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2022
report

Promoting innovation in technology and the natural sciences

The Werner Siemens Foundation supports groundbreaking projects in the natural sciences and technology. The selected projects in research and education are generally conducted at universities and higher education institutions in Germany, Austria and Switzerland; key requirements include upholding the highest standards and contributing to solving major problems of our time. The Foundation provides generous seed funding to innovative projects with the goal that, after a few years, the projects can be run independently and the results find industrial application. The Werner Siemens Foundation also promotes education and training projects and fosters young talent, particularly in the fields of mathematics, informatics, natural sciences, technology, medicine and pharmaceutical science.

Foreword

Since the start of our philanthropic activities, the Werner Siemens Foundation (WSS) has financed no less than twenty-five outstanding research projects in the natural sciences, life sciences and technology. Every year, up to three innovative endeavours are selected, and this past year was no exception. Two new promising undertakings are now receiving WSS funding: in Potsdam near Berlin, researchers at FutureLab CERES are seeking to identify the political measures that are most effective in protecting our planet's climate, biodiversity and soils (page 74); and in Aachen, the TriggerINK project team are working on a completely novel method for cartilage regeneration in damaged joints (page 54).

Readers will note that our 2022 report has a new layout. The centrepiece is the section on medical innovations, the theme of this year's report (starting on page 22), where we not only present the details on all WSS-funded projects in the area of medicine and medical technology, but also place them in a broader context. For instance, Thomas Südhof, Nobel laureate in physiology and medicine, shares his opinions on what constitutes good research funding and discusses why translating findings from basic medical research into medical care faces so many serious obstacles (page 66).

Last year saw publication of the handsome volume *Charlotte Siemens und Marie Siemens* by historian Béatrice Busjan and archivist Yvonne Gross (page 100). The book completes the biographical series on all five women who established or endowed the Werner Siemens Foundation—and the trilogy is also a wonderful prelude to the Foundation's centennial anniversary in 2023.

Indeed, this coming May, we will be honouring the Foundation's 100th year in a celebration with the descendants of Werner and Carl von Siemens. In connection with our centennial activities, the Werner Siemens Foundation also established the Ottara Foundation in December of 2021; more information will be forthcoming at the annual family assembly.

To mark our anniversary, we are also setting an accent in the Foundation's philanthropic mission: in the autumn of 2022, we launched an ideas competition for our "project of the century". Researchers from Germany, Austria and Switzerland were invited to submit project proposals for a WSS Research Centre dedicated to developing technologies for the sustainable use of natural resources. The winning project, which will be selected by a jury, will receive total funding of one hundred million Swiss francs over a ten-year period.

I am curious to see the bold and creative ideas our unique project attracts. And I also very much look forward to all new proposals that are submitted during our centenary year.

And now nothing remains but to cordially invite you to explore our report.

Hubert Keiber,
Chair of the Foundation Board of the Werner Siemens Foundation

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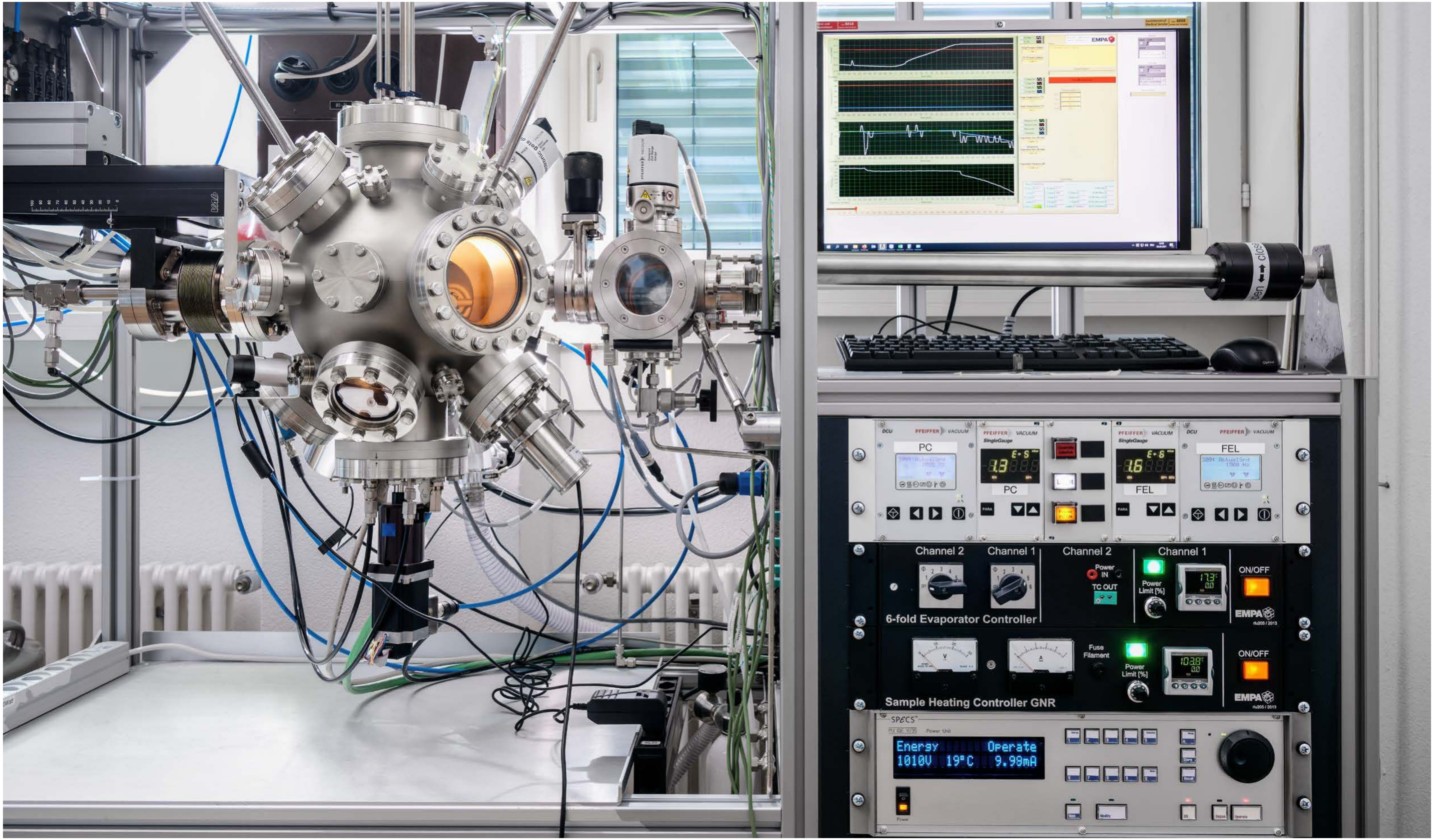
In the TriggerINK project, microgels are created to help cartilage heal.

Researchers in the MIRACLE II project plan to use models and implants from the 3D printer to improve bone surgery.

The team from the Center for Artificial Muscles conducting an experiment on their aorta ring.

When constructing a single-atom switch, contamination of any kind must be avoided.

Highly focused students at the Swiss Study Foundation summer camp in southern Switzerland.

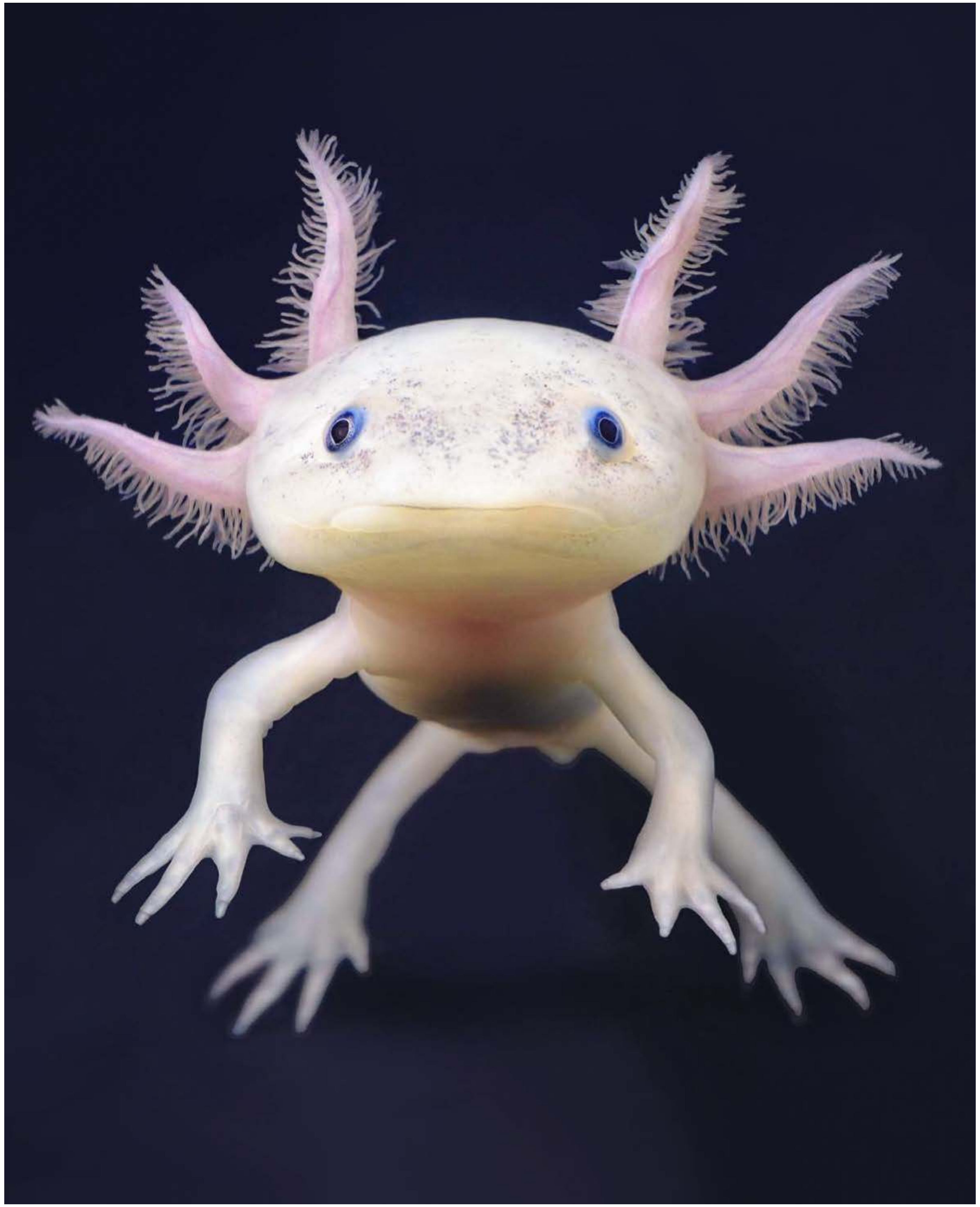


In the CarboQuant project, materials are measured in the scanning tunnelling microscope.

Researchers collect valuable climate data with the measurement instruments on board the *Eugen Seibold*.

Medical innovations

Health is our most valuable asset—and throughout history, humans have attempted to manage pain and cure disease. On the following forty-six pages, readers are introduced to the novel treatments being developed in projects financed by the Werner Siemens Foundation. In addition, a Nobel laureate explains why it's so important that we also invest in basic research.



Technology-enhanced medical care

If the salamander-like axolotl should lose a limb, it can just regrow it. Because we humans lack this rather convenient capability, doctors have been experimenting with prosthetics since the days of ancient Egypt. However, it's only today that implants are becoming a major factor in medical care. Three innovative projects financed by the Werner Siemens Foundation illustrate the advances in this area.

Humans are—quite obviously—not axolotls. For one, we lack the salamander-like animal's astonishing ability to regenerate body parts. While it's true that the human body is constantly renewing cells and cellular components, when we break a bone, lose a tooth or sever a finger in an accident, our bodies have no spare parts at the ready. By contrast, axolotls, which are native to Mexico, have a lifelong capacity to regrow almost every body part: legs, testicles, a severed spinal cord. It can even repair parts of its brain.

Perhaps these remarkable amphibians are what inspired healers in the ancient Maya civilisation—also in Central America—to implant artificial body parts into humans. Records show that, already in the seventh or eighth century of the Common Era, a Maya doctor implanted three prosthetic teeth made of polished conch shells in the mouth of a young patient. Yet the Maya weren't the earliest civilisation known to use implants: in Egyptian tombs, archaeologists have found prosthetic devices such as a wooden toe and a dental bridge made of gold to support a broken molar.

Götz of the Iron Hand

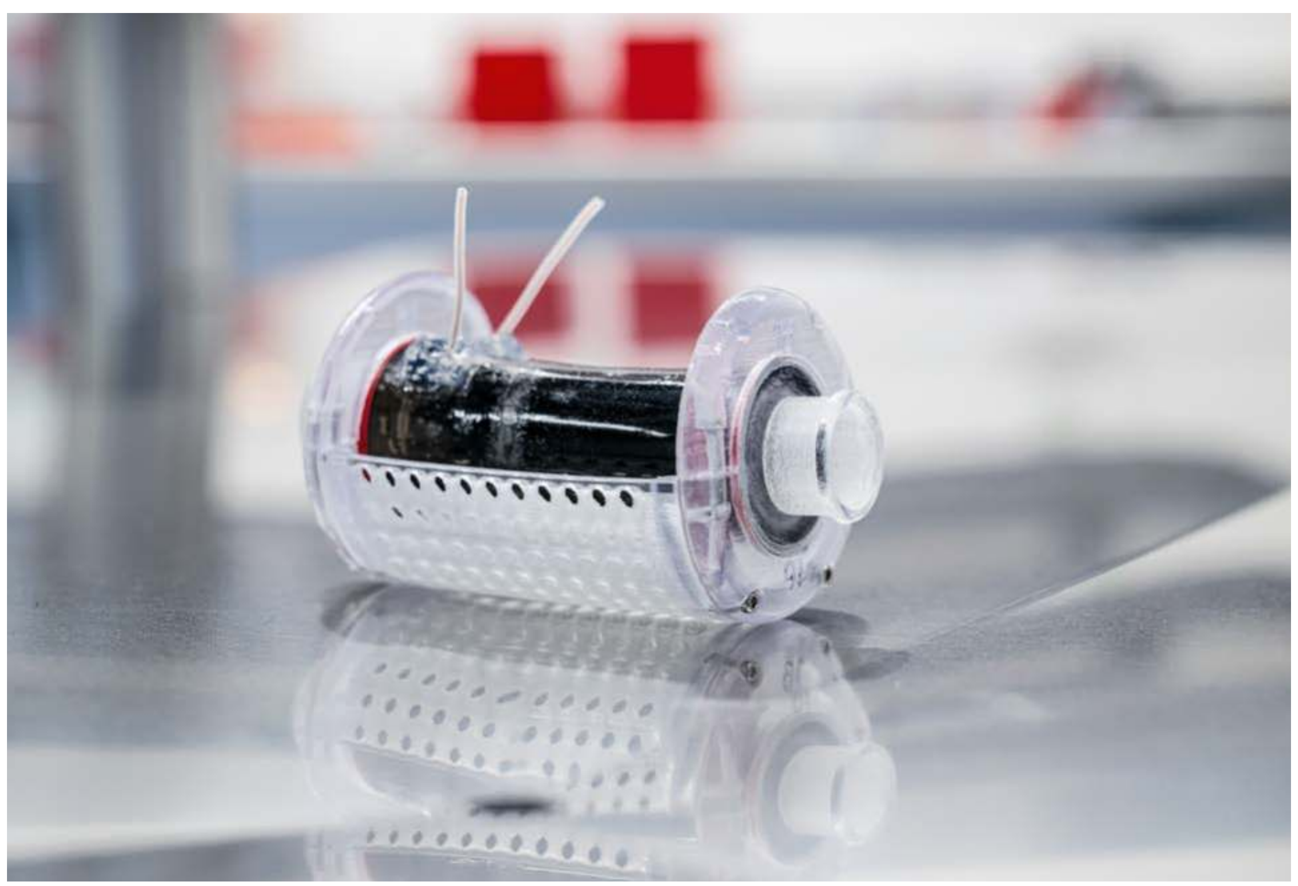
Over time, prostheses became more sophisticated. A famous example is found in Götz von Berlichingen, the Franconian imperial knight who could grasp and hold objects with his iron hand—for the early 16th century, it was a remarkable technical feat indeed. For centuries, however, prosthetics were restricted to use *on* the body. Implanting them *inside* the body was deemed impossible, and related attempts inevitably led to haemorrhaging and infections. Advances weren't made in this area until the 19th century when, for instance, Berlin surgeon Themistocles Gluck successfully implanted the first knee prostheses in 1890 by using cement to affix ivory replacement parts to bones infected with tuberculosis.

During and after the First World War, the development of—and, sadly, the need for—prosthetics made great advances due to the many war wounded. And the period following the Second World War saw a veritable surge in medical technology: metallic plates to stabilise hip fractures entered the market as did titanium hip and knee replacements as well as splints for backbones damaged by cancer. The first artificial cardiac pacemaker was implanted in a patient in Stockholm in 1958, and the first artificial heart valves were developed in the 1960s.

First artificial kidney—a washing machine drum

Since then, research into implants and prosthetics has progressed rapidly, and today scientists are experimenting on devices capable of carrying out actual body functions—a development that would astound earlier generations. One such project is underway at the Center for Artificial Muscles, located on the Neuchâtel campus of the École polytechnique fédérale de Lausanne (EPFL), where microengineer Yves Perriard and his team are creating an artificial muscle to help patients with cardiac insufficiency. The Werner Siemens Foundation has been financing the Center since 2018.

The researchers at the Center for Artificial Muscles are using a membrane made of a highly elastic material (black) to support the aorta's functioning in patients with cardiac insufficiency. A protective cover of hard plastic prevents the membrane from coming into contact with other substances.



Combining microengineering and state-of-the-art medicine: Yves Perriard (centre) in discussion with his colleague Yoan Civet (left) and cardiac surgeon Paul Philipp Heinisch from the Deutsches Herzzentrum in Munich.

Something of a buff in the history of prosthetics, Perriard relates the story of Dutch doctor Willem Johan Kolff, who invented the artificial kidney. Kolff constructed his first model in the 1940s, a device that resembled the drum of a washing machine but was made of wood and wrapped in a membrane. The contraption was placed next to patients whose blood was transferred in tubes through the membrane. The drum's rotations are what propelled the blood in the tubes through a cleansing solution—the principle behind modern-day dialysis. "Those were very different times in implant research," Yves Perriard says. "Kolff was a medical doctor who developed these technical devices himself."

In general, Kolff is considered a pioneer in the field of artificial organs: in addition to inventing the artificial kidney, he helped develop the Jarvik-7, the first artificial heart to be successfully implanted in a patient in 1982. "At the time, Kolff predicted we'd be able to replace all body organs with artificial organs in a few decades," Perriard says. "But he didn't quite account for how complex the human body is."

The advent of novel materials

Still today, even seemingly trivial processes in the body pose nearly insurmountable challenges to researchers. A prime example is blood flow, Perriard explains. The extreme delicacy of blood cells makes the dynamics of blood flow highly complex in comparison to fluids like water. "Many blood cells are damaged when they come into contact with the hard materials of artificial devices—even in pumps like the Jarvik artificial hearts, which are really quite gentle."

This line of thinking is what sparked the idea that would later give rise to the Center for Artificial Muscles. "I was saying we needed a system that works without copper or steel," as Perriard explains. Although not entirely serious at the time, he came across the principle of dielectric elastomer actuators (DEA) in 2012. DEA are novel, highly elastic materials that convert electric energy into mechanical work on the basis of a simple functioning principle. "That's when I began thinking we could use the principle for a novel kind of implant," Perriard says.

At the Center for Artificial Muscles, the micro-engineers are now applying the principle to develop an elastic membrane that fits like a ring around the aorta. An electrical impulse causes the ring to dilate and contract, thus supporting the aorta's functioning. In 2021, the team, which includes doctors such as cardiac surgeon Thierry Carrel, implanted the first-ever artificial muscle in a pig. “The concept worked,” Perriard says, “but the mechanical energy generated was too weak to support the heart.” To increase pumping capacity, the researchers decided to build a new implant capable of withstanding a higher voltage. New animal experiments are planned for the end of 2022.

Helping children with heart defects

This past year saw the team make two additional advances. First, they reduced the size of the power source: a wireless device that supplies electric energy to the artificial muscle and that patients are to wear on their belt. “Before, it was the size of a box, and now it’s ten by ten centimetres,” Perriard says.

The other major development is a new subproject in the group. As Perriard explains, “The cardiac centre in Munich approached us with the idea of using our technology to treat children with univentricular hearts.” Normally, bypass surgery is the solution in such cases, but there’s no pressure to support pumping in the bypass. “It’s possible that our system could deliver this pressure.” One problem, however, is that no laboratory animals have this heart abnormality: “It means we have to model our solution with extreme precision.”

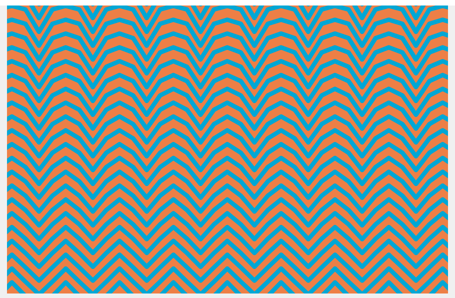
Challenges like this are what Perriard finds most interesting in today’s implant research. “The entire field is seeing exciting developments right now,” he says. In addition to novel materials making entirely new approaches possible, the branch of implant research is now inherently interdisciplinary—unlike in Willem Johan Kolff’s day. In addition to the doctors in Perriard’s team, materials researchers as well as modellers and electrical engineers all play a vital role.

Implant to promote healing

Tim Pohlemann, director of the Department for Trauma, Hand and Reconstructive Surgery at the Saarland University Medical Center, agrees: “Looking beyond traditional disciplinary boundaries is incredibly important. Today, major advances in medicine are often driven by new technologies, not medical research.” He and his colleague Bergita Ganse lead the “smart implant” project, which has been financed by the Werner Siemens Foundation since 2019.

It’s precisely with the help of novel technologies from materials science and engineering that the team in Saarland are designing their intelligent implants. Their devices are designed to promote healing in complex bone fractures by monitoring the healing process, detecting incorrect weight-bearing—and stimulating the healing process through targeted, autonomous movements at the site of a break. Indeed, fractured bones knit faster when the break is stimulated through micromovements, as earlier studies have shown.

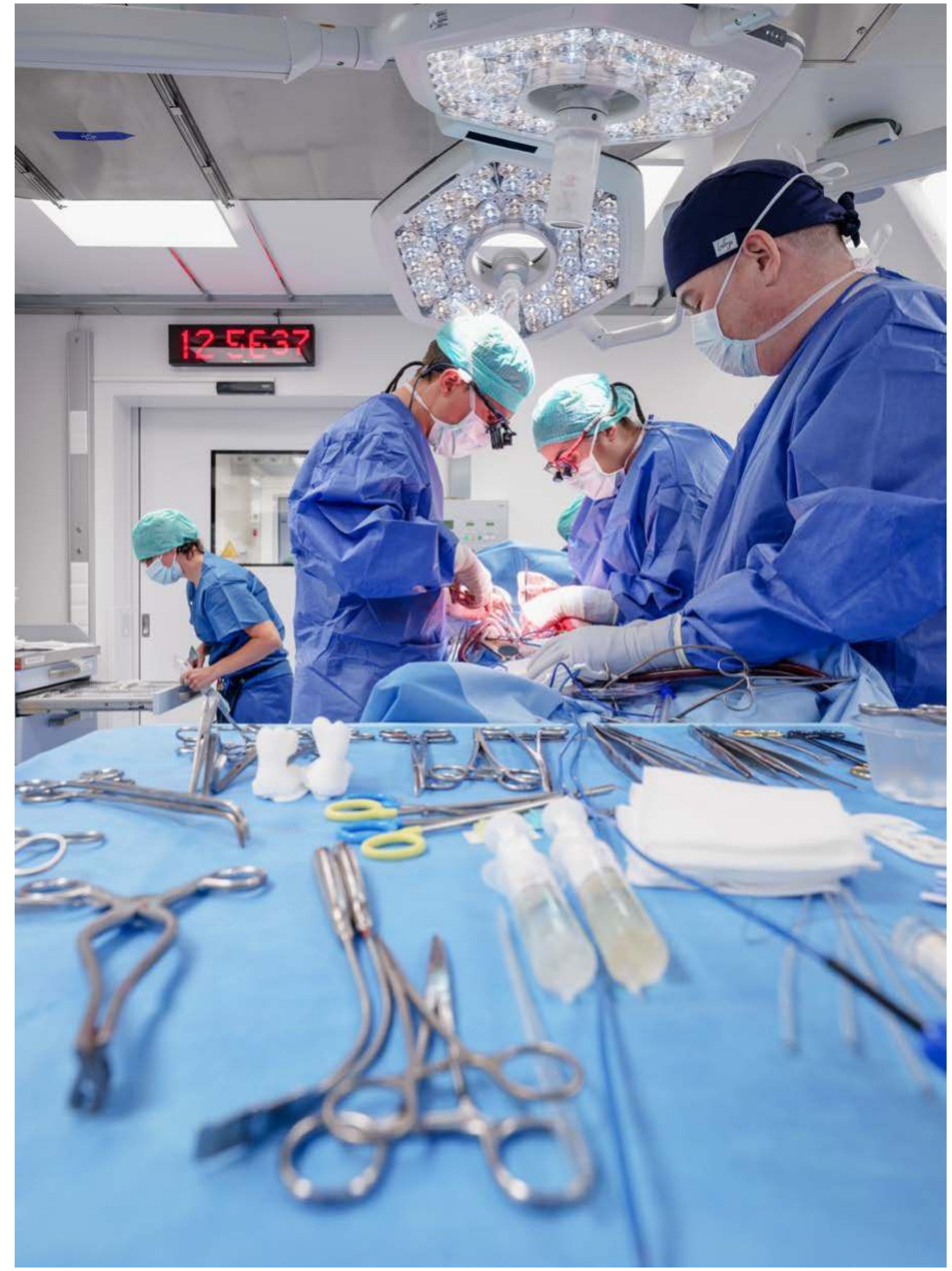
To trigger these micromovements, a smart implant must have the capacity to move or change its shape in response to an electric signal, and then return to its



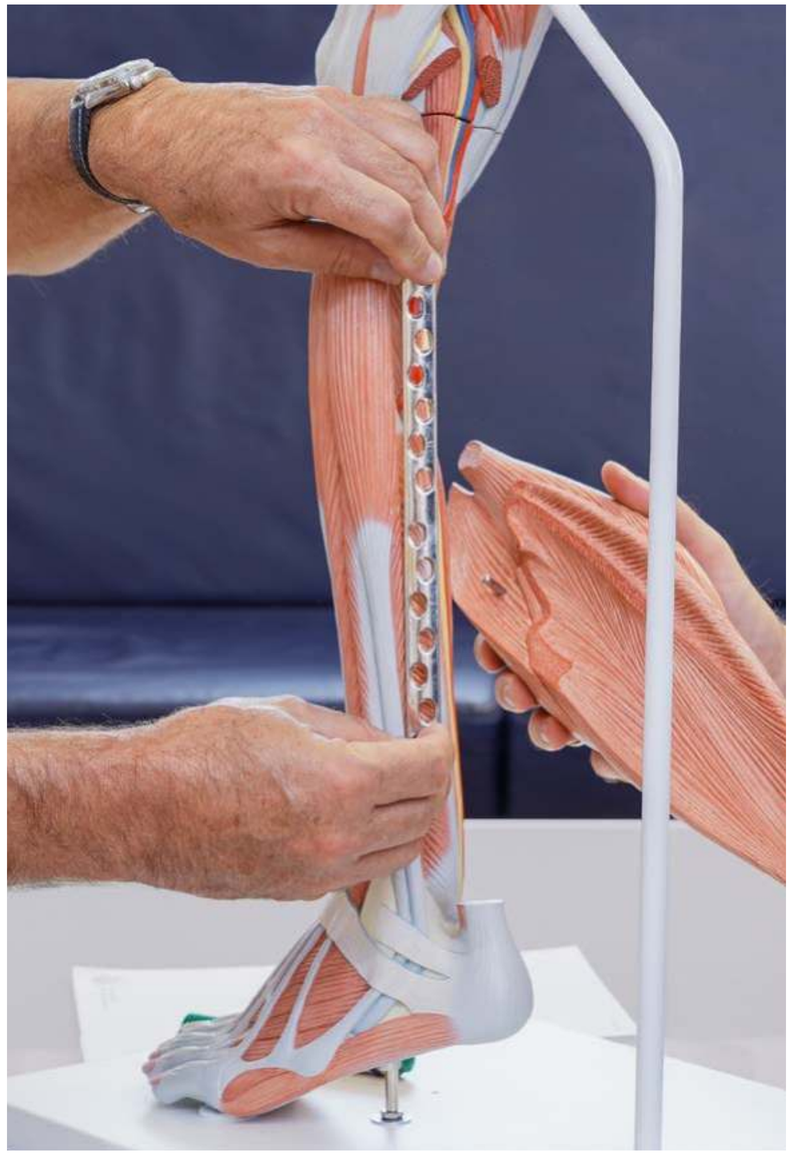
Artificial muscles

Cardiac insufficiency is a common disease, affecting one in every fifty adults. At the Center for Artificial Muscles, located on the Neuchâtel campus of the École polytechnique fédérale de Lausanne (EPFL), researchers are working on a state-of-the-art solution to help patients—they’re creating an artificial muscle that will give weak hearts a boost. Their idea is to place a ring-shaped electroactive polymer around a patient’s aorta. Powered by an external battery worn by the patient, the ring dilates to expand the artery in rhythmic intervals.

