scintillator inside Borexino – in which some neutrinos generate their revelatory light flashes – contains trace elements of uranium and thorium with a concentration of less than 10^{-19} g/g. This means that, in reference to uranium and thorium, the liquid scintillator is 10 trillion times purer than any natural building material. "Borexino is now the purest spot in the world when it comes to radioactivity," claims Lothar Oberauer.

Nevertheless, a certain trace of radioactivity can never be fully avoided. In recent years, however, researchers have continually increased the precision of their measurements over a number of test series using artificial sources of radioactivity. They have identified an inner core of the liquid volume of around 100 tons, into which external interference can practically no longer penetrate. If only the measurements performed in this "fiducial volume" are accepted as valid, overall uncertainty concerning the measurements of ^{7}Be neutrinos can be reduced to about 5 percent. "It is interesting that theoretical predictions in astrophysics have an error margin of 8 percent," notes Oberauer. "That means that we measure more precisely than theory can predict." To get an idea of what kind of precision this means, consider that, of the 1.5 x 10^{21} (1.5 trillion billion) neutrinos that fly through the fiducial volume every day, only 48 are detected on average. And most of these are emitted due to the proton-proton fusion reaction in the Sun.

The new results, published in "Nature", present the first experimental proof that the release of energy inside the Sun has remained unchanged for a very long time. To prove this, researchers compared the values of current solar energy – which can now be measured using the new method – with values of the solar energy from more than one hundred thousand years ago – which can be calculated from solar radiation. The results of the comparison ▷

2,200 sealed, custom-made photomultipliers are arranged around the innermost sphere. These were subject to intensive prior testing to ensure that the material they are made of releases practically zero radioactivity. In addition, all electrical wires fed through the outer water-filled tank had to be completely sealed, which made assembly much more difficult.

Picture credits: Eckert;
Top right: Paolo Lombardi Infn Mi/LNGS

"We were able to measure in real time neutrinos with particularly low energies. This was impossible with previous experiments."

Stefan Schönert

tally with current theoretical solar models. In this way, the picture we have of the fusion processes inside the Sun is gradually coming together, although many of the measurements have yet to be more closely verified.

Do sterile neutrinos exist?

Nonetheless, fundamental questions remain unanswered, and these will command the attention of particle physicists in particular. Neutrinos have a characteristic that makes them very enigmatic: they exist in three different forms and change from one to the other – what physicists call neutrino oscillations. Previous measurements as well as Borexino have confirmed this theory, even if they do not seem to match the theoretical constructs of the standard model. In Borexino analysis, the solar matter effects on these oscillations were observed with unprecedented accuracy. There are now signs that there are "sterile" neutrinos, which are not subject to weak interaction. The existence of such exceptional particles is an as yet unproven hypothesis. "Many people are skeptical and their existence is the subject of a lively debate in the scientific community," says Oberauer. Stefan Schönert adds: "It must be examined experimentally in any case, since the consequences would be immense for particle physics. The proof of existence of sterile neutrinos would represent a revolution of sorts."

Schönert and Oberauer therefore co-initiated the setting up of a new experiment in Italy whose purpose is the search for sterile neutrinos.

Both physicists are also involved in preparing and developing other future neutrino experiments in China and Italy – these will build on the insights gained thus far and will be able to measure with even greater precision. Yet another objective at Borexino is to measure the neutrinos from the Bethe-Weizsäcker cycle more precisely, thus eliminating all remaining uncertainties regarding the generation of energy in the Sun. The topic is one that has taken a firm hold of Oberauer: "I think neutrinos are the most interesting objects any physicist can study. We have only just celebrated the discovery of the Higgs boson – a fantastic achievement, as it represents the final cornerstone in the standard model. Nevertheless, I am certain that the neutrino masses are not created due to the Higgs mechanism. These particles are, so to speak, our link to a new, unknown world."

Brigitte Röthlein

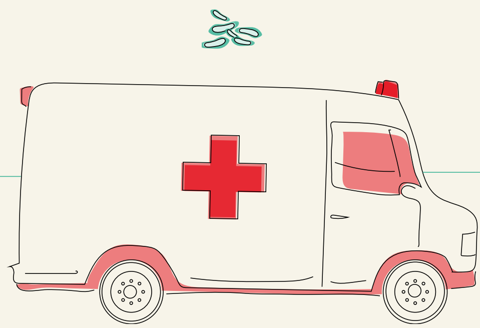
Physics professors Lothar Oberauer (above left) and Stefan Schönert (above right) jokingly refer to themselves as part of the "bedrock" of the Borexino research facility. They have been there from the beginning and will lend a hand in the conception and planning of future experiments. They are pictured here working on a detector for a new neutrino experiment.

Picture credits: Eckert

Graphics: ediundsepp; source: GERMAP2012

Overcoming
Antibiotic Resistance

Pathogenic bacteria are becoming increasingly resistant to standard antibiotics – and overcoming this public health risk calls for fresh approaches. That is why Prof. Stephan Sieber and his team are on a quest for totally new targets and their corresponding inhibitors. Rather than killing bacteria, his anti-virulence strategy is looking to neutralize or "tame" them – removing their claws, so to speak.



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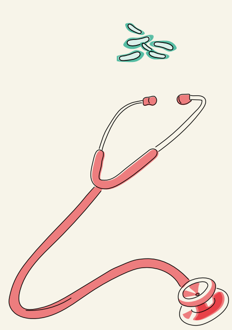
human

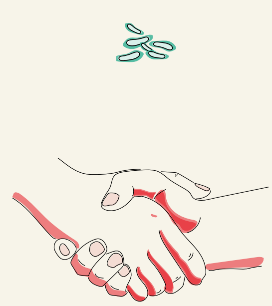
Hospitals account for
10–20% of antibiotic use

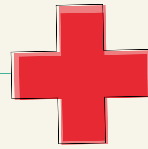
The use of antibiotics can result in the development of resistant bacteria

Antibiotics

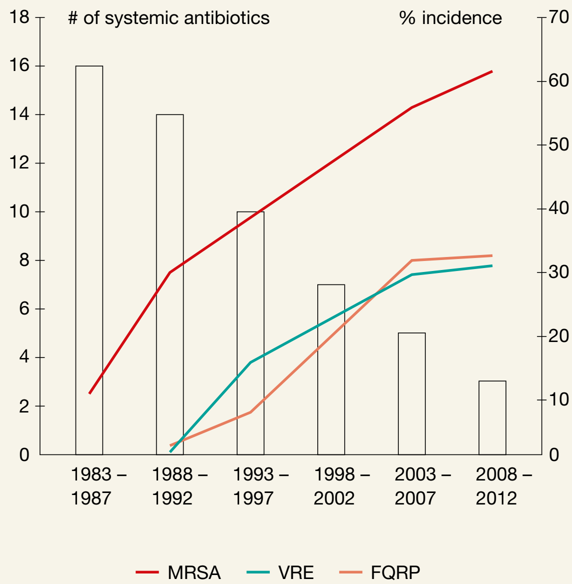


Resistant bacteria can develop inside the hospital or they can be brought in by patients. If they colonize doctors and nurses or contaminate surfaces, they can transfer to other patients

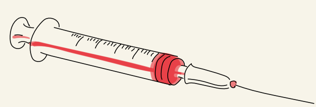




The use of antibiotics can result in the development of resistant bacteria



Between 1983 and 2012, the number of new systemic antibiotics approved by the US federal Food and Drug Administration continously declined. During the same time, the incidence rates with multiresistant bacteria rose. Shown here: methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococci (VRE), and fluoroquinolone-resistant Pseudomonas aeruginosa (FQRP).



