LICHTGEDANKEN 03
The Magazine of the Friedrich Schiller University Jena
ENGLISH

IMMUNOLOGY
FROM HARMLESS FUNGUS TO DEADLY THREAT
What disrupts the equilibrium of the intestinal flora

PHOTONICS
RAPID TEST FOR ANTIBIOTIC RESISTANCE
How a chip improves the effective use of drugs

ECOLOGY
SURVIVAL SPECIALISTS IN THE UNDERWORLD
How microorganisms conquer underground habitat



FEATURE

Microscopic worlds

Virtually every habitat on Earth has been colonised by microbes, and so have all higher organisms, from plants to people. All about the great significance of these tiny organisms.



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Prof. Dr Thorsten Heinzel
Vice-President for Research at Friedrich Schiller University Jena

Tradition and innovation—microbiology in Jena

For science in Germany, 2018 will be a year of important decisions in the Excellence Strategy programme of the German federal government and federal states. A total of 195 draft proposals for Clusters of Excellence have been submitted in this national competition. Of the 88 drafts that will be developed into full proposals by February, two are from Friedrich Schiller University, Jena (FSU). From 2019, between 45 and 50 Clusters of Excellence will be funded with 385 million euros per year.

The Cluster proposal »Enlightening the Receptome« is a joint application of FSU and the University of Würzburg. Its key objective is systematically to unravel the »receptome«—the sum of all receptor molecules of an organism—and make use of it in treating diseases (see p. 49). The Cluster proposal »Balance of the Microverse« focuses on microorganisms and their interactions with other microorganisms, and with their environment—the »Microverse«.

The diversity of these »microworlds« is the focus (see p. 8—46) of the present issue of LICHT**GEDANKEN**. Current FSU research topics in microbiology concern vital issues for the future, such as fighting infectious diseases, sustainably securing our basic needs, as well as ensuring a stable climate.

With these topics, the University is continuing the long tradition of microbiology in Jena, initiated by Hans Knöll in the 1940s when he first started the industrial production of penicillin here. The Central Institute for Microbiology and Experimental Therapy (ZIMET), led by Hans Knöll, gave rise to today's Leibniz Institute for Natural Product Research and Infection Biology–Hans Knöll Institute (HKI). The University benefits greatly from its close cooperation with the HKI and other non-university research institutes of the Leibniz Association, the Max Planck Society, the Fraunhofer Society, and the Helmholtz Association, in particular in preparing the »Microverse« Cluster proposal.

The Cluster combines the expertise of the FSU's profile lines LIGHT and LIFE, and builds on the very successful Excellence Graduate School »Jena School for Microbial Communication« (JSMC), which was set up in 2007. Based on strategic cooperation between participating institutes, several large third-party funded projects such as Collaborative Research Centres have been successfully established. Obtaining funding for the Microverse and the Receptome Clusters would represent a continuation of this positive development and enhance the international visibility of the FSU.

I hope that you enjoy reading this issue of LICHT**GEDANKEN**.



Jena, January 2018

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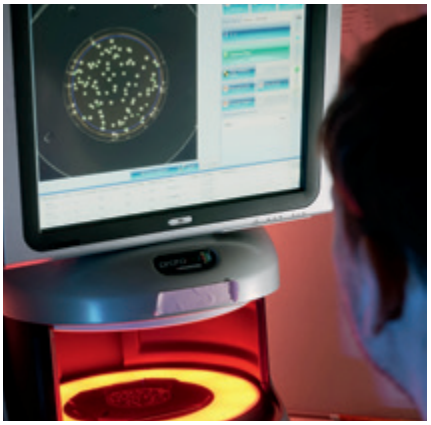
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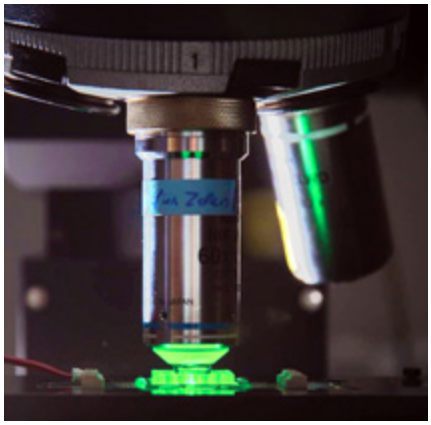
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Biomarkers for healthy food

Junior research group »Nutritional Concepts« is developing plans for different dietary types and has received federal government funding of some 2.7 million euros

Vegetarian, vegan, flexitarian—people nowadays follow many different diets. However, anyone who shuns particular foods runs the risk of suffering from a deficiency in important nutrients. Although there is plenty of advice available regarding various diets, for most approaches a valid scientific database is missing. Nutritionists in Jena want to change this. Over the next five years, the junior research group »Nutritional Concepts« aims to develop specific nutritional plans for a variety of diets. These concepts will be validated by human intervention studies.

The group is integrated within the Competence Cluster for Nutrition and Cardiovascular Research (nutriCARD) of the Universities of Jena, Halle and Leipzig, and is being supported by around 2.7 million euros in funding from the Federal Ministry of Education and Research (BMBF).

»Our aim is to develop nutritional plans or concepts for healthy people with various different dietary habits, which ensure an adequate intake of all essential nutrients,« explains Dr Christine Dawczynski, who leads the new junior research group.

In order to give nutrition-related studies greater and lasting value, the group focuses on identifying and validating biomarkers that reliably reflect specific nutritional patterns and thus reveal connections between the intake of nutrients and an individual's state of health. Scientists can already detect omega-3 fatty acids of marine origin in the blood, for example, and the objective of the junior research group is to establish and validate biomarkers that reflect, for example, the consumption of cereals, meat, dairy products, chocolate, fast food or fruit, and vegetables. sh

Healing chronic wounds

Research group »InflammAging« aims to achieve better wound healing using nanocellulose—700,000 euros funding by the federal state

The interdisciplinary research group »InflammAging« at the University of Jena has being funded for three years by the Free State of Thuringia with 700,000 euros from the European Social Fund. The research consortium aims to develop new therapeutic approaches for treating chronic wounds—especially for older people. The team, bringing together researchers from pharmacy, nutrition sciences and medicine, is pursuing its aim using a combination of bioactive natural products and an innovative carrier material made from bacterial nanocellulose. The idea is to develop innovative wound dressings based on this material—created through biotechnology research—in order to treat chronic inflamed wounds more effectively.



Researchers aim to pack anti-inflammatory molecules into wound dressings made from nanocellulose to treat chronic wounds more effectively.

In Germany, some 400,000 people a year develop a form of decubitus that requires treatment. Decubitus ulcers, also called bedsores or pressure sores, occur in response to damage to the skin and the underlying tissue that can develop into a »silent« inflammation. »Anti-inflammatory strategies for the prevention and treatment of such inflammatory conditions are therefore an important field of research,« explains the coordinator of the new research group, Prof. Stefan Lorkowski. Wounds are treated using bioactive natural products, such as triterpene acids from frankincense, which are anti-inflammatory. AB

Two research proposals reach the final

The University of Jena has been asked to submit two full proposals for research clusters as part of the Excellence Strategy programme of the German federal and state governments. The proposals »Balance of the Microverse« and »Enlightening the Receptome: From Biophysics to Clinical Applications« have to be submitted by 21 February.

The Friedrich Schiller University Jena (FSU) is enjoying success with the Excellence Strategy and has entered the final round of the competition with two proposals for Clusters of Excellence. The proposals, one of which is a joint proposal with Würzburg, cover the areas of life sciences and natural sciences. From 2019, the Clusters of Excellence will be funded with 385 million euros per year. The decisions on funding will be made in September 2018.

»Balance of the Microverse«

The aim of the Cluster »Balance of the Microverse«, whose speaker is Prof. Axel Brakhage, is to study microorganisms and their interactions with other microorganisms, as well as their environment—the Microverse. In order to build up a comprehensive picture of these interactions, Jena is pooling its expertise, with cooperation between microbiology and environmental microbiology, infection biology, chemical biology, bio-geo-interactions, systems biology, optics/photonics, material sciences, and further disciplines.
Apart from making technological progress in the laboratory, the researchers anticipate finding many possible applications for the benefit of people and the environment. Under the auspices of the FSU, the Cluster also involves Jena University Hospital; the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI); the Fraunhofer Institute for Applied Optics and Precision Engineering (IOF); the Leibniz Institute of Photonic Technology (IPHT); the Max Planck Institutes for Chemical Ecology, Biogeochemistry and the Science of Human History; the Helmholtz Institute, Jena; and DLR Institute of Data Science

»Enlightening the Receptome: From Biophysics to Clinical Applications«

The proposal »Enlightening the Receptome: From Biophysics to Clinical Application« aims systematically to unravel the »receptome«—the sum of all receptor molecules of an organism—and harness it to treat diseases. The Cluster proposal has been submitted by the universities of Würzburg and Jena, and their university hospitals. Research groups from the Leibniz Institute for Age Research—Fritz Lipmann Institute and the Max Planck Institute for Chemical Ecology are also involved. Speakers are Prof. Markus Sauer from Würzburg, and Prof. Klaus Benndorf and Prof. Christian Hübner, both from Jena University Hospital. With this Cluster, the scientists want to continue to build on their successful collaboration in the Collaborative Research Centre »Receptor-Light«. AB

New driver of innovation

A new Innovation Center for Quantum Optics and Sensor Technology (InQuoSens) is being created in Thuringia

The new centre is being funded with 1.5 million euros from the European Union and the same amount from the Free State of Thuringia. The Friedrich Schiller University (FSU) in Jena and the Technical University of Ilmenau (TU Ilmenau) will share responsibility for the dual-site innovation centre. »With InQuoSens, an effective research consortium has been created, which is active in a field that continues to be the subject of excellent basic research, but has also already been driving real innovations in optical sensors,« said the FSU's President Prof. Walter Rosenthal at the presentation of the funding awards at the end of October 2017.



Presentation of the funding awards (from left): Andreas Tünnermann (Fraunhofer Institute for Applied Optics and Precision Engineering and FSU), Walter Rosenthal (FSU), Wolfgang Tiefensee (Thuringian Ministry of Economy, Science and Digital Society), Kai-Uwe Sattler and Jens Müller (TU Ilmenau).



Fungus cultures in the »Jena Microbial Resource Collection« (JMRC), a shared facility of the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI) and Friedrich Schiller University. The JMRC curates a collection of around 50,000 microorganisms for research purposes.

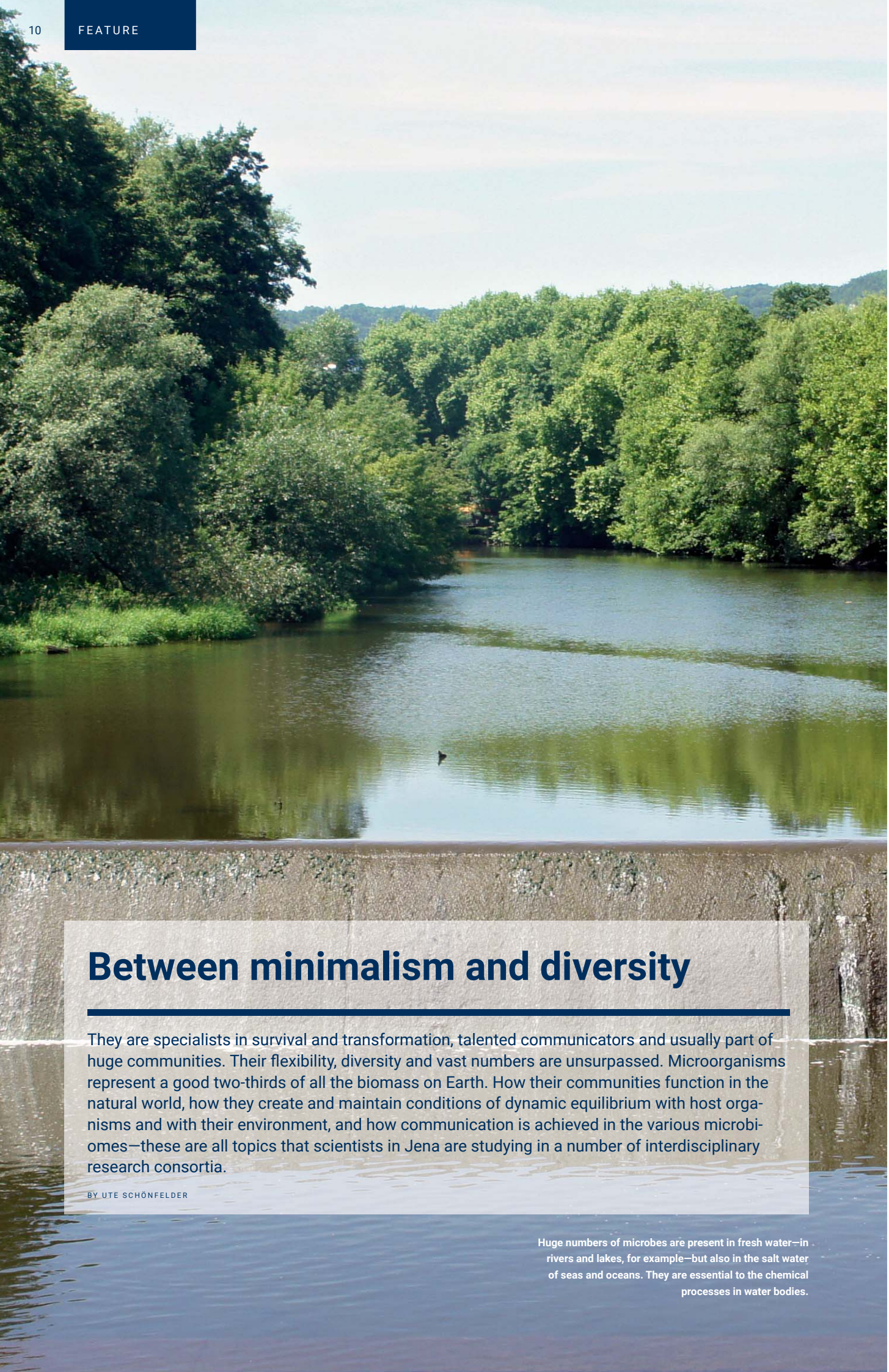


FEATURE

Microscopic worlds

Tiny organisms of great significance

Microorganisms are secretly the rulers of the world: not only have they colonized virtually every spot on Earth—all higher organisms, whether plants, animals or humans, have communities of microbes living on them. Innumerable processes of life and abiotic processes such as the climate are influenced by interactions with complex microbial communities. These diverse microscopic worlds have long been the subject of intensive research in Jena, at the University and Jena University Hospital, as well as at non-university research institutes such as the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI). »



Between minimalism and diversity

They are specialists in survival and transformation, talented communicators and usually part of huge communities. Their flexibility, diversity and vast numbers are unsurpassed. Microorganisms represent a good two-thirds of all the biomass on Earth. How their communities function in the natural world, how they create and maintain conditions of dynamic equilibrium with host organisms and with their environment, and how communication is achieved in the various microbiomes—these are all topics that scientists in Jena are studying in a number of interdisciplinary research consortia.

BY UTE SCHÖNFELDER

Huge numbers of microbes are present in fresh water—in rivers and lakes, for example—but also in the salt water of seas and oceans. They are essential to the chemical processes in water bodies.



Microorganisms consist of just a single cell or aggregates of single cells. These microscopic organisms include bacteria, archaea, most fungi (including yeasts), microalgae, and protozoa (amoeba). Viruses, which are not actually living organisms, are also usually counted among the microorganisms. Microbial life is very limited, reduced to the bare minimum. However, despite their minimalistic structure, microorganisms have a wide diversity of metabolic paths and products at their proposal, which makes them extremely adaptable.

Virtually every habitat on Earth is colonized by microorganisms

At a rough estimate, there are around 10^{30} microorganisms on Earth—1 followed by 30 zeros—and the majority of them are as yet undiscovered. According to estimates, we know only one to five per cent of all microorganisms. What is clear, however, is the huge significance of these minute organisms for life on Earth. Microbes play a decisive role in material cycles in nature and thus ensure the essentials of life for all higher organisms.

Water as habitat

Whether a puddle, garden pond, river or an ocean, all bodies of water are swarming with microorganisms—from bacteria and algae, through paramecium and ciliates, to amoeba. It was the Dutch naturalist and cloth merchant, Antoni van Leeuwenhoek, who first discovered and described the microbial life that he found in a pool of water in the 17th century.
Algae are responsible for around half of all the oxygen produced on the planet and also bind the greenhouse gas carbon dioxide. They are therefore a key primary producer in the food chains of lakes and seas. At the University Jena,

Microbiological research at the Friedrich Schiller University Jena and non-university institutions in the region

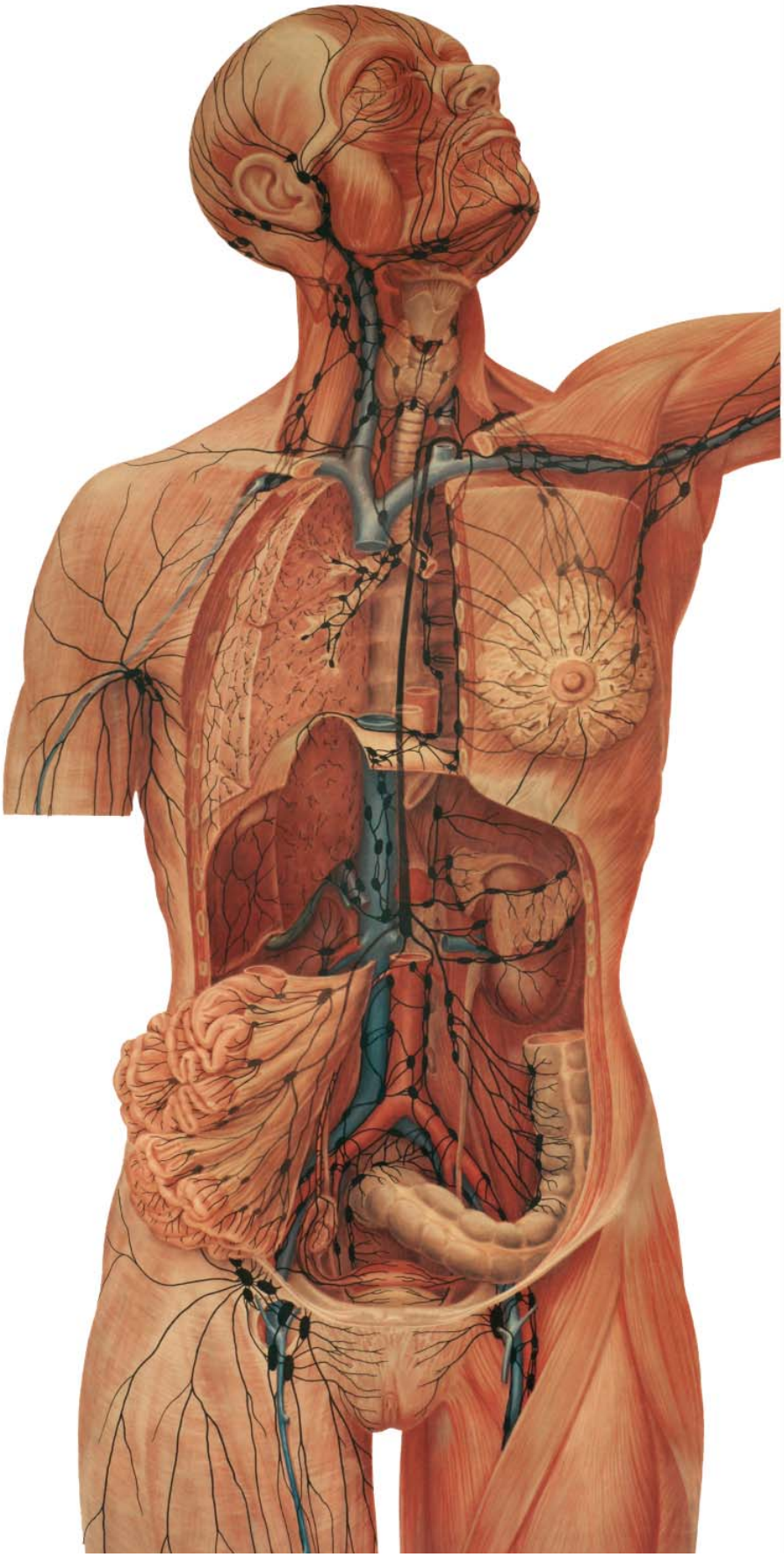
The Graduate School **»Jena School for Microbial Communication«** (JSMC), founded at the University in 2006, has been funded within the Excellence Initiative of the federal and state governments since 2007. The school brings together scientists from the natural and life sciences, for example biology, chemistry, medicine, pharmacy, biotechnology, geology, physics, and informatics. The JSMC's key objective is to decipher the »language« that microorganisms communicate with each other and higher organisms, and with the environment. This is a prerequisite for a better understanding of many diseases or the causes of environmental damage. Many findings from basic research form the basis for developing innovative technologies and new active substances. Since the school's foundation, more than 130 doctoral candidates have obtained their doctorate. The JSMC currently has 135 active doctoral candidates, of whom one in three come from abroad.

The Collaborative Research Centre/Transregio **»FungiNet«** is working on pathogenic fungi. In the research consortium launched in 2013, scientists from the University, Jena University Hospital and the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI) are collaborating with colleagues from the University of Würzburg and its university hospital to gain a better understanding of life-threatening infections caused by fungi and develop new therapies to tackle infections.

Also since 2013, ecologists, geoscientists and chemists have been working in the Collaborative Research Centre **»AquaDiva«** to analyse the links between the habitats of plants and microorganisms above and below ground, as well as the processes that take place in those habitats. The aim is to use the knowledge gained to make recommendations for sustainably protecting these ecosystems and the services they provide to humans. This specifically concerns protecting the natural groundwater reservoirs, among other things. Apart from the scientists from the University, »AquaDiva« also includes researchers from the Max Planck Institute for Biogeochemistry, the Leibniz Institute of Photonic Technology (IPHT) and the Helmholtz Centre for Environmental Research (UFZ).

Chemical mediators—signal molecules that determine the interactions between cells and organisms of one or more species—have been the focus of the Collaborative Research Centre **»ChemBioSys«** since 2014. In this work, researchers from the University of Jena, the HKI and the Max Planck Institute for Chemical Ecology are listening to—and deciphering—the chemical »babble« of these signals in biosystems that include fungi, bacteria, microalgae, plants, animals, and human cells in order to clarify how such community structures arise and function, and how their diversity is maintained.

In the Collaborative Research Centre (CRC) **»PolyTarget«**, which started in 2017, researchers from many disciplines aim to develop nanoparticles with which drugs to treat microbial infections can be steered precisely to where they are required. This CRC brings together chemists, materials scientists, pharmacists, medical experts, and biochemists of the University and the University Hospital, as well as scientists from the IPHT, the HKI and the Leibniz Institute on Aging (FLI). This initiative further strengthens the already strongly positioned research in Jena on sepsis and infection.



biologists and chemists are studying the interactions between the freshwater alga *Chlamydomonas reinhardtii* (see p. 33) and various bacteria, among other things. Researchers at the Institute of Inorganic and Analytical Chemistry are focusing on marine diatoms and studying the influence of chemical signal molecules on their way of life, reproduction or susceptibility to viruses. Geoscientists and ecologists are also on the trail of microbial life in groundwater (see p. 36).

Humans as habitat

Microorganisms not only colonize every habitat on Earth, but also live on, and in equilibrium with, virtually every higher organism, including humans. We are all walking »ecosystems«. Every one of us carries about a kilo of microbial biomass on and in our bodies (see interview p. 14). The intestines in particular are colonized by several hundred species of bacteria, archaea and fungi, with completely individual compositions in every organism. The microbes living inside us help with our digestion, breaking down indigestible food for us, for example. They also support our immune system, produce vitamin K, which is essential for blood coagulation, and break down harmful substances.

Research groups in Jena are looking at the pathogenesis of systemic fungal infections (see p. 18), identifying and characterising novel active substances from nature for the treatment of infections (see p. 30) and developing, in interdisciplinary research consortia, new methods of diagnosing and treating serious infectious diseases which can lead to sepsis (see p. 20 and p. 24).

Soil and rock as habitat

There is a wide diversity of microbial life not only in habitats on the surface, but also—and especially—underground. Researchers assume that one third to one half of all the biomass on our planet is produced below ground – by microorganisms.

Whether in woods, fields or in your garden at home: the soil is teeming with a wide variety of life forms. Soil bacteria and fungi live mainly among the roots of plants in the soil. There, they help make organic material decompose, provide nutrients and break down harmful substances.

However, microorganisms are also at home in layers of rock deep underground. Some bacteria and archaea are capable of living at depths of several kilometres, at extreme temperatures and under high pressure. They need neither organic material nor light in order to survive, but use inorganic rock to generate energy. These organisms have very slow metabolism and it is estimated that some divide only once every 1,000 years.

In current research projects, microbiologists of the University of Jena are studying, for example, how fungi break down rock and how bacteria form minerals (see p. 40). Geoscientists and ecologists are seeking out hitherto unknown microbes in rocks in Thuringia's Hainich National Park and in the Thuringian Basin (see p. 36). ■



Microbes living in the soil break down dead wood and other plants, and turn them into valuable humus.

Microscopic friends and helpers

In view of growing threats from global infectious diseases, multiresistant bacteria and dwindling numbers of effective drugs, microorganisms and fungi do not enjoy the best of reputations. However, these threats to our health, which must undoubtedly be taken seriously, can easily blind us to the huge significance of microbes in maintaining human health, an intact environment and a stable climate. In an interview, Jena microbiologist Prof. Axel Brakhage discusses what makes microorganisms so successful and what we can learn from them.

INTERVIEW: UTE SCHÖNFELDER

Prof. Axel Brakhage is Professor of Microbiology and Molecular Biology at the University of Jena and director of the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI). He coordinates the Excellence Initiative Graduate School »Jena School for Microbial Communication« (JSMC) and is, among other things, speaker of the Collaborative Research Centre/Transregio »FungiNet« (see box p. 11) and of the research consortium »InfectControl 2020«.

Microorganisms are present virtually everywhere: in the soil, the water and the air. How do bacteria, fungi or microalgae manage to colonize just about every habitat on Earth?

A key characteristic of microorganisms is their metabolic diversity. They have at their disposal an improbably large number of metabolic pathways—more than any higher organism. This makes them very flexible, so that they can adapt rapidly to any environmental conditions, even those that are very extreme, such as temperatures over 100 degrees Celsius, absolute aridity, high pressure or nuclear radiation. This enables them in principle to colonize all parts of the planet and, of course, all higher organisms. Plants, animals and humans provide habitats for a huge number and diversity of microorganisms. Every one of us carries a kilo or so of bacteria in our intestines, in our mouths and on our skin.

Can we therefore consider diversity to be the microbial recipe for success?

Without a doubt. But there is a second important factor for success, which is their abundance. There are just so many microorganisms! Their numbers exceed



those of all other organisms in the world. As a result, the number of microbial genes also far exceeds that of the higher organisms. They reproduce quickly and their genetic material is highly dynamic. Various different species of bacteria are able to exchange genes with one another, through what is known as horizontal gene transfer. This creates a large gene pool, which enables rapid changes in the genomes of various species.

What can we then learn from this extremely successful microscopic world?
From microorganisms we can learn, for example, how to break down harmful substances in the environment or how to make use of microbial metabolic pathways in biotechnology. We can learn from them how to make natural products—active substances—to treat diseases, for instance. Above all, however, it is important for us to learn how microorganisms manage to communicate with each other and with their environment, and how they succeed in maintaining their communities in a dynamic equilibrium.

Why is that important?
Take human beings as an example. We live with around the same number of microorganisms as our body has cells. The question here is how do these microorganisms manage to live in such harmony with us that we provide them with a suitable habitat and they do not make us ill? They have learnt this over the course of evolution: they »communicate« with each other and with our immune system using small chemical molecules, and in this way, they create an equilibrium. Our own bodies benefit from this in a variety of ways. We want to learn how this works, in order to be able to influence such microbial communities.

Which ones, for example?
The microflora in our intestines, for example. It is not only important for our digestion, but it is also decisive for a multitude of processes that affect our state of health and our well-being. If the flora is not in equilibrium, we become ill. There are millions of people who suffer from chronic bowel inflammation, for example, because their microflora is not in equilibrium. If we knew how to influence this flora—which microorganisms we should encourage and which ones we should inhibit—this would bring great relief to these patients.
In addition, there are challenges that affect the whole of humanity, or even the entirety of life on Earth, such as climate change. A major problem in this context is the greenhouse gas methane, which is many times more potent than carbon dioxide. And methane is generated exclusively by microorganisms that live in the stomachs of ruminants or in the soil. If we managed to manipulate the hordes of microbes currently producing huge amounts of methane, in such a way that methane production was stopped or at least reduced, we would have one less climate problem.

