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Max Planck RESEARCH

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Parasites

INTERNATIONAL LAW
Trawling in Outer Space

POLYMER RESEARCH
Plastic – Kind to the Environment

METEOROLOGY
Climate Slashing

CRIMINAL LAW
Anti-Espionage Strategies

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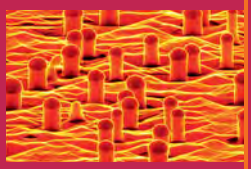
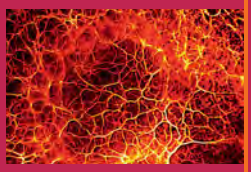
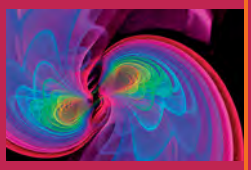
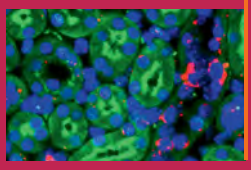
Connecting **Science and Business.**









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

Connecting Science and Business

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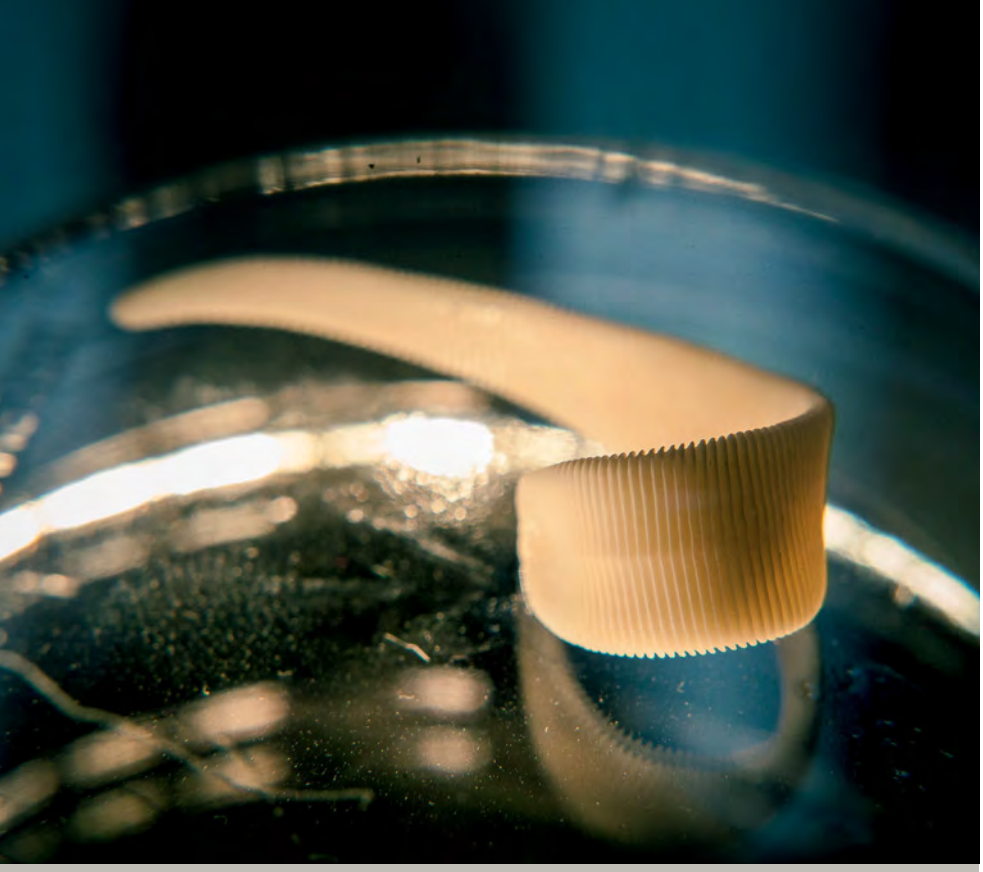
Photo: Sonja Metzger/Max Planck Institute for Evolutionary Anthropology

Daily Life in the Jungle

West Africa, Republic of Côte d'Ivoire, not far from the border to Liberia: the camp of the Max Planck researchers is sited in the middle of the Taï National Park rain forest, a 12-hour drive from the port city of Abidjan and three hours along a dirt road from the nearest village. For several years now, a team of scientists headed by Christophe Boesch has been observing three neighboring chimpanzee groups with a total of around 100 animals.

These animals are so used to the presence of humans that they practically take no notice of them – as if the researchers are merely a part of the surroundings. Achieving this usually takes many years of the scientists carefully and gradually approaching the primates. The actual research can begin only when, even in the presence of people, each chimpanzee behaves as it normally would when alone.

The scientists follow the chimp groups everywhere they roam and observe their day-to-day life, making sure, however, that they behave in a completely neutral way in the animals' presence: they don't feed them, don't eat in their presence, don't play with the young chimps – even when the latter are curious and seek out the humans' company. And the researchers never come into physical contact with the animals. This last point is crucial for the health of the primates: even a seemingly harmless cold can wipe out an entire chimpanzee family. Consequently, there are strict rules of behavior and hygiene measures: every person who enters the camp must be vaccinated against numerous diseases; in addition, he or she must initially spend five days in quarantine in the camp's outstation. Anyone who shows even the slightest symptoms of an infection is forbidden from entering the forest in the vicinity of the apes. On site, each observer must maintain a distance of at least seven meters from the animals – and always wear a protective mask, which can become quite uncomfortable at 95 percent humidity and temperatures that often exceed 30 degrees Celsius.



18 PARASITES

ON THE COVER A human whipworm of the genus *Trichuris* can grow as long as five centimeters. This intestinal parasite comprises a thread-like anterior end connected to a thicker posterior end containing the internal organs, making the worms resemble a whip. Some species infect animals, such as dogs, cats or pigs, but humans, too, can serve as hosts for whipworms. Infections are usually imperceptible. Only very severe cases might result in intestinal bleeding and diarrhea.

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Photos: Shutterstock/Mohamed Abdulraheem, iStockphoto, dpa (left to right)

Ethics, Economy and Social Change

New Max Planck Center launched with the University of Cambridge

Acclaim for Anglo-German initiative: Max Planck President Martin Stratmann (left) and Stephen Toope, Vice Chancellor of the University of Cambridge, at the launch of the joint venture.

How do moral and ethical convictions impact a local economy, and how do they influence the global capitalist system? These questions are at the heart of the research conducted at the Max Planck Cambridge Center for Ethics, Economy and Social Change, which was formally launched in early March. The collaborative project's search for answers will see researchers from the UK's elite University of Cambridge work together with scholars from the Max Planck Institute for Social Anthropology in Halle and the Max Planck Institute for the Study of Religious and Ethnic Diversity in Göttingen. At the inauguration ceremony, Max Planck President Martin Stratmann expressed his delight that "in this period of uncertainty caused by Brexit, we have established another highly visible collaboration with top British scientists." The Center's four Co-Directors – James Laidlaw and Joel Robbins from the University of Cambridge, and Max Planck researchers Chris Hann and Peter van der Veer – are aware of the considerable public interest in the ethical principles of capitalism generated by the global financial crisis. One of the aims of their work is to develop new approaches to respond to urgent social issues.

High Accolade for Science Historian

Max Planck Director Lorraine Daston receives Israel's Dan David Prize

Lorraine Daston, long-serving Director at the Max Planck Institute for the History of Science in Berlin, won a prestigious international award in recognition of her scientific work. She received the prize, which carries an endowment of 1 million US dollars (more than 800,000 euros), for her "groundbreaking research on the 'Ideals and Practices of Rationality'." In its statement, the jury noted that Prof. Daston's work had demonstrated, among other things, "how such seemingly universal concepts as 'fact' and 'proof' have changed since the 17th century." *Objectivity*, a book co-written by Lorraine Daston and Peter Galison, was singled out for particular praise, which the jury called "one of the most discussed and reviewed works in the history of science."

Named after Israeli businessman Dan David, the prize is awarded each year to individuals with proven excellence in the sciences, arts, humanities, public service and business. This year, three scientists were honored in each of the following fields: history of science, bioethics and personalized medicine.

International recognition: Lorraine Daston has made a name for herself through her research into the cultural history of rationality.

Photos: Alice Boagey/Max-Cam-Centre (top); Skúli Sigurdsson/MPI for the History of Science (bottom)

"In ten years, we will know which animals can predict natural disasters"

Interview with Martin Wikelski on the Icarus antenna's successful voyage to the *International Space Station*

It is expected to launch by mid-year: Icarus – the first satellite-based program to research animal migration. With the help of tiny transmitters that send data to the *International Space Station (ISS)*, Martin Wikelski's team of scientists at the Max Planck Institute for Ornithology in Radolfzell hope to understand the factors that impact migratory patterns of different animal species. The Icarus program's two key components have been in space since mid-February, after a *Soyuz* rocket transported the Icarus antennas to the *ISS*. Martin Wikelski talks about experiencing his first countdown and what the future holds for the project.

Dr. Wikelski, you were at the rocket launch in Baikonur. How did you feel at that moment? There was an awful lot at stake.
Martin Wikelski: The spaceport in the heart of the Kazakh Steppe is quite a special place. When you stand beside the massive gates and the rocket comes rolling out of the hangar, you feel a bit uneasy. My colleagues and I put so much time and energy into developing Icarus – and it could all go up in smoke in a matter of seconds. After all, we know that not every launch is successful.

Now that the antenna has arrived safely at the ISS, *what happens with it next?*
For now, it is stored in the station's Russian module. Then, in August, the antenna will be mounted on the station's exterior. That will be another critical moment. If everything goes well during the spacewalk for the two Russian cosmonauts Oleg Artemyev and Sergei Prokopiev, we'll have overcome the last remaining major hurdle.

2018 is a decisive year for Icarus. What are you most looking forward to in the months to come?
The first data transmission from the *ISS* – no question! The moment we receive the first test data from the Space Station and know that the system works, I'll be the happiest man in the world. We will then spend two months testing whether the antennas and on-board computer are functioning and making sure the data transmission is working properly. And then, in the fall or toward the end of the year, we can finally get going.

Icarus will allow scientists the first-ever opportunity to observe thousands of animals on their journeys around the globe – over months and years, 24/7. What are the most pressing questions that Icarus can answer?
The most significant thing for me would be migratory birds. Their numbers are falling dramatically around the world. We often don't know where they disappear to or why. Unless we find answers fast, so we can take countermeasures, it will soon be too late for many species. The same applies to heavily exploited fish populations and many marine mammals in our oceans. We also urgently need to learn more about how animals spread pathogenic agents. How does bird flu travel to Europe? Which animals carry the Ebola virus? This is why we want to track the flight paths of waterfowl in Asia and fruit bats in Africa. Both are possible carriers of these pathogens. And last but not least, in ten years, we'll know which species can predict natural disasters. Initial scientific data on earthquakes and volcanic eruptions suggests that certain animals can sense such events hours ahead of time. If we can provide solid evidence of these abilities, it could soon save the lives of hundreds of thousands of people.

Looking to the future now – what will Icarus look like in ten years?
To begin with, the numbers of research projects using Icarus will increase significantly in the coming years. I imagine that, by 2028, several thousand projects will be able to collect scientific data thanks to the Icarus system. Our transmitters, which by then will be even smaller, could be fitted to hundreds of thousands of animals. In addition, in ten years, Icarus will probably not only be installed on the *ISS* but also on a series of other satellites. This will also allow us to survey areas that Icarus is currently unable to cover. Above all, additional satellites will enable us to examine regions of particular scientific interest above the 55th parallel in Europe, Asia and North America.

Martin Wikelski

As soon as Icarus is up and running, a lot will also change for you personally. How will it affect your everyday work?
I will be able to work on my own research projects again, thank goodness! Unfortunately, during the last few years, I've sometimes had to put my scientific work on the back burner in favor of Icarus. That should certainly change now. Starting in July, I will take a sabbatical for science and go back to focusing completely on my research.

Interview: Harald Rösch

Photo: MaxCine

Rust Protection from Nanocapsules

New technology prevents metal from corrosion

Effective anti-corrosion protection: An environmentally friendly plastic coating with self-healing properties is designed to protect iron components against rust.

Costs resulting from corrosion total some 3.3 billion US dollars annually. Currently, varnishes, enamel, rubber and metallic surface layers are applied to materials to prevent rust damage, but these often contain harmful substances and do not provide long-term protection. German company Enviral has now acquired a license for a brand new anti-corrosive technology that was developed at the Max Planck Institute of Colloids and Interfaces and is based on "smart" pigments. The process enables anti-corrosive coatings to repair damage, similar to the self-healing mechanism of human skin. To achieve this, micro- and nanovessels are filled with organic corrosion inhibitors, encapsulated in a polyelectrolyte shell and subsequently embedded in the coating. If the protective layer is damaged – by scratches or fissures, for instance – the embedded vessels at the site of the flaw open, releasing the corrosion inhibitors and immediately protecting the damaged area. Enviral plans to further develop the smart pigments and promote their production and marketing.

Potential Tuberculosis Vaccine Draws Closer

A promising vaccine is being tested on patients with recurrent tuberculosis

Tuberculosis remains one of the world's most dangerous infectious diseases. Healthcare professionals and policymakers are particularly troubled by the increasing number of multiresistant pathogens. Researchers at the Max Planck Institute for Infection Biology laid the scientific foundation for a potential new vaccine that is now entering the decisive Phase III clinical drug trials. The vaccine, called VPM1002, is currently being tested in a study involving some 2,000 participants in India. This study began early this year and is slated to run until mid-2020. Researchers are testing the potential vaccine on patients who have already suffered from tuberculosis and successfully undergone treatment. For reasons that are currently unknown, around 10 percent of these patients contracted the disease again within a year. In the trial, a portion of the participants are inoculated with VPM1002 a few weeks after being discharged as healthy. "If the vaccine candidate can reduce the reinfection rate in this particularly challenging group and proves to be well tolerated, it will have cleared a major hurdle on the path to approval," explained Stefan Kaufmann from the Max Planck Institute for Infection Biology, who made a significant contribution to developing the scientific concept for VPM1002.

Immune system in action: A while blood cell (shown in red) ingests tuberculosis bacteria (yellow), confining them. However, the bacteria can survive for years in these phagocytic cells.

Photos: iStockphoto (top); Volker Brinkmann / MPI for Infection Biology (bottom)

Foundation for Heidelberg Research Network

Max Planck Society and Baden-Württemberg agree on a new building for the joint "Biology at the nanoscale" project

The Baden-Württemburg State Ministry of Science has agreed to support the collaboration between Heidelberg University and the Max Planck Institute for Medical Research in Heidelberg. Minister for Science, Research, and the Arts Theresia Bauer, Max Planck President Martin Stratmann and President of Heidelberg University Bernhard Eitel signed a declaration of intent to this effect in early March. The document details the federal state's commitment to provide 25 million euros to fund the construction. The new building will be erected on the "Heidelberg 4 Life" life sciences innovation campus, directly adjacent to the Max Planck Institute. It will become home to the planned "Biology at the Nanoscale" research network, which was born of an initiative by Nobel Prize laureate Stefan Hell. The University and the Max Planck Institute hope to use the research network to expand their collaboration in basic research in bioscience and biomedicine. Additional partners, including the German Cancer Research Center (DKFZ) and local clinical researchers, will also be integrated into the network. The scientists also aim to cultivate industry contacts so that their discoveries can be quickly translated into medical applications.

Innovation in sight: Bernd Bukau and Bernhard Eitel from Heidelberg University, Baden-Württemberg's Minister of Science Theresia Bauer, and Martin Stratmann and Stefan Hell from the Max Planck Society (from left) after signing the agreement.

Photo: Heidelberg University

On the Net

Flight and Trauma
Some 20 to 30 percent of refugees suffer from severe depression or post-traumatic stress disorder. A short film by the Max Planck Institute of Psychiatry uses animated images to show that insomnia, obsessive brooding and physical complaints such as headaches and shortness of breath can be symptoms of a mental illness. The film aims to relieve the pressure on those affected and encourage them to seek help. The two-minute film is available in ten languages, for example German, English, French, Italian, Arabic, Dari and Kurdish.
http://bit.ly/2M2GbV3

Passion for Science
This is the motto of the Max Planck Schools – an innovative national network for excellent graduate education. Preparations to launch the first three Schools are in full swing. The Max Planck Schools will issue a call for applications in the fall of 2018, and the first students will commence their studies 2019. Applications will also be open to students with a bachelor's degree, who can then complete a two-year master's degree followed by a three-year PhD program. The Schools have a joint website where those interested can find detailed information about the program.
https://www.maxplanckschools.de/en

Copy and Original
Through his copies of Italian paintings and frescoes, Johann Anton Ramboux (1790-1866) left a lasting imprint on art history research. Generations of artists and art researchers have relied on Ramboux's museum of copies. Before photography became the main form of documenting works of art, his drawings, tracings, lithographs and watercolors were often the only accessible source of these works. The Max Planck Society's Kunsthistorisches Institut in Florenz created an online exhibition juxtaposing Ramboux's copies with the original works.
http://photothek.khi.fi.it/documents/oak/00000331

Trawling in Outer Space

Luxembourg is the first European country to pass a law guaranteeing companies entitlement to raw materials obtained in outer space – as long as the companies are based in the country. The Grand Duchy is also using loans and research investments as incentives. The rationale behind this is Luxembourg's desire to become the leading international center for mining in outer space, in the hope that the companies involved will then pay tax on their profits there. However, this farsighted policy is more than a little dubious with respect to international law, as our author explains.

TEXT **LORENZO GRADONI**

In 1973, the President of the United States of America sent an unusual gift to the Grand Duchy of Luxembourg – the nation's flag in the size of a handkerchief, and a slightly smaller piece of rock. The flag had just travelled to the Moon and back on the *Apollo 17* mission, and the rock came from a Moon valley near Mare Tranquillitatis. The fragment of the Moon's surface, which is now housed at the National Museum of Natural History, was presented to Luxembourg "as a symbol of the unity of human endeavor."

> The words "in accordance with international law" were omitted

Today, the right to own and sell such rocks can be obtained in Luxembourg, regardless of whether they come from the Moon, a near-Earth asteroid or a mining facility on Mars. The only requirement is that they be extracted by a company under Luxembourg law that has obtained "written authorization for the mission" from the competent ministry. The procedure is governed by a law adopted on July 20, 2017, Article 1 of which states: "Resources in outer space may be appropriated."

This statement will come as a surprise to anyone who believed that outer space was the province of mankind under international law. How can it be lawful for somebody to own space resources and exploit them for their own advantage? Aside from the US, which adopted similar legislation in 2015, and the United Arab Emirates, where a comparable bill is being prepared, what are other countries doing?

Let's say that a company is the owner, under Luxembourg law, of a ton of heavy metals obtained from an asteroid. Doesn't it run the risk of having its valuable assets seized in the port of Antwerp? Belgium, which is a member of the United Nations Committee on the Peaceful Uses of Outer Space, has clearly opposed unilaterally promoting the privatiza-

No shoal of fish: The Outer Space Treaty seemingly prohibits the appropriation of entire asteroids. Whether international law permits them to be mined is a contentious issue.

Photo: iStockphoto/dottedhippo

tion of resources in outer space. One need only look at the Benelux countries to witness this "extraterrestrial" dispute. But the new law is controversial in Luxembourg, too.

On November 15, 2016, Etienne Schneider, Luxembourg's Deputy Prime Minister, presented to parliament a draft bill whose first article stated: "The resources of outer space may be appropriated in accordance with international law." Readers will undoubtedly notice the difference between this provisional wording and the final version of the law cited above. In the final version, there is no reference to international law, as if it had been overlooked. The Luxembourg government seems convinced, however, that international law can't stand in the way of its "space resources" project. So why was the reference to international law removed? Doesn't it look like an admission of culpability?

The headquarters of the Conseil d'Etat, which was responsible for deleting it – involuntarily as we will see – is just a few hundred meters away from Parliament. Its task is to check whether bills comply

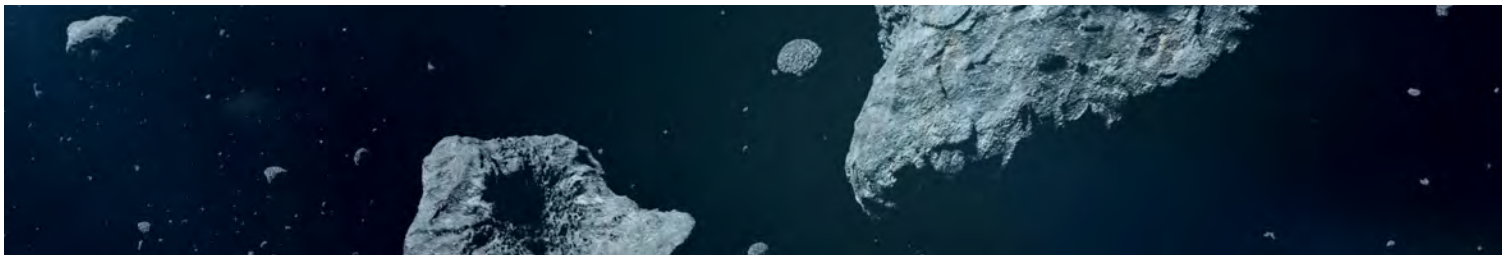
Are asteroids like small islands, boulders or icebergs?

with Luxembourg's Constitution, as well as with international agreements and EU law. While the Conseil didn't find any significant discrepancy between the bill and international law in its position statement issued on April 7, 2017, it did question the project's raison d'être.

The Conseil couldn't conceal its unease about international law on outer space – a law it deems to be vague. Nevertheless, the government of the Grand Duchy declared that the "primary aim" of the bill was to "establish legal certainty as regards the ownership of minerals and other valuable resources obtained in outer space and, in particular, from asteroids." But Luxembourg law can't offer this legal certainty alone if international law itself doesn't provide it. The practical conclusion drawn by the Conseil was quite radical: "Article 1 of the bill" – the emblem of the entire project – "had to be deleted." At the same time, it didn't wish to torpedo the legislation. Instead, its message to parliament was this: a bill that indicates that international law generally tolerates the appropriation of space resources would simply be misleading, and the legislator should confine itself to introducing an approval procedure to decide on outer space "permits" on a case-by-case basis.

As outlined above, only half of the message was taken on board. Article 1 of the bill was retained, albeit without any reference to international law, as if to protect the Luxembourg legal system and investors hoping to take advantage of Article 1 from the legal uncertainty highlighted by the Conseil. It is therefore not by chance that the bill's legal basis, as spelled out in the commentary thereto, refers not so much to international law as to domestic and natural law. It is the Napoleonic code that paved the way for the appropriation of space resources, to which it is said to apply by analogy. According to the bill's authors, the "analogy between outer space and the ocean" is "legally [...] evident." They seemingly took a decisive cue from François Laurent, a famous lawyer born in Luxembourg in 1810, who wrote a 33-volume "Principles of Civil Law" (*Principes de droit civil*) and the 18-volume Studies on the history of humanity (*Études sur l'histoire de l'humanité*). According to Laurent, who had a good understanding of the "nature of things," one couldn't assert that ownerless things, such as crustaceans and fish, "are intended by nature for use by all mankind. In reality, they are of no use to anyone unless they have an owner, and as soon as they have an owner, they are of use only to those who have appropriated them."

In the view of the Luxembourg government, the resources of outer space can, therefore, "like fish and crustaceans," be appropriated, but "celestial bodies and asteroids can't, in the same way that the oceans can't be appropriated." According to Article 116 of



the United Nations Convention on the Law of the Sea, "All States have the right for their nationals to engage in fishing on the high seas." The same rule would apply to outer space. This is provided that they can locate what counts as a fishing ground in outer space and distinguish it from things that can't be appropriated.

Anyone wishing to cast their nets to capture an asteroid would, according to the Luxembourg government, be trying to catch a celestial body that – even if relatively small – isn't legally the same as a tuna fish. What position would the extremely diverse family of asteroids occupy in the analogy between ocean and outer space? Should they be regarded as uninhabited small islands or as underwater boulders or pebbles washed up on the beach? Perhaps they should be viewed as icebergs? Can they be distracted from their orbit or mined until they are just empty shells without this being deemed illegal appropriation? More importantly, can we really be certain that François Laurent himself wouldn't have seen them as fish? Investors in space resource exploration and exploitation would be delighted to treat an asteroid like a big fish, but what does international law say? Nothing specific, according to the authors of the draft legislation. In their view, the "predominant school of thought suggests that appropriation of these resources is possible."

The notion of interpreting outer space law through the categories of law of the sea is certainly not arbitrary; international lawyers have frequently relied on that analogy. Yet its applicability is far from being uncontroversial. This is clearly reflected by the problems encountered when attempting to define the maritime equivalent of an asteroid. It is also worth remembering that the cornerstone of the law on outer space – that is, the exclusion of sovereignty – was established, not on the basis of the analogy between the sea and outer space, but rather in contrast to it.

"Outer space is to Earth what the ocean is to the continents," wrote René-Jean Dupuy, a famous French international lawyer, in 1989. But if celestial bodies were the equivalents of continents or islands, then states could make them their own, as they did when they sailed their ships across the oceans in search of unknown lands. "A planet becomes the extraterrestrial possession of the state that acquired it through conquest or peaceful occupation," wrote Joseph Kroell in 1953 in a journal on outer space law.

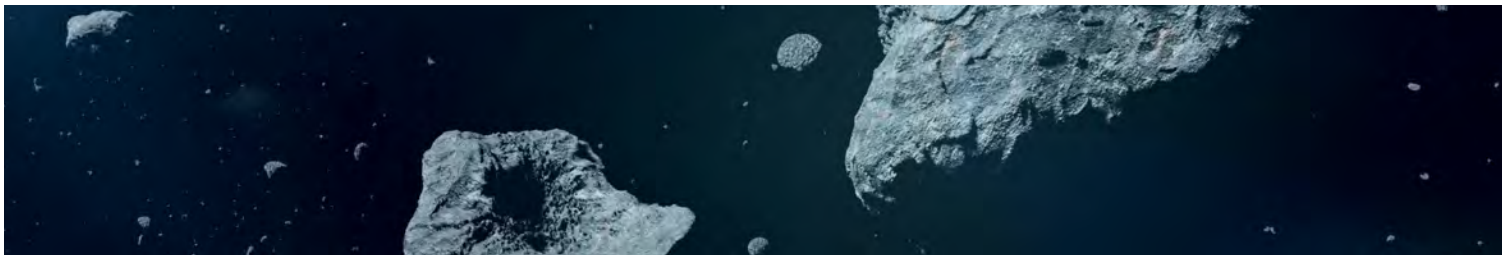
Only 18 states expressly recognize the Moon as the common heritage of mankind

But the international community took a different view in the first half of the 1960s. That was the decade in which the international community began to establish the law of outer space – a positive law that could sometimes run contrary to the "nature of things" and seemingly supported the call for justice coming from the nations that had just freed themselves from colonial rule. What does this law say about the legal status of space resources?

Outer space law can be found in five major treaties concluded under the auspices of the United Nations between 1967 and 1979. Only two of them matter for our discussion. The first of these agreements, the Outer Space Treaty, entered into force in 1967. Today, it has 107 signatory states, including Luxembourg and all the space-faring nations. The Agreement Governing the Activities of States on the Moon and other Celestial Bodies, known as the Moon Agreement, entered into force in 1984, but it has only been ratified by 18 countries, none of which are space powers. So far, it has been a failure.

How can these very different outcomes be explained? The two treaties don't contradict each other, but the second one goes further in advocating a collective approach to the use of space resources, generally in the interests of newly independent states. And that sealed its fate as the conservative revolution set in in the 1980s. Not only does the

Photo: iStockphoto/dottedhippo



Moon Agreement state that "the Moon and its natural resources" are "the common heritage of mankind" (which also applies to other celestial bodies in the solar system, except for the Earth), it also directs the small group of signatory states to establish "an international regime, including appropriate procedures," to govern the exploitation of natural resources in outer space, "as such exploitation is about to become feasible." The reasons why this paragraph has come to nothing are of a political rather than a technical nature.

Just how contentious the idea to create an international authority to administrate "the common heritage of mankind" had become by then is illustrated by the discussions on the legal regime of the deep seabed at the third United Nations Conference on the Law of the Sea. In 1982, the negotiations ended in an atmosphere of gloomy hostility between the states

Russia reacted with outrage to a similar law in the US

that were ready to invest in the exploitation of seabed resources, but less ready to share the proceeds thereof, and the numerically superior emerging nations. This eventually forced the adoption of a treaty text that provided for the creation of a powerful International Seabed Authority to act on behalf of "all mankind." It was a Pyrrhic victory. The agreement didn't enter into force until 12 years later, when a supplementary agreement was adopted that significantly weakened the Authority and the redistributive mechanism it was intended to govern.

Article II of the Outer Space Treaty, to which Luxembourg is a party, states: "Outer space, including the Moon and other celestial bodies, isn't subject to national appropriation by claim of sovereignty, by means of use or occupation, or by any other means." Does the new Luxembourg law comply with this principle? While Article II has often been interpreted in contradictory ways, it doesn't say much about the question as to whether resources in outer space can be appropriated. It could be argued that the term "national appropriation" was chosen to also exclude appropriation by non-state actors. That would also apply, for example, to a company based in a signatory state seeking to take ownership of a plot of land on the Moon.