Graphics: ediundsepp (source: TUM, GERMAP2012, Stellungnahme zur Antibiotika-Forschung, Leopoldina und Akademie der Wissenschaften in Hamburg, 2013)

Antibiotika-Resistenzen besiegen

Es ist eine gefährliche Kombination: Herkömmliche Antibiotika werden wirkungslos, weil immer mehr pathogene Bakterien resistent gegen Antibiotika werden – nicht nur gegen eines, sondern gleich gegen mehrere. Und es kommen kaum neue Antibiotika auf den Markt. Die Angriffsziele von Antibiotika in den Bakterien – die Bildung von Zellwand und von Proteinen sowie die Vervielfältigung der Erbinformation – sind abgenutzt. Deshalb ist es äußerst wichtig, neue Angriffsziele für Antibiotika oder Antibiotika-ähnliche Stoffe zu finden. Diesem Ziel hat sich der Chemiker Prof. Stephan Sieber mit seinen Mitarbeitern an der TUM in Garching verschrieben. Er verfolgt bei seiner Arbeit ein noch junges Konzept: die Anti-Virulenz. Hierbei geht es darum, die Bakterien durch Substanzen nicht abzutöten, sondern zu „zahnlosen Tigern" zu machen. Er spricht von Inhibitoren. Dies soll erreicht werden, indem sich geeignete Verbindungen an neue Angriffsziele in den pathogenen Bakterien binden und so verhindern, dass bestimmte Proteine, die zum Beispiel dem Ausbreiten der Bakterien im Körper und dem Kampf gegen das Immunsystem dienen, freigesetzt werden. Sind die Bakterien „zahnlose Tiger", kann das Immunsystem abschließend das Aufräumkommando spielen. Resistenzen können sich dabei nicht bilden. Sieber begann seine Forschungsarbeit mit ß-Lactonen, also Naturstoffen, die Bakterien nicht abtöten, aber bekämpfen. Mittlerweile konnte das Sieber`sche Team zwei Zielproteine in Bakterien identifizieren: Das erste ist ein proteinspaltendes Enzym (Protease) namens ClpP (caseinolytische Protease). Es schreddert nicht nur fehlgefaltete Proteine, sondern hat auch wichtige regulatorische Funktionen im Zusammenhang mit der Fähigkeit der Bakterien, den Menschen krank zu machen. Diese Fähigkeit bezeichnet man als Virulenz. ß-Lactone binden sich auf raffinierte Weise an das ClpP, sodass dieses durch strukturelle Veränderungen inaktiv wird. Damit wird das Bakterium an die Leine gelegt. Das zweite Angriffsziel ist ein sogenannter Transkriptionsaktivator, der aktiv wird, sobald die Bakterienzahl groß genug ist, um das Immunsystem erfolgreich anzugreifen. Er leitet dann in der Bakterienzelle das Ablesen wichtiger genetischer Informationen ein, sodass das Bakterium krankmachende Stoffe herstellen kann. Sieber und seine Mitarbeiter haben bereits die Substanz gefunden, die das verhindern kann. *Gerlinde Felix*

Link

www.oc2.ch.tum.de

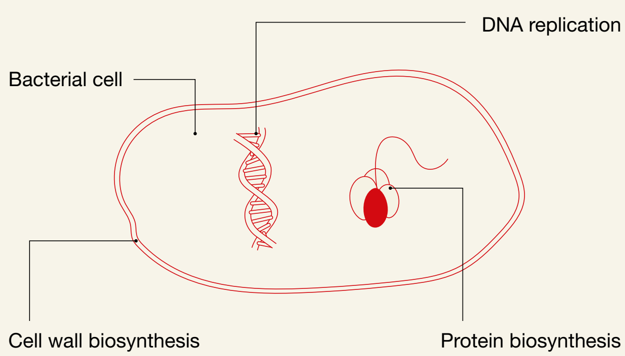
We all have our dreams – whether it be a sports car, the lottery jackpot or Olympic gold. A passionate researcher through and through, Stephan Sieber dreams of finding active agents that will prevent the growing resistance to antibiotics becoming a full-blown crisis. His priority is to develop agents with concrete medical applications. Since taking over TUM's Chair of Organic Chemistry II in Garching in October 2009, he has worked doggedly toward this ambition, building up a team that now numbers 24 researchers. Emphasizing the pressing nature of the problem, he points to a chart that shows a dramatic drop in the number of systemic antibiotics approved by the FDA in the US since 1983 – and an ominous rise in multidrug-resistant bacteria over the same time frame. This is partly due to a general lack of new antibiotics being developed. And this trend looks set to continue. Hospital "superbug" MRSA is a case in point. Though short for methicillin-resistant Staphylococcus aureus (S. aureus), the bacteria in question has built up a resistance not just to methicillin, but to a range of other antibiotics as well. In a future without either new antibiotics or fresh approaches to battle the onslaught of bacteria, mild infections could become severe or even fatal. The challenges are huge. But Sieber sees the answers to these challenges in his team members, giving them as much freedom as possible to work independently. "I hope that I can continue to work with such excellent and inventive self-starters – the quality of our research is largely in their hands." The team is focusing on the search for new targets within the bacteria, and effective agents with the ability to inhibit these target proteins.

From hostile pathogen to toothless tiger

Each of us carries bacteria like S. aureus. As long as they are only present in small quantities, these bacteria are able to hide from the immune system. They produce autoinducing peptides (AIPs), which they release into the surrounding environment to communicate with other bacteria. Only when the AIPs – and thus bacteria – reach a critical level do the bacteria switch from "stealth" to "attack" mode. "At that point, they know they are powerful enough to wipe out the immune system," explains Sieber. When they go into attack mode, the bacterial cells produce a selection of proteins or virulence factors. These include proteins that enable the bacteria to spread through the body, destroy cells, feed on those cells and weaken the immune system. Other proteins can cause tissue death, blood ▷

poisoning (sepsis), severe organ failure and circulatory collapse (toxic shock). The bacterial processes targeted by conventional antibiotics – cell wall synthesis, protein synthesis and DNA synthesis – have been exhausted. Over the years, bacteria have developed ways to sidestep the attacks launched by antibiotics, for instance through genetic mutation, and become resistant to them. Hence Sieber's quest for completely new targets, building on the relatively recent concept of anti-virulence. Here, Sieber and his team are focusing less on the bacteria-killing potential of new substances, and more on their ability to prevent the bacteria from producing virulence factors. The immune system can then take care of the rest. The major advantage of this approach is the fact that there is no selection pressure so that, according to Stephan Sieber, the risk of building up bacterial resistance ought to be relatively modest. An added benefit is that the normal flora in the intestines are not destroyed.

"The combination of biology, chemistry and structural chemistry all in one building is hugely beneficial to our work. It saves us a lot of time and makes it easy to try out new ideas spontaneously." — *Stephan Sieber*



Conventional antibiotics attack bacteria by blocking the building of cell walls or the replication of DNA, or by hindering the synthesis of proteins. Bacteria have developed ways to sidestep these attacks and thus become resistant to them.

Beta-lactones make a comeback: disarming rather than killing

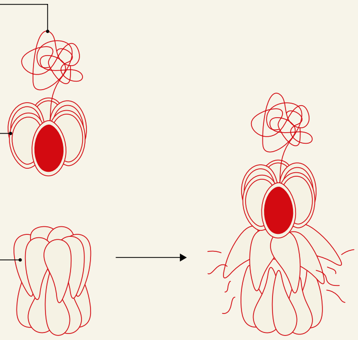
Now just turned 39, Sieber has been driven by a keen interest in bacteria and natural substances produced by organisms ever since working on his doctoral thesis in Germany and the US. Unsurprising, then, that on coming to TUM, the sporty chemistry professor chose to continue where he left off at Munich's Ludwig Maximilian University (LMU), researching the function of naturally occurring beta-lactones within the bacterial cell. A long-neglected substance class, ß-lactones are similar in structure to ß-lactams – a broad class of antibiotics that includes penicillin. In contrast ▷

Graphics: ediundsepp (source: TUM); picture credit: Eckert

Substances that do not kill the bacteria but prevent them from producing virulence factors help avoid resistance developing

Left: Chemist Prof. Stephan Sieber has a keen interest in bacteria and natural substances. His research focuses on finding natural substances that help disarm bacteria and thus offer an alternative to traditional antibiotics.

The protease ClpP acts as a sort of molecular scissors with 14 blades, snipping misfolded proteins into short segments. While ClpPs play a positive role in humans, they are also responsible for the pathogenic effect of bacteria.



to ß-lactams, however, ß-lactones are ill-suited to killing bacteria, leaving them sidelined by research. "But I was convinced that nature wouldn't simply produce a second-rate solution," recalls Sieber – and he proved to be right. As it turns out, ß-lactones can indeed prevent microbes such as S. aureus posing a threat to human health. This is because ß-lactones are anti-virulent, meaning that they strongly impair the pathogenic effect of S. aureus, in essence rendering the bacteria a "toothless tiger." But which proteins do the ß-lactones bind to in S. aureus? To find out, Sieber turned to activity-based protein profiling (ABPP) to monitor ß-lactone behavior with proteins – a complex method he learned during his postdoc period with US researcher Benjamin F. Cravatt at the Scripps Institute in La Jolla. ABPP enables examination of bacterial cells in aqueous solution with tagged chemical probes. The probe used by Sieber is a ß-lactone and the attached tag is an alkyne, or unsaturated hydrocarbon, which would not normally be present in S. aureus. An additional reporter tag that reacts with the alkyne enables visualization of the ß-lactone target protein in S. aureus using fluorescent in-gel analysis (SDS-PAGE analysis) and identification by mass spectrometry.