Microorganisms have formed and changed us in the course of our joint evolution.

It is not only scientists like you and your colleagues from universities and non-university research institutes who are concerned about microorganisms: at the 2017 G20 summit in Hamburg, the heads of state and government leaders of the most powerful countries in the world discussed the usual economic and financial topics, but also talked about diseases caused by microorganisms. Why is that?
Because infectious diseases are a major and growing problem, here and around the world. In Germany alone, 60,000 people a year die of infectious diseases, an estimated 30,000 of them due to multiresistant microorganisms. This is a ticking time bomb. We are in a race against time, as new pathogens are developing means of resistance, and that significantly faster than we can develop new active substances—new antibiotics. It is true that throughout human history there have been epidemics caused by microorganisms, which have depopulated whole areas. However, today the risk is much higher that infectious diseases could develop into pandemics, spreading extremely quickly across national borders and between continents. With air travel, pathogens can go around the world in 36 hours.

What are the most dangerous pathogens that currently represent a threat to human health?
These definitely include multiresistant strains of bacteria—of *Klebsiella pneumoniae* or *Pseudomonas aeruginosa*, for example—against which there is no longer any effective antibiotic. These bacteria can trigger life-threatening lung diseases, especially in people with a weakened immune system. There are also other multiresistant bacteria, and we are simply no longer able to treat such infections. There are additionally a few human-pathogenic fungi, such as yeast fungi or moulds, which cause invasive infections and against which there are as yet no effective drugs or treatment strategies.
Recent data suggest that an intact microbiome helps to boost our natural defences against infections, but a microbiome that does not function properly opens the doors to infections and other diseases.

The human-microbe relationship therefore appears to be quite ambivalent: are there good bacteria and bad bacteria?
No, that would be too anthropomorphic a perspective. There is no question that it is important to be concerned about in-



Microscopic world with spruce (see also cover photograph): At the Institute for Microbiology, scientists study the interaction between tree roots and fungi.

fectious diseases and to do everything possible to stop them from spreading. However, we must not forget that the vast majority of microbes are completely harmless to us or are even useful. There are an estimated three to five million fungus species, of which only 150 are known to be pathogens. And what is more, we live off microbial products: we eat bread, cheese and yoghurt—and we drink alcohol (*he laughs*).

So, does that mean we need microorganisms more than they need us?

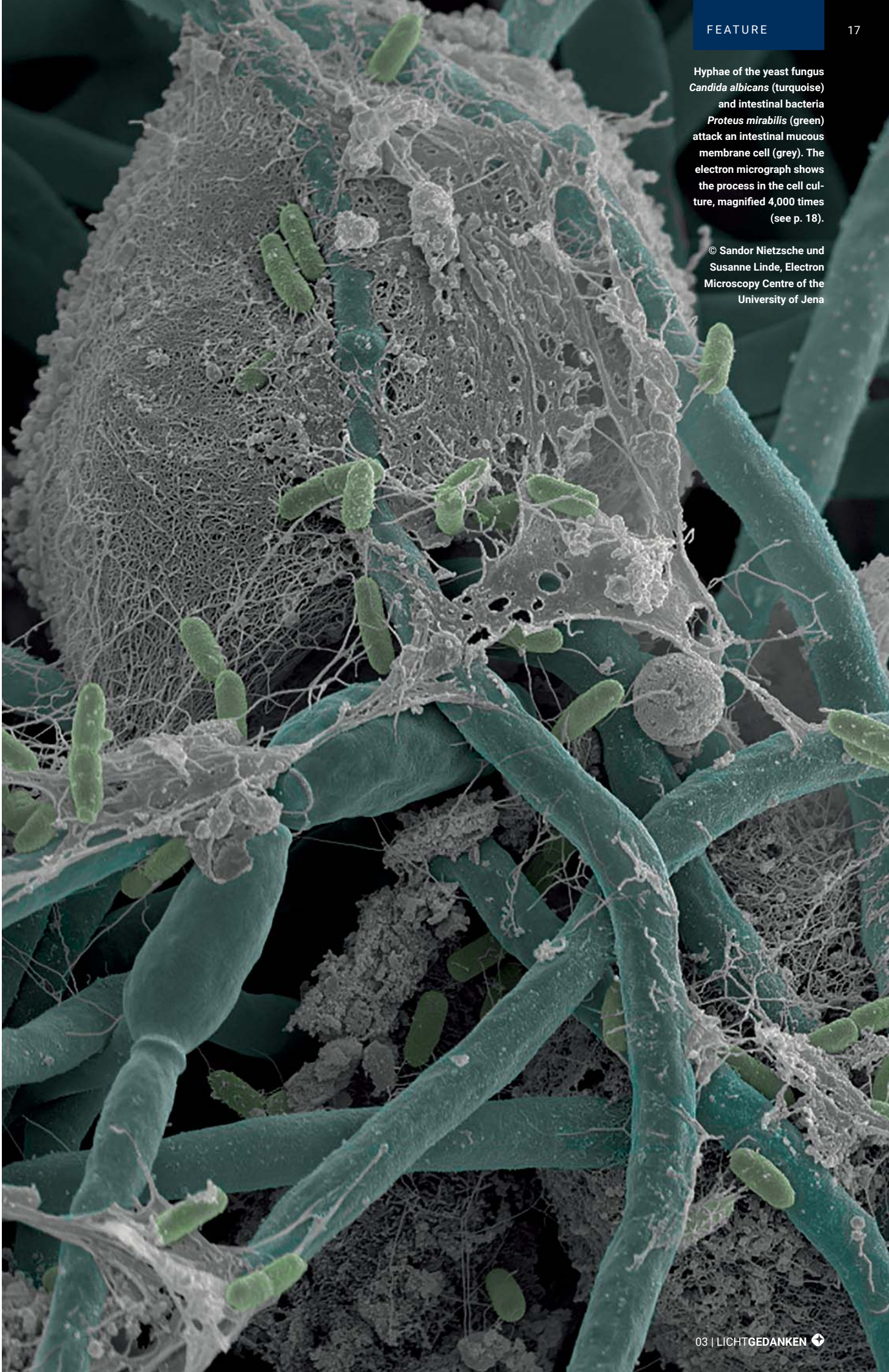
That means that the coexistence, the interaction between microorganisms and humans or other higher organisms is the result of millions of years spent evolving together. We are mutually dependent on one another. What is certain is that microorganisms were the first organisms on Earth—and they will probably be the last. The evolution of all higher organisms always involved interaction with microorganisms and this continues in the present day. We can see this in our immune system, for example, which would not even exist without microorganisms. We have a multitude of immunoreceptors, which exist exclusively to interact with various different microorganisms, because these can be either dangerous or useful to us. This means that in the course of time, microorganisms have formed and changed us, just as we have also formed the microbial communities. Similar examples can also be found in plants, which have used the interaction with microorganisms to develop efficient defence strategies. There is a constant competition between microbes and higher organisms.

What challenges must microbiological research therefore meet in the future?

What we have achieved to date is a comprehensive analysis of microbial communities. We can sequence and compare their genomes and their metabolisms, their proteins and natural products. We can precisely describe the organisms and the consortia they form. But describing is far from understanding. The next research step therefore consists of function analyses.

In order to understand why microbes coexist in one composition or another and what influence they have on their environment and on their hosts, such as humans, plants and animals, we have to conduct mechanistic analyses. For this, we need a panoply of new methods: good computer model systems in order to perform simulations; and new methods of optical and chemical analysis, with which we can observe the vital processes within the organisms in real time and *in situ* (in their real surroundings). We want to image single cells and molecules with the highest resolution possible and be able to see how individual microbes »talk« to one another and to us. And materials scientists are also required, because we need artificial cells and organs, which we can use to study and manipulate microbial communities.

These are major research goals for the years to come and in Jena we are well-placed to pursue them. We expect this research to yield decisive findings for the treatment of diseases, for agriculture and for environmental protection. ■



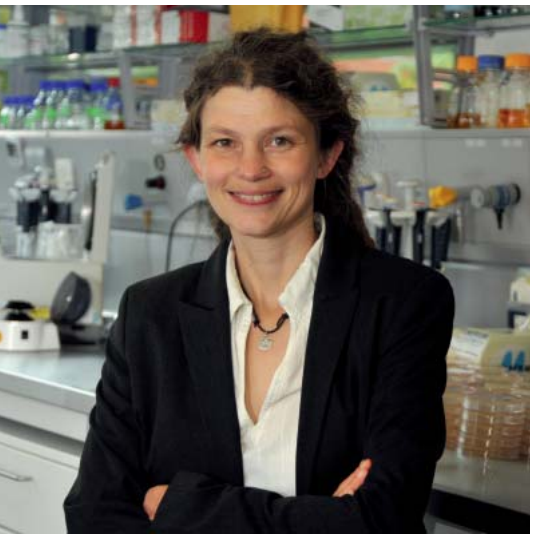
Hyphae of the yeast fungus *Candida albicans* (turquoise) and intestinal bacteria *Proteus mirabilis* (green) attack an intestinal mucous membrane cell (grey). The electron micrograph shows the process in the cell culture, magnified 4,000 times (see p. 18).

© Sandor Nietzsche und Susanne Linde, Electron Microscopy Centre of the University of Jena

»Dr Jekyll and Mr Hyde« in the intestine

Prof. Dr Ilse Jacobsen and her team examine how harmless inhabitants may become dangerous intruders. The team researches into the pathogenesis of systemic fungal infections. Together with other microorganisms, facultative pathogenic intestine inhabitants, for example *Candida albicans* and *Proteus mirabilis*, assist us in suppressing other intestine pathogens and train our immune system. Nevertheless, they may also cause life-endangering infections, including sepsis. A decisive factor for the transformation of »Dr Jekyll« into »Mr Hyde« in the intestine microbiota is the interplay of microbes in the »ecosystem human«.

BY UTE SCHÖNFELDER



Prof. Dr Ilse Jacobsen is head of the research group Microbial Immunology at the Leibniz Institute for Natural Product Research and Infection Biology, Hans Knöll Institute (HKI) and Professor for Microbial Immunology at the University Jena.

As humans, we are changing habitats —even in a complete isolation, we are never left alone. Humans and trillions of microorganisms form a highly complex ecosystem. Carrying hundreds of various species of bacteria, fungi and other microbes around with us, we share nutrition and protect each other. This means that it is not only our digestion which benefits from our intestine microbiota. Increasingly, studies suggests that the intestine microbiota also participate in a variety of life processes, for instance from our immune response and circulatory system to our mental state.

One of the most prominent »inhabitants« of the human intestine is the yeast *Candida albicans*. Despite the fact that every human being has an individual composition of microbiota, *Candida albicans* can be found in the majority of the population. Having a size of a few micrometres only, these unicellular organisms usually live in balance with other microorganisms as commensal organisms not only in the intestine but also in the oral cavity or on the skin.
»Under certain circumstances, however, this rather unspectacular fungus may become a truly life-endangering pathogen,« says Prof. Ilse Jacobsen. As the Professor of Microbial Immunology at the Leibniz Institute for Natural Product Research and Infection Biology, Hans Knöll Institute (HKI), she and her team do research into the reasons for such a serious change. Usually, the yeast cells live isolated and have a round form. However, the fungus is also able to grow into long, multicellular filaments or hyphae. Using its »tentacles«, which may grow up to 100 micrometres, *Candida albicans* can penetrate the cells of the intestinal epithelium and bore holes into the barrier.
»Consequently, it is not only the fungus itself that may reach the surrounding tissue but also other microorganisms as well. Both may infect internal organs and, under circumstances, spread to the blood circulation resulting in infections throughout the body,« explains Ilse Jacobsen. In a worst-case scenario, patients suffer from sepsis—a systemic inflammatory response affecting the whole body. Approximately a quarter of the infected persons do not survive such an infection (see p. 20).

What might lead to such a dramatic transformation? How is it possible that *Candida albicans* abandons the peaceful community of intestine population and turns against its host organism in such terrific manner? Paradoxically, one of the risk factors is the progress of the modern medicine. For systemic fungal infections affect already seriously ill patients in particular. »Patients in intensive care often receive antibiotic therapy,« points out Jacobsen. However, this does not only mean a targeted reduction of germs, it may also lead to a particular illness.
The microbiologist further explains: »Taking antibiotics may seriously influence the microbial life communities of the patient and disrupt their natural balance.« Numerous studies prove that the changed constellation in the »ecosystem human« is particularly advantageous to *Candida albicans* and to a series of bacteria. They gain an advantage in terms of growth and force other organisms to the margins.



Dr Maria Joanna Niemiec (left) and the master's student Isabel Auge are plating mouse excrement to culture medium in order to determine the microorganisms in there. They want to find out how yeast fungi and intestine bacteria communicate with each other.

Yeasts spur bacteria to produce more toxin

Similarly as *Candida albicans*, various intestine bacteria also belong to the facultative pathogenic species and may cause life-endangering infections, including sepsis. In the current research project CanBac by the Center for Sepsis Control and Care (CSSS), the researchers in the Jacobsen's team, their colleagues from the HKI and the University examine the interplay of the organisms among themselves and towards their host – the human.

»We cultivate intestinal absorptive cells, so-called enterocytes, and infect these with combinations of the examined microorganisms,« explains Dr Joanna Niemiec their experimental approach. »In the project, we want to understand how fungus and bacteria influence each other regarding their pathogenicity.« Dr Niemiec is a postdoctoral researcher and leads the project team CanBac within the Jacobsen's research group.

Among others, the researchers study the interplay between *Candida albicans* and the intestine bacterium *Proteus mirabilis*. The cell culture shows that both microorganisms, respectively, may damage the intestinal cells on a limited. If the intestine cells, however, are infected by both pathogens at the same time, the picture the researchers see is a striking one: »In this case, almost every cell comes to its end,« sums up Dr Niemiec. »Here, we do see a synergetic, mutually intensified effect of both pathogens.«

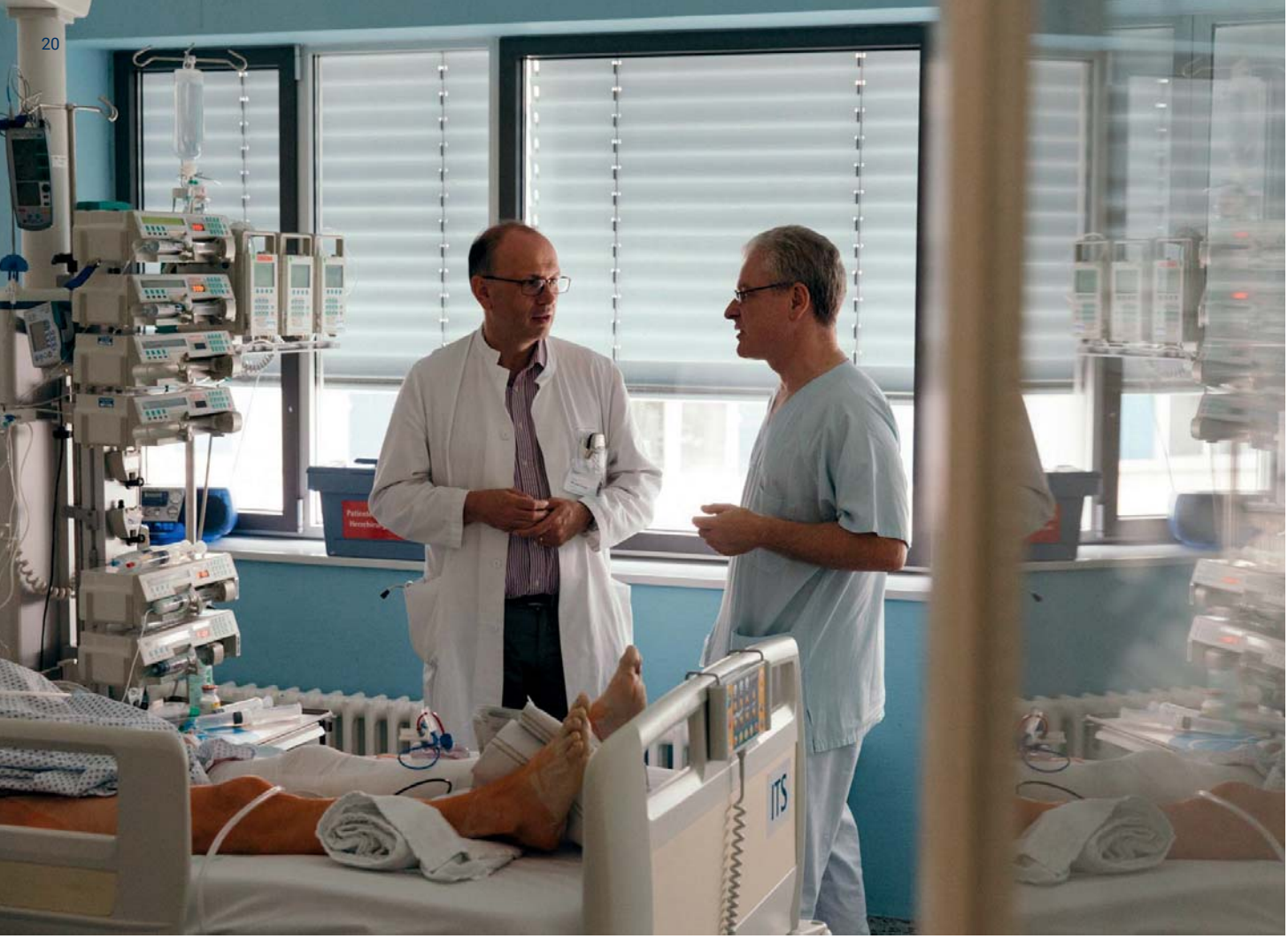
The first, yet not published findings from the Jena research team reveal the reasons for the devastating effect. There are various indications that the bacteria *Proteus mirabilis* produce an increased amount of toxin in the presence of *Candida albicans*. This hemolysin is a protein which lyses, i.e. dissolve, the cell membrane of the host organism. As a result, the cells die. »Essentially, the fungus makes the bacterium more toxic,« illustrates Prof. Jacobsen. In comparison to this, the »aggressiveness« of the fungus—this being pathogenic, too—is not stimulated by the bacterium. Indeed, *Candida albicans* may produce a lethal toxin, i.e. candidalysin. However, it is rather unlikely that its production may be additionally boosted by a co-infection with *Proteus mirabilis*.

In the current examinations, the researchers want to find out by which chemical »means of communications« the microbes communicate with each other. It is already clear that also other yeast fungi, for instance the common baker's yeast *Saccharomyces cerevisiae*, spur *Proteus mirabilis* into the intensified production of hemolysin. »Additionally, we also want to find out whether the effects observed in the cell cultures are reproducible in vivo,« reveals Dr Niemiec. In this regard, studies on roundworms and mice are being planned.

A targeted-oriented prophylaxis against fungi

»Nonetheless, we can derive some useful aspects for the treatment of patients in intensive care from the findings already,« makes Prof. Jacobsen clear. According to her, every seriously ill patient should undergo an individual risk assessment on how probable an emergence of sepsis may be. »If, for example, *Candida albicans* reduces other microorganisms after the patient has received an antibiotic therapy and the germ content of *Proteus mirabilis* or another comparable pathogen increases at the same time, a concrete, serious risk for the patient exist.«

In her opinion, a prophylactic therapy concentrated on fungi is advisable in such cases. On the other hand, Prof. Jacobsen is critical of general prophylactic measures against fungal infections using agents. »All in all, there are only a few antifungals; if they are generously used for prophylaxis, the fungi may become resistant, similarly to antibiotics.« Therefore, these agents should be used for specific purposes only. ■



Achilles' heel immune system

Despite modern medicine—or perhaps because of it—sepsis ranks among the most frequent causes of death in Germany. Although sepsis is predominantly triggered by bacteria, it is fungi, for example *Candida albicans*, which increasingly cause a deadly course. Prof. Dr Michael Bauer investigates severe and life-threatening infections at the Jena University Hospital and at the Center for Sepsis Control and Care (CSCC). In order to understand how microorganisms communicate within the human body, he wants to learn from biologists.

BY JULIANE DÖLITZSCH

It is not only its name which seems devastating, it is devastating itself: sepsis is a false, self-destructive reaction of the human body. »According to the current definition, sepsis is an organ failure resulting from inadequate response of the organism to an infection,« explains Prof. Dr Michael Bauer, an expert in intensive care medicine at the Jena University Hospital. During sepsis, a life-threatening infection gets out of control and the stress response of the body harms its own tissue and organs: »Instead of directing its full rage against the pathogen, the immune system turns against the host itself. The body's repair systems fail.«

Sepsis may lead to shock, multiple organ failure, and ultimately to death, especially if it is not recognized early and treated promptly. Sepsis is the leading cause of death from infection in the world. In Germany, for instance, approximately 280,000 new cases of sepsis occur every year killing almost a quarter of the affected patients. The situation in Jena reflects these data. »Out of 400 patients, we lose around 100 because of the insidious disease,« reports Bauer, who is also the speaker of the CSCC. Sepsis may occur as a complication of any infection, for example pneumonia, tonsillitis or urinary tract infections, not to mention those following injuries or surgical procedures. Thus every medical speciality has to deal with the problem.

In most cases sepsis is caused by bacterial pathogens, for instance *Staphylococcus aureus* or *Escherichia coli*. When the disease seems to be overcome, danger can be still imminent: »A second septic episode is, in more than 30 percent of the cases, due to a fungal infection,« specifies Michael Bauer. »It is rather difficult to detect fungi and our diagnostic methods are not fast enough. Detection using blood cultures takes days, but pa-

INFECTIONS, SEPSIS AND THEIR CONSEQUENCES

Infectious diseases are on the rise throughout the world. More and more pathogens are becoming resistant to antibiotics and thus threaten the health of many people. A **»postantibiotic era«** is looming, in which harmless diseases may end up tragically. A network of leading scientific institutions led by the Leibniz Association and with participation of the Friedrich Schiller University Jena is calling on the next German federal government to increase its support of the struggle against multiresistant pathogens. Research on new therapies and diagnostic procedures requires an improved interdisciplinary collaboration in hospitals as public-private partnerships. In a joint call for action, presented in November 2017 during the **World Antibiotic Awareness Week** in Berlin, the signatories claim that the patients should benefit from research results earlier than it has been the case until now. (For more details on the appeal, please refer to www.leibniz-ipht.de/fileadmin/user_upload/Aufruf_Infektionskrankheiten.pdf.)

Not only sepsis (colloquially: **»blood poisoning«**), but also the consequences of this disease pose a heavy burden on patients and their relatives. After awakening from an artificial coma, which might have lasted a few days or several weeks, many patients are unable to move. Often they have to relearn particular body movements whereas the body and the damaged organs have to gradually regain their normal functions. Quite often a lack of oxygen during sepsis causes serious tissue damage on peripheral limbs. As a result, the dead tissue has to be surgically removed, which can include amputations. In addition, patients may face **long-term consequences**, for example weight loss, fatigue, headache, joint and muscle pain. Further problems include cognitive impairment, such as poor concentration and loss of memory, deafness, and paralysis. Finally, the experiences in intensive care can seriously affect patients' mental health and require therapeutic intervention (see the interview on p. 22).

On the left photo: Prof. Dr Michael Bauer is one of the three speakers of the Center for Sepsis Control and Care (CSCC). At the Jena University Hospital, the expert in intensive care medicine and his colleagues treat around 400 patients per year suffering from sepsis. For about a quarter of them, the disease is fatal. Among frequent causes of sepsis are bacterial and fungal infections.

tients pass away within a few hours.« It is therefore critical to close fundamental research gaps. The Jena research campus InfectoGnostics, for instance, has already been working on better and faster procedures. Three partners join their forces and share their expertise in the research campus: the Leibniz Institute for Natural Product Research and Infection Biology, Hans Knöll Institute (HKI), the Jena University Hospital, and the Friedrich Schiller University Jena.

Bauer points out the urgency of this research topic: »The number of the septic infections is increasing.« Taking the modern, highly advanced medical technologies into consideration, this may be surprising at first. However, this very medical care provides the favourable conditions for invasive infections. »More and more people achieve rather advanced ages. Often, persons over 80 years receive a new knee joint or a hip joint,« explains Bauer. »But even a successful surgery may weaken the immune system. At that very moment, facultative pathogens often hit.« According to him, the human body usually harbours such germs without developing disease – they only trigger disease under certain circumstances. The fungus *Candida albicans*, for example, colonizes more than 50 percent of the population: it can be found in the mouth and in the throat, in the genital region or in the digestive system (see p. 18).

»The human immune system limits the success of the modern medicine – it is the Achilles' heel,« Bauer illustrates. To be more accurate, many drugs and therapeutic procedures affect the immune system, and make it more susceptible to pathogens—also to those germs residing in the body, for instance *Candida albicans*. In particular the intestinal microbiome, also known as gut flora, which consists of millions of microorganisms, is »a decisive factor for the human health«. When these microbes turn against the body, physicians are often at their wits' end.

»It is thus essential for us to understand how microorganisms function in ecosystems and how they communicate,« Prof. Bauer is firmly convinced. »In this regard, I want to learn from biologists.« Applying their findings to medical problems might lead to completely new perspectives beyond the simple concept of aggressively treating all pathogens with antibiotics. Otherwise the number of multiresistant germs will continue to increase which – in the worst case – may end in a »postantibiotic era« (see the box above).

Body has to find the suitable stress response on its own

»Finally, a better understanding of microorganisms will help us to find novel approaches to strengthen the body's defence and the immune system. The body itself should find a better stress response to sepsis and become more resistant,« hopes Michael Bauer. »To achieve these goals, it is our top priority to team up and to combine our interdisciplinary expertise.« ■

»We take the therapy to the patient«

Sepsis is the most frequent cause of death among infectious diseases. Those having survived it not only suffer from considerable physical impairments, also their mental health is impaired because of the experience of a life-threatening disease and intensive care. The experiences change the patient's life and that of the partner. A therapy is often inevitable to overcome the experiences. One of the projects at the Center for Sepsis Control and Care (CSCC) aims to help the persons affected by offering them an Internet-based writing therapy. The treatment »zwei leben« is accompanied by a study examining its efficacy. More about the project and the therapy in the following interview with the psychologists PD Dr Jenny Rosendahl (project manager) and Romina Gawlytta (project coordinator).

INTERVIEW: JULIANE DÖLITZSCH

In Jena, the research on sepsis is rather intensive at the moment. Your project was launched in February 2016. Could you explain your approach please?
Rosendahl: As part of our research at the CSCC, we have been dealing with the psychological long-term consequences of those who had survived sepsis. Some of these consequences are, for instance anxiety, depression, adjustment disorder, and post-traumatic stress disorder (PTSD). This may occur as a psychological response to an extremely overwhelming event, i.e. a trauma. For example, a trauma may be a traffic accident or experiencing violence, but also a death threat in extreme medical cases. For many, the helplessness encountered then is inescapable.

What are the effects of PTSD?
Gawlytta: Patients often have nightmares, they experience flashbacks and intrusions reminding them of intensive care. They also suffer from sleep disturbances or may have a lack of concentration. As a result, the quality of life may be reduced and they may encounter an enormous emotional stress frequently. Most of them are not able to overcome the experiences without professional assistance.

What is new about the project?
Rosendahl: In our study, we examine the efficacy of the Internet-based writing therapy which is applied after intensive care of a critical illness. In this regard, we apply a new approach: the partners of our patients participate in the treatment actively, too, and are being treated themselves if they also suffer from PTSD. If the partners are not affected, they still receive information on the therapy and attend the first telephone interview. This is reflected in the project's name zwei leben; firstly, it is about both partners, secondly, the patients often consider their life after intensive care as their second chance.

So the partners could also be affected, couldn't they?
Gawlytta: Yes, some of the partners are also affected due to their experiences. While the patients are in a life-threatening condition over a period of several days or even weeks the partners are also in a stressful situation. They do not know whether their partner will still be alive when they will be back for a visit in the hospital. Sometimes they fear the situation when they have to decide whether the life-sustaining medical devices should be switched off or not. Many of the partners still deal with these memories even weeks or months after their partner has already left the intensive care unit.

How many patients suffer from PTSD?
Rosendahl: The numbers vary depending on the respective study. Generally, every fifth patient with sepsis and every fifth partner suffers from PTSD. If the patients themselves are affected by PTSD, often their partners are affected, too. They share the same fate, yet from two perspectives.

How does your project help them?
Rosendahl: After being affected by sepsis, the patients are discharged even if they still have residual symptoms. The process of physical recovery often evokes negative memories. As a consequence, a trauma therapy is necessary. However, long waiting times and great distances, particularly in the countryside, often hinder the patients. We therefore offer an Internet-based writing therapy and take the therapy to the patient. In recent years, psychological treatment via the Internet has become an important treatment method. Various research projects have been working on its improvements. In comparison to the common face-to-face psychotherapy, the therapist and the patient are in contact with each other via computer.