Funding from the Werner Siemens Foundation 12 million Swiss francs
Project duration 2018 to 2029
Project leader
Prof. Dr Yves Perriard, director of the Center for Artificial Muscles and the Integrated Actuators Laboratory (LAI), EPFL

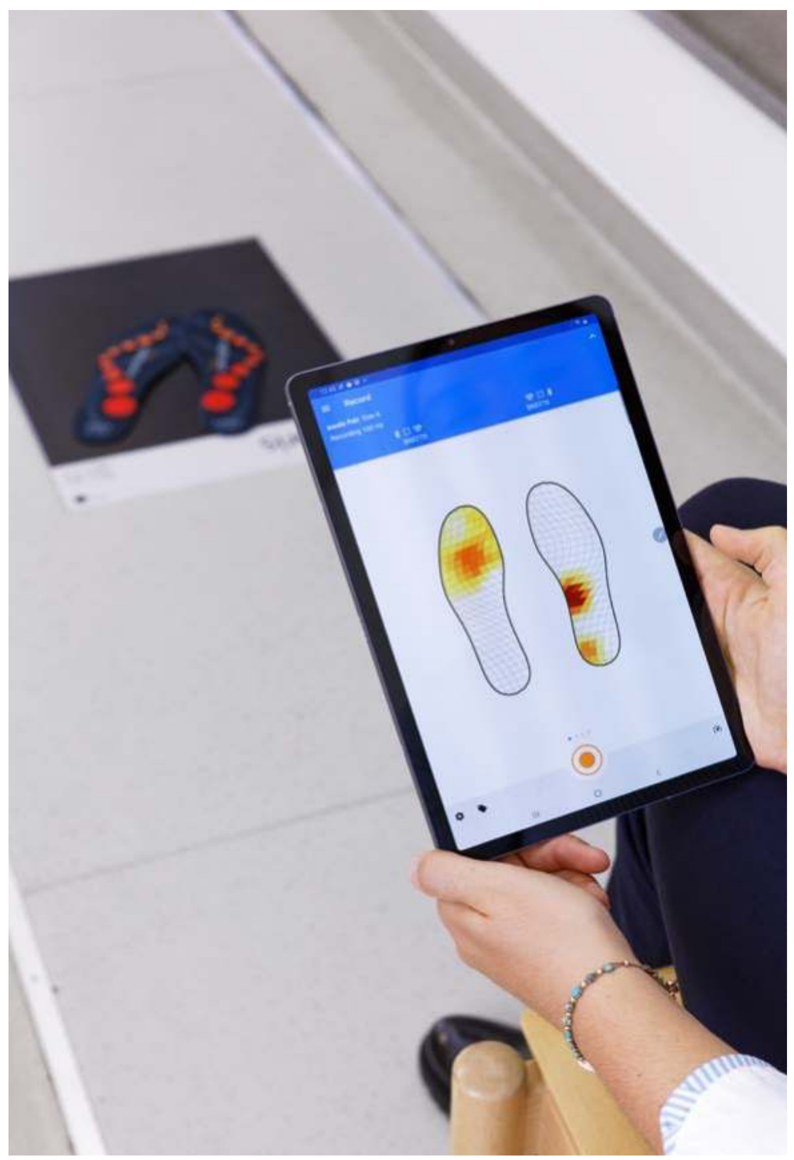


Tests on animals: before clinical trials on humans can be conducted, the researchers at the Center for Artificial Muscles must first test the aorta ring on laboratory animals.



Hitting the spot: correct placement of the smart implant in a shin bone is all-important.

The results of a gait analysis show the Saarland researchers how much weight a patient is placing on a broken leg.



original shape. For their prototypes, the team are currently working primarily with superfine wires made of nickel-titanium alloy that are embedded in the implant. “But we need to keep our eyes open,” Pohlemann says. “There are hundreds of different materials—one of them might be a better fit for our project.”

Controlled movements permitted

When completed, the active implants would represent nothing short of a quantum leap in the history of treating broken bones. When the use of plates to set fractures was first introduced back in the 1960s, surgeons had a simple task, as Pohlemann explains: “Their goal was absolute stability. After an operation, the idea was to leave no gaps at the fracture site.” Later, “relative” stability was the aim, and a little bit of leeway was accepted after the role of motion in fostering healing became clear. “The objective today is controlled stability, meaning we allow only very specific movements,” says Pohlemann.

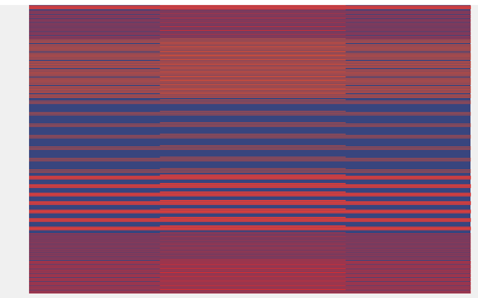
Although the path to market entry remains long, Pohlemann says the project is “skipping several generations in implants”. In fact, the advances the team have made are impressive: for example, the researchers succeeded in building a so-called demonstrator—an implant made of metal and synthetic material that is small enough to fit into the shin bone. Depending on the electric signal sent, the implant expands or contracts.

When developing an active implant, the meticulous investigation of each and every technical aspect is essential. However, it’s equally critical to understand the medical processes involved in healing. “To this day, we don’t understand why every seventh lower-leg fracture fails to heal properly, even with an implant,” Pohlemann says. That’s why the completion of the gait analysis lab was one of the year’s highlights. Roughly twenty patients have already been equipped with sensors, and detailed measurements of real-world healing trajectories are being compiled in the lab, Pohlemann explains, adding, “We’re now building a data pool that will grow rapidly.”

3D printers by the score

Developing smart implants is also one of the goals pursued in the MIRACLE and follow-up MIRACLE II project at the University of Basel and the University Hospital Basel, which the Werner Siemens Foundation began financing in 2015. The researchers are constructing a surgical robot that will one day be capable of using a laser to make minimally invasive incisions or drill holes in the diseased or fractured bones of cancer or accident patients (see page 44). Because the laser can cut different shapes in the bones, the innovation opens the door for entirely new ways of using implants. For instance, bones and implants could be fitted together like puzzle pieces—and remain in place without screws or plates, as is currently the practice.

To manufacture the customised implants, Florian Thieringer, co-project leader of MIRACLE II, is working with 3D printing technology. 3D printing has been used



Smart implants

In future, intelligent implants fitted in a bone will be able to directly monitor how well a lower-leg fracture is healing. A research team at Saarland University Medical Center are working on the innovative smart implants that, in addition to stabilising a broken bone, will provide information on how well the fracture is healing and detect incorrect weight-bearing. If a break isn’t healing well, the implant will react and, if necessary, trigger targeted movements to actively stimulate healing at the site of the fracture.

Funding from the Werner Siemens Foundation 8 million euros
Project duration 2019 to 2025
Project leaders
Prof. Dr Tim Pohlemann, Prof. Dr Bergita Ganse, PD Dr Marcel Orth, Prof. Dr Stefan Diebels, Prof. Dr Stefan Seelecke, Prof. Dr Phillipp Slusallek at the Department of Trauma, Hand and Reconstructive Surgery, Saarland University Medical Center

MIRACLE II

Gentle, minimally invasive, robot-guided and highly precise bone surgery—this is the aim of the MIRACLE II project at the University of Basel. Researchers in the project are constructing an endoscopic laser robot capable of making ultrafine incisions in bones, while miniature sensors and a 3D software program are designed to promote patient safety during surgery. In the hospital's in-house 3D printing lab, made-to-measure implants will be fabricated to fit in the pre-cut bones. All these developments mean that bones can heal faster after an intervention.

Funding from the Werner Siemens Foundation 12 million Swiss francs
Project duration 2022 to 2027
Project leaders
Prof. Dr Philippe Cattin, head of the Department of Biomedical Engineering (DBE) at the University of Basel
Prof. Dr mult. Florian M. Thieringer, senior physician for oral and cranio-maxillofacial surgery and head of the Swiss MAM research group at University Hospital Basel
Prof. Dr Georg Rauter, head of Bio-Inspired RObots for MEDicine Lab (BIROMED-Lab) at DBE at the University of Basel

in medicine for over thirty years, says Thieringer, who was recently appointed professor at the University of Basel and named senior physician for oral and cranio-maxillofacial surgery at University Hospital Basel. For example, he says, in the 1980s, printed models of skulls were very useful in planning surgical interventions: "For the first time, doctors were able to hold the anatomy of a patient in their hands and, quite literally, grasp it." Later, the technology advanced so far that perfect, made-to-measure implants could be produced.

Folding implants

To begin, only expensive supercomputers had the capacity to print 3D objects, but today, commercial computers can also master the task. For several years, the University Hospital Basel has maintained its 3D printing lab, mainly to fabricate patient-specific models; now, the lab is being certified to produce patient-specific implants. Thieringer explains the benefits: "It shortens pathways and production times, it lowers costs—and we can offer our patients individualised medical care."

To fit the made-to-measure implants into an operation site during minimally invasive interventions, Thieringer has opted to work with an origami-like technique. In future, he would like to create implants consisting of several small parts that are inserted one by one into the body and then assembled during the operation. "This is already 'smart'," Thieringer says. "But we also want to adapt the material to meet the precise needs of individual patients. And we want to equip the implants with sensors that deliver information about the state of an implant and how the body is reacting to it."

In short, prosthetics and implants will soon be much more than rigid replacement parts in the body. Good prospects for patients indeed.

In the 3D Print Lab at University Hospital Basel, doctors can order patient-specific models to help them plan an operation.

In addition to the 3D models, made-to-measure implants will be printed in the Basel lab in the near future.

At the office or the beach, while taking a walk in the woods or when talking with other researchers: innovative thinkers like Francesco Stellacci, Christina Warinner and Pierre Stallforth (left to right) hit upon brilliant ideas just about anywhere.

In the 19th century when Werner Siemens discovered the dynamo principle and established the field of modern electrical engineering, inventions were often born of sudden inspiration: extraordinary individuals like the Siemens company founder had a brilliant idea and were able to quickly convert it into a workable product. And now? How is innovation born in the 21st century?

The Werner Siemens Foundation supports researchers who pursue innovative, often unusual approaches. Molecular archaeologist Christina Warinner and biotechnologist Pierre Stallforth are a prime example. In their project, the two scientists have joined forces to solve the growing problem of antibiotic resistance, and they're looking in a place where no one has ever thought of finding antibiotic agents: in the mouths of prehistoric humans.

Francesco Stellacci, too, is pursuing an unconventional strategy to combat viral diseases. The materials scientist at the École polytechnique fédérale de Lausanne (EPFL) is aiming to develop a broad-spectrum antiviral as well as specific medications to treat a wide range of infections caused by viruses. His innovative approach transfers findings from materials science to the field of medicine: he and his team have designed an artificial molecule that can "capture" viruses and "crush" them using hydrophobic pressure.

How do researchers come up with these kinds of innovative ideas? A conversation with three scientists and professors: Christina Warinner, Pierre Stallforth and Francesco Stellacci.

"The most important thing is having time and space"

Looking back, when were you most creative in your career?

Warinner: I had the most freedom when I was a student at the University of Kansas. I took every course that interested me: Middle Egyptian hieroglyphs, physics, organic chemistry, microbiology, Celtic archaeology. Although I needed an extra year to finish my degree, after I earned my PhD in anthropological archaeology, this innate ability to pursue my own interests proved very useful. For example, I was a postdoc at the University of Zurich at a new institute where there was no supervisor in my research group for two years. So, it was up to me to develop ideas. I also had to knock on doors and ask other researchers for feedback on my work.

> "Talking to experts from other disciplines opens my eyes to holes in my own logic."
>
> *Christina Warinner*

At first, this freedom was a little frightening, but over time I realised it was a fantastic opportunity—and I found traces of DNA and protein where no one expected to find anything at all: in the dental plaque of prehistoric humans.

Stellacci: The postdoc phase was a very creative and inspiring time for me, too. It's also when I realised that a professorship would be interesting because it would allow me to devote my time entirely to research. However, a professorship also comes with numerous obligations—HR, project management, administration. Having all these duties is counterproductive, as conducting research is a creative process, similar to the work of an artist. In the music industry, no one expects musicians to be creative on command—it's not a case of: release a fantastic new album every year! But we professors are indeed subject to this kind of regime—we're obliged to regularly publish relevant research findings.

Does that mean having a professorship doesn't offer the best opportunities for conducting innovative research?

Stallforth: Not until you've become established in your field. Then you can step back from the pressure to publish as much and as often as possible. Also, with generous benefactors like the Werner Siemens Foundation, there's less worry and less need to spend so much time searching for new financing. Long-term funding means we don't have to prove every single day that we're worth the money that's been invested in us.

Are younger or older researchers more creative?

Stellacci: It's proven that we have fewer ideas as we age—but we get better at seeing how things are connected. When we're young, it's the opposite: the ideas flow freely. That's why we should involve junior researchers more closely in the activities of the established scientific community—through work with mentors, for example. It's important to find ways to channel the creativity of young researchers.

Warinner: I agree. When I used a new measurement instrument as a postdoc and met with such incredible success, I was handed a list of bacterial species—and I had to google every single one of them. I suddenly had a huge amount of prehistoric DNA on my hands, but I didn't know a thing about the oral microbiome. As a matter of fact, I didn't even know the word.

Have you ever worried about hitting a dead end with your approach?

Stellacci: All researchers have their doubts—it's normal. I began looking for antivirals in 2010, and I made good progress. I published articles, but always out of my own pocket. Five years later I was awarded a grant from the Swiss National Science Foundation, but after the funding ended, I thought I would have to give the project up. Then the coronavirus pandemic began in 2020, and WSS pledged their support.

Does secure financial footing promote innovation?

Stallforth: There's an interesting observation from theoretical physics: in the 1950s, Russian physicists were extremely innovative and successful—and they worked with pencil and paper …

Stellacci: … Right, but they also supervised just one or two gifted students and taught a single course. The example is a good illustration of how the ability to innovate depends on having enough time.

Stallforth: True. And, of course, in a field like palaeobiotechnology it's also indispensable to have good technical infrastructure. Without sequencing instruments, it would be impossible for us to make rapid progress—and today's state-of-the-art technology is extremely expensive.

Stellacci: Indeed it is, and the Russian physicists from the 1950s ultimately failed because they didn't have the financing to pursue their ideas. To be innovative, researchers need to work in a system that wants, needs and funds innovation.

Pierre Stallforth, was your idea a sudden inspiration, or did it evolve from years of work?

Stallforth: Today, anyone looking for new antibiotics is forced to be creative, as there's a limited number of possible "sites"—we can look into exotic organisms or underexplored habitats. And although the past fifteen years have seen scientists finding new chemical compounds in bacteria that live in symbiosis with insects, for instance, we generally rediscover already-known substances. The field is literally crying out for new, innovative strategies.

In many ways, your approach is a result of systemic limitations—but how did you come up with the idea to look for antibiotic agents in early human history, of all places?

Stallforth: It was in 2018 at a cluster of excellence meeting in Jena, when I got to know Christina Warinner and her work. We started talking and quickly realised that combining our core areas of expertise—molecular archaeology and biotechnology—would open up entirely new perspectives in antibiotics research.

Warinner: Exactly, because it's possible that there were chemical compounds in prehistoric times that no longer exist today—or that maybe do! That's what we want to find out. It's a wide-open field with many surprises in store.

What made you think that prehistoric agents could be "reanimated"?

Warinner: When I was doing my postdoc at the University of Zurich, I read a publication maintaining that it's impossible to find prehistoric DNA in dental plaque. I wasn't so sure, so I tested it. My first experiments were negative, but then measurements I made with more advanced lab equipment showed that my tests didn't fail because there was no DNA—they failed because there was such a huge amount of preserved DNA fragments that it overloaded the old instruments. No one saw that coming.

So your persistence paid off.

Warinner: It did, and dental plaque has turned out to be a unique window on how humans lived tens of thousands of years ago.

Stallforth: In the oral microbiome of early humans, we've found genes that enable the production of potentially novel antibiotics as well as antimicrobial resistance genes. So we know we're on the right track with our hypothesis.

What else do researchers need to get their ideas off to a good start?

Warinner: We need a place for interdisciplinary dialogue, collaboration, research, teaching, further education. The facilities at the department of palaeobiotechnology at the Leibniz Institute for Natural Product Research and Infection Biology in Jena offer this kind of amazing space.

But interdisciplinary research is also complex and time-intensive.

Stallforth: That's true. It took us a good year before representatives from all the disciplines involved—anthropology, archaeology and analytic chemistry—had presented their methods, ways of thinking and technologies, and for us to get to know and better understand each other. But it was definitely worthwhile.

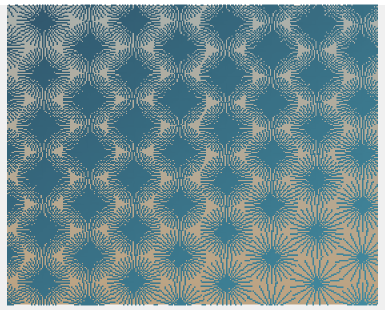
Francesco Stellacci, what motivated you, a materials scientist, to focus on treatments for viral diseases?

Stellacci: At a certain point in my career I realised that science had achieved major milestones, but that we bury our heads in the sand when it comes to recurring problems like war, earthquakes, droughts or pandemics.

Why precisely antiviral drugs?

Stellacci: I attended a conference where a speaker reported that every day, worldwide, a thousand children die of diarrhoea, mostly as the side effect of a viral infection. In the meantime, the figures have dropped by half, but it's still far too high and we're not doing anything about it.

Persistence pays off: Francesco Stellacci (left), Pierre Stallforth and Christina Warinner in conversation about inspiration and innovation.



Update: palaeobiotechnology

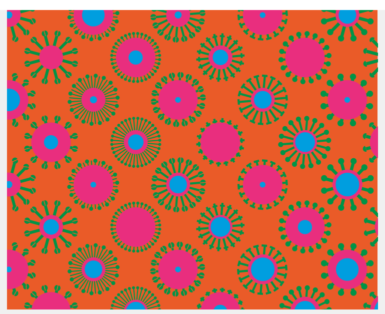
Bioinformatic brilliance

2022 was a good year for the department of palaeobiotechnology at Leibniz-HKI in Jena. Pierre Stallforth was appointed professor, and he and his colleague Christina Warinner moved with their teams into a state-of-the-art lab at the new HKI Biotech Center. The bioinformatics tool they developed has also proven effective in the search for ancient DNA: the researchers have succeeded in reconstructing their first prehistoric natural product.

In 2020, the Werner Siemens Foundation began funding the promising new research discipline of palaeobiotechnology. This support has acted like a catalyst, triggering positive advances and, at the end of 2021, leading to biotechnologist Pierre Stallforth's appointment as professor of bioorganic chemistry and palaeobiotechnology at Friedrich Schiller University Jena. Stallforth is also head of the department of palaeobiotechnology at Leibniz-HKI, the Leibniz Institute for Natural Product Research and Infection Biology in Jena.
In April of 2022, the core palaeobiotechnology team of around twelve researchers moved into the new HKI Biotech Center. "The research conditions are perfect," Stallforth says with evident satisfaction.

Generating natural products from ancient DNA
For the past two years, Stallforth's team has been working with the group led by molecular archaeologist and co-project leader Christina Warinner to develop bioinformatic tools capable of scanning vast amounts of data for prehistoric information while also differentiating it from present-day genetic information. If a DNA fragment is identified as prehistoric, other related DNA fragments must then be found, put together correctly to form a bacterial genome. "It's a bioinformatic tour de force," Stallforth says. The newly assembled genome is then tested for errors. If none is found, the two groups then work to determine the functions of the genes in the genome. For this, experts from the fields of archaeology, biotechnology, bioinformatics and organic chemistry contribute their knowledge.
Research leader Pierre Stallforth says, "Our broad focus on the ecological and archaeological context is highly innovative and new."
The researchers have already reconstructed bacterial genomes that existed between 16 000 and 100 000 years ago; a publication on this development is forthcoming. "It's fantastic that we can go back as far as 100 000 years. We now understand what kind of genomic information we need for our work and where the difficulties lie," is how Stallforth sums it up.

Funding from the Werner Siemens Foundation 10 million euros
Project duration 2020 to 2029
Project leaders
Prof. Dr Pierre Stallforth, professor of bioorganic chemistry and palaeobiotechnology at Friedrich Schiller University Jena and head of the department of palaeobiotechnology at the Leibniz Institute for Natural Product Research and Infection Biology (Leibniz-HKI) in Jena
Prof. Dr Christina Warinner, Max Planck Institute for Evolutionary Anthropology, Jena and Leipzig; head of the archeogenetics research unit at Leibniz-HKI in Jena; associate professor at Harvard University in Cambridge, Massachusetts



Update: antivirals

Vanquishing viruses

Materials scientist Francesco Stellacci and his team have developed artificial molecules that, by means of hydrophobic pressure, destroy viruses before they can enter a human cell. In the first preclinical study, the innovative approach has proven to be highly effective against influenza viruses. What's more, no side effects were observed. Now, the next step in the project is a long-term series of additional preclinical trials.

Francesco Stellacci is pursuing a two-pronged approach to combatting viral infections. On the one hand, he envisions a broad-spectrum antiviral drug that—much like penicillin—can be used to treat a wide range of viruses. Then, in the event that this general drug is ineffective against a certain virus strain, he aims to develop a method for quickly designing a specific antiviral. Currently, Stellacci and his team at the École polytechnique fédérale de Lausanne (EPFL) are focusing on coronaviruses as well as the influenza and dengue viruses—thanks to funding from the Werner Siemens Foundation.

Preclinical studies off to an ideal start
An independent lab in the US has already conducted toxicology experiments on mice to test the specific agent against influenza viruses. In this first preclinical study, no side effects were observed, not even when high doses were administered over several days. In addition, the therapeutic window for the drug is six times longer than with Tamiflu, the drug that is currently most commonly prescribed. In short: the preclinical studies are off to a great start. In the coming years, however, Stellacci will have to dedicate much of his time to organising additional preclinical trials: when developing medications for humans, toxicology testing is a complex, demanding and long-term procedure.

Deadly viruses
Stellacci is particularly interested in finding a treatment for dengue fever. With this disease, the initial infection is generally not too dangerous, but a later infection is fatal in nearly half of all cases. An inexpensive antiviral medication would also be very useful to treat rota- and noroviruses, which cause diarrhoea and kill hundreds of children in poor countries every day.
Because viruses are so dangerous, Stellacci is convinced that we need a centre for viral research dedicated to broad, interdisciplinary research on different virus types. Indeed, until an antiviral drug has been developed, there's a danger that a future virus will wreak as much devastation on the human population as the plague bacteria in the 14th century—when antibiotics were as yet unknown.

Funding from the Werner Siemens Foundation
5 million Swiss francs (2020–2021: development of a broad-spectrum antiviral)
4.5 million Swiss francs (2021–2023: Werner Siemens Foundation Center for Antiviral Research (WSS-CARe)
Project leader
Prof. Dr Francesco Stellacci, Supramolecular Nano-Materials and Interfaces Laboratory, Institute of Materials, École polytechnique fédérale de Lausanne (EPFL)

That's what first inspired me to work on viral diseases.

So it was a conscious departure from classical questions in materials science?
Stellacci: That's right. Viruses are really the most elegant and complex materials in nature—an assemblage of proteins, DNA and fatty acids. They're not classed as living organisms because they rely on a host to reproduce.

Were you always interested in virology?
Stellacci: Well, I have many interests, including physical virology. In this discipline, researchers examine how viruses can be broken down into their individual components in order to insert tiny particles in them when they're putting them back together again. I figured that if it's possible to reassemble viruses, it shouldn't be too difficult to destroy them. After all, it's always easier to destroy something than to build it.

When do you think about these kinds of things?
Stellacci: Usually when I'm alone, either at my office or at home. The idea to destroy viral material occurred to me during my summer holidays at the beach. I kept mulling over the possibilities and tried to imagine the various processes that viruses undergo when they replicate. At some point I came to the conclusion that it should be possible to deconstruct them. When I was back at work, I drew sketches of my idea and thought: now I need to find virology specialists who are willing to work with me, an "ignoramus".

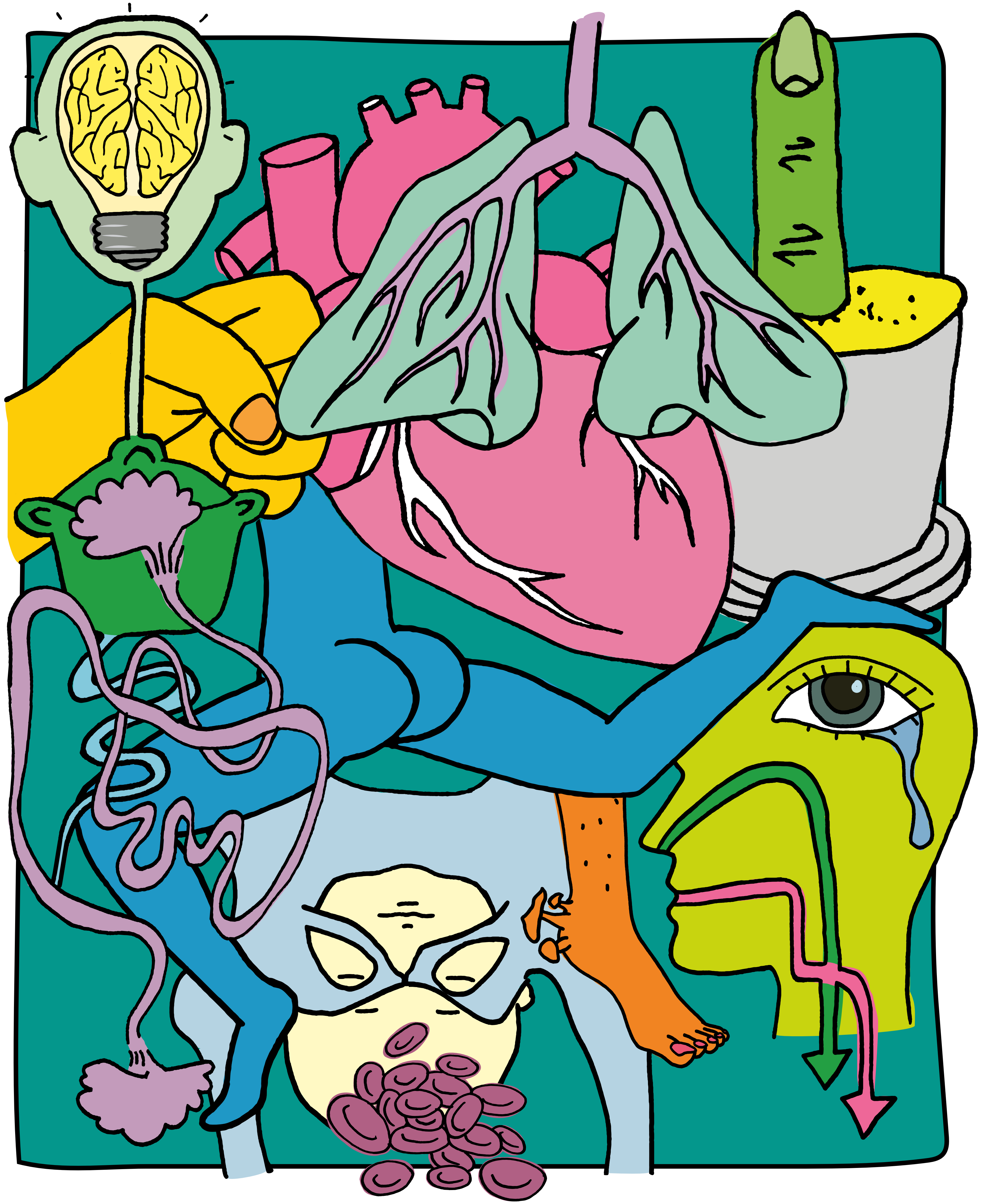
So some ideas are born of inspiration or a sudden revelation after all?
Warinner: There are definitely those wonderful and productive "eureka" moments, but with me, they generally happen after a discussion in the group. Everyone formulates their thoughts, the arguments fly back and forth, but without arriving at a solution. Then later, when I think about what we talked about, sometimes the scales fall from my eyes and I know what the answer is.