Targeting a specific protease

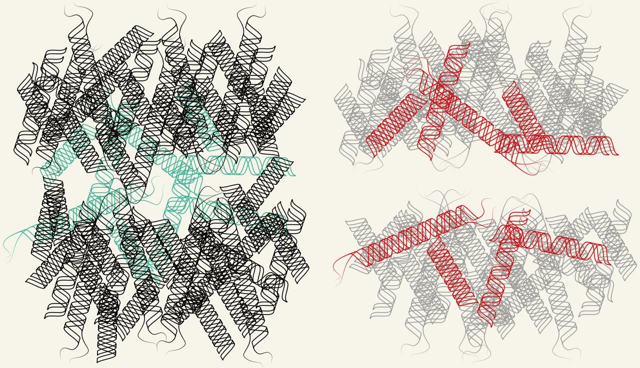
Sieber and his team established that their ß-lactone probe attaches to a proteolytic (or protein-splitting) enzyme or protease – in this case, caseinolytic protease, or ClpP. "ClpP is a giant protease consisting of 14 subunits – so a tetradecamer – and looks like a double donut," according to Sieber's brief description. Proteases are vital proteins that ensure order within a cell – hence they are often referred to as "housekeeping" proteins. If the bacteria cause an infection, oxidative stress ensues, triggering misfolded bacterial proteins. Here, ClpP acts as a sort of molecular scissors with 14 blades; each of its subunits houses an active site that can snip misfolded proteins into short segments. Since a serine atom is located in each active site, researchers also refer to ClpP as a serine protease. However, ClpP is more than just a housekeeping protein: it is also responsible for the pathogenic effect of S. aureus and other types of bacteria. So if it were possible to deactivate this serine protease, that would deal S. aureus a serious blow – which is where the ß-lactones come in. The Munich research team has determined that ß-lactones with a particular structure make good inhibitors and ▷

Picture credit: Ecker; graphics: ediundsepp (source: TUM) are able to bond very well with the reactive serine in a pocket in each of the ClpP's active sites – as long as the ß-lactone side chain is only eight carbon atoms in length. This bond renders the protease harmless. The structure of ß-lactones incorporates a characteristic electrophile four-ring form. "Without this quadruple ring and specific lactone geometry, the bond wouldn't be possible. But this is ideal," enthuses Sieber. So far, the Garching chemists have synthesized around 60 lactone derivatives in an effort to understand the exact relationship between ß-lactone structure and ClpP activity, and to identify the optimum candidates for a new antibiotic.

ClpP consists of 14 subunits – so a tetradecamer – and looks like a double donut

Double donut with a weak point

So how do the appropriately structured ß-lactones set about deactivating the ClpP? In one of two ways: If the ß-lactone has a side chain with residual hydrocarbons, they fill the pocket in each of the 14 active subunits, essentially disabling the blades of the molecular scissors. But the ClpP itself remains intact. Or – and this way only half of the active sites need blocking – they split the dual structure into two "donuts," so ending up with two heptamers. This is the case when the ß-lactone has an aromatic ring in its side chain. Each heptamer on its own is then completely inactive. "Incredibly, nature has fitted the ClpP with a predefined breaking point, which certain ß-lactones don't hesitate to use." Crystal structure analyses in collaboration with biochemist Prof. Michael Groll, based two floors above in the same building, have played an important role in revealing various secrets of the ClpP. Sieber views this extremely fruitful partnership with his colleague in crystallography as a major advantage over other research groups in the same field. Team members can just drop by at a moment's notice: "This combination of biology, chemistry and structural chemistry all in one building is hugely beneficial to our work. The physical proximity saves us a lot of time and makes it easy to try out new ideas spontaneously," declares Sieber. ▷



Right: Disarming bacteria: S. aureus with disabled ClpP cannot act on the blood sample (red), while untreated S. aureus does kill blood cells (dark area).

Left: Splitting the ClpP into a double "donut" disarms their virulent function: certain ß-lactones, which have an aromatic ring in their side chain, can do that.

Graphics: ediundsepp (source: TUM); picture credit: Eckert

> *"I hope that I can continue to work with such excellent and inventive self-starters – the quality of our research is largely in their hands."* *Stephan Sieber about his team*

Promising inhibitors in the pipeline

Despite the general euphoria, it has to be said that ß-lactones come with a catch: they are unstable and need to be injected. So oral administration would not be an option. But: "We can do better than that," resolved Sieber, thinking that there must be more stable compounds that would also be suitable. Sure enough: "Working with the Max Planck Institute of Molecular Physiology in Dortmund, we used high-throughput screening of 138,000 chemical compounds to identify a few that can block or completely deactivate the ClpP even without the ß-lactone four-ring structure." The outcome was seven or eight compounds that bind to the ClpP's active sites. Each compound contains a phenyl ester and splits the ClpP into two "donuts." These phenyl ester compounds have actually proved more stable and effective than ß-lactones in tests to date. "But we don't yet know how they behave in animals." ß-lactones, on the other hand, have already proved effective in mice and could progress to clinical trials in three to four years' time – provided a major investor is found. Meanwhile, another group of new compounds with properties similar to antibiotics has also been identified. For the moment, though, Sieber is keeping them under wraps, divulging only that they do hold great potential.

Second target: stopping armament

The second target Sieber and his team have isolated within S. aureus is associated with production of the virulence factors previously described. When the bacteria determine that it is worth launching an assault on the human organism, a cascade of reactions is triggered in the bacterial cell. These culminate with a molecule capable of binding to genetic information – known as a transcriptional activator – which is slightly but effectively modified so that it can form a strong bond to genetic material from S. aureus. In this way, it initiates transcription of the genes that carry the blueprints for the bacteria's virulence factors or "weapons." So the transcriptional activator and necessary bond to the genetic material present another target for anti-virulence efforts. But what compound could be used to sabotage this bond to the genetic information? Here, Sieber turned his attention to alpha-methylene-gamma-butyrolactones – a large class of natural compounds – to select an inhibitor, synthesizing numerous derivatives with his team. And not without success: When these substances are added to S. aureus, hemolysin – one of the most important virulence factors – is no longer released, for example. A drawback of this particular source of hope, however, is that it is toxic to human cells. But Sieber is not giving up just yet: "We're trying to alter the compound accordingly. Though it's unfortunate that the toxicity stems from the exact part we need for the bond to the transcriptional activator."

Alongside his research efforts, Stephan Sieber also gives lectures – by preference on natural substances. His trademark black suit makes him TUM's best-dressed chemistry professor, as far as students are concerned. And every December, it accompanies him on his trips to the German Institute of Science and Technology (GIST) at TUM Asia, founded in 2002 in Singapore, where he holds intensive lecture series for chemistry students. At around two meters tall, his size alone sets him apart there – and he frequently gets caught on Christmas decorations on the escalators. Fortunately, in life, as in research, obstacles leave Sieber undeterred. *Gerlinde Felix*

Picture credits: Eckert

Link
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Neuroscience Award Honors Optical **Technique That sheds Light on the Living Brain**

TUM Professor Arthur Konnerth is one of four winners of this year's Grete Lundbeck European Brain Research Prize, a million-euro award for neuroscience. The 2015 Brain Prize is being awarded for "the invention, refinement and use of two-photon microscopy to provide detailed, dynamic images of activity in individual nerve cells, dendrites and synapses, thereby transforming the study of development, plasticity and functional circuitry of the brain."

Arthur Konnerth has led pioneering studies of how the brain works – in good health as well as under the effect of neurodegenerative diseases such as Alzheimer's – from intra- and intercellular functioning to behavior. Several ground-breaking discoveries have been enabled by his use of optical techniques, including two-photon microscopy, which allows highly specific observation of brain activity in living animals. Konnerth first worked at TUM in 1999–2000, when he conducted an essential part of the award-winning research (published in 2003). In 2006 he became the founding chair of TUM's Friedrich Schiedel Institute for Neuroscience. He is also a Carl von Linde Fellow of the TUM Institute for Advanced Study and a principal investigator in the Excellence Clusters SyNergy (Munich Cluster for Systems Neurology) and CIPSM (Center for Integrated Protein Science Munich).

From cells to circuits, in illness as well as health

In 2003 Konnerth and colleagues pioneered an imaging method that permitted for the first time the analysis of cortical circuits with single-cell resolution. This method is nowadays used in many laboratories worldwide to improve

TUM Prof. Arthur Konnerth, Friedrich Schiedel Institute for Neuroscience, shares in the million-euro Brain Prize for 2015.