What are the advantages of the Internet-based writing therapy?
Rosendahl: In particular it is the fact that it can take place everywhere and at any time. Patients do not have to wait for a therapy as it is common to the face-to-face therapy and can plan their writing sessions at home easily instead. Especially for disabled persons it is a real benefit. In addition, some patients may become more accessible since they do not have to sit in front of their therapist. For some of them, it may be easier to write about feelings of guilt and shame.

The project »zwei leben« is a cooperation project – with whom do you work?
Rosendahl: On site, we cooperate with an



PD Dr Jenny Rosendahl (right) and Romina Gawlytta, psychologists from the Institute of Psychosocial Medicine and Psychotherapy at the Jena University Hospital.

IT specialist who administers the portal. In Berlin, we collaborate with Prof. Dr Christine Knaevelsrud, and two other therapists from the Freie Universität. They are responsible for the therapeutic part—they read the texts and give their feedback to the participants. Having applied the Internet-based writing therapy for treatment of traumatic experiences of refugees and of soldiers or persons traumatized in World War II, they contribute their expertise to the project.

What do the participants write about?

Gawlytta: The first three texts have a biographical focus. The participants write about their childhood, their youth, and their life before the disease. In the following four texts, they are supposed to reflect on their experiences at the intensive care unit and to describe their memories and their fears concerning the intensive care as detailed as possible. The last three texts shall give the patient the chance to think about the experiences from another point of view. They should not consider themselves as victims anymore since they have already overcome the disease, they are not helplessly exposed to the situation anymore, and can deal with their future expectations.

Rosendahl: Apart from these texts, the partners write a letter to the affected partner in which they should find some comforting and sympathetic words regarding the past and current strain. Moreover, they should point out their belief in the partner's abilities and competencies. The letter is completely confidential and the therapists do not read it. If both partners participate in the therapy, they have to write letters to each other.

Have you received any feedback from the participants, yet?

Gawlytta: Yes, we have. After the treatment had been completed, I called the participants for a diagnostic interview. Although some of them were sceptical before starting the treatment, their feedback is positive without exceptions. They are glad that they had taken part in the project. They do not have as many nightmares and flashbacks as before. And even if some occur, they can cope with them in a different way.

You carry out diagnostic telephone interviews to find out suitable candidates. Who cannot participate in the project »zwei leben«?

Rosendahl: Unfortunately, all who do not have a partner—our study focuses on couples.

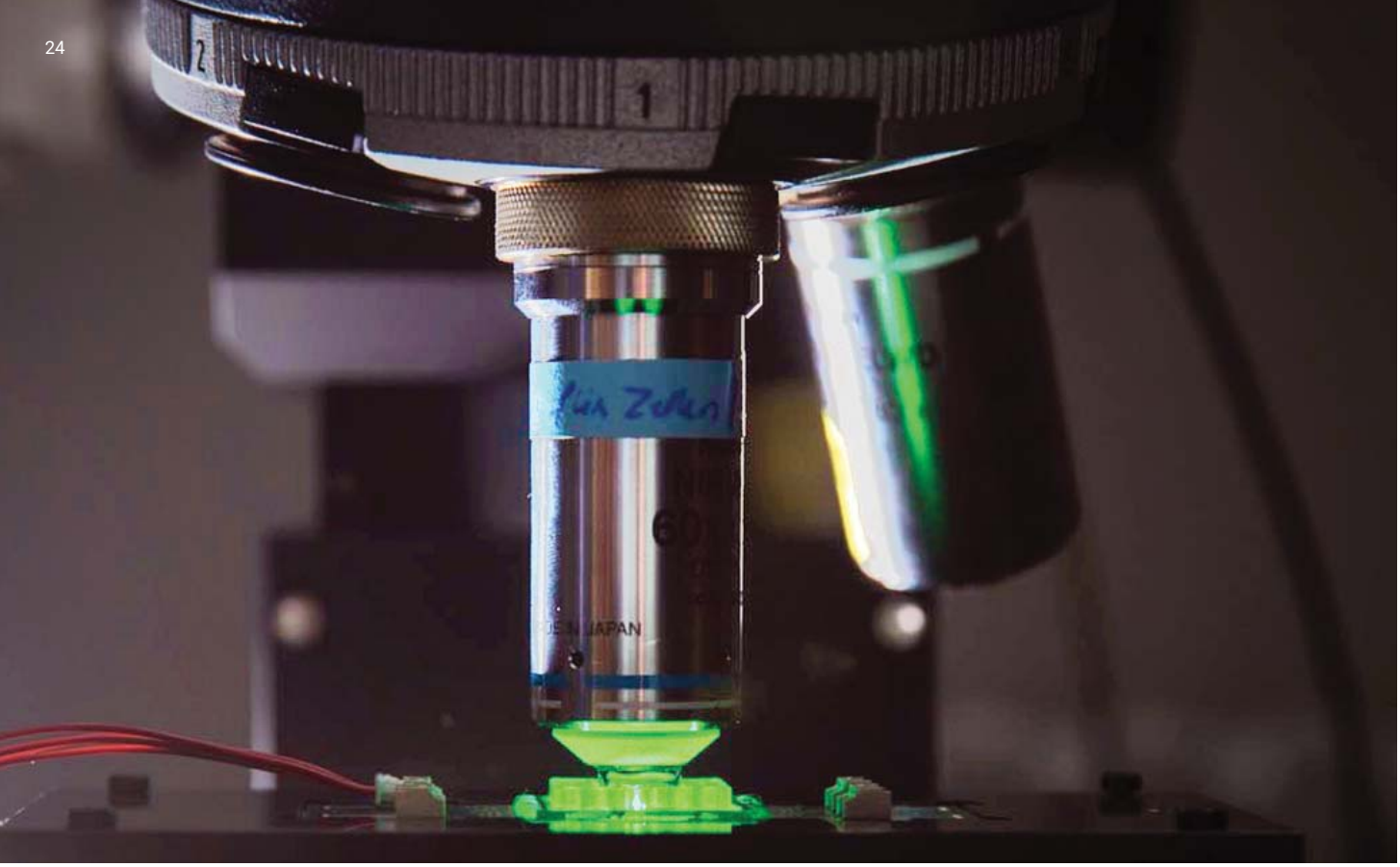
Gawlytta: Everyone who is undergoing a psychotherapeutic treatment elsewhere cannot take part in our study. Otherwise we cannot measure the success of our offer. Apart from those, neither persons addicted to medication or alcohol nor those with suicidal tendencies can participate. Of course, we do support those persons in finding an appropriate therapy for them. However, sepsis is not an exclusive criterion. As a result, also someone who underwent intensive care because of other reasons may participate in the study.

What will happen next?

Rosendahl: We will have been recruiting participants until the summer 2018. Our aim is to include 70 couples in total. Up to now, 14 couples have already begun their treatment or completed it. We would thus welcome any further patients. At the beginning of 2019, the study will have been completed. When we are able to prove the efficacy, we would like to continue the project. We are completely sure that the persons affected do benefit from the therapy.

How might the project »zwei leben« evolve in the long term?

Rosendahl: For example, we might offer our treatment to individuals so that singles or people whose partner died of sepsis could attend it, too. I can also imagine internationalizing the project. ■



Rapid test shows antibiotic resistance

Ironically, it is the very use of antibiotics in the fight against infectious diseases that is partly responsible for one of the most pressing health problems of the 21st century. Increasingly, pathogens are adapting to the active substances in antibiotics, thereby making some drugs ineffective. Hardly any new antibiotics have been developed over the last 20 years. In Germany, around 500,000 patients a year contract a hospital-acquired infection—and 15,000 of them die as a result. Faster and more precise diagnostic methods could lead to more targeted use of antibiotics, thus reducing unnecessary prescriptions. Researchers from the University of Jena, the Leibniz Institute of Photonic Technology (Leibniz-IPHT) and the Center for Sepsis Control and Care (CSCC) offer a solution to this problem.

BY SEBASTIAN HOLLSTEIN

»All organisms—and especially microorganisms—adapt to their environment in order to ensure the survival of their species,« asserts Prof. Jürgen Popp. »Resistance to antibiotics can therefore not be prevented—but it can be delayed.« To achieve this, a doctor would have to be in a position to prescribe the drug that specifically treats the infection in question. However, up to now it has been usual to tackle a pathogen using broad-spectrum antibiotics, which also kill other bacteria. This encourages many more bacterial strains to develop resistance. If a doctor knew exactly which pathogen was involved, he would be able to prescribe a targeted remedy that only affects the bacterium concerned. However, this usually requires elaborate diagnostic procedures, which can take up to 72 hours and hinder rapid treatment of the illness. »So we need tests that quickly show how a pathogen reacts to an antibiotic,« explains Popp.

Popp, who heads the Institute of Physical Chemistry at the University of Jena and leads the Leibniz-IPHT, has developed such a procedure over the last few years, together with colleagues from the CSCC and the InfectoGnostics Research Campus. At the centre of this procedure is a chip of about four square centimetres. On this chip patient samples, such as urine, are brought into contact with antibiotics, which react with the bacteria in the sample. To be able to examine them more closely, dielectrophoresis is used to concentrate the pathogens on the chip into an area of just a few micrometres. To this end, the surface of the chip carries electrodes, which generate inhomogeneous electric fields when a voltage is applied. In turn, the effect of these fields holds the bacteria in place at specific points, without damaging them. If the pathogens are

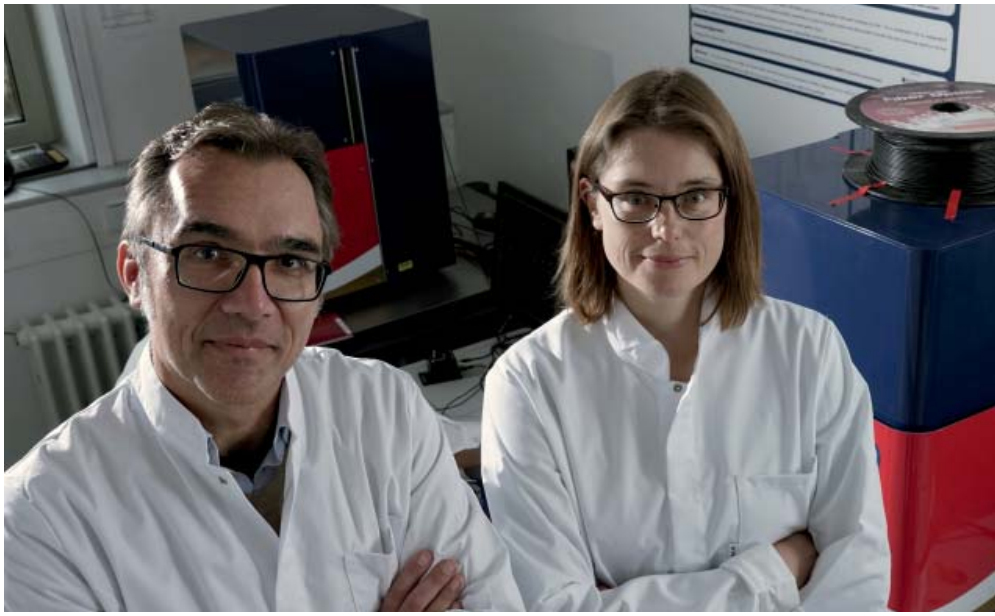


Photo left: Raman spectroscopy using the chip that not only allows pathogens to be clearly shown within a few hours. This innovation from Jena can also indicate whether the pathogens react to the antibiotics administered or whether they show resistance. This saves valuable time in treating patients. Photo right: Prof. Jürgen Popp and Prof. Ute Neugebauer head a team of scientists that developed the new system of analysis.

concentrated in this way, researchers can carry out the actual analysis. »For this, we use Raman spectroscopy—an analytical method based on optical light scattering. It enables precise identification of individual bacterial strains,« says Prof. Ute Neugebauer, who is closely involved in developing the new analysis system. »Bacteria are irradiated with light and the light scattering is analysed. Each bacterial strain then shows an individual, unique spectral pattern, with which the pathogen can be clearly identified.« For this, the scientists use multivariate statistical algorithms in order to match the measured patterns to known spectral patterns of bacteria in a database.

To treat patients successfully, it is necessary to check not only the pathogen, but also for existing types of resistance. In developing the chip system, the researchers in Jena focused first on enterococcus bacteria. Some strains of these intestinal bacteria can cause urinary tract infections, but also sepsis and endocarditis. As early as 30 years ago, it was reported that some enterococci had become resistant to the antibiotic vancomycin, and this has become a worldwide medical problem. For this reason, Popp, Neugebauer and their colleagues have developed a rapid test that specifically verifies whether or not this pathogen reacts to vancomycin. In this case too, the researchers use Raman spectroscopy to get their results. They bring samples of the bacteria into contact with the antibiotic and observe changes in the spectral pattern. After just 90 minutes or so, it is possible to see whether or not the pathogens react to the drug and die. Even with the necessary preparation and post-processing, the procedure takes at most three-and-a-half hours. This method of analysis can also be applied to other pathogens and antibiotics. Furthermore, it should be possible to test several antibiotics simultaneously on the recently developed chip.

Easy-to-use chip system for doctors to start a correct antibiotic treatment

»Our aim now is to develop a closed rapid test system that doctors can use both in the hospital and in a doctor's surgery,« explains Jürgen Popp. »For the system you need of course the chip as well as associated reading devices, which provide the result. We want to present a first prototype within two to three years; initial contacts have already been made with partners from industry.« In general, Popp is very committed to interdisciplinary cooperation, and he has found optimal conditions for this in Jena. The InfectoGnostics Research Campus alone enables fruitful cooperation with doctors, scientists from other disciplines and partners from industry. In addition, the proximity to Jena University Hospital is crucial, because such a method of analysis cannot be created without knowledge of the daily routines at a hospital, medical work processes and safety standards. It is therefore important that his colleague, Ute Neugebauer, for example, does research in the CSCC at Jena University Hospital.

Popp also stresses, however, that technical developments alone are not sufficient to combat antibiotic resistance, because what use are even the best methods if they are not applied for reasons of cost? »It is therefore important to bring the health insurance funds on board to address those aspects in the next few years.« The urgency expressed by the current figures on hospital-acquired infections should raise awareness of the problem. ■



Drops of blood in focus

At the Leibniz ScienceCampus InfectoOptics, scientists in the research project BLOODi are developing a dynamic haemogram. They want to use new optical technologies to recognise infectious diseases and their pathogens in whole blood in the fastest way possible. In order to discover how individual blood cells behave in the case of an infection and how they interact with pathogens, biologists, physicists, bioinformaticians and mathematicians need to pool their expertise and find a common language.

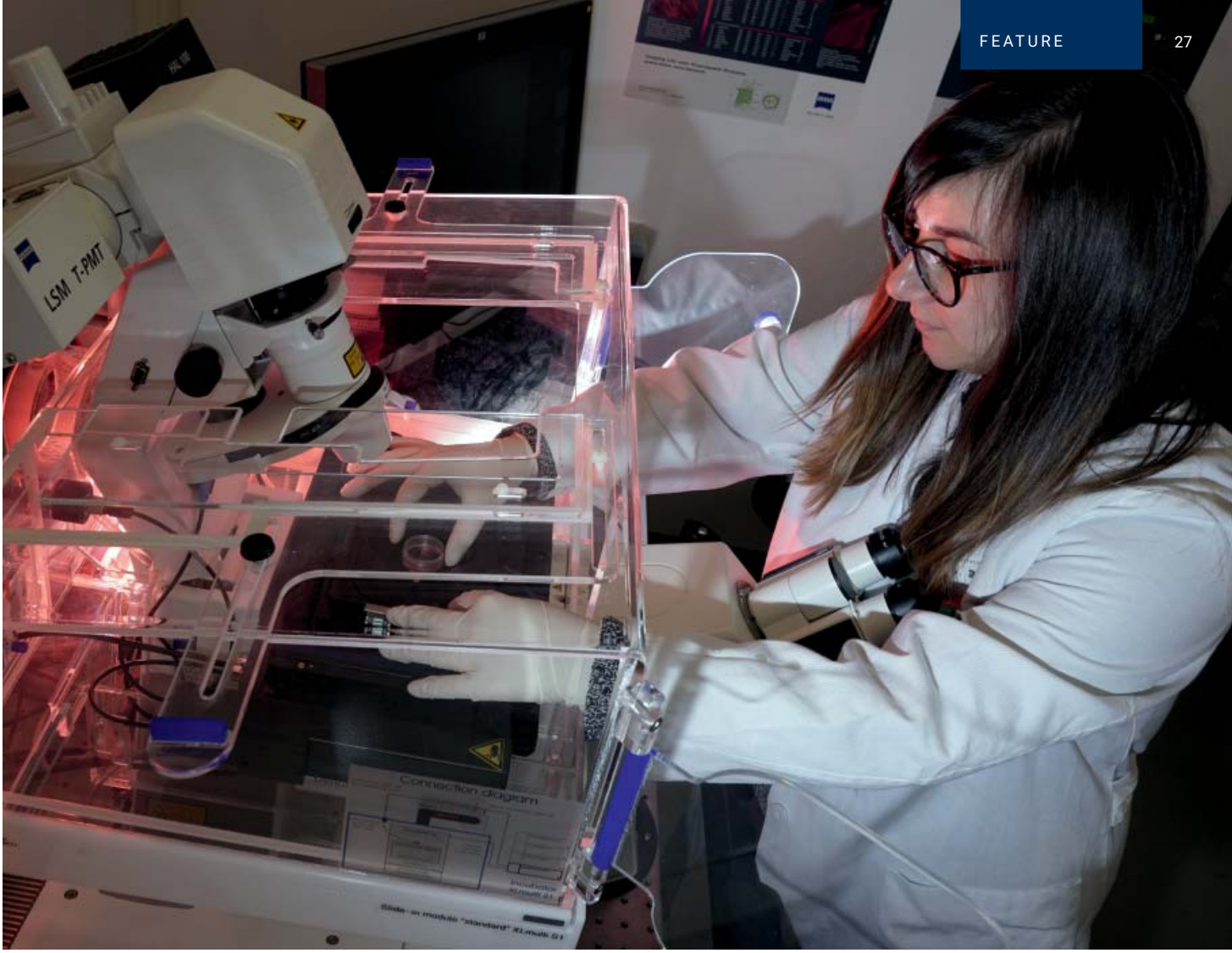
BY JULIANE DÖLITZSCH

BLOODi is as gruesome a project name as you could imagine and it conjures up horrifying images in my mind. However, BLOODi is anything but bloodthirsty. On the contrary: the aim of the project, which brings together the University of Jena and a number of non-university research institutes, is that a single drop of blood should ideally be enough to provide extensive information. The lower-case »i« in the name stands for Imaging and the complete project name is »Whole Blood Imaging«. The objective is to capture the dynamics of the blood components by means of microscopic »snapshots«, in order to be able to say as quickly as possible which pathogen has triggered an infection.

In Jena, short distances and short lines of communication are important—that much has become clear to me. Easy accessibility is a feature of the town, but also of the University and other research institutes. The fact that, on a small scale, BLOODi reflects the wider scientific landscape here is quickly apparent to me when I look at the organisational structure and then meet a number of researchers from the project group. They include biologists, physicists, mathematicians and bioinformaticians. One goal unites them all: »With the help of optical technologies, we want to develop a dynamic haemogram and use it to enable the rapid and targeted treatment of infectious diseases,« explains Prof. Marc Thilo Figge, who heads the project. »The special feature is that we want to leave the blood intact, in order to observe the interactions between cells. To achieve this, we are bringing together various different scientific disciplines and institutes.« This does not seem at all easy to me, and Prof. Figge concurs. »We first had to get talking to each other and develop a common basis and language,« the physicist recalls. The BLOODi team comprises 18 researchers, including seven doctoral candidates who ensure that BLOODi is well-positioned, not only as regards its interdisciplinary nature, but also its multinationalism. Three of the doctoral candidates come from Germany and the others hail from Italy, India, Russia and Syria. The young researchers' fresh ideas and open-minded outlook on research contribute towards the enthusiasm for innovation that characterises BLOODi.

Short distances between labs

The project, which was launched 18 months ago, is based very strongly on exchanges between researchers, says Figge. »We regularly get together in a large group to discuss results and new approaches. And of course, we also make contact in smaller groups, whenever the need arises.« Communication is greatly eased by the fact that everyone is close together on the Beutenberg Campus. In just a few minutes you can



Doctoral candidate Alessandra Marolda is studying neutrophil granulocytes, by comparing two blood samples from the same person. One sample is infected with the yeast *Candida albicans* and the other is not. Investigations using a laser scanning microscope reveal significant differences between the neutrophils from infected blood and those in the control sample.

be knocking on the door of a fellow researcher, so that you can discuss work and swap ideas.

While Alessandra Marolda, Italian doctoral candidate at the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI), explains her role in BLOODi, I am aware of other researchers in the lab. In the background, I can hear the eager whispering of the other project members, who are not chatting about what they did at the weekend, but are discussing current results from the lab.
Ideally, at the end of the project it would be possible to investigate whole blood, with as little effect as possible on the blood samples, the young biologist Marolda explains. Scientists have thus far been unable to do this. Nevertheless, she has already reached a small milestone with her investigations in the initial stage of the project at the Centre for Innovation Competence (ZIK) Septomics. »At the beginning we do indeed investigate single cells, but without marking them.« The cells are thus not stained, but are left as intact as possible, in order to produce valid results in spite of the cells having been extracted.

Neutrophils react to fungus infection

To this end, she took two blood samples from the same person, infecting one sample with the yeast and leaving the other as a control. »After one hour, I isolated neutrophil granulocytes from both samples,« says Marolda. These cells, often known simply as neutrophils, are by far the most common white blood cells. »As part of the innate immune response, they help to identify and destroy microorganisms—for that reason, it seemed to us promising to examine them more closely,« adds Marolda. When I make initial attempts with the laser scanning microscope, I too can see that the isolated neutrophils from the infected blood can indeed be distinguished from those of the non-infected blood: their shape has altered slightly, as they are somewhat flatter. »Their morphokinetics have been influenced by the pathogen,« explains Alessandra Marolda. In the next step, she is going to study, by infecting the blood samples, how the immune cells react to other fungi and bacteria: in exactly the same way? Differently? Do they only help to signal an infection or can one use their characteristics to identify a specific pathogen? How do other blood cells behave? In the case of sepsis, for example, starting treatment as early as possible is crucial to its success—a rapid identification of the bacteria and the appropriate medical response can, in extreme cases, mean the difference between life and death.

Impressed by the significance of the investigations, I leave the laboratory. The others also stop their shop talk, which



Prof. Dr Thilo Figge (left) and doctoral candidate Ivan Belyaev analysing experimental data. Here they take a closer look at images of granulocytes produced by time-lapse microscopy.

now touches on the similarities between the microscopes used by biologists and physicists. It appears that they cannot be easily compared in the case in question. Together, we swap lab coats for jackets and set off, arriving just a few minutes later in a physics lab of the Abbe Center of Photonics.

Microfluidics gives information on composition of blood samples

Now equipped with shoe covers, I examine a microscope. Under the lens is a chip stamped with fine, winding lines. Susanne Pfeifenbring, who works here most of the time, explains to me what this is all about. This chip measuring about one by one-and-a-half centimetres forms the foundation of drop-based microfluidics. Physicist Pfeifenbring, who is doing her doctorate at the Leibniz Institute of Photonic Technology (IPHT) within the framework of BLOODi, responds to my puzzled look by explaining further: »We place a drop of blood on the chip and examine the blood cells using non-linear oscillation spectroscopy.« Little the wiser, I study the chip, but Pfeifenbring continues: »Every cell consists of various macromolecules, such as proteins, lipids and DNA. If we irradiate the whole blood with two laser pulses, we selectively cause different molecules to oscillate and observe their distribution in the cells. As the oscillation spectrum of the cell is as specific as a fingerprint, we can use it to identify the biochemical composition. This is how we find the neutrophils in whole blood, for example.«
This is important, because in the physics lab, too, researchers aim to have as little impact as possible on the blood samples and, unlike in the flow cytometry procedure commonly used to date, they do not want to mark cells. Using oscillation spectroscopy, also called Raman spectroscopy, they could determine in this way which cells are involved and, ideally, whether they have been in contact with particular pathogens. »Combining non-linear laser spectroscopy with microfluidics in order to examine whole blood is completely uncharted territory,« adds Susanne Pfeifenbring.

As we slowly make our way back outside, Marc Thilo Figge once again highlights the key feature of BLOODi: »Here, physicists develop new optical methods for which they on their own do not see any necessity. And our biologists know what they want to study and what they want to find, but they are not able to create the necessary methods.« The close cooperation between laser physicists, biologists and immunologists thus stimulates fruitful research ideas and the possibility of making them a reality through the collaboration between the various disciplines.

Time-lapse microscopy makes differences visible

And because someone is also needed to analyse and interpret results from the laboratory, scientists such as Prof. Figge himself and doctoral candidate Ivan Belyaev complete the team. At the Center for Systems Biology of Infection at the HKI, which we visit last, the experiments are mathematically analysed. For example, they receive data from Alessandra Marolda and take a closer look at the development of neutrophils in the individual »snapshots«. The sequences of images produced using the time-lapse microscope—also called Live Cell Imaging—enable researchers to determine dynamic characteristics of the cell shapes. »This allows us to capture diagnostic criteria for cells under health

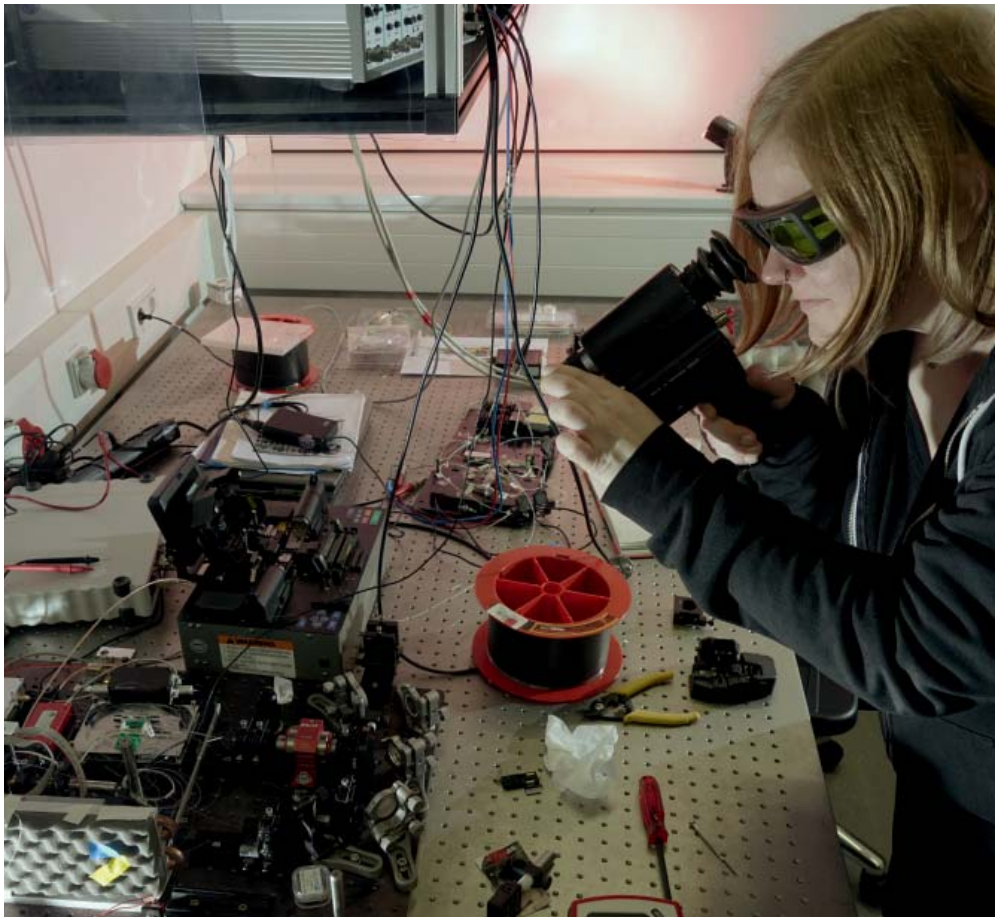
»BLOODi« is a subproject of the Leibniz ScienceCampus »InfectoOptics«. Researchers from both Life Sciences and Optics/Photonics are working closely together in an effort to understand and fight infectious diseases better with the aid of innovative optical technologies. **Project partners** include Friedrich Schiller University Jena, the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI), the Leibniz Institute for Photonic Technologies (IPHT), the Fraunhofer Institute for Applied Optics and Precision Engineering (IOF), the Institute of Molecular Pathogenesis at the Friedrich Loeffler Institute, the Federal Research Institute for Animal Health (FLI), as well as BLINK AG.