Researchers have to be able to deal with uncertainty—they can never be sure that an innovative idea will bear fruit.
Stallforth: I really enjoyed the uncertain phase when we were establishing the palaeobiotechnology research unit. Probably because I've always worked between disciplines—chemistry, molecular biology, physics, mathematics, microbiology, genetics—and I've never claimed to be "the" expert in a particular field. Over time, though, I've come to appreciate this role, and I've learned to ask questions with no sense of false shame if something isn't clear to me.
Stellacci: Researchers are like strikers in football matches. Sometimes they run around for 89 minutes with nothing to show for it. But if they score the decisive goal in the last minute, their job is well done. So the bottom line is: seize your opportunities and don't be discouraged by setbacks.

To sum up, what do researchers need most to realise their innovative ideas?
Stellacci: Most innovations come about when we leave our comfort zone and dare to take a new approach—an approach that we pursue relentlessly, tweaking our idea until it works. Beat it and buff it, as it were.
Warinner: To be creative, the most important thing is having time and space to think, to experiment, to pursue an intriguing notion. Talking to experts from other disciplines is what gives me new ideas most often. These discussions force me to think about aspects that are entirely foreign to me, and I can more easily identify holes in my own logic. It's both revealing and constructive.
Stallforth: No single person will ever be able to solve today's problems. Innovation happens through interaction, interplay, human contact, through honest feedback and constructive criticism. And then it's a question of testing feasibility—and deciding whether the massive amount of research required is really worthwhile.

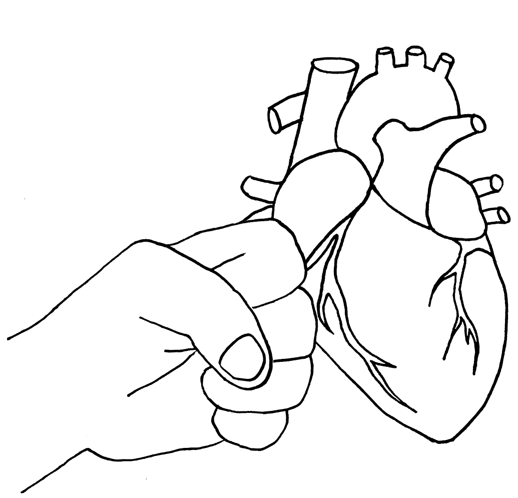
"No single person will ever be able to solve today's problems."
Pierre Stallforth

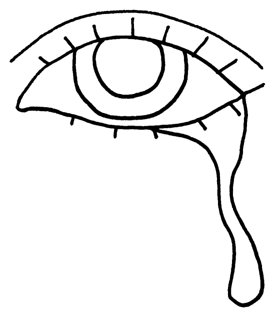
"We can't be creative on command."
Francesco Stellacci

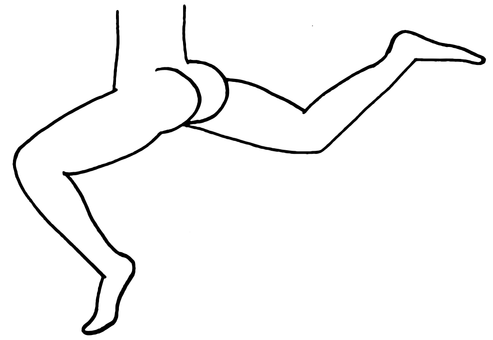


Twelve surprising facts about the human body

Medical research is mainly concerned with malfunctions in the human body. But our bodies are a miracle of nature, full of quirks and quiddities ranging from fingertips that regrow, outsourced digestive systems and scent receptors in our lungs—on to a veritable petting zoo in our belly buttons.







Anger not the best medicine

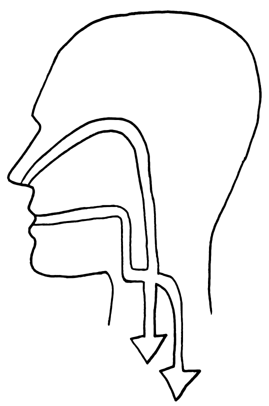
Caution advised! Throwing a temper tantrum increases the risk of heart attack by a factor of eight—and the danger can last several hours. Contrary to popular belief, blowing off steam is bad for our health, and trying to work off frustration by hitting a punching bag will only make us angrier.

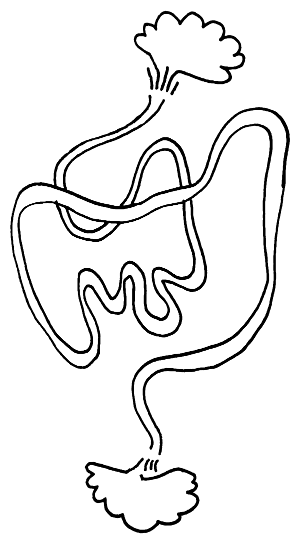
Tears are a turn-off

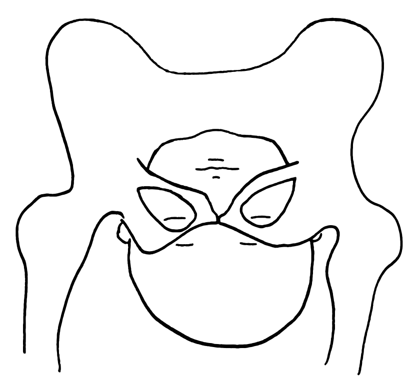
When women cry, men lose interest: experiments have shown that sexual arousal in men diminishes when they smell women's tears. It's believed that the phenomenon is due to a previously unknown chemical messenger that men don't consciously perceive.

Powerful posteriors

Compared to other primates, the buttocks of humans are generously endowed. Indeed, the gluteus maximus is the largest muscle in the body, and it's what makes us so good at walking and running. In addition to the sheer strength it supplies, it also ensures stability. Whereas other bipedal animals—the kangaroo, for instance—have large tails to counter-balance their forward-leaning torsos, this task is performed by our dutiful derrières.







The hazard in our throats

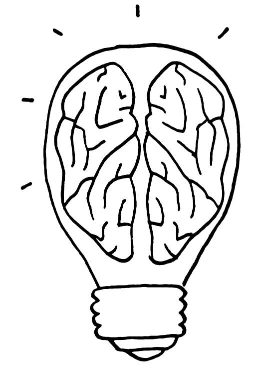
The pathways for food and air converge in our throats. When we choke, food sometimes goes down the windpipe—oft-times with fatal consequences. The faulty design came about when our earliest ancestors evolved from water creatures to living on land, making a separation of food and air passages necessary. Because fish breathe water, they don't have the problem.

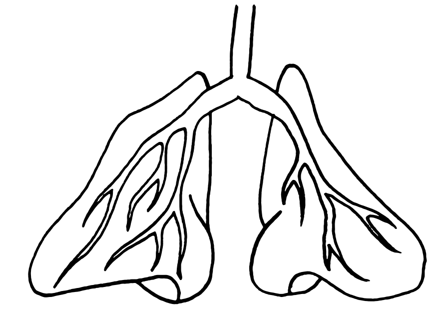
Airy intestines

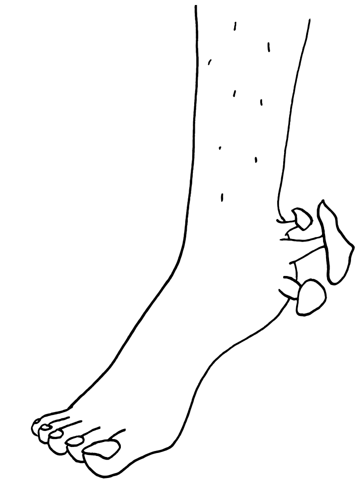
Only thirty percent of all intestinal gas is a result of digestion. The majority of air is swallowed when we eat and drink. Most of this gas is absorbed by the intestinal wall, transported to the lungs and eliminated when we exhale. Only a small amount takes the rear exit: on average, about forty millilitres of gas is passed fifteen times every day.

Birthing pains

Two typical traits of human beings aren't very compatible: our upright gait and our large brains. While bipedal movement requires a narrow pelvis, a wide pelvis would be better for birthing babies with large heads. On average, the birth canal in humans is 2.5 centimetres too narrow, making labour very painful. In the past, this was a leading cause of maternal death—caesarean sections have helped to reduce the risks.







Supercharged brains

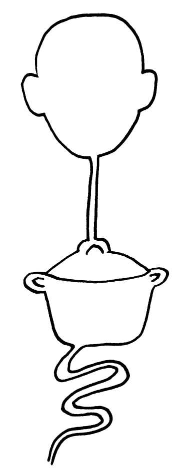
While it's true that the brain expends quite a large percentage of the calories we consume, it's highly efficient, requiring no more energy than an energy-saving bulb. That said, to simulate a human brain in all its complexity, we would need the electricity generated by several nuclear power plants.

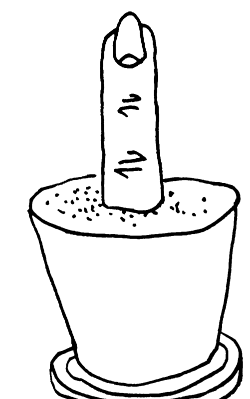
Lungs can smell

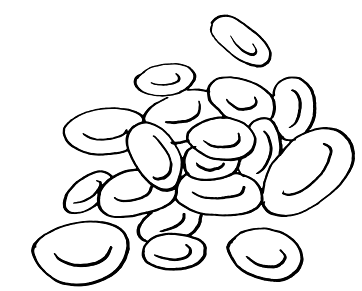
Scent receptors aren't limited to the nose: they're also found in our lungs, although we don't notice anything, as the smelling process happens unconsciously. When the lungs perceive a toxin in the air, they temporarily constrict the airways. It all happens without switching on the brain—and very fast.

Personal petting zoo

The human skin offers a natural habitat to all manner of creatures. On average, eighty kinds of fungi live on our heels, and a good sixty bacterial species dwell in our belly buttons. What's more, a few hundred tiny mites live on our faces, where they feed on sebum secreted by our pores. But not to worry—they're completely harmless.







Pre-digestion in the kitchen

Although the human gut is only half as big as the intestines in primates of a similar size, we have no problem digesting our food—because we cook it first. Our comparatively small jaws are also a consequence of outsourcing some of our digestion to the stovetop. An unpleasant side effect of our small mouths is that our wisdom teeth often don't fit.

Regrowing fingers

If a salamander loses a leg, the entire limb will regrow. We humans aren't so lucky. However, if the fingertip of a young child is severed, it will grow back without scarring as long as the wound hasn't been stitched up. And even in adults, an injured fingertip will regenerate over time if the cut is covered in a special dressing.

Blood-cell factories

Our bone marrow produces more than two million red blood cells every second, making a total of two hundred billion new cells every day, with the same amount being removed or recycled. The wear and tear is so high because one blood cell per minute is squeezed through the entire circulatory system to deliver oxygen and carry away carbon dioxide.

Better images, better treatments

Although the human body still harbours many secrets, it's no longer a black box—thanks to modern medical imaging. These innovative techniques are capable of making highly accurate images of processes inside cells and tissues, and their potential for application in medical care is great, as can be seen in two innovative projects that receive financing from the Werner Siemens Foundation.

In future, researchers in the MIRACLE II project plan to use 3D goggles and virtual reality technology to peer into the body of patients.

A chance discovery made 127 years ago initiated a revolution in the world of medicine. It was 8 November 1895, and German physicist Wilhelm Conrad Röntgen was in his lab conducting experiments with a cathode-ray tube. After sending electricity through the tube wrapped in thick black cardboard, he spotted a glow on an object he had left lying on his lab table. His apparatus produced rays! And he realised that the rays could even pass through dark-coloured materials like the cardboard. Röntgen continued with his experiments, and on 22 December 1895, he X-rayed his wife's hand, capturing the image on a photographic plate—her wedding ring and every detail of her finger bones all clearly visible. Röntgen's discovery was a veritable sensation in the world of medicine: now doctors could peer into the human body without having to cut it open.

The new technology spread like wildfire. The university hospital in Vienna set to work and began producing the first medical X-ray images already in January 1896. That same year, Scottish doctor John Macintyre established the first radiology department in a hospital, and just one year later, every hospital in Scotland had an X-ray machine. The earliest radiology journals were issued in Germany and the US, and in 1901, Wilhelm Röntgen was awarded the first-ever Nobel Prize in Physics.

X-ray technology is based on the phenomenon that more rays are absorbed by tissues with high density than those with a lower density. The greater the difference between tissue type, the more information an X-ray image will provide, which is why X-rays are particularly useful for examining bone fractures. In the decades following Röntgen's discovery, the technology became increasingly sophisticated—through the introduction of contrast agents, for example. Computer tomography (CT) was then developed in the early 1970s thanks to recent advances in computer science. In computer tomographic imaging, the source of the X-rays and a detector rotate around the patient's body, recording cross-sectional images of the various tissue layers as they move; the slice-like images are combined to create an overall picture.

Pioneering methods

The same period saw the advent of groundbreaking magnetic resonance imaging techniques (MRI). With this technology, a strong magnetic field aligns hydrogen nuclei—protons—which are then excited by a radio frequency to set them oscillating. The energy the atoms emit is received, processed and converted into images by a computer. Because this technique does entirely without X-rays, it's particularly gentle and safe to use. Moreover, MRI scanners deliver a higher-contrast image of soft tissues in the body compared to X-ray technologies, making them more suitable for examining internal organs.

The advances in imaging techniques have continued unabated in recent decades, says Philippe Cattin, professor of image-guided therapy and head of the Department of Biomedical Engineering (DBE) at the University of Basel. "Resolution is improving all the time, and radiation levels are decreasing." Cattin is co-project leader of MIRACLE and the follow-up MIRACLE II project, which the Werner Siemens Foundation began financing in 2015. The MIRACLE researchers are constructing a surgical robot that, in future, will use a laser to perform minimally invasive surgery on diseased or fractured bones in cancer or accident patients (see page 28).

For the exact planning and monitoring of these interventions, Cattin and his team have already designed SpectoVR, a virtual and augmented reality system. The navigation software links medical data from CT or MRI scans, recalculates them and renders them as three-dimensional images. When wearing 3D goggles, doctors can literally peer into the bodies of their patients and view tissues, bones and blood vessels from all angles. The system makes surgery more accurate, safer and faster, and SpectoVR has already become a standard instrument in certain procedures at University Hospital Basel.

Sensors in the endoscope

Last year, the MIRACLE team were pleased to announce a major milestone: for the first time, the researchers united the components of their system to form a modular robot, which they presented at a media conference. Nevertheless, much work remains to be done before their robot will be ready to operate on living humans. Researchers in the SpectoVR project group are now working on ways to introduce haptic components to their system. Their goal is for surgeons to not only see a tissue or fracture, but to also feel it.

In surgical interventions, it's critical that doctors can maintain a general overview of what's happening inside the patient's body. This is naturally made more difficult when the operating tool is a laser integrated into an endoscope tip—measuring just a few millimetres. To enable surgeons to see more, Cattin and his team plan to mount wafer-thin fibres on the endoscope; the fibres are equipped with optic sensors that provide real-time information on the position and curvature of the endoscope. These data are then fed into the navigation system and transmitted to the 3D goggles worn by the surgeon, thus supporting decision-making during an operation.

See more, understand more

Medical imaging techniques are, however, not only useful for treating patients. They also drive medical research forward. Cattin gives an example: "New multiple sclerosis medications promise to reduce the size of lesions on the brain. But to know whether these therapies actually work, we need technologies capable of making accurate measurements of the inflammations in clinical trials."

Developing precisely these kinds of innovative imaging technologies for preclinical research and clinical trials is the objective at the Werner Siemens Imaging Center (WSIC) at the University of Tübingen. The Werner

MIRACLE II

Gentle, minimally invasive, robot-guided and highly precise bone surgery—this is the aim of researchers in the MIRACLE II project at the University of Basel. The team are developing an endoscopic laser robot capable of making ultra-exact incisions in bones, while miniature sensors and a 3D software program are used to promote patient safety during surgery. In the hospital's in-house 3D-printing lab, made-to-measure implants will be fabricated to fit into the pre-cut bones. All of which means that bones can heal faster after an intervention.

Funding from the Werner Siemens Foundation 12 million Swiss francs
Project duration 2022 to 2027
Project leaders
Prof. Dr Philippe Cattin, head of the Department of Biomedical Engineering (DBE) at the University of Basel
Prof. Dr mult. Florian M. Thieringer, senior physician for oral and cranio-maxillofacial surgery and head of the Swiss MAM research group at University Hospital Basel
Prof. Dr Georg Rauter, head of Bio-Inspired RObots for MEDicine Lab (BIROMED-Lab) at DBE at the University of Basel

Professor André Martins (centre) at the Werner Siemens Imaging Center uses cutting-edge medical imaging techniques to study the metabolic activity in cancer tissues.

Several PET scanners number among the state-of-the-art instruments at the Werner Siemens Imaging Center in Tübingen.

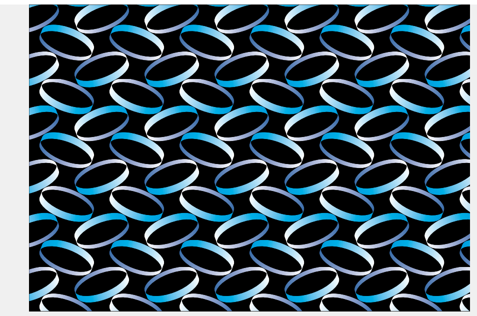
Siemens Foundation has been financing this research since 2007. Roughly ninety employees now work at the centre, which was established in 2014 with the aim of better understanding how medical conditions arise, develop and spread through the body—ultimately in order to offer improved patient treatments. The spectrum of disciplines at WSIC encompasses oncology, neurology, cardiology and immunology.

One key technique that researchers at WSIC work with is positron emission tomography (PET), which creates images of physiological and biochemical processes in the living body. PET uses weak radioactive, biologically active substances—called biomarkers or tracers—that have been introduced into an organism. The tracers are designed to carry out a specific task: detecting cancer cells, for example. Using cross-sectional images, a picture of how the tracers are distributed throughout the body becomes visible. The search for disease-specific tracers is currently a major priority in medical research.

Clinical trials with tracers

As an example, Professor Kristina Herfert and her group in Tübingen designed a tracer that binds to the protein alpha-synuclein; in this project, the researchers worked closely with biotech company MODAG and the Max Planck Institute for Multidisciplinary Sciences in Göttingen. "We know that alpha-synuclein aggregates and is deposited over time in the brains of patients with neurodegenerative disorders, especially in cases of Parkinson's," Herfert explains. One possible application of the tracer would be for detecting Parkinson's disease. "Until now, no PET tracer for the early diagnosis of Parkinson's—or for monitoring new treatment methods—has been developed," she says. Last year, her new biomarker was tested on primates to determine its safety for use in clinical trials with humans. "The data look very promising," Herfert says, and preparations for an initial clinical trial are now underway.

WSIC director Professor Bernd Pichler and his group have also taken a major step forward. For over ten years, they have been developing a tracer that can be used to detect "dormant" (senescent) tumour cells in the body. "When tumour cells are senescent, they're still alive but they stop dividing," Pichler explains. What sounds good, however, is in reality dangerous, as these sleeper cells secrete substances that trigger strong growth in the remaining tumour cells. To avoid this scenario, the researchers want to use drugs to destroy the senescent cells at the right time—thereby preventing suppressed tumours from regrowing. The new senescence tracer would help pinpoint the optimal point in time to use the medications. Pichler and his team have already concluded a phase I clinical trial with positive results. "We're now in the middle of a phase II study," he says. "The data we've collected on tumour patients are very encouraging. It would be the first time ever that senescence could be detected in a living patient."



Werner Siemens Imaging Center

The Werner Siemens Imaging Center plays in the premier league of research on medical imaging techniques, and the Center's work on personalised tumour therapies forms part of Germany's national Excellence Strategy. Thanks to the new, combined medical imaging techniques developed at WSIC, tissues and molecules can be studied in greater detail, and the innovative technologies also reveal which therapies work best for which patients.

Funding from the Werner Siemens Foundation
18.4 million euros (2024–2033)
15.6 million euros (2016–2023)
12.3 million euros (2007–2016)

Project duration 2007 to 2033
Project leader
Prof. Dr Bernd Pichler, Werner Siemens Foundation Endowed Chair and director of the Werner Siemens Imaging Center at the University of Tübingen

High-precision immunotherapies

Pichler's research group are also off to a good start in their work to develop a wide range of other tracers capable of improving immunotherapies for cancer patients. For instance, in therapies using chimeric antigen receptor T cells (CAR T cells), a sample of a patient's blood is taken, and the body's own white blood cells in the immune system are modified in the lab to improve their ability to recognise and target cancer cells. The patient is then given an infusion to reintroduce the modified cells back into the body. "These therapies can cost up to 400 000 euros," Pichler says. "They have numerous adverse side effects and, unfortunately, far from all are effective." He and his team hope that using tracers for individual immune cells will one day aid doctors in discovering whether and how well a patient is responding to the form of immunotherapy selected.

In his research, WSIC group leader André Martins, who was appointed professor by the university management in Tübingen in 2022, is also aiming to predict which tumours will prove resistant to a therapy. His main area of interest is the metabolic activity in and surrounding cancerous tissue. "A cancer resembles a society of cells where anarchy is one of the driving forces," Martins says. "We want to understand how metabolic activity changes when cancer cells transform into more aggressive types." In their work, he and his team use state-of-the-art, non-invasive imaging techniques, including hyperpolarised imaging, which changes the magnetic state of a metabolic molecule, thereby rendering it up to 100 000 times more visible in an MRI scan. Martins says he and his team are currently preparing several publications that discuss this and other types of metabolic imaging methods—hybrid metabolic PET/MRI measurements, for example, or pH imaging. And with a method called quantitative deuterium metabolic imaging, Martins is now leading the first-ever clinical trials in Europe.

Full-body microscopy

In another part of the project, Professor Bettina Weigelin and her team are looking at microscopic investigations of cancer cells and their interactions with the immune system. "Microscopy is extremely useful for cancer studies," Weigelin explains, "as cancer is ultimately a cellular disease." At the same time, however, tumours don't remain confined to just one part of the body; rather, they also spread to other tissues or organs, which is why Weigelin and her group are developing techniques capable of depicting larger tissue sections or even entire organs in model organisms—while maintaining a high microscopic resolution. "It's often the case that a therapy proves more effective in some organs than in others. We want to understand these differences—and this knowledge will lay the foundation for improved treatments for patients with advanced cancer," she says.

Weigelin uses cutting-edge technologies, including intravital microscopy and three-dimensional light sheet fluorescence microscopy. She says the latter technique makes it possible to scan large tissue sections and construct them as 3D models. The trick behind the method is a chemical cocktail that dissolves dyes out of the organ and aligns the refractive indices of the organ parts. Or put more simply: "It enables us to virtually look through an organ and see it as a whole under the microscope." In the past two years, the group have worked on getting the necessary technologies up and running. As Weigelin says, "This is a big achievement. Now we can start collecting biological data."

Massive datasets

The ability to simultaneously capture images of ever-larger sections of the body is one of the most important advances in medical imaging of recent decades, Bernd Pichler says. "We can now go from the very specific level of the cell up to full-body medical imaging." He believes that this capacity is extremely useful for better understanding systemic diseases affecting the entire body, and that the combination of different methods and techniques needed for this kind of imaging is a highly relevant, future-looking area of research. Nevertheless, Pichler spots a challenge: how can the massive datasets be adequately evaluated? "In the coming years, machine learning will become a key factor in our branch of research."

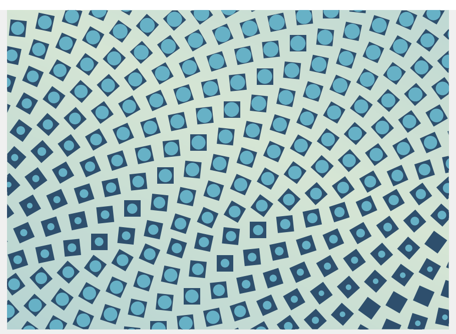
While precise predictions on how pioneering imaging techniques developed by top researchers will promote human health are difficult to make, several methods will certainly find use in medical care. Philippe Cattin thinks magnetic resonance imaging with lower magnetic fields—Low-field MRI—is a promising candidate. "The most interesting part of this technique is that no separate rooms are needed, as is the case with MRI scanners with their strong magnetic fields," Cattin says. "It would even be feasible to install a Low-field MRI device on a hospital bed or in an ambulance." In addition to the added comfort for patients, this set-up would also facilitate faster diagnoses—and better treatments. "Patients with a brain haemorrhage and those with clogged arteries exhibit the same symptoms," Cattin explains. "But while blood thinners should be given to the patient with clogged arteries as soon as possible, the treatment would be fatal in the case of a brain haemorrhage."

The example illustrates that a closer look into the body would indeed save lives in acute medical care.

Medical imaging techniques are delivering ever-more precise information on the body's inner workings.
Now, new technologies are needed to analyse the massive datasets they generate.

Measuring fatigue

Computer scientist Pietro Oldrati is preparing to launch a digital measurement platform to help people suffering from fatigue—thanks to a MedTechEntrepreneur Fellowship from the University of Zurich.



From idea to company

The University of Zurich Entrepreneur Fellowships were created to help talented junior researchers establish a firm—and enable them to translate their research findings into real-world applications. Thanks to funding from the Werner Siemens Foundation, fellowships in the field of medical technology were added to the programme in 2018. Since then, a total of eighteen junior researchers have received a MedTechEntrepreneur Fellowship and six new companies have been founded.

Funding from the Werner Siemens Foundation 10.67 million Swiss francs
Project duration 2018 to 2027
Project leader Prof. Dr Elisabeth Stark, Vice President Research, University of Zurich

Chronic illnesses often go hand in hand with a broad range of symptoms. One of the most frequent—and underestimated—is fatigue. People with multiple sclerosis, cancer, rheumatic diseases or long Covid often experience physical and mental exhaustion. Even sleep and rest fail to bring relief, and everyday life can become a struggle. “People with fatigue are forced to limit their activities and workload. Their lives change completely,” says Pietro Oldrati.