Picture credit left: Heddergott/TUM
Graphics right: ediundsepp (source: Christine Grienberger/TUM)

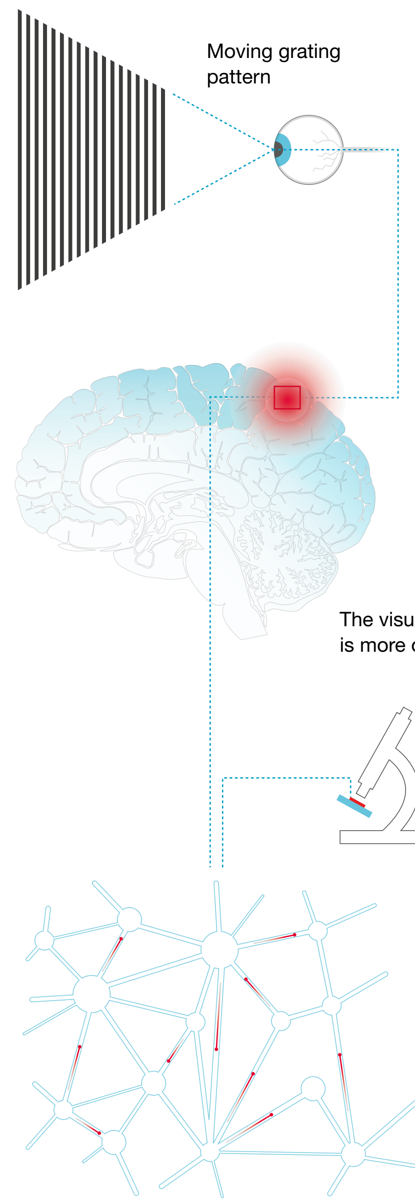
our understanding of how the brain controls behavior in animals. More recently they further improved their method, allowing them in 2010 to observe a mouse in the act of seeing, with resolution that went beyond a single nerve cell to a single synapse. This achievement enabled them to map the functional links between brain cells in detail. The scientists combined two-photon flourescence microscopy – making it possible to look up to half a millimeter into brain tissue and view not only an individual cell, but even its fine dendrites – with the so-called patch-clamp technique, which let them conduct electrical signals to individual dendrites. This study showed for the first time that an individual neuron integrates input representing multiple sensory features into a well-defined, unique output signal: a decision, in essence, made automatically by a single nerve cell.

Observing distinct stages of Alzheimer's disease

Another key discovery came in 2012, from in vivo single-neuron experiments with a mouse model of Alzheimer's disease. Konnerth's group observed correlations between increases in both soluble and plaque-forming beta-amyloid – a protein implicated in the disease process – and dysfunctional developments on several levels: individual cortical neurons, neuronal circuits, sensory cognition, and behavior. Their results showed that these changes progress in parallel and that, together, they reveal distinct stages in Alzheimer's disease with a specific order in time.
In 2013, a combination of optical techniques shed light on the brain's "slow waves," rhythmic signal pulses that sweep through the brain during sleep and are assumed to play a role in processes such as the consolidation of memory. The slow waves can be observed in very early stages of development, and they may be disrupted in Alzheimer's and other diseases. In this study, two-photon microscopy was used in conjunction with optogenetics, an approach that enabled spatially defined stimulation of small numbers of neurons. Konnerth's group showed conclusively that slow waves start in the cerebral cortex, ruling out other longstanding hypotheses. The researchers also found that such a wave can be set in motion by a single tiny cluster of neurons. "Out of the billions of cells in the brain," Konnerth explained, "it takes no more than a local cluster of fifty to one hundred neurons in a deep layer of the cortex, called layer 5, to make a wave that extends over the entire brain."

Patrick Regan (TUM)

Studying the brain activity of a mouse while it is being visually stimulated with a moving grating pattern of light and dark bars. By observing in vivo with two-photon flourescence microscopy how neuronal signaling responded to the stimulation, Konnerth's team could characterize the visual circuit as being more or less "tuned" to specific orientations and directions of movement. The scientists were able to correlate these dysfunctional developments with distinct stages of Alzheimer's disease.



The Brain Prize

The Grete Lundbeck European Brain Research Prize – "The Brain Prize"– is awarded to one or more scientists who have distinguished themselves by an outstanding contribution to European neuroscience and who are still active in research. The sponsor of the prize is the Grete Lundbeck European Brain Research Foundation, a charitable, non-profit organization founded by the Danish Lundbeck Foundation. Arthur Konnerth shares the 2015 Brain Prize with Winfried Denk (Max Planck Institute of Neurobiology, Munich, Germany), David Tank (Princeton University, New Jersey, USA), and Karel Svoboda (Howard Hughes Medical Institute, Maryland, USA). The million-euro award is a personal prize, to be shared equally among the awardees. It was presented in Copenhagen on May 7 by Crown Prince Frederik of Denmark.

Authors

Gerlinde Felix is a freelance medical and science journalist. She studied physics and medicine. Gerlinde Felix works for newspapers, magazines and online publications, as well as for research institutions. In 2011, her book “The Healthy Liver” was published.

Birgit Fenzel studied German language and literature, philosophy and educational sciences before starting her career in journalism. After finishing university and completing a year of voluntary service, she worked as an editor for a daily newspaper, also completing freelance assignments for other public service broadcasters. She worked on scientific articles for the ddp news agency and was most recently employed as an editor at the Max Planck Society.

Patrick Regan has been a member of the TUM Corporate Communications Center since 2009. He came to TUM from PBS and NPR affiliate New Jersey Public TV and Radio in the US, where he produced 800 news reports on science and technology and hosted two interview series. In prior work at Bellcore and Bell Labs, he served as a science writer, magazine editor, executive speech writer, media relations manager and corporate spokesperson. He is a senior member of the IEEE.

Dr. Brigitte Röthlein has been working since 1973 as a science author for magazines, TV and radio broadcasting and for newspapers. She holds a degree in physics and a Ph.D. in communication science, education science and history of natural sciences.

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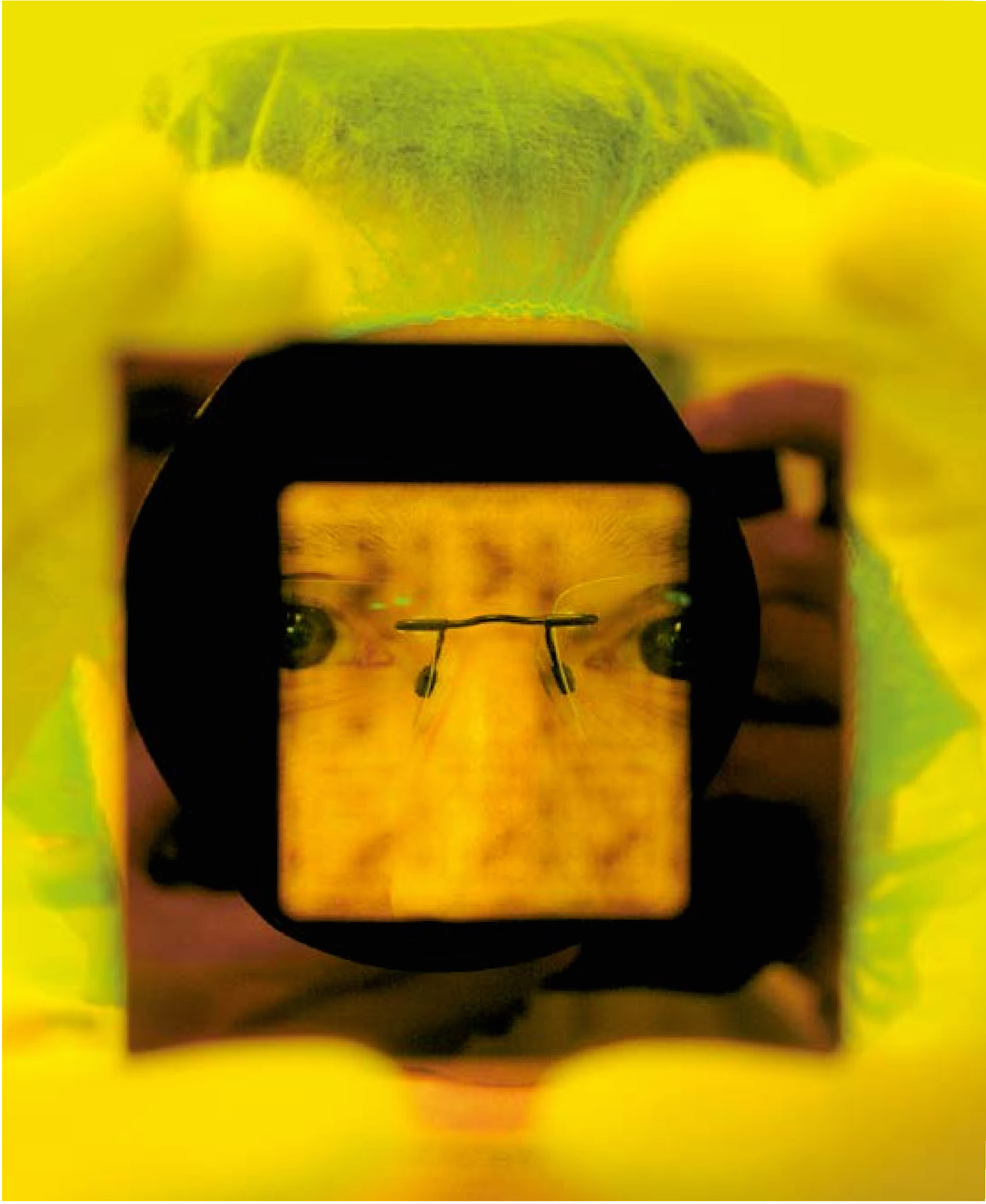