Fundamental to **droplet-based microfluidics** is a chip (Photo).



and disease conditions,« explains Belyaev, who is doing his doctoral research at the HKI. He refers to some diagrams on his computer, which are based on investigating the morphokinetics of the neutrophils. »As a result, we know that we should take this aspect into account when performing the microfluidics tests with whole blood. That takes us a big step further.« The Russian physicist is working on the BLOODi project for one reason: »Scientific curiosity.«

It is clear to me that this is also what drives his colleagues. With BLOODi, Alessandra Marolda values the fact that blood is studied in different ways and the results are brought together in the group. »Here, we approach a problem from various different angles and try to solve it together,« she notes. She and the other researchers have a good two years left for this work, after which the project will come to an end. In view of the significant initial results, Figge is optimistic. »We can learn a lot from the dynamics of whole blood. The snapshots that we have obtained so far give us hope that we will find characteristic biomarkers for pathogens, and that in future we will be able to make quicker prognoses regarding infections.« ■



Doctoral candidate Susanne Pfeifenbring checks the setting of a laser using an infrared viewing device. In the BLOODi project, blood cells are irradiated with laser pulses in order to find out, by means of their oscillation spectrum, which blood cells are involved and whether they have had contact with pathogens.

Termites have »green fingers«

In a termite colony, there is—quite literally—the right chemistry. Busy termites cultivate a fungus in large fungus gardens and feed on them. They are assisted by bacteria in protecting this valuable source of nutrients. These live in the termites' gut and in their garden, and produce natural products that prevent hostile fungi from infesting the termite mound. Christine Beemelmanns, with her team at the Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (HKI), is investigating the relationship between host and bacteria, and in the process she is discovering new natural products.

BY MONIKA WEISS

We humans are colonized by many different microorganisms. Not only have we become used to one another, we are also interdependent, as evidenced by our intestinal flora, for example (see p. 18). Although a few bacteria or fungi frequently cause serious illnesses, we could not survive without most microorganisms. The same is true of other organisms that coexist with microbes. For example, microorganisms in the root environment in the soil have a symbiotic relationship with plants and help them to absorb nutrients. And insects, too, have their own very individual intestinal flora, on which they depend.

Termites create gardens in their mounds to cultivate fungi

»In the gut and the fungus gardens of termite species that cultivate fungi, we find what are called actinobacteria. They play an essential role for the insect community,« says Beemelmanns. The chemist leads a junior research group at the HKI, which is studying the interrelationships between microbes and their host at the chemical level.

In 2015 and 2016, together with an interdisciplinary research group, Beemelmanns undertook expeditions to South Africa, where fungus-cultivating termites live. With her colleagues, she took samples from termite mounds: »We had to dig deep in order to reach the termites' fungus garden,« she adds. »Similar to our cultivation of grain, termites cultivate a fungus of the genus Termitomyces in order to feed on it,« explains Beemelmanns. Many different factors have to be in equilibrium for such a highly complex and fragile society as that of the termites to remain intact.



Mound of a *Macrotermes* colony in South Africa.

In addition to abiotic factors such as the composition of the soil, it is the interaction between the organismic partners that is of decisive importance. Only if the fungus used as a source of nutrition and the termites' supporting microbes are in a balanced relationship can such a complex system survive. Bioactive substances, as they are known, are particularly important in this process, because they serve the organisms concerned as signal and communication substances.

In this way, the microorganisms regulate their interactions and keep the system in equilibrium. In a similar way to human beings with their complex microbiomes, insect communities form a kind of superorganism. However, these ecological systems are also vulnerable and are occasionally infested by pests or succumb to infections. For example, parasitic fungi can overrun the vital nutritional fungus and cause the entire colony to collapse.

Christine Beemelmanns's junior research group is working on these microbe-host relationships. She believes that they hold great potential for finding new natural products that could be used in fighting human infections, for example. Instead of randomly extracting substances from samples, Beemelmanns's team first studies bioactive natural products within the organismic



Termite queen and king of the species *Macrotermes natalensis*. The queen (left) can grow to a length of 15 centimetres. Clearly visible is her enlarged abdomen for egg production. The king (right) reaches a size of only two to three centimetres. The queen is surrounded by a number of »workers« and small »soldiers«. The workers cultivate the fungus gardens and supply the queen and king with food. The soldier termites protect the gardens and the royal couple.

relationships to determine their possible biological function. This enables the researchers to kill two birds with one stone: at the same time as finding new natural products, they gain a better understanding of fundamental mechanisms in complex symbiotic systems.
»We have already found a few new molecules,« says Beemelmanns. One of the molecules formed by the actinobacteria in the termites' gut is of particular interest to the researchers, because it has an as-yet-unknown structure. It is a hybrid molecule that is composed of three different building blocks—a sugar, a polyketide and an amino acid—through the interaction between many different enzymes. »The final finished molecule is biologically inactive, as far as we have been able to assess that to date. However, some intermediate products show antimicrobial activities,« explains Beemelmanns. The natural product researcher and her team assume that these tropolone derivates, as they are called, along with a few other natural products that have been found, prevent the harmful fungus from infesting the termite mound. That is to say, they form a natural pesticide combination, which supports the termites in cultivating their food source.

Active substances turn fungi into parasites and disarm hospital-acquired bacteria

In further investigations, Christine Beemelmanns and her research group examined another parasitic fungus more closely. They observed that this fungus, of the genus *Pseudoxylaria*, acts like an invasive weed, overrunning the fungus that is essential to the termites. Beemelmanns explains how this works: »From this harmful fungus we were able to isolate cyclic tetrapeptides, which are probably in part responsible for its parasitic lifestyle.« In further experiments, the researchers discovered that these active substances are also effective against the bacterium *Pseudomonas aeruginosa*. This is an interesting finding, in particular because *Pseudomonas aeruginosa*—a typical hospital-acquired bacterium—can trigger serious wound infections in patients. Such »gram-negative« bacteria are difficult to tackle. The researchers in Jena therefore thought that they had a potential new substance for treating wound infections. However, the substance turned out to be toxic, so that it was unsuitable for use as an antibiotic for humans. »We have other substances in the pipeline, however, which we hope will show better pharmacological characteristics,« adds Beemelmanns with confidence.

The HKI, together with the University of Jena, is currently applying for a patent for a new natural product, which could be used in developing a new drug for cancer therapy..

Original Publication
Isolation, biosynthesis and chemical modifications of rubterolones A–F, rare tropolone alkaloids from Actinomadura sp. 5 – 2 (2017), DOI: 10.1002/chem.201701005

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»Fungus gardens« established by termites, with white fruiting bodies of the garden fungus *Termitomyces*. The oval fruiting bodies grow to a size of 1 cm.



Infected fungus garden with harmful fungus *Pseudoxylaria*. The parasite acts like a »weed«, overrunning the nutritional fungus essential to the termites.



Agar plate with green algae cocultivated with bacteria (center) and bacterial extracts respectively. In the center algal growth arrest is visible as a halo.

Ambush in a petri dish

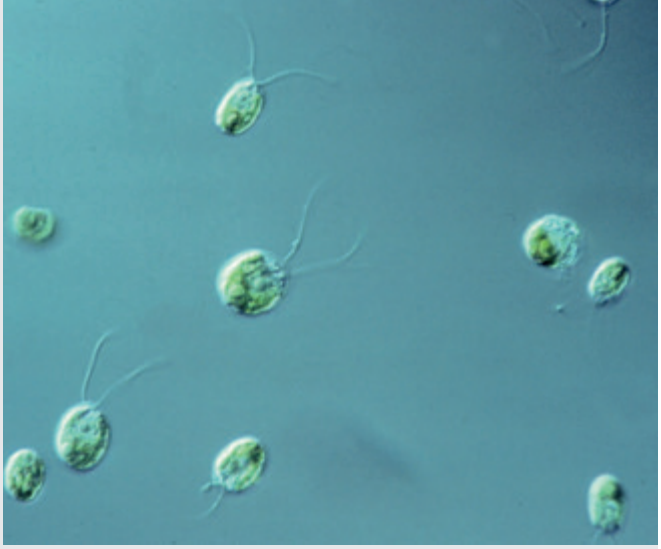
If green algae of the species *Chlamydomonas reinhardtii* meet *Pseudomonas protegens* bacteria, their fate is sealed. The bacteria, measuring only some two micrometres, surround the algae, which are around five times larger, and attack them with a deadly toxic cocktail. The algae lose their flagella, which renders them immobile. The green single-celled organisms then become deformed and are no longer able to proliferate. The chemical mechanism underlying this extremely effective attack has now been uncovered by botanists and natural product chemists.

BY UTE SCHÖNFELDER

It is a gruesome spectacle that meets the eyes of Prasad Aiyar as he looks down the microscope. The doctoral candidate from India, who came to Jena to do his Master's degree in Molecular Life Sciences, examines the species *Chlamydomonas reinhardtii* on a microscope slide. The oval-shaped microalgae, a good 10 micrometres in size, have two flagella with which they busily swim around—that is, until Prasad Aiyar uses a pipette to add a drop of a bacterial solution. The even smaller bacteria gather together into swarms, which surround the algae. Just 90 seconds later, the algae are motionless and when one looks more closely, one can see that their flagella have fallen off.

The Jena researchers have discovered why these bacteria have such a devastating effect on the green algae. It seems that a chemical substance plays a central role in the process, as the teams under Prof. Maria Mittag and Dr Severin Sasso of the Matthias Schleiden Institute (University Jena) and Prof. Christian Hertweck of the Leibniz Institute for Natural Product Research and Infection Biology—Hans Knöll Institute (HKI)—report in the journal Nature Communications.

Orfamide A, as the substance is called, is a cyclic lipopeptide which the bacteria release, together with other chemical compounds. »Our results indicate that orfamide A affects channels in the cell membrane, which leads to these channels opening,« explains Dr Severin Sasso. »This leads to an influx of calcium ions from the environment into the cell interior of the algae,« adds the head of the Research Group Molecular Botany. A rapid change in the concentration of calcium ions is a common alarm signal for many cell types, which regulates a large number of metabolic pathways. »To be able to observe the change in the level of calcium in the cell, we introduced the gene for a photoprotein into the green algae, which causes luminescence if the calcium level increases. This enables us to measure the amount



Chlamydomonas reinhardtii

Tiny, nimble and quick: the single-celled green alga *Chlamydomonas reinhardtii* measures just 10 micrometres—a good 10 times thinner than a sheet of paper. But with their two flagella, these algae can really speed up. Taking its size into account, *C. reinhardtii* swims as much as 12 times faster than a human being. This tiny alga is usually in a hurry because of changes in the light. Depending on the incidence and intensity of the light, it seeks out the best position for **photosynthesis and energy generation**. These microalgae live in fresh water all over the world and, in addition to bodies of water, they also occur in damp soil.

To perceive light, *C. reinhardtii* uses a large number of photoreceptors. Some of these are located in what is called the **eyespot**, which is on the »equator« of the single-celled organism and is coloured orange by carotenoids. Work on these receptors has opened up a new field of research—optogenetics—in which particular proteins from Chlamydomonas are put to use in neurobiology as »molecular light switches«.

The alga has a pronounced day-night rhythm, which is controlled by an **»internal clock«**, similar to the way this operates in humans. Even if the algae are kept in the dark for an extended time period, this rhythm continues to work, with a period of around 24 hours, which means that the algae »know« when it is actually day or night. Chronobiologists call this a circadian rhythm and distinguish between a subjective day and a subjective night. If the green algae register light pulses during their subjective day, they swim towards the light. If light pulses are shone on them during their subjective night, however, they do not react.

C. reinhardtii is also interesting for research because this simple organism can be used to study many fundamental processes of developmental biology and physiology. As the green alga only has a **haploid (single) chromosome set**, targeted manipulations of the microalga's genetic material can be immediately studied. *C. reinhardtii* was one of the first green algae for which the genome was fully sequenced, which underlines its importance as a model organism. Its genetic material comprises more than 15,000 genes, some of which correspond to plant genes, while others show similarities with animal genes.

What is more, the green alga is increasingly important for **biotechnological processes**. For example, it is used to produce biodiesel or alternative energy sources such as hydrogen. *C. reinhardtii* is also the first plant organism that is known to digest cellulose, i.e. other plants, in order to generate energy. If its environment contains too little carbon dioxide, which it needs for photosynthesis, the microalga forms enzymes that enable it to break down cellulose instead. This makes the alga an interesting organism for the **generation of biofuels** from plant waste containing cellulose.

As early as 2014, the phycology section of the German Botanical Society named *Chlamydomonas reinhardtii* **»alga of the year«**.



Doctoral candidate Prasad Aiyar studies cultures of the single-celled green alga *Chlamydomonas reinhardtii*.



Research team head by Prof. Dr Maria Mittag (back row left) and Dr Severin Sasso (back row right): David Carrasco Flores, Dr María García-Altares (HKI), Prasad Aiyar und Daniel Schaeme (front row from left).

of calcium with the help of the luminescence,« explains Prof. Mittag, Professor for General Botany. In some cases, the changes in the calcium lead to changes in the direction of movement, for example after light perception. In other cases, for example after the bacterial attack, they cause the loss of the flagella.

Researching the »chemical language« between microorganisms and their environment

In addition, the teams were able to show that the bacteria can tap the algae and use them as a nutrient source if they are lacking in nutrients. »We have evidence that other substances from the toxic cocktail released by the bacteria also play a role in this,« says Maria Mittag. Her team, once again in cooperation with the teams of Prof. Hertweck und Dr Sasso, now also wants to track down these substances, in order to gain a precise understanding of this chemical communication between algae and bacteria. Numerous research groups have dedicated their efforts to studying the »chemical language« between microorganisms and their environment as part of the Collaborative Research Centre »ChemBioSys«. Microbial species communities occur in virtually every habitat on Earth. »In these communities, both the species composition and the interrelations between individual organisms of one or more species are regulated by chemical mediators,« says Prof. Hertweck, who is the speaker for the Collaborative Research Centre and head of the Biomolecular Chemistry department at HKI.

The aim of the interdisciplinary research partnership is to explain the fundamental control mechanisms in complex biosystems, which affect the whole of life on Earth. »We want to understand the mechanisms through which the microbial community structures are formed and their diversity maintained.« They are important, because essentials of life—not least for human beings—depend on them, for example food or air.

This is also true of microalgae such as *Chlamydomonas reinhardtii*. Such photosynthetic microorganisms (phytoplankton) make a contribution of about 50 per cent towards fixing the greenhouse gas carbon dioxide and, as a byproduct of photosynthesis, they supply the oxygen that is essential for our survival.

In addition, microalgae, which are found in fresh water, wet soils or the world's seas and oceans, represent an important basis for food chains, especially in aquatic systems. For example, zooplankton in the oceans feed on the algae and together they provide food for crustaceans, which in turn are eaten by fish, before these are eaten by bigger fish or caught by humans. »In view of the huge significance of microalgae for human life, we still know astonishingly little about the fundamental elements and the interactions in their microscopic world,« says Prof. Mittag. ■

Original Publication
Antagonistic bacteria disrupt calcium homeostasis and immobilize algal cells.
Nature Communications (2017),
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Entrance to the subsurface: groundwater study site in the Hainich National Park in Thuringia.

Surviving in the subsurface

The world beneath our feet is full of life, with a multitude of microorganisms constantly busy in the soils and sediments, in groundwater and even in the rocks. But life is hard underground, lacking in almost everything that organisms need in order to live: nutrients, light and energy sources. Moreover, the depths are exposed to extreme temperatures and high pressure. To date, very little research has been done on the microbes that brave such an inhospitable environment and the strategies they use to survive there. Ecologists, geoscientists and chemists from Jena are following the traces of this hidden life underground.

BY UTE SCHÖNFELDER



Measuring tube of a groundwater well, used for various purposes, such as taking groundwater samples, monitoring probes or on-site experiments.

There is a saying that necessity is the mother of invention. When people lack food or other necessities of life, they are more willing to share, exchange and improvise. Things are no different in the microscopic world underground, for example in groundwater. Deep in the rocks, where rainwater accumulates after seeping through the soil, microorganisms cannot expect to live the high life. If they want to survive on the scarce supply of nutrients down below, far from the metabolic cycles above ground, they need reliable partners.

Live reduced to the bare minimum

»There is a whole range of microorganisms that have made their home in groundwater,« says Prof. Kirsten Küsel. The lives of bacteria and other single-cell organisms here are reduced to the bare minimum. »Most of these organisms have extremely reduced genomes and depend on partners for their survival,« according to the ecologist. In order to save energy, many microbes have simply »shut down« or »done away with« some of their metabolic pathways and maintain only the most basic emergency programme. This helps them survive, but it means that they need metabolites from other organisms that have opted for a different energy-saving strategy, so that they can exchange substances essential to life. Such a precisely interconnected survival network makes the ecosystem in groundwater aquifers extremely vulnerable, says Prof. Küsel. »If one species suffers damage or becomes extinct, its partners are also impacted.« How this subsurface microbial balance is maintained, how it arises in the first place, and what influences it, are all topics being investigated by researchers from Jena, together with numerous partners, as part of the Collaborative Research Centre (CRC) 1076 »AquaDiva« (see p. 11)

To this end, they have established a unique research platform in the Hainich National Park in the German state of Thuringia: the Hainich Critical Zone Exploratory (CZE). In this open-air laboratory of more than 12 square kilometres, the researchers take samples of water, gas and other materials from underground compartments, soils, the unsaturated zone, and the groundwater, in order to understand their characteristics and functions.
The area known as the »Critical Zone« extends from the near-surface atmosphere down to the bottom of groundwater aquifers. A large number of measuring and sampling sites have been set up over a six-kilometre transect in the Hainich CZE. Starting in the forests of the Hainich National Park, across pasture and further on to cropland, the researchers have drilled into the ground down to the groundwater aquifers. »The boreholes go down nearly 100 metres through soil and rock layers from the quaternary period and the Upper Muschelkalk,« says Prof. Kai Uwe Totsche, hydrologist and coordinator of AquaDiva alongside Prof. Küsel and Prof. Susan Trumbore.
In this way, the researchers were able to use the drill cores to reconstruct the soils and the geological underground of this outdoor laboratory. In addition, the water and rock samples obtained are now also providing remarkable data on the microbial communities in the subsurface.

»Astonishing« single-cell organisms »washed« from soils into the groundwater

In a current publication, for example, the research team characterises the biodiversity of what are called Archaea in groundwater and rock. These primeval single-cell organisms frequently colonise habitats with extreme conditions. We know of Archaea that live at temperatures of over 100 degrees Celsius, for example in geysers in areas of volcanic activity. Others can withstand extremely high pressure or high salt concentrations. But substantial numbers of Archaea also occur in the soil.
The current Jena-based study shows that the Archaea living in the soil find their way into the groundwater when water



Photo above: drilling core from a Schillkalk bench (Upper Muschelkalk). The fissures widened by karstification represent groundwater flow paths.

Photo right: sampling groundwater in the »Hainich Critical Zone Exploratory« at a location used as pastureland.

BACKGROUND

Scientists today mainly use the methodology of **genome sequence analysis** to identify microorganisms in soil or water samples. Compared with earlier methods, such as culturing microbes on growth media, this has the advantage that one can also analyse organisms which it has not been possible to culture to date. In addition, the high-throughput technique provides results very quickly and is much less labour-intensive.

A **»genetic fingerprint«** of the microbes is used for identification. As with an actual fingerprint, it can be compared with the other samples and in this way, organisms that are already known can be clearly identified. However, this technique additionally enables researchers to identify previously completely unknown species and determine their relationships.

In the first step of the procedure, the DNA is extracted from the microorganisms found in the water or rock samples. Great care must be taken in doing this, to avoid contamination with other microorganisms present everywhere in our environment. The DNA fragments thus obtained – usually very few in number – are subsequently copied in large numbers using the **»Polymerase Chain Reaction (PCR)«** method. The genetic information is then »read out«, which means that the DNA is sequenced.

Among other things, what is known as **16S rRNA** is of interest in identifying microorganisms. This denotes segments of **ribosomal RNA (rRNA)** that are present in all organisms and are preserved throughout evolution. The ribosomes are complex structures made of nucleic acids and proteins, which occur in all cells and on which protein biosynthesis takes place—a universal process of life. The 16S rRNA gene is highly conserved, which means that it is present in all organisms, but it is also characterised by very high variability. In publicly accessible databases, there are now thousands of sequences of 16S rRNA genes available as reference sequences, which enable immediate identification.

This method is not only used for analysing environmental samples. It is currently applied virtually everywhere that microorganisms need to be identified, for example for detecting pathogens in clinical diagnostics.

Knowledge of 16S rRNA provides not only the basis for detecting a specific microorganism in a sample. As this ribosomal RNA has barely changed in the course of evolution, it is also a kind of **»molecular clock«**. It enables researchers to classify each species in the universal tree of life and identify the most closely related species.

With the aid of the ribosomal RNA gene sequences, the currently generally accepted **phylogenetic tree** has also been created. This divides the organisms living on Earth into three domains: Bacteria, Archaea and Eukarya—to which all the higher organisms such as plants, animals and fungi belong, among others. As far as microorganisms are concerned, it is currently estimated that only one to five per cent of all species are known to date. For more than 90 per cent of all Bacteria and Archaea, we only know their rRNA sequences, without ever having cultured them in a petri dish or having made them visible under a microscope.

and materials are transported from the soil through the underlying rock strata. »The microbiomes in the forest soil and groundwater are usually totally different worlds,« notes Prof. Küsel. These microorganisms are significantly different in the way they live. The professor for Aquatic Geomicrobiology adds: »Therefore, when we find soil-dwelling organisms in groundwater, it is no coincidence.« She cites the fact that surface organisms enter the groundwater as evidence for the close connection between habitats above and below ground.
Although most Archaea from the soil do not survive long in water, the researchers have found evidence of Archaea in groundwater samples over the entire transect. According to them, this shows that the microorganisms must enter the groundwater along the whole transect. »Above all in the Hainich area, where the groundwater aquifers are relatively close to the surface, there were large numbers of the microorganisms in the water,« says Küsel. The organisms that are most likely to survive their move from the soil into the groundwater were identified as »Thaumaarchaeota« (from the Ancient Greek »thauma«, meaning »miracle«) and »Woesearchaeota«, named after the US microbiologist Carl Richard Woese.



In a further study, the scientists investigated the drill cores obtained from the CZE to look specifically at the microorganisms living in them. Microbiologists and geoscientists from the teams of Prof. Küsel and Prof. Totsche took small rock samples from the cores, which were examined for traces of microbial DNA contained within them (see also box on p. 38).

Signs of life from ancient rocks

It was discovered that signs of life were also present in the rocks itself: in the finely crushed rock samples, researchers indeed found the genetic fingerprints of various microorganisms. »What we have discovered is that the microbial communities are linked to the permeability of the rock and therefore appear to depend on the rock's cavity structure,« says Prof. Küsel. »This controls the length of contact between water and the rock matrix, and thus determines the living conditions in the ecological niches,« explains Prof. Totsche. Areas of high permeability, where the water flows relatively quickly, are home to organisms that are different from those in areas of limited permeability. Furthermore, the organisms found in the rock samples differed from those in comparative samples from groundwater or soil.

However, there were similarities to organisms discovered during the INFLUINS research drilling project in the Thuringian Basin. »These were samples from the same geological layer that we sampled in the Hainich,« says Totsche. For this reason, it is conceivable that the organisms have the same origin – but this theory will have to be supported by future research. What is certain is that the calcareous limestone rocks are over 230 million years old and were formed from sediments from the seabed. »This soil, too, once teemed with life,« says Kirsten Küsel. »It is possible that the microbes from the rock are descendants of these ancient organisms of 230 million years ago.«

Original Publications

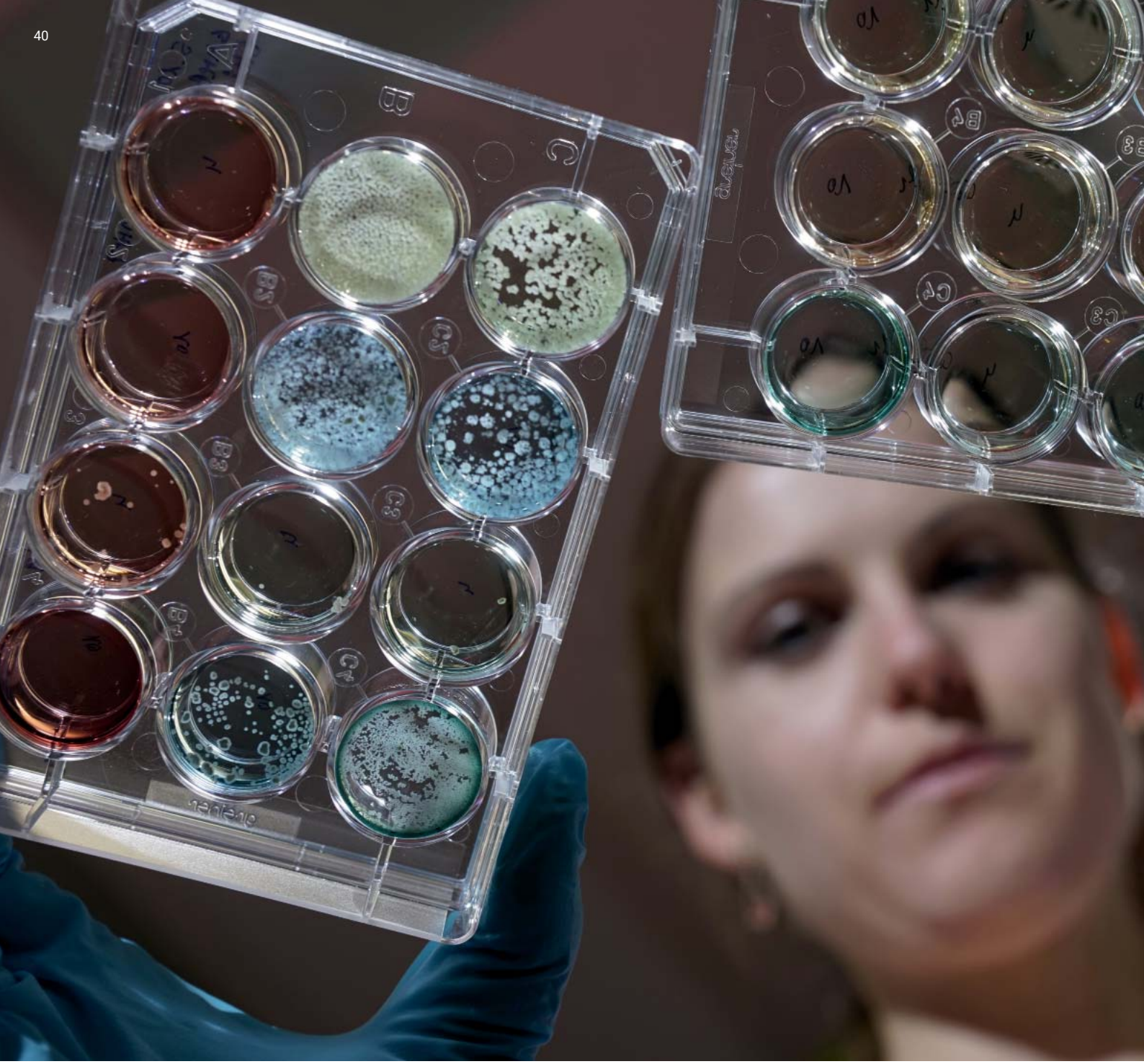
Archaeal diversity and CO_2 fixers [...]. Archaea 2017 DOI: 10.1155/2017/2136287

Aquifer configuration and geostructural links control the groundwater quality [...]. Hydrology and Earth System Science 2017 DOI: 10.5194/hess-2016-374

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Rocks and microbes

For a long time, geosciences and biology were seen as separate disciplines, one focusing on the abiotic world of rocks and minerals and the other on the living world. However, it has gradually become apparent that the two disciplines have more in common than previously thought. Microbiologists from the University of Jena, for example, are studying how bacteria form minerals and how fungi break down rocks.