However, it could also be contended that the wording refers only to states and perhaps also to new states that future settlers in outer space may establish, or to indirect expansions of states' sovereignty, for instance through the occupation of territories by contemporary equivalents of chartered companies. The only thing that can be said with certainty is that the authors' main aim was to ban sovereignty from outer space and that the cautious wording of Article II ("by any other means") simply aimed to prevent the ban from being circumvented.

The exclusion of sovereignty may nevertheless have consequences when it comes to the establishment of proprietary rights to resources in outer space. This is because the acquisition and protection of property depends on a state exercising sovereignty. In order to establish itself in outer space, property would first have to emancipate itself from sovereignty. According to Article VI of the Outer Space Treaty, on which much of the Luxembourg law on outer space is based, activities of non-governmental entities in outer space require "authorization and continuing supervision by the appropriate State Party." However, as a State performs this task, there is a danger that it will overstep the boundary between legitimate exercise of authority and what would be in essence a claim of sovereignty.

To date, the Luxembourg law on space resources hasn't attracted much interest in diplomatic circles, and it is difficult to predict how many states – apart from the US and the United Arab Emirates – will share Luxembourg's approach, but the issue is very

Photo: iStockphoto/dottedhippo

likely to prove contentious, as Russia's outraged reaction to the US legislation already suggested. In Russia's view, the US initiative was an "arbitrary self-extension of its own 'freedom'" and the result of the "notorious doctrine of supremacy in outer space." In the eyes of a leading space-faring nation, Luxembourg is therefore acting in the shadows of a self-proclaimed hegemon that seems to ignore the fact that mining in outer space – especially if small asteroids are deflected from their orbits in the process – "presents a high risk for the population of the entire world and should be regulated at the international level."

The issue hasn't yet been discussed within the EU; nevertheless, it is clear that the few EU states bound by the Moon Agreement (Austria, Belgium and the Netherlands) can't support Luxembourg without violating their international obligations. Belgium, in particular, has clearly expressed opposition to nations going it alone in this field. Instead, the country supports the negotiation of new international regulations to break the deadlock the international community faces due to the ambiguity of the Outer Space Treaty and the failure of the Moon Agreement. The fact that two countries (Armenia and Venezuela) recently ratified the long-neglected Moon Agreement may indicate that unilateral initiatives such as those in the US und Luxembourg are increasingly being viewed with skepticism, making it unlikely that other states will follow suit.

Andrew G. Haley, a pioneer in the law of outer space, prophesied in 1963 that "some day in the future companies will want to mine meteorite ore and then all the old law-of-the-sea problems will resurface under much more complicated circumstances." Luxembourg's law on space resources presents a good opportunity to tackle this issue and to define new shared approaches to international outer space law. ◀

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Photo: MPI Luxembourg

THE AUTHOR

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A Yearning for Roses

Max Planck scientists cooperate with partners in more than 110 countries worldwide. Here they relate their personal experiences and impressions. Lale Yalçın-Heckmann, who works at the Max Planck Institute for Social Anthropology in Halle, is studying values and moral ideas surrounding commercial transactions – taking traditional rose farming in Turkey as an example.

The story of roses and me goes back a long way. When I was a child, my maternal grandmother used to tell me fairy tales about women in traditional bathhouses, *hammams*, who would luxuriate in bath water infused with rose petals. In early Ottoman times, the roses from which the fragrant oil was obtained came from the Middle East. From there they spread to the Balkans – including Bulgaria, where they were cultivated by Turkish settlers.

Given my family's roots both in Bulgaria and in Isparta, Turkey, it is hardly surprising that I have had a fascination for roses – especially the culture surrounding their cultivation and the production of rose oil – ever since. There is an expression in Turkish that describes the feeling perfectly; it translates roughly as "the heart's yearning." My heart's yearning for culture and for roses makes perfect sense to the people I speak to in Turkey, especially around Isparta, where my father is from.

In my current research project, I am examining the values and moral ideas surrounding commercial transactions based on the example of how traditional rose farming and modern production processes in Turkey shape the regional community and its values. I spend weeks and months in Isparta, the traditional center of rose farming and rose oil production. I pick roses and talk with farmers, rose oil producers and seasonal workers. After all, social anthropology research is strongly dependent on local relationships, so it is essential to interact with people in order to fathom their knowledge of the economic situation.

Illustration: iStockphoto

Lale Yalçın-Heckmann, 62, studied sociology at Boğaziçi University in Istanbul before obtaining a PhD in social anthropology at the London School of Economics. Since moving to Germany in 1988, she has researched Turkish and Kurdish migrants and Islam in Germany and France. She qualified as a professor in 2009 and was a Group Leader at the Max Planck Institute for Social Anthropology. Since 2010 she has taught at the University of Pardubice in the Czech Republic and is a faculty member of ANARCHIE, an International Max Planck Research School. Within the ERC project entitled Realising Eurasia: Civilisation and Moral Economy in the 21st Century, she mainly coordinates scientific activities and her own research in Isparta, Turkey.

However, spending time with people "on the ground" can be arduous. As roses are extremely delicate and their fragrance quickly fades, the harvest begins at 5:00 a.m. – though this has the advantage that the work is normally done before the midday heat. Whether a rose picker is treated fairly depends very much on his or her relationship with the farmer and how many seasonal workers are at the farmer's disposal during the rose harvest. The amount picked by each worker is recorded at the end of every workday, and payment is made at the end of the harvest season. A strong worker can pick up to 40 kilograms a day, which in 2016 yielded a wage of 14 euros. Incidentally, my personal record is ten kilograms.

In the course of conversations and discussions, I've learned that rose farming – though characterized by expert knowledge and decades of experience – is by no means the only source of income for the farmers. In fact, mixed farming with apples or cherries or with dairy farming is what gives the farmers the leverage they need to negotiate prices with rose oil producers.

Rose prices saw a sharp rise in recent years, then rose oil prices recently plummeted. It is therefore in the farmers' interests to argue that they can easily switch to another product. Whether they keep a fruit tree or a rosebush depends on its market value. Since the farmers can usually adopt a flexible income strategy, and the factories are secretive about the actual volume of rose oil they produce, the pricing structure is highly opaque.

As in many rural areas, it's rare for the next generation to follow in their parents' footsteps. Families are migrating to big cities, and the rose harvest spans a period of just two months a year. The process of organizing workers for the season is thus heavily dependent on friendships and kinships. To put it simply, entire extended Turkish families gather in their native village to help with the rose harvest and ensure the survival of this age-old tradition. Ultimately, their heart's yearning leads them back to the roses.

Photo: Lale Yalçın-Heckmann

Genes as **Parasites**

Parasites exist not only in the plant and animal kingdoms, they are also a part of us. Our genome contains myriad short stretches of DNA that propagate at the genome's expense. For this reason, these transposons, as they are called, are also referred to as parasitic DNA. **Oliver Weichenrieder** from the **Max Planck Institute for Developmental Biology** in Tübingen wants to shed light on the processes by which transposons are copied – not only because they can cause disease, but also because they may be an important engine of evolution.

TEXT **TIM SCHRÖDER**

The object of his research work is tiny and sparkles like fine diamond dust. Oliver Weichenrieder slides a plastic plate containing small wells back and forth under the microscope. He searches for a while. "Ah, I can see a few in there. Pretty, aren't they?" The small crystals are invisible to the naked eye, but under the microscope they glitter in violet, pink and blue hues. "It takes a bit of luck for the crystals to form. That's why we use these plates with many small depressions," Weichenrieder says. That increases the hit rate.

Crystal – that sounds like materials science, like glass and ceramics, but that's not at all what Oliver Weichenrieder is concerned with. He is a biochemist, and the crystals he grows at the Max Planck Institute in Tübingen are molecules from living cells, specifically proteins or ribonucleic acids (RNAs). Weichenrieder is studying the crystals to elucidate the structure of these molecules with a view to solving one of genetics' enduring secrets: the puzzle of parasitic DNA, or parts of the genome that self-propagate independently of the rest of the genome.

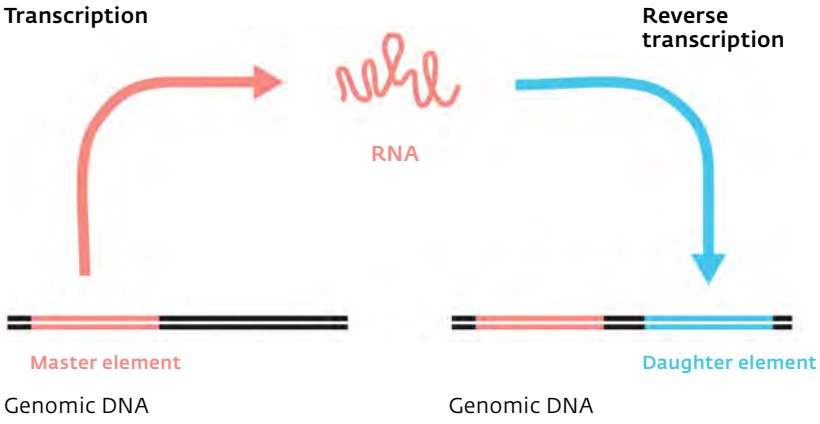
Parasitic DNA is a catchy description of genetic snippets known to scientists as transposons. Transposons are short sections of DNA that repeatedly replicate and insert themselves into new DNA sites in the genome. The term "transpose" is known from music and means writing or playing a piece of music in a different key. In the case of transposons, genetic information is transported from one site in the genome to another. This transfer process occurs during the development of germ cells and most notably in the early embryo when cells are dividing vigorously.

JUMP INTO THE GENOME

Each time this occurs, the DNA sequence is reshuffled – sometimes with serious consequences: "It can happen that a transposon lodges itself in a gene

Photo: Wolfram Scheible

The crystals of a transposon protein measure around one-tenth of a millimeter across. By analyzing the crystal structure, researchers in Tübingen have discovered how the protein is able to package transposon RNA.



Above For retrotransposons to be able to insert copies of themselves into the genome, their DNA, termed the master element, is first transcribed into RNA. The RNA is then transcribed back into DNA (reverse transcription), while the resulting DNA copy (the daughter element) is integrated into the genome.

Right Oliver Weichenrieder checks incubation cabinets for genetically altered bacteria. The microbes produce transposon proteins, which the researcher and his colleagues need in order to analyze the protein structure.

segment that contains information for a protein that is essential for metabolism," Weichenrieder explains. "The gene can then no longer be read correctly." The APC gene is a prime example. The protein it encodes can prevent the development of cancer. If it is disrupted by the incorporation of a transposon, colon cancer can result.

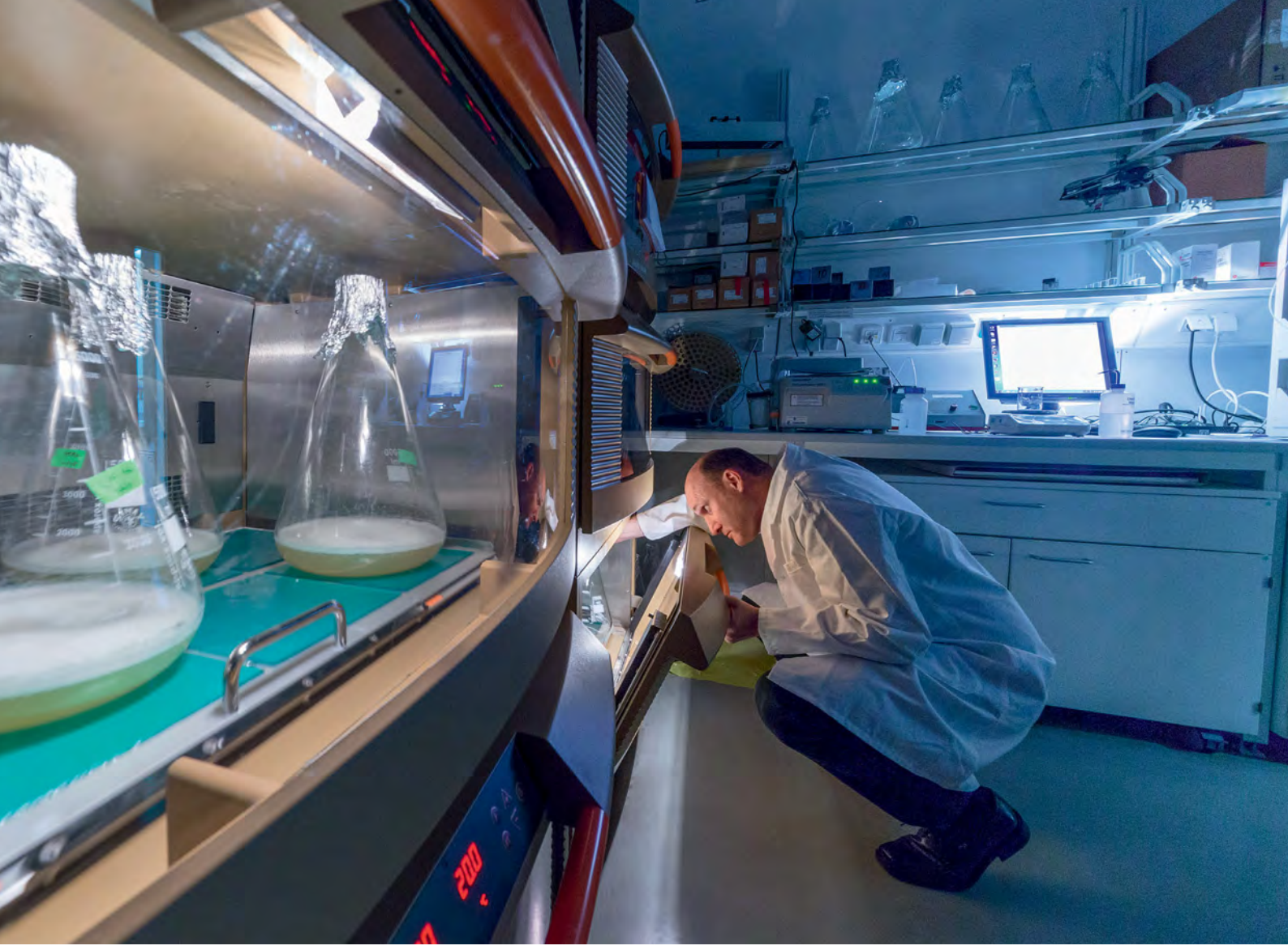
Proteins are essential for reading the information contained in DNA, transcribing it into RNA and translating the RNA into new proteins. Transposons, too, need various proteins to replicate and to insert themselves into the genome. "We still don't know exactly how transposons work," Weichenrieder says. "But if we elucidate the structure of the proteins involved in transposon replication, we might be able to better understand the whole process."

FLOOD OF TRANSPOSONS IN THE GENOME

Oliver Weichenrieder and his colleagues focus primarily on identifying the structure of two important parasitic DNA snippets known as the LINE-1 retrotransposon and the Alu retrotransposon, as both are extremely common in the human genome. A LINE-1 segment is about 6,000 DNA base pairs long – about as long as an average gene. The genome contains around 500,000 LINE-1 copies and fragments. In fact, the LINE-1 element alone makes up 17 percent of the genome. "This immense number has resulted from the creation of ever new copies in the course of evolution over millennia," Weichenrieder says. It's possible that more than half of our genome has been created from transposable elements. The proportion of transposons may be even higher in other organisms. In corn plants, for example, as much as 85 percent of the entire genome can be traced back to transposons.

Of course, the transpositions could only be passed on if they didn't kill the

Graphic: MPI for Developmental Biology; photo: Wolfram Scheible



individual, for example as a result of cancer. "Not every transposition is necessarily fatal for the individual or their offspring. It depends on which part of the genome the LINE-1 copy is incorporated into." In addition, many have been deactivated over time by mutations. At present, only around 100 of the 500,000 LINE-1 sections in the human genome are active and capable of parasitic behavior. The rest no longer work.

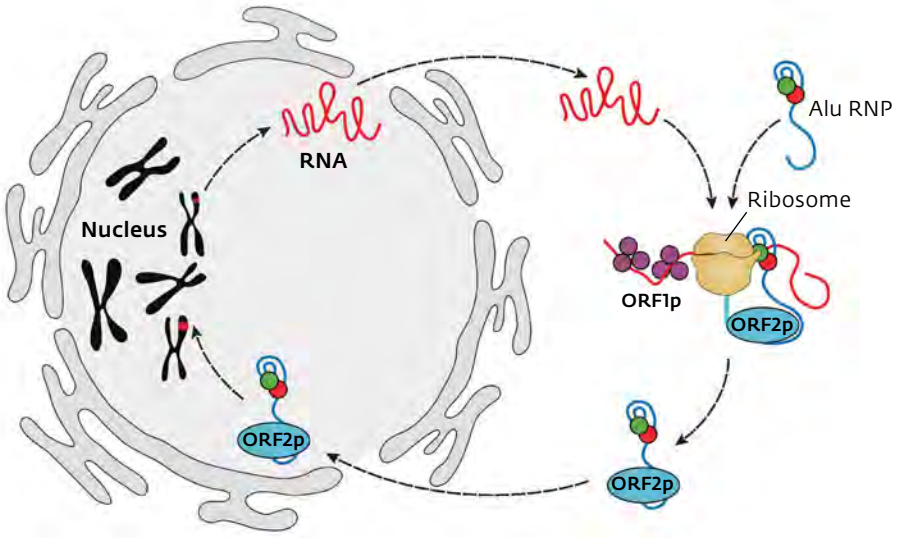
Weichenrieder is particularly fascinated by Alu retrotransposons, which are also distributed throughout the genome – not only because, with more than a million copies, they occur in great numbers and make up about 10 percent of the genome, but because, from a parasitic point of view, they take things a step further. They are parasites of a parasite in that they hijack the LINE-1 machinery and use it for their own replication. LINE-1 is able to replicate by itself. Alu, in contrast, requires LINE-1 proteins and uses them for its own purposes.

Transposons are therefore concerned only with their own propagation and don't appear to contribute anything to the organism's survival. The organism is just a means to an end. On closer inspection, however, it becomes clear that it can nevertheless benefit from transposons. Whenever transposons insert copies of themselves into the genome, they reshuffle the DNA, thus driving evolution. "That keeps the genome flexible," says Weichenrieder. "During times when the environment changes dramatically as a result of climate change or natural disasters, the organism is able to adapt more quickly." In fact, it has since been shown in plants that transposons are particularly active when the plants are under stress – for instance during a hot spell.

Many transposons are harmful, but sometimes they give an organism new characteristics that are vital to survival. "It has long been believed that evolution is driven by the exchange of individual letters of the genetic code, known as point mutations," Weichenrieder says. Now, however, many of his colleagues believe that transposons play an important role in vigorously reshuffling the genome, thus creating new variations.

PROTEINS FOR JUMPING GENES

In recent years, Oliver Weichenrieder and his team have used the small protein crystals to probe deep into the molecular structure of LINE-1 and Alu. Their laboratories in Tübingen contain equipment that allows them to extract the proteins required for the transposition of LINE-1 and Alu. These high-performance liquid chromatography systems separate a mixture of different proteins into its component parts so



that tiny amounts of a pure protein trickle out at the end. These are then mixed with a variety of substances on the microtiter plates and are concentrated in the hope that the small crystals will form.

FROM STRUCTURE TO FUNCTION

And then it's time to take a trip: the scientists bombard the crystals with intense X-ray light in particle accelerators in Zurich or Hamburg. The atoms of the proteins diffract the X-rays differently, producing a characteristic diffraction pattern. From this, computer programs determine the electron distribution in the crystal and, to a certain extent, the chemical structure of the protein molecule. "Nevertheless, there's still plenty of manual work for us to do. We need a great deal of chemical knowledge to reconstruct the entire protein from the fragments in the computer." This is how the researchers in Tübingen uncovered the structure of the LINE-1 proteins and of Alu RNA.

LINE-1 requires two main proteins to replicate successfully: ORF1p and ORF2p – that much was already known. The blueprint for those proteins is contained in the LINE-1 element. If LINE-1 is active, an RNA copy is first made. This migrates to the cell's protein factory, the ribosome, where it provides a template for synthesizing the proteins.

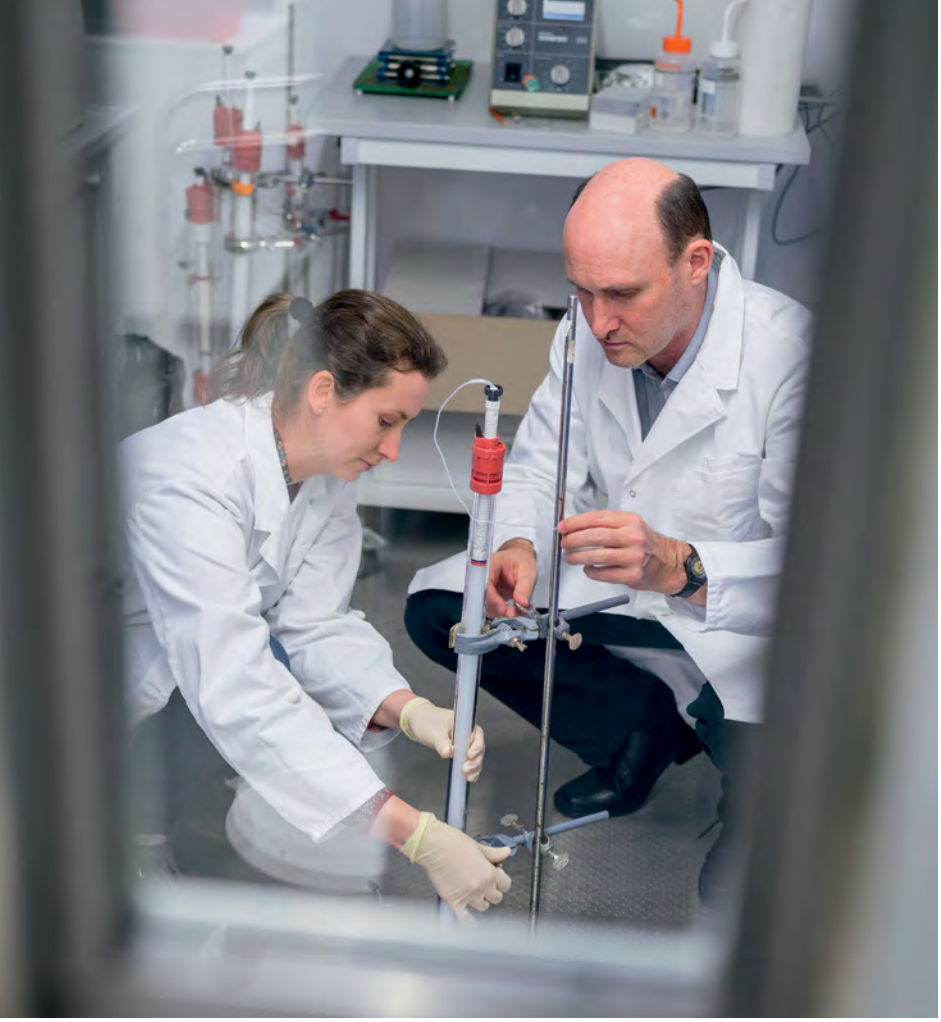
For a long time, it wasn't known how the two proteins function, but the identification of their spatial structure by the scientists in Tübingen provided clarity: ORF1p consists of three subunits, and the RNA is able to nestle between them. In addition, the ORF1 proteins always occur in bundles of three ORF1 protein molecules. "By all indications, the LINE-1 RNA is wound around the trimers of this protein to protect it from the cell's defense weapons," Weichenrieder explains. The cell is by no means completely at the mercy of a transposon; it can switch off the copying process in various ways, for instance with the help of proteins that destroy the transposon's RNA or attack ORF1p. The ORF1 protein protects the LINE-1 RNA from these countermeasures so that the RNA is able to go on to produce ORF2p.

ORF1p also resembles proteins that allow cell membranes to fuse. Accordingly, ORF1p might also help LINE-1 RNA conquer the nuclear membrane

Above A parasite attacks a parasite: A complex consisting of Alu RNA and proteins (Alu-RNP) recognizes the ribosomes that are currently translating the RNA of the parasitic LINE-1 element to produce ORF2p. The Alu complex hijacks the protein, which actually belongs to LINE-1, and hitches a ride with it into the cell's nucleus (gray), where ORF2p reverse-transcribes the Alu RNA and integrates the resulting DNA into the genome as a new Alu element.

Right-hand page Oliver Weichenrieder and Elena Khazina prepare a chromatography column (top). They inject a purified cell extract into the apparatus and then separate the protein mixture into its constituents (bottom).

Graphic: MPI for Developmental Biology



Photos: Wolfram Scheible (2)

to reach the DNA in the nucleus, to which it must return in order to replicate itself.

CUTTING AND TRANSCRIBING

ORF2p is needed for LINE-1 to replicate, and the researchers now have a more detailed understanding of its spatial structure, as well. It consists of two subunits: an endonuclease and a reverse transcriptase. The endonuclease first cuts the DNA. In doing so, it recognizes specific DNA structures that occur during the duplication of DNA or shortly before cell division, which clears the way for incorporation of the retrotransposon sequence. The reverse transcriptase then converts the RNA back into DNA and incorporates it into the genome.

The researchers' findings could lead to the development of drugs for forms of cancer in which the genome is damaged by transposons. Such drugs could block LINE-1 proteins, preventing transposition. However, Oliver Weichenrieder first wants to gain a thorough understanding of the underlying process, and Alu, being a parasite of a parasite, is particularly suitable for this purpose. "The Alu RNA evidently iden-

The crystal structure of an Alu ribonucleoprotein particle (RNP). The Alu RNA (blue) consists of ribonucleotides (adenine, guanine, cytosine and uracil), which fold into a well-defined structure stabilized by two proteins: SRP9 (red) and SRP14 (green). The actual molecular parasite is therefore the folded RNA.

tifies ribosomes that are currently producing ORF2p without directly recognizing the protein," he explains. "Once the ribosome has completed the ORF2p protein, Alu strikes and fishes it out." The Alu RNA then uses the hijacked endonuclease and reverse transcriptase to insert its own DNA into the genome. "So it depends on your point of view," Weichenrieder says, "because strictly speaking, the actual parasite isn't the transposon DNA but the LINE-1 or Alu RNA read from it."

STUTTERING ASSEMBLY LINE

It is estimated that only about one in twenty newborn babies carries a new Alu copy and passes it on to his or her descendants. The reason transposition isn't that common is that transposons are usually inactivated by cellular defense mechanisms. The transposition of LINE-1 is also fairly rare. "Alu RNA thus needs to be able to sense very precisely where LINE-1 is currently active and synthesizing ORF2p on a ribosome," Weichenrieder says – like a parasite that unerringly tracks down its host.

His results suggest that Alu may recognize a sort of stuttering that occurs during the synthesis of ORF2p on the ribosome. Some of the amino acids that are incorporated into the ORF2p protein during production are lysines, which don't readily pass through the ribosome's production channel. If they occur frequently, the assembly line can falter and stutter. It is very likely that Alu recognizes such stuttering and then arrives in time to pick up the finished ORF2p.

To date, no researcher has observed this process live, but all the evidence the scientists have gathered by analyzing protein structures points to this conclusion. In addition, the Alu retrotransposon is closely related to another particle known as the signal recognition particle (SRP), which regulates the production of specific proteins on the ribosome. Alu only emerged from SRP with the evolution of primates, which was a very recent event in evolutionary terms. The researchers in Tübingen have found that Alu RNA has retained substantial parts of the SRP structure and must also bind two

Graphic: MPI for Developmental Biology

Three scientists, one goal: By analyzing transposon proteins, Gabriele Wagner, Oliver Weichenrieder and Elena Khazina (from left) hope to gain an understanding of how parasitic DNA can spread in our genome.

small SRP proteins for it to replicate successfully as a retrotransposon.

For Weichenrieder, transposons are, in and of themselves, neither good nor bad. Nevertheless, he is intrigued by the idea of a molecular parasite: "Alu is so simple in structure: a short RNA segment and two small SRP proteins that fold the Alu RNA. It appropriates everything else it needs. By comparison, even viruses are enormously complex with their wealth of information on protein construction."

This raises the question of how small and simple a parasite can actually be and still function. Weichenrieder is therefore testing Alu variants to determine whether they can replicate. To this end, he gradually reduces their size and the number of proteins involved. In this way, he hopes to achieve his goal and find the "ultimate parasite" – a piece of RNA, pared down to the barest of necessities, that can still replicate successfully with the help of an organism's genome and at the organism's expense. ◀

www.tinyurl.com/y79ad2yp
(available only in German)

TO THE POINT

- **Parasitic DNA molecules are DNA segments that are able to replicate at the expense of the organism. In the case of LINE-1 and Alu, however, the corresponding RNA molecules are the actual molecular parasites.**
- **Large parts of the genome have developed from these transposons, which account for more than 80 percent of the genome of some plants. Most, however, are no longer active.**
- **Some RNA molecules, such as Alu RNA, exploit the copying machinery of other transposons, making them parasites of parasites.**

GLOSSARY

Reverse transcriptase: An enzyme used to transcribe RNA into the corresponding DNA sequence. Retrotransposons require this enzyme to transcribe a DNA copy from its RNA, and the copy is then reincorporated into the genome. The enzyme was first discovered in retroviruses, which have a genome consisting of RNA. In order for it to be incorporated in the host's genome, the reverse transcriptase must produce a DNA version.

Transposons: DNA segments that can change their location in the genome. They are sometimes referred to as "jumping genes." However, complete transposons often contain multiple genes. Transposons whose DNA-derived RNA is used not only for producing proteins, but also as a template for building a new DNA molecule, are termed retrotransposons. Retrotransposons probably also gave rise to retroviruses, which also insert themselves into the genome of the host, but can also leave it again as complete viruses.