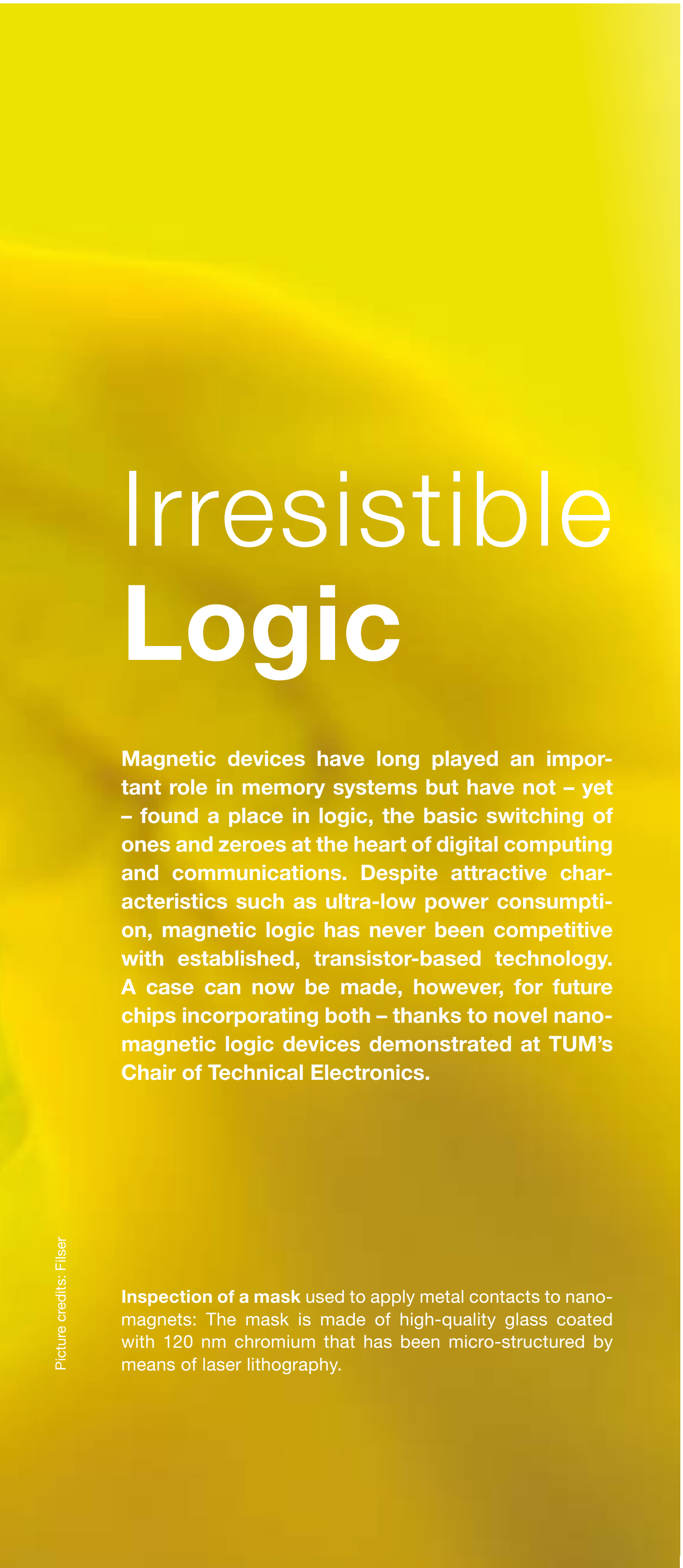

Irresistible **Logic**

Magnetic devices have long played an important role in memory systems but have not – yet – found a place in logic, the basic switching of ones and zeroes at the heart of digital computing and communications. Despite attractive characteristics such as ultra-low power consumption, magnetic logic has never been competitive with established, transistor-based technology. A case can now be made, however, for future chips incorporating both – thanks to novel nanomagnetic logic devices demonstrated at TUM's Chair of Technical Electronics.

Inspection of a mask used to apply metal contacts to nanomagnets: The mask is made of high-quality glass coated with 120 nm chromium that has been micro-structured by means of laser lithography.

Picture credits: Filser

3D-Anordnungen von Nanomagneten machen magnetische Computer attraktiv

In der Computertechnologie spielten magnetische Effekte bisher eine wichtige Rolle für Speicher. Im Hinblick auf logische Funktionen – dem allem digitalen Rechnen zugrundeliegenden Schalten zwischen Nullen und Einsen – konnte die Technik jedoch nie mit den auf Transistoren beruhenden integrierten Schaltungen konkurrieren. Mittlerweile steht der Industriestandard für digitale Computerchips, die CMOS-Technologie, vor grundlegenden Herausforderungen, denn die stetige Verkleinerung der Transistoren und die immer größere Packungsdichte der Schaltelemente auf einem Chip stoßen an Grenzen. Weltweit suchen Forscher nach völlig neuen Alternativen. Ein solcher Ansatz besteht im magnetischen Computer. Vielversprechende Experimente am TUM Lehrstuhl für Technische Elektronik zeigen auf, wie nanometergroße Magnete zu digitalen Logikgattern arrangiert werden können. Erzielt wurden diese Fortschritte im Rahmen einer langjährigen Zusammenarbeit mit der University of Notre Dame und dem TUM Lehrstuhl für Nanoelektronik. Der jüngste Durchbruch der Forscher war die Demonstration eines dreidimensionalen nanomagnetischen Logikgatters. Eine solche Struktur eröffnet die Möglichkeit, durch dreidimensional angeordnete Bausteine eine sehr hohe Packungsdichte auf der Chipoberfläche zu realisieren. Statt wie konventionelle Logik-Bausteine elektrische Ströme zu schalten, arbeiten die nanomagnetischen Strukturen durch Überlagerung magnetischer Felder. Einige ihrer Eigenschaften könnten für künftige Chips und Computersysteme hochattraktiv sein: Nanomagnetische Logikbausteine wären zum Beispiel nicht flüchtig, sie würden also ihre „1“ oder „0“ Zustände auch im ausgeschalteten Zustand behalten. Selbst im Betrieb würden nanomagnetische Schaltungen deutlich weniger Energie verbrauchen als vergleichbare Lösungen mit Transistoren. Außerdem könnten nanomagnetische Bausteine mit magnetischen Speichern integriert werden und so völlig neue Rechnerarchitekturen für Spezialanwendungen ermöglichen. Aus Sicht der TUM Forscher ist die Kompatibilität der nanomagnetischen Technologie mit CMOS besonders wichtig. Dadurch lassen sich zum einen gängige Produktionstechnologien einsetzen, um so ökonomisch von Skaleneffekten für die Massenproduktion zu profitieren, und zum anderen werden innovative Synergien zwischen den beiden Technologien möglich.

