Faszination **Forschung**

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The Physics of Self-Organization in Biology

Medical Materials – Enabling Patients to Grow a New Heart Valve
Architecture – Printing a House out of Sand
6G Network – Visions of Next-Generation Communication

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Dear TUM friends and associates,

If we are honest, in spite of geopolitical conflicts, the energy crisis as well as the climate crisis, we have a high standard of living and prosperity here in Germany. The fact that we enjoy a more comfortable position than many other people around the world, however, does not mean we can allow our readiness and willingness for change to wane. We certainly must not allow ourselves to slip into a false sense of security, beholden to the illusion that our prosperity will automatically continue in the future and things will always be this good. Quite the opposite: especially in times of turmoil and upheaval, our society's openness to new knowledge and acceptance of innovative technologies will play a decisive role in determining the role Germany and its economic power will play in a future world that waits for no one.

Picture credit: Astrid Eckert

At TUM, we have no intention of leaving the task of shaping the future to others around the world with the courage to pursue reforms. Our students, staff, alumni and partners are working hard to develop effective solutions to current challenges. Given the need for innovations to be responsible, trustworthy and sustainable, this work has mankind and nature at its heart.

In this issue of Faszination Forschung, we ask Prof. Sebastian Pfotenhauer a key question: what is a "good" innovation? This cannot be answered with technological knowledge alone. Instead, it requires a profound understanding of the social, political and ethical aspects of innovations.

Innovation is essential in biomedicine. Prof. Andreas Bausch researches the most minute building blocks of human cells, which are responsible for both cell stability and cell mobility. He aims to learn more about the forces that cause cells to move in biological processes, such as wound healing, and pathological processes like cancer and metastasis.

Prof. Petra Mela is applying a novel 3D-printing technique to develop a scaffold for growing a heart valve from a patient's own cells. Mela believes that a new heart valve made from the patient's own tissue will overcome the drawbacks of conventional, artificial heart valves, such as clotting disorders and calcification.

3D printing is also making headway in the construction sector – on a vastly larger scale. Prof. Christoph Gehlen has developed a procedure to the point of market maturity binding tiny sediment particles, layer by layer – a technique capable of producing concrete components in previously inconceivable forms. Prof. Katrin Dörfler is examining the potential use of robots on construction sites and how they could cooperate in human-robot teams. This would make construction faster, provide greater flexibility and, above all, conserve resources.

Putting people front and center is also the motto behind the new 6G mobile communication standard, which shifts the focus from the Internet of Things onto people and how they interact with their environment. In the 6G Future Lab, Prof. Wolfgang Kellerer is conducting research into the vital underpinnings of the new mobile communication standard. And now, dear reader, you are front and center, as we have conceived and created this issue of Faszination Forschung just for you. I hope you enjoy your read, and will benefit from new insights and fresh inspiration!

Yours sincerely,

Thomas F. Hofmann

Thomas F. Hofmann
President

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How the **Digital Transformation** is Changing Construction Sites

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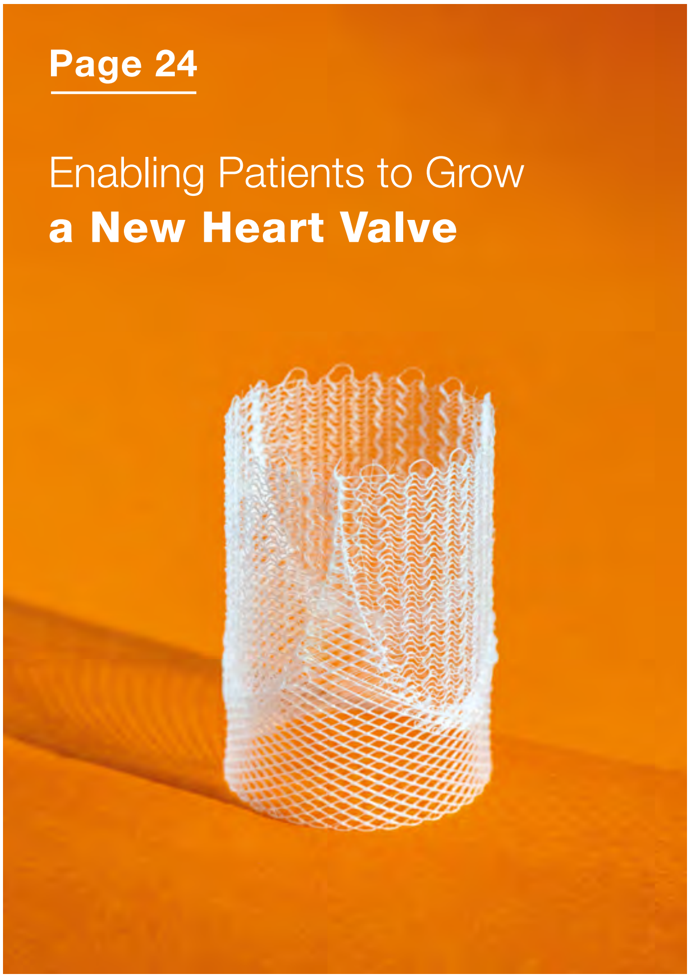
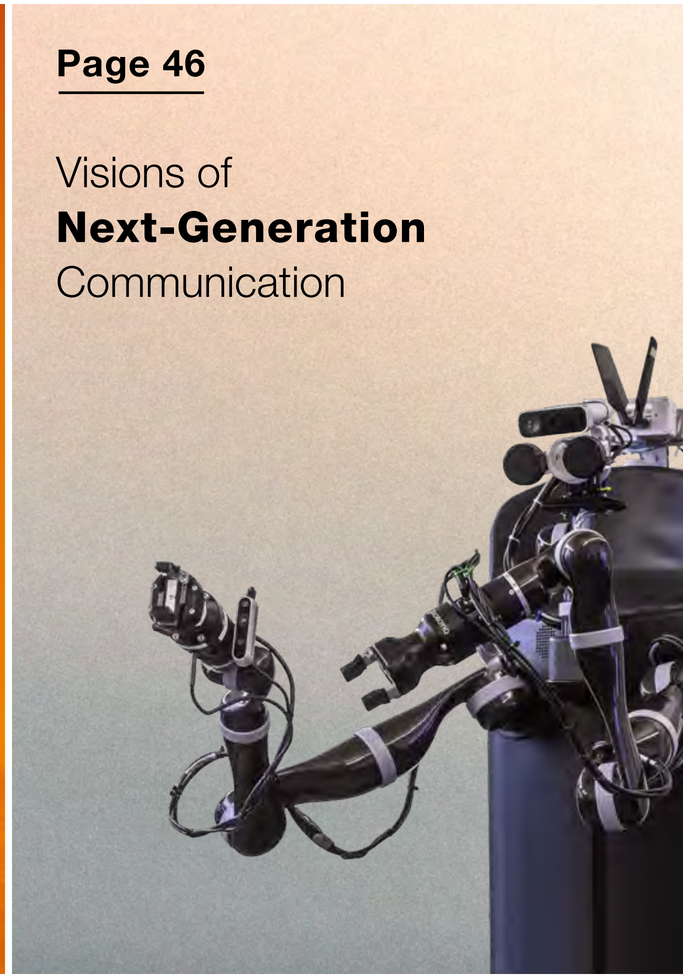




Picture credits: Juli Eberle, Astrid Eckert/TUM, Andreas Heddergott

In every Issue

Innovation is about **Social Change**

Sustainable Development is often associated with calls for more innovation. But what exactly is the “right” kind of innovation? And how does innovation relate to policy priorities and societal concerns? We spoke with Sebastian Pfotenhauer, Head of the Department of Science, Technology and Society and Professor of Innovation Research at the TUM School of Social Sciences & Technology and the TUM School of Management.

Gesamter Artikel (PDF, D): www.tum.de/faszination-forschung-29

Bei Innovation geht es um gesellschaftlichen Wandel

D

Innovationen werden in verschiedenen Gesellschaften stets unterschiedlich wahrgenommen, so Prof. Sebastian Pfotenhauer. In demokratischen Gesellschaften stoßen sie daher auf eine Vielzahl politischer Standpunkte und gesellschaftlicher Vorlieben, auch auf Widerstand. Pfotenhauer warnt davor, diese Konflikte durch ein pauschales Appellieren an die Vernunft der Menschen lösen zu wollen. Nachhaltige Innovation im eigentlichen Sinne beinhaltet nicht nur, Produkte und Dienstleistungen umweltfreundlicher zu gestalten, sondern muss auch gewährleisten, dass wir als Gesellschaft mit den Folgen von Innovation langfristig und sozial gerecht leben können. Hierfür müssen Innovationsprozesse im Hinblick auf eine stärkere Inklusion und Deliberation sowie im Hinblick auf die Legitimität von technologiegetriebenen Wandlungsprozessen und die Antizipation von unbeabsichtigten Konsequenzen verändert werden. Pfotenhauer leitet an der neuen TUM School of Social Sciences and Technology das Masterprogramm „Responsibility in Science, Engineering and Technology“. Es ist beispielhaft dafür, wie die TUM die gesellschaftliche Verantwortung in den Mittelpunkt ihrer Bemühungen als universitäre Einrichtung stellt. □

Link
www.mcts.tum.de/innovationsforschung/overview/

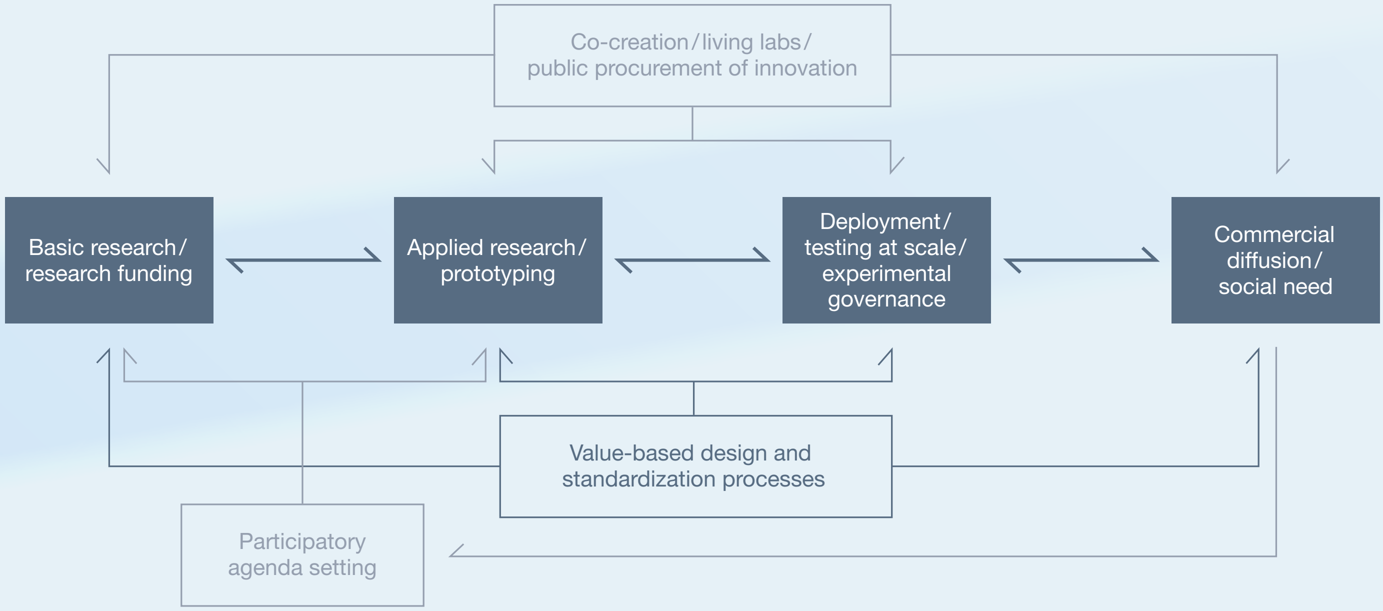
Picture credit: Magdalena Jooss

“People might reject innovations for reasons that have nothing to do with irrationality or ignorance.”

Sebastian Pfotenhauer

Professor Pfotenhauer, what is “good” innovation?
That’s the question, isn’t it? In the past, we have focused mostly on asking “What is innovation?” and “How can we get more of it?” Today, innovation is ubiquitous, both in the form of new products and services and also as a broader social discourse that drives companies and public policy. But the times are changing. In much of my research, I observe an increasing paradigm shift from simply “more innovation” – what I sometimes call a blind, one-size-fits-all “innovation imperative” – to a more nuanced understanding of *what kind* of innovation we actually want and need as a society.

So how does innovation play out in diverse societies and cultures?
Each society has its own way of dealing with, and producing, innovation. In a new paper, we analyze Bavaria’s innovation culture, which by and large tries to preserve socio-economic structures rather than radically change them – in contrast to the more free-wheeling, disruptive Silicon Valley culture. Likewise, new technologies are always received differently in different societies. In the 1990s, for example, genetically modified crops were seen



Innovation is still often conceptualized as a quasi-linear process, even though this depiction is highly reductionist. To account for more complexity, co-creative processes are often mobilized to explicitly blur the imagined stages of the innovation process. Participatory agenda setting, living labs, and value-based design and standardization are policy instruments that can help address societal goals, concerns and values during the innovation process.

in the US as an extension of existing biotechnologies, not fundamentally different or riskier, and were hence understood to be covered under existing regulations. In contrast, Britain chose an unusually scrupulous approach to genetically modified organisms after having recently been hit by the mad cow disease crisis, which considerably undermined public trust in risk management by government authorities and experts. Germany, against the backdrop of decades of strong environmental movements, took an extremely cautious, incremental course, with detailed regulation and publicly monitored, experimental procedures to test the effects of GM crops. Similar patterns can be observed with AI, robotics, neurotechnology, quantum technology or autonomous vehicles today – all technologies that we are currently studying in my group.

What conclusions do you draw from these findings?
At the heart of it all is a very simple insight: innovation is about social change. In democratic societies, new technologies will thus always encounter a diversity of political positions and social preferences, including resistance. Trying to resolve these conflicts of interests through appeals to the universal benefits of innovation or universal rationality fails to recognize that people might reject certain technologies or expertise for reasons that have nothing to do with irrationality or ignorance.

So people, or rather their attitudes towards innovation, are changing?
Correct – as are the questions that we as a society ask innovators today. Traditionally, science and technology have been shaped mostly by small expert communities, such as engineers, scientists, policymakers and entrepreneurs – unfortunately, mostly indeed men. Yet, in the current world, with controversial developments posing such a stark challenge – climate change, the power of Big Tech, autonomous vehicles – this traditional top-down model seems insufficient. Sustainable innovation in this sense is therefore not just about making products and services more environmentally friendly, but also about making sure that we as societies can live with the consequences of innovation over the long term and in a socially just manner. This means changing innovation processes to take account of inclusiveness and deliberation, public legitimacy for technology-driven change processes, as well as the anticipation of unintended consequences. ▷

Graphics: ediundsepp (source: TUM); Picture credit: Magdalena Jooss

Prof. Sebastian Pfotenhauer

is Carl von Linde Professor of Innovation Research at the TUM School of Social Sciences and Technology, where he heads the Department of Science, Technology and Society (STS). He shares a co-appointment with the TUM School of Management. He is also the coordinator of the federally funded "Munich Cluster for the Future of Mobility in Metropolitan Regions (MCube)". He tweets on all things related to innovation and society at @smpfotenhauer.

What needs to change to get everyone on board with sustainable innovation?

To address this, we need to focus more on the *process* dimension of innovation: How can we make meaningful changes "upstream" in innovation trajectories together with those that will be affected "downstream"? Let me give you two examples of large projects in which we've been trying exactly that. I am currently co-leading the large federal research cluster MCube – the "Munich Cluster for the Future of Mobility in Metropolitan Regions" – together with my colleagues Gebhard Wulfhorst (urban structure and transport planning) and Markus Lienkamp (automotive engineering). In this cluster, we have put a co-creative approach front and center by insisting that all projects need to involve TUM researchers, companies, and public sector partners, including civil society. We have also tried to balance technical with social science research programs, the latter, for instance on topics such as mobility justice, responsible innovation and local street experiments.