Photo: Wolfram Scheible

A Stickleback Full of Worms

Around 40 percent of all species on Earth are parasitic – apparently a highly successful way of life. Even a fish such as the three-spined stickleback is plagued by up to 25 different parasites. One of them particularly appealed to **Martin Kalbe**, **Tina Henrich** and **Nina Hafer** from the **Max Planck Institute for Evolutionary Biology** in Plön: the tapeworm *Schistocephalus solidus*. The scientists are researching the numerous tricks that host and parasite use to outdo each other.

Photo: MPI for Evolutionary Biology

TEXT **HARALD RÖSCH**

The three-spined stickleback is a cosmopolitan. Its geographic range extends across the entire northern hemisphere. Originally an inhabitant of the oceans, it probably first migrated to fresh water following the last ice age and now lives in rivers and lakes. Just as in the oceans, parasites are omnipresent in freshwater, too: roundworms, nematodes and tapeworms live at the expense of this small fish; carp lice attach themselves to its skin or in its gills and feed on its blood. Almost every part of the stickleback's body serves as a home for one parasite or another – even its eye lenses.

LOCAL DIFFERENCES

Schistocephalus, then, is just one of many pests that make life difficult for the fish. Together with Tina Henrich, Martin Kalbe has been collecting sticklebacks and their worms in different regions for many years and has discovered some astounding differences. In Norway, for example, the infection rate in some populations is almost 100 percent, while in others, not a single fish is infected. The fish in Plön come in more toward the bottom end of the scale: out of 4,000 animals, only one is infested with *Schistocephalus*.

One of the reasons for these differences is habitat. In rivers and streams, parasites are quickly washed away by the flow of water, so they are less common there than in calmer waters. Sticklebacks that live in small, scattered populations are also less afflicted by parasites. And finally, the fishes' predators also play a key role when it comes to the abundance of *Schistocephalus*, because only when the worm ends up in the right host can it complete its life cycle and produce eggs.

Initially, once the eggs have spent the winter at the bottom of a body of water, microscopically small, actively swimming larvae hatch. If they become prey and are eaten by a copepod – also known as a Cyclops because of its single eye – they continue to develop to the second larval stage. However, the tiny crustacean is only the first intermediate host. Next comes the stickleback. If the latter eats the Cyclops and the larva manages to pass through the fish's stomach without harm, it bores through the intestinal wall of the fish. The timing is important: the chances of success are greatest if the larva can develop within the crustacean for 13 to 15 days and then enter the stickleback.

The larva reaches the third larval stage in the fish's abdominal cavity and massively increases in size and weight. Then it must wait once again until the host is eaten. This is vitally important for the *Schistocephalus* larva. However, it is also crucially important that it land in the right stomach. In this case, that means the digestive tract of a warm-blooded animal. As a rule, these are fish-eating birds such as herons, kingfishers and cormorants. Only at an ambient temperature of at least 38 degrees can the larvae mature into fertile worms, find a partner and mate. "In Lake Plön, for example, most sticklebacks fall victim to cold-blooded species such as perch and pike. The parasite life cycle thus ends in a cul-de-sac, which is why so few sticklebacks are infected here," explains Henrich.

EVOLUTIONARY ARMS RACE

The stickleback and its worm are in a permanent competition against each other. Every advantage one of them gains is immediately countered by the other. The result is an evolutionary arms race in which the opponents permanently aim to outdo each other – like two wrestlers who have the appropriate defensive grip ready for each new attack.

The degree to which host and parasite struggle with each other is indirectly revealed when three-spined stickle-

A three-spined stickleback with the tapeworm *Schistocephalus solidus*: The parasite larva has bored through the intestinal wall and is growing in the fish's abdominal cavity, where it can become as heavy as the fish itself.

The three-spined stickleback owes its name to the three spines on its back, which it can position upright in case of danger. During spawning, the back of the otherwise inconspicuous males turns turquoise, and the throat and chest glow red. The males occupy a breeding ground and build a nest on the riverbed using parts of plants. After oviposition, they drive off the females and guard and take care of the eggs alone.

backs and *Schistocephalus solidus* from different areas meet: the tapeworms have even adapted to the small regional differences between the fish. Henrich and Kalbe have caught sticklebacks and their parasites in Canada, Norway and Germany and brought them together in various combinations in their laboratory in Plön. The worms are similarly infectious and grow to the same size when they have infected fish from their respective home. "*Schistocephalus* from Norway, however, seems to be more aggressive than its German conspecifics, because it infects fish from Lake Plön more often and grows faster in them than a German worm does in Canadian or Norwegian fish," says Henrich.

AGGRESSIVE WORMS

The researchers don't yet know why some local forms of worms are more aggressive than others, but one thing is clear: parasite and host have adapted to each other in such a way that the aggressive worms can exploit the differences between the fish populations to their benefit. And Kalbe and Henrich have gained another surprising insight: if a Norwegian worm and a German worm both infect a fish from Lake Plön, the Norwegian worm remains smaller than if it infects the fish alone. This is only to be expected – after all, it must share the nutrients. But oddly, the German worm, in contrast, grows larger than normal. The Norwegian worm seems to somehow benefit its competitor's growth – what remains unclear is how.

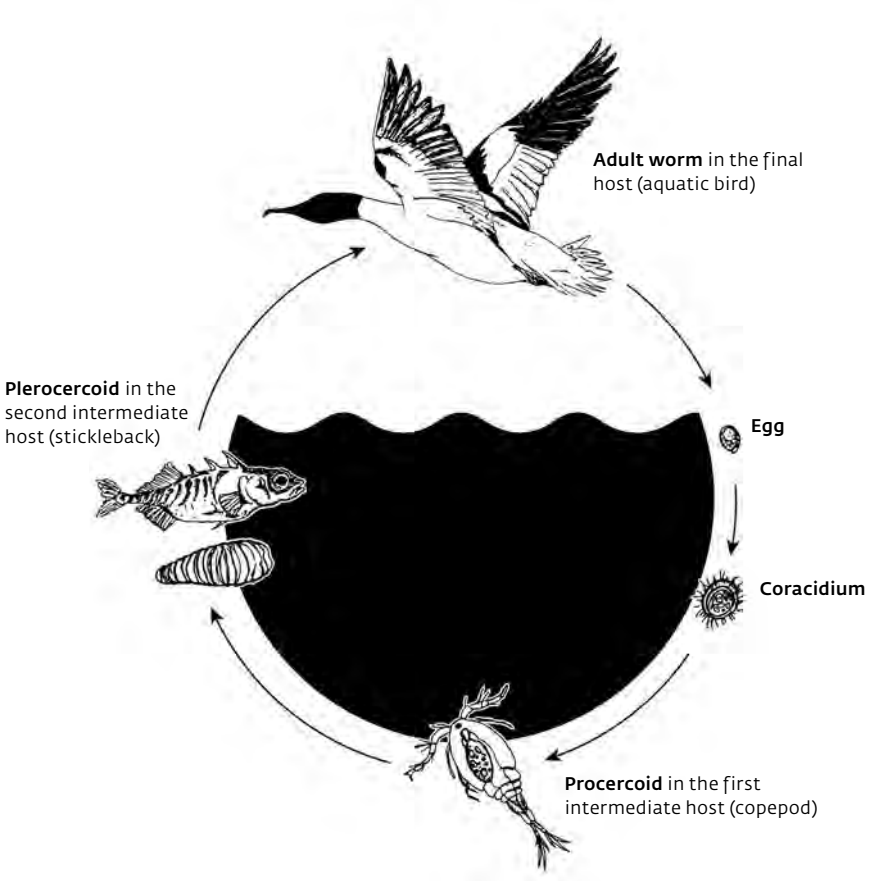
Differences in adaptation also explain why *Schistocephalus solidus* infects exclusively the three-spined stickleback: "It has simply become so specialized in this species that it can no longer overcome the defensive strategies of other fish," says Henrich. Those of the closely related nine-spined stickleback, for instance, which lives in the same waters as its cousin and is parasitized by *Schistocephalus pungitii*. Although the two tapeworms evolve only in their "own" species of fish, they can interbreed in the laboratory and produce fertile offspring. The hybrid worms that emerge from this interbreeding infest both the three- and the nine-spined stickleback. "So far, however, we haven't discovered such hybrids in any body of water. We still don't know why the two species don't mix in nature even though they could," says Henrich.

The scientists in Plön aren't the only ones researching the arms race between the three-spined stickleback and *Schistocephalus solidus*. The stickleback and its tapeworm have been investigated in the laboratory since the 1960s. Today, a number of research groups worldwide use this fish and its parasite as a model system. One reason for this is that both reproduce relatively easily in the laboratory. The sticklebacks are especially easy to keep; they aren't too demanding, and they easily lay eggs in commercially available aquariums.

LABORATORY LIFE CYCLE

As for the worm eggs, Henrich can store them in the dark for extended periods at four degrees. The larvae hatch when exposed to light. The scientist places each larva, together with a Cyclops, in the well of a laboratory cell culture plate and waits until the little

Photo: Michael Schwarz/MPI for Evolutionary Biology



The first larval stage (coracidium) hatches from the worm eggs. If the free-swimming larva is eaten by a copepod (Cyclops), it develops into the second stage, the procercoid, in the crustacean's abdominal cavity. The crustacean is a preferred meal for the three-spined stickleback. In the fish, the worm larva bores through the intestinal wall and becomes a plerocercoid. A fish-eating bird is then the parasite's final host. Once inside the bird's intestines, the adult worms produce eggs, which enter the water via the feces.

copepod has picked up the parasite larva. She then feeds the infected crustacean to a stickleback.

Only the last step of the cycle deviates from its natural model, as keeping waterfowl and multiplying tapeworms in them would be too time-consuming. Instead, Henrich and her colleagues use a replacement for the bird's intestine: a small bag of nylon gauze surrounded by a special nutrient solution. Although the bags were originally intended to hold tissue samples in medicine, Henrich must boil them in water for several hours. Only then do they cease to emit substances that are harmful to the worms. In these bags, submerged in a suitable nutrient solution at a pleasant 38 degrees, a worm couple willingly reproduces and eventually releases thousands of eggs.

In this way, the researchers in Plön managed to outwit the parasite and fool it into believing it was in a bird's intestine. "It's easier to simulate a final host than to develop an artificial intermediate host. In a bird, *Schistocephalus* can no longer grow, but only mate and produce eggs. Because the bird isn't harmed by this, it hasn't developed any defensive measures to which the worm must adapt. With the stickleback, in contrast, it has such an intimate relationship that it would be extremely difficult to reproduce it in the laboratory," says Henrich.

REMOTE-CONTROLLED HOSTS

But parasites are much more than just stowaways, living at the expense of their hosts and letting them provide their meals. They must first overcome their hosts' defense strategies. Then they frequently manipulate their hosts' metabolism in such a way that they themselves get as many nutrients as possible. But what is most intriguing – and simultaneously most unnerving – is their ability to reprogram their hosts' behavior. This can even go as far as an organism sacrificing its own life so that the parasite can reproduce. In such cases, the host is practically remote controlled.

"Some hosts hang on their parasites' strings like puppets," says Manfred Milinski, Director Emeritus of the

Sometimes several tapeworm larvae grow within a single stickleback – in some cases more than 20. Their final weight can be greater than that of the host. The parasites don't kill the fish, but they deprive it of nutrients, so the stickleback remains smaller than an uninfected conspecific.

Graphic and photo: MPI for Evolutionary Biology

Left Sticklebacks can be easily kept and bred in an aquarium. At the Max Planck Institute in Plön, the fish in the small tanks (center) are fed with infected Cyclops and thus deliberately infected with the tapeworms.

Right Daniel Martens, Tina Henrich and Christoph Gahr (from left) place sticklebacks raised in the laboratory in cages in the Great Plön Lake. This enables the researchers to investigate whether and to what degree the fish, which have never been exposed to parasites, are affected.

Evolutionary Ecology Department at the Max Planck Institute in Plön since April. He has been researching the stickleback and its worms since the 1980s. "If you consider that virtually no living creature exists without parasites, you have to ask yourself what an organism's actual behavior is and what is externally controlled."

SINGLE-CELLED ANIMAL MANIPULATES HUMANS

Not even humans are immune to manipulation from their parasites: the single-celled *Toxoplasma gondii*, for example, does everything it can to bring people and cats together. It needs humans as intermediate hosts to help it reach its final host, because the parasite can produce new eggs only in the intestines of predatory or domestic cats. Today, *Toxoplasma* is transmitted to domestic cats predominantly by mice and rats, and humans are a dead-end road for the parasite. However, when humans were still frequent prey of big cats in the early days of their development, they may have been frequent intermediate hosts for *Toxoplasma gondii*.

This would explain why infected individuals feel particularly attracted to cats. In order for its intermediate host to be more easily eaten by predator cats, *Toxoplasma* appears to reprogram the human brain so that people lose their innate caution toward all cats. According to one study, infected men find the smell of urine from domestic cats more pleasant than non-infected subjects do. The pathogen appears to have the same effect on mice and rats: while the rodents generally head straight for the next exit when they smell a cat, infected mice are even attracted to the smell of them.

A number of studies have now shown that *Toxoplasma* influences human behavior in other ways, too. According to these studies, this single-celled organism manipulates the nervous system in such a way that reaction times increase and people often defy social norms, with a possible consequence being that people infected

Photos: MPI for Evolutionary Biology (2)

Schistocephalus solidus isn't the only nuisance in the Great Plön Lake. Almost every water dweller has its own parasites. Martin Kalbe collects aquatic snails, for example, to investigate their parasites.

with *Toxoplasma gondii* are more frequently involved in road and workplace accidents.

The consequences could be dramatic: "It's estimated that more than 30 percent of the world's population is infected, so thousands of road deaths every year may be caused by this parasite alone," says Milinski.

THE FIGHT FOR CONTROL

Numerous cases of parasitic manipulation are now known, and many more are likely to be discovered. Another thing that remains largely unknown is how parasites manage to change the behavior of their hosts in their favor. "An infection by a parasite brings about more than just the immediate bodily reaction to it. If we can better understand how parasites manipulate their hosts, some seemingly preposterous behavior might perhaps make sense," says Milinski.

In addition, many organisms are infested with not just one but several different parasites that affect not only the host but also each other. "In these cases, we can speak of a veritable war for control over the host," says Milinski.

Nina Hafer from Milinski's department investigated one such case. In Lake Plön and elsewhere, the copepods can be infested not only with the tapeworm *Schistocephalus solidus*, but also with a nematode known as *Camallanus lacustris*. Both parasites must first develop in the crustacean for some time before they can infect a fish. During this phase, the crustacean should therefore be as inconspicuous as possible to prevent it from being eaten and the parasites dying with it. But as soon as they become infectious, they profit from greater host activity.

If this development runs in parallel, all is harmonious: both worm species have the same objective and control the copepod in such a way that it is initially placid and later as active as possible. But what happens when the copepod is infected by worms at different stages of development? "Such conflicts of interest between parasites of the same or different species must be the rule in nature, but this has scarcely been investigated to date," says Hafer.

CONFLICT OF INTERESTS

She keeps the infected Cyclops in the cell culture plates in the laboratory and determines its position every two seconds with a camera. Plate vibration then tricks the crustacean into believing that a stickleback is attacking. This allows her to identify possible differences in the activity of Cyclops that

Photo: MPI for Evolutionary Biology

Top The secret subletters become visible under suitable magnification: Several parasites often infect one and the same crustacean, such as the tapeworm *Schistocephalus solidus* seen here (green) and the tapeworm *Camallanus lacustris* (blue) in a copepod. If the parasites are in different stages of development, a conflict of interests results.

Bottom Copepods are the first intermediate hosts for the tapeworms. The approximately one-millimeter-long crustaceans can be easily observed in a drop of water under the microscope.

she has infected with different combinations of infectious and non-infectious thread- and tapeworms.

SABOTAGE IN THE CYCLOPS

Her measurements clearly show that the crustaceans are always more active if they are infected with an infectious worm – even if a non-infectious parasite is counteracting it. The infectious parasite sabotages the manipulations of the smaller, non-infectious worm. However, this isn't a consequence of size, because an infectious animal can also suppress two non-infectious worms that, together, bring more mass to the scales.

The biologist hadn't anticipated this result. "The infectious worm actually need only wait a while until it reaches the next host and can reproduce. The non-infectious parasite, on the other hand, inevitably dies if eaten too soon. It has so much more to lose and would have to try to outwit its competitors at any cost," explains Hafer.

Hafer doesn't yet have a definitive explanation for the surprising findings. "Perhaps the infectious parasite is more interested in rapid transmission to the fish than we thought. After all, the copepod could also simply die prematurely without being eaten. This would also seal the fate of the worm," Hafer says. However, it may simply be easier for the worm to outsmart its competitor; after all, an infectious parasite was, at one time, not infectious and manipulated the behavior of the crustacean. It appears obvious that it subsequently simply switches off old sabotage mechanisms – and, almost coincidentally, that of the non-infectious competitor.

In experiments using a variety of intermediate host and parasite populations from Germany and Norway, Hafer also discovered that the infectious *Schistocephalus* larvae from Germany manipulate the Cyclops to a greater degree – regardless of where the crustaceans originate. In addition, different combinations of Cyclops and worm larvae from Germany and Norway also display a comparable level of host manipulation. The larvae have

Photos: N. Hafer/MPI for Evolutionary Biology (top), Michael Schwarz/MPI for Evolutionary Biology (bottom)

apparently not adapted their ability to manipulate to different populations of intermediate hosts.

DISEASE PROTECTION

Hafer has thus demonstrated for the first time that a parasite sabotages a species of parasite that isn't closely related to it. This may influence the spread of diseases. "For example, it may be possible for a parasite to partially or completely disable pathogen manipulation and thus prevent the spread of infection," explains Hafer. Mosquitoes infected with malaria parasites, for example, sting less frequently if the pathogens aren't yet ready for transmission to humans. The tricks used by the parasites may thus provide infection biologists and doctors with ideas for new treatment methods. ◂

www.tinyurl.com/y9fd2l6y
(available only in German)

TO THE POINT

- **The tapeworm *Schistocephalus solidus* develops into a fertile parasite exclusively in the three-spined stickleback. The parasites are best adapted to the fish from their own region of origin.**
- **If larvae in different stages of development infect a Cyclops, conflicts of interest between the parasites may arise over how they manipulate their shared intermediate host. Here, an infectious worm larva prevails over a non-infectious one.**

GLOSSARY

Tapeworms: A class of parasites belonging to the flatworms. Around 3,500 species are known globally. As fertile worms, they generally live in vertebrate intestines, including in humans. Their larvae develop predominantly in arthropods, leeches, snails and vertebrates. They have no intestines and absorb their food over their entire body surface. The smallest species are just a few millimeters long; the fish tapeworm, in contrast, can be up to 15 meters long.

Toxoplasmosis: Fatigue, fever or headaches are usually the most common symptoms of a *Toxoplasma gondii* infection. Following the acute phase, the immune system encapsulates the protozoa permanently in cysts. These cause local inflammation in the affected tissues, including in the brain. In weakened immune systems, a severe, acute infection that can lead to fatal meningitis can develop from the latent infection. If infected immediately prior to or during a pregnancy, the pathogens can be transmitted from the mother to the child and lead to malformations of the fetus. The infection paths include the consumption of raw, pathogen-infected meat, the ingestion of eggs, contaminated vegetables and water, and bodily contact with infected domestic cats. *Toxoplasma* may potentially also be transmitted sexually.

Perilous **Puddles**

Admittedly, the research subject isn't particularly appetizing: *Strongyloides stercoralis* – small parasitic worms that live in their host's intestines and have the potential to cause severe problems. Nevertheless, **Adrian Streit** from the **Max Planck Institute for Developmental Biology** in Tübingen is fascinated by this threadworm. It has a unique life cycle, and to this day, no one really understands why.

TEXT **CATARINA PIETSCHMANN**

Referring to nematodes as unusual is almost an understatement, as strange behavior is completely normal for them. *Pristionchus pacificus*, which lives, among other places, on the Pacific island of La Réunion, seeks out a beetle larva, climbs up onto it and then stops developing. As soon as the beetle dies, the worm continues its development, gorges itself on the carcass and multiplies (MaxPlanckResearch 2/2014).

But compared with *Strongyloides*, that's almost boringly conventional. At the Max Planck Institute for Developmental Biology, Adrian Streit explores how this worm can survive in two worlds. Between parasitic generations, *Strongyloides* can also form free-living generations. Parasites are exclusively females that multiply in the host's intestines by parthenogenesis. "They produce both male and female eggs, which are excreted with the feces," explains Streit. "Either infectious larvae develop from the female eggs, which then immediately crawl back into the host, or free-living worms that mate with males are produced."

PARASITIC FEMALES

The male worms are exclusively free-living. If males and females reproduce in the soil, only parasitic female offspring are formed. This second generation of larvae thus needs to find another host to be able to multiply – which then once again takes place without a male partner.

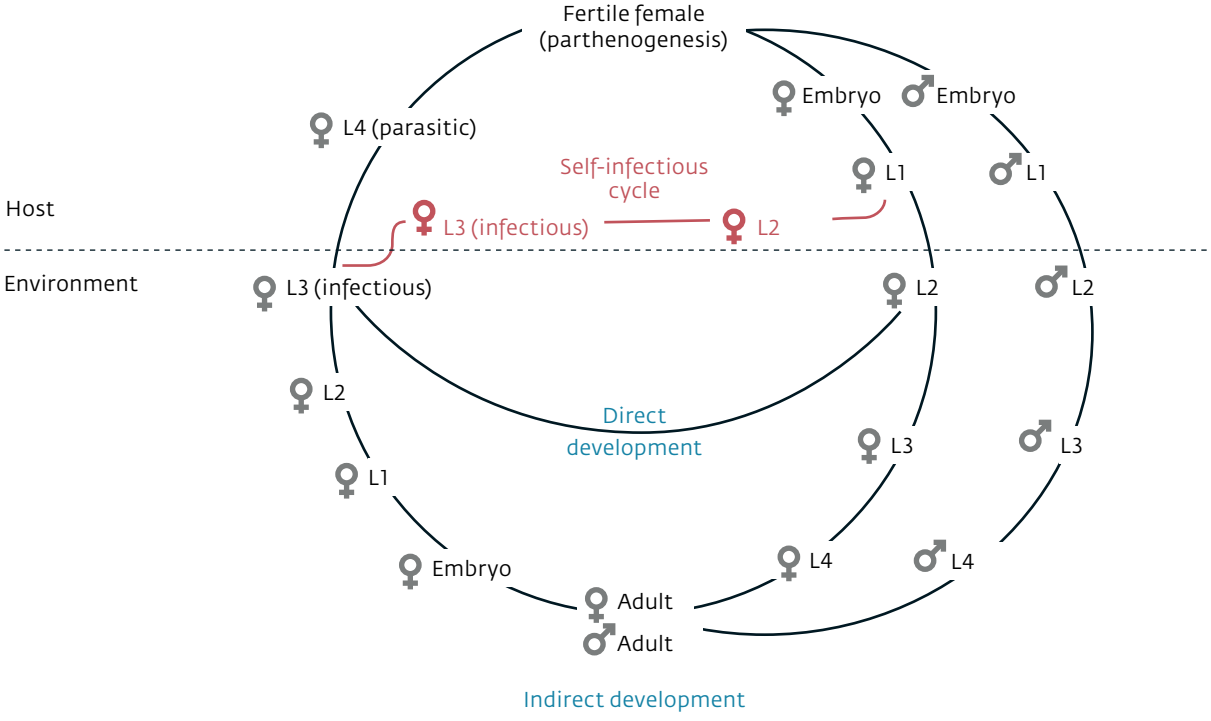
Many terrestrial vertebrate species have their own *Strongyloides* – including humans. The World Health Organization estimates that more than 300 million people worldwide are infected with the threadworm, especially in northern South America, Central Africa and Asia. A warm, humid climate and a lack of hygiene are an El Dorado for worms!

In healthy people, the infection usually goes undetected, as they harbor only comparatively few worms. In immunocompromised patients, however, the larvae in the intestines can infect other organs and cause a life-threatening infection called strongyloidiasis. "If the parasite isn't detected in cancer patients, for example, chemotherapy can end in disaster," emphasizes Streit.

Organ recipients are also at risk. Even in Western countries, deaths have occurred after transplants as a result of the worms. In the Netherlands, two cases were reported in which the infection was proven to have been transmitted

Photo: Kay Maeritz/LOOK-foto

Walking barefoot where the soil is contaminated with animal and human excrement should be avoided at all costs. Some parasites, such as the threadworm *Strongyloides stercoralis*, bore through their hosts' skin. The worm reproduces in the intestines and returns to the environment via the feces.



Strongyloides stercoralis life cycle: In a host, all worms are female. They produce female and male progeny by parthenogenesis (L1 to L4: larval stages 1 to 4). Females can enter one of three cycles: direct, indirect or auto-infectious. In the latter, the host is reinfected by parasites already present in the body. Males, in contrast, live exclusively in the indirect cycle and are free-living. All progeny from the indirect cycle are female and become parasites.

via donated organs – the donor had lived in South America 20 years previously. "In this country, the worms are not yet a major medical problem, but these cases are reason enough to take a closer look," says Streit.

It isn't unusual for the infection to remain undetected for a long time, as it can be completely symptom-free. In addition, the classic symptoms – skin rash, nausea, diarrhea, abdominal cramps – are unspecific, so it's easy to overlook the worms. The tragedy is that common worm remedies would have been sufficient to kill the parasites.

A lack of sanitary hygiene results in the worm being transmitted from person to person. But is this really the only way? Adrian Streit is driven by the question of whether strongyloidiasis is one of the zoonoses, meaning that it can be transmitted from animals – dogs, for example – to humans. If this is the case, worms with identical DNA would have to be found in both dogs and their owners.

FIELD STUDY IN CAMBODIA

To learn more about the transmission paths, Streit has teamed up with the Swiss Tropical and Public Health Institute in Basel and the Cambodian National Center for Parasitology, Entomology and Malaria Control. The two institutes maintain a field laboratory in northern Cambodia. The rural region is ideal for this purpose: the farmers' houses are built on stilts – the family lives upstairs, and the animals, generally pigs and dogs, live below. The sanitary facilities are anything but hygienic and residents go barefoot or wear open sandals.

Nematodes survive for weeks in the moist, feces-contaminated soil. The larvae bore into the skin and advance at ten centimeters per hour – pretty fast for creatures less than one millimeter long! That's why medical experts respectfully refer to them as "racing larvae." Skin irritations usually occur in the vicinity of the worms.

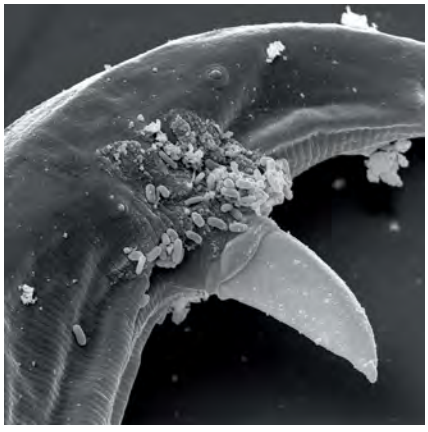
They then bore through the wall of a blood vessel and are flushed into the lungs with the blood. Here, they penetrate the tissue and migrate upward through the trachea. "First coughed up, then swallowed – that's how they enter the digestive tract," explains Streit.

In the small intestine's mucous membrane, each female lays up to a thousand unfertilized eggs per day. The majority are excreted in the feces. However, this human parasite has the unpleasant characteristic that a percent-

Graphic: MPI for Developmental Biology

Top A free-living *Strongyloides papillosus* female, about one millimeter long: The mouth opening with the esophagus is at the top end. The intestine is connected to this. The animal lays its eggs through the vulva, located at the right center of the image.

Bottom The copulation organ of a free-living male *Strongyloides papillosus*. The small rod-shaped structures are bacteria clinging to it.



Photos: Jürgen Berger/EM laboratory MPI for Developmental Biology (2)

age of the embryos develop into infective larvae within the host. These penetrate the intestinal wall or bore through the anal mucous membrane and reenter the body. This is why, if left untreated, the infection can persist for a very long time.

In Cambodia, with the consent of the villagers, Streit's doctoral students Tegegn Jaleta and Siyu Zhou took fecal samples from humans and animals. "This was a huge event for the people there," says Streit, smiling. "Many came to help." People were treated free of charge by staff from both institutes, and it was explained how they could protect themselves from infection.

The samples collected were first incubated for two days and placed in water, after which the worm larvae swimming in the water were separated out. However, genetic analyses weren't possible in the poorly equipped field laboratory in the village. The scientists thus had to fly the worms out to Germany, placing each one into a small tube containing ethanol. "Customs wasn't overly enthusiastic, but the officials were reassured once it became clear that the worms weren't being shipped alive and were in sterile packaging," explains Streit.

Streit and his colleagues then examined the worms' genetic material in their laboratory in Tübingen. The analysis revealed that one of the two *Strongyloides* populations that the researchers had identified in the dog feces was genetically identical to that in their owners' excrement. In other words, the populations overlap, so dogs must be seriously considered as carriers.

As a next step, Streit wants to investigate whether dogs are the only carriers for humans. Water buffalo may also be candidates, as peasants in many areas still plough their rice fields with the animals, and do so barefoot. Water buffalo are already known to be carriers of other zoonotic diseases; studies in southern China, for example, revealed that the animals were the main carriers of schistosomiasis, a disease caused by trematodes.