Oldrati, a computer scientist, is an academic associate at University Hospital Zurich. Since completing his master’s thesis in 2018, he has focused on developing new methods to measure fatigue, primarily in multiple sclerosis patients. Up to ninety-five percent of all people with MS suffer from fatigue; many describe it as the most debilitating symptom of their illness.

Lack of objective measurements

“However,” Oldrati says, “modern medicine has yet to understand what causes fatigue or how it can be treated.” This is because defining fatigue has proven elusive: it varies from patient to patient and, to date, no methods have been developed to objectively measure the severity of symptoms. Patients are typically asked to fill out a questionnaire. “But experiences and memories are subjective,” Oldrati explains. Moreover, the questionnaires are often completed only once a year. “Yet levels of fatigue vary, they come and go.”

This is why Oldrati is convinced that fatigue should be measured more frequently and more precisely in order to understand it—and to develop treatments. Today, doctors often have few options other than recommending a change in diet or prescribing medications such as Ritalin that haven’t been approved for fatigue syndrome.

Smartphones plus wearables

Together with a team of neurologists and other computer scientists at University Hospital Zurich, Pietro Oldrati has plans to develop a platform to measure fatigue levels. Their method uses smartphones and wearable technology—smartwatches and fitness trackers that record data.

In spring 2022, Oldrati was awarded a MedTechEntrepreneur Fellowship to pursue his project. The University of Zurich funding programme is financed by the Werner Siemens Foundation and endowed with a scholarship of 150 000 Swiss francs. The fellows are also mentored by experienced coaches who help them overcome the myriad obstacles on the rocky road to establishing a firm; they also have access to the UZH Incubator Lab and the opportunity to join a network of current and former fellowship holders.

Oldrati and his team are working on three measurement methods for their platform. The first is a patient questionnaire app that allows data to be collected more frequently than is currently the practice at medical centres. The second method involves tests completed on a smartphone to measure levels of fatigue throughout an activity. An example is a five-minute test requiring the patient to match patterns as quickly as possible. “Because the test is tiring, performance deteriorates over time,” explains Oldrati. “That can be measured objectively—and people with fatigue demonstrate a higher drop in performance.”

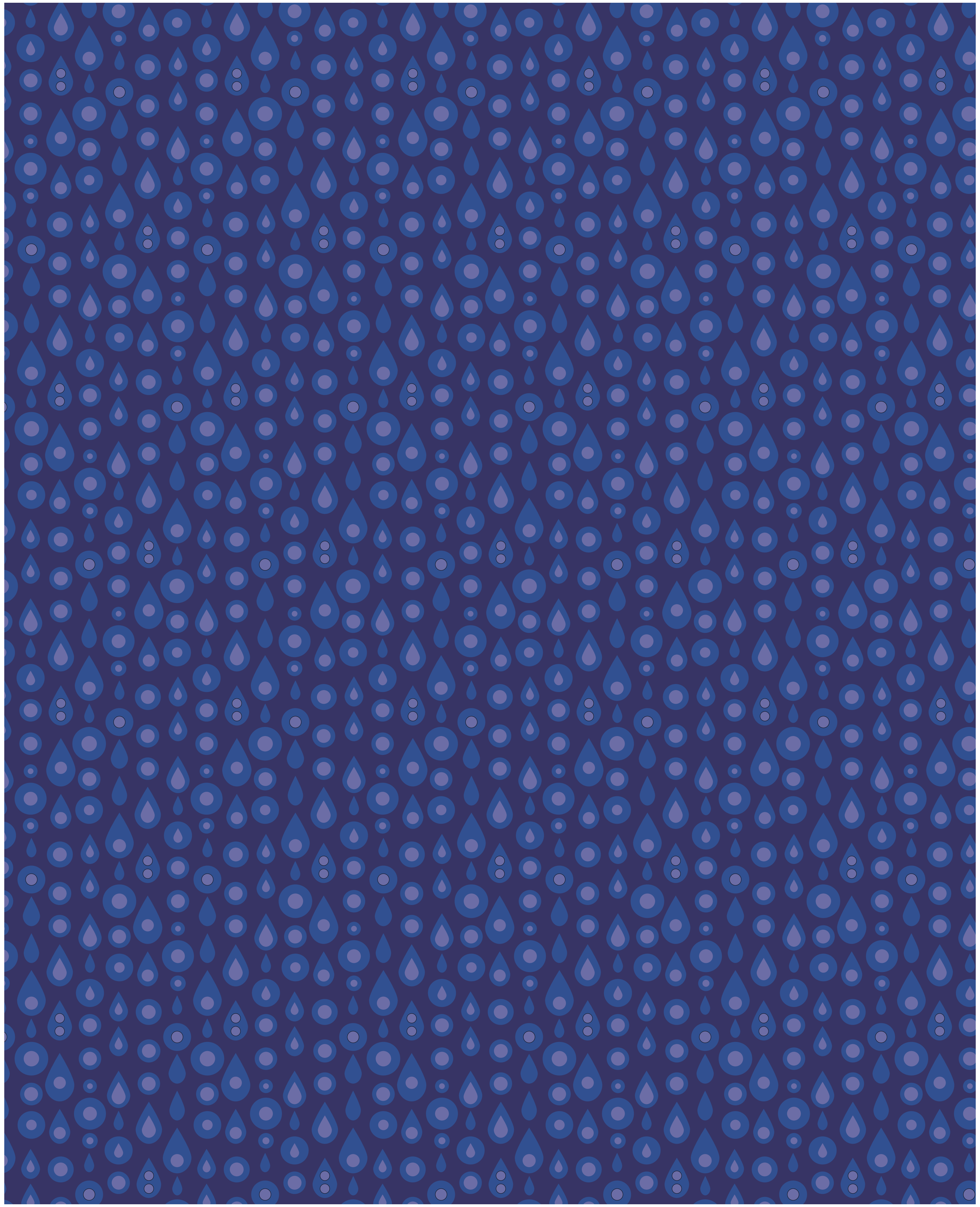
Irregular heartbeat

In the final method, the measurements are carried out directly on the body. A monitor worn on the patient’s upper arm functions as a pedometer and records the interval between two heartbeats. “People with multiple sclerosis and other diseases often exhibit fluctuations in heart rate variability,” says Oldrati.

Pietro Oldrati is convinced that combining the three measurement methods will enable medical professionals to make precise observations of fatigue without placing an undue burden on the patient. In order for his platform to succeed on the market, however, it must do more than just reliably prove the existence of fatigue. “It’s also important to find a simple way for doctors to integrate this information into everyday treatments,” Oldrati says.

If his endeavour succeeds, the outlook is promising—both for the planned start-up company and for people suffering from debilitating fatigue.

Pietro Oldrati is developing a system to objectively measure fatigue levels in patients with chronic illnesses. Smartphones and fitness trackers are used to record the data.



Cartilage regeneration

Newly supported project TriggerINK in Aachen

Healthy cartilage thanks to bio-ink

What can be done to aid cartilage regeneration in damaged joints? This question is at the heart of the TriggerINK project, which was recently awarded funding from the Werner Siemens Foundation. As a visit to the project team's lab at DWI – Leibniz Institute for Interactive Materials has made clear: regenerating cartilage takes novel materials, modern technology—and teamwork.

The project leaders at TriggerINK: Professor Andreas Hermann, Professor Stefan Hecht, Professor Laura De Laporte and Professor Matthias Wessling (left to right).

Laura De Laporte (left) and her colleagues are specialised in using novel materials to fabricate complex structures of natural tissues for medical application.

Conventional wisdom has it that the best researchers are loners—solitary introverts who shut themselves away from the world, poring over a problem until the solution reveals itself in a flash of inspiration. And while it's true that some of the great questions of our time have been solved this way, many research endeavours are simply too complex to be mastered by a single person.

That's why no less than four research groups are working together in the TriggerINK project at DWI – Leibniz Institute for Interactive Materials. The aim of the large-scale undertaking, which the Werner Siemens Foundation is supporting with 10 million euros over a five-year period starting in 2022, is to develop a visionary method for cartilage regeneration.

The project is led by Laura De Laporte, member of the scientific board at DWI in Aachen and professor of advanced materials and biomedicine at RWTH Aachen University. Also on the team are her RWTH colleagues: Stefan Hecht, DWI scientific director and professor of macromolecular chemistry; Andreas Hermann, DWI deputy scientific director and professor of macromolecular materials and systems; and Matthias Wessling, member of the scientific board at DWI and professor of chemical process engineering. A team of external experts also supports the project in an advisory capacity.

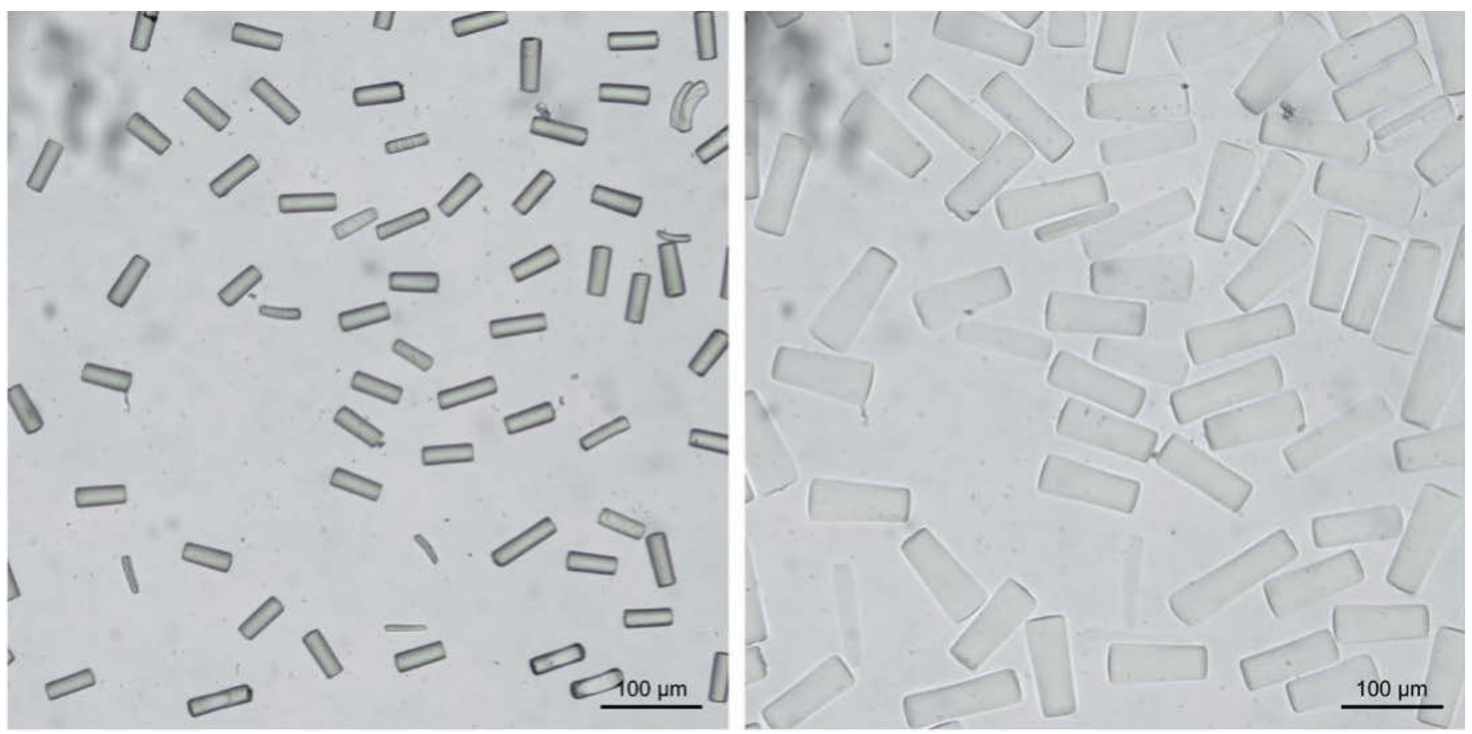
Problem point: the joint

TriggerINK aims to address one of the most common health issues of our time: joint pain. Although its causes are varied, cartilage loss (osteoarthritis) or a damaged meniscus in the knee number among the most frequent complaints. In Germany, one person in five has been diagnosed with osteoarthritis at some point in their life—and the numbers are set to increase as the population ages and obesity continues to rise.

Cartilage and the menisci have important functions: they absorb shock, they distribute the pressure exerted on the knee during movement and they enable bones in a joint to move quickly and smoothly, with minimal friction. However, worn or injured cartilage tissue can't regrow on its own, and although modern medicine has developed therapies such as cartilage transplantation as well as substances that promote tissue regeneration, these procedures are sometimes prohibitively expensive or their applicability is limited to a small subset of patients. And there's no guarantee of success.

One of the greatest difficulties in current cartilage regeneration methods is creating the tissue's structure, explains Laura De Laporte. Cartilage in the knee joint comprises different zones. First, and directly over the bone, it forms a hard layer with a vertical microstructure

The researchers test the consistency of their hydrogel on microscope slides.



A microscopic view of the microparticles in the bio-ink that change their size when exposed to light.

that new bone stem cells can penetrate only very slowly. The next and main layer, the middle zone, has a rather random cell structure. This is covered by the third zone, a smooth outer layer, whose cells and cell components are horizontally aligned. "Every tissue and every structure in our body has a clearly defined alignment," says De Laporte. "That's why it's imperative in tissue regeneration to steer cell growth in the right direction."

A sophisticated plan

To stimulate rapid and targeted cell growth, the TriggerINK team are benefitting from a broad range of sophisticated, cutting-edge procedures. Their plan to stimulate cartilage growth comprises the following steps:

- Using a 3D printer, hydrogel—a gelatinous substance made of mostly water and a small amount of a biocompatible polymer—is printed layer for layer onto the sterilised cartilage of a patient. The extremely porous hydrogel "bio-ink" forms a type of scaffold through which the cartilage tissue can regrow.

- The hydrogel is packed with particles that are important for cell growth in various ways. For instance, it contains magnetic gel rods with a diameter of two to five micrometres and a length of around fifty micrometres. As long as the hydrogel scaffold remains pliable, the gel rods can be aligned by activating a weak external magnetic field. The rods control the growth direction of the cartilage cells: the cells sense the resistance from the rods and grow parallel to their alignment.

- Particles containing growth factors or anti-inflammatory substances are also integrated in the hydrogel. As a remarkable feature, ultrasound can be used to stimulate the particles into releasing the substances locally and at specific times, thereby allowing the researchers to control various actions such as the activation of cell growth.

- A final component of the hydrogel are microparticles that can be manipulated externally using light. Depending on the intensity, the particles change in size, expanding and contracting and thus setting the surrounding tissue cells in motion. Previous research indicates that such movements accelerate the healing process.

First successes

A tour of the lab at DWI shows precisely how much research and collaboration is required to make this plan a reality. Nonetheless, it's equally clear that even after only one year, many components of the TriggerINK project are on a promising path.

For instance, Laura De Laporte's research group has already constructed a bio-ink. "We know that cells love this hydrogel and grow well in it," she says. In the patient, it's vital that the polymer strands of the hydrogel combine to form a hard, scaffold-like structure, but this crosslinking process should take place only after the magnetic rods in the gel are correctly aligned. This means the process must be activated externally.

Developing such an external control system is the work of Stefan Hecht's research group. One idea is to use chemical methods to affix certain molecules to the ends of the individual hydrogel polymer strands, thereby forming a type of protective cap that prevents crosslinking from occurring until the magnet rods are correctly aligned. Then, light is used to release the protective caps from the ends of the hydrogel strands, and the polymers are free to crosslink. One problem with this method is that the released molecules remain as a by-product in the body. "It's difficult to predict whether and how they may react with other substances," says Stefan Hecht.

Photoswitch trumps protective cap

Hecht and his team are therefore researching an innovative alternative: molecular photoswitches. This involves synthesising certain molecules that change their form and properties when irradiated with light. The approach has the advantage that no additional protective caps are required. The synthesis of photoswitch molecules is complex, but Stefan Hecht believes he and his team are on the right track. "The system works. After all, improving and accelerating syntheses is the core competency of a chemist," he says.

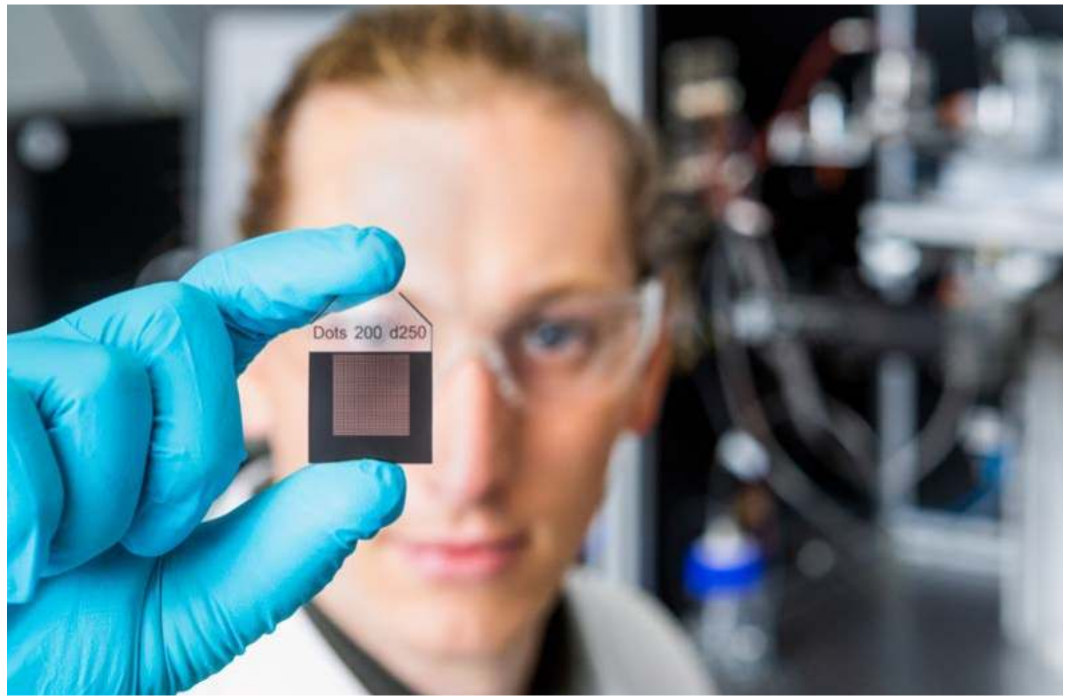
Producing the magnetic rods for the bio-ink is the terrain of Matthias Wessling and his research group. Like the bio-ink itself, the microrods are also made of a hydrogel; they contain magnetic nanoparticles. The rods are produced using a customised machine developed by the process engineers in Wessling's team. In a method called stop-flow lithography, the polymer flows through fine tubes and is then hardened in specific regions by ultraviolet light.

With the help of templates, the hydrogel can be shaped not only into rods but also an endless variety of other shapes. "We've already been able to substantially improve the stop-flow method in the first few months of the project," says Matthias Wessling. Among other developments, a new production machine is also in the pipeline.

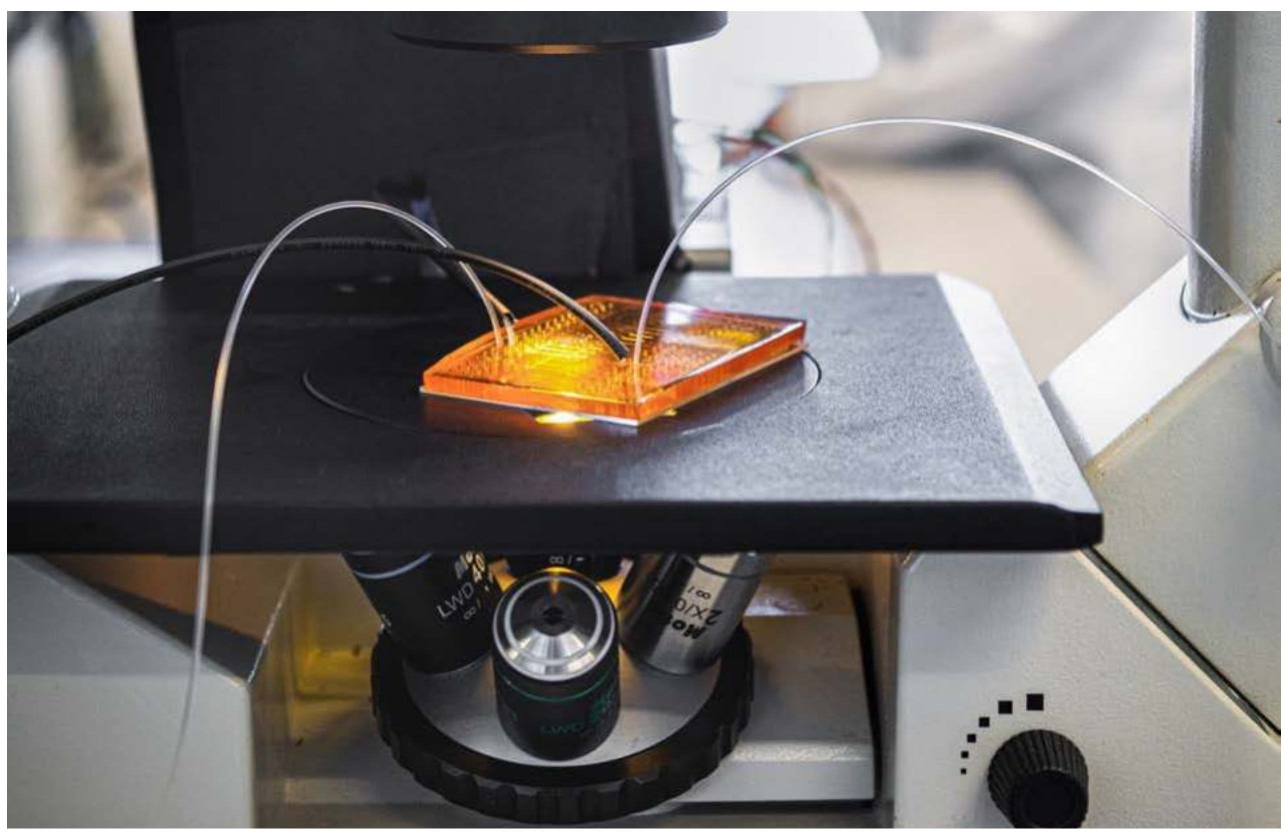
Reactions in the body

The team carefully study the properties of the produced rods and particles; models are used to show how the rods and particles react when, mixed into the bio-ink, they're introduced into the body using a cannula. Do they gather on a boundary layer? How do the rods and the ink interact? Answering such questions is essential if unintended outcomes are to be avoided. It also demands intense collaboration between the various groups.

The fruits of these efforts can be admired in another lab. A member of Laura De Laporte's team prepares a culture dish with bio-ink containing magnetic rods and



With the stop-flow lithography method, small templates are used to shape the hydrogel particles in a wide variety of forms.



In the TriggerINK lab, viscous polymer and oil are combined to create microgel droplets; after being exposed to light, they harden into different shapes.

Using a hand-held ultrasound device, the researchers can activate prepared molecules—both in a test tube and in the tissue of lab animals.

holds two magnets close to the dish. Viewed under the microscope, it becomes apparent that the rods have all turned in the same direction. The ink is then solidified and a new layer is applied, whose nanorods are facing in a different direction. With this process, the researchers are able to simulate the differently aligned cell layers in different cartilage zones.

Growth on demand

Andreas Hermann and his research group are responsible for the next step in the TriggerINK procedure—using ultrasound to externally control the release of biological substances. In the case of TriggerINK, these are growth factors and anti-inflammatories. These molecules are prepared with carrier particles that change when subject to mechanical force. For instance, the application of ultrasound causes the carrier particles to release the growth factors or anti-inflammatories deep in the tissue—at precisely the right time and location.

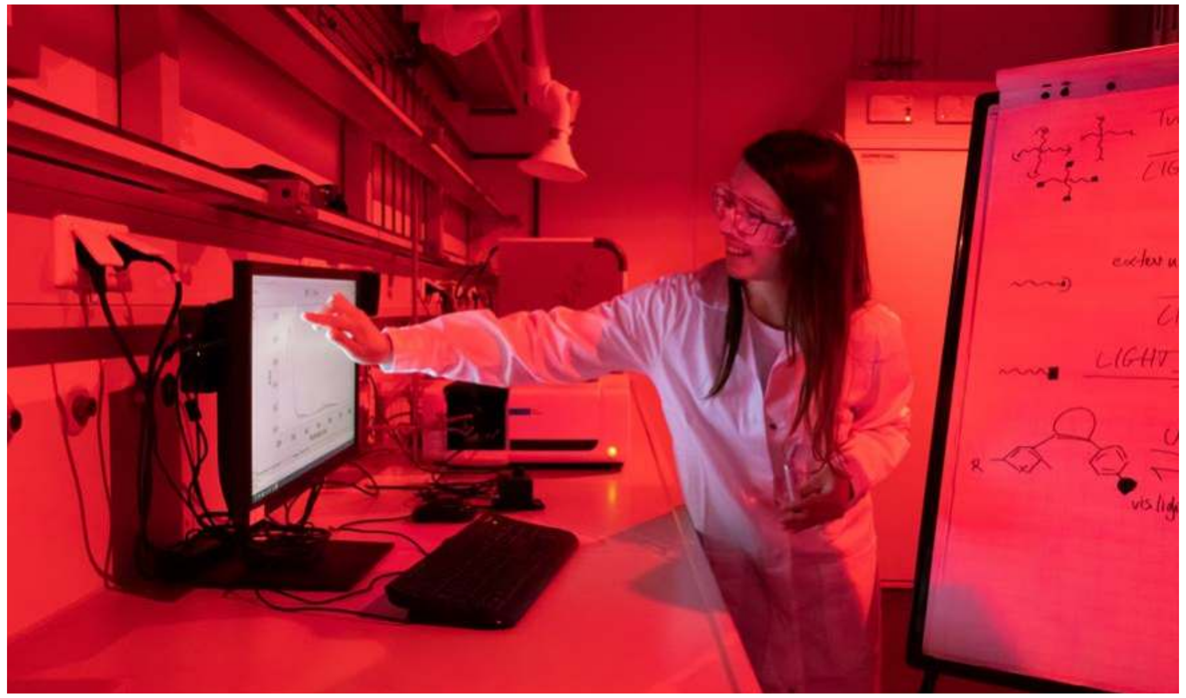
"Until now, one drawback with this type of activation has been the high ultrasound intensities required," says Andreas Hermann. One of his students demonstrates the problem by putting a transparent liquid in a small tube and inserting it in a box-shaped, high-powered ultrasound device. The sound pressure causes the liquid to turn blue—during the process, however, the researchers must either wear protective earmuffs or leave the room.

Such high sound pressures are obviously unsuitable for use in practice. "But recently we've achieved a breakthrough," says Andreas Hermann. "We proved that we could activate enzymes in the body also with much lower levels of sound pressure." In their tests using a hand-held ultrasound scanner, the researchers succeeded in activating the immune cells of sick mice, thus shortening their recovery phase.