Likewise, I coordinated a large European Horizon2020 research project called SCALINGS – short for "Scaling up Co-creation: Avenues and Limits for Integrating Society in Science and Innovation". There, we analyzed the scalability of "Co-creative" innovation approaches in robotics, energy and autonomous vehicles, together with partners from 10 countries. Our key finding was that co-creative approaches are not easily scalable. A nursing robot in a clinic in Munich will therefore not work without further ado in a clinic in Barcelona. The reason is that the exact ways in which technology, users, and economic and policy conditions need to come together vary dramatically. All the more reason to bring the social sciences on board early and on an equal footing.

How do you address these challenges in your teaching at TUM?

TUM has taken a number of commendable steps to put social responsibility at the heart of its institutional mission, most notably through the launch of the new School of Social Sciences and Technology (SOT) and the expansion of the social sciences as equal partners of the technical disciplines. At SOT, I head the Master's program in "Responsibility in Science, Engineering and Technology" (RESET), which is supported by the Elite Network of Bavaria. There, we teach students with both social science and technical backgrounds to tackle questions at this critical interface. At my secondary home, the TUM

“Questions about the relationship between technology and society won’t go away – on the contrary, they will become more central to everything we do.”

Sebastian Pfotenhauer

School of Management, we have embraced responsible technology leadership as a core value and put in place additional incentive structures to emphasize the Sustainable Development Goals in teaching and research.

How can we ensure responsible innovation practices to meet different needs?

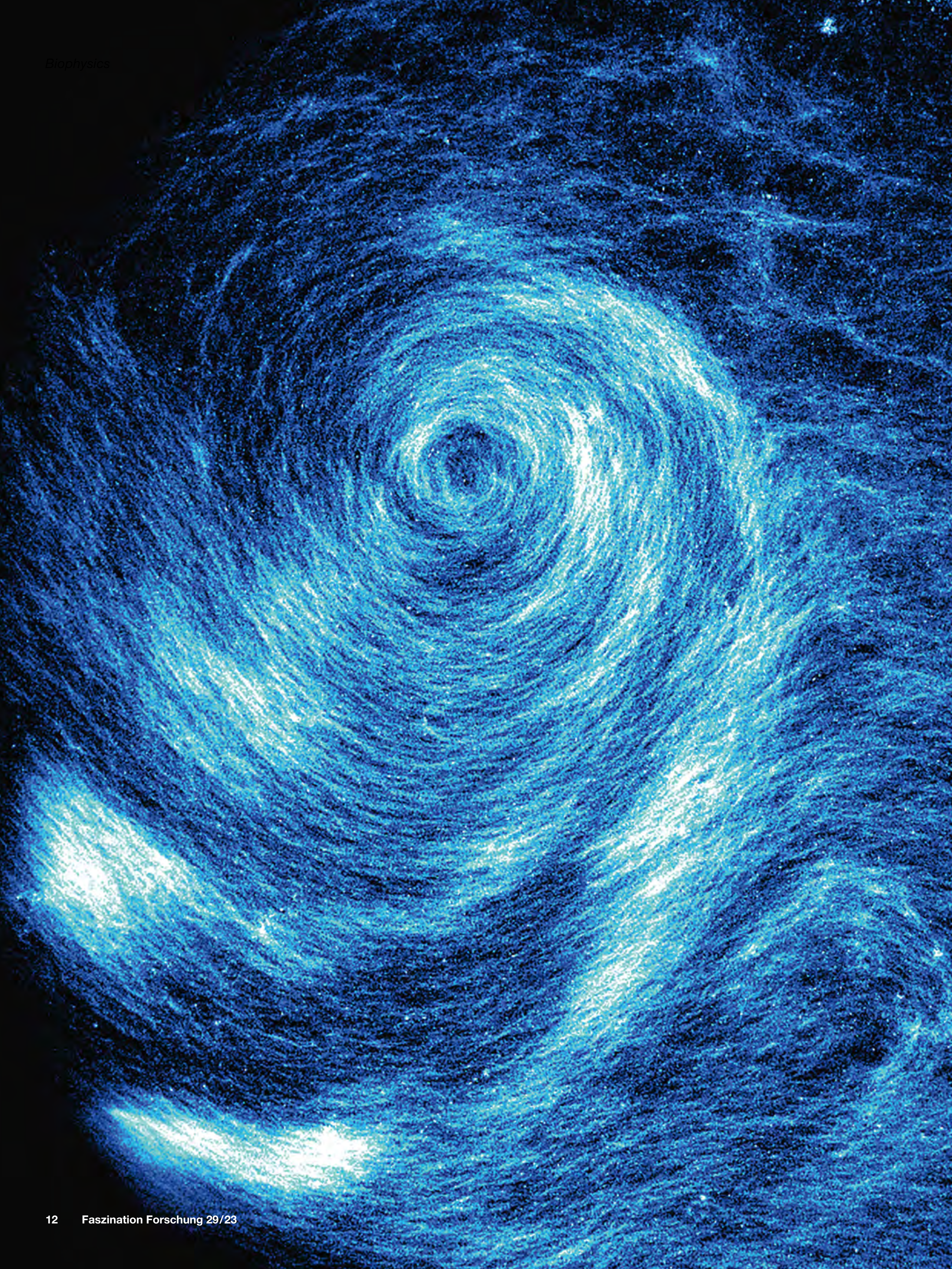
Well, what doesn’t work are mere “check-box” approaches to treat questions of ethics and responsibility – as currently embraced by many funding programs, including the European Commission. We need to build reflexivity into the processes themselves, which means improving our organizational capacity to be responsive and allowing social scientists and civil society to ask inconvenient questions. For me personally, the biggest unused lever rests with the private sector. We are now relatively good at requiring “responsible” approaches in publicly funded research. However, most companies still lack a “social responsibility” approach to innovation. This is highly problematic since companies are the driving forces behind innovation in many sectors! You can see this tension in the very visible failures and criticisms of initiatives such as Google’s AI Ethics Board or the Facebook Oversight Board.

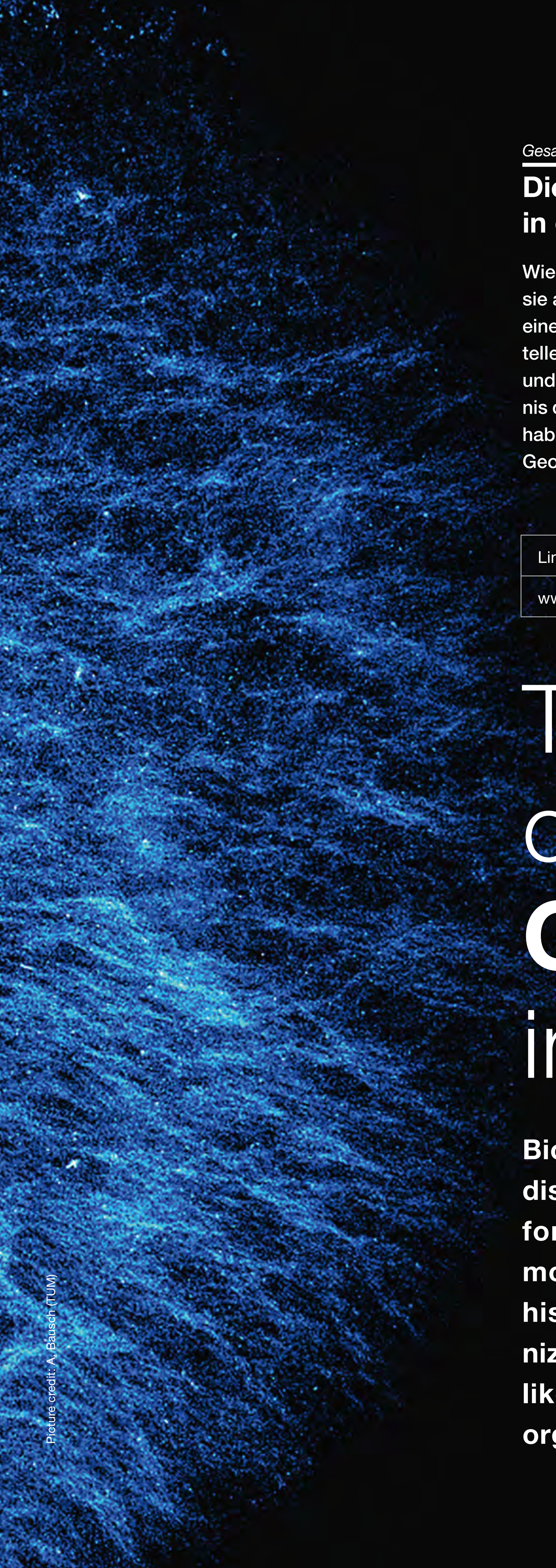
As a final thought, why is your research focus important right now?

Questions about the relationship between technology and society will not suddenly disappear or be resolved by a stroke of genius – on the contrary, they will become more central to everything we do as a society. Just think about how our understanding of sustainable mobility has changed twice over the past 3 years: starting with the pandemic, with massive implications for public transportation and remote work. And now again as a result of the Ukraine war, with supply chains disrupted and energy prices soaring. None of these are solely technological questions and they require a profound understanding of social, political and ethical aspects. ■ *Eve Tsakiridou*

Annotation:

This interview is an adapted version of a longer text originally intended for the PRME report 2021 of the TUM School of Management.





Picture credit: A. Bausch (TUM)

Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-29

Die Physik der Selbstorganisation in der Biologie

D

Wie genau findet biologisches Gewebe seine Form und wie erhält es sie aufrecht? Mit einem stark interdisziplinär orientierten Ansatz und einem Schwerpunkt auf der Entwicklung leistungsfähiger experimenteller Modellsysteme haben der Biophysiker Prof. Andreas Bausch und seine Kolleginnen und Kollegen wichtige Beiträge zum Verständnis dieses grundlegenden Geheimnisses des Lebens geleistet. Dabei haben sie viel über die Physik der biologischen Materie in komplexen Geometrien gelernt.

Link
www.bauschlab.org/home

The Physics of **Self-Organization** in Biology

Biophysicist Prof. Andreas Bausch wants to discover the minimal components required for different biological functions, like cell movement. His search has taken him from his discovery of how molecules can organize themselves into coordinated movement like swirling flocks of birds to the world of organoids.

Getting experimental control of biological systems requires well controlled sample preparations which are reconstituted by means of biomolecular methods.

The spanking new building of the interdisciplinary Center for Functional Protein Assemblies (CPA) graces the northern border of the TUM's Garching campus. From his third-floor office window, its founding director Andreas Bausch can look down on the construction site for the Center for Organoid Systems and Tissue Engineering, an institute he helped mastermind, and with which he plans to work closely when it begins operations next year. As a biophysicist, he is convinced that understanding the processes of life can only be achieved by biologists and physicists working together.

Bausch has always been drawn to the soft matter of biology, whose squishiness, seemingly against the odds, gives rise to the very precise and robust shapes of living tissue. During his PhD at TUM, he investigated the viscoelasticity of cytoplasm, the fluid contained within cells. At Harvard University his postdoc research, inspired by the question of how virus capsids assemble, focused on how crystals form on curved surfaces, and he also worked on the development of colloidosomes, tiny spheres that can encapsulate and deliver bioactive molecules. Colloidosomes have paved the way for the development of products in the pharmaceutical and other industries. Andreas Bausch returned to TUM in 2002 as assistant professor in the Department of Physics, set on investigating the mechanical properties of the cytoskeleton – the cell's scaffolding – and addressing pure physics questions like how its mechanical forces are transduced.

The cytoskeleton provides the cell with its structure and shape. Two of its main components are microfilaments, which are polymers of actin molecules, and microtubules, which are polymers of tubulin molecules. Stable as it is, the cytoskeleton can be induced to deform when the cell needs to move, for example during cell division, cell mi-

gration in development or wound healing processes. The process requires a molecular motor – myosin in the case of actin, kinesin for tubulin – and ATP as a source of energy.

Bausch began his research by making use of a very simple, two-dimensional in-vitro motility assay, which models some of the molecular aspects of cell movement. Myosin is immobilized on a cellulose gel and thereafter actin filaments are applied atop it. When ATP is added, the filaments begin to move randomly and can be tracked by confocal microscopy, with AI-based algorithms stitching the images together. “It’s a passive system where you throw in the basic ingredients and watch what happens – very simple, very beautiful,” says Bausch, describing the experiment. ▷

Picture credit: Stefan Woidig

“It’s great to see that our simple assays help understand the growth of organoid structures.”

Andreas Bausch

“These are the moments you live for in science.”

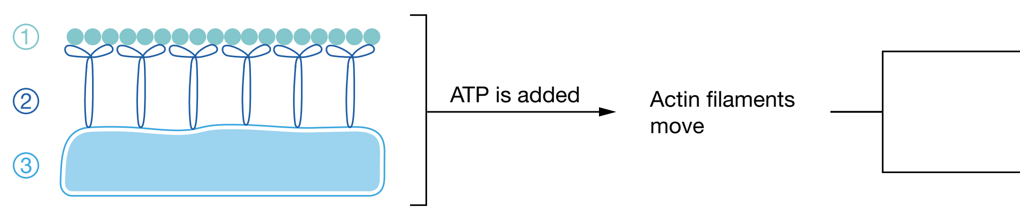
Andreas Bausch

A new phenomenon

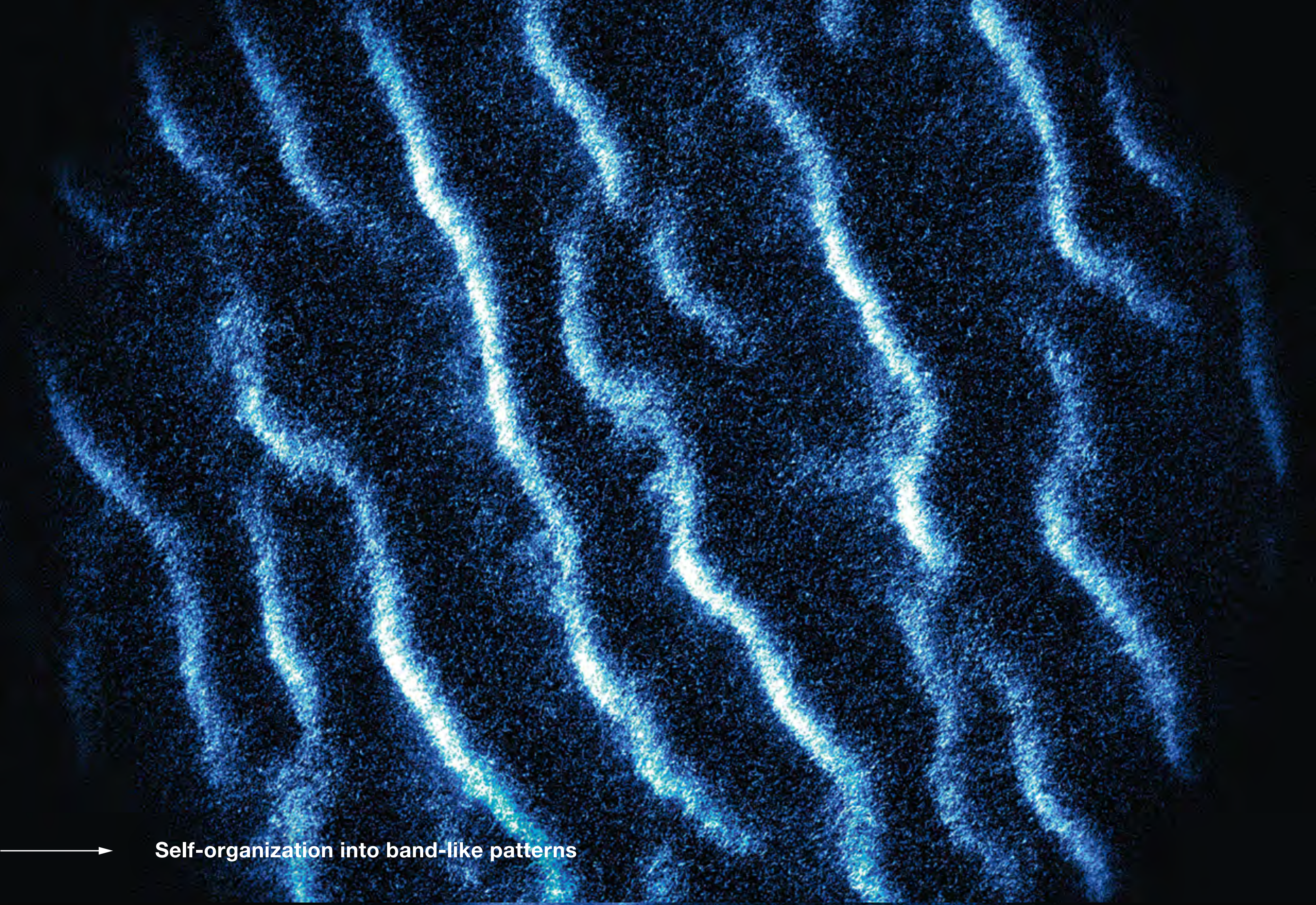
One Friday afternoon in the autumn of 2008, he and his group were casually wondering what would happen if they increased the density of actin filaments in the assay. They tried it, and were stunned to see the filaments suddenly aligning themselves into a collective motion, swirling in clusters around their coverslip in coherent patterns, like thousands of tiny synchronized swimmers. To biophysicists, this was an entirely new phenomenon. “We saw a switch from a disordered to an ordered state, clearly a very big deal,” says Bausch. “These are the moments you live for in science.”
They repeated the experiment numerous times and saw that patterns could take the form of bands as well as swirls. “But this one is my favourite,” he says, pointing to his laptop screen, his excitement seemingly as fresh as if he were seeing it for the first time. “The swirls are like galaxies; isn’t it cool?”