"Although treatment of the patients was quite successful, the worms could hardly be suppressed by treating humans alone. Nevertheless, the infection was brought under control in China, but only once the water buffalo were also dewormed," says Streit.

Could this be a model for dealing with strongyloidiasis? To find this out, Streit is planning a project similar to the one in Cambodia, but this time in southwestern China. Here, not only are there rural areas where the threadworms are abundant, but there are also

Top left For their field study in Cambodia, the researchers from Tübingen collect stool samples from villagers, mix the samples with sawdust and cultivate them in Petri dishes. This allows the worms in the samples to continue their development.

Top right In a field laboratory, Siyu Zhou and Tegegn Jaleta prepare the samples for transportation to Germany, where the worms can be genetically analyzed.

Bottom Village life in northern Cambodia: People and animals live in close quarters and constantly come into contact with each other's excretions, allowing intestinal parasites to be easily transmitted.

» A warm, humid climate and a lack of hygiene are an El Dorado for worms.

highly qualified scientists with well-equipped laboratories.

A worm infection can be identified under the microscope. With more than 25,000 species worldwide, nematodes are hardly distinguishable for the layperson, but not for biologists. "Apart from *Parastrongyloides*, a close relative, *Strongyloides* is the only nematode in which the infective larvae have a very long esophagus typical of these species.

However, the fecal samples contain predominantly other nematodes, such as hookworms, as both humans and animals in Asia are often infected with various worm parasites. It remains unclear whether the different parasite species compete in the intestines. "But one thing is certain: in a further infection, worms can suppress new arrivals of the same species," explains Streit. "We don't yet know how, but this could offer an approach for future treatment."

RELEVANCE TO VETERINARY MEDICINE

To discover the worms' tricks, Streit keeps two other *Strongyloides* species in Tübingen, where they live in rats or sheep (or, in the lab, in rabbits). Together with the University of Hohenheim, which maintains an animal breeding station in the Swabian Alb, he can also analyze the natural sheep parasite population for comparison.

In contrast to parasitic nematodes, *Strongyloides* doesn't play a major role in veterinary medicine. Unlike *Strongyloides stercoralis*, other *Strongyloides* species don't lead to long-lasting, self-sustaining infections. However, these species, which can also live outside the host, are suitable as study objects for basic biological research.

Streit also wants to investigate whether the threadworms possess something like "parasite genes" – that is, a group of genes that are necessary for this lifestyle. In 2016, scientists decrypted the genomes of four different *Strongyloides* and two other closely related species, one of which occasionally lives parasitically, while the other is free-living. A genome comparison revealed that the parasitic worms have more genes for two protein families that suppress the host's immune response than their free-living relatives do. "We don't yet know what role these genes play in a parasitic lifestyle," Streit emphasizes. "For this, we would need to switch off the individual genes – not very easy in an organism that lives in a host every second generation."

An additional peculiarity of these worms is that the free-living, bisexual generation produces exclusively female offspring, while the unisexual parasitic generation produces both males and females through parthenogenesis. Depending on the *Strongyloides* species,

PARASITES AND THE IMMUNE SYSTEM

Many parasites suppress their hosts' immune system, thus hindering a defense response. Long-standing host-parasite relationships can lead to an evolutionary race. This also applies to humans, who activate their immune system as a precaution to compensate for the suppressing effect of intestinal parasites.

This can become a problem if the immune system is constantly insufficiently challenged, for example in countries with high standards of hygiene. Scientists suspect that the immune system may then turn against its own body. This may explain why autoimmune diseases and allergies continue to increase in industrialized nations but are barely a problem in regions with many worm diseases. This is also suggested by the fact that parts of the immune system normally involved in parasite defense are overactive in autoimmune diseases and allergies.

This knowledge could be exploited medically. Some worm species are already being used to treat such autoimmune diseases as rheumatism, asthma, multiple sclerosis and Crohn's disease, but there have not yet been any large-scale studies.

Photos: MPI for Developmental Biology (3)

Left Adrian Streit spends most of his time researching in his laboratory in Tübingen. But in order to familiarize himself with the environmental conditions under which the threadworms live, he also conducts field studies – a welcome change from the daily routine at the institute.

Right Global distribution of *Strongyloides stercoralis*. The map shows that infection rates vary widely from country to country: more than 70 percent of the population may be infected with the worm in certain regions of some countries.

» Thanks to the two life cycles, a single, self-reproducing parasitic individual can establish a new population without sacrificing the benefits of sexual reproduction.

one chromosome must be completely or partially degraded so that males can develop without a father. The controlled degradation of genetic information is called *chromatin diminution* and was first identified in the equine roundworm. Such degradation is a rare occurrence in nature – outside of nematodes, it occurs, for example, in copepods, ciliates and lampreys.

GENERATION WITHOUT MALES

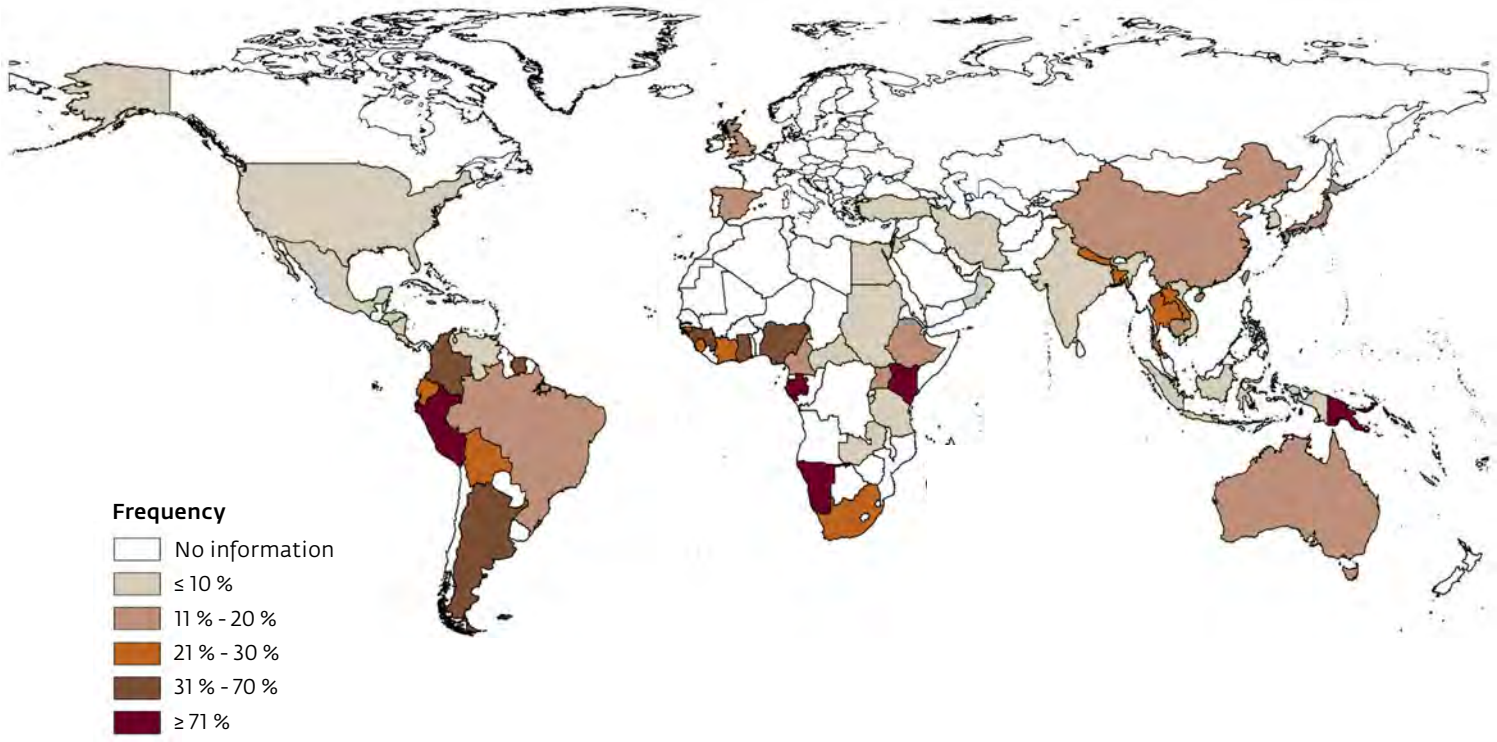
Different *Strongyloides* species also appear to have different means of preventing males from developing in the progeny of the bisexual, free-living generation. Similar to many nematodes, the females of the rat parasite also have two X chromosomes, whereas the males have just one. A Y chromosome as in humans doesn't exist in these species.

"While we didn't find mature sperm leading to males in sheep worms, there are sperm with and without an X chromosome in rat parasites," Streit explains. Some of these sperm would therefore have to lead to males, since an egg cell always carries an X chromosome. In contrast to the sheep, there are actually male worm embryos in the rat. However, they apparently die off, because neither of the two worm species forms male larvae. Still, when the male-designated sperm or the early male embryos are screened out remains a mystery.

Why is a parasite's life so complicated? As Adrian Streit sees it, the complex life cycle emerged gradually from a simpler one: numerous free-living nematodes occasionally form permanent stages to survive hard times. They often attach themselves to other animals, such as the previously mentioned worm living on a beetle. "Once such a larva is attached to an animal, the step to get inside the animal is no longer that great. This may lead to a life cycle similar to that of *Strongyloides*, where the worm is either parasitic or free-living," explains Streit. However, in the majority of parasitic nematodes, every generation is parasitic. Thus, in the course of evolution, the free-living phase may have been sacrificed in favor of a purely parasitic one in many parasites.

Strongyloides may be following the same path. But has it possibly taken a wrong turn? After all, the females multiply in their hosts exclusively by unisexual parthenogenesis, so "rejuvenation" of the genome by gene recombination doesn't take place in the parasitic generation.

Photo: Axel Griesch



In evolutionary terms, unisexually or asexually reproducing lines are generally young. It may even be assumed that they can't age, because the transition to a life without sexual reproduction is the beginning of the end. In other words, *Strongyloides* may have maneuvered itself into a cul-de-sac, making it impossible for it to now rescind the sexual free-living cycle.

But maybe the worm has found an ideal solution for itself: thanks to the two life cycles, a single, self-reproducing parasitic individual can establish a new population without sacrificing the benefits of sexual reproduction.

Whether and how *Strongyloides* will ever become a pure parasite, or whether its life cycle will become even more complicated, can't be predicted with certainty today. Evolution always finds a new, and sometimes curious, solution. ◂

www.tinyurl.com/yczguvf9 (available only in German)

TO THE POINT

- **There are more than 50 species of parasitic *Strongyloides* (a threadworm) that infect a wide range of terrestrial vertebrates. An estimated 300 million people worldwide are infected with the *Strongyloides stercoralis* worm.**
- **Dogs can also be infected with *Strongyloides stercoralis*. The parasites can infect people through the animals' feces. The infection is usually harmless in humans, but it can end in death in individuals with a weakened immune system.**
- **Genetic analyses have revealed that parasitic worms have more genes compared with free-living species, potentially reducing the host's immune response.**

GLOSSARY

Parthenogenesis: This type of unisexual reproduction leads to progeny from unfertilized eggs produced by female animals. In mitotic parthenogenesis, such as occurs in *Strongyloides*, diploid oocytes are formed without meiosis, and the genome isn't remixed by recombination. In other words, it is a form of asexual reproduction and the progeny are therefore genetically identical to their mother.

Graphic: Schär et al. (2013) PLOS Negl Trop Dis 7(7):e2288. doi:10.1371/journal.pntd.0002288

Dramatic Decline of Bornean Orangutans

The number of great apes in Borneo has plummeted by more than 100,000 in the last 16 years

The extinction of species on Earth continues unabated: the latest data from a research team that includes scientists from the Max Planck Institute for Evolutionary Anthropology in Leipzig indicates that the total number of Bornean orangutans dropped by more than 100,000 between 1999 and 2015. That leaves just 70,000 to 100,000 of these animals in Borneo, of which only a fraction live in viable populations. Persecution by humans is likely one of the main reasons why the greatest loss of great apes has occurred in selectively logged and primary forests. Many of them are killed for their meat and for the pet trade – but many also to protect crops from them. Although the numbers show that there are more orangutans than was previously thought, and that they can survive even in oil palm plantations, the rapid decline must be stopped. As a previous study showed, if only one in 100 adult orangutans is removed from a population per year, that population is very likely to go extinct. (www.mpg.de/11939623)

Habitat loss and poaching are the main causes of the disappearance of orangutans. In Borneo, for example, 10,000 orangutans live in forests that are slated for conversion into oil palm plantations. If this happens, most of these animals will die.

Fighting Malaria with Chemistry

The active ingredient artemisinin can now be produced more efficiently and economically and with less environmental impact

Developed in the lab, suitable for large-scale production: Obtained from plant waste, the source materials for manufacturing artemisinin (white powder) now no longer need to undergo cleaning, and the plant's own chlorophyll can be used as a catalyst.

Millions of people – especially in developing countries – who are infected with malaria may soon be able to access the key active ingredient against this disease more easily. Currently, 650,000 people die every year from the effects of malaria; of those, nearly 600,000 are children. Now we have the opportunity to prevent many of these deaths. Artemisinin, the key ingredient in the most effective anti-malaria drugs, can now be produced significantly more efficiently and economically and with less harm to the environment than before. This was made possible by researchers at the Max Planck Institutes for Dynamics of Complex Technical Systems in Magdeburg and of Colloids and Interfaces in Potsdam by refining a process the chemists in Potsdam presented a few years ago. They now no longer need to clean the raw materials used to produce artemisinin, which is obtained from waste from sweet wormwood (*Artemisia annua*), an annual plant. In addition, they use the chlorophyll from the plant as a catalyst, allowing them to forgo the expensive and environmentally harmful photoactivators they previously needed for this. ArtemiFlow, a startup founded by Max Planck researchers, is now working to implement the process on an industrial scale. (www.mpg.de/11958775)

Photos: Serge Wich (top), MPI of Colloids and Interfaces (bottom)

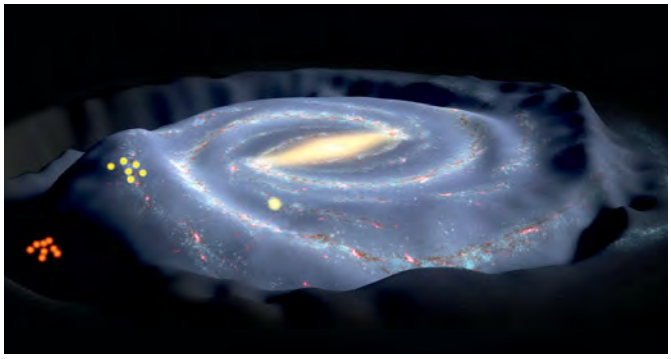
The Nose Knows

Study shows cognitive performance of dogs when tracking a scent

Dogs are well known for their excellent sense of smell, be it in searching for people or for a variety of substances. The question of how well dogs understand what they perceive with their sense of smell, though, remains largely unexplored. Scientists at the Max Planck Institute for the Science of Human History therefore subjected 48 dogs to a test: Each dog underwent a total of four trials in which they followed, unaccompanied, a scent trail marked using one of two of the dog's favorite toys. At the end of the trail, some of the dogs found, not the toy that was used to lay the track, but the other one. Many of the dogs seemed to be surprised by this, especially in the first test run. They continued to search even though they had obviously noticed the toy. However, this "surprise effect" disappeared in the subsequent test runs. Nevertheless, the results indicated that dogs have a mental representation of the target when tracking a scent. In other words, they have a specific expectation of what they will find at the end of the trail. (www.mpg.de/11966983)

Star Migration

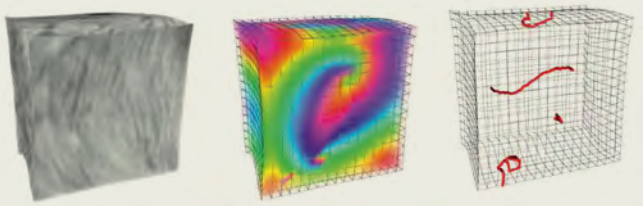
Our Milky Way is an average spiral galaxy. Most of its stars orbit the center within a disk, but some are also found in the surrounding halo, which is made up of dark matter. Many halo stars are grouped together in giant structures. These structures are considered to be signatures of our galaxy's turbulent past – debris from the many smaller galaxies that evidently collided with our Milky Way time and again, and that were torn apart in the process. A team of researchers headed by Maria Bergemann at the Max Planck Institute for Astronomy studied two groups of halo stars and discovered that their chemical composition is similar to that of the galactic disk. This is regarded as evidence that the stars they have now analyzed originated from within the disk and not, for instance, from trapped satellite galaxies. The scientists suspect that this stellar migration is caused by oscillations in the Milky Way disk as a whole, which in turn may have resulted from the tidal interaction between the disk and a passing massive satellite galaxy. (www.mpg.de/11959728)



A view of the galaxy: Illustration of a simulation of the Milky Way disk, perturbed by the tidal interaction with a dwarf galaxy. The locations of the two halo star structures the researchers studied – the Triangulum-Andromeda (Tri-And) and the A13 overdensities – above and below the galaxy disk are indicated.

Photos and graphic: MPI for Dynamics and Self-Organization (right), T. Mueller/NASA/JPL-Caltech (bottom)

Maelstroms in the Heart

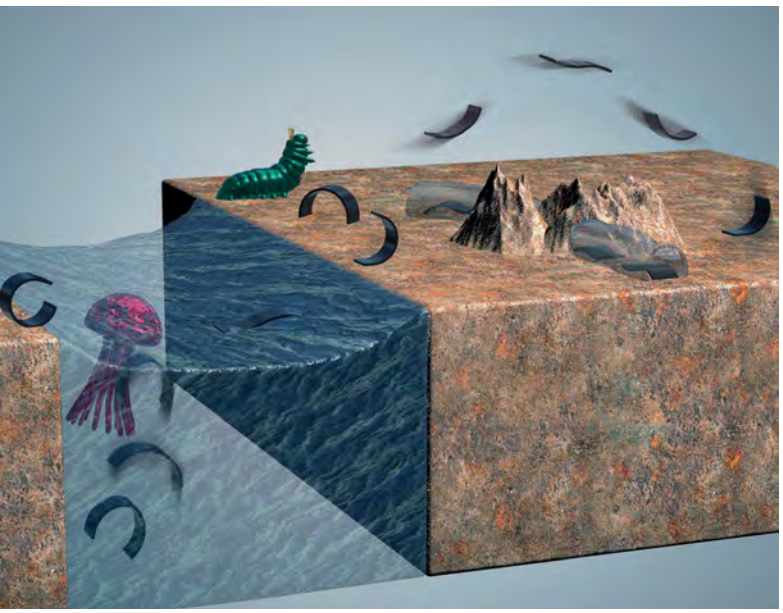


Getting to the core of ventricular fibrillation: From ultrasound images (left), Max Planck researchers reconstructed how the heart muscle contracts in a vortex-like manner in cardiac arrhythmia (center). In this way, they can also localize the filaments at the center of the vortices (right).

Every five minutes in Germany alone, someone dies of sudden cardiac arrest resulting from ventricular fibrillation, the most common cause of death worldwide. A new diagnostic method could help make future treatment of ventricular fibrillation and other types of cardiac arrhythmia more effective. An international team working with physicists and physicians at the Max Planck Institute for Dynamics and Self-Organization and the Heart Center at the University Medical Center Göttingen developed a technique that allows them to use common ultrasound devices to produce 3-D images of the vortex-like contractions that lead to the heart muscle spasms that occur in ventricular fibrillation. The researchers can even localize the eyes of the vortices and track them as their positions in the muscle change. A precise image of the vortex cores is crucial for stopping the ventricular fibrillation more gently than is currently possible. Today, this type of cardiac arrhythmia is treated with strong and very painful electric shocks from a defibrillator. This is why some patients with recurrent cardiac arrhythmias decline to have a defibrillator implanted, especially since these devices often emit electrical pulses unnecessarily. If the electrical shocks could be applied at the vortex cores, they could be much weaker, as they are particularly effective there. (www.mpg.de/11953915)

A Millirobot with a Talent for Movement

A magnetic drive allows a tiny vehicle to walk, crawl, jump and swim through a complex environment



Soon, tiny robots will be able to master any obstacle course. Scientists at the Max Planck Institute for Intelligent Systems in Stuttgart developed a four-millimeter-long strip of elastic silicone that can run, jump, crawl and roll through difficult terrain, as well as transport small loads and swim on and in liquids. The tiny vehicle owes its ability to perform these different types of movements to magnetic particles the researchers embedded in a sophisticated arrangement in the silicone strip. As a result, the rubber can be deformed in various ways depending on the orientation and strength of an external magnetic field. The researchers hope it will one day be possible to use this master of motion as a model to build tiny robots that perform medical procedures in the body. They could transport drugs to the source of an illness, for instance, or stop minor hemorrhages. (www.mpg.de/11895964)

The millirobot presented by the Stuttgart-based Max Planck researchers can move on land and in water. Jellyfish and caterpillars are just two of the natural role models that inspired the scientists who developed it.

Interconnected Sensory Impressions

It is estimated that one in 25 people have synesthesia, a union of sensory perceptions that are normally separate. Synesthetes may see or taste sounds, for example, or perceive them as geometric shapes. The phenomenon often occurs in multiple members of a given family, so it is likely hereditary. Researchers at the Max Planck Institute for Psycholinguistics and the University of Cambridge have now analyzed the DNA of three families in which several family members across various generations see colors when they hear sounds. They were able to identify genetic variants and see how they were passed on from one generation to the next. While the highlighted DNA variants differ between the three families, they also have one thing in common: a concentration of genes that are involved in axonogenesis and cell migration. Axonogenesis is a key process that enables brain cells to connect with the right partners. This tallies with findings from imaging studies that showed that the brain circuits in adults with synesthesia are wired somewhat differently than in people who don't experience these kinds of sensory couplings. (www.mpg.de/11964360)

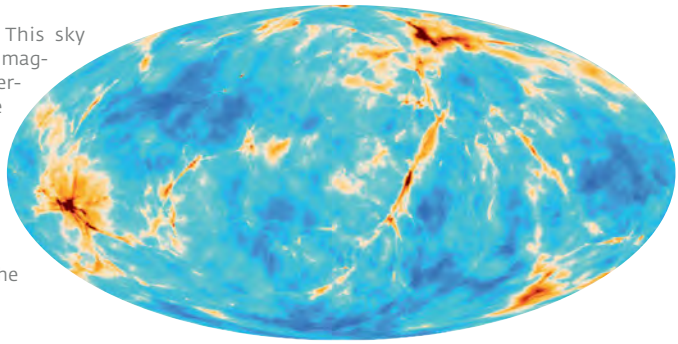
Colonial-Era Pathogen Identified

After the indigenous population in America came into contact with Europeans, numerous deadly epidemics swept through the New World. To date, contemporary reports have proved insufficient for identifying the causes. Now, for the first time, an international research team with significant participation of scientists from the Max Planck Institute for the Science of Human History has used DNA analyses to microbiologically identify the pathogen behind such an epidemic. The genetic material the researchers used was extracted from 29 skeletons in a cemetery associated with the epidemic in the abandoned Mixtec town of Teposcolula-Yucundaa in Mexico. The individuals buried there were victims of what is known as the cocoliztli epidemic, which took millions of lives in Guatemala and Mexico between 1545 and 1550. The team analyzed genetic material from the human skeletal remains using a novel computer program that enables them to examine the samples for non-specific bacterial DNA. Ten of the samples contained evidence of *Salmonella enterica* bacteria, which cause enteric fever – a disease that, similar to typhoid, causes fever, diarrhea and vomiting. The scientists consider it possible that the pathogen was introduced from Europe. (www.mpg.de/11884269)

Graphic: MPI for Intelligent Systems

A Relic of the Big Bang

Astrophysicists calculate the original magnetic field in our cosmic neighborhood



Viewing the invisible: This sky map shows the Harrison magnetic field strength, averaged across a sphere with a radius of approximately 300 million light-years. The two regions with particularly strong magnetic fields are the Perseus Pisces galaxy cluster (left) and the Virgo cluster (top).

The first fractions of a second following the birth of the universe saw the emergence of not only elementary particles and radiation, but also magnetic fields. A team headed by the Max Planck Institute for Astrophysics has now calculated what these magnetic fields in our vicinity should look like today – in great detail and in 3-D. To do this, the researchers first analyzed the distribution of galaxies around us and, based on this, calculated the distribution of matter at the time of the Big Bang. This is where the Harrison effect came into play: friction from what was then a very strong radiation field resulted in vortex movements in the plasma of the early universe, producing electrical currents and thus inducing magnetic fields. Subsequently, the scientists translated these fields back into the present and into our cosmic neighborhood, enabling them to predict the structure and morphology of the original magnetic field in the surrounding 300 million light-years. Unfortunately, this theory can't be tested through observation: the calculated magnetic field is 27 orders of magnitude smaller than that of the Earth, and thus far below the current measurement threshold. (www.mpg.de/11991394)

Brains of Jazz and Classical Pianists Work Differently

A musician's brain differs from that of a non-musician: making music requires a complex interplay of various skills, and this is also reflected in the brain structures. Scientists at the Max Planck Institute for Human Cognitive and Brain Sciences have now discovered that even the style of music plays a role: they observed that the brain activity of jazz pianists differed from that of classical pianists – even when they play the same piece of music. One major difference is in how they plan movements. While pianists generally have to know what they will play – that is, which keys they will press – and how they will play it, meaning which fingers they will use, the weighting of these two steps varies depending on the music genre. Classical pianists, for instance, focus particularly on the "how" – on their finger placement – in order to play a composition perfectly and with feeling. Jazz pianists focus primarily on the "what" so that they can improvise. (www.mpg.de/11881616)

The Spread of the Bell Beaker

DNA studies solve mysteries surrounding the spread of special ceramic vessels in prehistoric Europe

A popular burial object: Beaker vessels were often placed in the grave with the deceased. Today, scientists can determine how the pottery spread based on the skeletal DNA.

During the transition from the Neolithic to the Bronze Age, people in western and central Europe increasingly used pottery in a new, bell-shaped style. It was long debated whether the spread of the beaker ceramic style was due to migration or merely to the spread of new ideas. To shed light on the matter, an international team of researchers including members from the Max Planck Institute for the Science of Human History analyzed the DNA of 400 prehistoric skeletons that were buried together with beaker vessels. According to their findings, both explanations may be correct depending on the region. The beaker pottery must have initially spread between central Europe and the Iberian Peninsula without any appreciable migration, as the DNA of the skeletons in the two regions differs significantly. In ancient Britain, in contrast, among the dead who were buried with beaker vessels, the research team found genetic material from inhabitants of the eastern European steppe who migrated across central Europe to the British Isles some 4,500 years ago. At that time, they replaced more than 90 percent of the original population of Britain. Beaker pottery was not found in that region before the arrival of these immigrants. (www.mpg.de/11953055)

Neanderthals as Artists

New method yields older age of artwork in Spanish caves

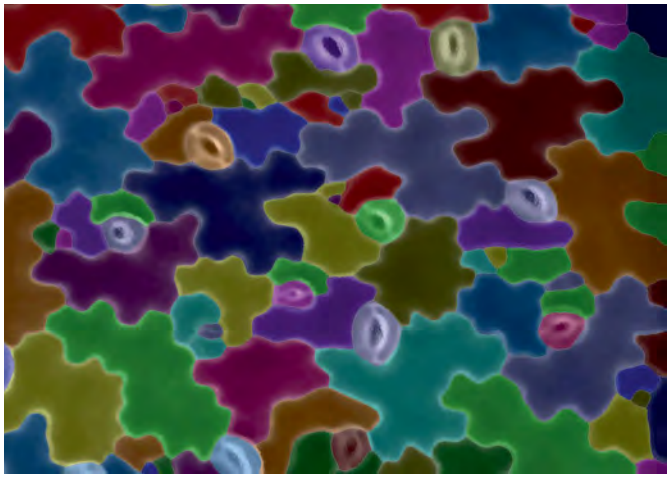
Anthropologists previously believed that only modern humans were capable of creating cave art, sculpted figures, decorated bone tools and jewelry. Previous analyses of such artifacts in Europe showed that they were created some 40,000 years ago, just as modern humans first settled the continent. Using a new measurement method known as uranium-thorium dating, an international research team including scientists from the Max Planck Institute for Evolutionary Anthropology in Leipzig has now obtained very different results: according to their findings, Neanderthals were already producing symbolic objects more than 115,000 years ago, and creating cave art in Europe more than 20,000 years before modern humans. This dating technique is based on the radioactive decay of uranium isotopes into thorium and facilitates age determination much further back in time than the commonly used radiocarbon method. In this way, the scientists dated carbonate crusts on paintings and on seashells with remnants of pigment and were thus able to determine the minimum age of the cave art. From this, the researchers conclude that Neanderthals, too, were able to think symbolically and were cognitively indistinguishable from modern humans. The origins of language and human perception and cognition must therefore go back to the last common ancestor of Neanderthals and modern humans, more than half a million years ago. (www.mpg.de/11948095)

Researchers analyzed carbonate samples that had formed over paintings on the walls of three caves in Spain. The paintings, mostly in red, but sometimes also in black, show groups of animals, dots, geometric signs and hand prints. According to the new measurements, the ladder-like painting composed of horizontal and vertical lines in the La Pasiega cave is more than 64,000 years old and therefore must have been created by Neanderthals.