BY SEBASTIAN HOLLSTEIN

Rock formation is generally considered to be a geological process, in which biological processes barely play a role. It has become clear, however, that microorganisms can also form minerals such as calcite (calcium carbonate) in freshwater springs. This mineral is present in many types of rock, for example in travertine (see box p. 43). Carbonate is normally precipitated when cold groundwater reaches the surface and becomes warmer there. With the help of microbial processes, carbon dioxide and



PhD student Hanka Brangsch from the Institute of Microbiology inspects bacterials cultures growing with heavy metals.

calcium eventually bind to form calcite. In this process, called »biomineralisation«, bacteria cause solid carbonate to precipitate, forming small crystals of various shapes, which settle as sediment in water, referred to as sinter rocks. It had previously been assumed that the pH value of the environment was the driving force for this process and that that this was how microbes could influence the mineralisation process. When the pH is high (i.e. under alkaline conditions), carbonate precipitates and sinter rocks consisting of calcium carbonate, or calcite, form. If the pH is low (i.e. under acidic conditions), the carbonate remains dissolved in the water. However, the scientists from the Institute of Microbiology in Jena made the surprising discovery that even in an acidic environment, bacteria ensure that carbonates are precipitated instead of being dissolved. Thus, the role of microorganisms in mineralisation may have to be re-evaluated.

Do bacteria secrete minerals?

»At the calcareous sites near Bad Kösen, we took samples of various bacterial strains from the groundwater, rocks and soil, and then investigated whether they could also achieve biomineralisation under laboratory conditions,« says Prof. Erika Kothe. »More than 92 per cent of microorganisms do indeed form carbonates, usually calcite, and in rare cases also calcite containing magnesium or vaterite.« Approximately a third of them created an alkaline environment in the process, while most others had no influence on the pH of the surrounding medium. Six strains even produced acidic conditions. »The process by which the formation of minerals at a low pH is achieved is so far unknown,« explains Kothe.

When they examined individual bacteria more closely, the researchers noticed that it was not essential for the newly created minerals to be deposited directly on the bacterial cells; they also occurred at a distance from the cells. This means that there must be a diffusion mechanism at work, which triggers the mineralization, and substances secreted by the bacteria probably play a role. In addition, the external form of the precipitate varies. »We have found very different morphologies of the crystals, from round through elongated to rosette-shaped,« says microbiologist Kothe. And the microbiologists in Jena have also discovered one more astounding connection: when extrapolated to one year's worth of formation, the new minerals total around two grams per litre, which closely matches the annual growth of a stalactite. The process that has been observed is therefore already known from nature.

The current results raise many new questions related to biomineralisation, which researchers want to answer in the years to come. »Our aim is to identify the process behind this mineralisation,« says Erika Kothe. »With one bacterial strain – a streptomycete – we have begun to switch off genes in order to find the genetic basis responsible for mineral formation. We have already obtained promising initial results.«

Applied research is already drawing on the fundamental processes of this mineral formation: the information can, for example, advance the development of self-repairing concrete. Spores could be integrated into concrete or road surfaces, which, when water entered, would germinate and start to induce mineralisation that would seal the cracks from the inside.

For Erika Kothe, the results demonstrate once again the benefits of cooperation between microbiologists and geoscientists. »We now know that mineral formation is far more complex than we thought, and that microbiological processes play a key role in it.« This would bring the two disciplines even closer together.

At Friedrich Schiller University (FSU) in Jena, this is already happening. Cooperative research initiatives have existed since 2000, and in 2005 these resulted in a BSc/MSc degree programme in Biogeosciences. Since 2006, young researchers have been working together in the »Jena School for Microbial Communication« (JSMC), which has been funded by the Excellence Initiative of the German Federal Ministry of Education and Research and the German Research



Historical photograph from 2005: point cone mine dump in Paitzdorf near Ronneburg in the former uranium mining area of Wismut. The mining landscape in eastern Thuringia has since been comprehensively reclaimed and regreened.

Foundation. In varied interdisciplinary projects within this initiative, researchers are uncovering the means by which microorganisms influence many different areas of life. In one example, the biogeoscientists are developing methods for remediating metal contamination at mining sites all over Europe, thus allowing the land of former heap sites to be reused. Another new research result offers a promising approach to this problem.

Fungi »nibble« on rocks

Here again, the biological version of a phenomenon known principally from the geosciences plays a major role. This time, the focus is not on the creation of rock, but rather the opposite—weathering. It is not only the effects of weather and physical processes that break down rocks: organisms also play a part in weathering. The FSU researchers have now found that fungi can attack rock and, in the process, dissolve heavy metals from this hard material.

»If one brings ground rock into contact with these fungi, metals can be released—we already knew that,« says Erika Kothe. »For this reason, we wanted to investigate more closely whether this was also possible in the case of compact rock samples.« The microbiologists suspected that the enzyme laccase plays a decisive role here. This protein is found mainly in wood-rotting white-rot fungi, which need it in order to break down lignin, a biopolymer present in wood that can only be completely broken down by fungi.
For this reason, the researchers grew such a fungus, with the Latin name *Schizophyllum commune* (see box on the right), on black slate slabs in the laboratory. The rock material from the spoil tip of the tourist mine Morassina or from the former uranium mining area near Ronneburg in Thuringia was then analysed after incubation with the fun-

penetrated the rock and formed etch pits under the growing fungal hyphae to a depth of approximately 200 nanometres,« explains Kothe. »Black slate is rich in organic material, which is used by the fungus for nutrition.«

To establish which factor is ultimately decisive for this behaviour, the researchers switched off individual genes of the fungus. After knocking out the gene responsible for the formation of laccase, they obtained confirmation of their hypothesis.
Furthermore, they discovered that *Schizophyllum commune* produces a particularly large amount of the enzyme when grown with the rock material present—probably because it needs more of this enzyme in order to gain access to its food source.

These findings might help to develop new methods for reclaiming land that has been mined. By breaking down the organic material in the rock, the fungus dissolves the heavy metals embedded in it. These metals are thus concentrated in the water. With the help of the fungus, such heavy metal residues could therefore be removed biologically. »This shows us yet again the potential of microorganisms,« says Erika Kothe, »and we will continue with our research on these interactions between biosphere and geosphere in the future, together with our colleagues from Geosciences.«



Calcite crystal on mineral realgar from China (mineralogical collection of the University Jena).

BACKGROUND

The mineral **calcite** consists of calcium carbonate. It is usually a colourless mineral, which dissolves with carbon dioxide emission in an acidic environment. Characteristic for calcite crystals is their birefringence: incident light is split into two rays of light with different refractive indices. Calcite is a rock-forming mineral and it occurs, for example, in marble and limestone. Stalactites and stalagmites in caves may also consist of calcite.

Vaterite, which is chemically related to calcite, also consists of calcium carbonate, but differs from calcite in its crystalline structure. As a result, the significantly rarer vaterite has different characteristics: it forms only small, filamentous crystals and is harder to dissolve than calcite. Vaterite forms in mineral-rich springs and also in organic tissue. It is a constituent part of gallstones and kidney stones, for example.

The rock called **travertine** consists mainly of calcite (calcium carbonate), which precipitates as »fresh-water limestone« from warm or cold springs. Well-known features are, for example, the »travertine terraces« in Pamukkale, Turkey, or in Mammoth Hot Springs, Yellowstone National Park, USA. The rock is light in colour, usually yellowish and brown, and has a porous structure. Travertine is used as building material, for example in many historical structures such as churches.



The fungus ***Schizophyllum commune*** (split gill fungus) is widespread and found all over the world. Especially interesting is the fact that this fungus forms more than 20,000 different »sexes« or mating types, enhancing the probability of reproducing sexually with outbreeding, and limiting inbreeding genetically. It occurs as a typical cause of white rot on deciduous and coniferous trees.

***Schizophyllum commune* produces fruiting bodies on dead wood, but also in petri dishes. Along with other fungi, it appears in the special exhibition, »Dem Geruch auf der Spur—Die chemische Sprache der Natur« (Following the scent—nature's chemical language), in the Phyletic Museum of the University Jena until autumn 2018.**

Original Publications
Stone-Eating Fungi [...]. Advances in Applied Microbiology (2017), DOI: 10.1016/bs.aambs.2017.01.002; Calcium carbonates: Induced biomineralization with controlled macromorphology. Biogeosciences (2017), DOI: 10.5194/bg-2017-251

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Imaging with »X-ray vision«

With ultrashort X-ray pulses, processes and structures can be resolved down to the nanometre range. X-ray pulses are usually generated in huge particle accelerators, such as the DESY in Hamburg. But the access to such facilities is limited and their operation is extremely expensive. Physicists in Jena are therefore developing »handy« laser systems, which enable ultrashort X-ray pulses at laboratory scale and thus allow a wide variety of applications in the lab.

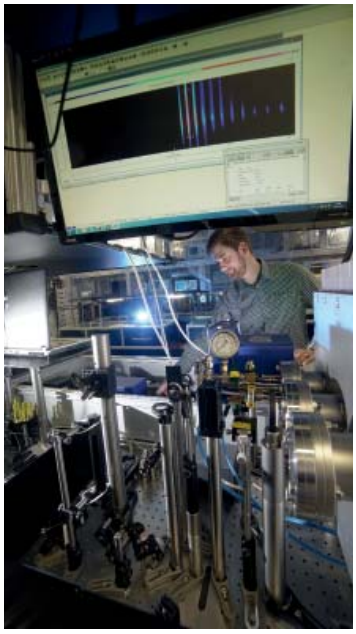
BY SEBASTIAN HOLLSTEIN

A visit to the optometrist often involves optical coherence tomography. This imaging process uses infrared radiation to penetrate the layers of the retina and examine it more closely in three dimensions, without having to touch the eye at all. This allows eye specialists to diagnose diseases such as glaucoma without any physical intervention.

However, this method would have even greater potential for science if shorter wavelengths were used, thus allowing a higher resolution of the image. Physicists at Friedrich Schiller University Jena have achieved just that and they have reported their research findings in the specialist journal »Optica«.

First XUV coherence tomography at laboratory scale

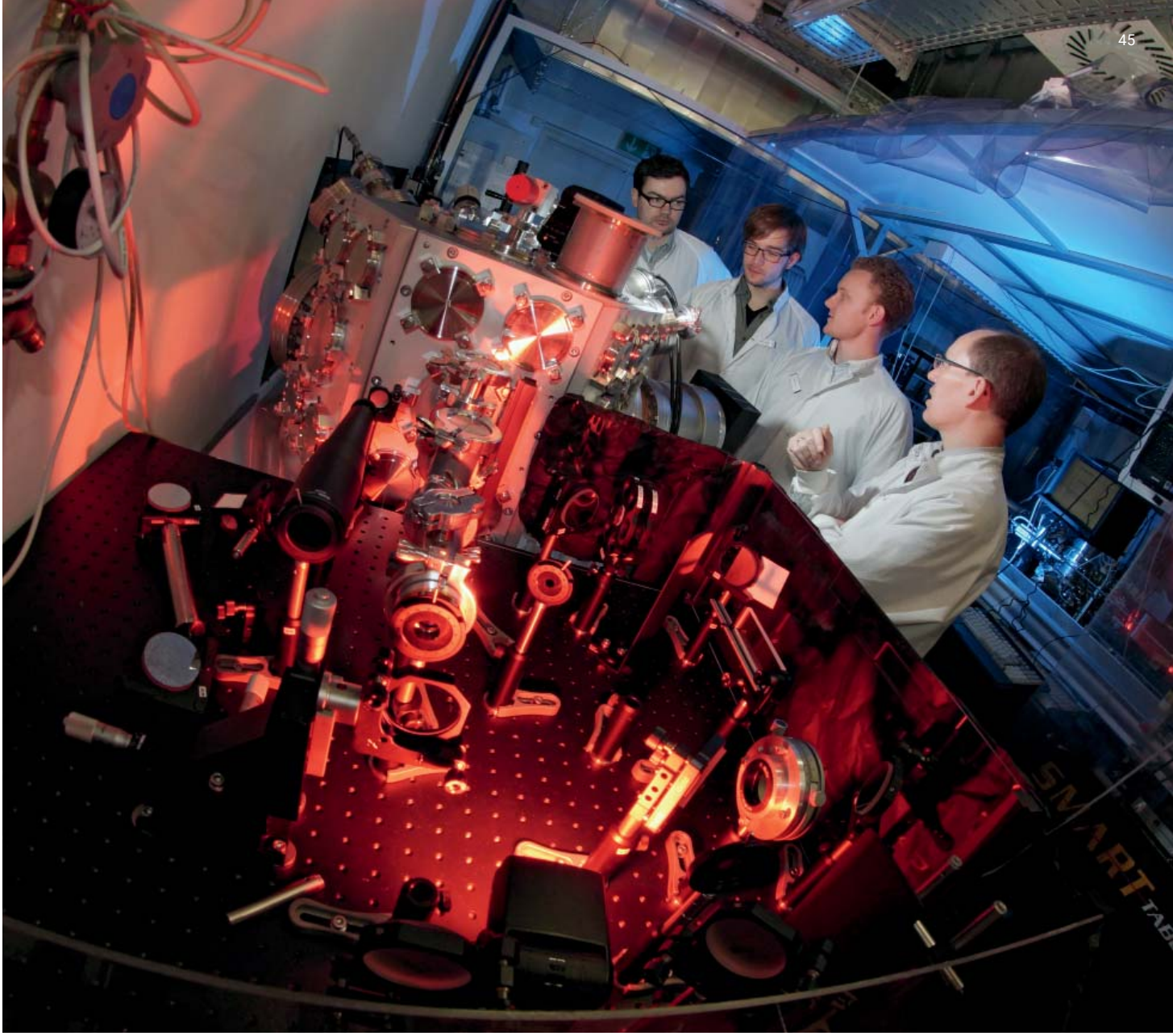
For the first time, the University physicists used extreme ultraviolet radiation (XUV) for this process, which was generated in their own laboratory, and they were thus able to perform the first XUV coherence tomography at laboratory scale. This radiation has a wavelength of between 20 and 40 nanometres—from which it is therefore just a small step to the X-ray range.
»Large-scale equipment, that is to say particle accelerators such as the German Elektronen-Synchotron in Hamburg, are usually necessary for generating XUV radiation,« says Silvio Fuchs of the Institute of Optics and Quantum Electronics of the Jena University. »This makes such a research method very complex and costly, and only available to a few researchers.« The physicists have already demonstrated this method at large research facilities, but they have now found a possibility for applying it at a smaller scale.
In this approach, they focus an ultrashort, very intense infrared laser in a noble gas, for example argon or neon. »The electrons in the gas are accelerated by means of an ionisation process,« explains Fuchs. »They then emit the XUV radiation.« It is true that this method is very inefficient, as only a millionth part of the laser radiation is actually transformed from infrared into the extreme ultraviolet range, but this loss can be offset by the use of very powerful laser sources. »It's a simple calculation: the more we put in, the more we get out,« adds Fuchs.



The generation and application of ultraviolet radiation has become a key topic at a number of research institutes in Jena. Physics doctoral candidate Robert Klas can be seen here behind such a test setup. He and his colleagues in the team led by Prof. Jens Limpert focus laser pulses in a birefringent crystal, which doubles the frequency of the original infrared light. As a result, laser pulses in the green wavelength range are generated. In a second step in what is called cascaded frequency conversion, these pulses are focused again, resulting in pulses of an even higher frequency in the extreme ultraviolet range (XUV). Limpert and his team are leaders in, among other things, the development of ultrashort pulse lasers with a very high medium-range performance, which can then be used to produce intensive XUV radiation.

Strong image contrasts are produced

The advantage of XUV coherence tomography is that, in addition to the very high resolution, the radiation interacts strongly with the sample, because different substances react differently to light. Some absorb more light and others less. This produces strong contrasts in the images, which provide the researchers with important information, for example regarding the material composition of the object being examined.
»For example, we have created three-dimensional images of silicon chips, in a non-destructive way, on which we can distinguish the substrate clearly from structures consisting of other materials,« adds Silvio Fuchs. »If this procedure were applied in biology—for investigating cells, for example, which is one of our aims—it would not be necessary to colour samples, as is normal practice in other high-resolution microscopy me-



From right: Prof. Gerhard G. Paulus, Silvio Fuchs, Martin Wünsche and Dr Christian Rödel by a laser-driven X-ray source. The physicists want to make it possible to use X-ray pulses for new imaging procedures, for example for studying cells.

thods. Elements such as carbon, oxygen and nitrogen would themselves provide the contrast.«

Before that is possible, however, the physicists of the University of Jena still have some work to do. »With the light sources we have at the moment, we can achieve a depth resolution down to 24 nanometres. Although this is sufficient for producing images of small structures, for example in semiconductors, the structure sizes of current chips are in some cases already smaller. However, with new, even more powerful lasers, it should be possible in future to achieve a depth resolution of as little as three nanometres with this method,« notes Fuchs. »We have shown in principle that it is possible to use this method at laboratory scale.«

The long-term aim could ultimately be to develop a cost-effective and user-friendly device combining the laser with the microscope, which would enable the semiconductor industry or biological laboratories to use this imaging technique with ease. ■

Original Publication
Optical coherence tomography with nanoscale axial resolution using a laser-driven high-harmonic source. Optica (2017), DOI: 10.1364/OPTICA.4.000903

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GPS for antibiotics

How does an active substance know where it should go? And how does the substance get from the bloodstream to exactly the right spot? Using polymer-based nanosystems, researchers in Jena want in future to direct drugs in a targeted fashion to the source of the infection and deliver active substances—antibiotics, for example—precisely where they are needed.

INTERVIEW: AXEL BURCHARDT



Chemist and materials scientist Prof. Dr Ulrich S. Schubert is coordinator of the Collaborative Research Centre (CRC) 1278 »PolyTarget« (see also box p. 11). With innovative carrier materials for the targeted application of medicines, the research consortium supports the diverse and broad-based sepsis and infection research being carried out at the University of Jena, Jena University Hospital and non-university research institutes in Jena.

You are an expert in innovative polymer-based batteries, self-healing materials and innovative applications of inkjet printing. Why are you and your team of chemists and material scientists now also developing new drugs?
Another of our specialist fields is that of pharmaceutical polymers, which are synthetic materials for use in medicine. Together with a strong University Hospital and the non-university institutes, we have been able to build up a solid position, which is reflected in the new Collaborative Research Centre »PolyTarget«, funded by the German Research Foundation. In this CRC, we want to package active substances in such a way that they can be sent directly to the location of the disease, without side effects.

Why should active substances be packaged in nanoparticles and why are these particles in particular well-suited for tackling infectious diseases?
There are many well-known antibiotics which cannot be used, because they have too many side effects: the dose is too high and the drugs are distributed throughout the body. And there are many potential new antibiotics which cannot be used, because they are not water-soluble and therefore not bioavailable. We offer solutions for both of these limitations. We package the active substances in tiny polymer-based nanoparticles. This causes far fewer side effects, partly because the doses can be smaller, as we ensure that they are taken up specifically by the organs and cells that are targeted. We are developing these new pharmaceutical polymers using robotics, with high-throughput methods, working together with our medical colleagues right up to the application stage.

Your nanoparticles are containers for these active substances. What does the ideal container for such substances look like?
The ideal container for an active substance is of course non-toxic and biodegradable, and all its harmless components should ultimately be excreted. Furthermore, it has a GPS system with which we can determine which organ and which cell the container must reach. The container also contains a dye, so that with a modern microscope, one can trace where the container is going and further optimise its path. The CRC is first of all a basic research project, with which we want to develop an understanding of the size, the load and the type of polymer we need to use in order to deliver genetic material or an antibiotic or peptide to the desired location. Our aim is to develop a platform that will also make it possible in future to develop new drugs in a relatively short time to the stage where they can be used to cure other diseases.

Up to now, you have never limited yourself to basic research. Are you also planning to put the nanocontainers to practical use in therapies and diagnostics?
That is of course also planned. We already have a spin-off, SmartDyeLivery GmbH, which, in collaboration with the University Hospital, will shortly be working with a large animal model on a very specific pathology—sepsis-induced cholestasis. At the same time, there are various application-oriented projects in collaboration with industry.

When can we hope to see the first polymer nanocontainers in use?
That will depend on how much time is needed for the medical formalities and the studies. The goal of the CRC is in any case to achieve some translation into practice within four years, so that follow-up projects can be carried out directly with companies.

The field is so huge—is it possible to deal with it, even with such a diverse team?
Naturally, we have restricted our work. We use the nanomedicine that we want to pursue really only for infection-related diseases, such as sepsis. Because here in Jena we have a strong position in this field, with the other priority areas at the University and the non-university institutes. Only together can we achieve critical mass. But in Jena we are lucky to have, among other disciplines, Medicine, Pharmaceutics, Biochemistry, Macromolecular Chemistry, and Material Science.
There are not many locations that can offer so much in one place.

Calendar: The myth of the October Revolution

Hundred years ago, on 25 October 1917, the Bolsheviks took over the reigns from the Provisional Government in Russia. The upheaval at the Winter Palace turned to a glorification of the Great October Socialist Revolution which was illustrated accordingly later. It is a myth that has endured to the present day.

BY STEPHAN LAUDIEN

The shot fired from the armoured cruiser Aurora (»red sky at morning«) was the signal for the storm on the Winter Palace and heralded the new era of Communism at the same time. Thousands of Bolsheviks attacked the hated palace of the Russian tsars in Saint Petersburg and gained the victory—a strong signal for the workers in the whole world.

What a story! Well, it is not a true one. »From its beginnings, the October Revolution was a myth arranged as such,« says the historian specialized in the East European history Prof. Dr Jörg Ganzenmüller. According to him, the term »revolution« itself is not tenable. In 1917, there were no revolutionary masses on the streets. It was rather a concentrated action in which the Provisional Government was arrested and strategic points in Saint Petersburg were occupied. Jörg Ganzenmüller describes it as an overthrow. In spite of this, the myth of the Great October Revolution lives on, even hundreds years later. It is the images of the events to be blamed for it, to be more accurate, those missing.

The people already rose in February 1917. The reason for the revolution was a provision crisis in the Russian Empire which had been due to the World War I. After the tsar Nicholas II. had been forced to abdicate, the power was shared by the Provisional Government and the soviets, i.e. workers' and soldiers' councils. Since the Provisional Government kept fighting in the unpopular war, Lenin and his Bolsheviks seized its power.

The vast majority of images originate in a film by Eisenstein

»The Bolsheviks had been enjoying the support among workers and soldiers,« explains Jörg Ganzenmüller. In the Constituent Assembly elections of 1918, they thus received 25 percent of votes. In the October Revolution, however, the masses were not involved. Later on, the event was therefore arranged accordingly. Apart from the events on the historic sites on the anniversaries, the images were provided by the film October: Ten Days That Shook the World by Sergei Eisenstein from 1927 primarily. In vast majority, the images of event, which we still have in mind, originate in this film. As Jörg Ganzenmüller comments, the Bolsheviks aimed at suggesting to posterity that the masses had been on their side. As a matter of fact, in 1918 the majority of population voted for the Socialist Revolutionary Party—agrarian socialists popular with the peasants. »After the Bolsheviks had won the civil war, they wanted to be seen as the revolutionary force,« says Prof. Ganzenmüller. At the same time, the competitive socialist parties should have been marginalized—apart from the social revolutionists, particularly the Mensheviks who had been defeated in the election. Having a great power, the myth of the storm on the Winter Palace made its way to German textbooks, too. Whereas in East Germany the Soviet interpretation was adopted, in West Germany one could find »images« of the October Revolution even in the nineties—despite the fact that none exist. Up until today, documentaries have been trying to replace the missing images by film clips, especially from the one by Eisenstein. But only a few of them refer to the source—enabling the myth to endure.



A bust of Vladimir Ilyich Ulyanov, alias Lenin. The October »Revolution« he led was rather an overthrow than a revolution. To the present day, false images have been circulating about the event.



MEDICINE

Surviving with leukaemia

Targeted therapy for chronic myelogenous leukaemia (CML) continues to be effective and to have few side effects, even over a period of 11 years. This was the result obtained by a team led by Jena haematologist Prof. Andreas Hochhaus in a fresh analysis of the IRIS study. This pioneering clinical trial underpinned the effectiveness of targeted therapy for CML and the accompanying molecular monitoring.

BY UTA VON DER GÖNNA



Haematologist Prof. Andreas Hochhaus and his team conducted a fresh analysis of the »IRIS« study, which began in 2000.

Chronic myelogenous leukaemia (CML) is the second most common form of chronic leukaemia. This disease of the haematopoietic system is caused by a specific genetic mutation (portions of chromosomes 9 and 22 switch places) which leads to a sharp increase in the number of white blood cells. The new active ingredient tested in this trial—a tyrosine kinase inhibitor—specifically inhibits the activation of the altered protein that causes continued division, i.e. reproduction, of the leukaemia cells. These new drugs have fundamentally improved therapy for this disease, which previously could only be cured by stem-cell transplantation.

»Currently, 83 per cent of CML patients live for 10 years after their diagnosis, which is close to the survival rate in the general population,« says Prof. Andreas Hochhaus, Director of the Department of Haematology and Medical Oncology of Jena University Hospital, describing a key result of a long-term analysis of the IRIS study data.

The study was begun in 2000 to compare the effectiveness of the tyrosine kinase inhibitor »Imatinib« with the standard therapy of the time, which was to give patients the immunostimulant interferon alpha. »IRIS« stands for »International Randomized Study of Interferon Versus STI571«.

The therapeutic response and the tolerability of »Imatinib« were so good that the majority of patients from the inter-

Cluster of Excellence »Enlightening the Receptome: From Biophysics to Clinical Applications«

The »receptome«, the sum of all receptor molecules of an organism, makes up more than five per cent of its proteins. Through interactions with other molecules, these **molecular switches** direct a large number of metabolic processes. Due to their function, receptors are ideal targets for therapeutic applications. The aim of the Cluster proposal is to unravel the receptome in all its diversity and use the knowledge thus obtained to develop **innovative diagnostic procedures and personalised therapies** for the treatment of diseases.
It is a joint proposal by the **Universities of Würzburg and Jena**, headed by Prof. Markus Sauer (Würzburg) and Prof. Klaus Benndorf and Prof. Christian Hübner (both in Jena).

feron group switched to the other therapy, and »Imatinib« became the standard medication for treating this form of leukaemia. The follow-up of the participants in the study is now providing valuable data relating to long-term therapy. Andreas Hochhaus: »The active substance is also effective when applied over the long term, so that patients are living free from CML symptoms for 10 years and longer. The IRIS study also showed that during this period, no critical side effects accumulate or intensify.«

Not least as a result of the experience gained from the IRIS study, chronic myelogenous leukaemia, with its characteristic mutation, has become the model disease for the diagnosis and treatment of many cancers with complex genetic causes. Findings relating to the individual tumour biology can be used, for example, to make targeted interventions in the molecular tumour mechanisms and develop new therapeutic approaches. Specific interactions of proteins and signal molecules—such that between »Imatinib« and the tyrosine kinase—are therefore the focus of a current joint Cluster proposal by the universities of Würzburg and Jena under the Excellence Strategy programme of the German federal government and federal states (see box above).

Standards established for therapy and monitoring

The effectiveness of a CML therapy is demonstrated by patients entering remission with a reduction in the proportion of genetically modified blood cells still present. To determine remission, a quantitative molecular genetic method of analysis was developed for the IRIS study. This method is now standard for monitoring CML. If the proportion of white blood cells with the characteristic mutation falls below a specific threshold, the disease is considered to be in complete remission.

»Recent therapy studies have shown that patients in deep remission can safely stop their therapy. This has major consequences for their quality of life and also for therapy costs,« notes Andreas Hochhaus, who coordinates the German CML Alliance in Jena. This is a network of university centres, outpatient haematology specialists and patient representatives. »Thanks to the fact that the IRIS study has substantiated the success of the targeted therapy in treating CML, we can turn our attention to questions that go beyond ensuring patient survival. These concern, for example, better procedures in CML treatment and the social and psychological aspects of living with the disease over the long term.«

Original Publication
Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. New England Journal of Medicine (2017), DOI: 10.1056/NEJMoa1609324

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Fossilised specimen of the »Bad Boy« *Ponomarenkia belmonthensis* (late Permian period, Age around 250 million years).

PALEONTOLOGY

»Bad Boy« of the beetles

An international team of insect researchers has succeeded in reconstructing a long-extinct beetle with the help of a fossil. Despite being an impressive 250 million years old, *Ponomarenkia belmonthensis* has astounded researchers with its very »modern« features, which present scientists with a real taxonomic problem.