Graphics: ediundsepp (source: TUM); Picture credit: A. Bausch (TUM)

Basic experimental set-up: Myosin (2) is immobilized on a cellulose gel (3) and actin filaments (1) are applied atop it. The filaments begin to move randomly when ATP is added. They switch into an ordered state beyond a certain filament density.

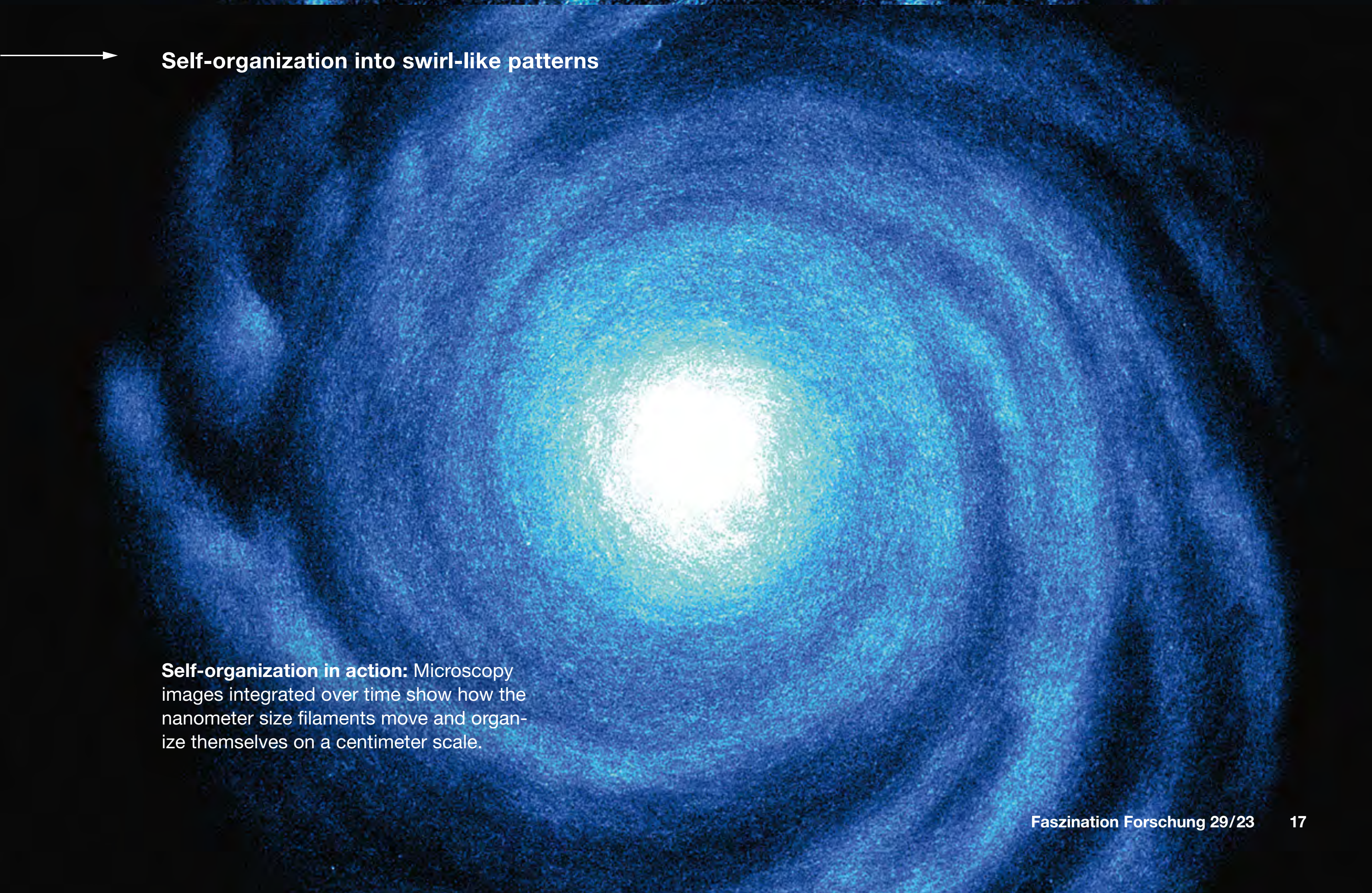


Bausch was aware of the theory of active matter, developed in the 1990s, which mathematically models how flocks of thousands of birds or schools of thousands of fish move together in bold patterns. But he hadn’t quite expected the molecules in their ultra-simple assay to self-organize in the same active-matter way. “Fish and birds are complex organisms, with brains and chemical sensing mechanisms that could be somehow influencing their coordinated movements,” he says. “Our system was as simple as it gets, and we were seeing the same sort of thing.”
The assay allowed for the first time the physics behind this order transition to be addressed experimentally. In the years since, he and his team have been using it to probe the mechanics and dynamics of this active matter. They added tubulin-kinesin to the repertoire. And, thinking back to the physics of crystallization on curved surfaces and colloidosomes that he studied during his postdoc, Bausch created a system whereby tiny samples of active matter can be inserted into droplets, this time spherical lipid-bilayer vesicles. The filaments arrange themselves on the vesicles’ inner curved surfaces where their three-dimensional motion can be studied.
A major part of his lab’s efforts now focuses on using these two- and three-dimensional assays to reverse-engineer particular cellular functions by adding cell components to the assay and adjusting conditions until functions can be replicated. In this way, they elaborated, for example, the physics of cytoplasmic streaming, a biological phenomenon occurring in oocytes and other very large cells where the cytoskeleton distorts itself to distribute molecules more homogeneously through the cell’s volume. One of his ultimate goals is to build minimal systems that can fulfill biological tasks – such as a minimal migratory system composed of just a handful of necessary proteins that is already capable of mimicking cellular movements. ▷



Self-organization into band-like patterns

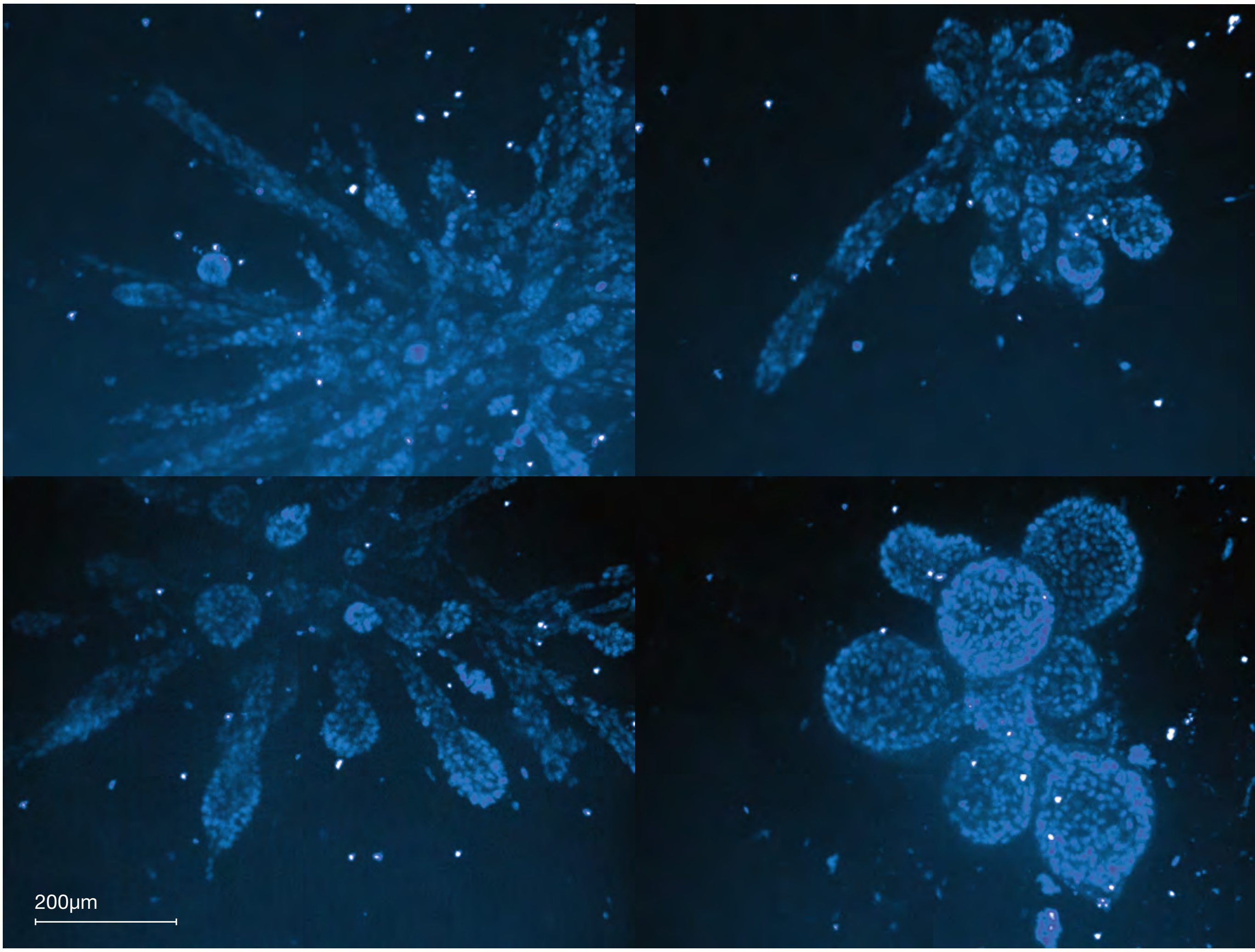
Self-organization into swirl-like patterns



Self-organization in action: Microscopy images integrated over time show how the nanometer size filaments move and organize themselves on a centimeter scale.

Prof. Andreas Bausch

discovered his passion for soft-matter biophysics during his doctoral studies at TUM's Department of Physics. PhD in hand, in 1999, he moved to Harvard University for a postdoc. In 2002 he returned to TUM as assistant professor and became a full professor in 2008. Bausch became founding director of the Center for Functional Protein Assemblies in 2014. He developed the concept for the Center for Organoid Systems and Tissue Engineering, which will open by 2024. In 2015-2016 Bausch was visiting Miller Professor at the University of California, Berkeley and has been a visiting scholar at Harvard since 2021. He received an ERC Starting Grant in 2011, followed by an ERC Advanced Grant in 2012, an ERC Proof of Concept Grant in 2017 and an ERC Synergy Grant in 2019.



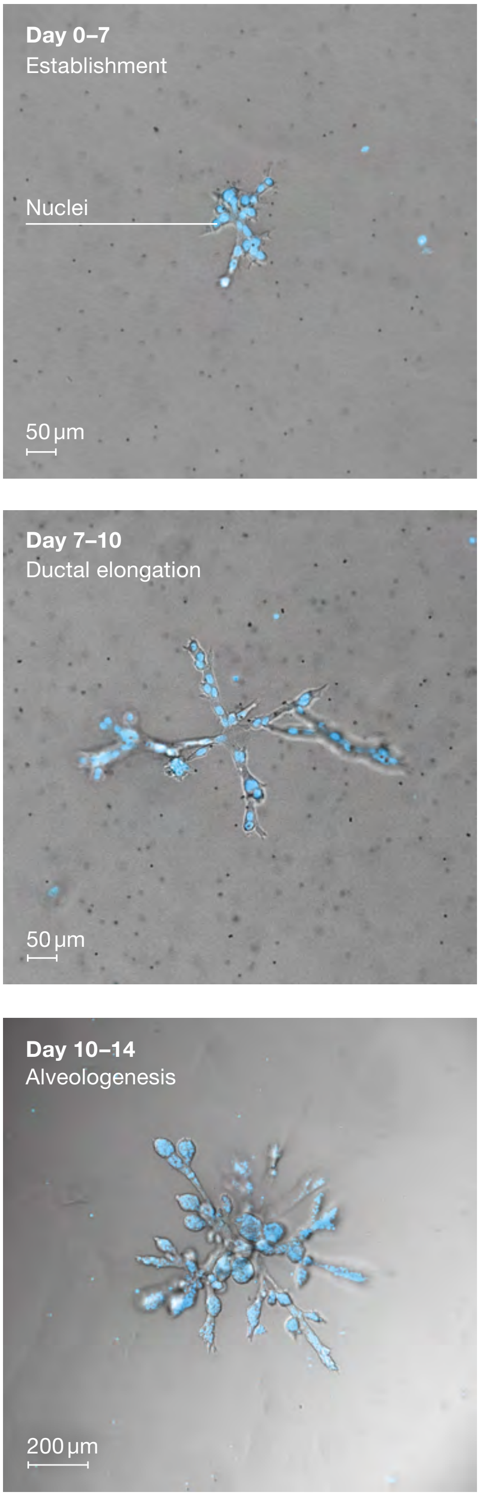
Picture credit: Stefan Woidig; A. Bausch (TUM)

From single human mammary gland cells complex structures of thousands of cells develop. Collective cell motion results in a rotary motion in the sphercial structures, which resemble alveoli.

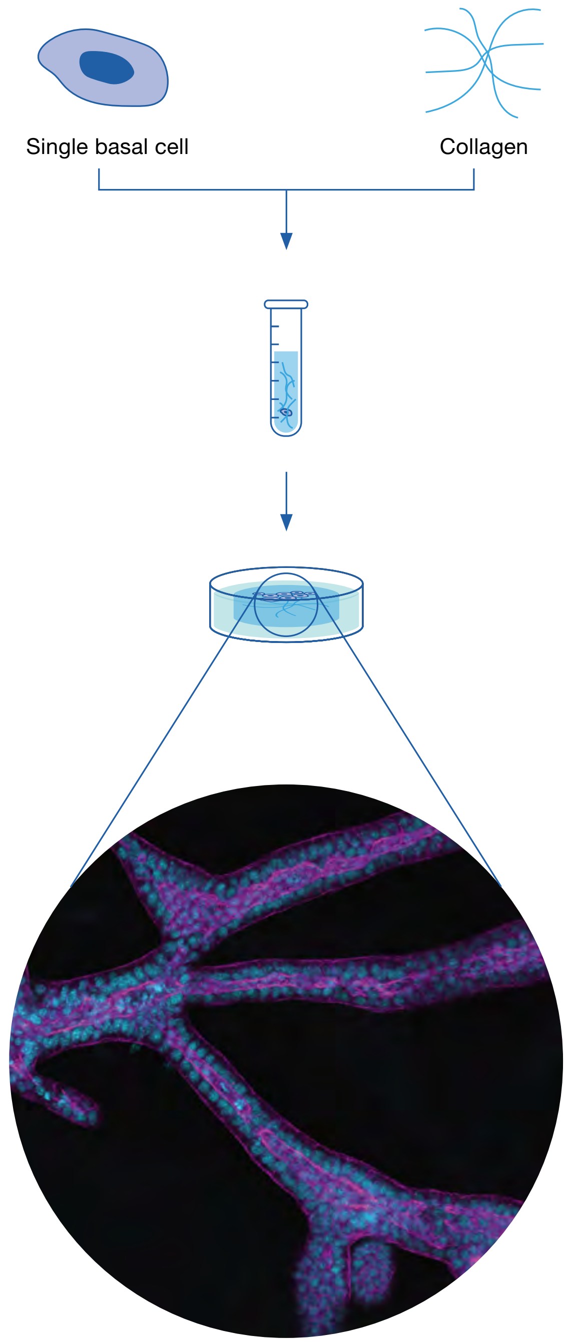
Moving to organoids

Six years ago, Bausch decided it was time to move to a larger scale, and investigate more complex systems and structures. He had always been struck by how little was understood about the forces that cause cells to move during significant biological processes like development and wound healing, or pathological processes like cancer and metastases. Would the principles his team had identified in the highly stripped-down assays also apply in vivo? Would they help fill in these knowledge gaps? He decided to test out the possibility in organoids, mini-organs growing in cell culture.