A Jigsaw Puzzle of Plant Cells

Their irregular shape enables epidermal cells to withstand the high pressure in their interior

Plant cells are under tremendous pressure, so they had to come up with a way to keep from bursting. According to scientists at the Max Planck Institute for Plant Breeding Research in Cologne, epidermal cells with an irregular shape can withstand the pressure in their interior better than round cells can. Using a specially developed computer model, the scientists simulated the pressure conditions in cells of various shapes. The researchers' calculations show that long, thin cells or those with an irregular shape can withstand turgor pressure better because they have no large, open areas, which tend to bulge out. The shape of these surface cells is determined by how a plant organ grows: epidermal cells of leaves, which grow uniformly in all directions, resemble pieces of a jigsaw puzzle, while plant organs that have a preferred direction of growth, such as roots and stems, usually have cylindrical cells. (www.mpg.de/11956824)



As the epidermal cells of thale cress (*Arabidopsis thaliana*) are shaped like puzzle pieces, they can withstand greater pressure. The interspersed guard cells of the stomata, which help regulate the plant's exchange of water and gas, are an exception. Their small size is what prevents them from bursting.

Photos: P. Saura (top), MPI for Plant Bleeding Research/Smith (bottom)

Humans Limit Animal Movements

Biologists identify decline in migration in areas with a high human footprint

While humans travel more and more frequently and cover ever greater distances, animals' freedom of movement is becoming ever more restricted. Researchers at the Max Planck Institute for Ornithology in Radolfzell, the Senckenberg Nature Research Society and Goethe University Frankfurt analyzed the GPS movement data of more than 800 animals and compared it with the Human Footprint Index of the areas through which they move. The results showed that mammals in areas that are influenced by humans move only one third to one half as far as in the wild. One reason for this is that the animals are impeded by human settlements and roads. Species such as deer and wild boars then increasingly retreat to smaller woodland areas that are surrounded by human infrastructure. Others, such as grouse, completely avoid regions with a significant human footprint, for instance with ski lifts, aerial cableways and alpine sports. In addition, some animals change their behavior in the presence of humans. Urban foxes, for instance, can find food more quickly in areas with a strong human presence, so don't need to cover as much distance. Human hunting and leisure activities also affect the animals: the research findings show that wild boars and other species alter their activity times and territories to avoid humans. (www.mpg.de/11892788)

Some animal species require large ranges, so they can no longer be found in the vicinity of humans. Zebras, for example, travel up to around 500 kilometers during their annual migration – more than any other mammal in Africa. From 1968 to 2004, a fence blocked the zebras' migration in the Okavango Delta in Botswana. Only after the obstacle was removed were the animals able to resume their migrations.

Photos: Franz Lanting/Fotolia (top), MPI of Molecular Cell Biology and Genetics/J. Rink (bottom)

Axolotl and Planarian Flatworm Genomes Decoded

The data from these DNA analyses is helping researchers understand the astounding ability of these animals to regenerate

Even when the flatworm *Schmidtea mediterranea* is cut into tiny tissue pieces, each piece regenerates back into a complete mini-flatworm. The worm owes this ability to regenerate to stem cells that remain active throughout the worm's life. Each one can form a complete worm.

When the Mexican axolotl loses a body part, it grows it back within just a few weeks. The planarian flatworm *Schmidtea mediterranea* can even form new mini-flatworms when it is cut into small tissue pieces. Thanks to new sequencing techniques, two international research teams have now completely decoded the genome of both of these animals – in both cases together with researchers at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden. With 32 billion base pairs, the axolotl genome is more than ten times larger than that of humans, making it especially difficult to sequence. Moreover, it consists of many long, repetitive segments. Large portions of the flatworm genome are also composed of these nearly identical sequences, so it, too, posed a great challenge for the researchers. In the axolotl genome, the researchers discovered several genes that occur only in amphibians and that are expressed in regenerating tissue. It is also striking that an important and widespread developmental gene named PAX3 is completely missing. The flatworm, on the other hand, is missing two universal genes that, during cell division, ensure that both daughter cells receive the same number of chromosomes. The researchers plan to use the new genome data to study why the axolotl and planarian flatworm can regenerate organs and body parts. (www.mpg.de/11886544, www.mpg.de/11886639)

In the Cosmic **Chemistry Lab**

As a young girl, she was a talented painter and had a keen interest in art. The course for her future seemed set. Then she happened upon a book – a book that transported her into the vastness of space and ultimately decided her career aspirations. **Paola Caselli** thus became, not an artist, but an astrochemist. As a Director at the **Max Planck Institute for Extraterrestrial Physics** in Garching, she is still just as fascinated by cosmic clouds as she was when she was 12.

TEXT **ALEXANDER STIRN**

In the beginning was a book: *The Black Cloud*, a science fiction novel about a monster made of gas and dust that, to astronomers' amazement, would later turn out to be an intelligent life form. It was written toward the end of the 1950s by Fred Hoyle, an astrophysicist who was as brilliant as he was controversial.

At the age of 12, Paola Caselli was blown away when her teacher handed her the book. The mere thought of peering into the depths of space through a telescope, studying clouds and possibly discovering extraterrestrial life captivated the schoolgirl. Finally, Caselli realized, she had found the mission she had dreamed of – her calling in life.

Now, 40 years later, Caselli is sitting in a bright, tidy corner office just outside Munich. Nevertheless, dark black clouds are omnipresent. Using the world's biggest and most powerful telescopes, the Italian scientist, a Director at the Max Planck Institute for Extraterrestrial Physics in Garching since 2014, investigates which molecules exist in interstellar clouds, which chemical processes take place there and how they could give rise to stars, planets and perhaps even life. Caselli – black hair, black glasses and words flowing like a waterfall – is driven by an overwhelming sense of curiosity and an almost Prussian sense of discipline.

A BOOK BY FRED HOYLE DETERMINES HER CAREER

"Fred Hoyle was a visionary, an idol," Caselli says with a twinkle in her eyes that leaves no doubt as to the fascination that must have captivated her then – and how strong that enthusiasm remains today. "His book opened my eyes. I connected the dots and I knew: Okay, that's exactly what I want to do. I want to use the short time I have in this universe to better understand it."

Though peppered with physics formulas, Hoyle's first work was science fiction through and through. In 1957, when the famous British astrophysicist wrote his book, experts knew of no more than a few simple organic molecules (CN, CH, CH+) in interstellar clouds, let alone any manner of life. The field of astrochemistry, in which Caselli is at home today, didn't even exist.

Science has since come a long way. Since the early 1990s there has been little doubt that molecules exist almost everywhere in the cosmos: in the black clouds of gas and dust that stretch between the shining stars, both in our galaxy and in the depths of the universe. Chemists have also succeeded in studying the properties of these molecules in detail in the lab.

Of particular interest to astronomers is how the molecules behave when excited by radiation and colli-

Ambitious: Even as a young girl, Paola Caselli was fascinated by the cosmos and doggedly pursued a career in science. Today, she is a Director at the Max Planck Institute for Extraterrestrial Physics in Garching.

Photo: Axel Griesch

» My parents taught me a great deal, especially about how to make ends meet. But science – that I had to learn myself.

sions with other molecules, particularly hydrogen (H_2), the most abundant molecule in the cosmos: following excitation, molecules can rotate, vibrate and emit electromagnetic waves of a precisely known frequency. A "glowing fingerprint" emerges that is characteristic of each molecule.

"These fingerprints allow us to study the physics in cosmic clouds from a great distance," says Caselli. Although the clouds appear dark and usually only shimmer faintly with low energy, large telescopes can detect their characteristic radiation. The data obtained gives astrochemists information about the composition of the clouds.

And not only that: the data also reveals a lot about conditions in space. For example, if the molecules are moving relative to the Earth, the frequencies of the fingerprints are shifted slightly by a phenomenon known as the Doppler effect – similar to how the pitch of an ambulance siren changes as it races past at high speed. "If a cloud collapses, as occurs before the birth of a star, we can detect such movements from Earth," Paola Caselli says.

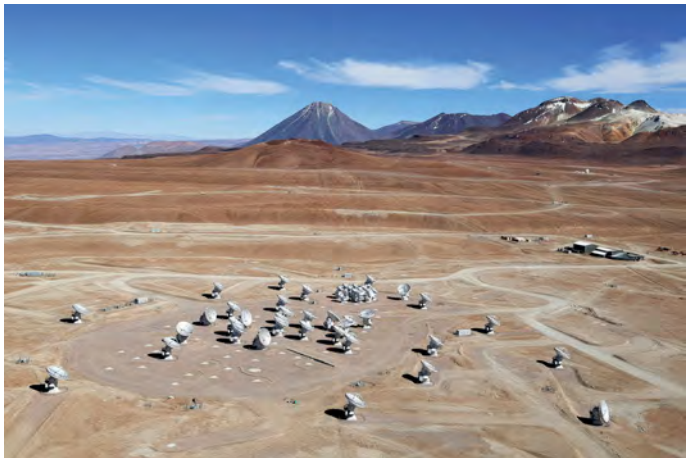
AMMONIA SERVES AS A COSMIC THERMOMETER

But molecules can do even more. Owing to its structure, a gas such as ammonia has various transitions. Several radiation lines emerge whose relative intensity depends on the ambient temperature. Astrochemists therefore use ammonia as a thermometer for measuring the temperature of distant clouds.

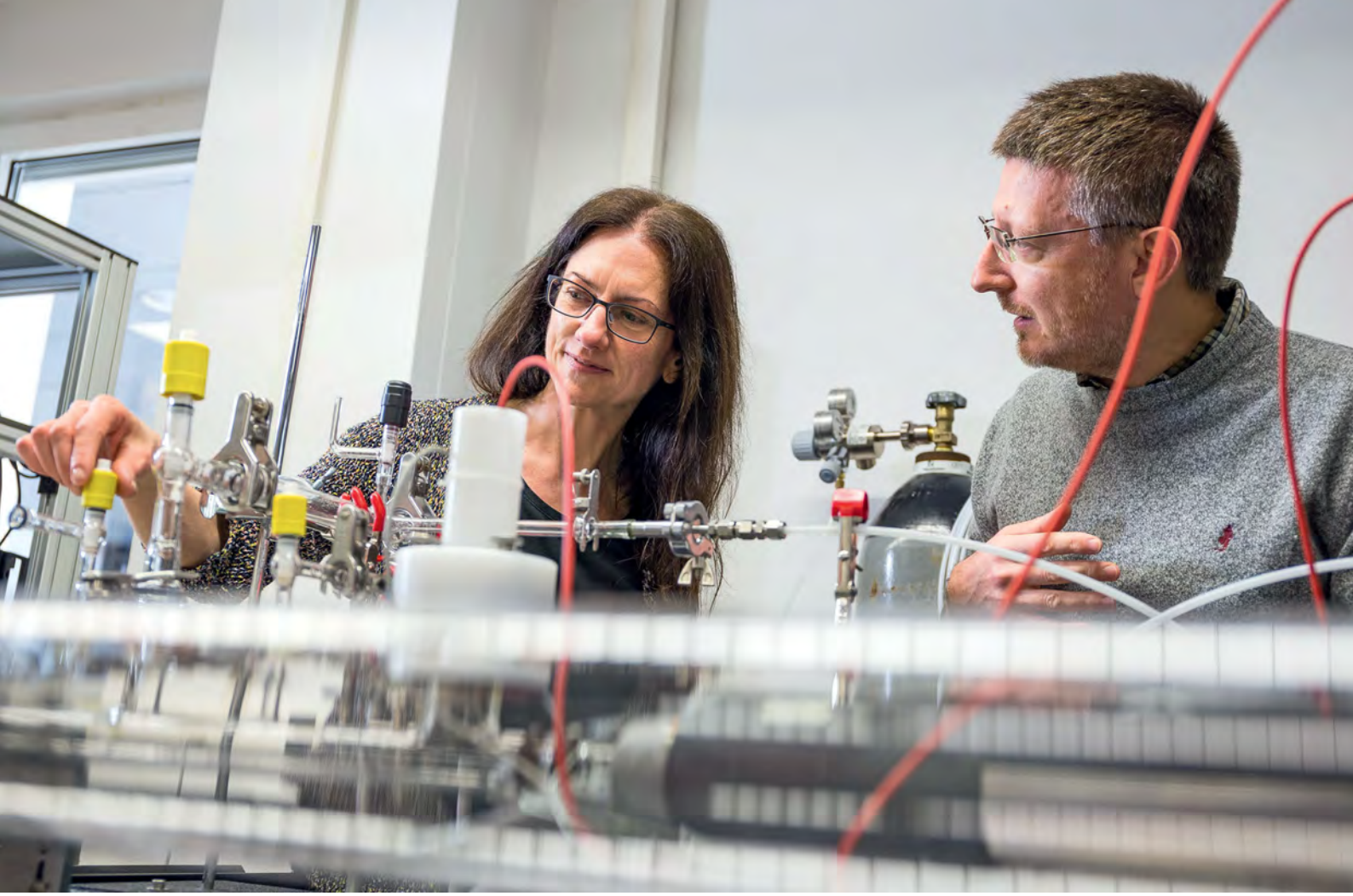
The chemical composition of the cosmic structures is also intriguing. A close look at the signals shows that most of the molecules are organic in nature, as Fred Hoyle predicted: they consist of carbon and, in many cases, nitrogen – the basic requirements for life as we know it. Some molecules are just one step away from the simplest amino acid, glycine, an important building block of proteins. Fatty acids, which are required for cell membranes, as well as nucleobases, which make up our genetic code, also exist in the primordial material of our solar system. And water is ubiquitous, too. "Basically," Caselli says, "we see everything that is needed to make up prebiotic material, everything needed to create a life form – and even from a time before life existed on Earth."

In the Tuscan seaside town of Follonica, where Caselli grew up, all this is at least as distant as the nearest stars and galaxies. Here, the closest they come to

A valuable tool: To obtain data and gain insights into cosmic molecular clouds, Paola Caselli and her team make observations using the world's biggest and best telescopes, including ALMA, an array of 66 radio antennas in the Atacama Desert in Chile (left) and the 30-meter telescope on Pico Veleta in Spain, which is operated by IRAM.



Photos: Clem & Adri Bacri-Normier (wingsforscience.com)/ESO/IRAM



The cosmos in a lab: It's not easy to replicate the conditions of cosmic gas clouds in an experimental setup, as they are extremely thin and very cold compared with the Earth's atmosphere. But Paola Caselli and her colleague Luca Bizzocchi succeeded in producing and studying reactive molecules. The light they emit can then be compared with observations of real molecular clouds in space.

exotic are the foreign tourists who stop off in Follonica on their way to the island of Elba just off the coast. Caselli's mother works there as a seamstress, mostly from home, at the same table where little Paola did her homework.

Her father also came from a family that wasn't blessed with wealth. He had no education, repaired shoes, worked in bars and shops, and eventually became a barber – an occupation that Caselli's younger brother still pursues today. "My parents are from a humble background," Paola Caselli says. "They taught me a great deal, especially how to make ends meet. But science – that I had to learn myself."

Initially, however, her focus was on art. Little Paola loved to paint, mainly with oils. She mostly painted colorful landscapes, birds and almost microscopically detailed insects. Later, in secondary school, she produced precise black-and-white images, abstract and with a calligraphic flair. "When I painted, I would completely lose myself in my work and only after five or six hours realize: Oh, maybe I should eat something," Caselli says with a laugh.

PROTOSTARS FORM AT THE CENTER OF DARK CLOUDS

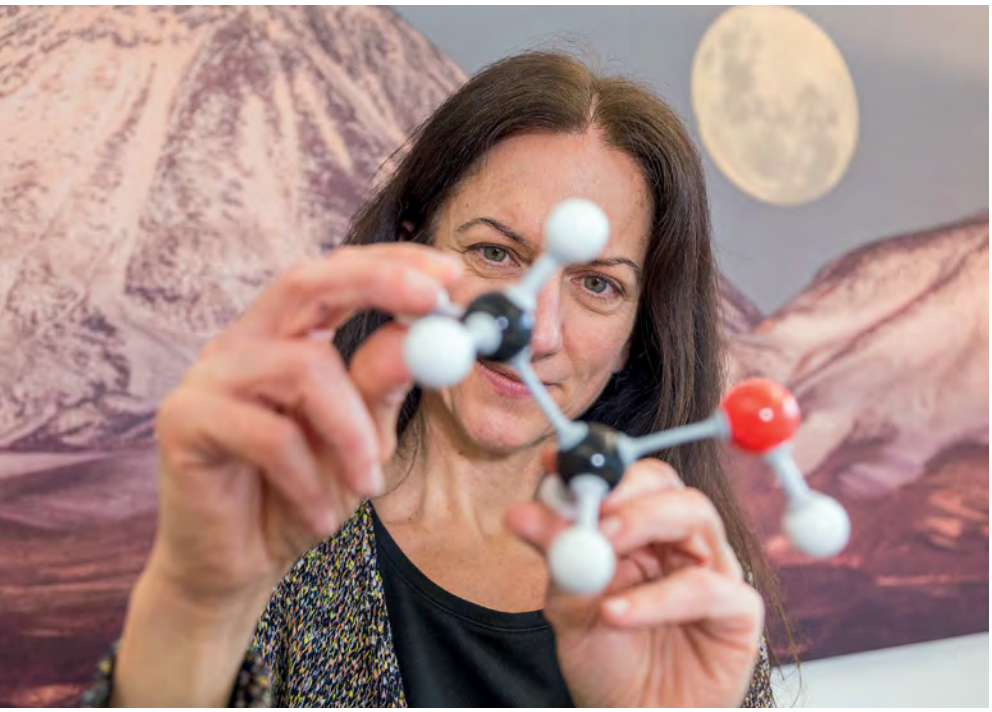
A difficult step came toward the end of secondary school. Fred Hoyle's book had long since made its impact and the previously indecisive student knew in her heart that she wanted to become an astronomer. "I decided to quit painting entirely," Caselli says. "If you want to do something, you must commit yourself fully – or just let it be."

Now, her attention is focused on the birth of stars and star systems: in the center of dark clouds, molecules gradually grow in complexity. The first delicate star structures form, known as protostars. They aren't yet dense enough to ignite the fire of nuclear fusion that lights up conventional stars; their pale light comes from molecular gas and dust that heats up and glows while raining down on the newly created protostars.

Yet the local conditions and the associated chemical reactions aren't easy to understand. At first, there are just a few thousand molecules in every cubic centimeter of space, in molecular clouds. In the end, when a protostar is born, there are one septillion particles per cubic centimeter. "We need to understand an enormous number of physical steps that occurred between those two states," Caselli says.

And that's not all: the remains of the original gas and dust clouds surround the newborn stars like a doughnut. It is precisely in those regions that planets are most likely to emerge, and with them entire star systems. The same processes that led to the birth of our solar system were at work. For Caselli, this is an extremely fascinating process: "Basically, it's about under-

Photo: Axel Griesch



Looking at our own history: Gigantic gas and dust clouds full of molecules roam the universe. So far, astrophysicists have identified around 150 chemical species, including organic compounds such as formaldehyde, formic acid and methanol. These and many other building blocks of life also accumulated in the material from which our Sun and the planets – and ultimately we humans – were formed.

standing our own history," the astrochemist says. And all this with nothing to go on but the ghostly light from distant molecules.

E-MAILS SENT OVERSEAS TO TWO PROFESSORS

Thirty-five years ago, when Paola Caselli finished secondary school and opted for science instead of art, astrochemistry itself was still in the "protostar stage." It didn't sparkle; it barely existed. Caselli went to Bologna, to one of only two astronomy departments in Italy at the time. It quickly became clear that astrophysics alone wouldn't lead her to her goal, so Caselli also attended chemistry classes, took the examinations for those and met people with whom she still works today. She completed her studies in overdrive. "Since my parents weren't rich and couldn't support me forever, I felt an obligation to not waste any time," says the Max Planck Director.

But for a master's degree in astrochemistry, it was clear that she would have to go abroad to study. One evening, Caselli was working with a telescope near Bologna. The weather was bad and there was nothing to do, so she sent two e-mails to American professors whose names she had found in the astrochemistry publications she liked best. "Those may have been the first e-mails I ever sent overseas," Caselli recalls. Both professors replied to the Italian student. Both invited her to study in the US.

Paola Caselli first went to Ohio and later to Harvard, where she completed her doctorate at the age of 28. A year later, she returned to Italy for the sake of her family. There, she obtained a permanent researcher position at Arcetri Astrophysical Observatory. "That was great, as I was close to my family, and my colleagues there were brilliant," she recalls. But it proved to be a constant battle there for students and research funding. So she returned to Harvard, and finally moved to Leeds, England, where she was offered a professorship. In other words, the usual nomadic wanderings of a scientist.

"If you want to do research, you have to seize every opportunity you're offered," she says. "Under no circumstances should you be afraid to move again and again." Not even if – as in Paola Caselli's case – you have a daughter who you have raised alone since she was three and a half years old. "Of course things are difficult sometimes, and you have to organize your life very efficiently. But children adapt quickly to new environments," says the 51-year-old. "As long as the parents are happy with what they're doing, it's okay for the kids."

Finally, in April 2014, now a Max Planck Director, she moved to Munich. There, in Caselli's corner office overlooking a stream flowing through the middle of the institute campus in Garching, there are no pictures of colorful nebulae or dark clouds. Instead, large-format photos of telescope systems adorn the walls. These are the tools of astrochemists, and Paola Caselli needs a lot of them. Depending on what excites the faraway molecules – cosmic rays, pale starlight or violent explosions – they emit radiation of different

Photo: Axel Griesch

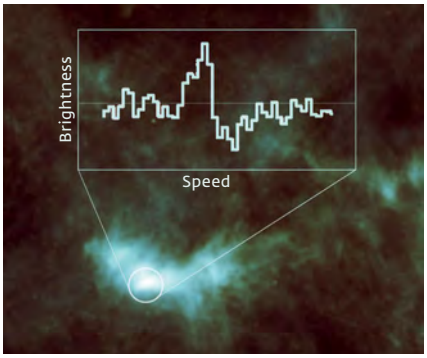
wavelengths: some secrets are revealed by radio waves or short microwaves, and others by infrared light. X-ray telescopes are also needed in order to complete the picture.

HUGE VIRTUAL TELESCOPE ON THE COMPUTER

But an assorted mix of radiation wavelengths isn't the only thing that can shed light on the molecules and their movements. To study the phenomena in detail, astrochemists also link numerous telescopes together to form what is known as an interferometer. By overlaying multiple signals, they can create a giant virtual telescope in a computer with immense resolution. In doing so, however, the big picture is lost, which is why individual telescopes are still needed. "Because we're unable to touch the clouds, it's extremely important to get as much complementary information as we can," Caselli says. "The only way to do that is by examining as many electromagnetic frequencies as possible."

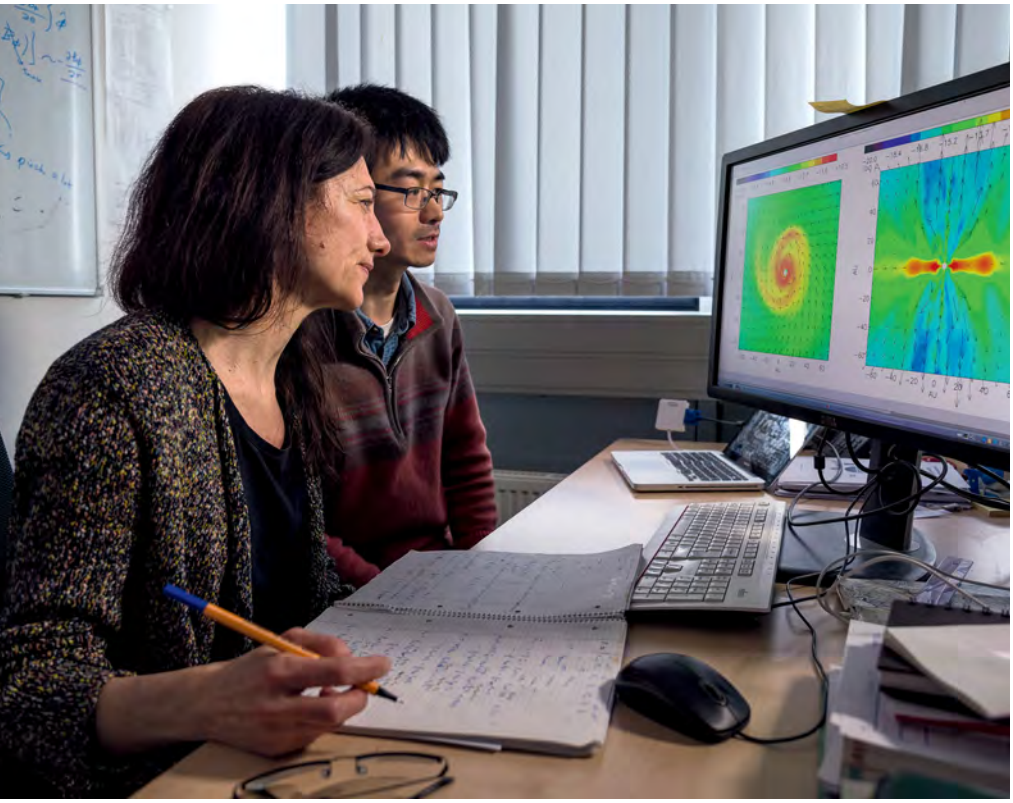
For astrochemists, this means that they are constantly on the move, visiting such far-flung corners of the Earth as Chile and Hawaii. "That can be pretty tough sometimes. You travel a lot and you have to stay up through the night and immediately comprehend what's going on. After all, you don't want to waste valuable telescope time," Caselli says. Now the researcher avoids this stress: she sends students and junior scientists – to learn, to familiarize themselves with the telescopes, but also to have a little fun exploring exotic places during their trips.

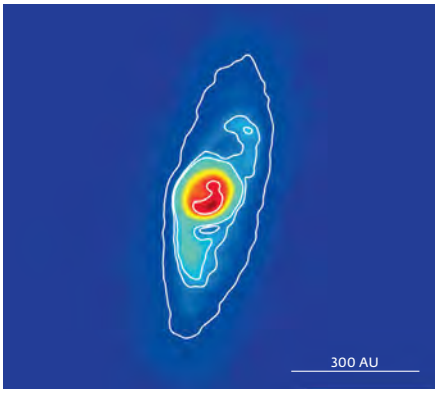
After all, having fun is crucial: "One of the most important things for young scientists is having motivation – combined with a willingness to dedicate precious time to science," Caselli says. For example, she herself had to observe the skies two Christmases in a row. The Italian researcher shakes her head. "Who would do that sort of thing if they weren't highly motivated?" So grades and letters of recommendation aren't everything for the astrochemist: "People can be as smart



In the stellar nursery: The Rho-Ophiuchi complex in the constellation Ophiuchus (top) is a shining example of the birthplace of stars. Researchers like Paola Caselli search such clouds for molecules. The smaller illustration shows the first evidence of water vapor – represented by the spectral curve – within the thick cloud in which a star will soon form. The region, named Lynds 1544, is located in the Taurus constellation and was captured using in the infrared range with the *Herschel Space Observatory*. The amount of water found in the cloud could fill around 2,000 terrestrial oceans.

Photos: Jim Misti and Steve Mazlin (acquisition), Robert Gendler (processing); ESA/Herschel/SPIRE





Back to the beginning: The group led by Paola Caselli – shown here with Bo Zhao – is concerned with the origin of stars and planets in theory and practice, on the computer and at the telescope. The bottom photo was obtained with the ALMA radio interferometer and shows a young protoplanetary disk embedded in the larger cloud in which it formed. Our solar system looked similar to this image around 4.6 billion years ago.

as they want, but if they're not enthusiastic, it won't work."

In selection interviews, Caselli therefore tries to gauge candidates' interest in the research subject and whether they have a real zeal for astrochemistry. If not? No problem. "As long as young people find a field they're passionate about, they'll be successful."

THE DAY BEGINS WITH PHYSICAL EXERCISE

When it comes to motivation and discipline, Paola Caselli sets the same high standards for herself. When it all becomes a bit too much – with work, with her daughter, who is about to graduate from secondary school and whose picture occupies a place of honor on Caselli's tidy desk – the scientist relies on good organization: "If you plan your daily routine without worrying about it too much, you don't notice how crazy it all is." Almost every day begins with exercise: on an exercise bike or stair stepper, but in any case, with stretching for the back. Even on trips, her gymnastics mat must accompany her. To save time, and because Caselli has no time for reading anyway, she listens to audiobooks while working out.

She is also disciplined when it comes to eating: healthy, not too much, and above all, fast, please. In Italy, she relates with sweeping gestures, half an hour was often wasted before everyone was ready to march off together to the cafeteria. Here in Garching, you set off at the agreed time. End of story. "I like the German way, the order, the rules," Caselli says, laughing. "I like clear messages."

Fred Hoyle, the idol with the black cloud, was different. The brilliant but controversial astrophysicist liked to make his own rules and formulate his own hypotheses. One of his most famous is that simple life forms are distributed throughout the universe, and thus also reached Earth – a theory known as panspermia. "I don't believe in it," Caselli says tersely. "It's interesting, but we need proof." So far, the only thing that is certain is that water and organic molecules regularly ride piggyback to Earth in meteorites. In the future, Caselli wants to team up with biophysicists to determine whether that is enough for life to emerge from the building blocks formed in space.

That won't be easy, and it will take time. It is, the astrochemist muses, a puzzle – a project for future generations. "It will be important to not get lost in the details," she says. "We must always keep the important questions foremost in our minds, the questions we would really like to answer. Only that will keep the motivation alive." ◀

Photos: Axel Griesch; MPI for Extraterrestrial Physics

God's law?