Patrick Regan (TUM)

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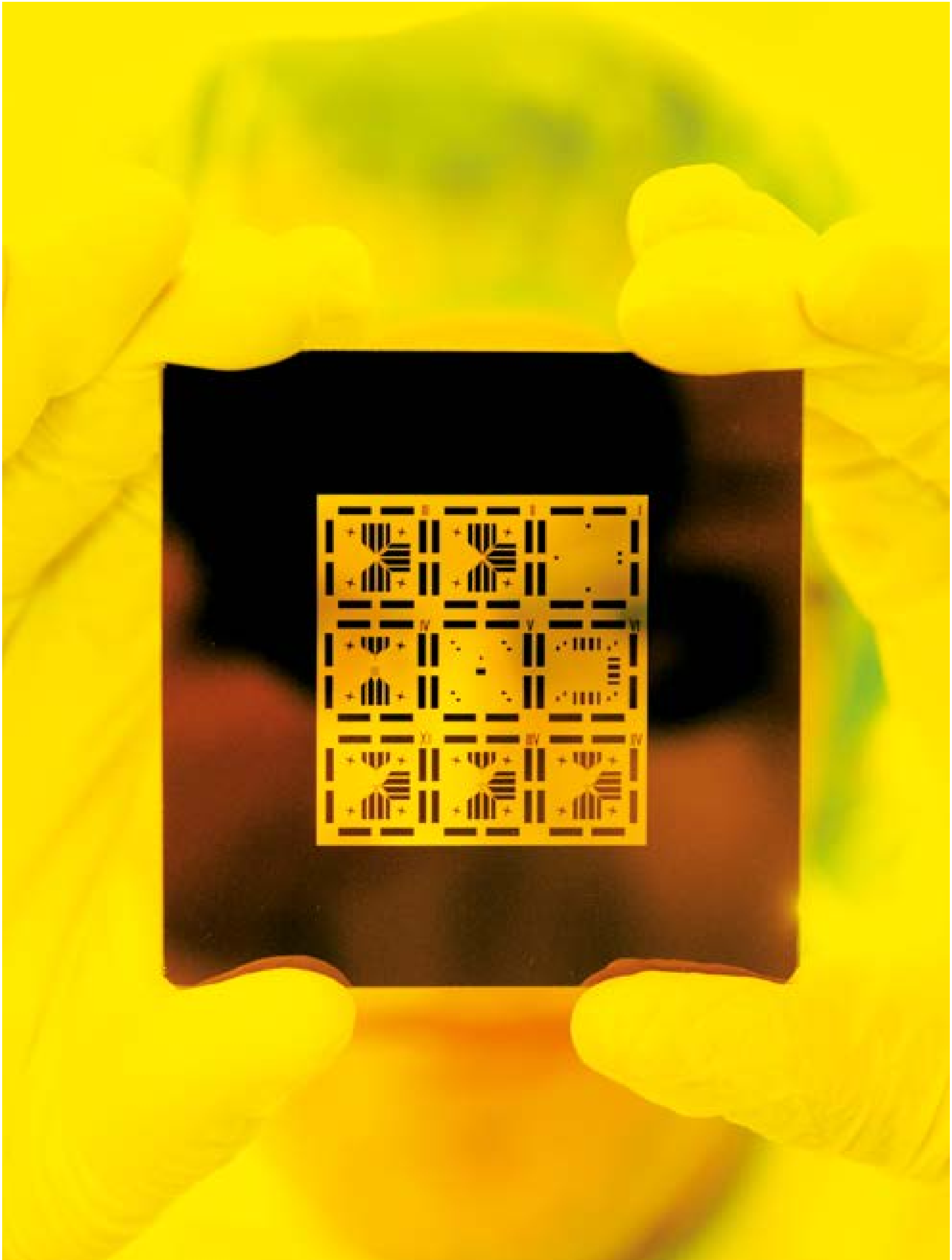
The transistor is one of the most basic building blocks of present-day civilization: This solid-state electronic gate switches the digital bits that define the information age. You can't see transistors any more, but they're everywhere you look. And in fact, they are everywhere you look largely because you can't see them. With features as small as a few tens of nanometers, transistors in the millions or even billions crowd the surface of integrated circuits – processors, memory components, controllers and single-chip realizations of whole systems. Beyond what they've done for computing, these chips, together with the intangible machinery of coding algorithms and software, have of course become the brains of the smart phone, the core of the car, part and parcel of everything from appliances to aircraft. This much of the story is widely known and fairly well understood.

"In applications such as parallel computing, data mining and pattern matching, nanomagnetic computing could have advantages over CMOS."
Markus Becherer

What most denizens of today's information society do not appreciate and ideally need not know is that the stream of innovations they rely on flows from a hidden source: a crucible of marketplace competition, proprietary research and development, and precompetitive cooperation. It's the cooperative effort of drawing up and periodically revising a "roadmap" that has enabled the semiconductor industry, for decades now, to deliver steady, even predictable improvement in the capabilities and performance of integrated circuits while also bringing down costs.

A particular focus is on reducing the size of transistors, thus increasing their density on a silicon chip – especially within the technology system known as CMOS, or complementary metal oxide semiconductor. The workhorse of the industry, CMOS has performed like a racehorse in negotiating the famous "Moore's curve," which charts an aggressive path for processing power or memory at a given price. The expectation of endless progress, which the public takes for granted, rests on a vast amount of behind-the-scenes effort, cooperative as well as competitive. Obstacles are identified many years in advance, spurring the intensive research and development needed to stay on track.

The obstacles now in sight may be the most challenging in the industry's history. Much progress to date has depended on scaling, with the development of ingenious ways to design and manufacture chips with ever smaller transistors. Make the transistor small enough, however, and quantum effects like tunneling come into play, exacerbating ▷

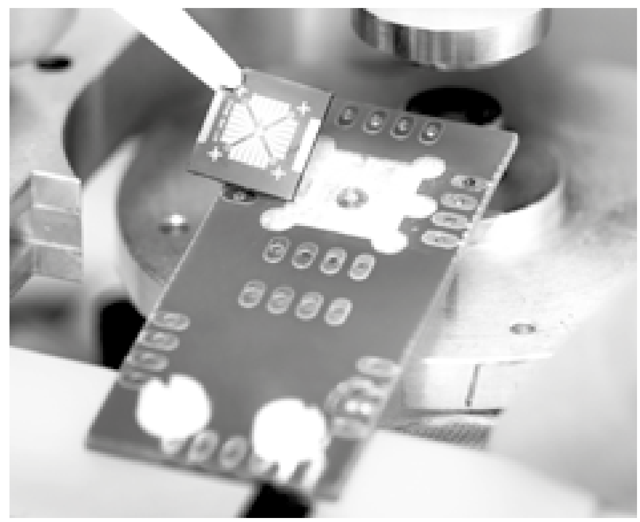


Picture credit: Filser

Picture credits: Filser

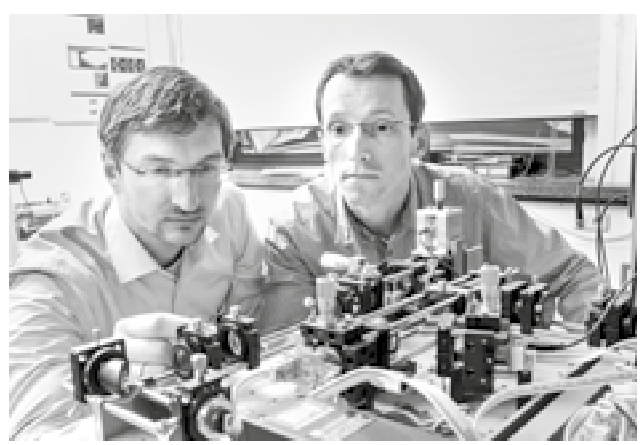
The nanomagnets are produced and characterized in the laboratory. Left: An electron beam evaporation system is used to deposit copper on the magnet sample's surface. The sample is placed above an electric coil (top right) to enable hysteresis measurements inside a magneto-optic Kerr microscope, which the scientists built themselves (bottom right).