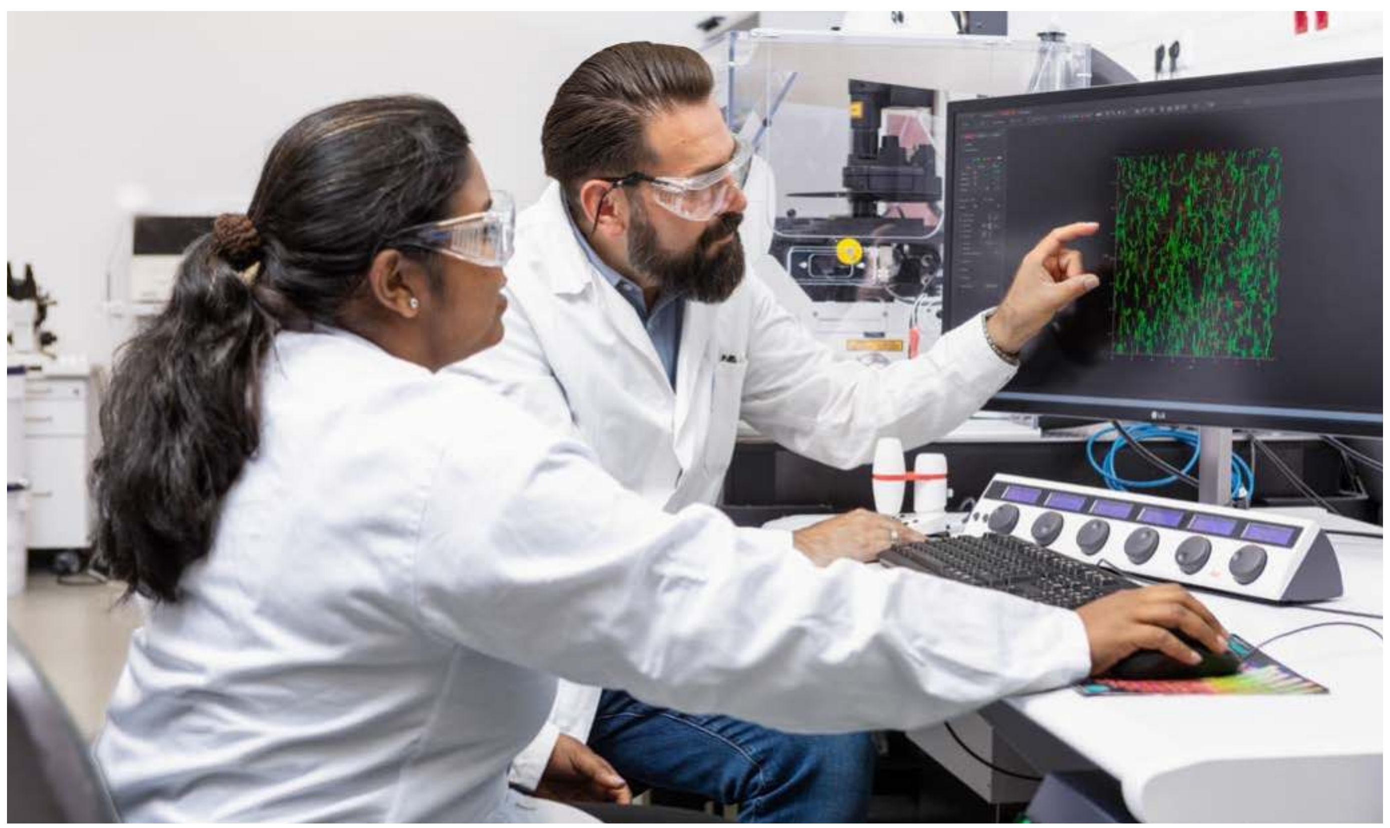
There remains just one final component to complete the cartilage-healing bio-ink of the future: contracting and expanding microgel particles that mechanically stimulate the cells. These particles are produced in Laura De Laporte's lab using a special technique to create a controlled emulsion. In tiny ducts, the liquid hydrogel forms small drops when it's mixed with oil. Depending on duct size, flow conditions and properties of the liquid, different drop shapes result. The drops are illuminated in the duct and harden as microgel in the form given by the conditions. The aim of the researchers is to produce a whole library of such microgel shapes and to test their properties. "We don't yet know which magnitudes are most suitable for our project," De Laporte says.

Healing through movement

The microgels are to function like tiny little sponges in the bio-ink: infrared light impulses that penetrate deep into the tissue will cause the microgels to collapse—they wring themselves out and become smaller. This shrinking



Chemistry or alchemy? Some molecules—so-called photoswitches—change shape when irradiated with light.



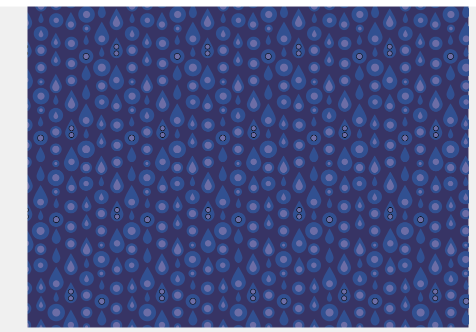
The data on the monitor show that the bio-ink growth can be steered through a scaffold made of magnetic rods—just as planned.

is what sets the surrounding hydrogel and the growing tissue in motion, thus accelerating the healing process.

Although regenerating cartilage with the TriggerINK method remains a long-term vision, the various subprojects are gradually forming a whole. Preliminary experiments have shown that the magnetic rods in the bio-ink influence the direction of cell growth. After the rods have been aligned in a certain direction, the cells are left to grow for several days. When observed under the microscope, it can be seen that they do indeed grow along the rods.

Teamwork and communication

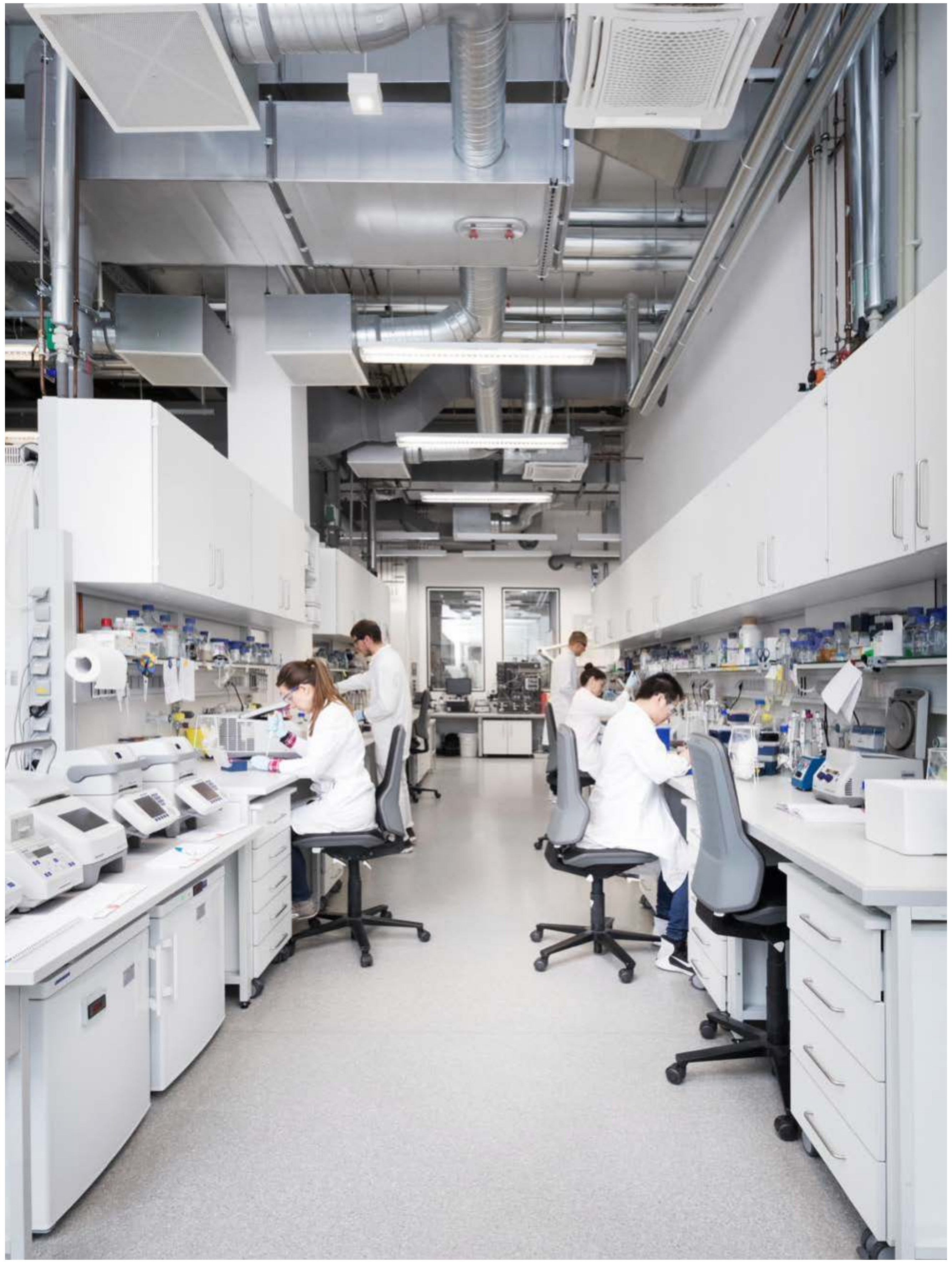
It's fair to say that the ambitious TriggerINK project is off to an excellent start. And that, explains Laura De Laporte, is also thanks to Arne Lüken, the project's outstanding coordinator. Depending on the issue and objective, one of his many responsibilities is bringing the individual research groups and subgroups together. Something he does very well, as Laporte says, adding: "The team are passionate about the project. It has led to new collaborations within DWI and allowed the researchers to get to know each other better. That's great for those involved, and the whole Institute benefits."



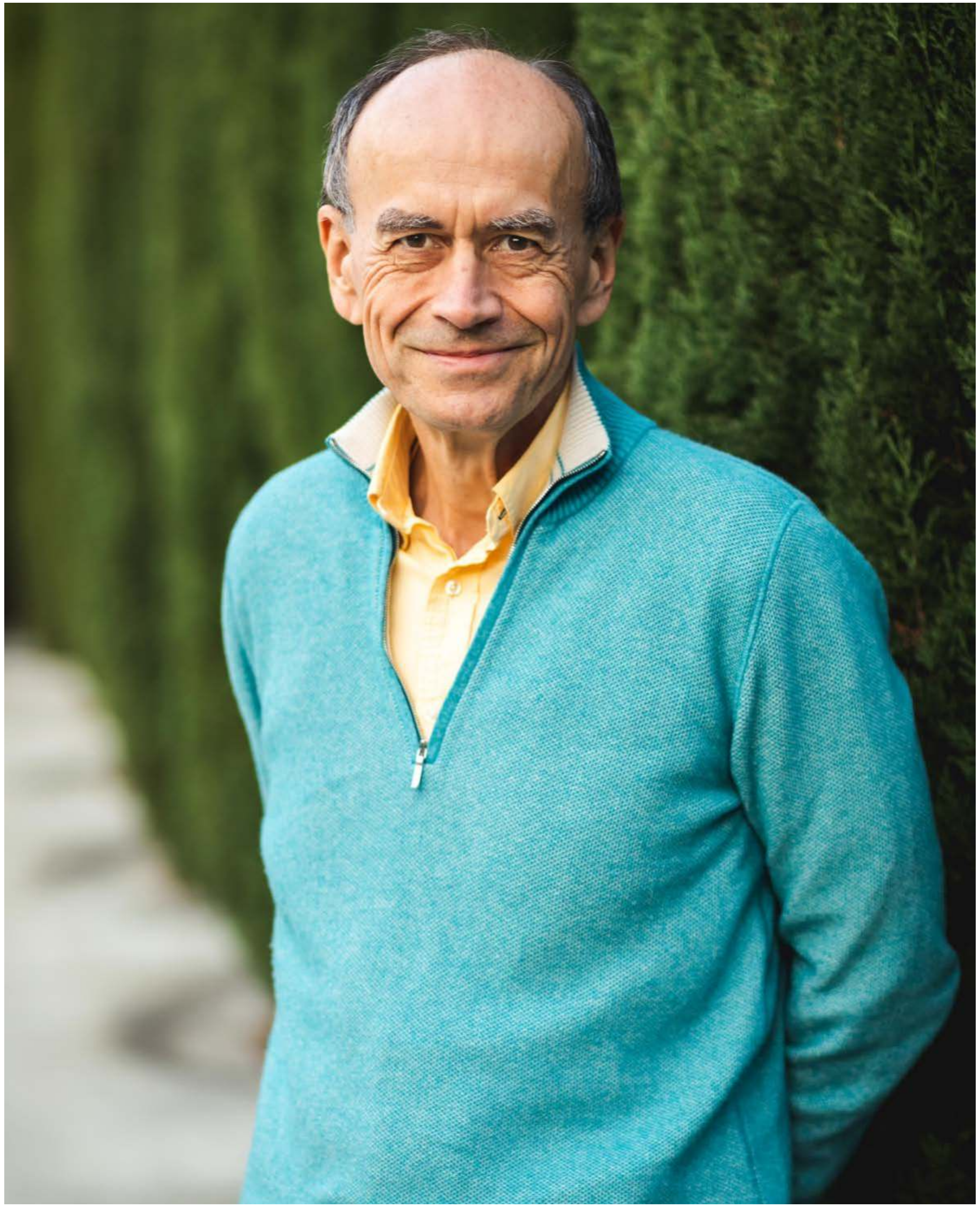
TriggerINK

A scaffold made of bio-ink to help damaged cartilage regenerate: this is the aim of the TriggerINK project at DWI – Leibniz Institute for Interactive Materials in Aachen. The innovation takes advantage of pioneering 4D printing technology.

Funding from the Werner Siemens Foundation 10 million euros over 5 years
Project duration 2022 to 2026
Project leaders
Prof. Dr-Ing. Laura De Laporte, member of the scientific board at DWI – Leibniz Institute for Interactive Materials and professor of advanced materials and biomedicine at RWTH Aachen University
Prof. Stefan Hecht, PhD, scientific director of DWI – Leibniz Institute for Interactive Materials and professor of macromolecular chemistry at RWTH Aachen University
Prof. Dr Andreas Hermann, deputy scientific director of DWI – Leibniz Institute for Interactive Materials and professor of macromolecular materials and systems at RWTH Aachen University
Prof. Dr-Ing. Matthias Wessling, member of the scientific board at DWI – Leibniz Institute for Interactive Materials and professor of chemical process engineering at RWTH Aachen University



To realise the ambitious TriggerINK project, researchers from a wide range of disciplines are combining their expertise in the labs at DWI – Leibniz Institute for Interactive Materials in Aachen.



“Keeping sight of the bigger picture is essential”

The stated aim of medical research is to cure disease. And yet, when clinical trials prove unsuccessful, research labs and pharmaceutical companies alike too often fail to adjust their strategies. A conversation with neuroscientist and Nobel laureate Thomas Südhof on abysmal studies, effective research funding—and the Alzheimer’s debacle.

Thomas Südhof, have you ever climbed Mount Everest?
No. (laughs)

I could well imagine you have. In your research, you set your sights on the highest peaks: you study what is possibly the most complex organ in our body, the brain. What led you to do so?
The brain may well be our most complex organ. It makes us who we are, something that has always fascinated me. But we shouldn't underestimate how many secrets other organs still hold. Even the cell, the smallest unit in an organism, whether animal or plant, is complex and not yet understood.

The more closely we look, the more complicated it gets.
Yes. Originally, I studied medicine. My desire to understand is what motivated me. After earning my doctorate, I began researching cholesterol transport because I wanted to gain deeper insight into how lipid metabolic disorders develop. Although I saw that much remained to be discovered in this area, I also realised that quite a bit was already known—and that outstanding scientists were hard at work on the problems. The brain was largely unexplored at the time, so there were great possibilities for researchers. That was what lay behind my decision to go into brain research.

You're specialised in synapses, the junctions between neurons in the brain. What makes them important?
Synapses are nodes where neurons communicate. But they're also the central processing units in our brains. When one neuron transmits information to another, the signal isn't simply passed on: it changes at the synapse. And still, most neurobiologists focus on the neurons—counting how many times they fire—without considering the synapses. What's truly significant, however, is how the information encapsulated in the firing of neurons is transmitted and, in the process, recalculated. This varies from synapse to synapse: there are many different kinds of synapse, with every neuron having thousands, tens of thousands and sometimes even hundreds of thousands of them.

It's an incredibly complex system.
That's why synapses are often overlooked in theories by systems neurobiologists, although they're involved in everything the brain does. Conditions like neurodegeneration, epilepsy, autism, schizophrenia or Tourette's syndrome are ultimately all linked to synapses. The problem is that we don't understand most brain disorders, we don't know what causes them. Alzheimer's disease is a prime example.

With regard to Alzheimer's in particular, many attempts have been made to cure it. But there have also been many setbacks. Are you surprised?
Not in the least. Roughly thirty years ago, it was discovered that a small peptide called amyloid beta is a major factor in Alzheimer's disease; its exact role, however, is still unclear. What we do know is that this peptide is deposited in the form of insoluble accumulations—plaques—that are found in the brains of all patients with Alzheimer's. These plaques are formed already ten, twenty, even thirty years before the first symptoms present. Among many researchers, the conviction that the peptide itself is toxic gained ground, so the pharmaceutical companies all began developing medications that alter the amyloid beta or its production, and millions upon millions were invested. That made sense, no question about it.

"Made" sense?
At first, yes. But after many, many clinical trials, it became clear that suppressing the enzymes responsible for amyloid beta exacerbates symptoms of Alzheimer's. In short, the medications were making the disease worse. This result is actually unsurprising, especially if we think that these enzymes process a range of different substances, making them important for the brain's functioning. Afterwards, there was a series of clinical trials that removed amyloid beta directly from the brain, but no substantial improvement in patient health was detected.

There seems to be a lack of basic knowledge about how the brain functions. Were the clinical trials started too early because a drug to treat Alzheimer's would be highly lucrative?
A very good question. The relationship between basic research and clinical studies is complex. Sometimes it's necessary to begin clinical trials before we understand everything to the last detail. This is the case when the need for a treatment is extremely dire and a mechanism seems plausible. With amyloid beta, the original trials were justified. But the real question is: what happens when it becomes clear that an approach won't result in significant progress? With amyloid beta, the original studies showed that it's possible to remove the peptide from a patient's brain—but without attaining a measurable improvement in patient health. That's why it really no longer made sense to continue working in this direction in order to develop similar, maybe minimally better antibodies. It would make more sense to invest in basic research and gain a better understanding of the disease.

"Conditions like Alzheimer's, epilepsy, autism and schizophrenia are ultimately all linked to synapses. The problem is that we don't understand most brain disorders."

What problems arise when an unpromising approach is nevertheless continued?
Ethical, financial problems—and those that implicate research practice itself. Patients are subjected to experiments that will clearly never succeed, which is unethical. In addition, clinical trials cost pharmaceutical companies billions, money that could be invested in other trials at these companies. Patients, too, are unavailable for other studies. And university hospitals, which are frequently involved in these projects, are left with fewer resources for other work.

Thomas Südhof
Thomas Südhof (1955) is a neuroscientist specialised in how neurons communicate via synapses. After earning his PhD at the Georg August University of Göttingen in Germany, he went to the US to conduct research on cholesterol metabolism and transport at the University of Texas Southwestern Medical Center in Dallas, where he was named professor in 1986. In 2008, he moved to Stanford University, where he was appointed head of the Center for Molecular Neuroscience in Health and Disease in 2015. Thomas Südhof has received numerous awards for his work, including the 2013 Nobel Prize for Medicine for his discoveries related to the transmission of stimuli between neurons. He also advises several pharmaceutical companies.

And so research stagnates?
Precisely. The wrong signals are sent. The pressure to conduct applied research is growing in numerous countries. When pharmaceutical companies invest billions in amyloid beta toxicity, governments believe it's the way forward —and they, too, fund projects in the same area. That means wasted money, lost opportunities. All this has consequences. Science currently has a credibility problem in society, and it's partly because so many mistakes are being made.

Is it also because study findings are later proven to be incorrect?
Yes, certainly, it's a huge problem. Science publishing is a broken business. We can no longer trust journals to honestly review articles, and pharmaceutical companies can no longer rely on published findings.

Not even research findings published in top-tier journals?
Exactly. Today, if a pharmaceutical company finds a study interesting, it repeats the investigation in-house, which is an absolute waste of money. But they do it because quality control is abysmal, even at the best journals.

Why?
Commercial reasons. The journals are interested in publishing as many papers as possible to make money.

Does this then impact research funding, which is awarded mainly on the basis of publications?
Of course. The publishing industry is currently the biggest problem in academic research. It's even worse than the lack of money, worse than anything else, in fact.

How could we solve the problem?
Through regulation. Science publishing is the largest industry in the western world that isn't regulated. Journals can publish what they want. They can make any assertion they please. There's no liability, no accountability. There are companies that own hundreds, even thousands of journals. It's like the Wild West.

So we have no way to know how good a journal is.
That's right, and if they publish incorrect information, it's never retracted.

"The publishing industry is currently the biggest problem in academic research. Worse even than the lack of money."

If false data are published, aren't researchers held accountable?
No. And while the system will correct itself eventually, it takes a long time. This mainly happens in that false findings never lead to anything viable. The studies are still accessible and are cited, but no therapies or real-world applications based on them are ever

developed. Amyloid beta is a good example. Many, many studies on the peptide have been published in renowned journals, but most are wrong.

For example?
One study maintained it's possible to diagnose Alzheimer's by detecting amyloid beta in skin biopsies. Utter nonsense. Other researchers removed the ovaries of mice to simulate menopause. The study—published in *Nature*—claimed this led to a loss of up to fifty percent of all synapses and would explain why postmenopausal women develop Alzheimer's more often. Can you really imagine that women generally lose half their synapses in the brain during menopause? It's not very plausible. And then there's the recent discovery that data in an influential *Nature* paper on amyloid beta published nearly twenty years ago were falsified. It all illustrates how problematic the business of science publishing is.

"The most important criterion for awarding funding should be quality. When evaluating proposals, keeping sight of the bigger picture is essential."

Has this uncovering of bad practices had a positive impact on Alzheimer's research?
I'm not certain, but I think so. In the meantime, it's become clear that studying amyloid beta alone won't get us anywhere. That's why all the research now is focusing on another aspect: immune cells called microglia. Suddenly, most researchers are convinced that Alzheimer's is linked to an immune reaction—certainly true, but it doesn't explain everything. The same labs that published papers in Nature about amyloid beta are now publishing articles about microglia in *Nature*. Just like lemmings. (laughs)

Do you think the people and institutions sponsoring and funding research should make an effort to help improve the situation?
Yes, and that includes foundations like the Werner Siemens Foundation. The most important criterion for awarding funding should be quality. When evaluating proposals, it's important for experts to not lose sight of the bigger picture, to keep track of an entire field—and not just focus on the latest findings and trends.

Do you see fundamental differences in how funding is awarded in the US and Europe?
Yes, I do. In the US, almost all research is financed through third parties. For example, Stanford University doesn't pay my salary: the money stems from third-party funds at the Howard Hughes Medical Institute—and I have to reapply for my research funding every five years.

I noticed you even have a donate button on your group's website. That's rarely seen in Europe.
(Laughs) Unfortunately, it doesn't work.

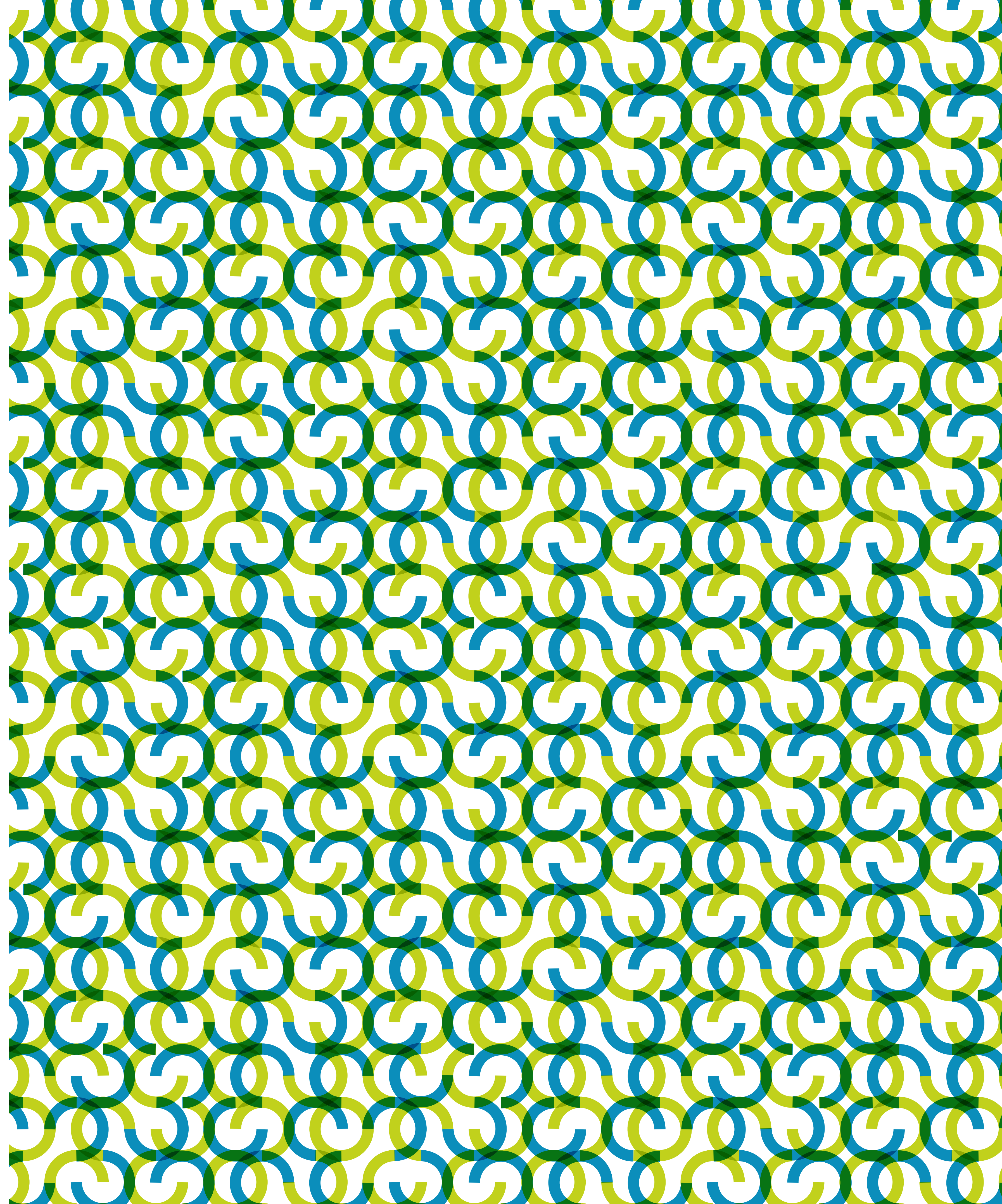
It doesn't hurt to try.
In Europe, at least in Germany, all major labs are permanently funded—and they're often huge. At Stanford, there are a few labs that are really big, but most—mine included—employ twenty-five researchers tops. A lot of my former postdocs in Europe have much larger labs. Although they, too, have to submit applications to third parties, these funds often make up less than half of the overall financing. Both systems have their advantages and disadvantages. The good thing in the US is that researchers are held accountable for their work at all times. As a result, the money is often awarded wisely.

And the disadvantage?
The pressure is huge. Fewer and fewer people are interested in pursuing a career in research. There's no security, you constantly have to work at drumming up money for your salary and research. It's especially difficult for women who want to have children. We need to do more there.

In Europe, too, there's no guarantee of a professorship after a postdoc.
But if you have a job in Europe, you have it for the long term. On the downside, however, this means that researchers might just keep doing the same thing. They're no longer motivated to prove anything, they're situated comfortably within a gigantic apparatus and don't produce much that's new. The other problem in Europe is that the research world is too small. In Germany, everyone knows everyone. Even more so in Austria and Switzerland. The result is that nepotism in research funding is on the rise.