The future of a research team comparing Islamic family and inheritance law was at stake. The Foundation bridged a funding gap at the Max Planck Institute for Foreign and International Private Law, enabling Nadjma Yassari to continue a vital contribution to research – and do more to show how changeable Islamic law applies in Germany.

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Plastics – Kind to the Environment

Plastics are practical – not least because they last. But when they find their way into the environment, this is precisely what becomes a problem. The amount of plastic waste in the environment is constantly increasing. A team headed by **Frederik Wurm** at the **Max Planck Institute for Polymer Research** in Mainz is therefore developing polymers that can be broken down by microorganisms once they have served their purpose. The researchers are applying what they've learned from their work on biodegradable polymers for medical use.

TEXT **KARL HÜBNER**

Every year, 380 million tons of plastic enter the material cycle. If it were to be loaded into 40-ton trucks, the line would encircle the Earth nearly four times. This figure includes plastics for bags, food packaging and cosmetic bottles, toothpaste tubes and tights, as well as plastics for computer monitors and smartphones, CDs, linoleum and laminate flooring. Similarly, car and aircraft manufacturers are continuously increasing the proportion of plastics in their products – to reduce weight and thus lower fuel consumption.

The reason plastics are so omnipresent is quite simply because they offer so many advantages. Not only are they lightweight and strong, they are also versatile and long-lasting. The key chemical characteristic of plastics is that they are made by joining basic building blocks – monomers – to form enormous chains, sometimes thousands of monomers long. Chemists use different types of monomers to modify the properties of a plastic, such as hardness, ductility, tensile strength, thermal stability and much more.

Once synthesized, most polymers are virtually indestructible. Even exposing them to weathering and light causes no more than slight discoloration. And microorganisms that use many other materials as food sources are at a loss when it comes to dealing with most plastics. Depending on the type of polymer and the conditions it is exposed to, it can take decades or even centuries before the giant molecules are fully broken down into carbon dioxide, water and other residues. Until then, they continue to represent a potential hazard to fish, seabirds and many other animals.

4.9 BILLION TONS OF PLASTIC WASTE

For many applications, the longevity of plastics is one of their major advantages, but today it is also considered to be one of their greatest disadvantages. About a year ago, a team of researchers in the US published some shocking figures on the fate of plastics. According to their calculations, between 1950 and 2015, 8.3 billion tons of plastic were manufactured worldwide, of which 6.3

Easy pickings for microbes: These phosphate-based plastic plates can be broken down by microorganisms –plastics like these wouldn't accumulate in the environment.

Photo: Thomas Hartmann

Almost indestructible: Plastic waste can endure for hundreds of years. Finding its way into a landfill, as here in the Maldives, must be considered a good outcome, as particularly in countries without a functioning waste collection system, colossal volumes of plastic end up directly in the environment.

billion tons have already become waste. Of that amount, just over a fifth has been recycled or incinerated. The remaining 4.9 billion tons have ended up as waste either in landfills or directly in the environment. The corresponding line of trucks would encircle the Earth almost 50 times.

Although some plastics are readily biodegradable, they currently make up only a very small proportion of total plastics. Polylactic acid, for example, is used in bags for compostable waste and plastic tableware for street festivals. However, if they are to actually decompose after use, the material must be correctly disposed of. "Little is gained when polylactic acid beer cups end up in normal household waste or in the recycling container," explains Frederik Wurm, Research Group Leader in Katharina Landfester's department at the Max Planck Institute for Polymer Research in Mainz. Only when disposed of in the organic waste bin or composter will polylactic acid come into contact with the microorganisms required to break it down.

Frederik Wurm and his colleagues develop polymers with customized properties, one of which is biodegradability. "This needn't necessarily involve the use of renewables," explains Wurm, clearing up a popular misconception: "Firstly, not everything that's based on biological materials is automatically biodegradable," says Wurm. "And secondly, not everything that's biodegradable is necessarily of biological origin." His group is doing a lot of work with phosphates and phosphonates, for instance, and although these substances are geological in origin, polymers produced from them are fully biodegradable.

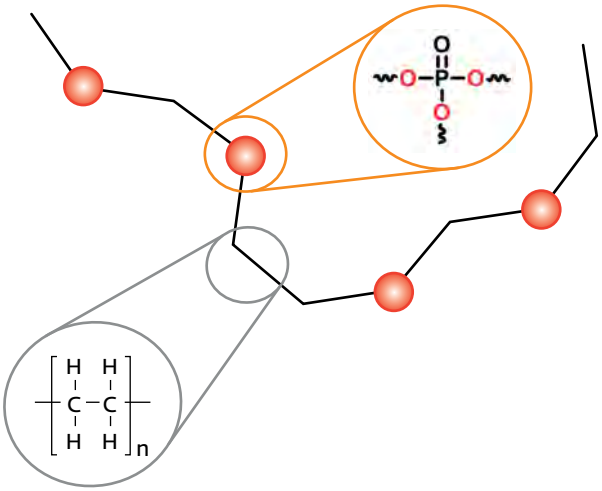
PE MOLECULES WITH BUILT-IN CLEAVAGE SITES

"The idea is actually very simple," Wurm says in reference to one of his current projects. "We make normal PE molecules, but we incorporate a few phosphate groups into them as cleavage sites." PE stands for polyethylene, one of the most widely used plastics in the world. It's used for making plastic films for the food industry and agriculture, as well as for shopping bags and containers for shampoo, cleaning agents and cosmetics.

Phosphate groups in the PE chain whet the appetite of certain microorganisms, giving them something to sink their metaphorical teeth into. A PE molecule with phosphate groups incorporated into it would therefore be readily broken down in the environment. All that would remain are the many small PE sections between each pair of phosphate groups. In contrast to the giant chains in normal polyethylene, if these sections are short enough, they, too, says Wurm, are readily biodegradable.

But does incorporating phosphate alter polyethylene's other properties? "Our aim is to make materials that can be used like PE, but are also biodegradable," explains Wurm. The mechanical properties are decisive here, and the key to these is how the polymer chains line up with each other. In pure PE, for example, it is known that the long molecules are folded like an accordion. The chemists in Mainz therefore wondered whether the polymer would behave in the same way with the added phosphate groups. With respect to biodegradability, there was another important point to consider: "To be accessible to microorganisms and their enzymes, the phosphate sections need to be on the outside of the kinks in the chain," explains Wurm.

Photo: Shutterstock/Mohamed Abdulraheem



Above Standard polyethylene consists of thousands of repeat units consisting of only carbon (C) and hydrogen (H). To make the plastic biodegradable, the chemists in Mainz add phosphate groups, consisting of phosphorus (P) and oxygen (O), at the kinks in the polymer.

Below Hisachi Tee, a member of Frederik Wurm's (right) research group, is using phosphorus chemistry to develop new polymers. The researchers are also trying to reproduce properties of common plastic films.

Graphic: MPI for Polymer Research; photo: Thomas Hartmann

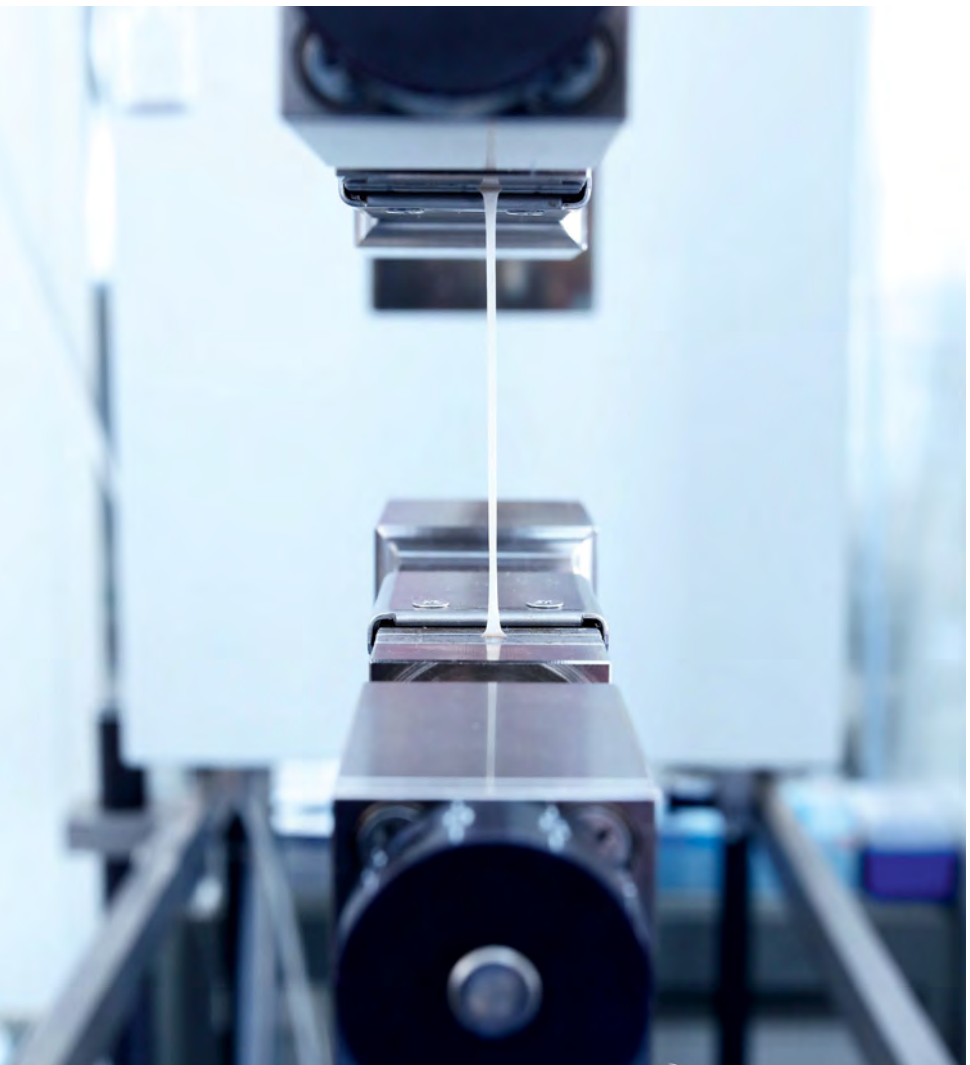
The researchers used transmission electron microscopy to confirm that both of these requirements are met. They found that their polymers folded in exactly the same way as pure polyethylene, and that the phosphate groups were located, as they had hoped, at the kinks in the chains.

The team isn't yet completely satisfied, though. "Our molecular weight isn't yet high enough for most practical applications," admits Wurm. In other words, the molecular chains the chemists produce in the laboratory aren't as long as standard PE chains. This is because, in order to incorporate the phosphate groups, they use a different technique to manufacture their polymer than that used to produce industrial polyethylene.

PAYING A BIT MORE FOR A BETTER ENVIRONMENT

Nevertheless, the team in Mainz now has a general approach to producing biodegradable PE. Frederik Wurm is, of course, well aware that not all PE users will immediately switch over to the PE-phosphate polymer. After all, the low cost of pure PE is currently unrivalled. Few manufacturers can afford to pass on the extra costs to their customers, especially when it comes to bulk products like packaging materials. But Frederik Wurm can imagine that some customers might be prepared to pay a little more for the environmental benefits – customers who shop in organic grocery stores or other relevant chains, for example.

In medical applications, in contrast, material costs are almost completely irrelevant, and it is precisely for the



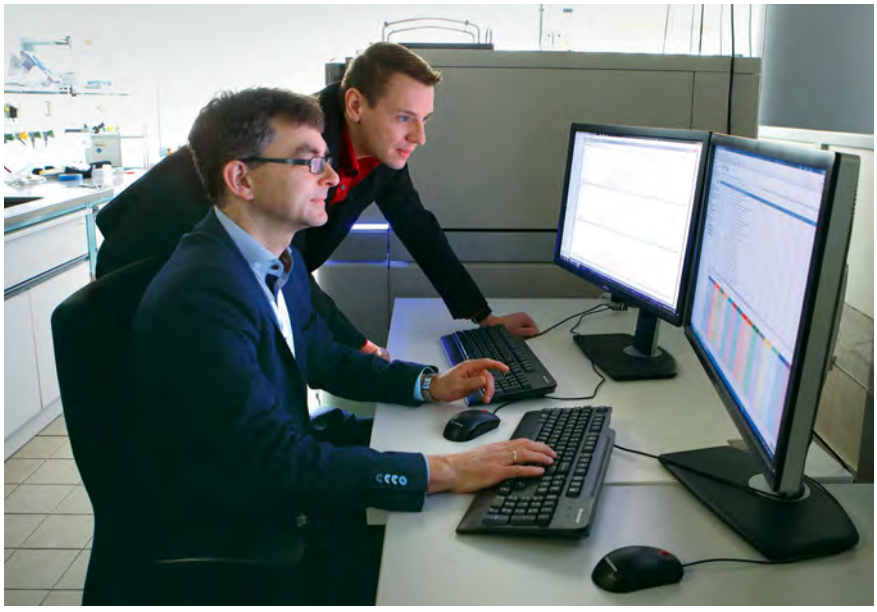
medical sector that Wurm's team developed the first phosphate-based biodegradable polymers. Their success in doing so is what gave the chemists the idea of incorporating phosphate groups into other common plastics, such as PE.

For medical applications, the primary focus is on polymer-drug conjugates. This involves embedding drugs, such as anti-cancer drugs, in nanoparticles. The particles, or sometimes the drugs themselves, are then coated in innumerable polyethylene glycol (PEG) chains, which flutter about the conjugate like fringes. These PEG chains act to hide the nanoparticles from the body's immune defenses, preventing them from being broken down prematurely. As a result, the conjugates circulate much longer in the blood than the drug alone, which also increases the duration of action. In addition, most conjugates are chemically programmed to deliver the drug to specific cells. This enhances the desirable effects while reducing side-effects.

"The market for such conjugates is already worth billions," notes Frederik Wurm. To date, however, the long-term fate of the PEG units remains unclear. Within the body, they are believed to be nondegradable; this, Wurm notes, is a good thing, as the monomer, ethylene glycol, is harmful to health. "If the PEG chains are short enough, they are excreted via the kidneys," explains Wurm. For longer chains, however, it

Polymers for testing: Max Planck researchers polymerize monomers, added via the turquoise syringe (top), in a reaction vessel heated in a water bath. They test the elasticity of their polymers using tension experiments (bottom).

Photos: Thomas Hartmann



Stealth effect uncovered: By analyzing mass spectrometry data, Volker Mailänder (left), Katharina Landfester (not pictured) and Frederik Wurm discovered that endogenous proteins attach themselves to their tiny drug delivery vectors. As a result, the body's immune defenses fail to recognize the payload as a foreign body.

should be assumed that they accumulate in the body, which could pose a problem in the case of drugs for chronic conditions. It's conceivable, for example, that PEG chains could form crystals at certain sites in the body.

POLYPHOSPHATES ARE BROKEN DOWN IN THE BODY

In collaboration with the University Medical Center Mainz, Wurm is currently investigating whether his phosphorus-based polymers could be used as an alternative to polyethylene glycol. In contrast to the above-mentioned PE, in which the chemists incorporate only isolated phosphate groups into the PE chains, here they use polymers constructed almost exclusively from phosphate groups. But what makes these substances particularly suitable for use as medical polymers? "We know for certain that polyphosphates can be broken down into phosphate within the body, which is then entirely harmless," explains Wurm. One polyphosphate that has proven particularly suitable in terms of water and thus blood solubility, as well as biodegradability, is poly(ethyl ethylene phosphate), or PEEP for short. Frederik Wurm's Group has already developed a clever technique for synthesizing the polymer.

In contrast to polyethylene, in which the ethylene monomers form an endless chain, in PEEP each ethylene monomer is sandwiched between one phosphorus and one oxygen atom, making it much easier for enzymes to break these bonds as compared with pure PE. So, once the drug delivery vector has delivered its payload to the target, the enzymes cleave one ethyl ethylene phosphate monomer after another from the PEEP chain. "These small phosphate molecules are easily excreted via the kidneys," explains Wurm.

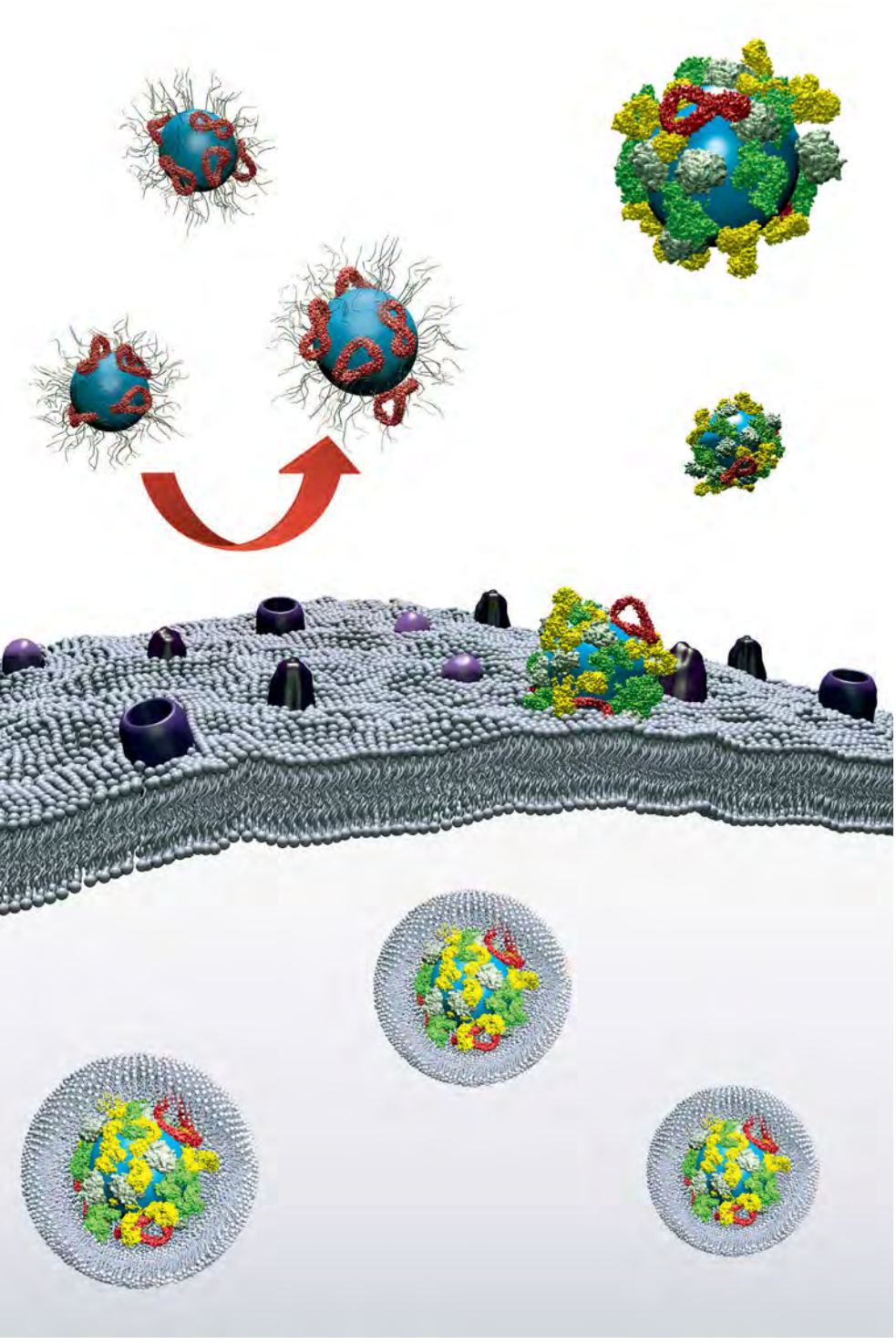
"The degradability in the organism and even in individual cells is very important and makes these polymers of great interest for further development," emphasizes his collaboration partner Volker Mailänder from the University Medical Center Mainz. The physician is currently researching ways to replace PEG with readily degradable polymers and is collaborating with Frederik Wurm to achieve this. One of the researchers' current goals is to develop vectors for delivering a drug to immune cells. The substance is designed to reprogram the immune cells to attack melanoma cells.

But before PEEP can be used in actual medical practice, there are a number of questions that Wurm and Mailänder still need to answer. For example, whether polymers such as PEEP can achieve the same stealth effect, allowing the polymer-drug conjugate to reach its target undetected. For test purposes, the researchers created stand-in nanotransporters for the drug payload, and then attached their PEEP fringes to these tiny particles. "We were able to show that these also circulate in the blood for a long time, proving that they aren't attacked by immune cells," says Wurm.

With the help of a special type of mass spectrometry, the researchers in Mainz have since also determined how the stealth effect actually works. "The polymer chains, whether PEG or PEEP, recruit from the blood specific proteins that attach to the conjugate," explains Mailänder. This shell, made up of the body's own proteins, gives the conjugates a sort of free pass, allowing them to circulate unhindered.

In and of itself, the long dwelling time in the blood is of no great benefit, medically speaking. The key thing is the

Photos: Thomas Hartmann



It's all in the mix: When a variety of endogenous proteins attach to particles camouflaged with polymer fringes, the potential drug delivery vectors are absorbed by the cells and, enclosed in membranes, transported into the interior of the cell, as shown on the right in this image. If, in contrast, the particles attract only one type of protein, they remain unable to enter the cell.

address label that the PEEP-nanotransporter conjugate uses to reach its intended target. In the cooperative project with the University Medical Center Mainz and other researchers in Landfester's department, sugar groups serve as address labels, as they stick to very specific immune cells. But there are still a few details to be fine-tuned. According to Wurm, it isn't all that easy, for example, "to strike the right balance between adequate camouflaging and sufficient pinpoint accuracy."

Because phosphate-based polymers are so readily biodegradable, the researchers in Mainz want to use them in other areas, too. In one project with a commercial partner, they are developing a kind of bone cement such as surgeons use for minor bone repairs, for instance. At present, the main types of adhesives used in this area are acrylic acid polymers. An adhesive that would disappear without a trace after a certain time would be a big plus.

PHOSPHORUS CHEMISTRY YIELDS NEW FLAME RETARDANTS

Of course, for that kind of application, the material needs to exhibit a certain robustness. "The first materials we made were as brittle as cold candle wax," Wurm recalls with a smile. To refine their phosphate polymer bone cement, the chemists once again had to reach for their box of chemistry tricks. "On the one hand, we needed to increase the molecular weight," explains Wurm. The chains needed to be made much longer than the fringes for the drug vector, the maximum length of which was a little over a hundred phosphate groups. On the other hand, to make the cement both more elastic and harder, the chemists needed to tinker with the design of the side chains.

The possibilities for this kind of tinkering are exactly what Frederik Wurm loves about phosphorus chemistry. Owing to their nature, phosphorus atoms are able to form one more bond than carbon – the backbone of traditional polymers. This gives synthetic chemists like Wurm more leeway. With poly-

Graphic: Nature Nanotechnology 2016

phosphates, for example, chemists can attach one more chemical group to the phosphorus atoms than they would be able to with the carbon atoms in analogous carbon-based polymers. "We can design this group any way we need to in order to achieve a particular property, such as stickiness," gushes Wurm, describing the possibilities this opens up as an "enormous playground."

The Max Planck researchers in Mainz also want to use their expertise in phosphorus chemistry to develop new flame retardants. Phosphorus compounds are already used as flame retardant additives, as they release flame retardant substances upon burning, while they themselves merely carbonize. Until now, these additives have generally simply been mixed with existing plastics. "We are working on incorporating such phosphorus groups directly into other polymers to make them flame resistant," says Wurm.

The chemist admits, however, that for the time being this solution isn't going to be used in areas where the emphasis is on price, simply because such plastics are too expensive. But epoxy resins and epoxy adhesives used for gluing floors, for instance, are a different matter. Here, the plastics being produced in Wurm's laboratory could well have a role to play. "We are currently looking at whether we can improve flame retardancy in such products," says Wurm. A further side effect would be that it would remove the need to use bisphenol A. This is currently an important starting material for the production of epoxy resins, but it is controversial, as it can be harmful to health.

As even the work of flame retardant products will one day be done, and they too will end up as waste, it would of course be good if they were readily biodegradable under normal environmental conditions. Existing flame retardants tend not to be, and may even be toxic. Against this backdrop, new solutions based on phosphates or related phosphorous compounds have a certain attraction.

MANY ALTERNATIVES TO LONG-LASTING PLASTICS

The researchers are testing how quickly their compounds really break down using the types of enzymes microorganisms release in the environment. These include lipases, proteases and depolymerases, as well as phosphatases and phosphodiesterases, which specifically target phosphorus groups. "We perform tests both with individual enzymes and with mixtures," says Wurm. The team also uses real-life fluids, such as blood plasma and sewage sludge.

Frederik Wurm is aware that the approaches his group is taking aren't going to revolutionize the world of plastics on their own. But they do offer a few possibilities among many others that, together, could ensure that plastics will one day no longer be a problem for the environment. "There's not going to be just a single solution," says Frederik Wurm. The problem of long-lasting plastics in the environment will require a range of alternative materials. His group, for its part, is working on a few of them. ◀

TO THE POINT

- **More than 8.3 billion tons of plastics have been produced since 1950. Of these, 4.9 billion tons have ended up in landfill or elsewhere in the environment. The majority of these plastics are not readily biodegradable.**
- **Scientists at the Max Planck Institute for Polymer Research are developing biodegradable polymers. To achieve this, they incorporate phosphate groups into polyethylene (PE). These groups can be attacked by enzymes present in the environment, cleaving the polymer molecules.**
- **In addition, the researchers in Mainz are producing polyphosphate polymers for medical use. They are also working on biodegradable polymers with flame retardant, adhesive and other properties.**

GLOSSARY

Mass spectrometry: A technique for identifying unknown substances. Large molecules such as polymers are split into often characteristic fractions. An electric charge is applied to these fractions and they are then sorted according to their mass-to-charge ratio by deflecting them in an electric field. This produces a characteristic spectrum.

Polymer: A molecule consisting of chains of a basic building block (monomer), often thousands of monomers long. Polyethylene (PE) consists of long chains of ethylene molecules, whereas poly(ethyl ethylene phosphate) (PEEP) consists of long chains of ethyl ethylene phosphate monomers.

Polymer-drug conjugate: A conjugate in which a drug – generally embedded in a nanoparticle – is coated with polyethylene glycol (PEG) or poly (ethyl ethylene phosphate) to hide it from the immune system. These conjugates remain in the body longer and can have chemical address labels attached to send them to specific cells.

Climate Slashing

Public debates on global warming focus on one main cause: CO_2 emissions from the combustion of fossil fuels. But humankind is also changing the climate by clearing forests and through farming, forestry and animal husbandry. Together with her Research Group at the **Max Planck Institute for Meteorology** in Hamburg, **Julia Pongratz** is investigating the consequences of these activities for the climate – and how these interventions could be used to counter global climate change.

TEXT **UTE KEHSE**

A large map of the world hangs on the wall in Julia Pongratz' office. The oceans on it are white, the continents multicolored. A mosaic of violet, green, brown and gray shades covers the land areas. "This map shows the world's different land use systems," explains the researcher from the Hamburg-based Max Planck Institute for Meteorology. Dark green represents virgin forest, and light green, forests in which forestry is carried out. The purple and pink shades symbolize different types of farmland, while orange shades are grasslands with different levels of livestock farming. The lighter the shade, the more heavily the land is used.

It is apparent that humans have taken over the great majority of the land on Earth. "Three-quarters of the ice-free land surface is anthropogenically influenced," says Julia Pongratz. On around a quarter of the world's continents, humans have destroyed the natural vegetation over time to create cropland, rice fields or pastures. This process has accelerated since 1950, as heavy deforestation in the tropics testifies. Around half of the land surface is still covered by the original type of vegetation, but even here, some form of management takes place. Studies show that humans thus account for almost a quarter of the global terrestrial net primary production, or more specifically, 24 percent of the annual renewable plant biomass.

Humankind has, one might say, truly subjugated the planet – and this comprehensive exploitation of nature

Photo: iStockphoto/AVTG

Photo: shutterstock

Forests with different climate impacts: An unmanaged forest with trees of different ages and a lot of deadwood (this page) exchanges different quantities of greenhouse gases, water and energy with the atmosphere than a spruce monoculture (left).

isn't without consequences for the climate. A total of one-third of the carbon dioxide ever released by humans – including historic deforestation – can be attributed to the original vegetation of the land surface being altered. Currently, changes in land use cause about 10 percent of human CO_2 emissions.