He teamed up with stem cell researcher Christina Scheel from the Helmholtz Center Munich who had developed a method for generating organoids from individual human mammary cells embedded in floating collagen gels. In this environment the cells develop into a branching network of ducts, recapitulating mammary gland structure. The team wanted to investigate the physical mechanisms that allowed the developing ducts to drive their way into the collagen matrix, which models the extracellular matrix in tissues. They stained the cells' nuclei so that they could follow their movement with confocal microscopy. They discovered – again, to their happy surprise, says Bausch – that the active-matter concepts did indeed apply in this case, too. When the cell numbers became large enough, the cells moved together in coherent clusters – and this collective movement provided a force strong enough to distort the collagen matrix into a kind of mechanical cage that both guided and constrained the cell movement, and thus the overall shape of the ducts. ▷



Starting with a single primary human basal mammary epithelial cell, a mammary gland organoid grows within about two weeks. The microscopy images show the different stages of growth; the nuclei are visualized using DNA stain.



The growth of organoids via self-organization starts with a single cell cultivated on a substrate made of collagen or similar materials. The image shows an organoid generated from pancreatic tumor cells.

Graphics: ediundsepp (source: TUM); Picture credit: A. Bausch (TUM); Stefan Woidig

Human cells are technically difficult to work with, so to investigate the phenomenon in more depth, he joined forces with Maximilian Reichert, a clinician specializing in pancreatic cancer at the Klinikum Rechts der Isar. Reichert, who now also runs a CPA lab, had created organoids from mouse pancreatic tumor cells. Their teams are applying the range of tools available for manipulating mouse genes and proteins as well as high-resolution microscopy methods to work out how the mechanical forces inside and outside cells are generated, and how they feed forward and back on gene expression. The big question, says Bausch, is to understand how the interplay of all these effects steers cells to create the correct structures and functions all by themselves during development of organ structures.
Both he and Reichert will establish research groups in the new Center for Organoid Systems and Tissue Engineering when the building is ready. Seven other interdisciplinary research groups will join them, providing expertise in other tissue organoids and technologies like CRISPR gene editing. There, Bausch hopes that collaboration across disciplines leads to developing a new understanding of organ growth as well as to the development of innovative high-throughput assays that can be used in drug discovery. For all the insights that his approach is providing to biologists, for Bausch the most compelling part of his research is very much about the physics of self organization. “It’s great if our simple assays help in understanding the processes to build organoid structures,” he says. “We are trying to understand these processes more fundamentally in order to work out the generic principles of the biological systems.” *Alison Abbott*

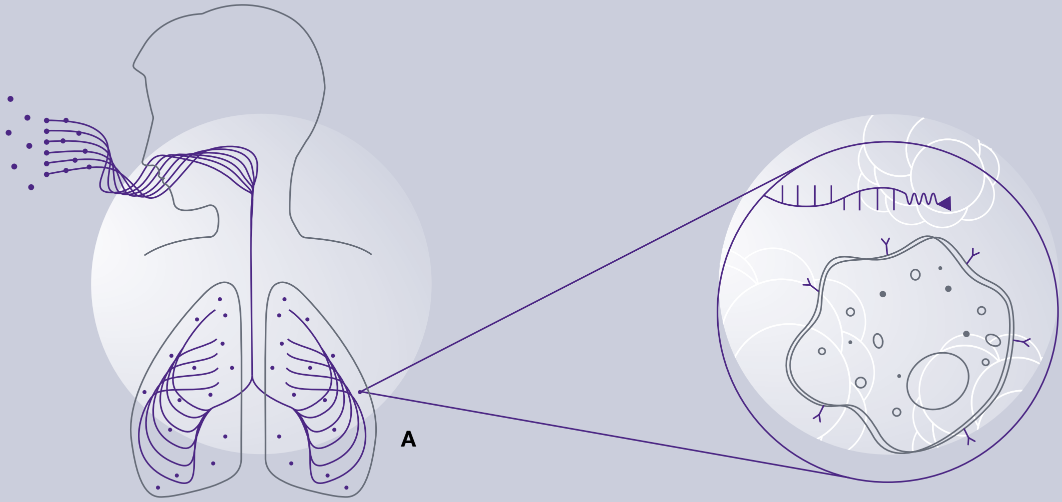
The micro-mechanical properties of the organoids during growth are determined with optical measurements.

TUM Center for Functional Protein Assemblies

The Center for Functional Protein Assemblies (CPA) is an interdisciplinary research center dedicated to understanding concepts of self-organization in biological tissues, and how functional properties of protein assemblies emerge as they interact with their cellular and extracellular environments. Twelve research groups investigate aspects of these functions, which range from protein folding and cellular transport mechanisms to cell migration via cell division. 150 biophysicists, biochemists, organic chemists, engineers and biomedical scientists collaborate across disciplines within the center. They moved together into the 4,000 m^2 building in spring 2022.

TUM Center for Organoid Systems

Organoid systems are rapidly emerging as a novel technology capable of fundamentally transforming the future of biomedical research. The Center for Organoid Systems (COS) is dedicated to generating and exploring relevant diverse human tissue organoid models using cutting-edge technologies in bioengineering, biophysics, nanotechnology and artificial intelligence. The overarching goal is to gain novel insights into human biology and to develop new, personalized therapies to improve human health by integrating this technology platform. It is scheduled to open in 2024.



Healing with RNA

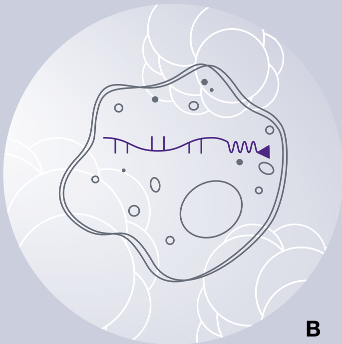
Link
www.rnatics.com

Everyone has been familiar with RNA-based vaccines since the COVID-19 pandemic. Yet RNA molecules also harbor major potential as drugs. One of the biggest challenges here is getting the active ingredients to their destination. RNATICS GmbH has come up with an elegant solution for the lung that is now set to revolutionize the treatment of COVID-19 and other diseases.

Prof. Stefan Engelhardt is often asked why he set up RNATICS. For him, the answer is simple: Wanting to help people by developing a drug and using it in real life is a noble aim, he says. That Engelhardt now has the opportunity to do just that is down to many years of academic research, an unusual field of study, and a few fortunate conditions. Though he had initially wanted a career in clinical cardiology, things turned out differently, and Engelhardt "got stuck in research at an early stage." After holding various positions, including at the Rudolf Virchow Center – the German Research Foundation's Research Center for Integrative and Translational Bioimaging in Würzburg – he was appointed to the Chair of Pharmacology and Toxicology at TUM in 2008. Not long before that, he had stumbled across a new class of molecule that continues to fascinate him to this day: noncoding RNAs, which are not translated into proteins but act mainly to regulate the cell's behavior.

Engelhardt first had the idea of a business start-up around three years ago, as he himself explains: "We'd devised a method for getting RNA molecules into macrophages in a targeted way. That meant we suddenly had the realistic prospect on our hands of developing a drug." This is because, as part of the immune system, macrophages have a hand in the pathophysiology of many diseases – including COVID-19, where they are mainly responsible for the overactivated inflammatory response that characterizes severe courses of the illness. Engelhardt and his working group were fortunate enough early on in the pandemic to get their hands on lung tissue from patients who had died from COVID-19. "We found that an especially large amount of a non-coding RNA that we'd been researching for 15 years had been produced in this tissue, particularly in the macrophages that it contained," he says. This made it clear that this so-called microRNA-21 might be involved in what was determining the course of the disease.

For Engelhardt and his team, all the pieces now came together. "The idea was to inhibit microRNA-21 with a suitable RNA molecule known as antisense RNA. This had to be designed in such a way that macrophages would absorb it without hesitation. And it was exactly this method that we'd already developed," the founder of RNATICS



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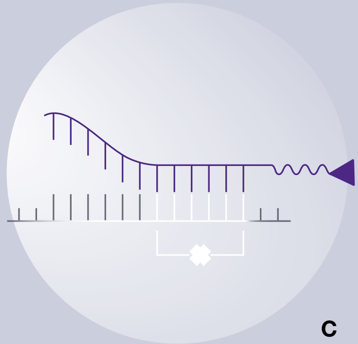


C

A The RNA therapeutic is inhaled

B The antisense RNA is designed in such a way that macrophages absorb it

C The antisense RNA inhibits the disease-causing microRNA

Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-29

Mit RNA heilen

D

Das Start-up RNATICS GmbH entwickelt RNA-basierte Medikamente für die Therapie von COVID-19 und anderen Krankheiten. Grundlage der Ausgründung sind die Forschungen von Prof. Stefan Engelhardt und seinem Team am Lehrstuhl für Pharmakologie und Toxikologie der TUM. Engelhardt arbeitet an nicht-kodierenden RNAs und hat eine Methode entwickelt, um RNA-Moleküle zielgerichtet in Zellen einzubringen. Die RNATICS GmbH wurde mit 7,5 Millionen Euro vom Bundesministerium für Bildung und Forschung gefördert, um ihr erstes RNA-Medikament in klinische Studien zu bringen. □

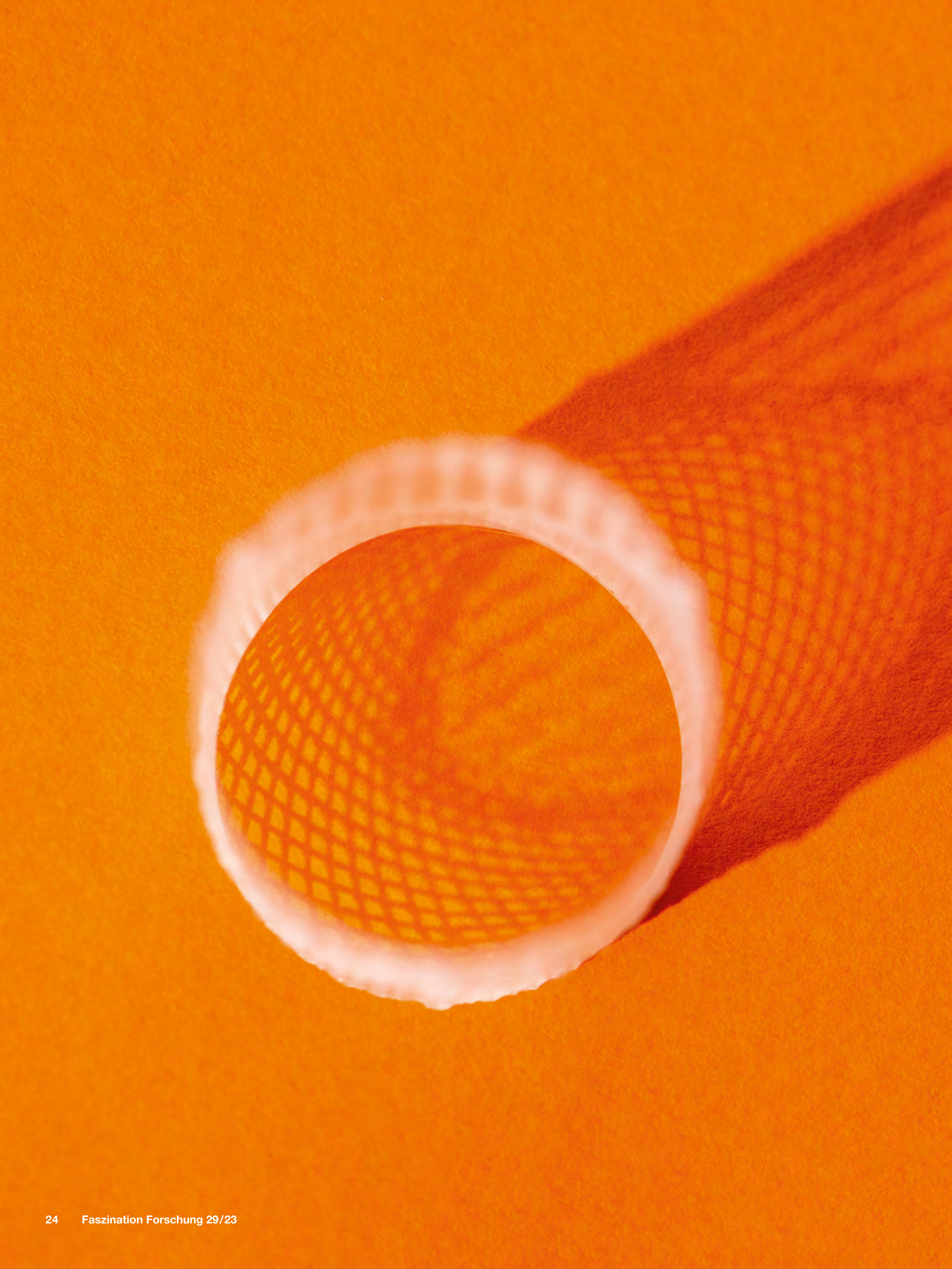
explains. The antisense RNA had sugar residues attached to it, which macrophages generally use to detect pathogens and which they therefore absorb without hesitation – thus taking in the antisense RNA at the same time. One advantage of treating the lungs is that the active ingredient can be inhaled, allowing it to be administered in a targeted way. “Local therapy like this generally causes very few side effects,” says Engelhardt, clearly pleased.

His spin-off got off the ground with a call for tenders issued by the German Federal Ministry of Education and Research (BMBF), which was making funds available for developing new COVID-19 treatments. Engelhardt set off on a hunt for suitable co-founders and is still delighted by the swift and enthusiastic “yes” he received from his two first choices: Dr. Thomas Frischmuth, an expert in nucleic acids and sugar coupling with extensive start-up experience, and Prof. Klaus Rabe, Director of LungenClinic Großhansdorf GmbH, who happens to be an eminent expert on clinical trials for lung disease. This marked the inception of RNATICS. Funding of EUR 7.5 million from the BMBF’s pot enabled it to commission the final toxicological studies and the production of the new RNA drug, with the first human clinical trials planned for 2023. A partnership agreement with ISAR Biosciences has brought another financial backer on board. This is the ideal solution for the fledgling firm because, in Engelhardt’s words, “it lets us stay independent.”

With Engelhardt deciding to retain his chair at TUM rather than working full-time in his company, an intensive search for a young leader to build up the RNATICS team step by step led to Dr. Johannes Schmidt. In his role as Managing Director of the TUM Venture Lab Healthcare, he had supported the spin-off process in its early phase and assisted with licensing negotiations. “Having the TUM Venture Lab Healthcare acting as intermediary enabled us to secure an exclusive licensing agreement for the necessary patents very quickly,” Engelhardt recalls. Schmidt adds: “The Venture Labs were able to connect with some key contacts, without whom the business set-up would have never been this fast.” TUM handled his switch to RNATICS in an extremely professional manner, he says. The company has already had confirmation this year that it has a highly promising future ahead of it: Besides winning the Innovation Prize of the German BioRegions, it was also placed in the top two for “Most Innovative Product” in the “Breakthrough Innovation” category at the Pharma Trend Image & Innovation Awards.