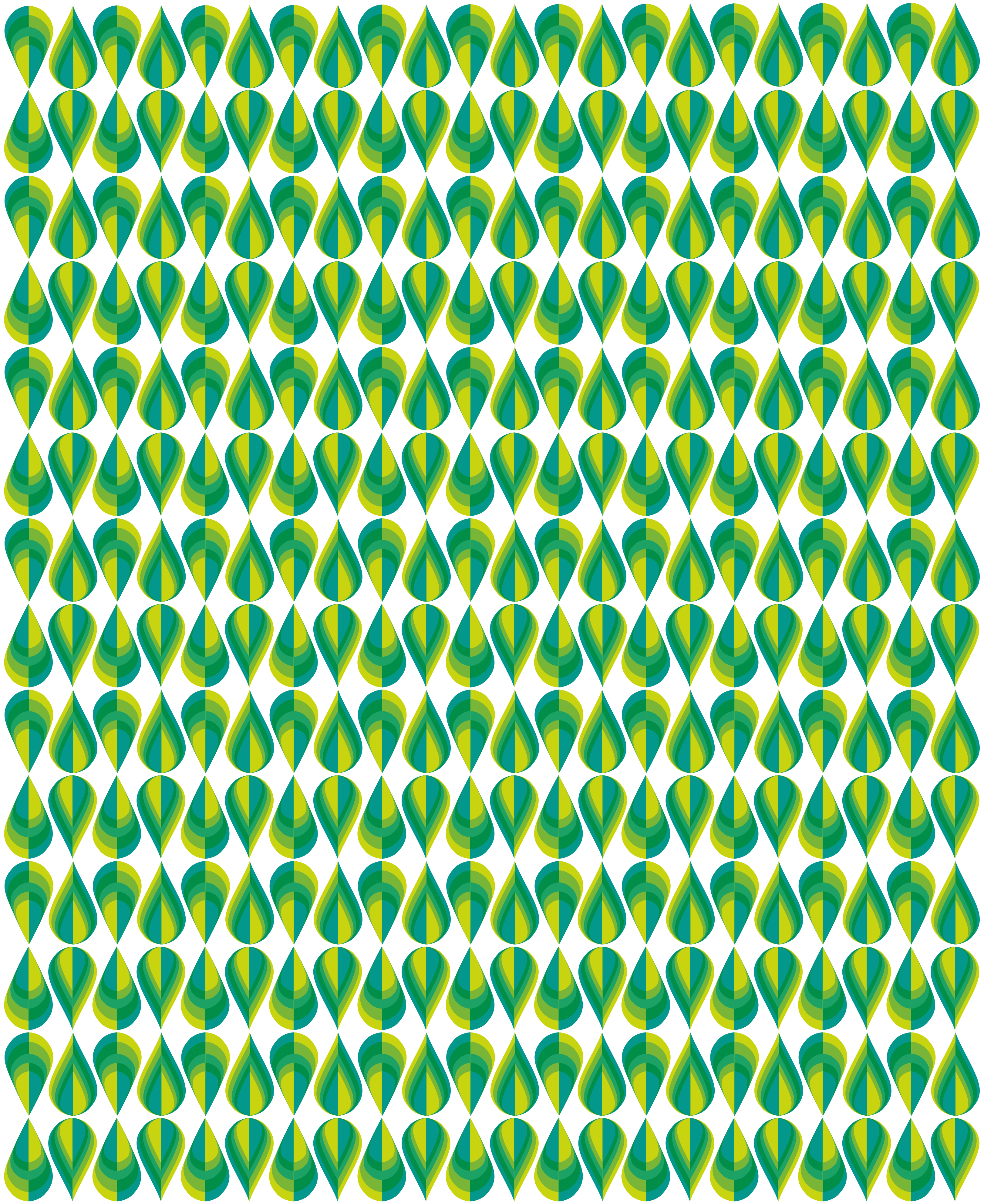
You've made major advances in your field and have received numerous honours, including the Nobel Prize, the most prestigious of them all. What makes you such a good researcher?
(Laughs and thinks for a long time) I have a strong tendency towards independence and scepticism, which is both good and bad. It's helpful in that these qualities make me resistant to trends and help me to critically question accepted opinions. Independent, critical thinking is of utmost importance in science. I believe it's my strength. But it's also a weakness. I don't feel comfortable working in bureaucracies or larger teams. I've never been president of anything, as other qualities are needed for those kinds of roles.

What's your advice for young researchers?
It's important to know your own strengths and weaknesses.
People who excel at devising specialised experiments should be the ones trying to solve scientific problems. But those with a talent for networking, teamwork and communication should work on interdisciplinary projects, or they should tackle issues that are of interest to governments. Both kinds of researchers should work and conduct research at universities. We need both.



Projects

In addition to projects in medical technology, the Werner Siemens Foundation also supports groundbreaking research in the natural sciences and technology. On the following pages, readers will learn about how the new WSS project FutureLab CERES at the Potsdam Institute for Climate Impact Research began its work—and discover what progress the other projects financed by our Foundation have made.

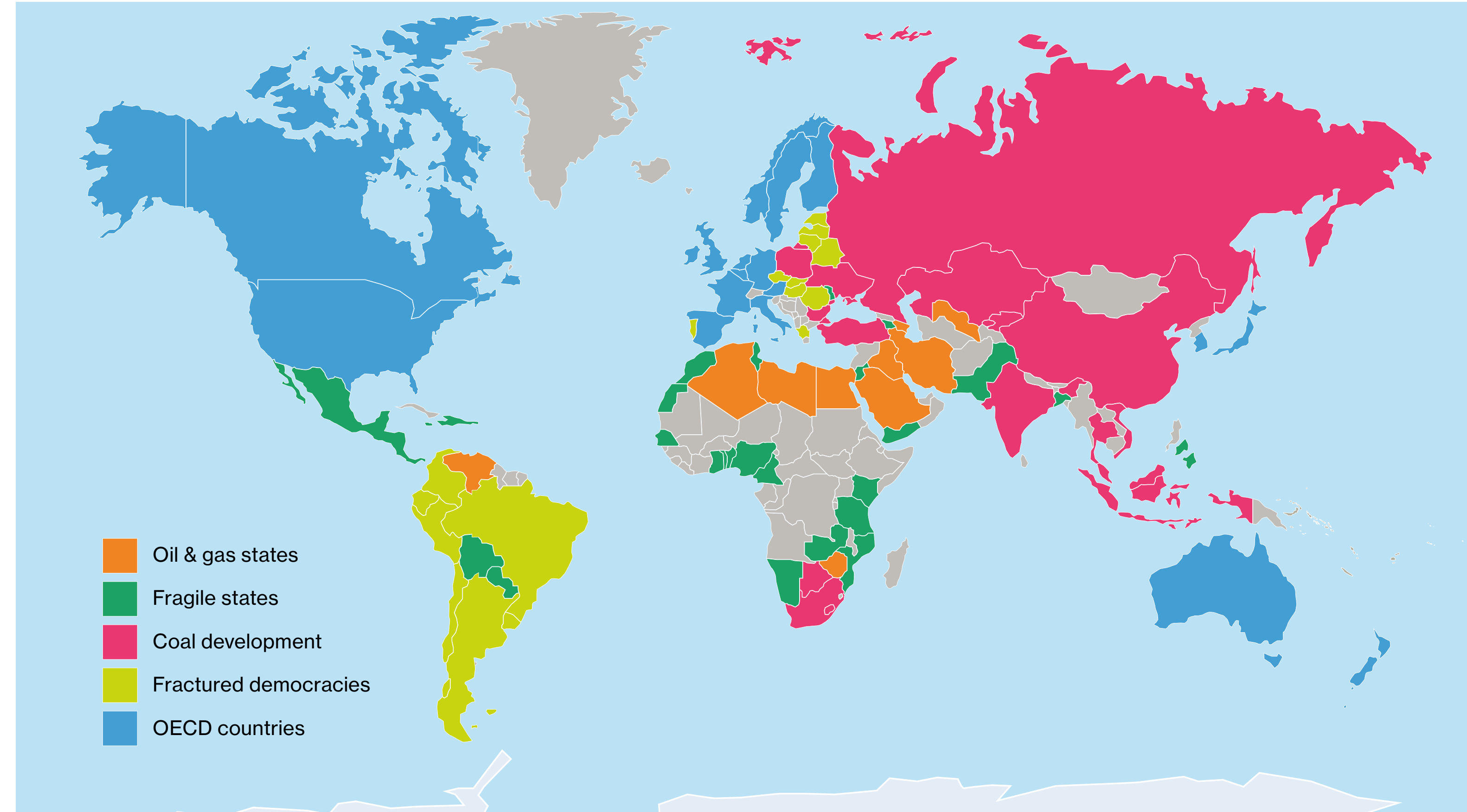


FutureLab CERES

Newly supported project FutureLab CERES

“Price is the main driver”

What political measures should be adopted to protect our planet’s climate, biodiversity and soils? Answering this question is the mission of FutureLab CERES, located at the Potsdam Institute for Climate Impact Research (PIK) near Berlin. The Werner Siemens Foundation began financing the project last year. PIK co-director Ottmar Edenhofer in discussion on how CERES is setting about the task.



What countries depend on coal, who profits from oil production and which nations are fragile? The FutureLab CERES project is studying how these factors impact climate protection.

Ottmar Edenhofer, the effects of global warming are becoming increasingly plain to see. Last summer, rivers nearly dried up, glaciers melted at a never-before-seen pace, and vast forest fires raged. How much more time do we have to turn things around?
To a certain extent, climate change is now inevitable. We can no longer stop it. We’ve already reached a global mean temperature increase of roughly 1.2 degrees Celsius. If we start reducing emissions now, we can hope to limit the increase to just under two degrees. In other words, we have no choice other than to adapt to much of what climate change will bring.

Is all really lost?
It would be an exaggeration to say that we’re heading for a precipice—and that when we get there, we’re bound to fall over the edge. When talking about climate policy, a marathon is the more apt metaphor. And to curb climate change, we have to reach the net zero mark by the middle of the century—that is, we must emit no more CO_2 than the atmosphere can absorb. To get there, emissions have to fall by six to seven percent every year. We’ve only just begun the marathon race.

Have you observed that nations are more likely to enact climate change policies now that the effects are becoming more obvious?
An estimate made by our researchers shows that, already today, the social cost of climate change is over one hundred euros per metric ton of carbon dioxide emitted. The cost increase will be more dramatic the further away we move from the two-degree target. So it’s clearly more cost-effective to meet the Paris Agreement goals than to accept unchecked climate change. And still: emissions continue to rise. The war in Ukraine has accelerated this trend because the price of natural gas has risen faster than the price of coal, which is even more harmful to the climate. This development has once again made coal an interesting source of energy. Especially countries in Southeast Asia have begun opting for coal. By contrast, other nations have taken action. But, in total, it isn’t enough.

At FutureLab CERES, researchers are investigating how global public goods like the atmosphere, oceans and biosphere can be managed sustainably. What more can be done when even the drastic events of the recent past have had no effect?
In reality, we’re flying blind. We don’t have an adequate understanding of which political measures to protect the climate have made a difference—and which have proven ineffective. The situation is comparable to a doctor who administers medications but doesn’t bother finding out whether, or in what combination, they improve their patient’s health. That’s why we’ve begun a large study at

About Ottmar Edenhofer
Ottmar Edenhofer is one of the world's leading experts on the economics of climate change. He is director and chief economist at the Potsdam Institute for Climate Impact Research (PIK), director of the Mercator Research Institute on Global Commons and Climate Change and professor of the economics of climate change at Technische Universität Berlin.

FutureLab. Our first step is to examine the EU's transport sector. Where were emission reductions achieved? What combination of political instruments facilitated this outcome?

How are you proceeding?
With big data. We're analysing massive datasets. What we already know is that most measures have done nothing. Only seven European countries have managed to reduce emissions in the transport sector.

Which countries?
Denmark, Finland, Germany, Ireland, Luxembourg, Portugal and Sweden. Our initial findings reveal that effective measures always involve pricing instruments—examples include a motor vehicle tax linked to CO_2 or subsidies for renewable energies. This is a key insight, as it shows that price is the main driver. We now want to apply the research method globally.

That's a lot of processing done by huge computers.
We have access to the large, high-performance computer at PIK, that's a big advantage. But first we have to find a way to establish causality between a policy measure and an intended result. To do this, my colleagues at the institute have

"The days of global appeals to morality are long past."

already developed several promising econometric methods. They collect and interpret data, all with the aim of deriving meaningful political recommendations. Because we're looking back—but we're also looking to the future. What will be effective? Which combinations of subsidies, taxes, standards and bans will bring about which results?

In a second work package, you're conducting case studies in several countries.
That's correct. We want to find out why governments continue to favour coal-fired power plants. To move away from coal, it's often not enough for a country to see the negative impacts of global warming. The reason is that many nations see coal as a fundamental guarantee for their energy security. As such, we need more than a replacement for coal: we also need changes within these political systems. With CERES, we're looking very closely at the economy and policies of different countries, and we're asking: who is pursuing what interests and how could an energy transition work in these specific conditions?

You're mainly investigating nations that are rich in natural resources but also very dependent on them—and that possibly lack the money to achieve a turnaround …
… or that have lots of money, but

whose elite classes benefit greatly from the export of fossil resources.

And therefore slow the transition.
We have to consider every aspect. If we don't take the trouble to truly understand the various interests involved, we'll never get anywhere. The days of global appeals to morality are long past.

You also visit the various countries—Brazil, for example, or the Congo.
Yes, we've already conducted several case studies and we have teams on-site. That's essential. It's not enough for

"We still have no adequate understanding of which climate protection measures are effective."

western European academics to sit in their offices and think about what these countries should do.

The Congo, where you're conducting a case study, wants to auction off oil and gas production rights in thirty different regions, many of which are located in protected peat swamp forests that store carbon dioxide. Do political decisions like this influence your work?
Definitely. That the war in Ukraine has driven global investments in fossil fuels is particularly worrying. As just one example: Ecuador is pushing forward with oil exploration. This kind of information is relevant for policy recommendations. That's why we're seriously considering the option of having multilateral development banks buy up and then decommission coal-fired power plants—while simultaneously offering reduced-rate loans to encourage these countries to shift to renewable energy sources.

What does Russia's war against Ukraine signify for your project?
It brings fundamental change. International cooperation projects are becoming much, much more difficult. And, as I said, coal is experiencing a renaissance.

So the war has had a negative impact on sustainability, climate protection and the environment?
Not only. It's true that the war is driving demand for fossil energies, but two major players have also set ambitious climate goals: the EU with the Green Deal and the US with the Inflation Reduction Act. These are powerful signals.

The EU and US are global economic powers. For emerging and developing countries that rely heavily on selling energy or raw materials, it's exponentially more difficult to enact political measures for sustainability and cushion any side effects with compensation. How can these countries find new sources of revenue?
This is a complex question that the CERES team is studying in our third work package. Many countries fail to diversify their economies as long as they're generating large revenues. One measure would be for exporting countries to tax fossil resources. But there will also always be a need for decision makers willing to invest in alternatives. Some countries are trying. Others want to maintain their fossil resource business for as long as they can. Our job is to understand their reasoning and then advise them accordingly.

Which countries are looking for alternatives?
South Africa is thinking about how it can manage an orderly phase-out of coal. And if development banks offered to buy up the coal-fired power plants and pay off debt in Vietnam and Indonesia, I think these countries would be very interested in phasing out coal.

In its fourth work package, CERES is looking at these kinds of international instruments and cooperation projects. But as you've mentioned, it's currently hard to put them into practice.
Yes, that's true, but Europe and the US are pursuing very similar goals. They

FutureLab CERES

The climate crisis has shown how overusing the earth's natural resources endangers the future of our planet—and of humanity. The team at FutureLab CERES at the Potsdam Institute for Climate Impact Research (PIK) are seeking to understand which political instruments will best promote the sustainable management of natural capital—and what stops decision makers from taking action.
The project's aim is nothing short of realigning our economic system along new, sustainable priorities. Today, gross domestic product (GDP) is the major indicator of a country's wealth and the success of its economy. However, GDP as a measurement takes no account of the natural world. According to some estimates, the earth's natural resources have shrunk by forty percent over the past thirty years. To protect and guarantee sustainable use of the oceans, biosphere and atmosphere, any future wealth index must include the global commons.
Research at CERES is divided into four work packages. The spotlight is placed on countries like Brazil, Indonesia, Columbia and the Democratic Republic of the Congo, which have a central role in the protection of natural resources. Although biodiversity in these nations is exceptional, they also face huge climate-related disasters—and they generate high revenues from exporting fossil fuels or natural resources.

Funding from the Werner Siemens Foundation 10 million euros
Project duration 2022 to 2031
Interim project leader
Prof. Dr Ottmar Edenhofer, co-director and chief economist at the Potsdam Institute for Climate Impact Research (PIK), Potsdam near Berlin

could think about forming a type of "club" that obliges members to commit to specific goals. The club members could agree on a CO_2 price and impose an import tariff on coal, oil and gas. They could also make climate-friendly technologies like carbon capture available. In light of the war in Ukraine, these kinds of ideas are promising. The German government has expressed great interest in this "club", and we've already initiated discussions there. With the CERES project, we're also examining how this kind of agreement might be structured.

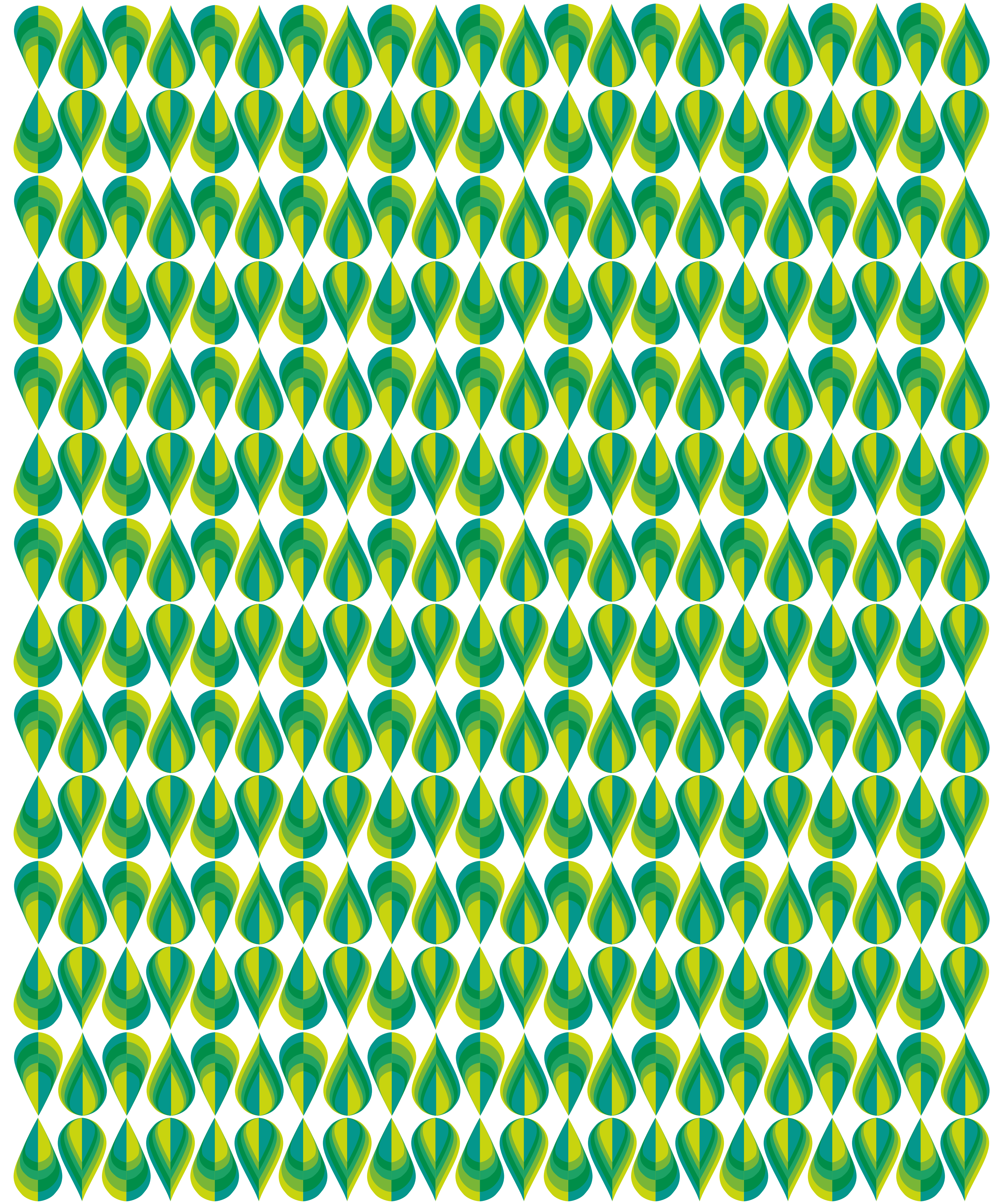
But relations between the West and other states have deteriorated.
Tensions between China and the US are high, but the countries will have to cooperate on certain issues. I certainly hope that climate is one of them. We're living in a world in which conflict and cooperation are increasingly interwoven.

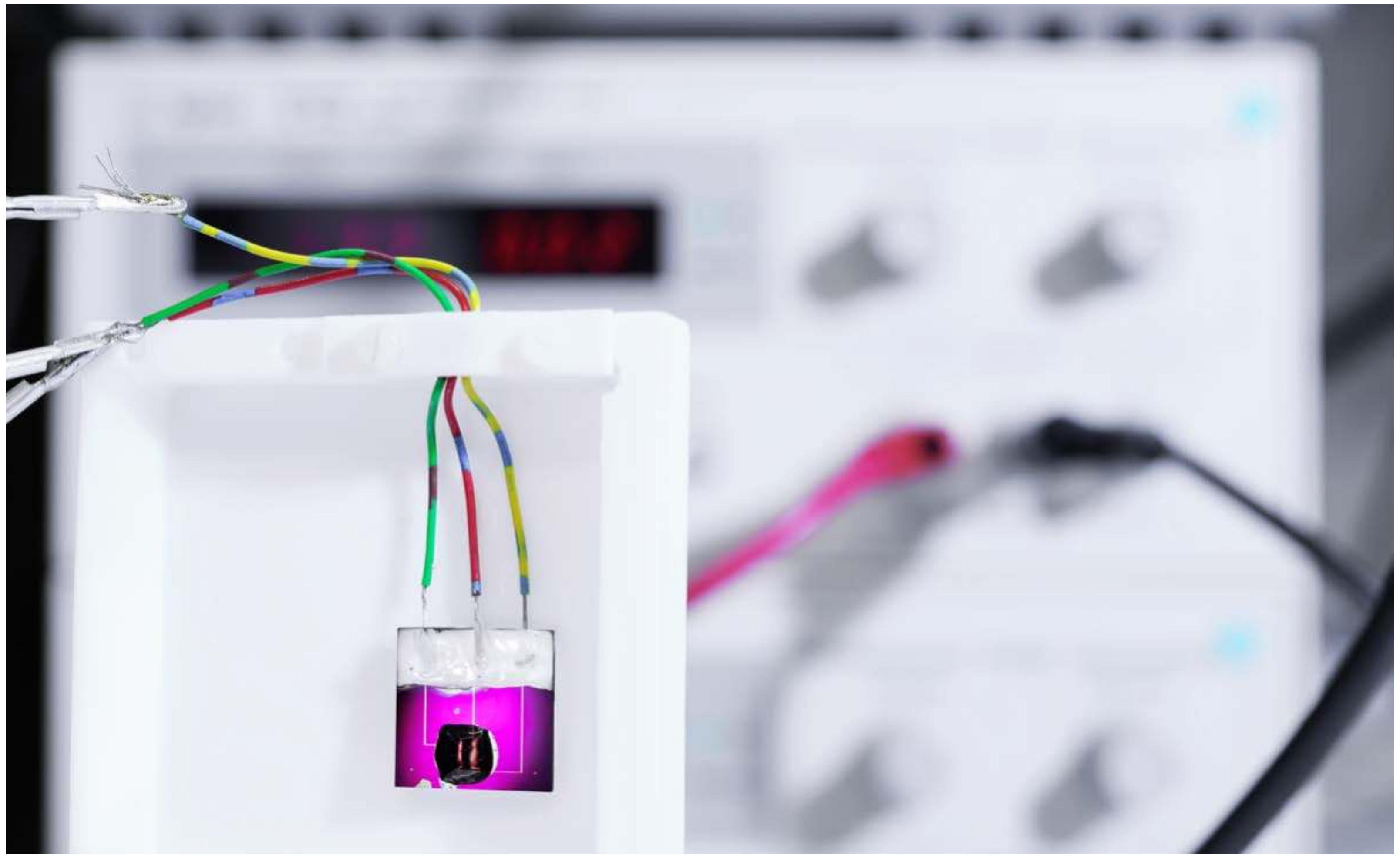
What else has the CERES project achieved in its first year?
We've been able to hire good researchers. And we're currently setting up a professorship for political economy. That said, we don't have to wait for the professorship to begin our research. We've already made a good start, and we're very much looking forward to tackling our research agenda with our new—and growing—team next year.

You've worked as a policy adviser on climate issues for quite some time. Is there a particular topic where you feel like a voice in the wilderness—an issue that politicians refuse to understand?
(Smiles) Yes. Climate- and sustainability-related issues pose the greatest dangers in the twenty-first century—but the dangers lie in the future. In politics, there will always be an event, crisis or trend that dominates in the short term. However, we should be thinking about the long term, because the interrelated crises surrounding sustainability, food, climate and biodiversity are escalating. This is actually what's most worrisome: we're dealing with multiple crises at the same time. We simply don't have the luxury of solving one at a time—we have to work on all of them at once. It's highly complex. The world of science acts like a radar that picks up the risks—and scientists must be able to advise policymakers.

How can researchers make themselves heard in the political sphere?
By offering impartial expertise—and being willing to be a pain in the neck. Also at PIK, our activities in the Intergovernmental Panel on Climate Change and the European Environment Agency enable us to maintain excellent networks in many different countries. For us, the CERES project is an additional reputational advantage: it helps open the doors of decision makers.

"We're living in a world in which conflict and cooperation are increasingly interwoven."





The single-atom switch project has made excellent progress, and the researchers are measuring switching speeds never seen before.

Record-breaking research

The miniature microchips of the future will function at the atomic level—and in their work to achieve the minuscule size-scale necessary, researchers at ETH Zurich and KIT in Karlsruhe have been busy setting records.

Boundaries are there to be tested. At least they are in the single-atom switch project, which the Werner Siemens Foundation has been funding since 2017. “This past year has shown that we haven’t yet reached the minimum physical limits of energy consumption in our switch,” says Jürg Leuthold, project leader and professor at ETH. In a first step, the project group led by Professor Thomas Schimmel at the Karlsruhe Institute of Technology (KIT) used tin electrodes to develop a transistor that switches on and off with a control voltage of just three millivolts, meaning it consumes some ten thousand times less energy than today’s conventional switches based on silicon semiconductor technology.

But no sooner had Schimmel’s group published an article on their record in July 2022 than they bested it: a few weeks later, the team reduced the control voltage by another factor of ten, down to 0.4 millivolts. Because the correlation between voltage and energy consumption is quadratic, energy consumption is reduced by a factor of one hundred: the new transistor is therefore a million times more energy efficient than today’s microchips—and it generates a million times less heat.

A mere fourteen picoseconds

Meanwhile, Leuthold’s group at ETH Zurich have set a different kind of record. Speed is an important metric for the single-atom switch, Leuthold explains: “The switches can be as small as you like—if they react sluggishly when turned on and off, no one will be interested.” Until now, the researchers did indeed fear this scenario, as the switching speeds in atomic switches are known to be much slower than in traditional microchips.

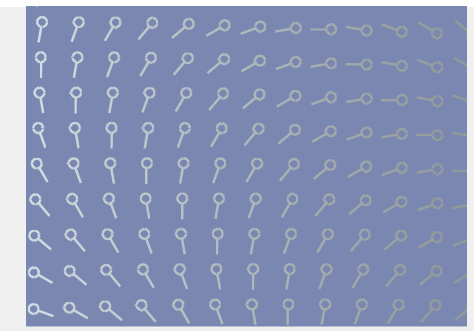
But not to worry: Leuthold and his team have reduced this value to a mere fourteen picoseconds. For clarity, that’s fourteen millionths of a millionth of a second. Leuthold says this tops the former world record for atomic switches and lies in the range of today’s silicon chips. In addition, he and his colleagues proved that the switch maintained its speed even after several dozen on-and-off cycles—and that resistance, hence the current, can be regulated. “Switching speed will no longer be a reason to rule out single-atom switches.”