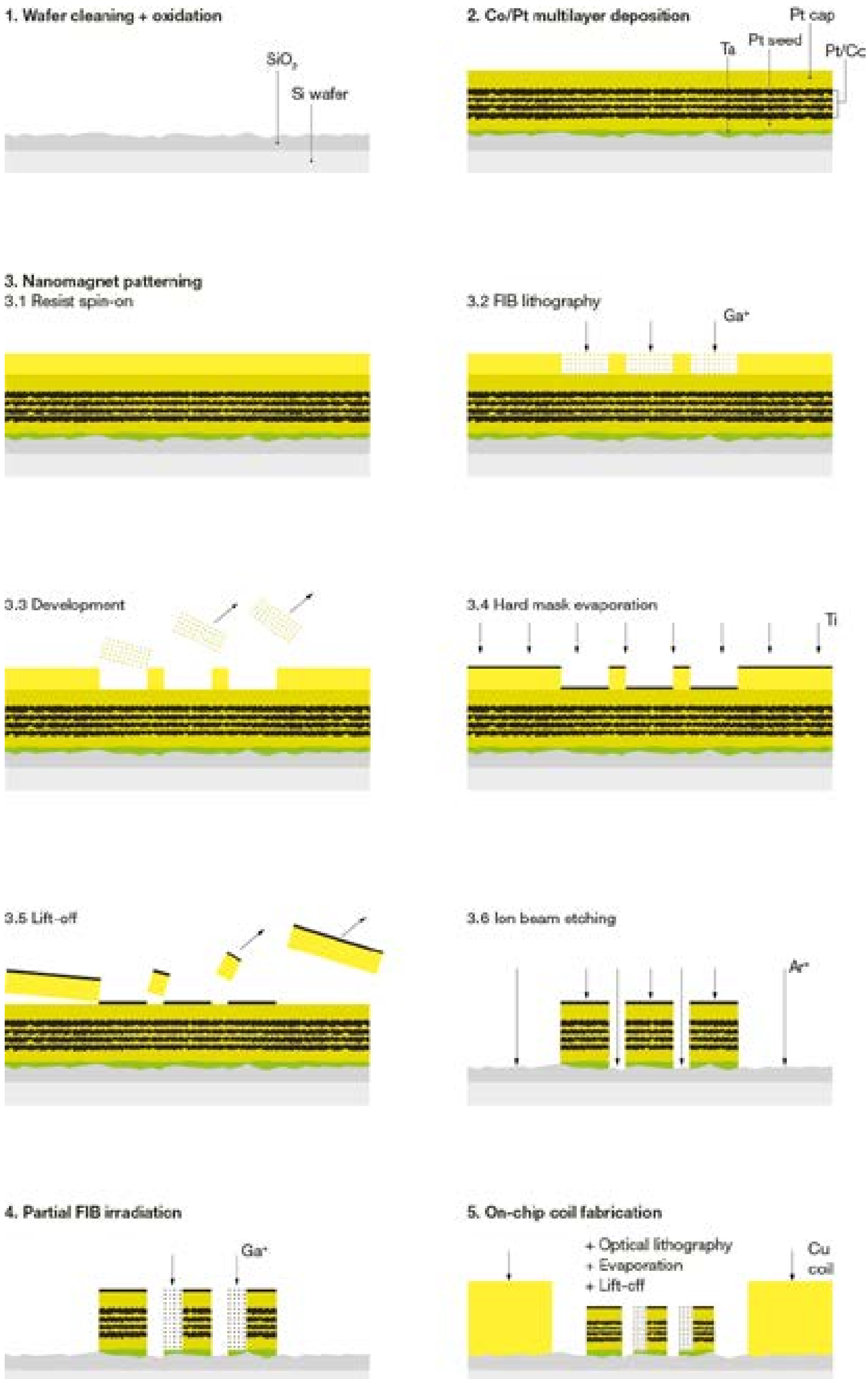
practical issues including power consumption. The smaller and more densely packed transistors are, the more power is wasted – not only when switching, but even in an idle state. These and other looming problems have created an opening for radical thinking. As the latest edition of the International Technology Roadmap for Semiconductors (ITRS) says: "Looking at long-term devices and systems (7 – 15 years horizon, beyond 2020), the 2013 ITRS reports on completely new devices operating on completely new principles amenable to support completely new architectures." In other words, it's time to consider a fork in the industry roadmap – if not several branching paths – to ensure that this foundational technology is not going to hit the wall. Groups around the world are probing a range of possibilities, even some that involve computing without transistors.



Magnetic computing now

The idea of magnetic computing goes back at least to the 1950s, and it engaged bright minds at research powerhouses including IBM and Bell Labs. Magnetic logic, however, was not viewed as being competitive with semiconductor-based technologies, which by the mid-1970s had already out-competed even the most successful magnetic technology, core memory. The idea never quite died, even as researchers moved on to greener pastures. Today, though, the approach under investigation at TUM truly could be considered, in the words of the ITRS, "completely new."
According to Dr. Markus Becherer, leader of a research team at TUM, computing based on nanometer-scale magnetic devices has some inherently attractive characteristics, ▹



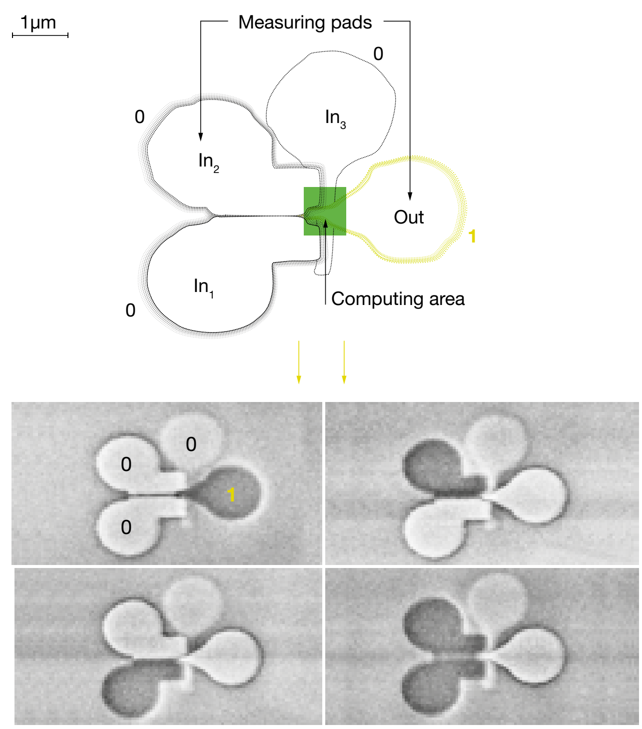


Picture credits: ediundsepp (source: TUM)

Stacking ten nanomagnetic gates yields a ten times higher area density

beginning with ultra-low power consumption. And it's fairly easy, he adds, to identify applications in which nanomagnetic technology could have advantages over CMOS, such as parallel computing, data mining and pattern matching. "The biggest questions arise," Becherer says, "when you think about all of the requirements that need to be fulfilled, all the numbers that have to be matched, to build a fully functioning and competitive system. If just one property fails to meet the mark – say, with regard to mass production, variability or manufacturing cost – then the technology cannot be exploited for applications." It's this big-picture view that motivates Becherer's team, based in Prof. Doris Schmitt-Landsiedel's Chair of Technical Electronics, and helps to prioritize goals for their experimental program.

Since 2009 the group has demonstrated several advances toward practical nanomagnetic logic. Key contributions have been made by doctoral researchers Stephan Breitkreutz-v. Gamm, Irina Eichwald, Josef Kiermaier, Xueming Ju and Gražvydas Žiemys. Also vital, from the start, has been collaboration with researchers at the University of Notre Dame and with TUM colleagues in Prof. Paolo Lugli's Chair of Nanoelectronics. Crucial early steps included novel techniques for fabricating nanomagnets and for characterizing the new breed of circuits that would employ them. By 2012 a new family of building blocks for digital integrated circuits – nanomagnetic logic gates – began to appear. With successive experiments, the researchers have strengthened the case that some future computer chips could be based on arrangements of nanometer-scale magnets. A major result in 2014 was the demonstration of a three-dimensional ▹



Magnetic force microscopy images of a 3D majority logic gate. In_1, In_2, In_3 and Out indicate the input and output nanomagnets (In_3 is located 60 nm below the others). The areas shown in the image are pads used by the scientists to measure the magnetic state of each magnet. The actual computing area is about 550 by 700 nm in size. Shown here is a NOR gate, which yields "1" whenever all inputs are set to "0" and "0" otherwise. For laboratory operation, the magnetization of the input magnets is set via copper coils on the chip. In practice, the magnets would be set by preceding magnets in the circuit.

The production process for nanomagnetic logic devices starts with a silicon wafer, onto which a multilayered sandwich of cobalt (Co) and platinum (Pt) is deposited via RF magnetron sputtering (1, 2). This multilayer film is patterned into isolated Co/Pt nanomagnets using focused ion beam (FIB) lithography for shaping the magnets and argon (Ar) ion beam etching to remove the remaining material (3.1 – 3.6). Partial FIB with Ga^+ ions is the key process to lower the magnetic anistotropy of the nanomagnets by disrupting the stable interfaces between the Co and Pt layers (4). The magnetization can then easily be set by an external magnetic field generated by copper coils, which are produced in a final step by optical lithography (5).