■ *Larissa Tetsch*

Graphics: ediundsepp (source: RNATICS)



Link
www.mec.ed.tum.de/en/mmi

Enabling Patients to Grow a **New Heart Valve**

Patients with heart valve disease may someday be able to grow their own healthy heart valves on an implanted scaffold thanks to Prof. Petra Mela, Chair of Medical Materials and Implants. Mela is leading the development of these game-changing scaffolds using melt electrowriting, a sort of 3D printing technique with a twist.

Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-29

Wie im Körper der Patienten neue Herzklappen wachsen

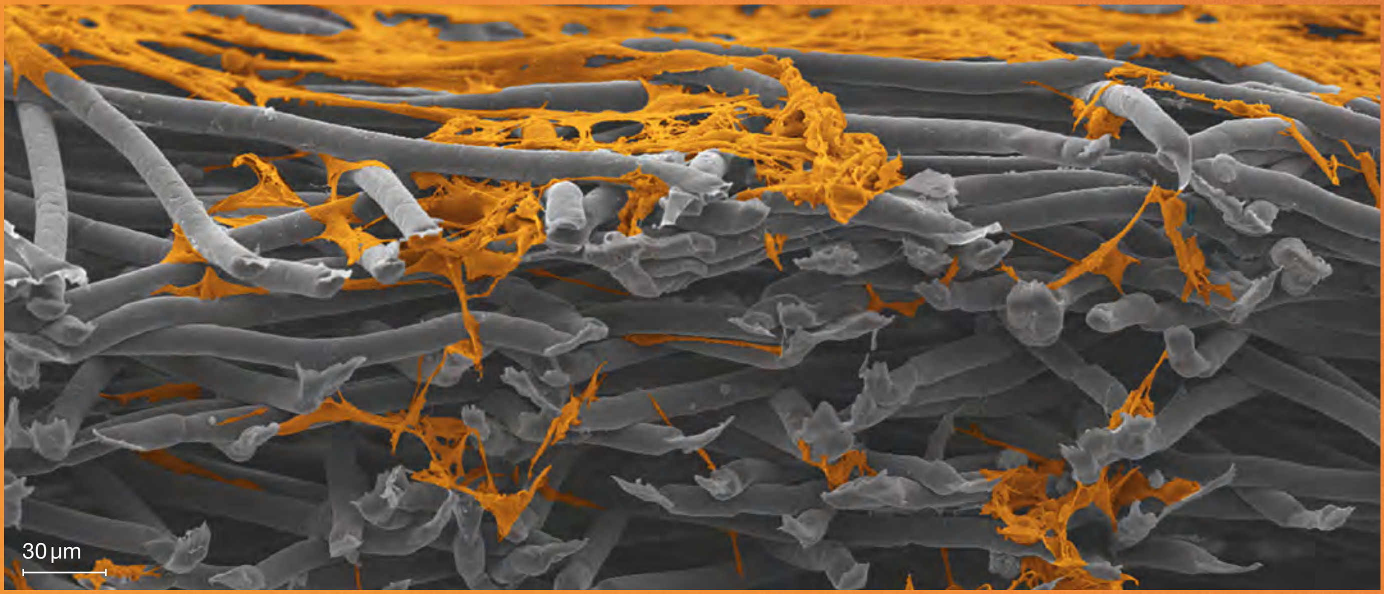
D

Für Patienten mit Herzklappenerkrankungen kann eine Klappenprothese lebensrettend sein. Aber viele Herzklappenimplantate verursachen Gerinnungsprobleme oder lassen mit der Zeit in ihrer Leistung nach. Gerade bei heranwachsenden Kindern müssen sie alle paar Jahre ersetzt werden. Hier kommt das neuartige Herzklappengerüst ins Spiel, ein Implantat, das mit dem sogenannten Melt Electrowriting-Verfahren gefertigt wird. Entwickelt haben es Petra Mela, Professorin für Medizintechnische Materialien und Implantate, und ihr Team. Das Verfahren funktioniert nach dem Grundprinzip des 3D-Drucks, weist jedoch einen entscheidenden Unterschied auf: ein elektrisches Feld. Dieses ermöglicht die Herstellung von Trägergerüsten aus filigranen Mustern dünner Fasern. Nach dem Einsetzen soll das Gerüst im Körper des Patienten als Stützstruktur fungieren, um die herum eine neue Herzklappe aus körpereigenem Gewebe entsteht. Das Gerüst wird vom Körper absorbiert, sodass nur die neue Herzklappe übrigbleibt. Mela ist optimistisch, dass sich dieses Verfahren als unschlagbar erweisen kann, wenn mehr darüber bekannt ist, wie sich die Immunreaktion der Patienten steuern lässt, wenn ihnen eines Tages ein solches Gerüst eingepflanzt wird. □

Picture credit: Astrid Eckert

Clinically used heart valve prostheses such as mechanical (left) and biological ones (middle) have inherent downsides. Petra Mela wants to overcome these with a tissue-engineered heart valve based on a melt-electrowritten bioabsorbable scaffold (right).

When Petra Mela was a researcher at RWTH Aachen University, she attempted to tissue engineer her first heart valve. Back in 2010, many researchers across the globe were failing to create heart valves that were strong enough to function and Mela, a newcomer in the field, wanted to know why. She noticed that the majority of researchers were using the same approach: the new valves they were creating to be implanted in patients were the same shape as the valves patients were born with, known as native valves. So Mela went in another direction. By drawing on a design principle originally developed by cardiac surgery expert Dr. Wolfgang Goetz, Mela attempted to create a better heart valve not by modeling the implant on the anatomy of a native valve but instead creating one with a tubular design reinforced by textiles. When implanted in a patient, she suspected it would function the way a native valve does, including being strong enough to withstand the high pressures exerted by blood flowing through the heart. "I remember when I proposed this, the response was, 'This will never work.' But it turns out it works very nicely. And if you look at the way many heart valves are currently made in tissue engineering, they are pretty much designed according to a tubular concept," she says. Now, Mela is pushing the boundaries of tissue engineering yet again. Along with her collaborators, she is currently working to digitally fabricate a tubular heart valve scaffold that, when implanted, can be colonized by a patient's own cells, a paradigm known as *in situ* tissue engineering. The goal is for a patient's body to use the scaffold as a support structure on which to reconstruct a new valve from its own living tissue. "If this is achievable, it's unbeatable. Because living tissue grown by the person's own body is the best biomaterial you can have," says Mela.



Picture credit: Astrid Eckert, P. Mela (TUM)

Scanning electron microscope image showing how cells (in orange) are infiltrating a melt-electrowritten scaffold (in gray).

The amazing heart

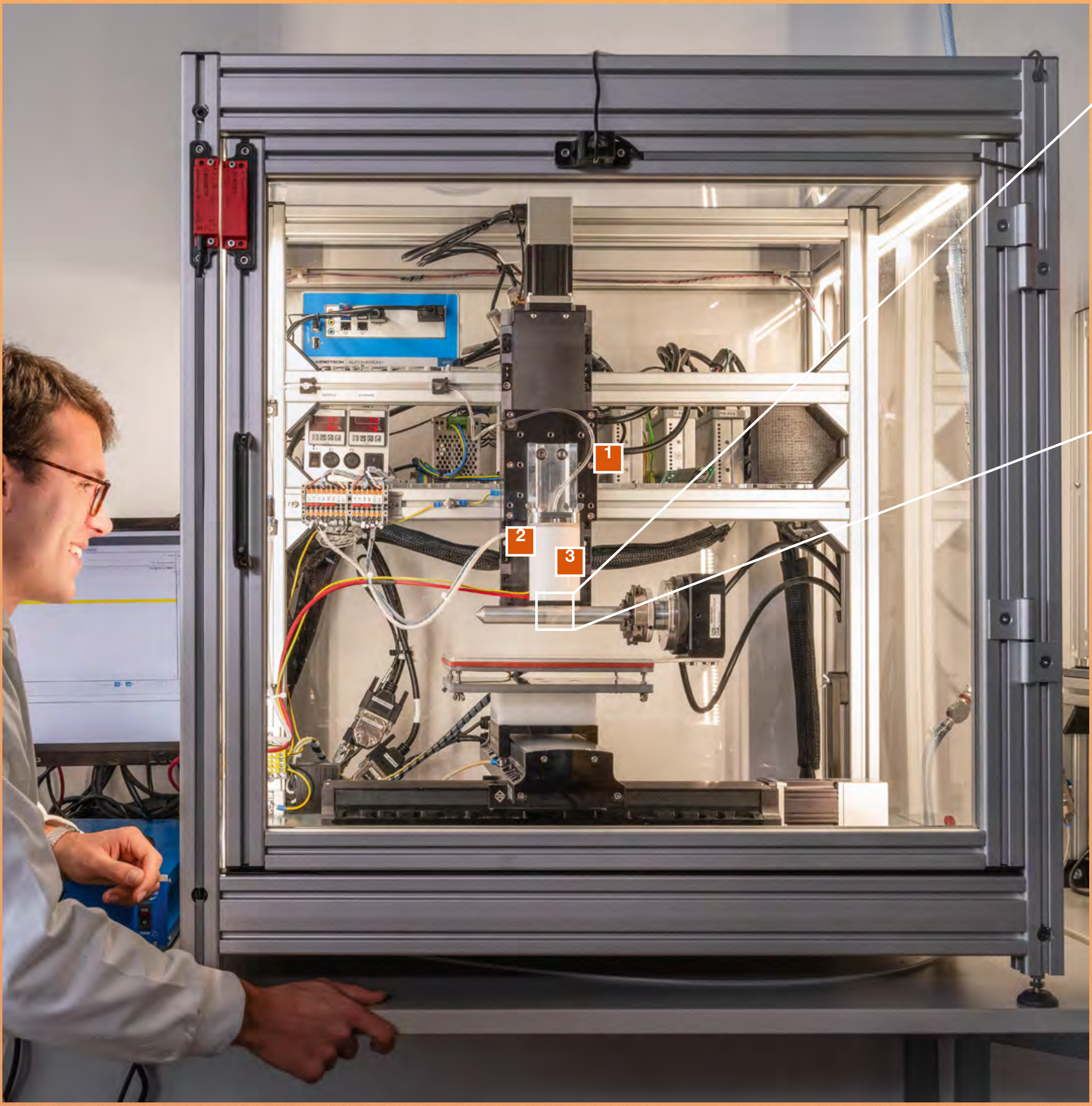
The heart, as Mela puts it, is a fantastic piece of engineering that we get for free. Within our hearts, each valve is essential for ensuring that blood flows in the right direction to remove metabolic waste products and provide oxygen and nutrients throughout the body. The tissue that makes up each valve is layered in such a way as to optimize its performance, varying in its quantities of elastin or collagen, among other materials, as well as in the orientation of the tissue's fibers, which function differently when the heart is in the midst of a beat or between beats. When a valve doesn't open or close as it should, the heart works extra hard to compensate. For those with malfunctioning valves, heart valve prostheses can be life saving. It has been projected that there will be over 850,000 patients in need of heart valve implants in the year 2050, according to a seminal 2005 paper in "Nature Clinical Practice Cardiovascular Medicine". And although the impact of these medical devices is undeniable, they do come with drawbacks, including damaging delicate blood cells, causing problems with coagulation, and calcification, preventing the valve from opening properly.

In addition, a prosthetic heart valve needs to be replaced every ten to twenty years in adults and far more frequently in children because of kids' stronger immune response and increased calcium metabolism as compared to adults'. And just as children outgrow their clothes, over time, they also outgrow their implants, requiring additional surgeries to replace them.

"The big motivation for me is helping the pediatric population," says Mela. "This is where my heart is." ▷

"Little by little, the bioabsorbable scaffold will disappear. All that is left is the tissue that the patient's own body has created."

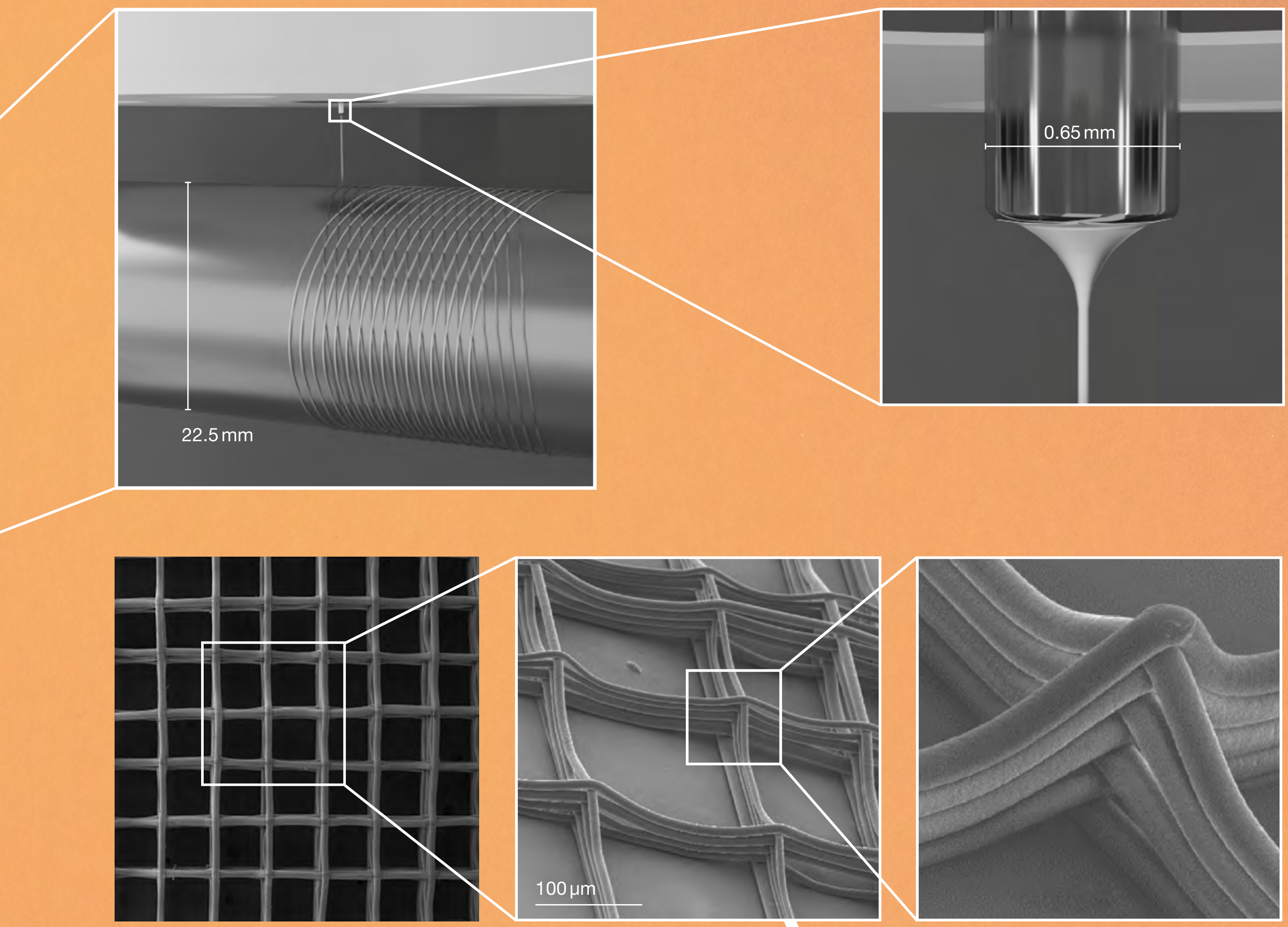
Petra Mela



Graphics: ediundsepp; Picture credit: Astrid Eckert, P. Mela (TUM)

The melt electrowriting device in Mela's laboratory.

1 Driven by pressurized air, 2 a polymer melt is extruded from a heated print head through a nozzle. 3 An electric field causes the melted polymer to form a fiber jet that decreases in diameter as it travels towards the grounded collector.



△ **Top row: 3D renderings** showing how a polymer fiber is deposited onto a cylindrical collector in a defined pattern.
Bottom row: Scanning electron microscope images that highlight layer-by-layer fiber stacking typical of additive manufacturing.

Typical diameter of the fibers:
about 10 µm

Typical thickness of a human hair:
60–80 µm

“At the moment, I think melt electrowriting is the only technology that allows us to do something so sophisticated.”