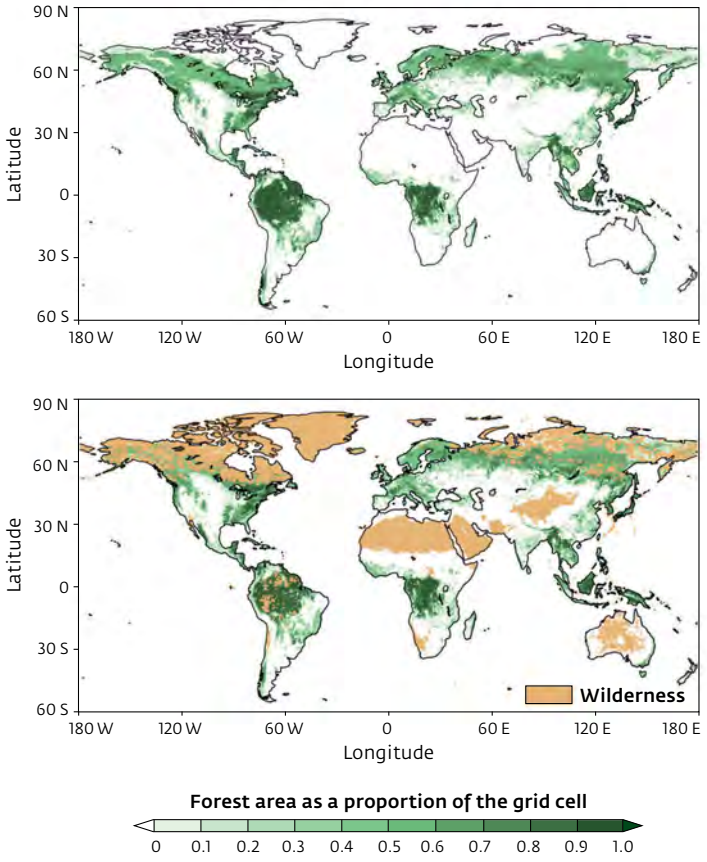
GREENHOUSE GASES FROM FERTILIZERS, LIVESTOCK AND RICE

The effect is even greater when climate-changing gases such as methane and nitrous oxide from agriculture are included in the balance sheet. These greenhouse gases enter the atmosphere through fertilizers, animal husbandry and rice cultivation, for instance. "If we add methane and nitrous oxide to carbon dioxide, the share of land use in today's greenhouse gas emissions increases to about one-third," reports Julia Pongratz. On the balance sheet of individual countries such as Brazil, land use emissions play an even greater role than fossil fuels.

When humans turn forests into fields, for example, they not only intervene in biogeochemical cycles, such as the carbon and nitrogen cycles, and alter the atmospheric CO_2 balance, they also influence various biogeophysical processes, such as albedo – the propor-

Complex climate factor: When a forest is cleared, not only does a carbon sink disappear – the albedo and other physical properties change, as well (top). However, how vegetation influences the climate also generally depends on which crops – corn or wheat, for instance – are cultivated on a field (center). These multifaceted effects should be taken into consideration, for example, when cultivating elephant grass as a substitute for fossil fuels (bottom).

Photos: shutterstock, Julia Pongratz, shutterstock (from top to bottom)



Ample forestry: Forest covers large sections of the tropics and the high northern latitudes (top). However, only around 40 percent of this area is wilderness, as the orange regions in the bottom map show.

tion of reflected sunlight – or the exchange of heat and moisture between land and atmosphere. These biogeophysical contributions can lead to atmospheric warming or cooling and thus enhance or counteract the climatic effect of an increase in the CO_2 concentration.

Because biochemical and physical factors interact in complex ways when land use is altered through agriculture and forestry, researchers currently understand the climate impacts of such interventions far less well than they do the effects of burning fossil fuels. The climate balance of the various factors can vary depending on the latitude or the assemblage of vegetation species – and as if that weren't enough, sometimes it can also take a different direction locally than it does globally.

Just how complicated the connections are is demonstrated by a relatively simple example: the transformation of a forest into cropland. The first effect is that there are now fewer forests available to absorb CO_2 and store it over the long term, fostering global warming. But there are also biogeophysical effects: at the site of the deforestation on the one hand, but also in more remote regions, on the other hand, because air currents carry the changes in the heat and hydrologic balances of the atmosphere further downwind.

Johannes Winckler, a mathematician in Julia Pongratz's group, was the first to make a clear distinction between the remote effects of these biogeophysical changes and the local effects. "The non-local effects were previously ignored because they weren't captured by observational data," says Winckler. However, he succeeded in unraveling the effects of massive deforestation worldwide and locally, and found that deforestation carried out to date has cooled more-distant regions. The non-local biogeophysical effects thus compensate for some of the global warming caused by the CO_2 emissions produced by clear-cutting.

For actual living conditions, though, the global mean temperature is far less relevant than the local climate. And even locally, the climate consequences of deforestation aren't easy to assess, because the change in vegetation typically makes the surface brighter – in other words, its albedo increases. Clear-cutting thus has a cooling effect, as more sunlight is reflected back into space. But deforestation can also induce a warming effect, since it reduces transpiration, or evaporation from the leaf surface. A field of grain often gives off less moisture than a forest, which normally has a larger leaf surface and deeper roots.

Which impact has the greater influence depends mainly on the latitude. At high latitudes, such as in northern Europe, the albedo effect is usually stronger, so deforestation tends to lead to local cooling. In the humid tropics, in contrast, the transpiration effect dominates, and deforestation here thus leads to warming. >

Graphic: Julia Pongratz/MPI for Meteorology

"One thing that is special about our group is that we consider both the biogeochemical and the biogeophysical aspects of land use," says Julia Pongratz. "This is important, because the climate sees both factors, and both are politically relevant." A geographer by degree, she finds the political significance of her research topic, which is essentially oriented toward basic research, particularly attractive.

CLIMATE-RELEVANT PROCESSES IN FORESTRY

Since the establishment of her Emmy Noether Group in July 2013, she and her interdisciplinary team have been working to investigate climate-relevant biogeophysical and biogeochemical processes that play a role in land use, and especially in forestry. In addition, the group aims to discover to what extent land management can be used in climate change mitigation. To this end, the ten researchers are working to incorporate some previously neglected processes into the MPI-ESM Earth System Model of the Max Planck Institute in Hamburg.

Such Earth system models are among the climate researchers' most important tools. They have long been capable of modeling what happens when forests, for example, must give way to grazing land or fields – that is, when the land cover changes. The more

The climate researchers and their tools: Julia Pongratz, Sebastian Sonntag and Julia Nabel (from left) between a few of the towers of the Mistral supercomputer at the German Climate Computing Center in Hamburg.

Photo: Tom Pingel

common case, however, when only the form of management in an area changes, hasn't yet been covered by the models. There are numerous variables in agriculture and forestry, such as fertilization, irrigation, harvesting cycles and grazing. They influence biogeophysical and biogeochemical variables, such as albedo, surface roughness, carbon uptake and other climatic factors. This is why Julia Pongratz' team takes both into consideration: changes in land use that alter the land cover and those that concern only land management.

The importance of considering changes in land management in climate models was demonstrated in a 2014 study by a team of researchers headed by Sebastiaan Luyssaert from the French Laboratory for Climate and Environmental Sciences in Gif-sur-Yvette. In the journal Nature Climate Change, the team – of which Julia Pongratz was also a member – reported that a change in land management, such as the transition from a virgin forest to a managed one, or the cultivation of different crop species – can affect temperatures just as strongly as changes in land cover.

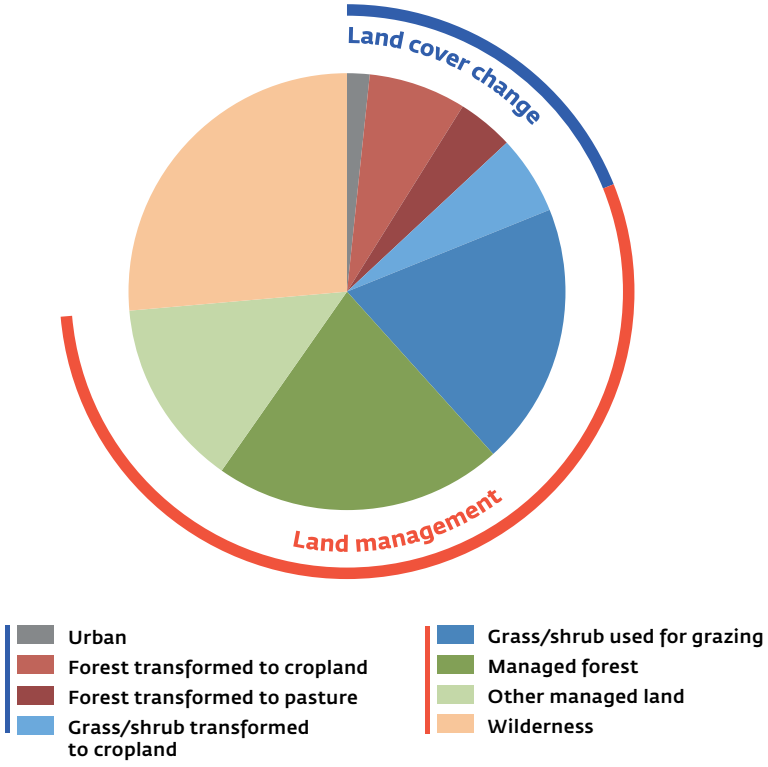
At the locations that the researchers compared, both activities produced an average warming of two degrees Celsius. The team thus concluded that climate mitigation strategies shouldn't address merely fossil fuel emissions and deforestation, but also take into account the consequences of agriculture and forestry, which will likely become more intensive in the future.

Julia Pongratz' group is therefore dedicated to the task of integrating various aspects of land management into climate models. A recently published study, in which Julia Pongratz played a key role, shows that the models didn't realistically simulate the effects of different types of land management.

In January 2017, a team of researchers led by Almut Arneth at the Karlsruhe Institute of Technology reported in the journal Nature Geoscience that land use and land management likely released more carbon dioxide in the past than was previously thought. This factor in the climate system would therefore have contributed more than a third to the increase in atmospheric carbon dioxide since humans took control of the Earth. Vegetation models have apparently underestimated these emissions to date because they didn't model land management realistically. "For example, the models don't currently address whether timber is harvested in a forest, and if so, how," says Julia Pongratz.

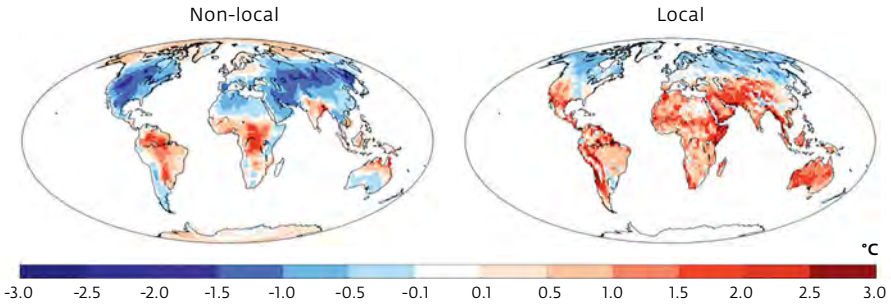
Post-doctoral student Kim Naudts is working on integrating the effects of land management into the climate models, assisted by Julia Nabel. As the group's scientific programmer, Nabel, a computer scientist, incorporates the processes being studied into the Max Planck Institute for Meteorology's complex Earth system model. She also ensures that the models run on the large supercomputer at the German Climate Computing Center. Efficient computing on the supercomputer is essential for modeling the diverse interactions between vegetation and atmosphere, as well as regional variations.

"We study primarily the effects of forestry," Naudts says. In an earlier study, the researcher, together with a



Diverse land-use changes: Wilderness is found on only around a quarter of the ice-free land surface. Often, regions are altered in a way that also changes land cover, for example from forest to cropland. More common, however, is a different type of management, such as when people start to use grasslands as pastures. Both types of change influence the climate to a similar degree.

Graphic: MPI for Meteorology



Globally, deforestation leads to warming due to the loss of a carbon dioxide (CO_2) sink. However, global deforestation has a cooling effect (blue) across large areas due to non-local biogeophysical effects. Locally, the biogeophysical factors can increase temperatures (red) or decrease them (blue). (Scale in degrees Celsius)

Extreme differences in albedo occur when – as here in Zillertal – snowy, well-reflecting surfaces meet dark coniferous forest, which absorbs most of the light.

team from the French Laboratory for Sciences of Climate and Environment (LSCE), investigated how species selection by humans affects a forest's climate impact. For example, as coniferous trees have been cultivated in Europe in recent centuries for economic reasons, the vegetation has absorbed more heat. Although the conifers stored more carbon than the deciduous trees grown previously, the albedo effect had a greater impact. "Coniferous trees are probably not the best species for mitigating climate change in Europe," says Kim Naudts.

Now she is looking at what influence a forest's age has on the exchange of carbon, water and energy with the atmosphere. In most climate models to date, the age structure of the forests has not played a role. The Belgian-born researcher therefore investigated different harvesting methods – and showed that there are significant differences in the amount of stored carbon or in albedo when forest age is taken into account in their management. "To properly assess how much forestry can contribute to mitigating global warming, climate models must also incorporate the age of the forests," says Kim Naudts.

HOW WELL CAN REFORESTATION MITIGATE CLIMATE CHANGE?

In addition to investigating the consequences of land use changes, Julia Pongratz and her team are also investigating climate mitigation strategies. Sebastian Sonntag, for example, is researching how well reforestation could mitigate climate change. Together with Pongratz and other colleagues, he found that reforestation reduces the CO_2 level in the atmosphere more than was previously thought: in some scenarios, the growth of forests on land no longer needed for farming could lower the CO_2 increase by 85 ppm by the year 2100 – current calculations show an increase from today's 400 ppm to around 700 ppm. Consequently, the average global temperature would increase, not by 3.7 degrees Celsius by 2100, but by just 3.4 degrees.

"The novelty of our study was that we incorporated feedback loops with the carbon cycle into the model – for example, that increasing carbon dioxide levels in the atmosphere stimulate plant growth," explains Sonntag. However, even the new model doesn't include all conceivable factors. In the future, for example, droughts or a shortage of nutrients could affect tree growth. "It's fairly unlikely that we underestimated forest growth, but it could also be less than in our model," says the physicist. The reason is that many models don't sufficiently account for the reaction of the forest to climate extremes. Droughts, for example, can cause forests to die, and their impact continues for decades: they reduce carbon storage in vegetation until young forest has been reestablished. "In the model, this legacy doesn't exist yet as such," reports postdoc Lena Boysen, whose work closes this gap.

In another paper, Sebastian Sonntag compared the reforestation scenario with another geoengineering method: ocean alkalization. "The idea is based on the fact that the oceans can

Graphic: MPI for Meteorology; photo: Julia Pongratz

bind more carbon dioxide if we increase the amount of acid-binding substances," says Sonntag. In practice, ocean alkalinity could be increased by enormous amounts of ground limestone. The results of his investigation reveal that this method may be more efficient than reforesting: because forests also have a warming effect, especially at high latitudes, it would be necessary to remove more CO_2 from the atmosphere with reforestation in order to achieve the same cooling effect as alkalization.

BIOMASS PLANTATIONS CAN HELP REDUCE EMISSIONS

In addition to reforestation, bioenergy plantations have also recently been discussed as a measure to combat global warming. "In some socioeconomic models, it is assumed that, in the future, large areas can be used for cultivating energy crops," says biologist Dorothea Mayer. "The harvested biomass would be converted into fuels or heating energy and thus reduce the consumption of fossil fuels." However, this kind of land use presents its own problems because energy crops can easily compete with food production or displace natural ecosystems, as Lena Boysen impressively demonstrated in previous studies with colleagues from the Potsdam Institute for Climate Impact Research. Therefore, in her scenarios, Mayer uses only arable land vacated as a result of intensified farming on other plots.

If biomass crops, such as elephant grass, were cultivated on such land in order to replace fossil fuels, this would mitigate the increase in CO_2 projected under unchecked emissions by a maximum of one-third – if all the material harvested were able to replace fossil fuels. "However, current techniques are not that good yet," Mayer points out. So according to her studies, biomass plantations can play a certain role in slowing down the increase in CO_2, but as before, the only way to stop it completely is to forego fossil fuels.

A final verdict on which forms of agriculture and forestry can contribute to mitigating climate change isn't easy to arrive at. As Julia Pongratz concludes, by constantly improving Earth system models, integrating key types of land management, and considering both local and global effects, climatologists can better understand the impact of changes in land use. At present, however, recommendations for policy makers remain difficult. "One can certainly argue whether land use should be exploited to mitigate climate change at all, as many processes are extremely complex and often not well understood," says the Research Group Leader. In her opinion, however, these considerations are useful. "We use the land anyway, there's no reason we shouldn't do it wisely." ◀

TO THE POINT

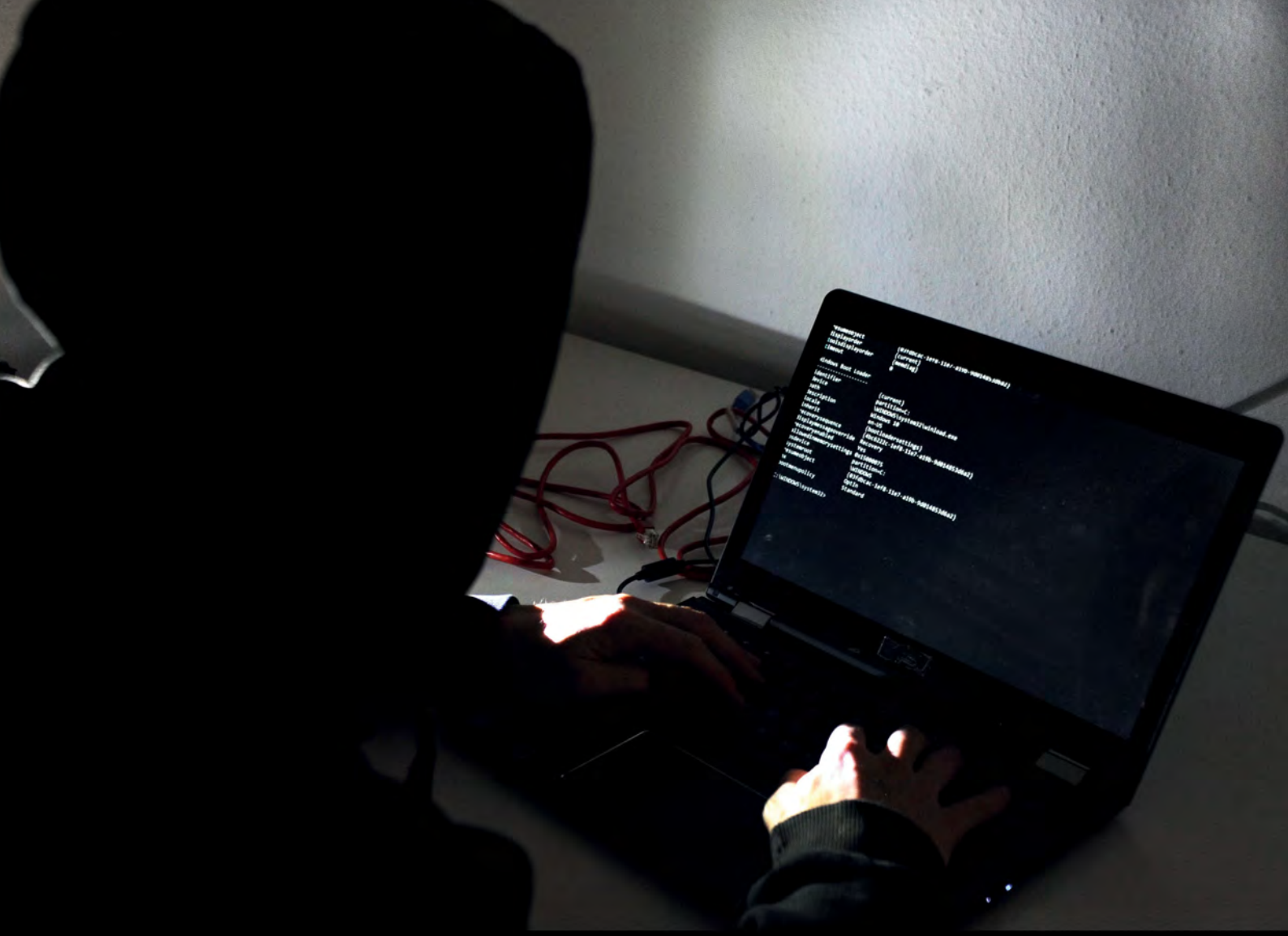
- **At least one-third of the CO_2 emissions caused by humans to date originate from land-use changes, such as deforestation.**
- **The effects of changes in land use are often difficult to assess. For example, to date, the conversion of forests into agricultural land has led to additional global warming owing to the release of CO_2, which, however, has been mitigated by changes in heat and water fluxes. At the site of deforestation, though, it may cause cooling at high latitudes due to increased albedo, while warming usually occurs in the tropics due to reduced transpiration.**
- **Different types of agriculture and forestry prevail on about half of the ice-free land surface and can affect the climate and atmospheric CO_2 levels as much as changes in land cover. This is why Julia Pongratz' team is also working on representing the effects of land management in Earth system models.**
- **Replacing fossil fuels with biomass energy sources would reduce the predicted increase in the CO_2 concentration by a maximum of one-third.**

GLOSSARY

Albedo is a measure of the amount of sunlight that is reflected into space without warming the atmosphere.

Alkalinity is the capacity to buffer acids, or in other words, to resist changes in pH that would make the water more acidic.

Land use encompasses all the ways in which humans intervene in an area's vegetation and soil. Changes in land use can lead to changes in land cover, for example from forest to cropland. However, an area – a forest, for example – can also simply be managed differently than previously.



Anti-Espionage Strategies

The competition isn't sleeping, it's spying. And especially small and medium-sized businesses are increasingly falling victim to criminal competitors or being targeted by foreign intelligence services. Nevertheless, most cases remain shrouded in mystery. **Michael Kilchling** and his team at the **Max Planck Institute for Foreign and International Criminal Law** in Freiburg are now attempting to shed some light on the phenomenon. Together with colleagues at the Fraunhofer-Gesellschaft, they are conducting research into the scale of industrial espionage in Germany, how companies are combating it and how the authorities could better support them in their efforts.

Photo: dpa

TEXT **BENNO STIEBER**

Rieder, a company specializing in concrete and headquartered in Kolbermoor, Bavaria, greeted the visiting Chinese CEO as a welcome partner. The firm is renowned for its innovative building materials – its fiberglass concrete slabs turned the Soccer City stadium in Johannesburg into an architectural showpiece at the soccer World Cup in 2010 – and it was delighted to have found a local partner for a Chinese construction contract worth millions. No one in Kolbermoor suspected that the Chinese company was really only interested in stealing cutting-edge know-how from Germany in order to take over the contract on its own.

While the CEO from the Far East was touring the plant, Rieder employees spotted a mini-camera attached to their guest's belt. Instead of allowing their visitor to continue exploring the company's inner sanctums, they called the police. Analysis of the belt camera's data later revealed that the material would have been sufficient to copy and reproduce the high-tech components in China. The damage to the medium-sized company would have been immeasurable.

The attempted espionage in the Bavarian province is a fortunate exception compared with other cases examined by the "WiSKoS – Economic and industrial espionage in Germany and Europe" research project. The perpetrator, objective and motive were all apparent. The case was quickly and successfully dealt with and no long-term damage was done. The Munich District Court handed down a suspended sentence to the spy and ordered him to pay damages.

Such outcomes tend to be the exception in cases of economic espionage by foreign intelligence services and, above all, spying by competitors. These kinds of attacks are often launched via fiberoptic cables, and victims don't notice that a remote computer has stolen valuable data until it's too late. Rarely is it established whether the aim was sabotage or actually to steal know-how. Was the attack sponsored by foreign intelligence services, or were the hackers hired by direct competitors? In many cases, it isn't even possible to quantify the damage caused to the company attacked. Particularly when attacks are carried out from cyberspace, the perpetrators, background details and frequently even the actual purpose of the strike remain shrouded in mystery.

This was the case in an attack on the German Aerospace Center (DLR) in 2014, when all of its operating systems were infiltrated by trojans over the course of several months. The IT experts from the organization's cyber defense unit discovered Chinese characters in the trojans' code, but this may have been a diversion tactic by another intelligence agency. At the time, the German news magazine Der Spiegel reported that the DLR had called in the National Cyberdefence Centre in Bonn, which specializes in this kind of attack. Still, it was never determined who was actually behind it.

Espionage takes place in gray areas, and it is most successful when it remains undetected. This makes it exciting material for films and novels set in the Cold War era. But also in today's globalized and digital world, it offers a highly promising opportunity for business competitors or governments in both industrialized and emerging countries to keep pace with leading-edge developments from rival research labs abroad. However, in times of open markets and international corporations, the conditions for such espionage have changed tremendously – largely unnoticed by politicians and scientists.

SPECIALIST LITERATURE FROM THE COLD WAR ERA

When the research team at the Max Planck Institute for Foreign and International Criminal Law in Freiburg and the Fraunhofer Institute for Systems and Innovation Research ISI in Karlsruhe, headed by Michael Kilchling and Esther Bollhöfer, started work on assessing the scale of the current threat to medium-sized businesses, the researchers were surprised by how little substantiated empirical knowledge there was on economic and industrial espionage in Europe. "We realized that it's a real blind spot," says Kilchling, a Senior Researcher at the Max Planck Institute in Freiburg.

And it's not just spy thrillers that are set in the Cold War period; most of the specialist literature on economic espionage is from that era, too. The insights

Attacks from the web: The perpetrators are often in far-away places such as Russia, India or the Caribbean. It is difficult for German investigators to track them down; they are often defeated by national borders.

Dangerous insights: Trade secrets are often worth millions. Small and medium-sized businesses in particular need more support from the government to protect themselves.

were obtained before borders were opened and the European single market created, during a time when national economies still existed and were widely regarded as an asset worthy of state protection.

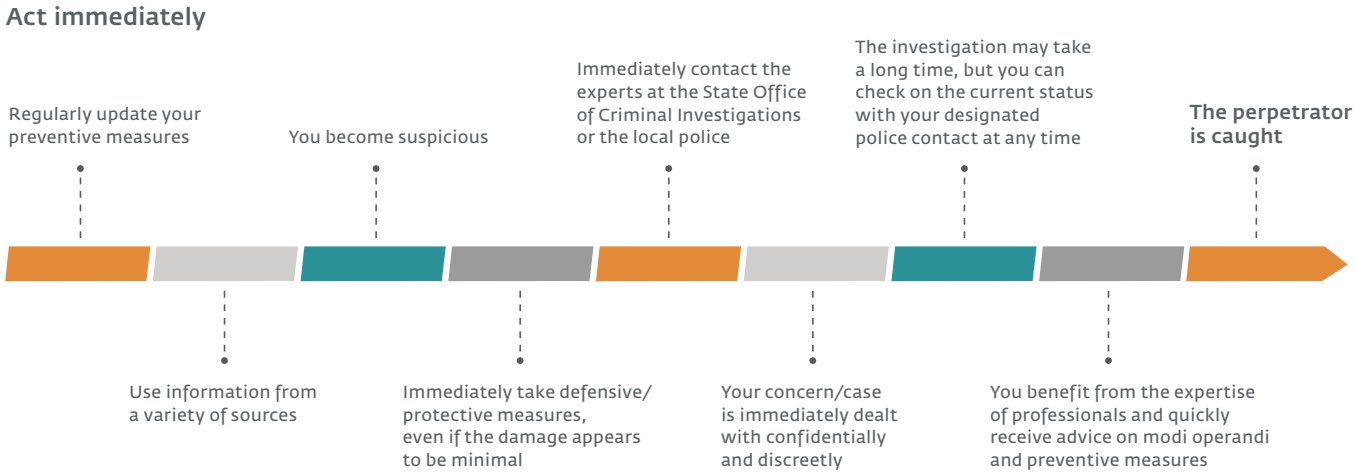
The joint WiSKoS research project aims to close this gap. The Max Planck Institute carried out the legal and criminological analysis of the cases and conducted expert interviews in other European countries, while the Fraunhofer Institute used its extensive connections with industry to conduct the survey of companies. "The collaboration proved extremely fruitful, as we have good access to public authorities and the Fraunhofer Institute enjoys an excellent reputation in industry," says Michael Kilchling. Nevertheless, the project was a challenge for everyone involved. The researchers used very different approaches and methods to analyze the status quo and, on the basis of their findings, to establish not only a core body of knowledge, but also a set of practical recommendations.

The team initially conducted a survey to obtain as comprehensive an overview as possible of the threats facing medium-sized companies in Germany. The researchers then examined the legal situation in Europe and how the authorities deal with the issue, so as to develop defensive strategies for companies and public authorities.

Esther Bollhöfer, an academic staff member at the Fraunhofer ISI, is managing the project modules that are under the responsibility of her institute. Her colleague who carried out the survey was surprised by the willingness of medium-sized companies to provide information about their shortcomings with respect to security: no fewer than 612 out of 8,300 randomly selected SMEs returned the questionnaire to the research group. One in five companies admitted they didn't have an anti-espionage strategy in place. Many of the companies would like to see the government provide more support with preven-

The team in Freiburg: Elisa Wallwaey, Michael Kilchling and Susanne Knickmeier (from left) are working on the WiSKoS project at the Max Planck Institute for Foreign and International Criminal Law.

Photo: CCO (top), Markus Herb (bottom)



Specific recommendations: The scientists advise companies to develop an anti-espionage strategy before it's too late. This includes suitable preventive measures and a plan governing how employees and management should respond in the event of an attack.

tion. Only ten companies rejected the idea of state intervention.

Despite the anonymity of the survey, few companies were willing to disclose how they deal with suspected cases internally. "This may mean that they don't wish to discuss it, but it could also indicate that they have no strategy in place," says Esther Bollhöfer. Of those who responded, the majority undertake their "own measures" – in other words, they conduct private investigations. Only a very few indicated that they would cooperate with the Office for the Protection of the Constitution, while cooperation with the police scored slightly higher.