Better components thanks to simulations

The team at the Center for Single Atom Electronics and Photonics have made remarkable advances in other areas as well. For instance, the researchers manufactured the first chip combining their single-atom switch with a traditional transistor; this experiment demonstrated that significant energy savings are already possible. And last but not least, the group led by ETH research partner Mathieu Luisier have taken an important step in their work on simulation models: they developed a platform on which the entire process of manufacturing the single-atom chip can be simulated—from the atomic-level structure to the completed component.

The simulations are crucial for better understanding the basic processes, says Leuthold, and they also show how the various components can be constructed to ensure the most reliable and energy-efficient functioning. The simulations also replace time-consuming and resource-intense tests, especially as researchers can otherwise easily spend several months building a new component after a “real-world” test has failed.

All in all, the prospects for a revolution on the electronics market are looking good, and Jürg Leuthold is now fairly certain that the new single-atom switch technology will one day replace silicon semiconductors as the standard technology.



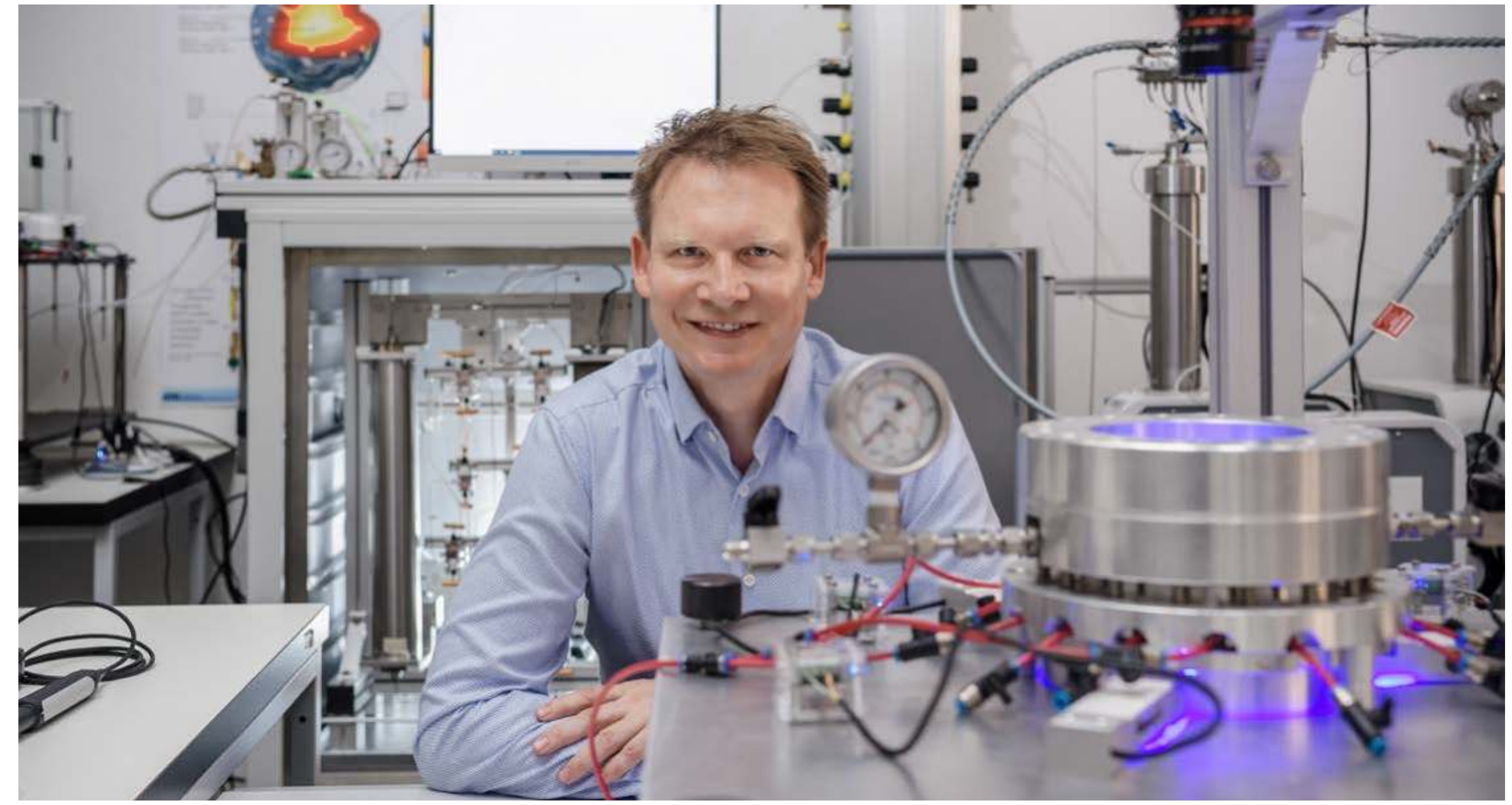
Revolutionary single-atom switch

From espresso machines to huge mainframe computers, microchips are in almost every electronic device we use. In recent years, researchers have succeeded in making microchips smaller and faster, but the push to get even more minuscule has now hit a wall, and the amount of energy the chips consume is a growing problem. That’s why researchers at the Center for Single Atom Electronics and Photonics at ETH Zurich and at the Karlsruhe Institute of Technology (KIT) are experimenting on a completely novel microchip—one that functions at the atomic level.

Funding from the Werner Siemens Foundation 12 million Swiss francs
Project duration 2017 to 2025
Project leader Prof. Dr Jürg Leuthold, head of the Institute of Electromagnetic Fields, ETH Zurich

Underground heating

With successfully concluded projects, a major new undertaking and negotiations with industrial partners: geophysicist Martin O. Saar, Werner Siemens Foundation Endowed Chair of Geothermal Energy and Geofluids at ETH Zurich looks back on a busy year.



Geophysicist Martin O. Saar has every reason to be satisfied: his innovative deep geothermal energy projects are meeting with great interest.

Deep geothermal energy

Geothermal energy is one of the largest unused energy reserves on the planet. Professor Martin O. Saar and his team at ETH Zurich are exploring ways to harness the earth's heat for large-scale energy production. In the project, Saar has developed a novel drilling technology—and an innovative concept for sequestering the greenhouse gas CO_2 underground while also using it to generate electricity.

Funding from the Werner Siemens Foundation 10 million Swiss francs
Project duration 2015 to 2024
Head of research
Prof. Dr Martin O. Saar, professor of geothermal energy at ETH Zurich

Renewable energies are the way of the future, a fact that even the most stubborn minds have been forced to concede following Russia's invasion of Ukraine and the heatwaves of the past summer. For Martin O. Saar, professor at ETH Zurich, the increased interest in his area of expertise—deep geothermal energy—is welcome news. Indeed, massive amounts of energy harboured in the earth's interior are simply waiting to be used.

Determining the extent of this potential is what Saar and his team are now investigating in a new project funded through a Swiss Innovation Agency "Innosuisse Flagship Grant AEGIS-CH" worth 11.4 million Swiss francs and spanning a period of four years. Saar, who leads the large-scale project, submitted the proposal with colleagues from research and industry. He says it was an honour to be selected, adding that the grant is also important for capitalising on the possibilities offered by deep geothermal energy.

Local geothermal energy plants

The project consortium aims to further develop the drilling method—Plasma Pulse Geo Drilling (PPGD)—which Saar helped to create. Instead of mechanically breaking up the rock, PPGD works with a type of electric shock: electric pulses blast through the rock via tensile force, starting at the bottom and moving up. The innovative technology requires only about a quarter of the energy consumed in standard drilling procedures, making it much cheaper to access geothermal energy at depths of roughly five to ten kilometres.

Saar hopes that the method can be used to build power plants that function much like the heat pumps used in residential buildings: two boreholes are connected at the bottom to create a U-shaped loop or circuit. Inside the loop, heat is extracted from the rock using carbon dioxide as a circulation fluid. The heat is then either used directly or converted into electricity in a power plant and fed into the grid. Saar estimates that a plant capable of extracting the earth's heat from depths of five to ten kilometres would deliver energy for 500 to 1000 people. These types of power plants could be constructed anywhere in Switzerland—by municipalities, for example—regardless of the specific geological conditions.

Cost-effective carbon sinks

Saar's second research priority last year was organising a consortium to facilitate pivotal advances in a method he's developed: CO_2 Plume Geothermal (CPG). Put briefly, CPG is designed to make the capture and underground storage of carbon dioxide cost-effective. When the greenhouse gas is stored between 2.5 and 3 kilometres below ground, it heats up to roughly 100 degrees Celsius. "It's this heat that we want to tap into," Saar explains. He envisions a cycle in which the heated CO_2 is transported to the surface, where it propels turbines. Afterwards it's returned to the underground reservoir to ensure that all carbon dioxide is permanently sequestered.

Because CO_2 is less viscous than water, the method is two to three times more energy efficient than technologies in existing or planned geothermal power plants, Saar says. He adds that he has contacted several leading firms as potential partners: "They're very interested, but we need a pilot project to prove the method works." And this is the precise aim of the new consortium. Saar hopes that work on the pilot can begin in 2023.

Hotspots in Aargau

In 2022, Saar's team completed their investigations into heat flux distribution in Canton Aargau, where there are "hotspots" with a heat flux density that exceeds the national average. The researchers simulated the underground heat flow on a computer using a novel approach—and thus laid the foundation for drawing up subsurface maps of the entire country. This information will aid public authorities in Switzerland in finding locations suitable for planning geothermal energy projects—and harness clean energy from the earth's interior.

Climate data from a yacht

Hard at work on the high seas: researchers aboard the *Eugen Seibold* use high-tech instruments to collect samples containing valuable climate data.

After three intense years spent collecting samples on the high seas, the team led by Gerald Haug from the Max Planck Institute for Chemistry in Mainz can now present the initial findings from their work on the research vessel *Eugen Seibold*. The data lay the groundwork for reliable forecasts on how global warming will impact the oceans.

From 2019 to 2021, the researchers on board the *Eugen Seibold* traversed the Atlantic Ocean, collecting samples and covering more than 20 000 kilometres along the way. Between Iceland and the equator, the crew analysed the seawater at depths of up to one thousand metres in the interest of gleaning precise details about the ocean-atmosphere exchange. Using their high-tech instruments, the crew measured a total of fifty biological, chemical and physical parameters and their interactions; their main focus was the greenhouse gas carbon dioxide. Now, terabytes of data and thousands of samples are available for a wide range of analyses.

Daily carbon dioxide exchange

The initial findings at the Max Planck Institute for Chemistry confirm the general assumption that three factors play a decisive role in the ocean's uptake of carbon dioxide: turbulence in the water masses, chemical absorption capacity and the conversion of CO_2 into oxygen by plants (photosynthesis). These processes also depend heavily on water temperature. Now, thanks to the detailed data and samples collected by the *Seibold* crew, it's possible to chart the CO_2 exchange in specific ocean regions over the course of a day.

Take, for instance, the nutrient-poor waters of the subtropical Atlantic Ocean east of the Azores. At sunrise, photosynthesis in plants (such as algae) increases, whereby carbon dioxide is absorbed and the concentration of oxygen at the water's surface rises. Algae that form in the morning are then eaten by zooplankton, whose respiration drives up CO_2 concentration in the water. By noon, solar radiation is so strong that the algae convert less carbon dioxide into oxygen, and after midday, the evaporation of seawater causes clouds to form, reducing the amount of solar radiation, whereupon photosynthesis—and consequently oxygen production—again increases. At sunset, oxygen production drops, the CO_2 concentration in the seawater remains high, and zooplankton graze on algae. With minor differences, this cycle was also observed in other marine provinces.

Complex ocean

"We now see that CO_2 uptake in the ocean-atmosphere exchange is much more complex than previously assumed," says Ralf Schiebel, head of research on the *Eugen Seibold*. "And this knowledge about the overall system, including the many physical, chemical and biological parameters that interact and influence each other, is essential for making forecasts on climate change." The data collected by the *Seibold* crew can now be used to improve current climate models, making it possible to formulate realistic future scenarios. As such, forecasts for how global warming will impact the oceans are placed on solid scientific footing. Project leader Gerald Haug calls it "a major breakthrough". When conducting the next analyses, the team will intensify their collaboration with the German Marine Research Alliance, and specialised IT firms will also be consulted. "It would be impossible for us to manage the data on our own," Schiebel says. "We need a large network."

Understanding El Niño

In December 2022, the *Eugen Seibold* will embark on its first voyage to the Pacific. The crew will set up base in Panama City; over the next three years, this will be the point of departure for their various research missions. "We now also have a better chance to observe an El Niño phase," says Schiebel. The natural extreme weather phenomenon is interesting for the researchers, as it radically changes the normal conditions in the Pacific and impacts the entire global climate.

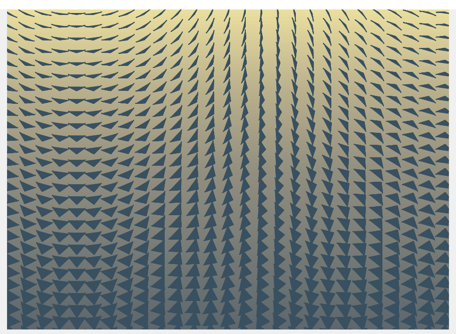
Eugen Seibold, the sailing research lab

Oceans play a decisive role in our planet's climate system. In particular, they absorb heat and carbon dioxide, although there are limits to this capacity. Since 2019, the crew on the world's most ecological research vessel, the *Eugen Seibold*—built and operated with funding from the Werner Siemens Foundation—have been systematically investigating how global warming is impacting ocean regions.

Funding from the Werner Siemens Foundation
3.5 million euros (2015–2019 construction, technical installations)
3 million euros (2020–2030 operating costs)
Project duration 2015 to 2030
Project leaders
Prof. Dr Gerald Haug, director of the Department of Climate Geochemistry at the Max Planck Institute for Chemistry in Mainz, and professor at ETH Zurich
Dr Ralf Schiebel, group leader of Climate Geochemistry at the Max Planck Institute for Chemistry in Mainz

Self-sufficient underwater robot

Researchers at the Innovation Center for Deep-Sea Environmental Monitoring have begun cultivating partnerships and promoting technology transfer with other marine organisations—a step that has already begun to bear fruit.



Innovation Center for Deep-Sea Environmental Monitoring

Hidden away in the deep sea are precious resources coveted by numerous countries and companies. However, deep-sea mining would cause irrevocable harm to this vitally important ecosystem. At the Innovation Center for Deep-Sea Environmental Monitoring at MARUM in Bremen—which is financed by the Werner Siemens Foundation—researchers are developing technical solutions to identify and monitor ecologically valuable deep-sea regions.

Funding from the Werner Siemens Foundation 4.975 million euros
Project duration 2018 to 2028
Project leader Prof. Dr Michael Schulz, director of MARUM – Center for Marine Environmental Sciences at the University of Bremen

Having laid the basis for their novel deep-sea environmental monitoring system, the project team are now shifting their attention to stages two and three: making their underwater robots first semi-autonomous, and then fully autonomous. In 2022, project leader Ralf Bachmayer hired two new specialists for these tasks: robotics engineer Dr Ehsan Taheri is in charge of optimising the robot's underwater steering and control technology, and physicist Dr Anna Kolomijeca will work on the optical sensor systems.

Expecting the unexpected

When gliding over the seabed, the autonomous underwater vehicle (AUV) must be able to identify sudden surprises like cliffs—and then to react accordingly, without losing sight of its pre-programmed task. "The problem is easiest to understand if we imagine we're flying over unknown terrain in the pitch dark using a simple torch to light our way—and we suddenly encounter a precipice," Bachmayer explains. Having no adequate lighting makes it difficult to know whether the wisest choice is flying across or around it. To provide the necessary overview, a remotely operated underwater vehicle (ROV) works in tandem with the semi-autonomous AUV. "The tandem vehicle is equipped and programmed to ensure that the AUV close to the ocean floor is able to carry out quick, agile actions; if necessary, the AUV can access data stored in the 'mother' ROV located higher up and then calculate the best way to get to the programmed target," Bachmayer says. His team of seven are already working on components for the fully autonomous underwater robots; once given a command such as "move along a temperature gradient", these vehicles can then independently collect and interpret data to find the optimal solution.

Characterising deep-sea matter

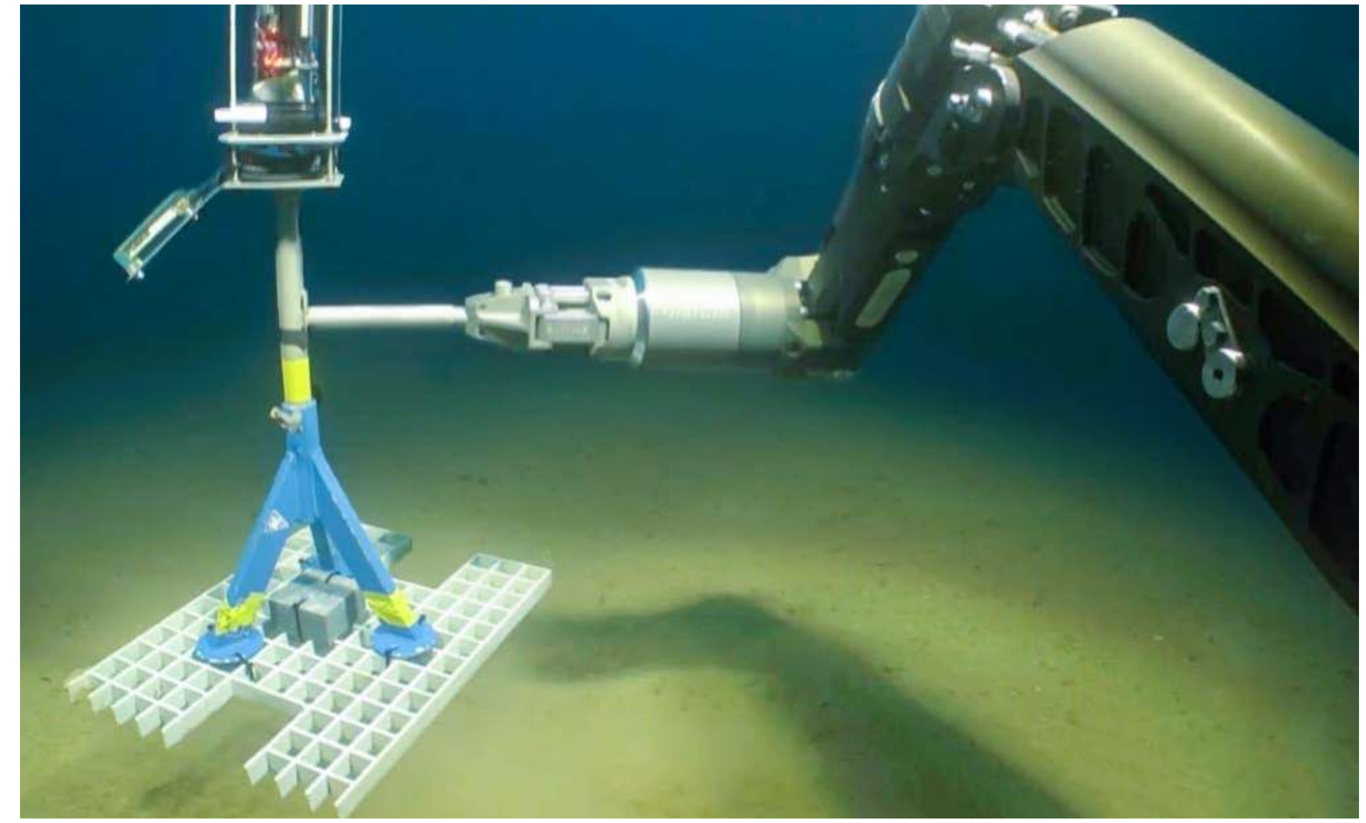
One of the AUV's key tasks in the deep sea is to identify matter in its immediate environment, be it rock, sand, suspended solids, gases or other chemical substances. For this work, the AUV is to be equipped with a Raman spectrometer, which will enable the autonomous vehicle to identify the composition of matter without even touching it—using back radiation of a substance that has been illuminated by a laser light source. Bachmayer says that "Raman spectroscopy is already being used today in drug tests". Now, Anna Kolomijeca has plans to adapt the optical sensor to the conditions of the deep sea, making it possible for the AUV to identify a black smoker, for example, and analyse its emissions on-site. The instrument could also be used to examine the "sediment clouds" stirred up by deep-sea mining that endanger life forms found at the ocean floor.

Despite pandemic-related problems as well as supply shortages, the team managed to conduct several deep-water tests in 2022. In one, Ralf Bachmayer worked with Dr Maren Walter and colleagues on the German research vessel *Meteor* to study the measurement-steered control systems of commercial underwater gliders. Their experiments were part of a larger mission in the southern Atlantic Ocean to examine flow energy and atmosphere-ocean exchange; while on the research voyage, Bachmayer and his colleagues also tested the use of "their" algorithms in the gliders.

Working with the *Eugen Seibold*

This voyage is an example of the increased collaboration with other research groups and organisations like GEOMAR and the Fraunhofer Institute for Physical Measurement Techniques in Freiburg, Germany. In 2022, the Innovation Center for Deep-Sea Environmental Monitoring also began participating in the German Marine Research Alliance (DAM), which five northern German states established to coordinate and advance German marine research. Within the scope of the DAM research mission "Marine carbon sinks in decarbonisation pathways", Bachmayer and his team are developing a mobile, long-term monitoring system whose sensors register the amount of carbon dioxide stored in the deep sea. When injecting CO_2 into the ocean floor, it's important to determine whether there are leaks and, if any are found, to measure how much CO_2 is escaping.

Bachmayer has also contacted geologist Ralf Schiebel, research leader on the yacht *Eugen Seibold*—another project funded by the Werner Siemens Foundation. Bachmayer has plans to connect his remotely operated underwater vehicle, the MiniROV, with the sampler on the *Seibold* to test the transmission of images from the Atlantic Ocean.



The deep-sea robots made in Bremen autonomously perform various tasks and are even able to mark specific points on the ocean floor.

A growing enterprise

In the long tunnels of the Bedretto Underground Lab, world-class research is conducted to better understand how deep geothermal energy can contribute to the energy supply.

Constructed in 2018, the Bedretto Underground Lab attracts researchers from all over the world. This past year, the unique facility was enlarged to allow even more experiments to be conducted: an additional tunnel was accessed for the subterranean research projects—once again with funding from the Werner Siemens Foundation.

Construction company Fretus began work on the extension in January 2022 and, until April, improved the infrastructure in a section covering 2.9 of the tunnel's overall 3.1 kilometres. Due to another long-term commitment, however, it was autumn before all work was completed. During the building hiatus, researchers took the opportunity to drill exploratory boreholes in what would be the new, second part of the lab.

There, the researchers studied methods of drilling deep holes for energy storage at medium depths that won't trigger discernible earthquakes. This preliminary work was also necessary for drilling additional boreholes and creating a planned side tunnel. In addition, another research project financed by the Werner Siemens Foundation has commenced: Mitigating Induced Seismicity for Successful Geo-Resources Application (MISS). The objective of MISS is to discover ways of keeping the subsurface immobile when fluids or gases are injected. For this work, the researchers stimulate the rock layers over a period of forty-eight hours by injecting water at four points in the first borehole, then observe the connection to the second borehole, where the heated water rises.

International interest

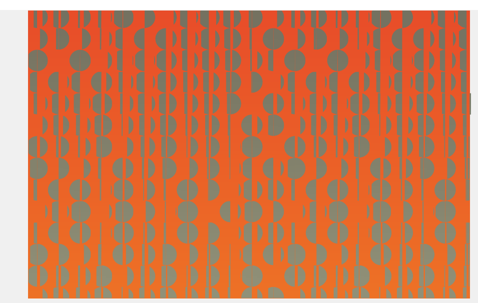
The new testing environment in the Bedretto Underground Lab will be ready for operation at the start of 2023. "We'll have double the capacity for further research into deep geothermal energy," says project leader Domenico Giardini. National and international research groups and organisations have shown strong interest in the facilities, with roughly two dozen projects currently underway or in planning. The European Research Council, too, is contributing to research in the Bedretto Underground Lab—in the form of the largest ERC grant ever awarded to an earth science project. In addition, three new EU projects were launched in 2022, and an international advisory board was constituted to oversee these research partnerships. Members include representatives from the GFZ German Research Centre for Geosciences at the Helmholtz Centre Potsdam, EGS Collab at the US Office of Energy Efficiency and Renewable Energy, and the research programme Geothermal Energy at the Swiss Federal Office of Energy. There are also plans to enlarge the board of the Bedretto Underground Lab.

Underground heat reservoirs

The growth in all these project areas is no coincidence: geothermal energy is looked on as a key component in future climate-neutral and diversified energy policies. Indeed, by 2050, Switzerland hopes to use geothermal energy to cover 25 percent of the country's heating needs. Russia's war in Ukraine and the related surge in energy prices have played a significant role in the fact that most European countries have begun reassessing their energy policies—in particular their dependence on Russian gas—and are seeking to invest in more autonomous energy production.

Heat reservoirs for energy storage located at medium depths are one way of achieving this, and researchers in the Bedretto Underground Lab are currently testing feasibility. Their idea is to create heat reservoirs in various locations at depths of around 1500 metres. During the energy-rich summer months, water can be pumped into the reservoirs, where it is heated. The heat stored in these reservoirs would then be available for generating power in winter.

This method of exploiting geothermal energy has two major advantages. First, costs would be reduced drastically, as drilling to a medium depth of 1500 metres is much less expensive than constructing reservoirs at depths as low as 5000 metres, which is currently the practice for deep geothermal power plants. Second, in summer, the energy to pump the water into the rock is available in great supply—and consequently much less expensive.



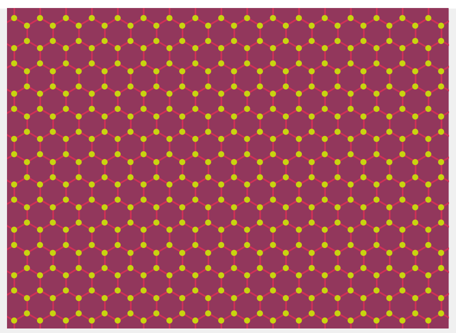
Bedretto Underground Lab for research into deep geothermal energy

In recent years, the Werner Siemens Foundation has financed the construction of two unique research facilities in an underground lab located in the southern Saint-Gotthard Massif, and it currently funds research into deep geothermal energy. In the near-authentic conditions of the Bedretto Underground Lab, ETH Zurich researchers and their partners from Switzerland and abroad have an ideal environment for studying the physics of earthquakes and testing methods to safely use and store geothermal energy.

Funding from the Werner Siemens Foundation 12 + 3.5 million Swiss francs
Project duration 2018 to 2024
Project leader Prof. Dr Domenico Giardini, professor of seismology and geodynamics, ETH Zurich

Tweaking at the nanoscale

The CarboQuant project at Empa has been financed by the Werner Siemens Foundation since 2022. Just one year into their work, the researchers have already achieved an important milestone.



CarboQuant

Researchers in the CarboQuant project at the Swiss Federal Laboratories for Materials Science and Technology (Empa) in Dübendorf, Switzerland, have plans to develop a materials platform for the second quantum revolution—on the basis of a novel method for synthesising carbon-based nanostructures. The project's overarching objective is to produce ultra-tiny quantum electronic components that function at room temperature, making them suitable for use in everyday devices.

Funding from the Werner Siemens Foundation 15 million Swiss francs
Project duration 2022 to 2032
Project leaders
Prof. Dr Roman Fasel, head of the nanotech@surfaces Laboratory at the Swiss Federal Laboratories for Materials Science and Technology (Empa), Dübendorf
Dr Oliver Gröning, co-project leader of CarboQuant and deputy head of the nanotech@surfaces Laboratory at the Swiss Federal Laboratories for Materials Science and Technology (Empa), Dübendorf

The CarboQuant researchers must first design their specific, graphene-based molecular structures on the drawing board and then fabricate them with atomic precision. The greatest difficulty in the process is that the resulting materials are practically insoluble and, in some cases, highly reactive—a "nightmare for any chemist", as CarboQuant co-project leader Oliver Gröning says. To solve the problem, the researchers began synthesising the materials on a metallic surface rather than in a liquid. Over the past fifteen years, the method has advanced so far that it's now possible to manufacture a wide range of completely novel graphene structures—nanoribbons, for example.