Petra Mela

Picture credit: Astrid Eckert

‘Writing’ a scaffold

To achieve this goal, Mela and her team used a new technique to manufacture a better heart valve scaffold.

The approach uses melt electrowriting, an extrusion-based technique that works according to the same basic principles as a 3D printer, with one additional key feature: it is assisted by an electric field. This electric field makes it possible to create a scaffold composed of thin fibers – typically as small as 10 microns in diameter, about seven times thinner than a human hair. By digitally controlling how the microfibers are collected, this technique makes it possible to produce scaffolds with optimal fiber architectures and tunable mechanical properties.

To create a scaffold using this new technique, a polymer is melted down in a cartridge, pressurized, and pushed through a nozzle, creating a filament. Then, an electric charge in the polymer causes the filament to thin down as it travels towards the oppositely charged collector. The fiber that is formed is then deposited in a particular pattern to form a scaffold that mimics critical aspects of a native heart valve, including the way collagen fibers elongate in the leaflets – the flaps of a heart valve – which, in turn, contributes to the dynamic way native heart valves open and close. “In addition, because the heart valve is attached to the aortic wall, which has different properties from the leaflets, we also developed a platform where we were able to assign different patterns to different regions. Each of these patterns, then, have specific mechanical properties or responses. And if you do this in a way that ensures everything does have the right properties, then the whole structure will be optimized in its physiological function,” Mela says. “Making these patterns and combining different patterns in a 3D construct – this is what we can do with melt electrowriting. At the moment, I think this is the only technology that allows us to do something so sophisticated,” she adds.

Perfecting the design

But the developments don't stop there. Mela has developed a way to overcome a problem that pervades the world of fibrous heart valve implants: a scaffold so dense, cells can't properly infiltrate it. She found that combining the melt-electrowritten scaffold with an elastin-like biomaterial makes it adequately porous. Kilian Müller, one of Mela's doctoral students, used this knowledge to develop a further system that is itself microporous, so that it doesn't require the addition of any other material or technique. Müller also led the work on incorporating another material – ultrasmall superparamagnetic iron oxide nanoparticles – that would make it possible for a melt-electrowritten scaffold to be detected by an MRI scan. This way, when these scaffolds are implanted into patients in the future, doctors will be able to monitor their functionality while the patients' own tissue grows inside them. ▷

△ **Petra Mela and her doctoral student Kilian Müller inspect a 3D-printed scaffold.** Müller works on incorporating ultrasmall superparamagnetic nanoparticles, which make the scaffold detectable by an MRI scan.

Prof. Petra Mela

studied Mechanical Engineering at the Politecnico of Torino (IT) and earned her PhD in biomechanics at the University of Twente (NL). She led the Cardiovascular Tissue Engineering group at RWTH Aachen, where she also did her Habilitation in medical technology. Petra Mela has been a visiting scientist at the British Heart Foundation, University of Liverpool (UK) and at Sandia National Laboratories (CA, USA). In 2019 she was appointed professor and chair of Medical Materials and Implants at TUM. She is a member of the Munich Institute of Biomedical Engineering (MIBE), the Integrated Research Institute "Materials, Energy and Process Engineering" (MEP) and the TUM.Additive cluster.

Picture credit: Astrid Eckert

“The big motivation for me is helping the pediatric population. This is where my heart is.”

Petra Mela

So far, all the testing has been done *in vitro* – no melt-electrowritten scaffolds have been implanted into patients just yet, although other valves based on the concept of *in situ* tissue engineering have undergone small pilot clinical trials. But Mela is acutely aware that the effectiveness of her team’s melt-electrowritten scaffolds can only be confirmed once tested *in vivo* – first in animals and eventually in humans. She looks forward to testing her team’s elastin-embedded scaffold, which she thinks holds particular promise.

“Within the patient’s body, the person’s cells should infiltrate the scaffold and start producing the right proteins and other components of a heart valve’s tissue. The scaffold guides this tissue regeneration, which would not otherwise spontaneously occur in a heart valve. Little by little, the scaffold, which is bioabsorbable, will disappear so that in the end, all that is left is the tissue that the patient’s own body has created.”

Collaboration is key

The key to making these heart valve scaffolds a success? Extensive interdisciplinary collaboration. As chair of Medical Materials and Implants, Mela understands how essential it is to collaborate with chemists, immunologists, engineers and clinicians, not only on heart valve implants but on other cardiovascular projects, too. Between working on projects on stents, grafts and conductive tissue, she is developing a better *in vitro* model for cancer patients that could enable researchers to test cancer medications on an individual’s own tumor in the lab. Mela is excited, too, to be part of the TUM Innovation Network for Artificial Intelligence Powered Multifunctional Materials Design. The support and interdisciplinary collaboration in this network enables her to work on a number of projects to develop new materials to be used in the cardiovascular system. “I think the biggest challenge in my work is putting these different disciplines and all this complementary knowledge together. The benefit, though, is that by working with so many people from different disciplines, you learn to speak their specific languages. I’m constantly encountering new things, new knowledge and new people. For me, this is what makes working at university unbeatable,” she says. ■ *Sarah Puschmann*

Printing a House out of Sand: **How the Digital Transformation is Changing Construction Sites**

Could the houses, bridges and train stations of the future be produced in 3D printers? Additive manufacturing has already made inroads into the construction sector. The digitally controlled process of applying layer upon layer of material promises to bring about swift, flexible and environmentally friendly construction. However, there is still a lot of work to do. Prof. Christoph Gehlen and Prof. Kathrin Dörfler at TUM have set about tackling this topic in their research.

Picture credit: Juli Eberle

Links

www.amc-trr277.de
www.arc.ed.tum.de/df
www.mae.ed.tum.de/cbm

Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-29

Ich bau’ dir ein Schloss mit Sand: Digitale Transformation auf der Baustelle

D

Häuser, Brücken oder Bahnhöfe aus dem 3D-Drucker? In der Baubranche hält die additive Fertigung gerade Einzug. Prof. Christoph Gehlen und Prof. Kathrin Dörfler von der TUM packen mit ihren Forschungen kräftig an. Gehlens Team hat das Verfahren Selective Paste Intrusion – also das selektive Verbinden mit Zementleim – zur Marktreife entwickelt. Dabei werden winzige Gesteinskörner Schicht für Schicht genau an den Stellen mit Zementleim verfestigt, die das Datenmodell vorgibt. So lassen sich Betonbauteile in Strukturen fertigen, die bisher nicht herstellbar waren. Dörflers Forschungsinteresse wiederum liegt auf Robotern, die sich auf der Baustelle für die additive Fertigung einsetzen lassen. Sie sollen flexibel von Einsatzgebiet zu Einsatzgebiet flitzen und direkt dort tätig sein, wo sie in dem Moment gebraucht werden. Sie sollen Mauern bauen, schweißen, verschiedene Bauteile zusammensetzen und additiv fertigen. Mit solchen Robotern und neuen additiven Fertigungsprozessen lassen sich in Zukunft Häuser, Brücken und Bahnhöfe schneller, flexibler und vor allem viel umweltfreundlicher und ressourcenschonender als bisher bauen. □

In 2020, a small house in Beckum, North Rhine-Westphalia made headlines, having been built in around a hundred hours of additive manufacturing. Such developments have so far been one-off prestige projects rather than everyday reality in the construction industry. Nevertheless, computer software has long since replaced the architect’s drafting table. Digitally planning buildings has now become standard practice. However, when projects move into the execution phase, the digitalization soon ends. Construction site foremen and laborers predominantly continue to rely on paper plans – and contend with the resulting difficulties. A prime example is the fact that paper-based plans cannot be updated in real time to reflect changes, which costs time and can lead to errors. Even the project to construct the house in Beckum was not without its challenges: while the 3D printer produced the walls in record time, additive manufacturing processes were not able to supply the windows, doors, ceilings and interior fixtures.

“Closing this digital gap between planning and execution, and establishing additive manufacturing on construction sites in support of a sustainable, resource-conserving construction culture – that’s our goal,” says Kathrin Dörfler. She is one of around 80 researchers at TUM and TU Braunschweig who collaborate in the DFG Collaborative Research Center Transregio 277 “Additive Manufacturing in Construction (AMC)”, which was established in 2020 for a maximum term of 12 years. “From architecture to construction engineering to robotics, every engineering discipline is involved – which makes our research particularly exciting,” enthuses Christoph Gehlen. He and Dörfler are both members of the Collaborative Research Center’s management board.

Germany's first 3D printed residential building (design: Mense-Korte ingenieure+architekten).

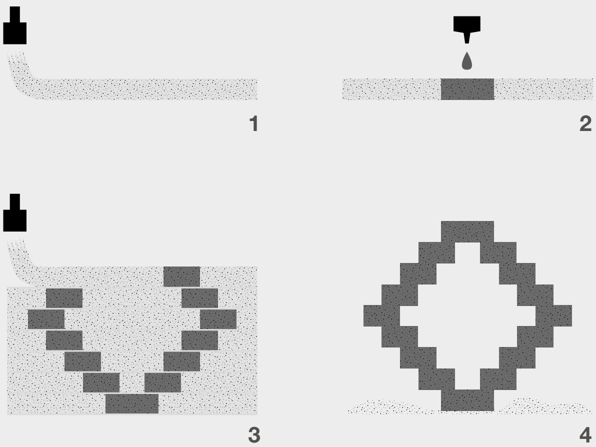
Picture credit: PERI Vertrieb Deutschland GmbH & Co.

New geometric freedom

Additively manufactured products have already become ubiquitous, from mascara brushes to airplane engine components to bone implants. These products' special attribute lies in their design and construction, having been manufactured on the basis of a digital data model and assembled layer by layer without any tools, molds or formwork. "This process opens up entirely new design possibilities and geometric freedom," says an effusive Dörfler. Components that were once impossible to produce can now be created. And that's not all: because materials are only placed where they serve a specific function, additive manufacturing reduces material consumption compared to conventional techniques and is almost entirely waste-free. Another benefit is the ability to manufacture components on site, which removes the need for environmentally damaging transport. And, as additive manufacturing replaces a large proportion of manual work processes, it is also an economical option.

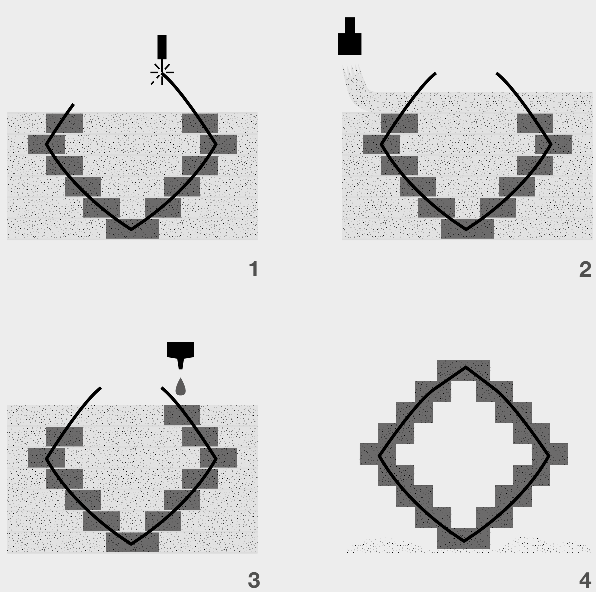
In light of this, many sectors of industry have already adopted additive manufacturing to produce delicate or complex forms. However, this is not yet the case on construction sites. There are several reasons for this. First of all, construction sites are considerably more exposed environments, making them less controllable than specialist manufacturing halls. Secondly, buildings are subject to stringent safety and quality standards, yet generally applicable regulatory frameworks have still not been developed or implemented for 3D printing techniques and materials. And thirdly, applying 3D printing in the construction industry would involve working at extreme scale. After all, additively manufacturing a building presents a significantly larger challenge than printing a toothbrush. ▷

3D printing of concrete components by means of selective paste intrusion:



1 | A layer of sand is applied **2 |** Cement paste binds these particles at precise locations **3 |** Layer by layer, the desired concrete component is formed **4 |** The particle bed is removed

3D printing of steel-reinforced objects:



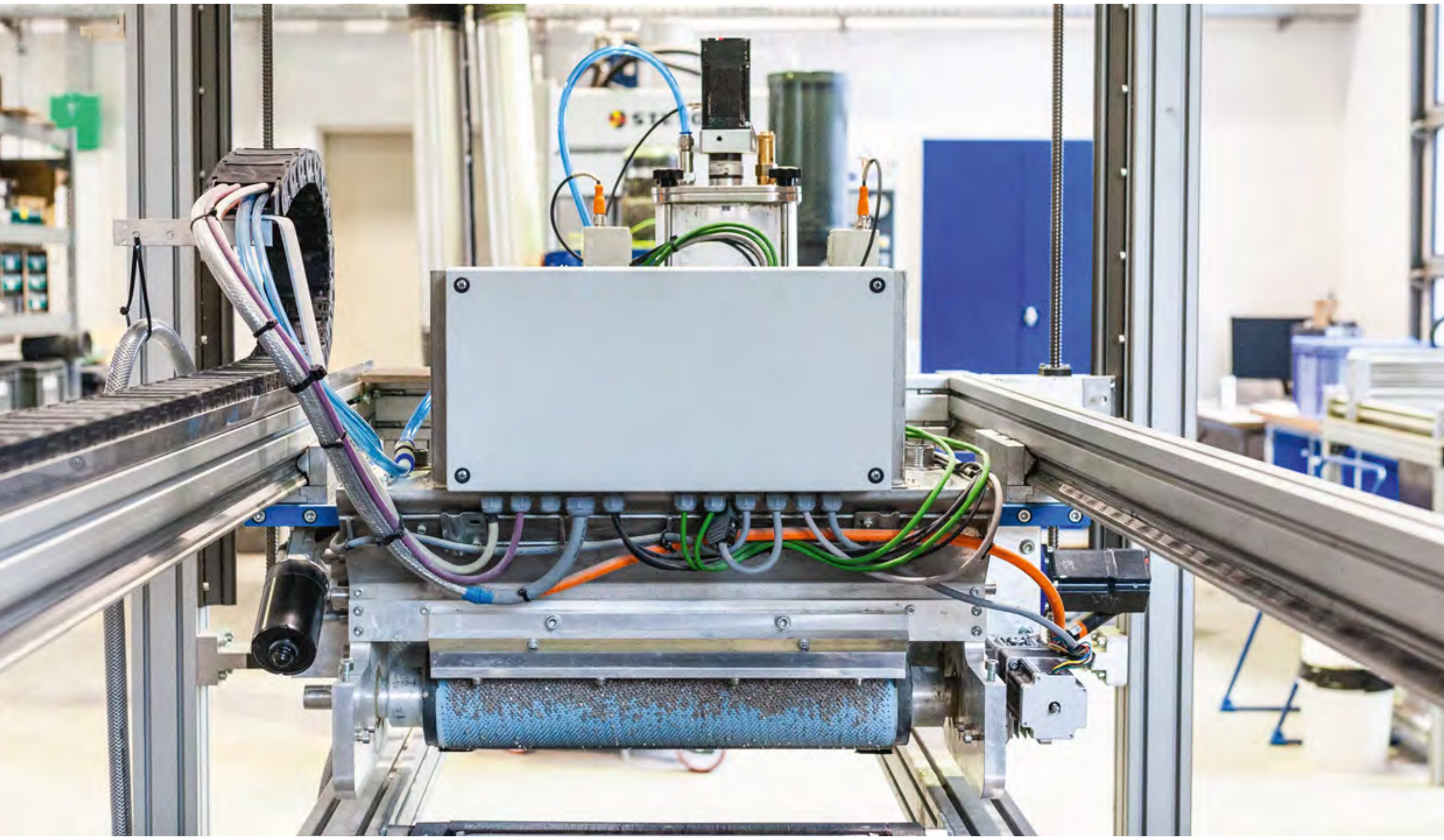
1 | Printing of the steel reinforcement **2 |** A layer of sand is applied **3 |** Cement paste binds the particles **4 |** The particle bed is removed

Produced in a particle bed

A whole array of techniques is now available to produce technically demanding components using different materials. Selective paste intrusion, which involves a selective binding of cement paste, is one of them. Gehlen and his team have developed the technique specifically for use in the construction industry.