BY JULIANE DÖLITZSCH

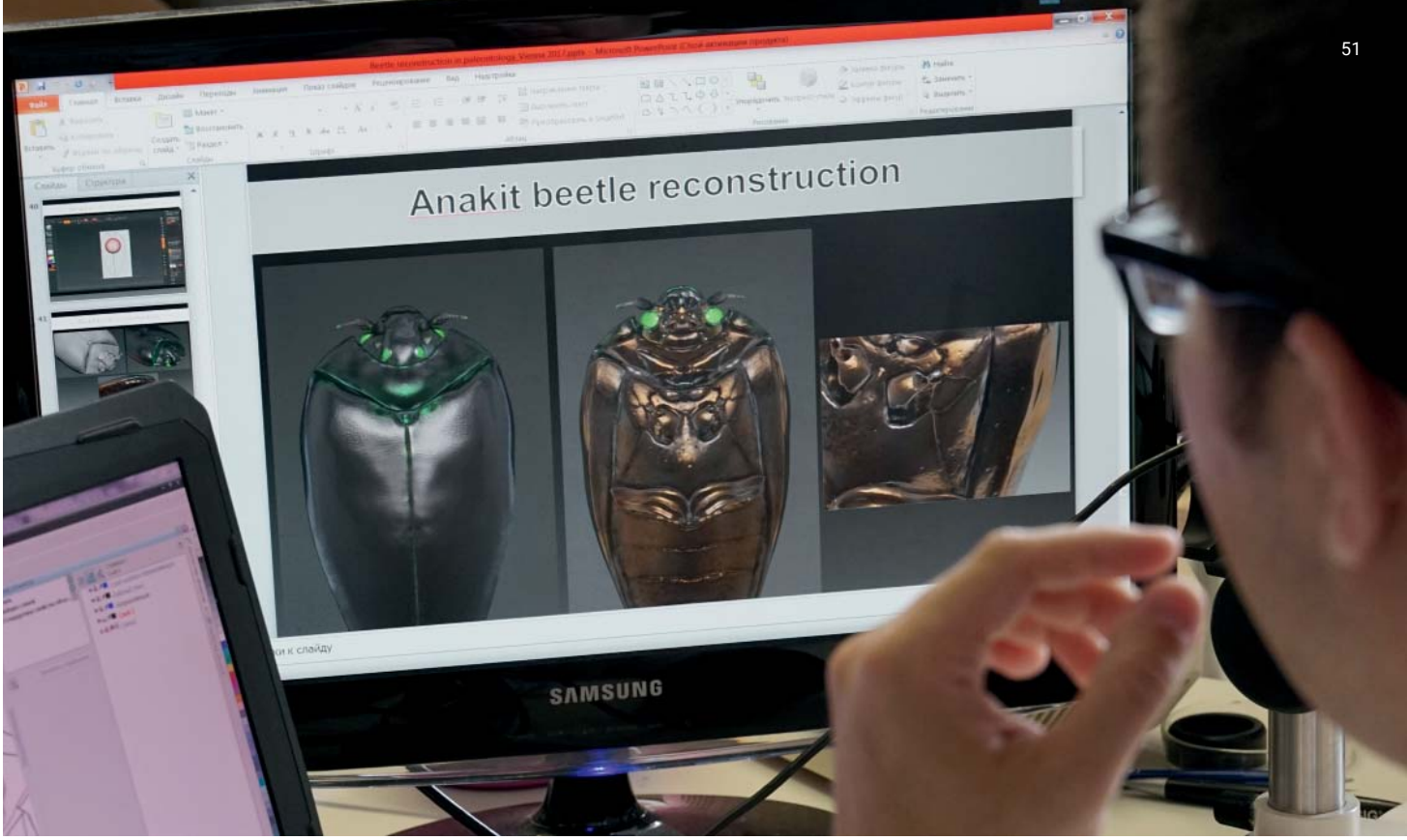
He is Australian, around half a centimetre long, fairly nondescript, 250 million years old—and he is currently causing astonishment among both entomologists and palaeontologists. The discovery of a beetle from the late Permian period, when even the dinosaurs had not yet appeared on the scene, is throwing a completely new light on the earliest developments in this group of insects.

The reconstruction and interpretation of the characteristics of *Ponomarenkia belmonthensis* was achieved by Prof. Dr Rolf Beutel and Dr Evgeny V. Yan of Friedrich Schiller University Jena. They have published this discovery together with renowned beetle researcher Dr John Lawrence and Australian geologist Dr Robert Beattie in the »Journal of Systematic Palaeontology«. It was Beattie who discovered the only two known fossilised specimens of the beetle in former marshland in Belmont, Australia.

»Beetles, which with nearly 400,000 described species today comprising almost one-third of all known organisms, still lived a rather shadowy and cryptic life in the Permian period,« explains Jena zoologist Beutel. »The fossils known to date have all belonged to an ancestral beetle lineage, with species preferring narrow spaces under bark of coniferous trees. They exhibit a whole series of primitive characteristics, such as wing cases—elytra—that had not yet become completely hardened or a body surface densely covered with small tubercles.«

Earliest form of the »modern« beetle

In contrast, the species that has now been discovered, assigned to the newly introduced family *Ponomarenkiidae*, can be identified as a »modern« beetle, in spite of its remarkable age. Modern characteristics are the antennae resembling a string of beads, antennal grooves, and the unusually narrow abdomen, tapering to a point. What is more, unlike previously known Permian beetles, the wing cases are completely hardened, the body's surface is largely smooth, and the thoracic segments responsible for locomotion show modern features, notes insect palaeontologist Yan. In ad-



Insect palaeontologist Dr Evgeny V. Yan in front of the computer reconstruction of »Flat Bob«, the oldest known whirligig beetle and a contemporary of »Bad Boy«.

dition, it appears that this little beetle had stopped living under tree bark, the habitat favoured by its contemporaries, and had adopted a much more exposed lifestyle on plants. A significant fact is that, due to its unorthodox combination of ancestral and modern characteristics, this genus does not fit in any of the four suborders of beetles that still exist, which is why Yan and Beutel have given it the nickname »Bad Boy«.

»*Ponomarenkia belmonthensis* shows above all that the first major events of radiation in the evolution of beetles took place before the Permian-Triassic mass extinction,« says Rolf Beutel. Beetles as a whole survived this dramatic event, which saw the acidification of the seas and major volcanic eruptions, considerably better than most other groups of organisms—presumably because of their terrestrial life style and hardened exoskeleton. However, the »Bad Boy« ran out of luck, as there are no more traces of its existence in the Mesozoic era.

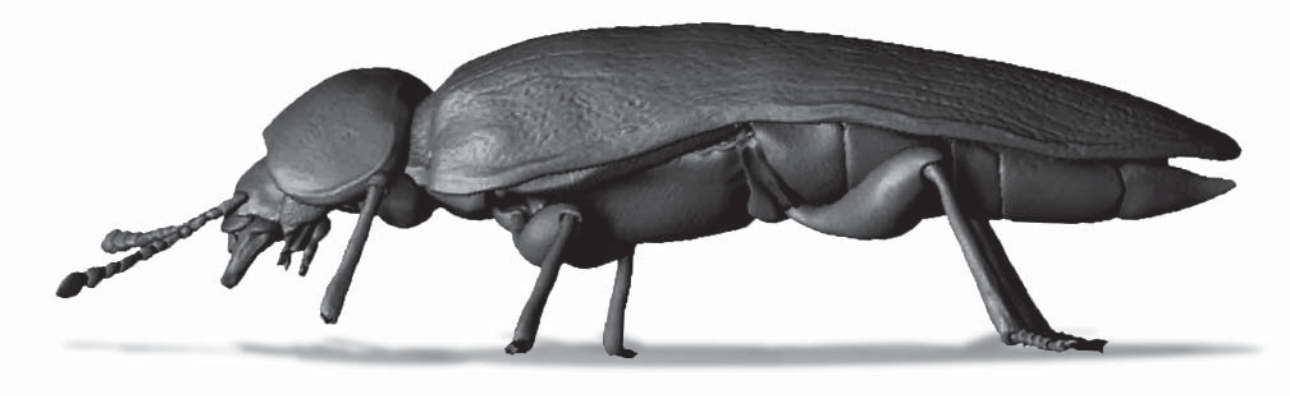
The Jena researchers dedicated the genus and family to Moscow palaeontologist Prof. Alexander G. Ponomarenko. He has had a strong influence on beetle palaeontology for decades and supervised Dr Evgeny V. Yan's doctorate. It is Yan's elaborate reconstructions on the computer that have provided the precise insights into *Ponomarenkia belmonthensis*.

Informative 3D model was created

In the first stage, some 40 photographs were taken of the two specimens, which were available as impressions on stone. »With this series of photographs an accurate 2D reconstruction was possible, with which we were able to correct for deformations in the original fossil. This allowed us to get closer to the actual beetle,« explains Dr Yan. Based on precise drawings and with the help of a special computer program that is also used for animation and computer games, a very informative 3D model was created. »The 3D reconstruction also enables us to draw conclusions about the way the beetle moved and lived,« the palaeontologist adds. He has developed this method of visualisation, as well as the analytical process in which he also includes hypothetical ancestors of the beetle, since his arrival in Jena. »We have already been able to apply this process to three newly discovered ancient beetle species,« Prof. Beutel is happy to report. »In this way, we have made significant steps towards deciphering the earliest stages in the evolution of an extremely successful order of animals.«

Original Publication
At the dawn of the great rise: †Ponomarenkia belmonthensis [...]. Journal of Systematic Palaeontology (2017), DOI: 10.1080/14772019.2017.1343259

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3D reconstruction of *Ponomarenkia belmonthensis* based on precise drawings of the holotype and an accurate 2D reconstruction. Due to its combination of ancient and modern characteristics, this genus cannot be assigned to any of the four extant suborders of beetles, which is why it has the nickname »Bad Boy«.

Outliving life itself

When researchers immortalize themselves as part of the tree of life, their choice is not always a happy one

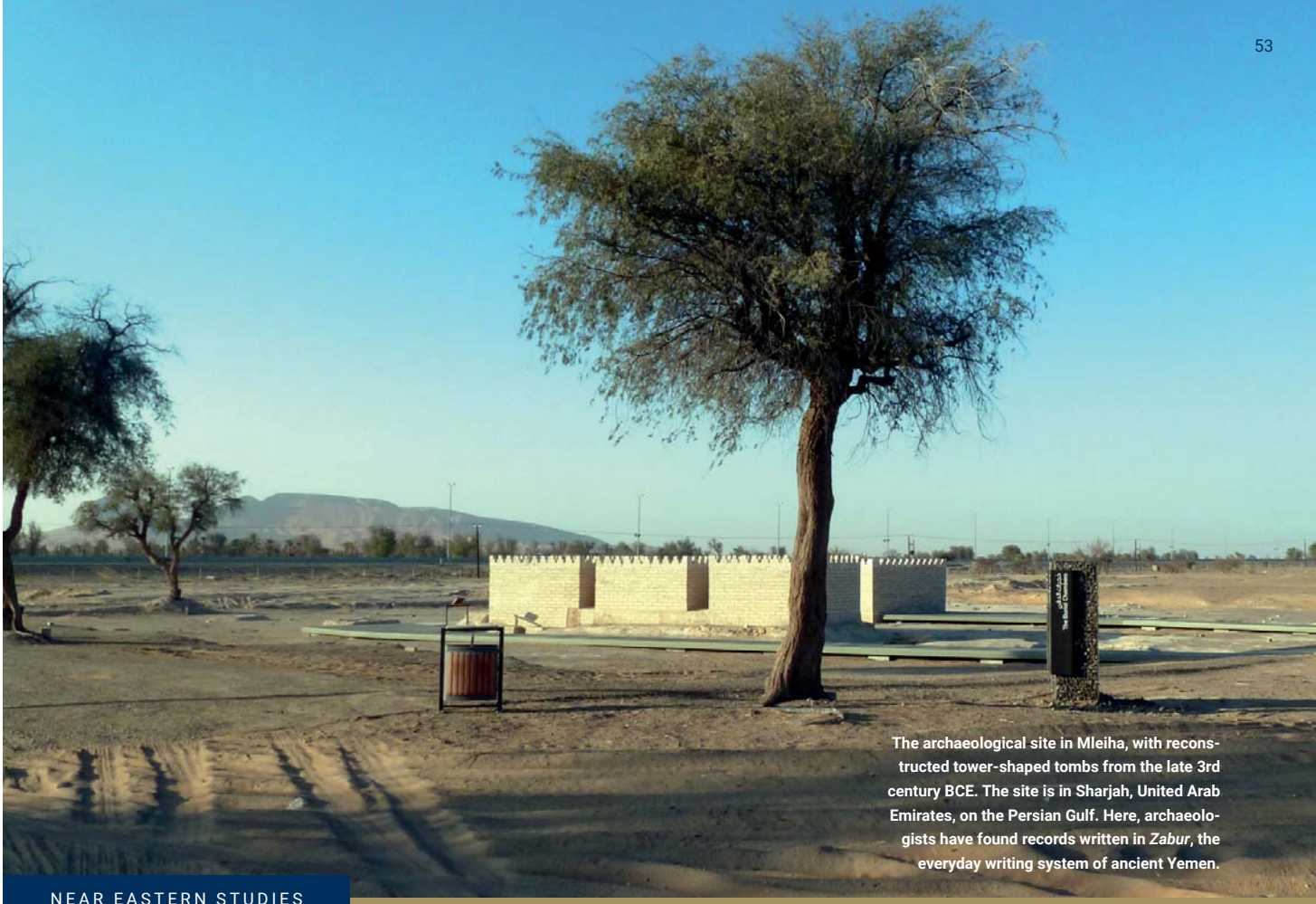
COMMENTARY BY UTE SCHÖNFELDER

Donald Trump was recently in the headlines again. »Oh, really?«, I hear you say, »so what?« After all, when does Donald Trump not cause controversy? In this case, however, it was not the man himself who was to blame, but a newly discovered species—a moth—which was named after Donald Trump in early 2017. *Neopalpa donaldtrumpi* sports a crown of yellow-white scales that bears an undeniably striking similarity to the human Trump's blow-dried hairdo. Whoever saddled the poor creature with this name presumably thought it was funny. But should the classification of species be seen as a source of jokes?

Plants, animals and microorganisms—whether long extinct or still caught up in the treadmill of evolution—everything that walks, crawls, swims or flies, and that grows, metabolizes and reproduces is systematically classified. Thanks to the meticulous work of taxonomists, no creature goes missing—at least on paper. And if a species quits this earthly life, because it cannot find food, a sexual partner or a habitat, or because climate change, an unfortunate mutation or a motorway has led to its extinction, its name and its place in the eternal tree of life will endure—classified and described for all time. How long will *Neopalpa donaldtrumpi* last? Or the huntsman spider *Heteropoda davidbowie*, or the South American frog *Hyloscirtus princecharlesi*?

This is a question that does not arise in the case of *Ponomarenkia belmonthensis*, as this beetle became extinct more than 250 million years ago. Nevertheless, *Ponomarenkia belmonthensis* has only recently been discovered by a research team led by the Jena entomologist Rolf Beutel (see p. 50), phylogenetically classified and scientifically »christened«.
The long-extinct insect is named after the Moscow palaeontologist Prof. Alexander G. Ponomarenko. Nothing is publicly known about his hairstyle. However, his work as a scientist is obviously highly appreciated in Jena, which is why the beetle—combining characteristics of both ancient and modern species—was given the professor's name. However, what is the significance of such appreciation if a dyed-blonde pompadour is clearly just as suitable an inspiration for a name as academic merit?
I am sure that we do not need an official body to vet names, in the way that the registry office in Germany ensures that parents do not call their children »Darth Vader« or »Facebook«. But please, dear taxonomists, preserve the nameless, as-yet-undiscovered beetles, worms or moths from a fate like that of *Neopalpa donaldtrumpi*! Be aware of the far-reaching consequences of your decision when you name a previously unknown creature: you are recording it in the eternal book of life. Heed the example of those who christened *Ponomarenkia belmonthensis*! Ultimately, politics and evolution both teach us that presidents and species come and go, but the scientific names of all beings remain.

Name your own species: if you feel called upon to give a name to a new species, get in touch with the Phyletisches Museum (Phyletic Museum). In exchange for a donation to the museum's association, anyone can choose a name for a tropical moth or butterfly species. For more information, please visit: www.phyletisches-museum.uni-jena.de/falternamen-zu-vergeben.html.



The archaeological site in Mleiha, with reconstructed tower-shaped tombs from the late 3rd century BCE. The site is in Sharjah, United Arab Emirates, on the Persian Gulf. Here, archaeologists have found records written in *Zabur*, the everyday writing system of ancient Yemen.

NEAR EASTERN STUDIES

Gifts to the gods

Travelling broadens the mind, as getting to know other people and cultures makes us see our own lives in a different light. Travellers bring something back from foreign places and leave traces in those places that they have visited. Such exchanges go back thousands of years, as evidenced by the latest research results of the Jena University Semitist, associate professor Peter Stein. In the Persian Gulf area, he deciphered the inscription on a silver plaque, which is evidence that people in the Gulf region worshipped the goddess Allāt. Previously, such gifts to the gods were only known from southern Arabia—the area that is now Yemen.

BY JULIANE DÖLITZSCH

In Mleiha, an archaeological site some 55 kilometres east of Dubai in the Emirate of Sharjah, local researchers made two discoveries a few years ago. In excavations they found a small silver plaque and a handle broken off an amphora, both dating from the late 3rd century BCE. Both finds bear inscriptions in Hasaitic, the language spoken in the region 2,000 years ago.

However, the writing on the two objects presented the researchers with a puzzle, because it did not resemble the letter forms known from the region up to that point. Peter Stein, a researcher in Semitic languages, cultures and histories, who in recent years has been working intensively on the written culture of ancient South Arabia, was able to solve the puzzle. With support from the Director-General of the Sharjah Archaeological Authority, Dr Sabah Jasim, Stein has been able to study the original inscriptions and decipher them.

The *Zabur* writing system

What made the inscriptions initially so »unreadable« was the fact that they were written in *Zabur*, in cursive letters that were commonly used for writing daily matters in ancient Yemen. »*Zabur* was usually scratched into small wooden sticks,« explains Stein. Letters, contracts and other official documents were written down and distributed in this way as far back as the early 1st century BCE. The »ancient South Arabian minuscule script«, as *Zabur* is also referred to, was previously only known from the south of the Arabian Peninsula, but not from the Persian Gulf region.

The content of the inscriptions was also a source of astonishment for the researchers. Whereas the writing on the handle of the amphora refers only to its



The silver plaque from the 3rd century BCE was found at the archaeological site in Mleiha in the Persian Gulf. The text was written in *Zabur*, which is actually typical of the southern Arabian region. The plaque bears the inscription: »Liʿaḏḏim, the daughter of Maʿūnlāt, has offered (the goddess) Hallāt this metal plaque.«

owner, the inscription on the seven-by-six-centimetre silver plaque is evidence of a religious custom hitherto also unknown in the Gulf region.
»In material and shape, the plaque resembles the bronze plaques that were typical of southern Arabia. There, they were used as votive offerings to the gods,« adds Stein. The letters, six to eight millimetres in size, are punched into the smooth metal surface. As was the usual practice in ancient South Arabia, the individual words are separated by vertical lines.

Votive offering to the goddess Allāt

Now that the content of the inscription has been deciphered, we can see clearly that the plaque was offered to Allāt, a goddess worshipped throughout Arabia. Peter Stein suspects that the goddess »might have been worshipped here as a major goddess of the area, under the local name of Hallāt«. Starting from South Arabia, the *Zabur* script and the custom of dedicating metal plaques to the gods must have travelled many hundreds of kilometres in order to have become a local custom at the site in the Gulf region where it was found. This probably happened through trade along the famous Incense Route. From numerous inscriptions found in Yemen, it is known that around 300 BCE there was lively trade between the ancient trading city of Gerrha in the east of the Peninsula and the region that is now Yemen. »The eastern Arabian traders, who had not developed their own local written language, must have used the South Arabian writing system and then brought this knowledge back home with them,« says Stein.

A second route that the *Zabur* script and the religious custom might have taken runs along the south coast of the Arabian Peninsula, through the region Hadramawt—now the eastern part of Yemen—to Oman. Here too, people communicated using wooden sticks inscribed with the *Zabur* script. »The local form of the ancient South Arabian writing system that was developed in eastern Arabia is referred to by scholars as Hasaitic,« explains Stein. The other writing system we know of from the Gulf Region is Aramaic, which served as a lingua franca throughout the Near East from the middle of the 1st millennium BCE. An Aramaic votive inscription to the same deity on a bronze plaque was already discovered in Mleiha a considerable time ago. However, it was only possible to identify this votive offering correctly against the background of the recently discovered silver plaque.

Temples still to be discovered

What is exciting about these votive plaques is not least the knowledge that there must have been temples or shrines near Mleiha. »However, apart from tower-like tombs, no evidence has as yet been found for solid constructions in that period. The permanent settlement of the location by the previously nomadic population apparently began only 100 to 200 years later,« explains Stein. The finds do answer some questions, but also pose new riddles, which need to be solved. ■



Associate professor Peter Stein has deciphered the inscription on the silver plaque (photo p. 54). He is one of the few experts in the world able to read the ancient South Arabian minuscule script *Zabur*.

Original Publication
South Arabian zabur script in the Gulf: some recent discoveries from Mleiha (Sharjah, UAE). Arabian archaeology and epigraphy (2017), DOI: 10.1111/aae.12087

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CHEMISTRY

To attract—or not attract

Jena chemists have developed a magnetic polymer, the »attractive« properties of which can be potentially switched on or off. The secret behind the material bearing the name »Jena University Magnetic Polymer« (JUMP) lies in its structure: the regularly structured three-dimensional framework is peppered with nano-pores in which various chemical molecules can be embedded, thus controlling the properties of the polymer.

BY UTE SCHÖNFELDER

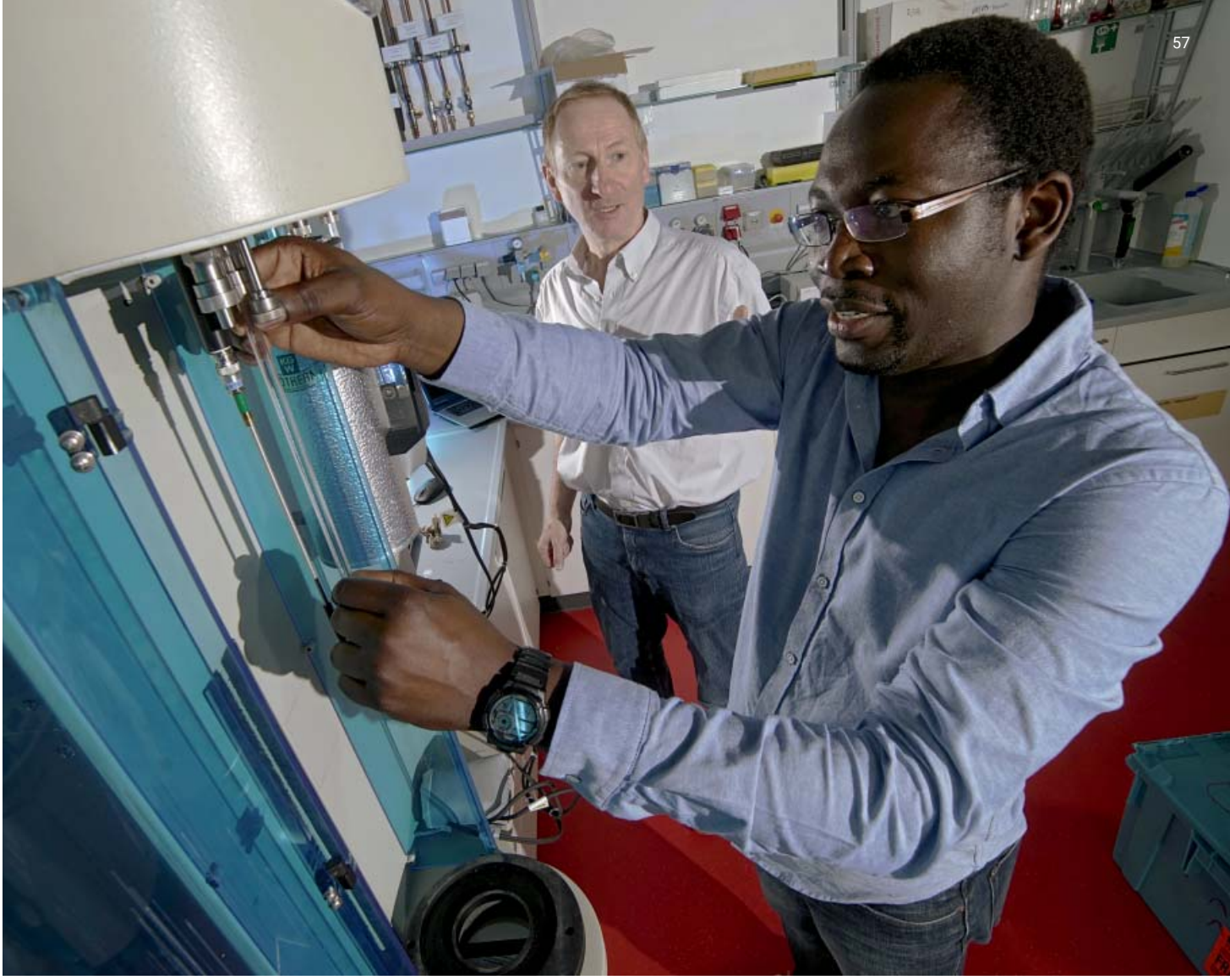
Photo left: In a laboratory at the Institute of Inorganic and Analytical Chemistry, doctoral candidate Oluseun Akintola from Nigeria shows a small glass tube containing a tiny sample of a porous polymer. The innovative material, which demonstrates a combination of fascinating properties, opens up new possibilities in the area of switchable magnetic materials.

Photo right: Oluseun Akintola prepares a sample of the magnetic JUMP polymer for examination on a sorption-analyser. He is a doctoral candidate under Prof. Winfried Plass (in the background) at the Institute of Inorganic and Analytical Chemistry.

In the glass vessel that chemist Oluseun Akintola holds up to the light, one can see just a few small crystals. There is a violet shimmer to the fragments of polymer, which otherwise do not look at all spectacular. What is special about them, explains Akintola—a doctoral candidate from Nigeria working at the department of Inorganic Chemistry II—is in the detail. »The crystals have a huge inner surface,« he says. One gram of the material, which fits in a teaspoon, has a pore surface of at least 150 square metres. The »Jena University Magnetic Polymer« – JUMP for short – has been developed and characterised by Oluseun Akintola, who is supported by the Evangelisches Studienwerk Villigst, as part of his doctoral research under Prof. Winfried Plass, together with colleagues in the department. The researchers have reported the material JUMP-1 in the specialist journal »CrystEngComm« of the Royal Society of Chemistry, and Prof. Plass's team also designed the cover.

Three-dimensional framework with numerous cavities

In addition to its appreciable interior size, the second special feature of this porous polymer is its magnetic properties. »What's more, these properties are potentially switchable, which means that we are currently working on chemical modifications of the polymer that can turn the magnetic property of the material on or off,« explains Prof. Plass. The material consists of layers of a two-dimensional network made of magnetic cobalt clusters and organic linkers, which are then connected by regularly arranged bridging molecules. Plass



adds: »This produces a three-dimensional crystal, the volume of which is more than 50 per cent cavities.« Various tiny ions or molecules can be embedded in these cavities. »The properties of the polymer change according to the properties of these guest molecules,« says Plass. Such porous framework substances, or MOFs (Metal-Organic Frameworks), were not invented in Jena, but have been known in a variety of forms for some years.

The novel feature of JUMP-1, however, is that the linking molecules are redox-active: they can give up single electrons, which makes it possible to control the magnetic properties of the layers of cobalt ions. Furthermore, positively charged counter-ions can be selectively embedded in the overall negatively charged polymer framework. These positively charged ions regulate the capacity of the lattice framework to take up guest molecules and, as it were, selectively open and close the »door« to the pores. »In this way, we can fashion the polymer to fit the possible application,« says Plass.

Future switchable magnetic materials could be used, for instance, as highly sensitive sensors for small charged molecules. Thanks to their appreciable interior surface area, such polymers could also be of use as catalyst for chemical reactions.

Original Publication
A robust anionic pillared-layer framework with triphenylamine-based linkers: ion exchange and counterion-dependent sorption properties, CrystEngComm (2017), DOI:10.1039/C7CE00369B

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Excavating traces of ancient earthquakes

If there is an earth tremor anywhere in the world today, technical devices record even the tiniest movement. And if an earthquake causes serious damage, the media ensure that we know about it and that it is not so quickly forgotten. However, even catastrophes for which we have no records have left traces underground. Geoscientists are now uncovering this evidence.

BY SEBASTIAN HOLLSTEIN

Over the next three years, geoscientists from Jena will be working in a little-known earthquake zone in Europe: Slovenia and eastern Italy. »Today, we are particularly aware of the major disasters of recent years in the centre of the Italian Peninsula, but similar events can also occur in neighbouring areas,« explains Dr Christoph Grützner. He leads a project that is part of the priority programme SPP 2017, funded by the German Research Foundation (DFG). Scientists from FSU Jena, RWTH Aachen and GFZ Potsdam are working together in this programme, doing research on the tectonic movements in this region.

»The Adriatic Plate is continuously moving northwards towards the Eurasian Plate, at a rate of about two millimetres per year,« says Grützner. This may be very slow when compared with other earthquake zones, but it does not mean that there is no seismic activity. Earthquakes in May and September 1976 killed approximately 1,000 people and caused considerable damage in a number of towns.