Embedding spin

Indeed, so much progress has been made that the CarboQuant team are now able to control the production of even complex graphene nanoribbons. And the researchers have managed to incorporate and link so-called spins in the nanostructures. A fundamental property of elementary particles, spins are quantised magnetic moments. "In quantum physics, they're looked on as a highly promising building block in new quantum technologies," Gröning says.

Now the team are turning to the next step: developing a technology platform that makes the unusual quantum properties of their graphene nanoribbons available. Before this happens, however, the researchers must first characterise and analyse the quantum effects, and then integrate them into electronic components. As Oliver Gröning explains, "These are all extremely broad research fields that we need to approach from an interdisciplinary perspective."

Integration the main challenge

In 2022, the Materials to Devices research group received a major boost thanks to the appointment of Gabriela Borin Barin to lead this activity. Borin Barin and her team have taken on the challenge of integrating the graphene nanoribbons into microchip-like structures and measuring the electronic transport properties under different conditions. "The work is highly demanding, as our nanostructures are much smaller than the components in even the most recent commercial chip generation," says Roman Fasel, co-project leader of CarboQuant. "In order to build these kinds of minuscule chip components, we first need to conduct more basic research and acquire specific know-how from a wide range of disciplines." In this regard, Fasel sees himself as a networker: his goal is to unite research groups from across the globe in the CarboQuant project.

Materials engineer Dr Gabriela Borin Barin from the CarboQuant team examining a sample of carbon nanoribbons in the scanning tunnelling microscope.

Collaboration a recipe for success

Recent successes have proven Fasel right: in 2022, a consortium of research groups from the US, Germany, China and Switzerland published an article on the integration of graphene nanoribbons—measuring just 0.6 nanometres—in field-effect transistors and on their electronic transport properties. "But it was also the expertise within our own ranks that led to another breakthrough," Fasel says with evident satisfaction. In collaboration with the Transport at Nanoscale Interfaces Laboratory at Empa, the CarboQuant team manufactured components of complex electronic graphene nanoribbons, which integrate several control electrodes in an extremely minute space. Another achievement was establishing an electronic contact between individual graphene nanoribbons and electrodes made of single-wall carbon nanotubes—the cylindrical variant of graphene nanoribbons. "The incredibly tiny proportions made this challenge seemingly insurmountable," as Roman Fasel explains. "But thanks to the in-house collaboration at Empa, we've now brought manufacturing precision down to a scale that has never been seen before."

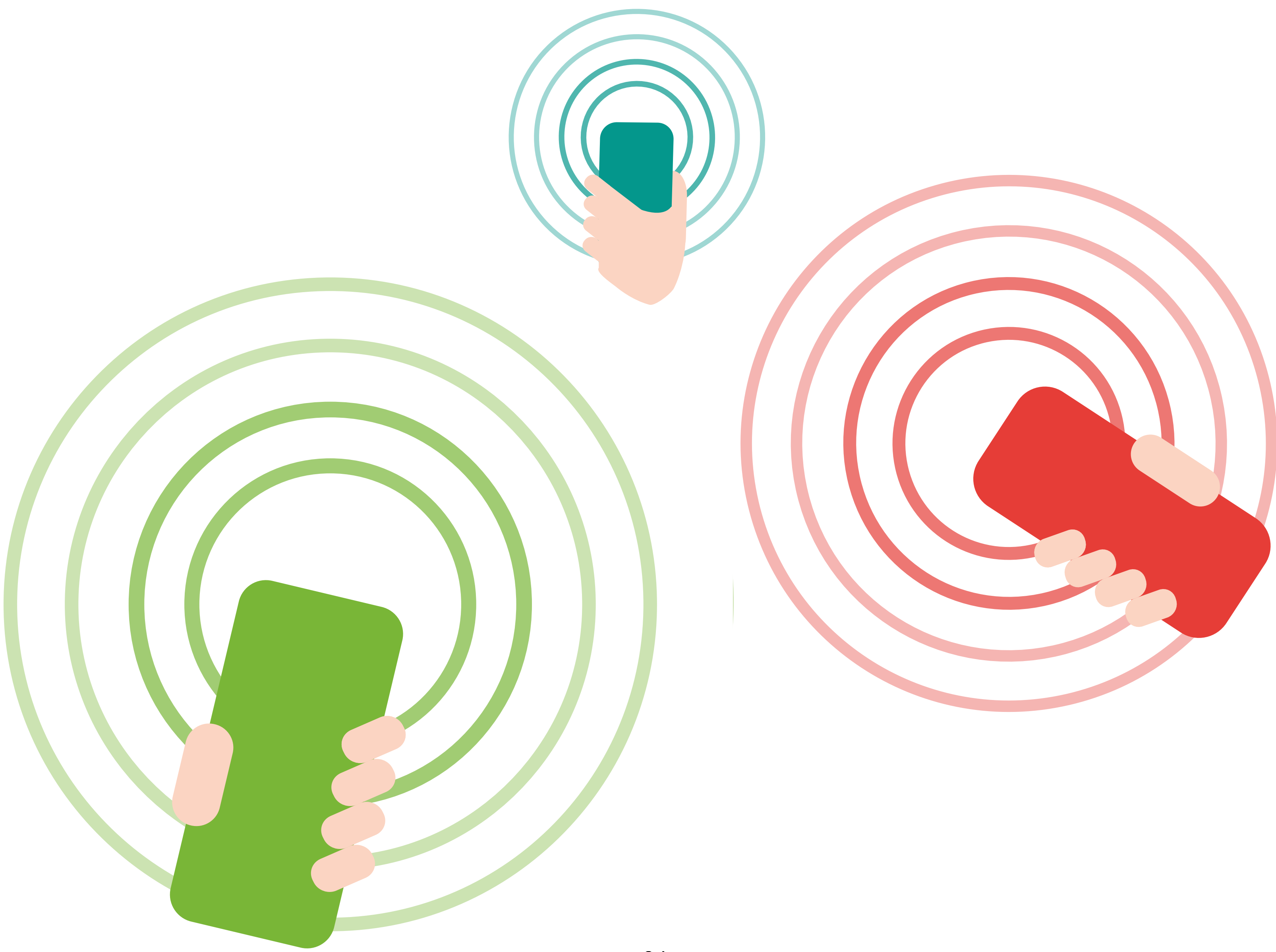
In the latest measurements, the components demonstrated very clear characteristics of a single-electron transistor, meaning they have the hallmarks of a quantum effect. "With this work, we've already achieved an important milestone that we can build on for the integration of more complex electronic and spin functionalities," Fasel says.

Manipulating and understanding spin

Although the researchers currently have the capability of making atomic-resolution characterisations of their graphene nanomaterials' spin properties, the goals of manipulating spins and understanding their dynamics are impossible to reach with the existing infrastructure at Empa. Now, however, thanks to financing from the Empa directorate and the Swiss National Science Foundation, a new scanning tunnelling microscope will be set up, making it possible to perform electron spin resonance on single atoms. To operate the microscopy unit, CarboQuant is creating a new research group for molecular quantum magnetism.

Lessons from a Covid warning app

Whether users trust a digital application depends on a variety of interrelated factors. At the Centre for Cyber Trust, these relationships are being studied by Matthew Smith and his team from the University of Bonn. One case study in their work is the German “Corona-Warn-App”.



Digital technologies are an integral part of our everyday lives. Yet when we download apps, open websites or use online payment systems, we’re exposed to risks: hackers crippling websites, cybercriminals intercepting data, and corporations and authorities collecting personal data without us knowing how they may be used in the future.

That’s why the Centre for Cyber Trust at ETH Zurich and the University of Bonn—which has been funded by the Werner Siemens Foundation since 2019—is aiming to develop cybersecurity systems such as certification and authentication methods that users can trust one hundred percent. But it’s not enough to simply program new software. “Ultimately, it’s the human factor that decides whether a new technology is accepted,” says Matthew Smith, professor of computer science at the University of Bonn and the Fraunhofer Institute for Communication, Information Processing and Ergonomics, also in Bonn.

User studies show the way

With his team, Smith is investigating the interface between humans and software. He wants to find out how well users understand new technologies, how they use them—and whether they trust them. “Computer scientists like me sometimes see the world differently,” says Smith. “User studies are important for finding out whether we’re on the right path.”

The Covid-19 pandemic provided an excellent opportunity for such a study. Shortly before and after the “Corona-Warn-App” was introduced in Germany, the researchers surveyed a representative sample of the population about the app, specifically about their knowledge, their attitudes and their user experience. According to Smith, the results showed that the broader population sometimes had diametrically opposed views to the software developers. “One way that developers foster trust is by working with open-source software, whose code is publicly accessible,” he explained. This principle was also applied to the Corona-Warn-App.

However, in contrast to the hopes of the developers, only around a quarter of the persons surveyed said this had a positive effect on their willingness to download the app. Many German speakers were unfamiliar with the term “open source”, said Maximilian Häring, lead author of the study. “One respondent wrote that the survey was interesting, but it used too many foreign words like ‘open sourse’ [sic].”

Digital applications, real-world trust

Shortly before the app launched, many survey participants still had questions about how the app functioned and how well their privacy would be protected. For instance, over half thought the app would warn them when an infected person was close by. A central factor driving acceptance of the app was a user’s attitude to the German government’s coronavirus policy. “The degree of trust in government was the most significant variable in predicting whether someone would download the app,” says Häring. While some respondents ruled out using the app under any circumstances, others indicated they would definitely download the app—regardless of any data protection concerns.

In the follow-up study conducted after the app’s launch, new sticking points were detected. While privacy protection issues took a back seat, user-friendliness became more important. Depending on age group, up to twelve percent of all respondents cited technical problems as their reason for not installing the app.

Overall, says Matthew Smith, the Corona-Warn-App provided valuable lessons on introducing digital innovations, and it showed that software quality doesn’t determine whether users accept and trust new applications: “It’s the trust-based relationships in the real world that are decisive. We need to transfer this trust to the digital realm,” he explained. In the coming years, the project aims to show how this can be achieved. Smith is convinced: “Applications shouldn’t be developed by techies alone. The general population needs to be involved from the very outset.”

Centre for Cyber Trust

The actions of cybercriminals and hackers undermine society’s faith has in online data exchange. To remedy this, computer scientists at the Centre for Cyber Trust of ETH Zurich and the University of Bonn are developing a fundamentally new security infrastructure for the internet. Their aim is to transfer traditional relationships of trust from the physical world to the digital realm.

Funding from the Werner Siemens Foundation 9.83 million Swiss francs
Project duration 2019 to 2027
Project leaders
Prof. Dr David Basin, Department of Computer Science, Information Security, ETH Zurich
Prof. Dr Peter Müller, Department of Computer Science, Programming Methodology, ETH Zurich
Prof. Dr Adrian Perrig, Department of Computer Science, System and Network Security, ETH Zurich
Prof. Dr Matthew Smith, Institute of Computer Science, Usable Security and Privacy, University of Bonn

Thermoelectrics, ultra-fast

Testing materials for their capacity to efficiently convert temperature differences into electricity is a complex, time-consuming process. That's why Maria Ibáñez and her team at IST Austria are looking forward to the day that their new high-throughput unit is in operation.

Novel materials are the essence of physicist Maria Ibáñez's work. But fabricating new materials requires not only profound knowledge—a great deal of time and patience are also necessary. As are the right tools. It often takes numerous attempts before a material presents the right properties, and when researchers have to make every new mixture by hand in their lab and then test it individually, progress is painfully slow.

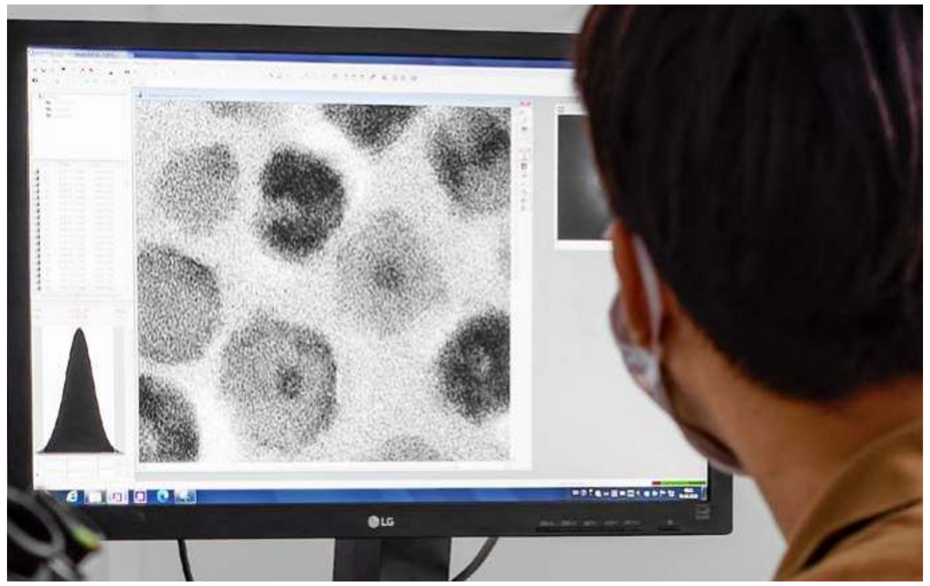
The materials that Ibáñez and her team are developing have precisely defined nanostructures. The researchers grow polycrystals of a thermoelectric material—tin selenide, for example—in an aqueous solution and then coat the surface with the molecular complexes of a second material, for instance cadmium selenide. "To test this kind of new material system by hand and also vary the different parameters, a researcher would need eight months, even a year," Ibáñez says.

This is what makes her all the more excited about the high-throughput infrastructure currently being built in her new lab. To be sure, there have been several delays due to supply shortages and because it was difficult to hire specialised engineers during the coronavirus pandemic. "But now we're working on a prototype." The new unit is capable of fabricating material combinations and testing them at the same time. Ibáñez hopes that the prototype will be in operation by spring 2023. The finished equipment, which has several other functions, should be ready for general use a few months later. "That's my big goal for the year," Ibáñez says.

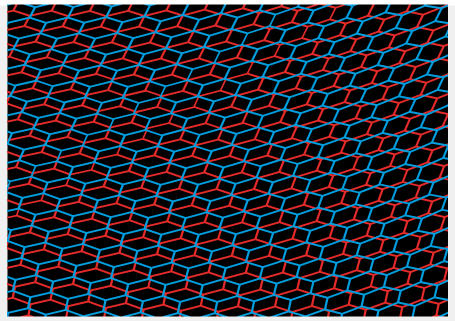
High-performance polycrystals

Despite the pandemic-related delays, Ibáñez is satisfied with her group's progress, saying, "We've now laid the cornerstones for our work and have decided which methods we'll use to test which materials in the high-throughput lab." The team have recently published a number of promising findings in top-tier journals. One article discussed their development of a new way to fabricate tin selenide using a polycrystalline structure that is more cost-effective to produce; the resulting thermoelectric performance is on a par with the best materials in the—costly—single crystal form.

In another important development, Ibáñez says the team "can now control how big the grains in the crystals grow, which in turn affects the grain boundaries". The boundaries are the decisive factor in how heat is transported. In future, the researchers will be able to use them for optimising the thermoelectric performance of their materials. And this new knowledge can also be applied to improve polycrystalline materials, Ibáñez adds. "Solar cells are one example."



Manufacturing new thermoelectric material systems is still largely done by hand. This is now set to change thanks to a new high-throughput infrastructure.



Thermoelectric materials

Whether in a computer or a refrigerator, on a windowpane or the human body: wherever temperature differences are found, they can in theory be used to generate electricity. Existing methods, however, are inefficient and expensive. The aim pursued by Maria Ibáñez and her research group at the Werner Siemens Laboratory for Research on Thermoelectric Materials at the Institute of Science and Technology Austria (IST Austria) is to find cost-effective solutions—hence her search for new materials. Precisely defined nanostructures are what will give these new materials the right properties.

Funding from the Werner Siemens Foundation 8 million euros
Project duration 2020 to 2028
Project leader Prof. Dr Maria Ibáñez, Institute of Science and Technology Austria (IST Austria), Austria

Who we are

Charlotte (left) and Marie, who established the Werner Siemens Foundation, were close throughout their lives.

Great blessings, bitter losses

This past year saw publication of a double biography of Charlotte von Buxhoeveden und Marie von Graevenitz. The book is the third and final work about the lives of the five women who established or endowed the Werner Siemens Foundation. All three books are now available in bookshops and libraries.

All information presented here stems from the book by Béatrice Busjan and Yvonne Gross: *Charlotte von Buxhoeveden und Marie von Graevenitz. Die Töchter des Carl von Siemens*, ed. Werner Siemens Foundation (Schwerin: Thomas Helms Verlag, 2022).

Just a few years ago, very little was known about the women who established the Werner Siemens Foundation—Charlotte and Marie—or those who later endowed the Foundation with generous legacies—Anna, Hertha and Nora. Indeed, any scant knowledge about their lives had more to do with their famous fathers (or, in Nora's case, father-in-law) Werner and Carl Siemens. Now, in the biographies written by historian Béatrice Busjan and archivist Yvonne Gross, readers can discover the personal histories of the five women who lived through the upheavals of the late 19th and early 20th centuries. The authors relate how the importance of family ties was impressed upon the Siemens daughters, how they were constant companions from a young age, and how the sisters, in their married lives, supported one another during the political turmoil before and after the First World War. Finely written and illustrated with striking photographs, the books offer deep insight into the circumstances that led the daughters of Carl von Siemens (Charlotte and Marie) to establish the Werner Siemens Foundation on 7 March 1923, and why the daughters and daughter-in-law of Werner von Siemens (Anna, Hertha and Nora) later left generous legacies to the Foundation.

The third and final volume—*Charlotte von Buxhoeveden und Marie von Graevenitz. Die Töchter des Carl von Siemens* [Charlotte von Buxhoeveden and Marie von Graevenitz. The daughters of Carl von Siemens]—was published in 2022.

Charlotte von Buxhoeveden, née Siemens

Charlotte von Buxhoeveden, née Siemens

Charlotte, the second child of Carl Siemens and his wife Marie (née Kap-herr), was born in 1858. She and her siblings spent their early childhood in a modest home located directly next to the Siemens factories in Saint Petersburg. In 1853, Father Carl had begun managing the Russian branch of Siemens & Halske, the company his brother Werner founded in Berlin in 1847. The firm's telegraph lines were in high demand in the Russian Empire, and business thrived under Carl's leadership.

As a girl, Charlotte was said to be happy, outgoing and strong-willed. However, her childhood in bustling, diverse Saint Petersburg was cut short when her younger brother died at the age of one. The event broke the spirit of her once vivacious mother, who suffered several miscarriages as well as a stillbirth and was often confined to her bed. To improve Marie's health, the family moved to the Georgian spa town of Borjomi when Charlotte was nine, and then later to Berlin. But the doctors there, too, were unable to find a cure for Marie Siemens, who had also developed tuberculosis. She died in 1869; one month later, Charlotte's youngest sister also passed away.

Life in London

Charlotte was ten years old at the time. She and her siblings, Werner Hermann and Marie, were placed in the care of a changing series of governesses. To provide a better upbringing for his offspring, widower Carl Siemens moved with them to London, where his brother Wilhelm lived with his wife, Anne, who had no children of her own. The couple took charge of raising their nieces and nephew, who spent eleven enjoyable years in London before returning to Russia with their father. In 1881, Carl and his three children again established a home in Saint Petersburg, this time in a large house near the Winter Palace, the residence of Tsar Alexander II. He and his now adult children re-entered high society, attending balls, dance parties and social gatherings. This carefree life, however, took a temporary end with the assassination of the Tsar.

In 1884, Charlotte wed Axel Baron von Buxhoeveden. The couple spent their winters in Saint Petersburg and summers on the Estonian island Saaremaa at the Buxhoeveden family estate. Axel pursued a political career, and Charlotte was content with her life at his estate. They had the means to afford a glamorous lifestyle, even after Charlotte's favourite castle in Haimre was burnt down in the revolution of 1905.

Already in her youth, Charlotte suffered physical complaints in response to traumatic life events; as an adult, her anxiety increased and she experienced several nervous breakdowns. To recover, she frequently sought treatment at Sanatorium Bellevue in Kreuzlingen, Switzerland—she was staying there in 1911 when her daughter Lolotte died of scarlet fever.

Dispossessed and stateless

During the First World War, Charlotte left Saint Petersburg to receive medical care in Stockholm. After the communist revolution made a return to Russia impossible, she travelled to Switzerland in 1918. There, again as a patient at Sanatorium Bellevue, she learned that Axel had been killed in the civil war on Saaremaa—due to his rank as a nobleman.

Widowed and stateless, Charlotte, then 63 years old, made a fresh start in Berlin with the help of her children and other family members. To be sure, she had lost her properties in Russia and Estonia, but she and her sister had inherited a large share in the German and English Siemens factories upon their father's death. In 1923, they used a part of this fortune to establish the Werner Foundation (later the Werner Siemens Foundation) with the purpose of supporting impoverished relatives of Siemens founders Carl and Werner.

Like many other Russian emigrants, Charlotte settled in Baden-Baden. In 1924, she obtained Liechtenstein citizenship, a new passport—and once again the freedom to travel. Against the advice of her doctors, she embarked on journeys throughout Western Europe. On 26 March 1926, Charlotte died in the Zurich hotel "Elite" and was buried in Baden-Baden.

"When Charlotte would tell her grandchildren stories about Russia and Estonia, it was like listening to magical tales from times long past," writes author and historian Béatrice Busjan. "Indeed, throughout her entire life, Charlotte von Buxhoeveden moved in circles that, with her generation, have long ceased to exist."

Marie von Graevenitz, née Siemens

Marie von Graevenitz, née Siemens

Marie, the fourth child of Carl and Marie Siemens, was born in Saint Petersburg in 1860. Reserved and shy, she was content to live in the shadow of her older, more extroverted sister Charlotte. The two women were in close contact throughout most of their lives; they shared major life experiences such as the deaths of their mother and brother as well as the family relocations to London and back to Saint Petersburg.

In 1884, Marie married Georg Baron von Graevenitz. Her new husband was a member of the Tsar's diplomatic corps in Saint Petersburg, and he was promoted to the rank of valet de chambre in 1890. The couple had six children, and when Georg was transferred to the Russian embassy in London, the entire family moved with him for five years. At diplomatic receptions in the following years, Marie regularly took the place of her husband, who suffered from alcoholism.

Overcoming depression

Much like her sister Charlotte, Marie also experienced episodes of depression. When her condition worsened, she too sought treatment at the renowned Sanatorium Bellevue in Switzerland in 1903. Unlike Charlotte, however, Marie recovered from her depression and was again able to lead an independent life.

In 1904, Marie's husband was appointed head of the Russian diplomatic mission in Weimar, and the family moved to Germany for four years. When the legation was closed, they returned to Saint Petersburg, maintaining communications with foreign envoys from there. The family moved between their city residence in Saint Petersburg's diplomatic neighbourhood and their country estates in Gostilitsy and Chmelewo, which Marie had inherited from her father. Her three sons were trained for service in the Tsar's court at the military academy.

Supporting Charlotte

Marie also frequently took care of Charlotte's children during her sister's bouts of illness. It was Marie who sat at Lolette's deathbed in 1911 and, starting in 1915, she looked after of her nephew Charles when Charlotte travelled to Stockholm for medical treatment.

In the spring of 1917, Marie witnessed first-hand the Russian Revolution and abdication of the Tsar. She fled to Helsinki, where her husband and sons soon joined her. This fateful event was to be followed by yet more misfortune: in the following year, her oldest daughter died of tuberculosis, and two of her sons later succumbed to the same disease.

Georg von Graevenitz remained loyal to the tsarist court until his death; he and Marie chose to remain stateless after the Bolsheviks stripped them of their Russian citizenship. However, Marie maintained ownership of her Russian properties in Gostilitsy and Chmelewo throughout her life.

Inheritance as a lifeline

Marie's fortune as heiress to the property of her ennobled father, Carl von Siemens (died 1906), was the basis for the family's finances. She also provided for the financial security of future Siemens generations when she established the Werner Foundation in 1923 with her sister. Indeed, Marie dedicated many years of her life to caring for family members, with her deep faith in God supporting her during times of trial. After Charlotte's death, Marie also established the Maria Foundation in 1927—against the wishes of her children—and endowed the fund with shares worth 2.1 million Reichsmark to support Siemens descendants, former servants and friends. Marie died on 2 October 1939, just weeks after her husband.

Governing bodies

Siemens Family Advisory Board

Descendants of Werner von Siemens and his brother Carl von Siemens sit on the Siemens Family Advisory Board. The Siemens Family Advisory Board supports the work of the Foundation Board and holds important veto rights.

Oliver von Seidel
Chair
Düsseldorf, Germany

Dr Christina Ezrahi
Member
Tel Aviv, Israel

Alexander von Brandenstein
Member
Hamburg, Germany

Foundation Board

The Foundation Board manages the ongoing activities of the Werner Siemens Foundation.

Dr Hubert Keiber
Chair
Lucerne, Switzerland

Prof. Dr Peter Athanas
Member
Baden, Switzerland

Beat Voegeli
Member
Rotkreuz, Switzerland

Scientific Advisory Board

The Scientific Advisory Board is an independent body that supports the Foundation Board in identifying suitable projects. Board members are responsible for reviewing and assessing the quality of proposals submitted to the Foundation.

Gianni Operto, Chair
Ebmatingen, Switzerland

Prof. Dr Gerald Haug, Member
Max Planck Institute for Chemistry
Mainz, Germany, and
ETH Zurich, Switzerland

Prof. Dr-Ing. Dr h. c. Matthias Kleiner, Member, former President of the Leibniz Association, Berlin, Germany

Prof. Dr Bernd Pichler, Member
University of Tübingen, Germany

Prof. Dr Peter Seitz, Member
EPFL, Switzerland

Selection process

Selection criteria

Every year, the Werner Siemens Foundation finances up to three new groundbreaking projects in the fields of technology and the natural sciences. The projects are generally conducted at higher education institutions in Germany, Austria and Switzerland. Requirements include upholding the highest standards and contributing to solving key problems of our time.

As a rule, each project is awarded generous funding of five to fifteen million euros or Swiss francs. Projects are selected in a multistep procedure by the Scientific Advisory Board, the Foundation Board and the Family Advisory Board of the Werner Siemens Foundation.

In addition to projects, the Werner Siemens Foundation funds exceptional programmes in education and in the promotion of young talent in STEM subjects.

The Foundation does not support activities in the arts, culture, sports, leisure, politics, disaster relief, nor does it support permanent projects, commercially oriented projects, project co-sponsoring with other foundations, individual scholarships, costs of studying or doctoral theses.

Project application

Project proposals must be submitted in writing to the Werner Siemens Foundation. The selection process is as follows:

1 Project proposal is appraised for compliance with the Foundation's funding criteria
2 The Scientific Advisory Board evaluates the project
3 The Scientific Advisory Board presents its recommendation to the Foundation Board and the Siemens Family Advisory Board
4 The Foundation Board and the Siemens Family Advisory Board consider the project for approval
5 Final decision
6 Contract

The selection process takes approximately six months.

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bigfish AG, Aarau

Articles

Brigitt Blöchlinger, Zurich
pp. 34–39, 86–93, 100–103

Simon Koechlin, Brittnau
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Mathias Plüss, Vordemwald
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pp. 12–21, 26–29, 82, 85, 86, 90, 93, 97

Oliver Lang, Fotografie, Lenzburg
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Hannes Woidich, Fotografie, Dortmund
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at the University of Bremen, p. 89 (video still)

MIRACLE II, University Basel
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David Ausserhofer, p. 78

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Stock, p. 24

Siemens Historical Institute, Berlin, pp. 100–103

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