It involves loosely applying a layer of sediment particles, such as sand, in a thin layer measuring two millimeters thick on a platform and then binding these particles with cement paste in the precise locations specified by the data model. New particle layers are applied and the process repeated over and over again. The particles gradually form the desired component, with the particle bed serving as a support structure. “This way, we can produce fine concrete components in structures that were previously not possible to manufacture,” explains Gehlen.

Together with his team, he has developed this technique to the point of market maturity, with a research project set to trial it on a larger scale in the near future. Gehlen’s team is now researching how steel-reinforced concrete components can be produced through additive manufacturing. This would involve printing concrete and steel simultaneously. The challenge lies in the very different composition of the two materials. “The process of welding steel involves heat, which is not compatible with the selective binding of sand with cement paste,” explains Gehlen. “The water in the cement paste would evaporate straight away, which would prevent the paste from hardening.” Despite this, Gehlen and his team are searching for ways to combine the two processes. ▷



Selective paste intrusion machine in Christoph Gehlen's laboratory. The blue roll applies the particle bed layer by layer. The cement paste container is located behind the gray metal plate.

Graphics: ediundsepp (source: TUM); Picture credit: Juli Eberle

Prof. Christoph Gehlen

holds the Chair of Materials Science and Testing at TUM. After studying chemistry and mineralogy in Bonn, he qualified as a civil engineer at RWTH Aachen, where he went on to obtain his doctorate. Gehlen then teamed up with two partners to found an international engineering firm in Munich. After being appointed to a chair at the University of Stuttgart, he moved to TUM in 2008. He served as Dean of Studies from 2012 to 2016 and was Dean of the TUM Department of Civil, Geo and Environmental Engineering from 2016 to 2021. He became the Founding Dean of the new TUM School of Engineering and Design (TUM SoED) in 2021.

Prof. Kathrin Dörfler

is an architect and researches computer design and robot production in this field. She has a Master's degree in Architecture from TU Vienna and a PhD in Digital Fabrication from ETH Zurich. In 2019, she became a Tenure Track Professor at the TUM School of Engineering and Design (TUM SoED), where she is establishing a Digital Fabrication research group in the Department of Architecture. In this role, she also serves as co-spokesperson of the DFG Collaborative Research Center Transregio 277 "Additive Manufacturing in Construction (AMC)".

Mobile robots on construction sites

Dörfler's research interests primarily lie in additive manufacturing processes involving mobile robots that can be deployed directly on construction sites. These robots should be able to move flexibly between different areas on the site and operate wherever they are needed at any given moment. Another benefit, of course, is the fact that robots can work around the clock.

The challenge lies in the fact that the robots would not be operating in production halls but rather on a construction site that, given its complexity, offers far less protection and controllability. Ultimately, robots have been used most successfully to date when fixed in one place and repeatedly performing the same task. By contrast, each construction site is unique. This means that robots must use sensors and control methods so that they can react to unforeseen events.

Dörfler and her team have developed two robot prototypes as research platforms. These nimble assistants can maneuver in all directions and, thanks to their sophisticated sensor systems, are capable of registering and interpreting their surroundings. However, the issue of navigation poses less of a challenge for the research team than making sure the printhead's precise guidance system, which is accurate to the millimeter, can move freely and adapt to each new application. As it stands, the robots can build and weld walls and assemble various components. The team is now working to enable the robots to produce components using additive techniques. To achieve this, the robots need to be able to travel the printing path specified by the digital data model with millimeter precision.

Another research question Dörfler addresses is how to facilitate robot-robot and human-robot collaboration. "In my team, we are researching how to build strong teams of humans and machines, making the most of their complementary strengths – the speed and precision of machines, and their ability to process vast quantities of data, combined with the human ability to work creatively, flexibly and collaboratively to solve problems," says Dörfler.

Stone by stone

In the future, such robots and new additive manufacturing processes will make it possible to build houses, bridges and train stations faster and more flexibly – and, above all, present a far more environmentally friendly alternative. However, both aspects entail high upfront costs for construction companies, with research and development work still very much needed. Dörfler and Gehlen have observed that it is above all start-ups driving technological development forward. These smaller, younger companies seem to find it easier than established companies, particularly because manufacturing, supply and delivery operations now need to be fully integrated, which requires entirely new processes. With this in mind, Dörfler and Gehlen hope to encourage experts to found start-ups. Step by step, layer by layer, the digitalization of the construction site is well underway. ■ *Gitta Rohling*

Picture credit: Juli Eberle

Material cartridge

Collaborative robotic manipulator

Sensors for precise end-effector localization

Material extrusion

User interface

Mobile robotic platform

Sensors for precise base localization

Gido Dielemans, doctoral researcher in Kathrin Dörfler's team presents a mobile robot prototype.

> *"Additive manufacturing opens up entirely new design possibilities and geometric freedom."*
>
> Kathrin Dörfler

Additive Manufacturing **In-Flight**

Link
www.mlr.in.tum.de/home

An international team of researchers have created a fleet of bee-inspired flying 3D printers for building and repairing structures in-flight. The technology could ultimately be used for manufacturing and building in difficult-to-access or dangerous locations such as tall buildings or help with post-disaster relief construction.

3D printing is gaining momentum in the construction industry. Both on-site and in the factory, static and mobile robots print materials for use in construction projects, such as steel and concrete structures. In “Nature”, an international team of researchers describes Aerial Additive Manufacturing (Aerial-AM), a new approach to 3D printing using flying robots that use collective building methods inspired by natural builders like bees and wasps. The drones work cooperatively from a single blueprint, adapting their techniques as they go. They are fully autonomous while flying but are monitored by a human controller who checks progress and intervenes if necessary, based on the information provided by the drones.

Drones must navigate very precisely

The team was led by Imperial College London and Empa, the Swiss Federal Laboratories of Materials Science and Technology. Stefan Leutenegger, Professor of Machine Learning for Robotics at TUM since 2021 and a Reader at Imperial, is one of the project’s principal investigators. “The big challenge my team and I were tackling was to make the drones navigate very precisely, which includes the use of on-board sensors – such as cameras – to accurately map and adapt to the structure they are printing,” said Leutenegger. Lead author Prof. Mirko Kovac, of Imperial’s Department of Aeronautics and Empa’s Materials and Technology Center of Robotics, said: “We’ve proved that drones can work autonomously and in tandem to construct and repair buildings, at least in the lab. Our solution is scalable and could help us to construct and repair buildings in difficult-to-reach areas in the future.”

Two types of drones

The Aerial-AM fleet consists of so-called BuilDrones, which deposit materials during flight, and quality-controlling ScanDrones that continually measure the

Picture credit: Vijay M. Pawar & Robert Stuart-Smith / University College London, Department of Computer Science, London

BuilDrones deposit materials during flight

ScanDrones measure the BuilDrones' output and inform their next steps

BuilDrones' output and inform their next manufacturing steps. To test the concept, the researchers developed four bespoke cementitious mixtures for the drones to build with. Throughout the build, the drones assessed the printed geometry in real time and adapted their behavior to ensure they met the build specifications, with manufacturing accuracy of five millimeters.

The proof-of-concept prints included a 2.05-meter-high cylinder printed in 72 layers with a polyurethane-based foam material, and a smaller cylinder (18 cm) printed with a custom-designed structural cementitious material. The technology offers future possibilities for building and repairing structures in tall or other hard-to-access locations. Prof. Kovac said: "We believe our fleet of drones could help reduce the costs and risks of construction in the future, compared to traditional manual methods."

Digital fabrication using robots at construction sites

Stefan Leutenegger will continue his robotics research at TUM. For a current project, he will join forces with Kathrin Dörfler, Professor for Digital Fabrication at TUM. Their project "Spatial AI for Cooperative Construction Robotics" will start in October. It is supported by the TUM Georg Nemetschek Institute Artificial Intelligence for the Built World. One of the goals is to teach robots to navigate and make sense of actual building sites with all their changing structures and machinery and workers constantly moving about. "We want to help robots to cooperate safely," says Stefan Leutenegger, "with one another and with humans." Future projects will combine these new approaches with additive manufacturing technologies as described in the current research paper. ■ *Paul Hellmich (TUM)*

First Neutrino Image **of an Active Galaxy**

For over ten years the IceCube Observatory in the Antarctic has been monitoring the light traces of extragalactic neutrinos. While evaluating the observatory's data, an international research team led by TUM discovered a high-energy neutrino radiation source in the active galaxy NGC 1068, also known as Messier 77.

Picture credit: NASA/ESA/A. van der Hoeven

Hubble image of the spiral galaxy Messier 77, also known as NGC 1068.

The universe is full of mysteries. One of these mysteries involves active galaxies with gigantic black holes located at their centers. “Today we still don’t know exactly what processes take place there,” says Elisa Resconi, Professor for Experimental Physics with Cosmic Particles at TUM. Now her team has made a major step towards solving this puzzle: The astrophysicists have discovered a high-energy neutrino source in the spiral galaxy NGC 1068.

It’s very difficult to investigate the active centers of galaxies using telescopes which detect visible light or gamma or X-ray radiation from space, because clouds of cosmic dust and hot plasma absorb the radiation. Only neutrinos can escape the infernos at the edges of black holes; these neutrinos have no electric charge and almost no mass. They permeate space without being deflected by electromagnetic fields or absorbed. This makes them very difficult to detect.

The greatest obstacle in neutrino astronomy has until now been the separation of the very weak signal from the strong background noise created by particle impacts from the earth’s atmosphere. It took many years of measurements using the IceCube Neutrino Observatory and new statistical methods to make it possible for Resconi and her team to accumulate enough neutrino events for their discovery.

Detective work in the eternal ice

The IceCube telescope, located in the ice of the Antarctic, has been detecting the light traces resulting from incident neutrinos since 2011. “Based on their energy and their angle of incidence we can reconstruct where they come from,” says TUM scientist Dr. Theo Glauch. “The statistical evaluation shows a highly significant cluster of neutrino impacts coming from the direction of the active galaxy NGC 1068. This means we can assume with a probability bordering on certainty that the high-energy neutrino radiation comes from this galaxy.”

The spiral galaxy, 47 million light-years away, was discovered as early as the 18th century. NGC 1068 – also known as Messier 77 – resembles our galaxy in shape and size, but has a highly luminous center which is brighter than the entire Milky Way, although the center is only approximately the size of our solar system. This center contains an “active core”: a gigantic black hole with a mass of about one hundred million times that of our sun, which is absorbing large amounts of material.

But how and where are neutrinos generated there? “We have a clear scenario,” says Resconi. “We think the high-energy neutrinos are the result of extreme acceleration which the matter in the vicinity of the black hole undergoes, raising it to very high energies. We know from particle accelerator experiments that high-energy protons generate neutrinos when they collide with other particles. In other words: We’ve found a cosmic accelerator.”

Neutrino observatories for new astronomy

NGC 1068 is the statistically most significant source of high-energy neutrinos to be discovered as yet. More data will be necessary in order to be able to localize and investigate weaker and more distant neutrino sources, says Resconi, who recently launched an international initiative for the construction of a neutrino telescope several cubic kilometers in size in the northeast Pacific, the Pacific Ocean Neutrino Experiment, P-ONE. Together with the planned second-generation IceCube observatory – IceCube Gen2 – it will provide the data for the neutrino astronomy of the future. ■ *Monika Weiner*

Links
www.ph.nat.tum.de/cosmic-particles www.icecube.wisc.edu Video about NGC 1068 galaxy and IceCube neutrinos: youtu.be/uV0eumyRlww

Links
www.6g-future-lab.de/ www.ce.cit.tum.de/en/lkn/

Visions of **Next-Generation** Communication

Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-29

Visionäre Pläne für das Netz der Zukunft

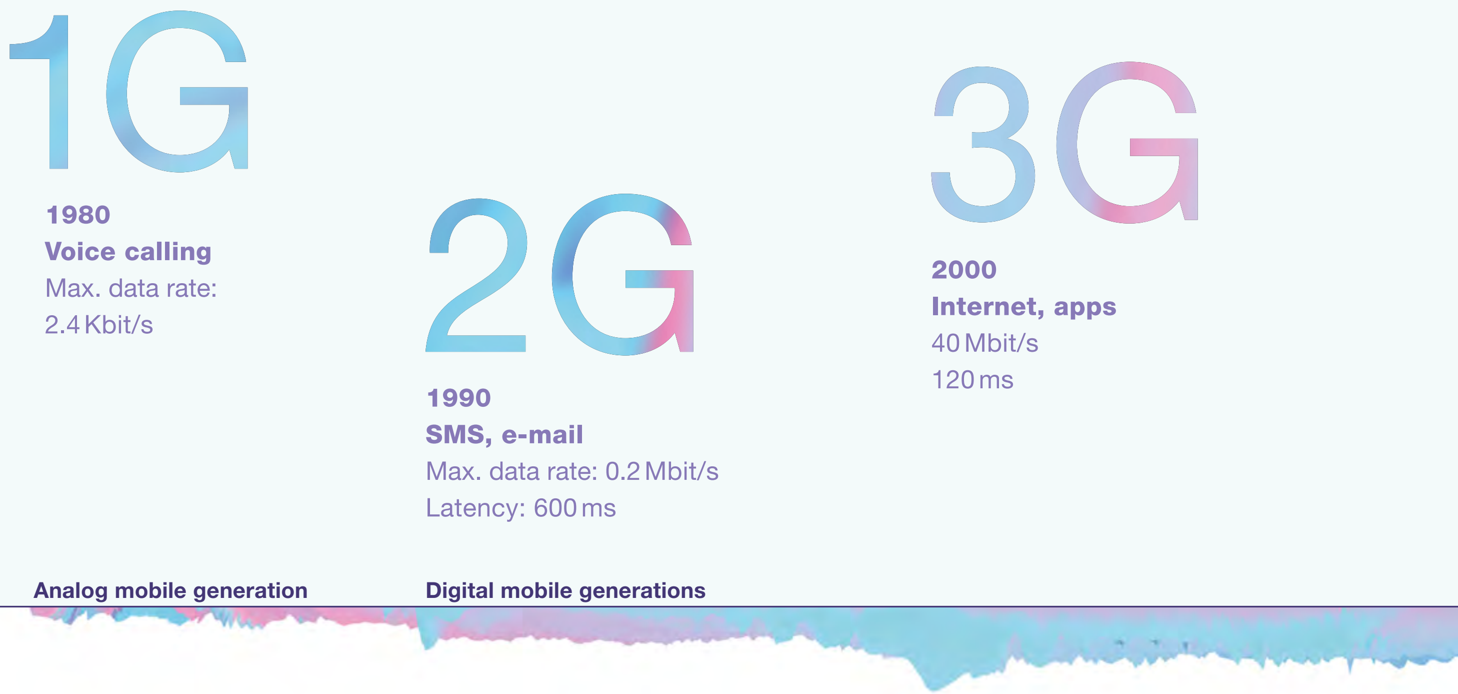
D

Im 6G Zukunftslabor Bayern arbeiten zwölf Lehrstühle der TUM zusammen, um schon heute die Voraussetzungen und Möglichkeiten der nächsten Mobilfunkgeneration zu erforschen und zu definieren. Projektleiter Prof. Wolfgang Kellerer, Inhaber des Lehrstuhls für Kommunikationsnetze: „Die aktuelle Generation 5G spielt eine entscheidende Rolle für die Industrie 4.0. Sie ermöglicht eine neue Dimension der Kommunikation von Maschinen untereinander. Bei 6G sollen hingegen der Mensch und seine Umgebung im Mittelpunkt stehen."

Er und seine international renommierten Kolleginnen und Kollegen entwickeln in dem dreijährigen Projekt, das vom Bayerischen Wirtschaftsministerium mit 4 Millionen Euro gefördert wird, Ideen, Vorschläge und wissenschaftliche Grundlagen, die später in die konkrete Entwicklung einfließen sollen. □

Graphics: ediundsepp

The 6G Future Lab Bavaria brings together 12 TUM Chairs in an effort to research and define the requirements and possibilities of the next generation of mobile communications. Wolfgang Kellerer, holder of the Chair of Communication Networks at TUM, is the project coordinator. He and his internationally renowned colleagues are developing strategies and scenarios that might seem more suited to the world of science fiction. In the decades ahead, however, they could well become reality.