Written records of historical quakes are rare

There was a similar disaster in 1511, as evidenced by historical documents. Due to the long gap between the individual events, though, it is difficult to estimate average repetition rates at individual faults, which could contain important information about the seismic activity in this area. »At most, we can hope to get information from the Romans, who ruled the region around 2,000 years ago. There are no written records of any earlier earthquakes,« explains Grützner, a geophysicist. »This means that there could be geological time bombs ticking in this region, which nobody knows about because they only explode every few thousand years.«

However, a close look at and under the ground can help researchers to find traces of past earthquakes. Grützner explains: »First, I use the computer to analyse high-resolution terrain models and look for particular structures in the landscape that indicate tectonic seam zones—for example, characteristic-looking river valleys. And then I go in person to look at the area.«

At the site, he digs into the earth, exposing sedimentary layers in order to find striking deformation structures. Layers that are normally arranged horizontally can be deformed. »This is how I identify faults from which earthquakes have been triggered in the past and could again be triggered in future. In addition, by dating the sedimentary layers I can draw up a possible chronology of the seismic activity.«



Prof. Kamil Ustaszewski (l.) and Dr Christoph Grützner study a map of the Alps covering the area of Slovenia and north-eastern Italy.

Researching the origins of the Alps

However, this Adriatic region is interesting not only in relation to earthquakes. The tectonic movements of the two plates are also responsible for the emergence of the Alps, says Prof. Kamil Ustaszewski. The professor of structural geology heads the working group of which Grützner's work is also a part. »We are investigating how the Alps were formed and how the deep structures beneath them were created,« explains Ustaszewski.



Securing, using and sharing

Constantly increasing amounts of scientific data from observations, experiments or measurements not only require greater computer storage capacity, but also sustainable research data management. This is currently being significantly expanded at Friedrich Schiller University in Jena.

ARA Cluster of the Institute of Computer Science in the University's Computer Centre. The High-Performance Computer system (HPC) works with at least 300 processors. In order to obtain scientific information from the flood of digital data that is currently available, high-performance computing and data-based sciences are working hand-in-hand. Sustainable research data management secures the treasure trove of data for the worldwide scientific community and for future use.

BY UTE SCHÖNFELDER

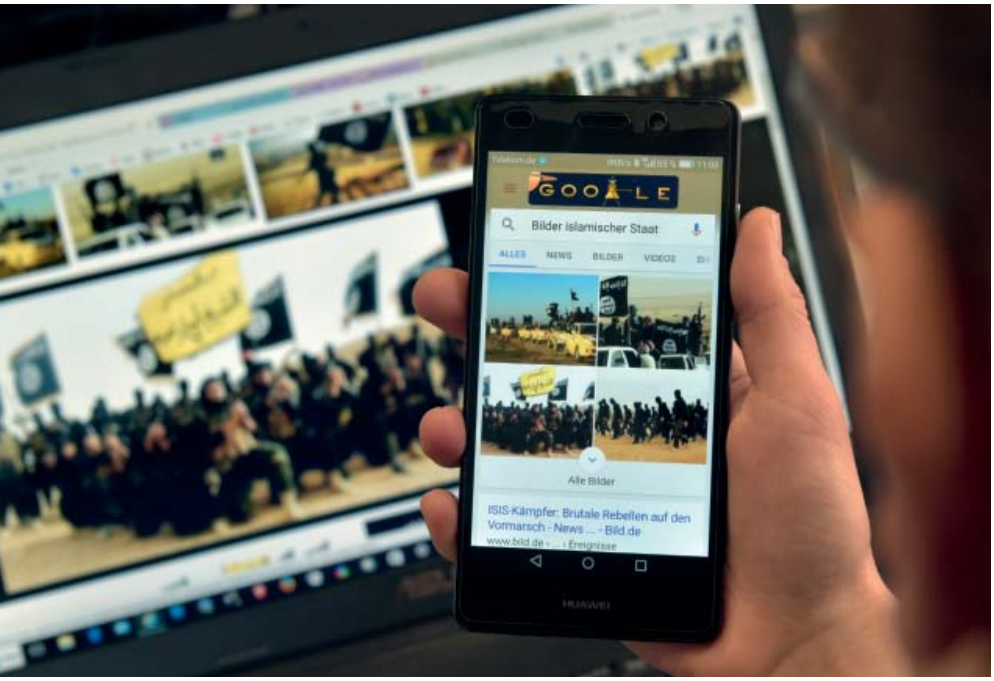
Satellite images of climate data, results of sociological surveys, as well as growth curves of national economies or microorganisms—in nearly all scientific disciplines nowadays, new findings are based on the analysis of large amounts of digital data. Scientist frequently work for years on accumulating these datasets, which then fill vast storage devices and require huge computing capacity for processing. This constitutes a veritable »treasure trove« of data. »In many cases, such measurements are unique and cannot easily be repeated,« notes Prof. Birgitta König-Ries. From the point of view of science, it is absolutely imperative to make efficient use of this wealth of data. However, to date only a small part of all primary data finds its way into scientific publications, databases or public archives, adds König-Ries, who holds the Heinz-Nixdorf Chair for Distributed Information Systems.

To change this situation, the University Jena aims to deal with digital data sustainably and efficiently, and to this end it is expanding its research data management. In a project funded by the Federal Ministry of Education and Research (BMBF), various building blocks for effective and efficient research data management will be developed and tested by 2019. The project is receiving around 467,000 euros in funding.

International infrastructure

»Our aim is to expand and improve our range of services in the area of research data management and of data collection, including secure data storage over the long term,« says Prof. König-Ries, who leads the project. In practice, the plan is to offer advice to researchers that is specifically relevant to their discipline and that informs them about data management plans, data platforms or metadata standards, for example. To this end, existing services will be brought together and coordinated in the »Research Data Management Helpdesk«, set up in 2015.

»Additionally, we want to professionalise the processes for sustainable research data storage, and integrate them into a national or international infrastructure,« adds Roman Gerlach, who works with Prof. König-Ries in the »Research Data Management Helpdesk«. With regard to the publication and long-term storage of research data, Gerlach refers to the existing »Digital Library of Thuringia«. Furthermore, project members will work with the international scientific community to develop criteria and methods for sustainable quality assurance in the area of research data management.



IS is using digital recruitment methods to further its radical aims.

Preventing terrorism

Psychologists want to prevent young people from becoming radicalized—an increasingly complicated endeavour in the digital age. The Federal Government is now providing three million euros to fund the development of preventive measures.

BY SEBASTIAN HOLLSTEIN

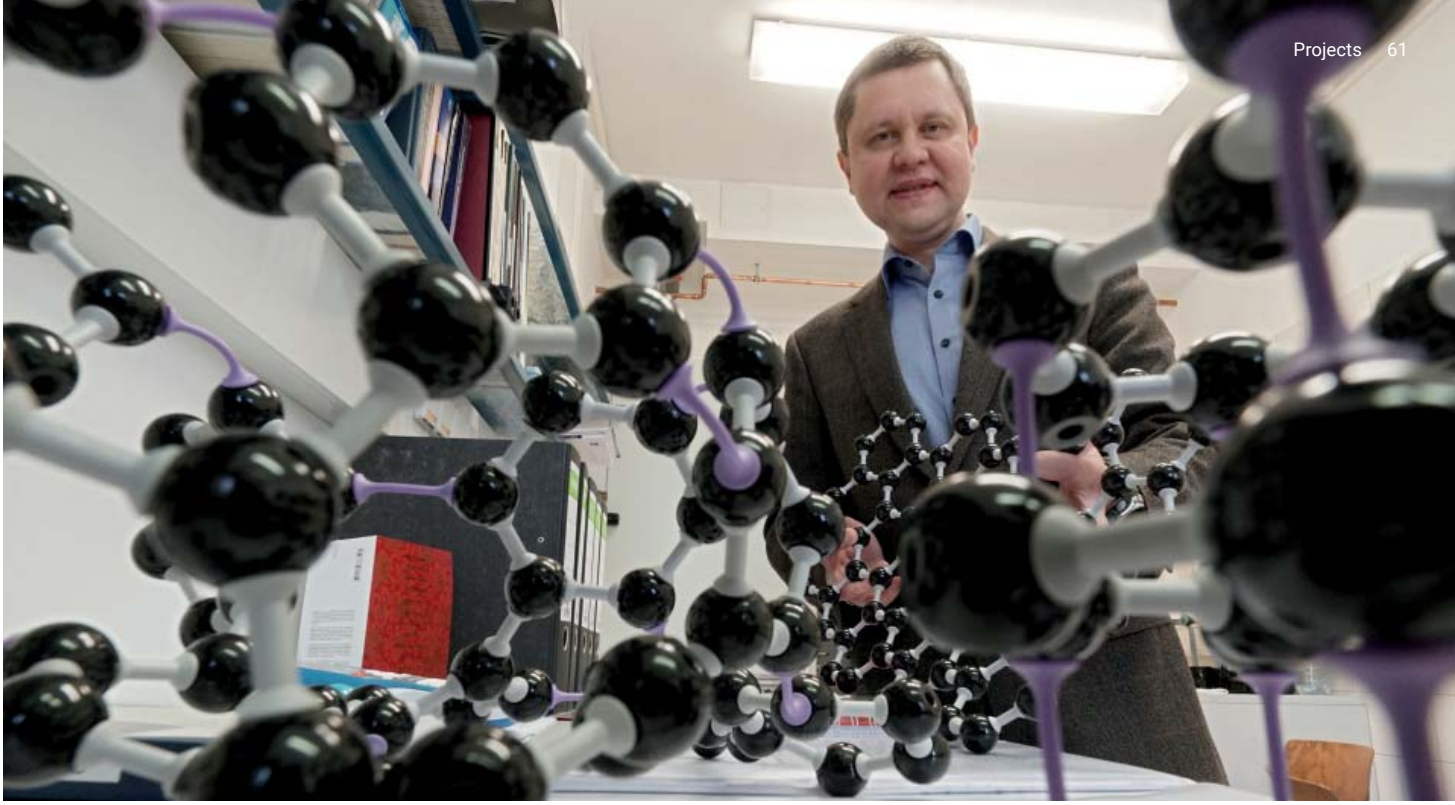
Discussions about fighting terrorism often centre on equipping the police or on military action. However, if one wants to find long-lasting methods for tackling politically or religiously motivated offences, the key task is to prevent the perpetrators from becoming radicalized at a young age. Hence, over the next three years, psychologists at the University Jena will be developing measures to prevent the radicalisation of young people as part of a project funded by the Federal Ministry of Education and Research. In the project »Radikalisierung im digitalen Zeitalter« (Radicalisation in the Digital Age)—RadigZ for short—they will be working with seven other institutions in Germany, organised by the Criminological Research Centre of Lower Saxony. The Ministry is providing three million euros for the project, of which 350,000 euros go to Jena.

»In principle, we assume that radicalisation processes work in very similar ways, regardless of whether right-wing extremism or religious fanaticism is involved,« says Prof. Andreas Beelmann, who leads the project at the University Jena. »However, because of the Internet, the situation has of course changed dramatically over recent years.« Whereas in the past, like-minded people had to make much more effort to make contact with each other, this has become much easier in the digital age, as well as much harder to monitor. However, this does not have to mean that young people are more likely to become radicalised. »It is still a minority of members of a cohort or generation who go on to express a radical ideology in criminal actions,« says Beelmann. Together with the psychologists, Dr Sara Jahnke and Clara Neudecker, he will be systematically collecting and analysing national and international research on radicalisation over the next few years. »We will first be checking which developmental factors in adolescents correlate with extremist views and actions,« explains Beelmann. »We will then take a close look at the preventive measures that have been taken and investigate how effective they turned out to be.« The psychologists want to use the results of these analyses to develop new, effective preventive measures, which can then be implemented in a variety of practical contexts such as schools or within civic education and staff training.

Beelmann began studying the topic of preventing violence in children and young people some years ago. »In the last 30 years, significant progress has been made in this field,« he notes. In the case of the radicalisation of young people, too, the task is now to let the findings on radicalization processes flow into the development of preventive measures. The psychologist also sees socio-political shortcomings, of which the scientists want to raise awareness: »For instance, young people without qualifications or career prospects are a high-risk group; in radicalization they see opportunities for gaining the recognition that they are denied elsewhere.«

»Centre for Research on Right-Wing Extremism, Civic Education and Social Integration«

The project also adds a priority research area to the work of the Centre for Research on Right-Wing Extremism at the University of Jena. In addition, the Free State of Thuringia has extended and significantly boosted its funding of the Centre, which, as a result of its new tasks and objectives, now bears the name »Centre for Research on Right-Wing Extremism, Civic Education and Social Integration«.



Prof. Andrey Turchanin investigates nanoscale 2D materials such as graphene.

The best of two nanoworlds

An international team of scientists coordinated by Jena professor of physical chemistry Andrey Turchanin is working on new applications in the area of flexible electronics by developing ultrathin hybrid sheets of organic semiconductors and inorganic atomically thin 2D materials. The research project is supported with 847,000 euros by the EU funding programme FLAG-ERA.

BY JULIANE DÖLITZSCH

It is every researcher's dream: an invention is followed by a patent application, a renowned scientific journal then publishes the research results, and, finally, a funding agency provides nearly a million euros in order to make the idea a reality. It is precisely what has come true for Prof. Andrey Turchanin of the Institute of Physical Chemistry.

In October 2017, the EU programme FLAG-ERA announced which proposals will be supported within the Flagship projects Graphene and Human Brain over the coming years. The only project to be selected that is coordinated from Germany was »H2O«—Heterostructures of 2D materials and organic, semiconducting nanolayers—which was funded with 847,000 euros for three years from January 2018. In this initiative, project leader Prof. Turchanin and Dr Bert Nickel from Ludwig Maximilian University in Munich are building on their invention of an ultrathin sheet made of organic semiconductor pentacene. Previously, the results of their research were published in »Advanced Materials«. In collaboration with scientists from the Netherlands and Sweden, the researchers are further developing this novel nanomaterial with a thickness of only 50 nanometres.

Assembly with atomically thin sheets

»We will use the funding to create new applications for organic semiconductor nanosheets, for which we have applied for a patent, by combining them with inorganic atomically thin 2D materials such as graphene and transition metal dichalcogenides, thus employing the best properties of these two complementary material classes,« explains Turchanin. The project will start with a thorough characterization of the properties through microscopy and spectroscopy. Using the layer-by-layer assembly of organic and inorganic nanosheets, the hybrids with the desired properties will be produced: »flexible, conductive, switchable, and environmentally friendly,« explains Turchanin. Among potential applications of these materials, he sees flexible electronic devices including displays, solar cells and sensors.

Since the discovery of insulated single-layer graphene sheets, research of graphene and related 2D materials has been one of the hottest topics in physics, chemistry and materials science. This field is considered to be so promising that since 2013 the European Union has dedicated one its two major research initiatives to developing and implementing these nanomaterials. Annual calls for proposals such as FLAG-ERA aim to attract innovative ideas to this initiative.



Haussknecht's oriental souvenirs

Botanists in Jena and partners are launching a project to publish the oriental travel diaries of Thuringian naturalist Carl Haussknecht. The cultural history project has been awarded some 400,000 euros in funding.

BY AXEL BURCHARDT

Travellers return home enriched by new experiences and often with a few souvenirs in their luggage. Carl Haussknecht (1838-1903), too, brought back »souvenirs«—thousands of them—from his journeys through the Ottoman Empire and Persia, which he started in 1865 and 1866. There, the naturalist found and collected plants, which represent a significant part of the herbarium that Haussknecht created. Raised as a foundation in 1896 in Weimar, the herbarium has long been in the possession of the University Jena. But besides plants, Haussknecht brought back 15 octavos closely written in Kurrent, an old form of German handwriting, totalling 1,000 pages describing his travels and the plants (photo top). These travel diaries, which are kept at the Institute of Ecology and Evolution, will now be digitally published and annotated in a large interdisciplinary project involving several universities. The German Research Foundation (Deutsche Forschungsgemeinschaft DFG) is funding the three-year project, which also involves the universities of Halle-Wittenberg and Marburg, with 400,000 euros.

Haussknecht's personal thoughts on people and politics

»On the one hand, we want to find out more about our collection,« says botanist Prof. Frank H. Hellwig. This is because the exact size of the collection is not yet known. On the other hand, the diaries help to investigate and deduce the designations of certain plants. »What we have seen so far shows that the information in the diaries, which extends beyond pure botany to take in a broad spectrum of disciplines such as geology, geography, cartography, zoology, local customs, and social and cultural history, is of importance in interpreting the botanical material,« says project director Hellwig. »The diaries are thus cultural and historical documents.« Important for this cultural dimension is also the fact that Haussknecht never intended for the diaries to be published, with the result that they contain very personal thoughts and impressions of people and of the political situation.

Project collaborator Kristin Victor and her colleagues face the challenge of deciphering and »translating« Haussknecht's antiquated cursive writing. Future tasks also include identifying and annotating plant names, geographical designations, local conditions and events, as well as evaluating their scientific, cultural and historical relevance.

In order to make the annotated writings accessible worldwide, the team is receiving support from the Thuringian University and State Library. Finally, science historian Dr Andreas Christoph is responsible for designing the digital presentation of the research results. The project's comprehensive Internet presence is planned to go online before the end of the project in 2020.

His and hers medicine cabinets

Testosterone makes anti-inflammatory drugs work differently in women and men

Susceptibility to particular diseases is different in men and women, with inflammatory diseases such as asthma, psoriasis or rheumatoid arthritis being much more common among women than men. Pharmacists working with Prof. Oliver Werz, together with colleagues from Italy, Denmark and Sweden, have uncovered a significant cause for these sex differences at the molecular level. In two high-profile publications in the »Journal of Clinical Investigation« and »Scientific Reports«, they show how the male sex hormone testosterone interferes with the biosynthesis of inflammatory substances, and additionally reduces the effectiveness of anti-inflammatory drugs (DOI: 10.1172/JCI92885; DOI: 10.1038/s41598-017-03696-8).
To this end, the researchers comprehensively analysed and compared inflammatory processes in diverse animal models, but also in immune cells from the blood of male and female human donors. »We investigated the formation of inflammatory substances, such as leukotrienes and prostaglandins, and looked at whether the effect of anti-inflammatory drugs differs in male and female cells,« explains Werz.



Do we need separate »his and hers« drugs? Pharmacists show that inflammations need to be treated differently in men and women.

As expected, the effect of the drugs under investigation was significantly stronger in the female samples than in the male samples—after all, the inflammatory process is much more pronounced in women. However, these differences are completely abolished by the administration of testosterone. Previous studies—including work by Prof. Werz's team in Jena—have already shown that testosterone can protect against inflammatory reactions. »However, now we have been able to throw light on the molecular mode of action and show that testosterone also influences the therapeutic effect of drugs,« notes Werz. With this work, the researchers have once again provided concrete evidence supporting the need for gender-specific medicine. US



Costly decisions

Economist uncovers irrational management decisions for product innovations

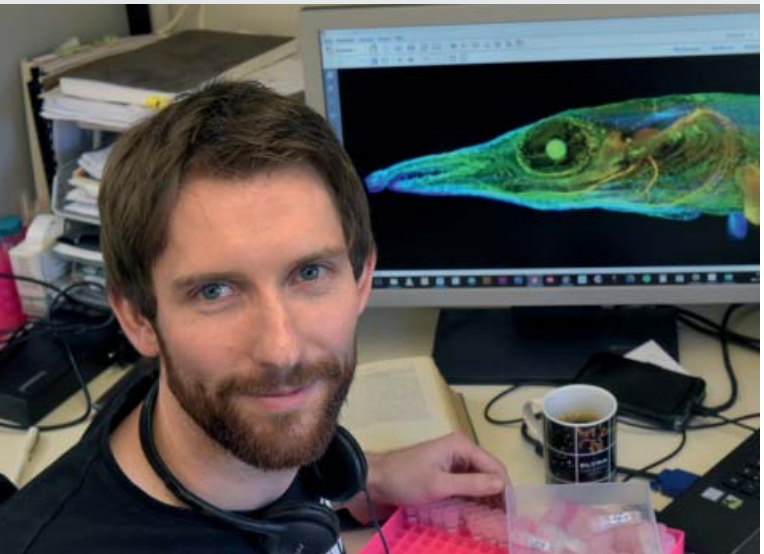
Disadvantage is a fact of life: women have a hard time in areas traditionally dominated by men; foreigners often have to struggle against prejudice; and in Germany, people from the former East Germany are less likely to be in senior positions. These are facts that have been scientifically studied and substantiated. Economic researcher Ronny Reinhardt (photo above) has now discovered yet another group facing discrimination: cheap new products. It appears that managers and decision-makers in companies avoid these and show a preference for expensive product innovations. This is demonstrated by Reinhardt and his co-authors from Switzerland and the USA in their essay »The High-end Bias—Investigating the Irrational Preference for High-end over Low-end Innovations«.
In their recent study, the researchers found out that in innovation projects, managers opt for products from the more expensive end of the range in around 80 per cent of cases. »With the same investment and the same return for the company, decision-makers are more likely to choose to bring expensive products to market.« They give preference to the higher-class products and would rather have fewer customers with more money than a lot of customers with little money. »They tend to reject low-cost innovations,« explains Reinhardt.
The study gives clues to possible reasons for this: expensive products have positive connotations, reflect high value and a certain status—factors that are clearly important to managers at manufacturing companies.
»These feelings influence investment decisions, although they are not appropriate. This ultimately means fewer new products for those with limited budgets,« adds Reinhardt.
The economists collected their data by means of experimental surveys and two reaction tests in which associations were recorded that were made by over 500 participants from small and large companies in a wide variety of sectors. A study of a dataset relating to more than 2,000 product launches in the USA additionally shows that in supermarkets, the result was high product diversity in the high price range and little choice in new low-cost food products—even though from 2010 to 2011 cheaper products accounted for twice the turnover of expensive ones. jd

How fish made the move to land

The garfish's cucullaris muscle give insight into the evolution of terrestrial vertebrates

The garfish has been swimming in the waters of our planet for more than 140 million years, yet it still holds secrets. Evolutionary biologists from Jena have unravelled one of these secrets gaining important information about how fish developed into terrestrial vertebrates. Benjamin Naumann (photo below) and Prof. Lennart Olsson from the Institute of Evolutionary Biology have succeeded for the first time in correctly identifying the »cucullaris« muscle in this fish species. This muscle shows many similarities with the cucullaris muscle of terrestrial vertebrates. The scientists reported on their research results in the specialist journal »Evolution & Development« (DOI: 10.1111/ede.12239).

»We have corrected an error made over a century ago, because in earlier investigations a different muscle was classified as the cucullaris muscle in the garfish,« says Benjamin Naumann. The evolutionary biologists are interested in the muscle which connects the head to the shoulder girdle in particular because it is present both in ancient fish and in mammals, although its function has changed substantially during evolution. »In fish, the head rests directly on the shoulder girdle, which means that the head cannot move independently from the body,« explains Prof. Olsson. This direct connection has been done away with in terrestrial vertebrates. They developed a neck which enabled them to move the head independently from the torso.
This new study in Jena has made it clear that in the garfish, too, this muscle is present between the body and the head. Previously, researchers had erroneously assumed that a different muscle near the gills was the cucullaris. »The position of the cucullaris muscle is important because it reveals to us that it is formed exactly as it is in mammals, for example,« says Naumann. »Developmental biology therefore shows us a homology in this case indicating that the muscle has a common evolutionary origin in both animal groups.« sh



What makes mushrooms »magic«?



»Magic mushrooms« have their strong psychedelic effect due to a substance called psilocybin, which has been known for nearly 60 years. One mystery remains, however: how exactly do mushrooms of the genus *Psilocybe* (on the photo) form this active substance? A team led by Jena-based natural substance and fungi expert Prof. Dirk Hoffmeister has now solved this mystery. The researchers succeeded in identifying the enzymes that help the mushrooms to form their magic substances. In addition, through their research they established that the biosynthesis occurs in a different order from that described in earlier studies. Their results appear in the journal »Zeitschrift Angewandte Chemie« (DOI: 10.1002/anie.201705489).
Using the model bacterium *Escherichia coli*, it was possible to produce the previously identified enzymes. In this way, Hoffmeister and his colleagues were able to reproduce the synthesis of the active substance and produce psilocybin without fungal cells. In future, this very effective molecule could be produced more easily in this fashion, as apart from its use as a recreational drug, this substance also has useful healing properties. In small doses, for example, it can reduce anxiety in patients with life-threatening cancers or relieve the symptoms of depression and lethargy. MR

How mammalian teeth get their shape

The teeth of hairless dogs are giving scientists clues to the development and evolution of teeth in mammals. Hairless dogs differ from other dogs not only due to their lack of fur, but also in the number and nature of their teeth. Researchers from the Max Planck Institute for Evolutionary Anthropology in Leipzig and Friedrich Schiller University Jena have re-examined almost 100-year-old skulls and teeth of hairless dogs from the collection of Jena's Phyletic Museum, and they have established that a gene called »FOXI3« is involved in the development of teeth. They presented their results in the journal »Scientific Reports« (DOI: 10.1038/s41598-017-05764-5).
The team, led by associate professor Kornelius Kupczik and Prof. Martin S. Fischer, was able to show that in the hairless dogs, nearly all the permanent teeth that replace milk teeth (i.e. incisors, canines and premolars) were missing, while the molars were present. It was also noticeable that on these teeth, certain dental cusps on the side nearest the tongue had not developed. The researchers assume that »FOXI3« also plays a role in the development of teeth in other mammals, including humans. US

Crossing borders

Four-volume encyclopaedia provides first comprehensive overview of private international law

In the 21st century, many people's lives are very international. They travel all over the world, buy goods from countless countries and marry people from other cultures. But what happens if the flight is cancelled, the car breaks down or a couple falls out of love? »Law has not managed to keep pace with the dramatic internationalisation of our lives. It is still to a great extent national and looks different in Germany from the way it looks in England, France or Italy,« says Prof. Giesela Rühl (photo on the right). Her area of expertise, private international law, is concerned with the question of how to solve the problems of cross-border legal relationships.

Rühl explains that with globalization the number of international disputes and legal proceedings has increased. National and international lawmakers, but especially the European Union, have responded to this situation in recent decades and have adopted appropriate regulations. However, an overview of this confusing and rapidly growing area of law has been lacking – until now. The »Encyclopedia of Private International Law«, coordinated by Prof. Rühl's department, has just been published. The four-volume English-language work contains 4,000 pages that comprehensively describe the history, methods and content of private international law. As the central coordination point, Giesela Rühl's department brought together all the threads of the mammoth project funded by the Fritz Thyssen Foundation, which involved 181 authors from 57 countries. The first two volumes of the encyclopaedia contain contributions on private law topics. Volume three encompasses country reports on private international law from 80 states, including Thailand, Tunisia and Nigeria, which had hardly been described before. Finally, the fourth volume contains a collection of legal texts from all over the world, translated into English. »This volume is of central importance for further research, because it makes many laws available to an international readership for the first time,« says Prof. Rühl. The entire work will soon be found on library shelves, mainly of universities and other educational institutions. jd



Laser beams from the sky

Laser beams are frequently used to study the chemical composition of the atmosphere. Researchers send laser pulses into the sky and then analyse the light that is scattered back. However, it would be better if the light could also return to earth as a laser beam, because its light sends a stronger signal and it is easier to read information from it. Dr Daniil Kartashov of the Institute of Optics and Quantum Electronics in Jena and Prof. M. Shneider of Princeton University (USA) have now established the theoretical principles for such sky lasers (DOI: 10.1063/1.4978745).