The most basic building blocks are around 30 by 60 nanometers in surface area

nanomagnetic device – implementing a so-called majority logic gate – that could operate in vertical stacks.
Devices based on this approach would compute not by switching electric currents but by controlling coupled magnetic fields – more specifically, through the influence of each nanomagnet's "stray field" and the propagation of tiny "magnetic domain walls." Thus, the devices would be non-volatile, meaning that logic elements could remember their states even with the system turned off. Drawing no current at all when idle, such circuits would consume very little power even when operating – and would waste next to nothing, since magnets don't "leak." An additional advantage is that they should be more resistant to electromagnetic radiation than CMOS integrated circuits, particularly at the short wavelengths of X-rays and gamma rays. Finally, the option of stacking large numbers of magnetic gates on top of each other might make them irresistible in terms of integration density: having ten gates stacked, for example, the density is ten times higher within the same footprint.
The researchers explain the underlying principle of the nanomagnetic majority logic gate with a simple illustration: Think of the way ordinary bar magnets behave when you bring them near each other, with opposite poles attracting and like poles repelling each other. Now imagine bringing several bar magnets together and holding all but one in a fixed position. Their magnetic fields can be thought of as being coupled into one, and the "north-south" polarity of the magnet that is free to flip will be determined by the orientation of the majority of fixed magnets. Gates made from field-coupled nanomagnets work in an analogous way, with the reversal of polarity representing a switch between Boolean logic states, or the binary digits 1 and 0. In the team's 3D majority logic gate, the state of the device is determined by three input magnets, one of which sits 60 nanometers below the other two, and is read out by a single output magnet. ▷

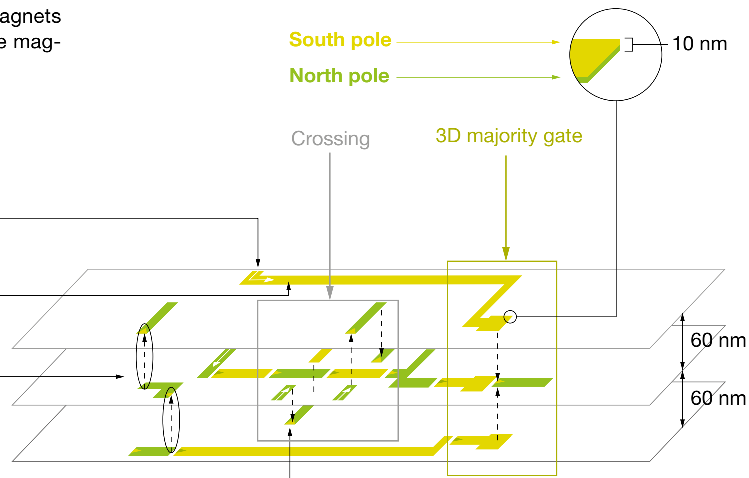
A fruitful collaboration

These advances in computing based on nanomagnets are the fruit of a longstanding collaboration between TUM and the University of Notre Dame in South Bend, Indiana, USA. The work builds on capabilities ranging from sophisticated simulations of magnetic behavior to innovative fabrication and measuring techniques.
A central figure is Gyorgy Csaba, who did his doctoral research with Prof. Wolfgang Porod at Notre Dame. Csaba did the initial proof-of-concept simulations on nanomagnetic logic. He then moved to Prof. Paolo Lugli's Chair of Nanoelectronics at TUM but continued to provide modeling support for Notre Dame's emerging experimental program. He realized that similar ideas could also be tested with technology available just three buildings away, at Prof. Doris Schmitt-Landsiedel's Chair of Technical Electronics: specifically, the ability to grow cobalt-platinum multilayers and to pattern devices using focused ion beams. Markus Becherer took the lead in starting the experimental work there, while doctoral candidates in the Chair of Nanoelectronics did some of the important simulation research under Csaba's guidance.
Over the years, members of the TUM team have spent time at Notre Dame. Porod, as a Fellow of the TUM Institute for Advanced Study, has made many visits to Munich. And when Csaba eventually returned to Notre Dame as a research associate professor, the strong ties were kept up. The experimental programs at Notre Dame and TUM are based on different types of structures, different materials and different patterning techniques. Yet throughout, the researchers' partnership has been extremely productive, with mutual feedback and strong complementary contributions.

A team that thinks outside the box: Stephan Breitkreutz-v. Gamm, Markus Becherer, Gražvydas Žiemys and Irina Eichwald (from left) are investigating the potential of 3D nanomagnets for a radically new computing technology.

Picture credit: Filser

Cross-section through a 3D nanomagnetic device: Nanomagnets can be arranged in several layers. Signal transfer between the magnets happens via magnetic coupling fields, without wires.



The road ahead

There are several reasons why nanomagnetic logic can allow very dense packing. The most basic building blocks, the individual nanomagnets, will be around 30 by 60 nanometers in surface area and thus are comparable in size to individual transistors. Furthermore, where transistors need contacts and wiring, nanomagnets operate purely with coupling fields, requiring only on-chip copper coils to control the magnetic field of the nanomagnets. Also, in building CMOS and nanomagnetic devices that have the same function, it can take fewer magnets than transistors to get the job done. For example, a so-called full-adder demonstrated by the TUM team consisted of just five interacting magnets whereas, depending on the architecture, 20 to 30 CMOS transistors would be required. Finally, breaking out of the 2D design space with stacks of 3D nanomagnetic logic gates is a step with truly disruptive potential.

The 2013 International Technology Roadmap for Semiconductors gave some serious attention to magnetic computing

In its 2013 edition, the International Technology Roadmap for Semiconductors gave some serious attention to magnetic computing, in a chapter on "Emerging Research Devices." Soon after, the "Journal of Physics D: Applied Physics" published "The 2014 Magnetism Roadmap," which featured a review of nanomagnetic logic by TUM's Stephan Breitkreutz-v. Gamm. The challenges outlined in his paper are daunting, but the evidence and arguments in favor of this technology are compelling.

One of the most provocative observations is that the strict separation of logic and memory in the classic "von Neumann" computer architecture – which underlies most of the computers that have ever existed – is redundant if your logic runs on non-volatile nanomagnets instead of transistors. Thus, progress in magnetic logic might inspire, or require, rethinking some of the basics of computer science.

A higher priority for Becherer's team, however, is ensuring that there will be a constructive synergy between magnetic computing and CMOS. The best outcome they can envision is not for their nanomagnetic logic technology to "beat" the competition, but rather to join it.

Patrick Regan (TUM)

Picture credits: ediundsepp (source: TUM)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Academia and Industry – **Partners in Innovation**

Never has innovation been viewed as more critical to growth, employment and prosperity than today. For Europe, stepping up its game is a must.

Dr.-Ing. habil. Carlos Härtel

Carlos Härtel is Director of GE's European Research Center in Garching, near Munich, a position he has held since 2007. In addition, Härtel is a member of the management board of GE Germany. He is also President of EIRMA, the European Industrial Research Management Association. Prior to joining GE, Carlos Härtel held positions as a scientist and manager in the development of gas turbines at Alstom in Baden, Switzerland. He studied aerospace engineering at RWTH Aachen and TUM, and received his doctorate from the Institute of Fluid Mechanics of the German Aerospace Center (DLR) in Göttingen. Subsequently, he spent several years at ETH Zurich, where he qualified as a university lecturer in 1999.

When launching the flagship initiative "Innovation Union," the European Commission acknowledged that Europe needs to become much better at turning research into new services and products that can compete successfully on the world stage. A strong linkage between public and private actors, especially academic institutions and technology enterprises, will be a key enabler here. This not only creates pathways for taking early-stage ideas to market; it also exposes our students of natural sciences, engineering and entrepreneurship to the cutting edge of what's technically feasible today. This offers invaluable learning experiences. And it provides inspiration to those who are eager to push the limits of science and technology in their own future careers.

For academic research, the main objective is the understanding of basic phenomena. Industry, on the other hand, is keen on mastering the application. Technology is the point where both parties meet: creating the know-how, the recipe for how scientific insights can be put to practical use. But while there's a natural connection, there's a natural divide, too. Universities and companies are fundamentally different entities, and so differ in their work cultures, their priorities and their ambitions. Effective collaboration therefore requires teams from both sides to be well integrated and to work in synch during the duration of a project: from jointly defining the objectives, through to the execution phase with regular progress assessments, to decisions on adjustments that need to be made along the way. In fact, geographic proximity is ideal for achieving the intensity of engagement that leads to highly successful collaborations. Many regions and governments have begun to realize this, as evidenced by the emergence of technology parks and clusters with co-location of academic institutes and industrial labs. Our European Research Center is also situated on a research campus in Garching, a privilege that none of our other global R&D facilities enjoys. Consequently, the interaction with TUM has developed into a relationship that is richer and deeper than most other university programs of GE.

The symbiotic relationship between universities and private companies around Silicon Valley has led many to assume that business and academia are more tightly connected in the US than in Europe. But this is not generally true. Rather, Europe has a unique tradition of research partnerships, which we should build upon and expand to create a pillar of regional competitive advantage. Occasionally, this closeness is even criticized as an alleged threat to academic freedom. However, this has very little substance. Keeping an eye on potential conflicts of interest is, of course, important; but in my own experience, the vast majority of industry-funded university research is far from having such conflicts. On the contrary, it's devoted to questions of fundamental scientific relevance. Through EIRMA, the European Industrial Research Management Association, leading companies from across Europe have been working with partners in academia and public research organizations to build a framework for how the private and the public sector can cooperate in ways that are fair, productive and mutually beneficial. The outcome is summarized in the guideline "Responsible Partnering," which has served the community well for many years and which will continue to be updated and contemporized in the future. □

Picture credit: Jooss