The research team believes this reluctance to turn to the authorities is explained by the fact that it isn't easy in Germany to determine which authority to contact for which type of espionage. Responsibility for the prevention and criminal prosecution of espionage in industry is divided between the federal intelligence service and their 16 counterparts at the state level (intelligence services of the federal states), the Federal Police Office (Bundeskriminalamt), the Federal Attorney General (Generalbundesanwalt) and the local public prosecutor's offices for economic crimes, depending on the offense. These authorities incidentally also often compete for the scarce number of specialists available in the field.

The researchers identified the legal distinction between economic and industrial espionage under German criminal law as the biggest stumbling block to criminal prosecution. This is also a relic from the Cold War period, when the state had to focus primarily on protecting its own economy against espionage from the Eastern Bloc. Currently, if a foreign intelligence service is behind an attempt at espionage, the secret service may be responsible in addition to the police. The Federal Attorney General is then generally responsible for criminal prosecution, assigning the case to either the federal or state police authorities for criminal investigations.

If there is no evidence of the involvement of foreign intelligence services, it is a case of industrial espionage, for which the local public prosecutor's office is responsible with the support of the local police force. Often, the perpetrators have vanished or covered their tracks, and the investigation must be terminated.

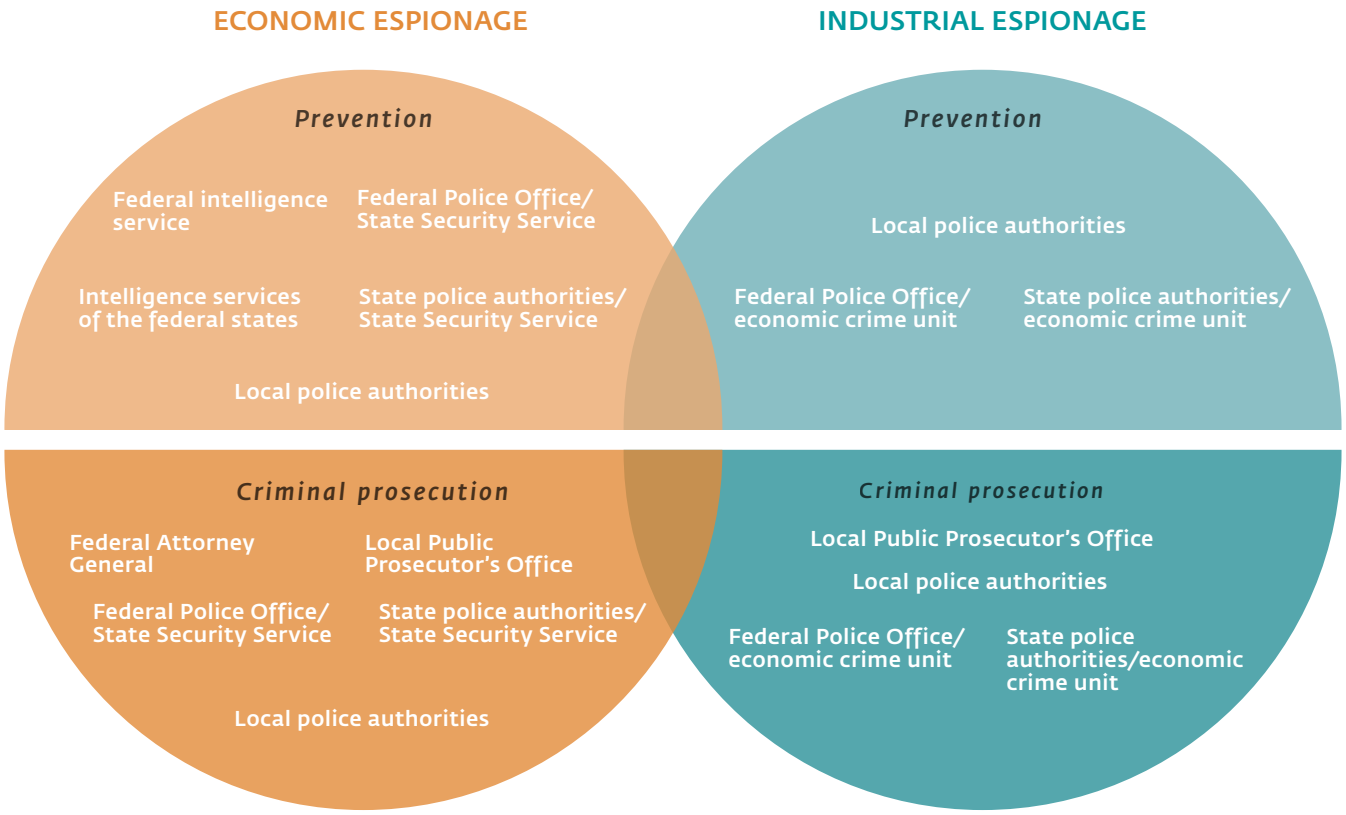
This is precisely what happened in a case that Susanne Knickmeier at the Max Planck Institute in Freiburg discovered in the investigation files. A large German company discovered that considerable amounts of data were being pulled from its datacenter. Instead of plugging the data leak, the employees responsible for the matter tried to set a trap for the cybercriminals. They allowed the data thieves to carry on with what they were doing while at the same time setting up a new system where they could secure important data. This led the spies to believe they could continue their activities undetected, and gave the authorities enough time to trace the data flows to another country.

THIN FILE DESPITE INTENSIVE INVESTIGATION

There, however, they were unable to intervene. The Federal Police Office was unable to identify the real culprits behind the attack, and the Federal Attorney General dropped the investigation. The local public prosecutor's office then took over the case and tried to determine exactly who was behind the attack – also in vain. The proceedings were eventually terminated.

"There is only a thin file," says Susanne Knickmeier, "but we know from the interviews with the investigators

Graphic: MPI for Foreign and International Criminal Law



Complex distinction: Depending on whether an intelligence service (economic espionage) or a competitor (industrial espionage) is spying, different authorities are responsible for prevention and criminal prosecution. The scientists recommend bundling these areas.

the great lengths they went to, despite ultimately failing to achieve a positive outcome." The case shows that the investigators' remit is restricted by national borders, which can only be resolved by international cooperation agreements. However, it also indicates that much time is often lost during investigations due to the different scopes of responsibility of the German authorities.

Following their interviews with companies and authorities, the research team from the Fraunhofer ISI and the Max Planck Institute in Freiburg believe that the legal distinction between economic and industrial espionage and the various areas of competence associated with it are outdated. In particular, they recommend a legislative reform that puts the focus on the companies that suffer damages. "In the era of the European single market, the national economy as a legal asset no longer exists," says Michael Kilchling, and the companies attacked aren't concerned about the political motives.

They want the leak to be plugged as quickly as possible, the perpetrator to be prosecuted, and to claim compensation, if possible. This is also reflected in the survey: the companies are willing to cooperate with the authorities if the cost-benefit ratio is reasonable and if they themselves believe there is a genuine chance of resolving the matter. Anonymity when notifying the authorities, on the other hand, was important to only a small number of the companies surveyed.

BREAKFAST MEETINGS ON ESPIONAGE PREVENTION

Kilchling and Bollhöfer see prevention as another key factor in protecting companies effectively, and suggest adopting approaches used in other European countries. Just how differently the issue is dealt with from one country to the next reveals a great deal about the relationship between government and business in the country concerned, says Michael Kilchling. In France, where the two sectors traditionally have close ties, the "Economic Warfare School of Paris" was established in 1997. At this postgraduate institution, 50 students spend ten months learning about the principles of economic warfare – that is, how to obtain strategic information about competitors – as well as about how to protect against espionage. Those who complete this postgraduate program often go on to work for security consulting firms or in the strategy departments of major corporations.

With regard to prevention, Germany could learn a great deal from the UK and Denmark. In the UK, espionage prevention is conducted primarily in informal groups and breakfast meetings to which companies gain access only once they have completed advanced training courses funded by the government. Business leaders, security experts and public prosecutors get to know one another here and establish

Graphic: MPI for Foreign and International Criminal Law

networks of trust. Trust is vitally important to successful cooperation in the event of an actual attack.

Denmark has also been successful with informal networks. Here, there is also an extensive informal flow of information between authorities and the business community, with SMEs also participating. The Danish government also requires all listed companies to document and assess their espionage risks and anti-espionage security measures.

As a result, general security standards have become prevalent in Denmark – and not just in listed companies. Numerous German companies would also voluntarily comply with these government requirements. More than half of the companies surveyed deemed a kind of state espionage certification to be "very good" or at least "good." They would also like to see more information events organized by the government and have personal designated contacts at government agencies.

But a comparison with other European countries also shows that German companies aren't spied on more often than firms in other countries. This is reassuring, in one respect, but also something of an affront in view of German industry's reputation for innovation worldwide. Companies that have not only a production facility abroad, but also research and development departments, are spied on more often. These branches, which are usually smaller and less secure than departments at the head office, are particularly vulnerable. "Conversely," as Esther Bollhöfer interprets it, "this also suggests that spies find it hard to penetrate headquarters in Germany."

An often-underestimated risk, as also revealed by the WiSKoS Research Group, is espionage at universities. Researchers and students, particularly at technical universities, often work with confidential data from industry, which frequently passes through the hands of dozens of research assistants. This makes protection quite difficult. Spies also try to steal research data via the internet.

RESEARCH INSTITUTES TARGETED BY SPIES

The Max Planck Institutes themselves are constantly being targeted by hackers. Rainer Gerling, an IT Security Officer at the Max Planck Society, can recall many ingenious attacks. The spies weren't only interested in discoveries in biomedicine or new developments in materials research. "Researchers who examine political and economic relationships and who possibly offer consulting in these fields are targets, too," reports Gerling. "When social scientists delve into the social structures of minorities in certain countries, there is always interest in obtaining this information."

The fact that science depends on international exchange complicates efforts to protect research data. Visiting scientists from all over the world spend several weeks or months at research institutes, work in their laboratories and take part in meetings, obtaining insight into technologies, methods and approaches that have not yet been published. "Many research institutes aren't even aware of the danger," points out Max Planck researcher Susanne Knickmeier. Visiting professors and students from abroad obviously can't be placed under general suspicion. On the other hand, the intelligence service also warns that countries such as China expect their students abroad to maintain contact with their embassies, enabling the intelligence service to enlist them at any time.

Universities could therefore be expected to show some degree of awareness. However, when the WiSKoS researchers were looking for universities willing to discuss the dangers of espionage, Elisa Wallwaey from the Max Planck Institute recalls this reply from one institution: "We would be pleased to discuss this matter with you. But what makes you think that we could be at risk?"

The WiSKoS team has since finished evaluating the results. In May, the researchers presented their findings at a closing conference in Brühl, near Bonn, under the aegis of the Federal Police Office. At the same time, they also published their own guidelines with practical recommendations for companies, police authorities and scientific organizations. After all, the project's stated goal is to apply the findings as directly as possible so as to make the work of the spies at least a bit more difficult. ◀

TO THE POINT

- **Industrial espionage, especially via electronic means, poses an increasing risk to small and medium-sized businesses in Germany; very few are equipped to deal with this.**
- **The legal distinction between economic and industrial espionage under German criminal law makes it more difficult to prosecute the perpetrators. It would be better if the authorities joined forces.**
- **To improve prevention, the researchers recommend government-defined security standards and better networking between authorities and industry before espionage occurs.**
- **Academic and research institutions should also protect themselves against espionage.**

Molecules – On Ice

Cryo-electron microscopy facilitates the precise imaging of tiny structures, such as molecules, right down to the atomic level. For their contribution to the development of this technology, British molecular biologist Richard Henderson, German-born American researcher Joachim Frank and Swiss biophysicist Jacques Dubochet were awarded the Nobel Prize in Chemistry in 2017. At the **Max Planck Society's Fritz Haber Institute** in Berlin, former Research Group Leader Friedrich Zemlin was also involved when the method carved out a place for itself in biology in the 1980s.

TEXT **ELKE MAIER**

In order to make inroads into the tiniest dimensions of life, scientists like to put their research objects on ice: they place them on a tiny grid and immerse them at lightning speed in an ethane bath at minus 196 degrees, causing the sample to freeze within a few thousandths of a second. They then use electron beams to X-ray their flash-frozen specimen.

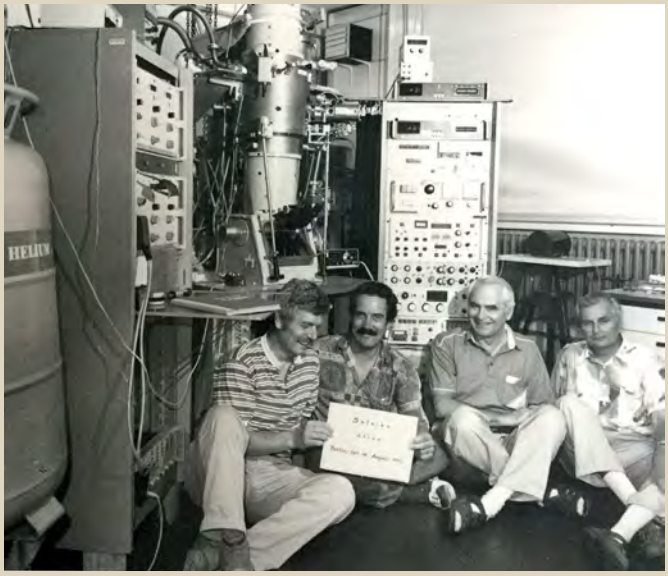
Using this cryo-electron microscopy (*kyros* means "cold" in Greek), they compile thousands of individual images to form one composite image – with spectacular results. Bacteria that attack cells, the most delicate structures on the surface of the Zika virus, and incorrectly folded proteins in the brains of Alzheimer's patients are just some of the images they've obtained. Researchers can even "freeze" molecules in motion to visualize the complicated processes in the cell interior, such as the manufacture of proteins in the ribosomes, the protein factories of the cell.

For a long time, though, no one believed that the electron microscope would ever be suitable for imaging biological objects: to ensure that the electrons are diffracted solely by the specimen, there is a high vacuum in the interior in which hydrated specimens, such as cells, would normally dry out immediately and shrivel up into unrecognizability. On top of this, there is the damaging effect of the radiation: Ernst Ruska, the inventor of the electron microscope, once even caused a metallic filament to evaporate – not a good sign for the far more sensitive biological samples!

Richard Henderson, too, who carried out research on membrane proteins at the MRC Laboratory of Molecular Biology in Cambridge in the 1970s, initially didn't even consider the electron microscope. Instead, he tried to ascertain the structure of proteins using X-ray crystallography – the method of choice at that time. However, he soon reached the limits of this technology: some proteins couldn't be obtained in sufficient quantity, while others didn't form any crystals at all. That left the electron microscope as the only device capable of displaying the molecules in their natural environment – the cell membrane.

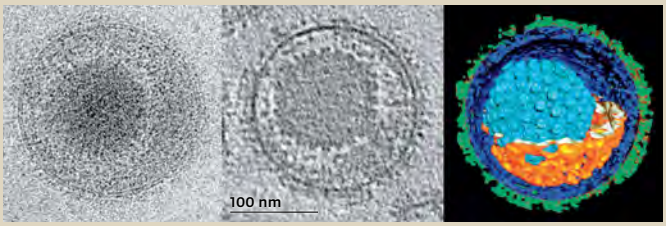
Henderson's favorite protein was bacteriorhodopsin – a red pigment that exists in the cell wall of the halophilic (salt-loving) archaeon *Halobacterium salinarum* and sometimes colors entire salines red. To image the protein in its original state, he and his colleague Nigel Unwin placed the entire membrane in the microscope and selected the lowest radiation dose possible. The trick that helped the researchers was to coat their specimens with a sugar solution, which proved to be effective protection against dehydration. Because the protein had such a regular shape, it was possible to reconstruct its structure in 3-D even with the low-contrast images.

The photo appeared in the journal Nature in 1975 and shows how the molecule's protein chain weaves its way through the cell wall seven times. The resolution is 0.7 nanometers (billionths of a meter) – roughly the length of seven atoms laid side by side. At the time, it was the best depiction of a protein that had ever been achieved with an electron microscope.



Saying goodbye to SULEIKA: Friedrich Zemlin and his team gather one last time in front of the cryo equipment that was used to produce the Nobel Prize-worthy images of bacteriorhodopsin. The famous lens was subsequently removed and installed in a more modern microscope. From left: Friedrich Zemlin, Rolf Meilicke, Erich Beckmann and Klaus Heinrich.

Photo: Bärbel Lehmann



History of a virus: The researchers capture their object from various angles to get a 3-D view of *Herpes simplex*. They combine these 2-D snapshots to form a composite image. Shown here are a microscope image (left), the reconstructed and denoised tomogram (center) and a 3-D reconstruction (right).

But Richard Henderson wasn't yet satisfied. He wanted to show the precise atomic structure of his molecule. In particular, the work that was being done by a team in the Electron Microscopy Department at the Max Planck Society's Fritz Haber Institute (FHI) in Berlin convinced him that there was still room for improvement: in 1984, Elmar Zeitler and Friedrich Zemlin, together with colleagues from the University of Arizona, published the structure of the rattlesnake venom Crotoxin with a resolution of 0.35 nanometers.

"We had a superb microscope at the Institute," says Friedrich Zemlin. "In particular, the helium-cooled, superconducting lens developed at Siemens in Munich by physicist Isolde Dietrich was fantastic. It was part of a laboratory setup that we had put together at the FHI and dubbed SULEIKA, a German acronym for *supraleitende Kryo-Apparatur* – superconducting cryo-equipment." From 1984 on, Richard Henderson frequently traveled to Berlin to work with SULEIKA.

On the other side of the Atlantic, at the New York State Department of Health, Joachim Frank had already been tinkering with image-processing algorithms for several years. The German-born researcher, who later acquired American citizenship,

DIE ZEIT, January 22, 1982

» It seems that low-temperature microscopy and deep-freezing herald a new chapter in molecular biology: the direct observation of the most elementary vital processes under the microscope.

had been a doctoral student at the Max Planck Institute for Protein and Leather Research in Munich, the forerunner to the Max Planck Institute of Biochemistry in Martinsried. His mentor was Walter Hoppe, an expert in X-ray crystallography who had moved into electron microscopy in the early 1970s.

Hoppe's specialty was the 3-D reconstruction of complex molecular structures, such as enzymes. Using tomographic technology, he imaged one object from various angles and combined the images on the computer to form a three-dimensional composite image. The main problem with this was that the harmful radiation dose increased as a result of the multiple photos.

Frank tried to avoid this by producing a single snapshot of several identical particles in a solution. This reduced the radiation exposure considerably. However, it made analyzing the image all the more complicated, as the particles were jumbled up and crisscrossed and often didn't stand out well from the background. Contamination also occurred, which was a huge challenge, particularly given the lack of computer processing power at the time.

Nevertheless, Frank managed to develop algorithms to search through the widely scattered particles for recurring structures and to form from them a sharp, three-dimensional composite image of the structure. Together with physicist Marin van Heel, who later also worked as a researcher at FHI and who is considered to be a pioneer in the imaging of individual molecules, Frank published the first programs in 1981. Frank's SPIDER software package, a comprehensive tool for computer-based image analysis, was published that same year.

One issue remained outstanding: how to protect biological samples from drying out in the vacuum of the electron microscope. Richard Henderson used a sugar solution in his bacteriorhodopsin studies, but that wasn't suitable for all specimens. Some researchers had already tried to freeze their samples, but ice crystals formed in them, which destroyed the delicate structures in the sample and also deflected the electron beam.

That ice really was the way forward was proven by Jacques Dubochet, who was researching precisely this issue at the European Molecular Biology Laboratory (EMBL) in Heidelberg at the time. One idea was to chill the sample so quickly that there was no time for ice crystals to form. Many colleagues considered this to be a utopian dream, as, in order for this to happen, the sample would have to reach a temperature of less than minus 150 degrees Celsius within a few thousandths of a second – a cooling rate of more than 10,000 degrees Celsius per second.

But Dubochet managed to achieve the seemingly impossible. To do this, he cooled water in fractions of a second in an ice-cold ethane bath, freezing the liquid as a glass-like mass – a state researchers call vitrified water. The method proved to be ideally suited to keeping biological specimens from drying out in the vacuum of the electron microscope: vitrified water doesn't form destructive ice crystals, and it allows the electrons to pass unhindered. In addition, the low temperature protects against radiation damage. "Using cryotechnology, we succeeded in imaging paraffin molecules with an electron microscope in the mid-1980s," says Friedrich Zemlin. "That was a real breakthrough, as the long hydrocarbon chains are extremely sensitive to electron beams."

Soon afterwards, the electron microscope became firmly established in biology, as well. Richard Henderson and his colleagues published the first image of a protein at atomic resolution in 1990: after years of painstaking work, the researchers finally succeeded in imaging bacteriorhodopsin at a resolution of 0.35 nanometers. To do this, they combined hundreds of individual snapshots in the computer to form a high-resolution 3-D structure; most of the images came from SULEIKA. Friedrich Zemlin and his colleague Erich Beckmann are two of the co-authors of this pioneering work.

The legendary lens that was used to capture the images was later installed in a more modern Philips microscope and is now located in the Max Planck Institute for Biophysical Chemistry in Göttingen. Institute Director Holger Stark, formerly a doctoral student with Friedrich Zemlin and Marin van Heel at the FHI, had "inherited" the device and taken it with him when he moved to Göttingen in 2001. It was used successfully there for several more years.

Photo: Science 302, 1396-1398 (2003)

Countdown to Summer Schools

The courses offered by the Max Planck Institutes will again reach around 900 young scientists this year

The idea of universities offering summer schools during the course-free period originated in the US, but it has since found its place at the Max Planck Institutes, too. Although they are not universities, programs like these still open the doors to young academics and offer insight into research. Frequently organized by the International Max Planck Research Schools (IMPRS) for doctoral education and with other partners, this summer, more than 15 such specialized courses are being offered.

The courses differ from one institute to the next, both in duration and content. Group sizes can also vary according to focus, and there is generally a selection procedure for each program. Such is also the case for the 8th IMPRS NeuroCom Summer School at the MPI for Human Cognitive and Brain Sciences in Leipzig, where around 140 participants are expected. For three days in late June, lecturers will introduce and expand on cognitive neuroscience techniques and tools; two of the focus topics are "Modeling the Mind" and big data. In the words of the organizers: "We've invited leading international experts as well as lecturers from Leipzig and around Germany." Together with other building blocks, such as the Summer School Poster Award, they aim to offer an "unforgettable experience with inspiring lectures, discussions and icebreakers to help participants get to know one another."

As here at the MPI for Computer Science Summer School in Saarbrücken last year, the MPG will again offer more than 15 such specialized courses in 2018.

The Max Planck Summer Academy for Legal History will be hosted at the MPI for European Legal History in Frankfurt/Main for the fifth time. The motto of this two-week course is "The world and the village – the global and local dimensions of legal history" and it is fully booked with around 30 participants, mostly doctoral students. Material will be conveyed in two stages: the first block provides insight into the scientific study of sources, including use of the institute's library, and into basic methodologies, theories and controversial schools of thought in the field of legal history research. In the second part, the focus will be deepened and students' own research discussed.

And like many of the MPI Summer Schools, the curriculum in Frankfurt isn't restricted solely to academic activities. It also includes, for instance, participation in the institute's summer festival, a group tour of the city and a visit to the university campus.

https://www.mpg.de/10704527/summer-schools

German-Chinese Exchange in Shanghai

Varied program addresses trends in research and provides career advice

Max Planck Partner Groups reinforce the bond between international researchers who return to their homeland after their stay at an MPI and their former institute. One focus of this program is China, which is why the Partner Group leaders there were offered the opportunity to get to know each other better. The opening keynotes were delivered by chemists Klaus Müllen, Director Emeritus of the MPI for Polymer Research (photo: back left), and Markus Antonietti, Director at the MPI of Colloids and Interfaces, who also maintain contact with young Chinese researchers through the Partner Group program. In addition to the opportunity to network, several panels were held in which individual research projects were discussed. The Chinese scientists work at facilities of the Chinese Academy of Sciences (CAS) or at universities such as Shanghai Jiao Tong University, where this meeting took place.

Photo: Oliver Dietze / MPG

Minerva Fellows Meet in Munich

Fifteen young scientists receive new scholarships from the Foundation

The selection committee meets twice a year, once at the Weizmann Institute in Rehovot and once in either Munich or Berlin. This working session is traditionally linked to a framework program. While the German Minerva Fellows employed at local research institutions are invited to the meeting in Israel, the Israelis working in Germany gathered in Munich. Together, they went on a guided city tour that, in addition to the tourist highlights, also included places of interest with regard to past and present Jewish life here. A series of scientific talks rounded out the program. Foundation officer Lou Bohlen describes the day as "very communicative, humorous, and cosmopolitan."

The following day, the Selection Committee, headed by Max Planck Director Stefan Offermanns, discussed the applications for scholarships and for German-Israeli conferences, the Minerva Schools, and the awarding of the Arches Prize.

Fifteen new scholarships – doctoral students and postdocs funded as visiting scholars for up to three years or two years, respectively – were awarded. The Minerva Foundation has been operating under the aegis of the MPG since its founding in 1959.

Silvia Jonas, a Minerva Fellow at the LMU Munich Center for Mathematical Philosophy, gave one of the lectures.

PhDnet Visits Administrative Headquarters

MPG doctoral student representation presents a comprehensive analysis of the doctoral degree situation

"Of 4,525 doctoral students, 2,218 participated in the 2017 survey. We are pleased that the PhDnet communication strategy is so well received by the institutes," says spokesperson Jana Lasser of the MPI for Dynamics and Self-Organization. This survey among MPG doctoral students – the most comprehensive one to date – shows that striving to improve working conditions, such as vacation time and compensation, will continue to be a main concern of PhDnet.

The PhDnet board: Spokesperson Jana Lasser (center) with BMS representative Ezgi Bulca (left) and Julia Misersky (right) for the HS Section. Second row: Secretary General Mohamed El-Brolosy, CPT representative Severin Daiss and treasurer Greta Giljan (left to right).

In general, the doctoral students value the excellent facilities and the environment at the MPIs and are very satisfied overall, "but they also highlight topics such as support, mental health and career strategies," says the head of the working group, Miguel Borges of the MPI for Psycholinguistics. Among other things, his team of nine wanted to investigate the relationship between support quality and the ability to achieve a healthy work-life balance. The survey does indeed reveal a significant statistical correlation between the quality of support and stress-related symptoms. More than two-thirds of doctoral candidates state that they suffer from at least one stress-related symptom. Accordingly, PhDnet supports the fact that the MPG has now implemented initial occupational health management measures. The survey also clearly reveals that the switch from scholarships to contracts has been completed at almost all MPIs – a development that PhDnet strongly supports.

Furthermore, 45 percent of respondents state that they have little interest in a scientific career – mainly due to the difficulty of planning and reconciling such a career. In this context, the PhDnet board welcomed the important role of the new Human Resource Development and Opportunities Department at Administrative Headquarters in the future of doctoral students, as well as the introduction of the childcare allowance. On April 20, the team visited Administrative Headquarters to continue the constructive dialogue with the President.

Photo: Denise Vernillo (top), PR (bottom)

When the Senate Gets together with Iron Researchers

After the meeting, a special surprise awaited

"100 years of cutting-edge research in Düsseldorf" – a fitting motto for celebrating the anniversary of iron research (MPIE) in 2017, as the MPG Senate was able to verify for itself when the high-ranking representatives of public life once again gathered together at an MPI. "It's a great pleasure to have such an eminent body as our guests and thus to support the discussion of current topics pertaining to excellence in research," said Dierk Raabe, Director at the MPIE.

The Senate members were impressed, too – by the venue and its industrial charm, as the meeting took place in the middle of a production hall that houses laboratories with high-resolution transmission and scanning electron microscopes. These are used mainly by the Department of Nanomechanics to analyze, test and optimize various metals down to their atomic structure.

Following the session, a tour of the laboratories allowed the Senate members to paint their own picture of what the MPIE scientists do in the laboratories and workshops to develop and improve materials. In the company of external guests, such as State Secretary Cornelia Quennet-Thielen, President Martin Stratmann also took the opportunity to take part in the tour. "It is a special pleasure for me to be back here in my workplace of many years and to discuss the future of basic research. After all, the Max-Planck-Institut für Eisenforschung, with its 100 years of integrating science and industry, is also a very special think tank, in the truest sense of the word," said Stratmann.

During the tour, Michael Rohwerder introduced the Kelvin sensor, which was originally enhanced by Stratmann to detect corrosion processes at an early stage. Today, it is additionally used to detect hydrogen in metals and to understand the phenomenon of hydrogen embrittlement.

Afterwards, doctoral student Priyanshu Bajaj explained to the Senate members the principle of additive manufacturing, or 3-D printing of metals. Here, a laser beam repeatedly passes through a metallic powder. The powder layer melts, cooling shortly thereafter, and a new layer of powder is applied, creating the desired 3-D product layer by layer. Bajaj and his colleagues are working on developing new alloys using this method. Following the tour, the Senate members received a 3-D printed shopping chip with the head of Minerva. Bajaj and Group Leader Eric Jägle had the idea for the chip – it was actually intended for Max Planck Day, which invites the public throughout Germany to visit the institutes on September 14.

State Secretary Cornelia Quennet-Thielen during the tour. Doctoral student Priyanshu Bajaj explains how metallic powders can be improved for 3-D printing.

Photo: MPI für Eisenforschung

Research Establishments

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

The Netherlands
- Nijmegen

Italy
- Rome
- Florence

USA
- Jupiter, Florida

Brazil
- Manaus

Luxembourg
- Luxembourg

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