For this, the researchers exploit the properties of the air. The use of ultrashort laser pulses creates a kind of »lens« in the air. This lens focuses more strongly the laser beam that is emitted and creates fine plasma channels. The light in these filaments, as they are called, supports a broad spectrum of radiation, which can provide information on the chemical composition of the environment. By selecting suitable parameters, such as plasma temperature and density, the laser can interact with the nitrogen in the atmosphere in such a way that a real sky laser is produced. sh

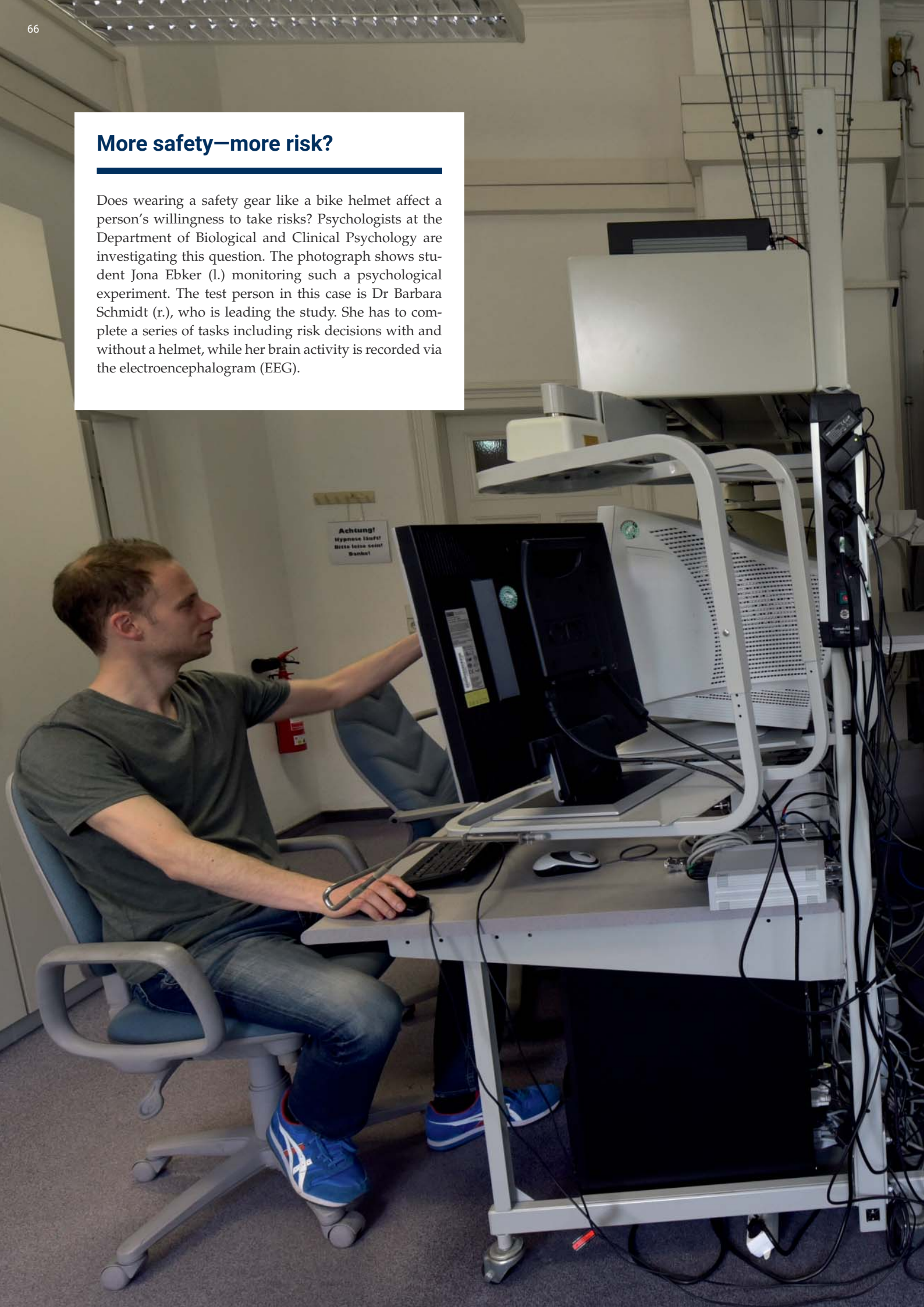
How does hypnosis work?

Psychologists at the Department of Biological and Clinical Psychology have shown that even an imagined »obstruction« can disrupt a person's vision. In the journal »Scientific Reports« they presented the results of a study that reveals what happens in the brain of a person under hypnosis when processing visual stimuli (DOI:10.1038/s41598-017-05195-2).

For her experiment, Dr Barbara Schmidt of the working group led by Prof. Wolfgang Miltner tested three groups of participants: people who were very suggestible and easy to hypnotize; people who were moderately suggestible; and a group of people who were more resistant to hypnosis. Under hypnosis, participants had to count symbols on a screen in front of them. At the same time, they were told to imagine that there was a wooden board in front of their eyes. The suggested visual blockade made the number of counting errors rise sharply. The participants' brain activity, which was recorded via EEG during the task, showed that their basic visual perception was intact, even with the imagined obstruction. However, secondary processing operations, such as counting the symbols, were impaired. sh

More safety—more risk?

Does wearing a safety gear like a bike helmet affect a person's willingness to take risks? Psychologists at the Department of Biological and Clinical Psychology are investigating this question. The photograph shows student Jona Ebker (l.) monitoring such a psychological experiment. The test person in this case is Dr Barbara Schmidt (r.), who is leading the study. She has to complete a series of tasks including risk decisions with and without a helmet, while her brain activity is recorded via the electroencephalogram (EEG).







Christoph Redies with one of his abstract works from 2001.

The art of science and science of art

Unlike most medical students, Prof. Christoph Redies never wanted to practise medicine. Instead, from early on in his research career, he wanted to pursue, in a scientific way, his second great passion: art.

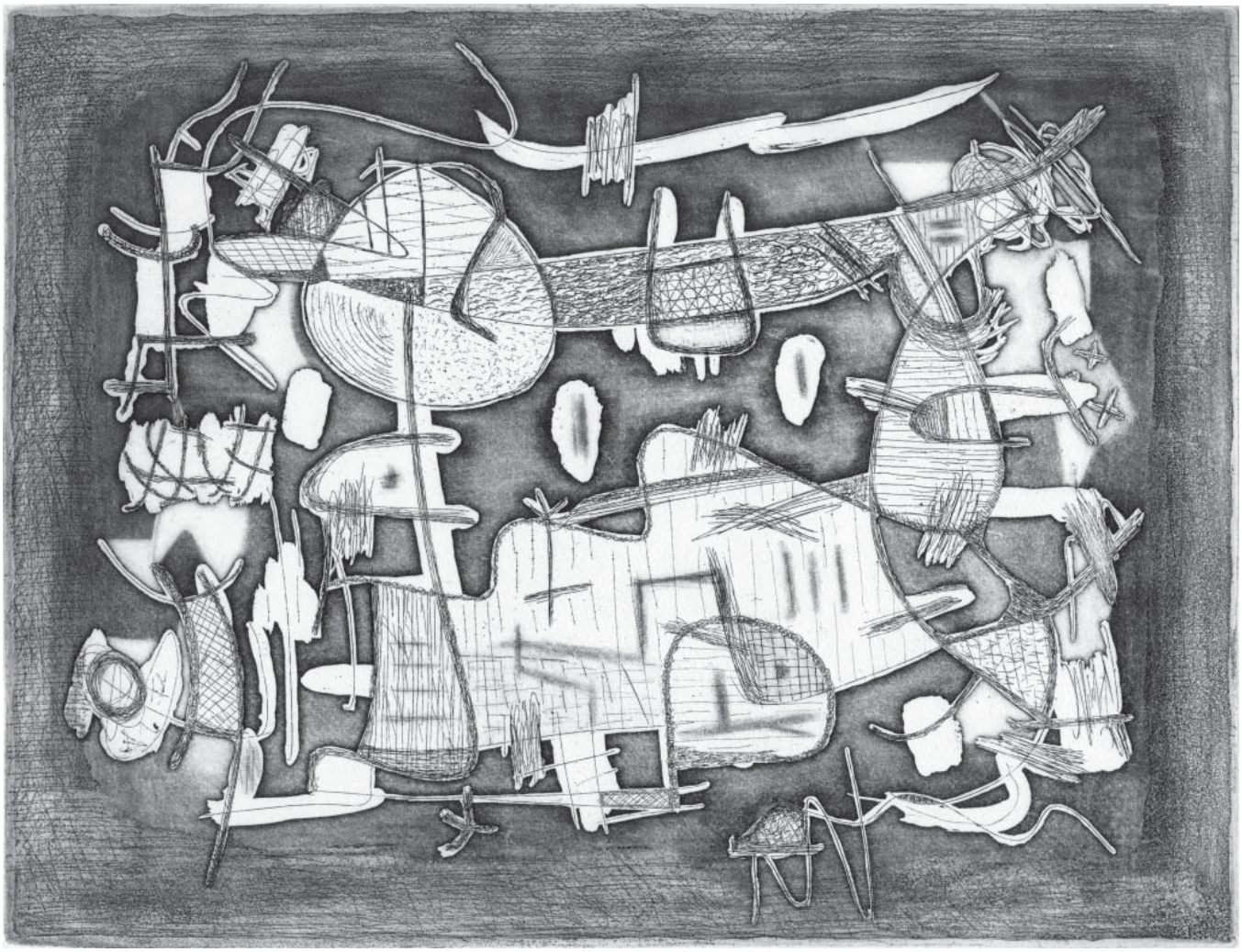
BY JULIANE DÖLITZSCH

During last year's Jena University Summer Party, anyone who took a look at the small art exhibition in the canteen on Philosophenweg was bound to be attracted by the abstract compositions framed in heavy, valuable wood. Their creator, Prof. Christoph Redies of Jena University Hospital, was always to be seen nearby. The professor of Anatomy was very happy to answer the call for University staff to exhibit their photographs and paintings in the Summer Party's artists' studio. Redies not only showed watercolours, oil paintings, pastels and etchings, but also set up a video installation and displayed a collection of his scientific publications. The topic was Experimental Aesthetics. With great enthusiasm, he explained his research to a large number of visitors.

»I would like to find out what constitutes the structure of a beautiful piece of art,« explains Christoph Redies. »What does a picture have to be like in order to be considered aesthetically pleasing?« This question has always preoccupied the 59-year-old professor, just as art has always been an integral part of his life. The son of international art dealers, who ran a gallery for modern art in Düsseldorf, Redies began painting at the age of 16. The self-taught artist spent the summer of 1977 in a studio in Paris, but subsequently decided to study medicine in Essen. »I was not ready to cope with the uncertainties of an artist's existence,« he recalls. However, he does not want to describe his academic choice as simply being a rational one: »I have always been interested in the natural sciences.« He did not necessarily wish to become a doctor, but wanted to keep other options open.

After the first years of medical studies in Essen, he considered studying the biological foundations of art. However, in the 1980s the time was not yet ripe for such research. Redies specialized in vision research and the molecular basis of brain development. The last year of his medical studies resembled a clinical world tour, taking him to Adelaide in Australia, Boston in the USA and Montreal in Canada. However, practical work in hospitals failed to stimulate his interest in working as a doctor. »After obtaining my licence to practise medicine, I hung up my white coat and never saw patients again,« notes Redies. And so, after finishing his medical dissertation at the Max Planck Institute in Göttingen, he wrote a doctoral thesis in neurosciences in Montreal, thus obtaining a PhD. After postdocs at the Massachusetts Institute of Technology (MIT) in Cambridge and Japan's Kyoto University, he returned to Germany. In 1997 he was appointed Professor of Anatomy at the University of Essen and in 2003 at the FSU. He attributes his successful academic career to his research in molecular biology and brain research, as his other research ideas relating to aesthetics were initially seen as fanciful.

However, Christoph Redies's research interests became acceptable at last when the state of Thuringia competed—



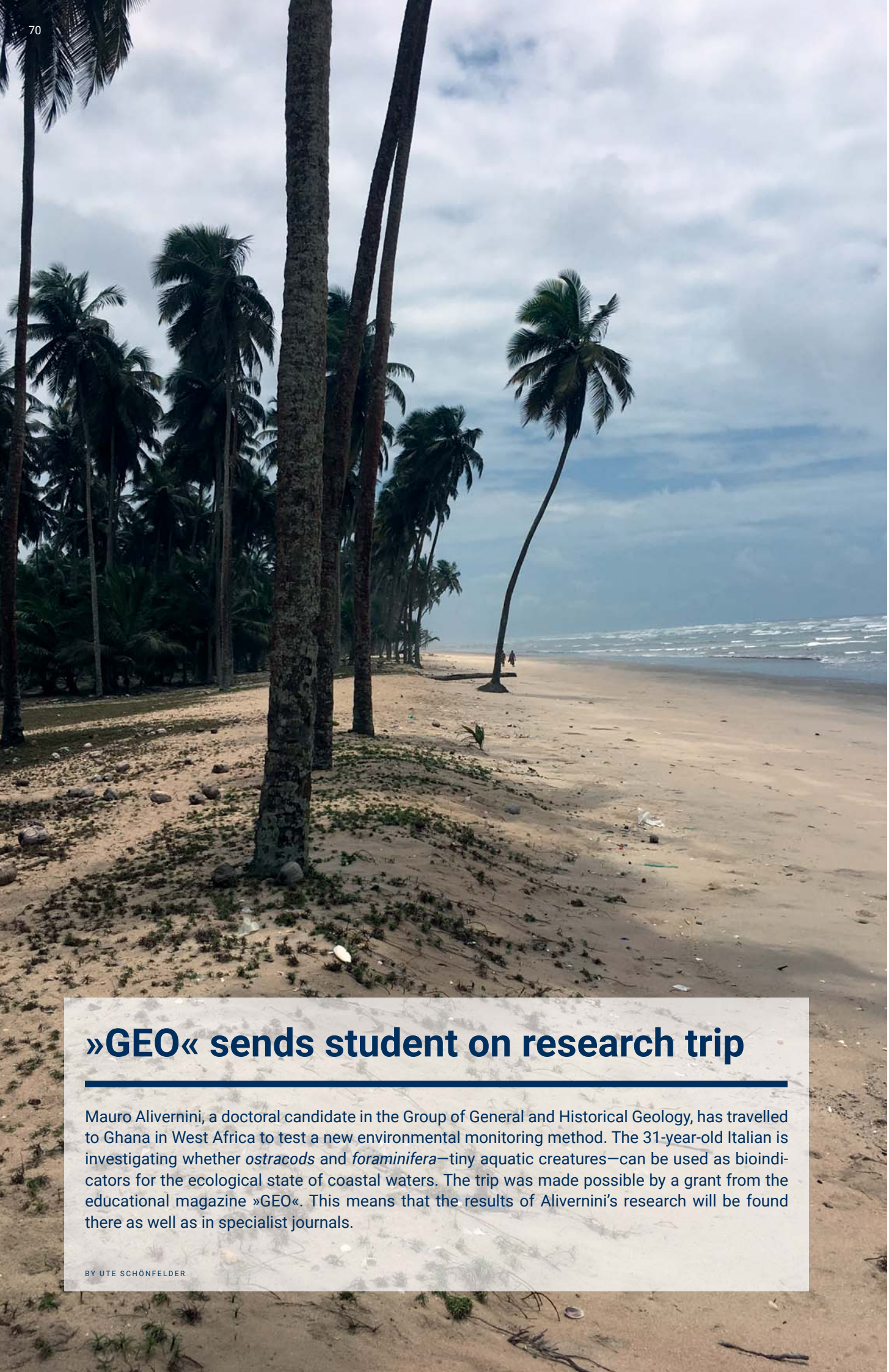
Christoph Redies created the etching »Paris« in 1977 during his stay in the French capital.

unsuccessfully—to become the site of the new Max Planck Institute for Empirical Aesthetics. »At the start of my career, I would have ruined my academic reputation if I had pursued my research interest in art, but technology has since undergone huge developments. In addition, as early as 2005 I found an open-minded collaborator in Prof. Joachim Denzler,« says Redies. Together, the physician and the IT specialist laid some of the foundations for research on the aesthetics of art. His research group currently works with a team from the Institute of Psychology. He does not see himself as a trendsetter, but readily admits that »it's exciting to be part of a new, developing field of research right from its beginnings«. Aesthetics has now actually become a trendy academic topic. As evidence for this trend, several research associations have thrived in this field, such as the International Association of Empirical Aesthetics, of which Redies is of course a member.

Structure of beauty in the visual arts and music

Does Redies paint differently since he has started studying the subject so intensively? »Thinking is not necessarily helpful when one is painting,« he replies, »but rather it is feeling that counts. And my feelings have not changed.« In any case, he does not have much time for painting at the moment—science is still the top priority, because there are many things he wants to accomplish in science before this father of four daughters retires. He would like to get even closer to the heart of what constitutes beauty in an artwork. In addition, in his research he would like to turn his attention to music. In his youth, Redies played the piano for nine years, »but not particularly well,« he says with a laugh. But his penchant for classical music has stayed with him.
Research is first and foremost an intellectual game for him, and he experiences joy in being curious and in making discoveries. Art, on the other hand, can connect people and cultures, and can move people more deeply. For a long time, it was his dream to combine the two, and he has now been able to fulfil his dream for the last 12 years at the Institute of Anatomy, of which he is the Director. In this position he benefits not only from being located in Jena: »As a professor at a German university, you have the freedom to investigate whatever you like—and that's fantastic.«

And what is the structure of a beautiful artwork all about? »The way in which an artist paints often imitates the structure of complex natural scenes,« explains Redies. As a result, because our visual system is adapted to process natural structure and patterns, humans find artworks familiar and perceive them as beautiful—and the richer and more varied they are, the more beautiful they seem. »It's difficult to express this in simple words,« notes Professor Redies. It would be easier using brushstrokes.



»GEO« sends student on research trip

Mauro Alivernini, a doctoral candidate in the Group of General and Historical Geology, has travelled to Ghana in West Africa to test a new environmental monitoring method. The 31-year-old Italian is investigating whether *ostracods* and *foraminifera*—tiny aquatic creatures—can be used as bioindicators for the ecological state of coastal waters. The trip was made possible by a grant from the educational magazine »GEO«. This means that the results of Alivernini's research will be found there as well as in specialist journals.

BY UTE SCHÖNFELDER



Photo left: Natural paradise on the west coast of Ghana. Photo right: Geoscientist Mauro Alivernini, accompanied by a Ghanaian fisherman, sails through a mangrove forest close to shore, near the Amanzule River.

It is early September and in Thuringia the weather is mild. Mauro Alivernini stands with a colleague in a pedalo in the middle of the artificial lake at Hohenfelden, some 20 kilometres south of the Thuringian capital Erfurt. The boat wobbles as, helped by Thomas Biehl, the athletic young man pulls a two-metre-long plastic cylinder, with metal weights attached, out of the water and into the boat. Water, brown from the churned-up mud, runs down the sides of the cylinder, soaking Alivernini's feet. He looks satisfied: the sediment sample from the lake bottom promises to provide sufficient research material. The sampling session was a success.

Four days later, Alivernini, Master's student Thomas Biehl and Ghanaian scientist Lailah Akita are on a plane to Ghana. Their destination is Accra: the country's capital and economic hub, and one of the most polluted places on Earth. On board are the scientists' sampling and measuring devices. Alivernini and his colleagues want to test a new environmental monitoring method in the West-African country. Ghana is a dumping ground for Europe's electronic waste. On huge rubbish dumps in Accra, computers, photocopiers, fax machines and television sets from the western world are disposed of. Workers extract valuable metals from the devices simply by burning the plastic housing in the open air, without any protection for the soil, water or the workers themselves. Rainwater washes away heavy metals and other harmful substances, which find their way into the lagoons on the city's edge, and from there they are carried out to sea. »These are extreme examples of environmental damage, which is being caused here and is spreading at an alarming rate,« says Mauro Alivernini. Ecological standards are virtually non-existent and few people in Ghana are environmentally aware. The environmental destruction is particularly severe along the coast, where the bulk of the population lives.

Sustainable coastal management

With their research, the scientists want to create the conditions for sustainable coastal management in Ghana, and to this end they have been doing ground-breaking work. Over a three-week period from 9 to 27 September, they took sediment samples from various bodies of water, first in Accra and its heavily contaminated surroundings, followed by the lagoons and mangrove forests in the less polluted western coastal area of the country. They analysed the first samples in Ghana, and also brought around 10 kilos of sieved and dried sediment back to Jena, in order to examine it in detail.

Back in their own laboratory, Alivernini and his colleagues are studying *ostracods* and *foraminifera*: microscopically small creatures that live in bodies of water around the world. Just a few millimetres in size, »they are normally completely uninteresting for people. After all, they don't transmit any diseases and you can't eat them«, jokes Alivernini. However, the tiny creatures are of enormous value for him and for other geologists: they accumulate in sediments and provide information about the state of the water in which they live.

Foraminifera are single-cell organisms—amoeba—which are usually enclosed in a calcareous shell. They occur principally in the sea. *Ostracods* are equally tiny crustaceans that live in all types of bodies of water. »These organisms react very sensitively to changing environmental conditions,« explains Alivernini. Temperature fluctuations, changes in the salt content of the water or influxes of contaminants quickly lead to morphological alterations to the creatures' tiny calcareous shells. For this reason, the creatures' appearance and the species composition enable researchers to assess environmental conditions such as water quality, and even to draw conclusions regarding climate change over the long term. »In some countries, *ostracods* and *foraminifera* are already used routinely for environmental mo-



Beach strewn with rubbish near the Ghanaian capital Accra. The ground is sealed by a thick layer of oil, which prevents rainwater from seeping away. Here too, Mauro Alivernini took sediment samples: within just a few minutes, the researcher sank up to his thighs in the mud. It was only with a great effort that he managed to free himself from the soft soil, which offers no support. Locals report that every year, a number of people simply disappear into this morass.



Local people help the researchers from Jena to load the inflatable boat and equipment near Keta Lagoon in the east of the country.

nitoring, for example in Norway,« says Alivernini. The researchers now want to make this possible in Ghana as well, because the method is simple, but very effective and—what is more—cheap.

Inventory of the microfauna

All one needs is an average optical microscope and knowledge of the typical composition of the local microfauna. The researchers used their expedition to Ghana to prepare a precise inventory of the *ostracod* and *foraminifera* fauna in the coastal waters. Some of the sediment samples are currently being analysed by scientists from the University of Accra. Other samples are being analysed by Alivernini and his colleagues in Jena, under the direction of micropalaeontologist Peter Frenzel.

Initial results from the heavily polluted region around Accra show a multitude of deformations in foraminifera shells. »We've never seen anything like it before,« remarks Alivernini. The aim is now to document the spread and ecology of the bioindicators for the Ghanaian coastal region, and assess the current environmental situation. »Over the long term we want to develop a monitoring programme for the West African coast, based on *ostracods* and *foraminifera*,« says Alivernini of the group's future plans. ■

BACKGROUND

With his research project on *ostracods* and *foraminifera* as bioindicators, Mauro Alivernini won »GEO«'s 2016 expedition grant. The 31-year-old geologist was chosen from among more than 50 competitors from all over Germany. Alivernini used the 10,000 euros for a trip to Ghana, during which he and two colleagues took extensive sediment samples for the current analyses. Two journalists from »GEO« magazine accompanied the Italian scientist for several days during his field work in Africa. The magazine will report on the young researcher's work in one of its next issues.

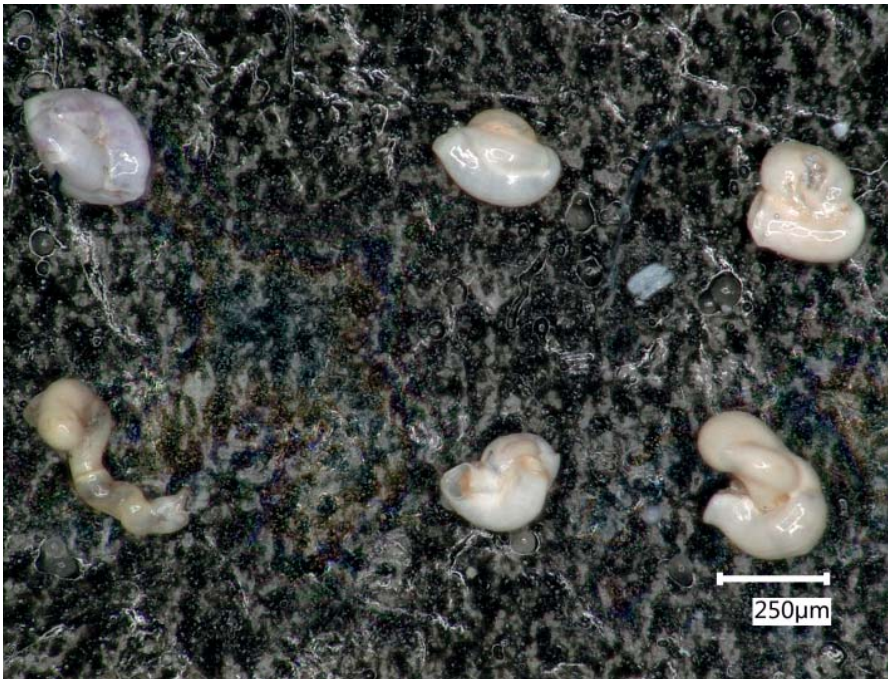






»GEO« photojournalist Dominic Nahr (centre) watches Thomas Biehl (left) and Mauro Alivernini preparing samples in their open-air laboratory at the University of Accra. The photographer and two journalists from the educational feature magazine accompanied the Jena scientists during their work for a whole week.

The sediment samples from the different coastal regions are washed, sieved and then dried, before they are put under the microscope. The researchers brought at least 10 kilos of dried material back to Jena, in order to analyse it further.



Foraminifera from sediment samples that Alivernini and his colleagues collected in the heavily contaminated region around Accra. The shells of the single-cell marine organisms are severely deformed. Above left is a normally shaped specimen of the genus *Quinqueloculina*.



Reaserch in Microgravity

The materials scientist, Prof. Markus Rettenmayr (Photo above), experienced a microgravity parabolic flight last summer. He talks here about the fascination of weightlessness and suffering in the cause of science.

BY STEPHAN LAUDIEN



Doctoral candidate Robert Hanke (seen here during a flight in 2016) remained earthbound in Bordeaux on this occasion and provided the team with technical support.

If you have a burning desire to float in zero gravity, there is no need to fly to the ISS, as you can experience this phenomenon on a parabolic flight. The European Space Agency (ESA) offers such flights in partnership with the German Aerospace Center (DLR), with a special airplane taking off from Bordeaux in France. Flights are carried out for the purposes of scientific research, but also for simple curiosity, as in some cases tourists can also book a flight.

»Weightlessness starts very suddenly—there's no transition phase,« says Prof. Markus Rettenmayr. You have to be careful, as spontaneous movements can quickly lead to violent collisions, adds the scientist from the Otto Schott Institute of Material Research. If you are squatting on the floor of the aircraft when weightlessness starts and try to stand up in the usual way, you will bash your head against the ceiling. Not for nothing are there four helpers and a doctor on board, and the ceiling of the plane is also padded.

Rettenmayr took his first parabolic flight last summer, and it was probably also his last. Not because he did not enjoy it, but rather because other scientists working on the same research project would also like to have a go at zero gravity. During the flights, Rettenmayr and his team investigate how melted metal alloys resolidify in crystalline or vitreous form. The aim is to eliminate the influence of gravity as much as possible in this process. Highly sensitive measuring devices are used, which measure factors such as viscosity, thermal conductivity and solidification velocity. »These experiments will be extended later on aboard the ISS,« says academic employee Robert Hanke. The parabolic flights are a necessary preparation for the experiments on the space station. The long-term goal is to obtain a model for the solidification behaviour of metal alloys that is as precise as possible. The plane used for the parabolic flights is the German Airbus A 310 that used to carry the German Chancellor. Where Angela Merkel and her entourage used to sit, there is now equipment to be used in a variety of experiments. There is also a system of belts and straps, so that weightless passengers do not completely lose control. Only in the rear of the plane are there still seats.

»It's like being seasick, but worse!«

Before the flight, passengers take medication against motion sickness. »It feels as if you're seasick, but worse,« says Rettenmayr. Headaches, nausea and vomiting are common symptoms, which is why parabolic flight aircraft have been nicknamed »vomit comets«. After taking off from Bordeaux, you first fly out over the open sea and a quiet area is sought for the parabolic flights. The Airbus pilots then accelerate to 2 g—twice the acceleration of gravity—and pull the nose of the plane up to an angle of 50 degrees. After the climb, the engines are throttled and the plane follows the path of a trajectory parabola, during which passengers experience 22 seconds near absolute weightlessness. The plane then returns to the horizontal. The changes in gravity imply flying close to the aircraft's technical limits, says Rettenmayr, adding: »This flying manoeuvre demands great skill.« It is no wonder that the crew consists of four former military pilots. One flight day involves around 30 parabolas, with a one-minute break after each period of weightlessness.

The passengers enjoy floating around inside the aircraft. The physical discomfort of motion sickness is the price that must be paid. However: »One or two days later, everything is fine again!«



UNIVERSITY INFORMATION DAY 2018

at the Friedrich Schiller University Jena
Saturday, 26 May 2018 beginning at 9.30 at Ernst-Abbe-Platz

On the University Information Day, the faculties will present around 200 study opportunities ranging from ancient history to zoology. We kindly invite future students and their parents to visit information stands and learn subject-specific opportunities. Do not miss more than 50 presentations and campus tours. If you are interested in the Student Paradise Jena, you may also join one of our sightseeing tours.

FURTHER EVENTS

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28 March and 4 October 2018

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from 16 April 2018 to 6 July 2018 (summer semester)
from 22 October 2018 to 1 February 2019 (winter semester)

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