As the great German philosopher Ernst Bloch once remarked: “Visions need roadmaps.” Evidently, the Bavarian State Ministry of Economic Affairs has embraced this notion, as it is driving forward a 6G initiative seeking to promote the mobile communications technologies of the future. One of the most important building blocks is the 6G Future Lab Bavaria at TUM, which has been awarded €4 million of funding over a three-year term. It features a team comprising 13 professors from 12 TUM Chairs, who have been tasked with developing ideas, proposals and scientific foundations for subsequent incorporation into practical development. “It is vital that the world of science knows what future users will require of the 6G network,” says Wolfgang Kellerer, the team’s project coordinator. “Only then will we be able to formulate the decisive research questions to help ensure that the next generation of mobile communications is an outstanding success.”

It all started in 1992

Nowadays, it is difficult to imagine what our lives would be like without mobile communications. Back in 1992, when the first cell phones hit the market, some were wary of this new technology. Then, in 2000, frequencies were sold off to interested suppliers in huge auctions, and the D1 and D2 networks offered by telecoms giants soon made it possible to make mobile telephone calls from virtually anywhere.

When the third generation – called UMTS – hit the market in 2004, significantly higher data transfer rates became possible. People became accustomed to using their cell phones not only to make calls but also for a range of other services. The fourth generation, now known as 4G, represented a significant step forward, offering further frequencies that made it possible to play online games and stream films wirelessly for the first time. This was all part of a continuous development process, which is why 4G was initially also known by the acronym LTE (Long Term Evolution). Since then, the demands of networks have continued to rise – but so too have the possibilities. The fifth generation, 5G, brought about a truly disruptive

4G

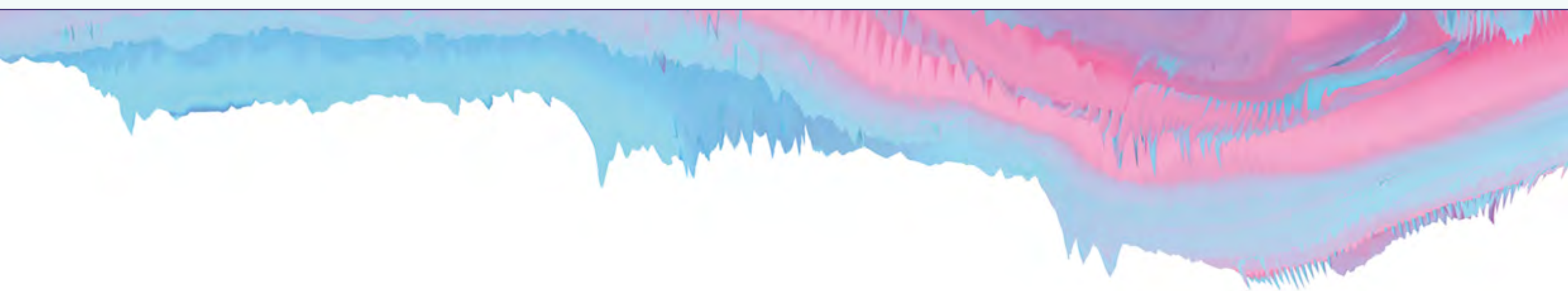
2010
Internet of Applications
1,000 Mbit/s
45 ms

5G

2020
Internet of Things, artificial intelligence
10,000 Mbit/s
≈1 ms

6G

2030
High-precision remote handling, automated vehicles, man-robot collaboration
1,000 Gbit/s
0.1 ms



Graphics: ediundsepp (source: TUM)

increase in technical options, and has spread considerably since its introduction in 2019. It is primarily focused on the requirements of industrial applications. These include the ability to transfer extremely high data rates with mobile broadband connections. This is fueling the rise of the Internet of Things, which involves wireless communication between robots and machinery as well as everyday devices and appliances. Thanks to this generation's high reliability and short transfer times, it is also laying the foundations for autonomous driving. Technical innovations based on this generation have primarily stemmed from Asian firms, with Germany often forced to play catch-up.

The 5G mobile communications standard has made it possible to increase the speed of wireless data transfer to up to 10 gigabits per second. This performance, however, is far from the end of the story.

Munich: An ideal location

This time, Bavaria wants to get it right. After delaying for too long in the development of 5G, researchers hope to set new benchmarks this time, including in research. "It was the other way around with 5G. There were major industrial consortia, and we were part of them, but this time we're setting the direction of the journey," as Kellerer enthuses. Work is already underway; the time required to introduce a new mobile communications standard is usually around ten years, meaning that 6G is expected to arrive around 2030.

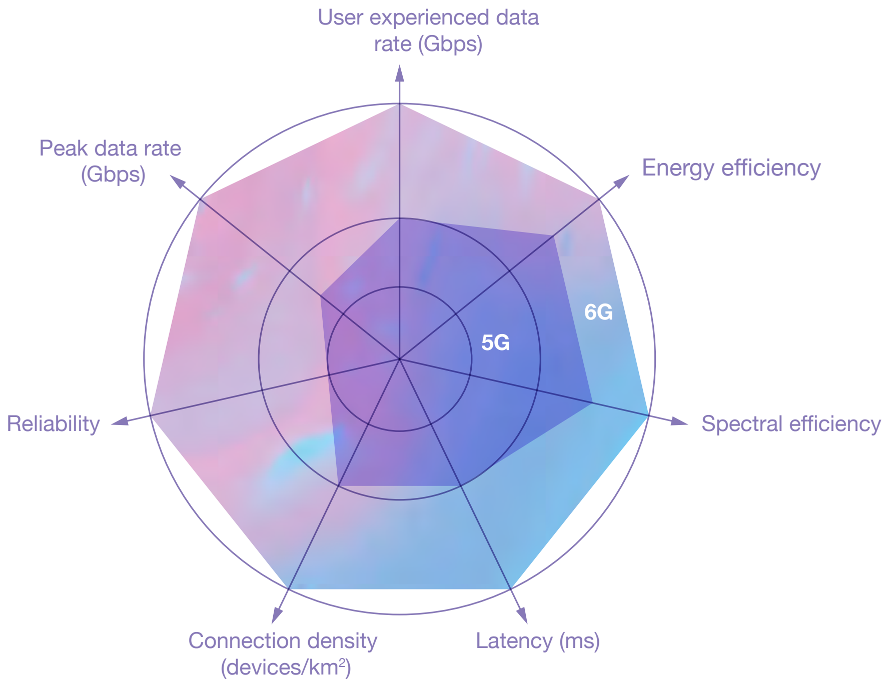
Munich provides near-ideal conditions for this work: leading IT firms such as Nokia, Google and Apple have major research and development centers in and around the city, while TUM also holds particular expertise. Consequently, numerous initiatives have been established in the Bavarian capital. These include, as part of the Bavarian 6G Initiative, Thinknet 6G – which aims to facilitate contact between research and industry players – and the 6G Future Lab Bavaria at TUM. In parallel with this, TUM has teamed up with TU Dresden to secure total funding of €70 million over four years for the 6G-life project.

“It is vital that the world of science knows what future users will require of the 6G network.”

Wolfgang Kellerer

Prof. Wolfgang Kellerer

His life has been dedicated to networks in every meaning of the word: Kellerer joined the TUM Chair of Communication Networks in 2012 but is also renowned as an exceptionally gifted networker. He is a member of numerous scientific organizations and also serves as a consultant for the European Commission and various other research programs. He began to learn his trade at TUM in the 1990s before taking up a guest researcher position at Stanford University after receiving his doctorate. In 2002, Kellerer joined the Japanese company DOCOMO Communications Laboratories Europe GmbH, the Munich-based European research institute of NTT DOCOMO. Wolfgang Kellerer holds more than 40 patents and patent applications in the field.



The evolution from 5G to 6G is not just about achieving higher data rates. For precise robotics control, for instance, latency is an essential parameter.

From the very outset, Wolfgang Kellerer has been determined to seize the initiative this time around. His vision impressed the Bavarian State Ministry of Economic Affairs and inspired his colleagues at TUM. Perhaps Kellerer was predestined to pursue a career intrinsically linked with the development of mobile communications networks, as key dates in his life run just about parallel with the emergence of new mobile communications generations. He turned 50 just as 5G hit the market, and will turn 60 around the time 6G is likely to launch.

Putting people front and center

While the primary focus of 5G is to facilitate communication between machines, 6G aims to switch the focus and put people front and center. This approach has three key aims:

- The transfer speed must be increased. Researchers are striving to transfer data wirelessly at speeds of up to 400 gigabits per second. This will require higher frequencies in the terahertz range. However, such high transfer rates are crucial for users to be able to immerse themselves in virtual reality environments in real time, such as for medical applications, disaster response operations, or for recreation and gaming.
- Communication reliability and precision must be increased to 99.999999999%. This is vital for applications in which humans interact with robots, such as remote-controlled operations, the use of robots in nursing care, and autonomous driving. In order to achieve this, all available means of communication must be intelligently combined, from satellites to optical fiber to mobile networks.
- Security must be further enhanced. This will involve the use of new, absolutely secure encryption methods, such as quantum cryptography.

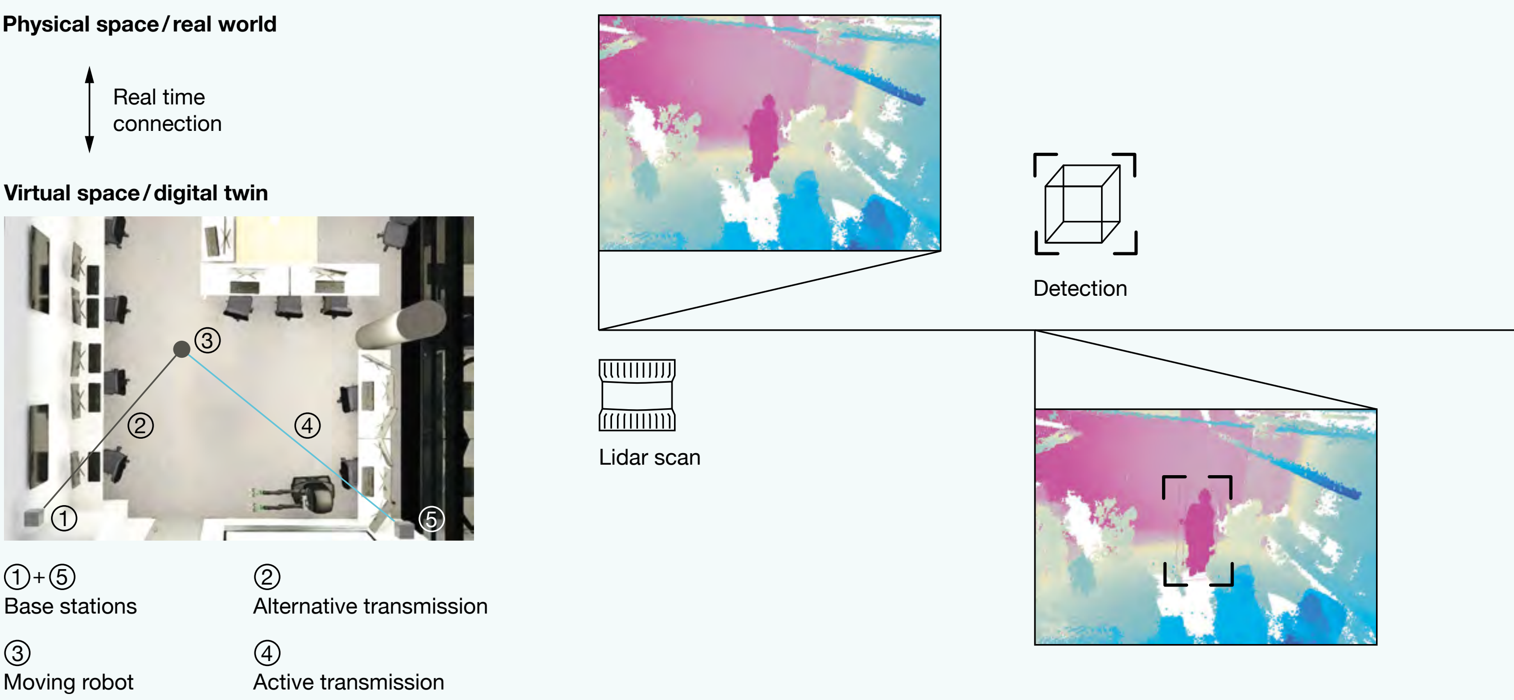
Digital twins

The researchers have set themselves some ambitious goals. Yet, since its inception in May 2021, the project has already produced initial results. These include, for example, the development of a “digital twin”, which aims to reproduce a communication device’s surroundings in real time in a virtual environment. The goal behind this is to improve the reliability of communication.
So, how does it work? As noted earlier, achieving higher transfer rates in 6G will require the use of higher frequencies. Yet, the higher the frequency, the more difficult it is for waves to penetrate barriers such as walls, doors or people. This means that, ideally, there would always be a clear line of sight to the base station. ▷

Picture credit: A. Heddergott; Graphics: ediundsepp (source: TUM)

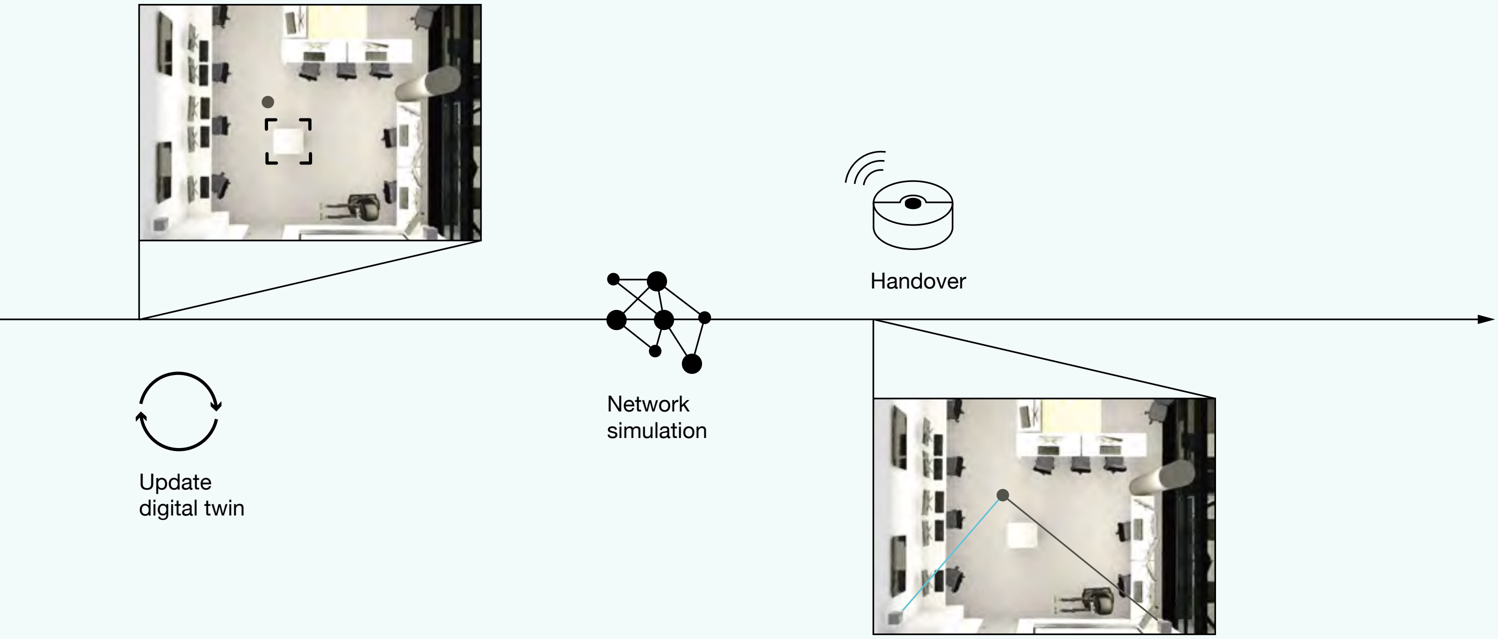
△ **The researchers use this robot** to develop and test precise controls and man-machine collaboration.

△ **The three main aims of 6G development** focus on the communication between man and machine.



▽ **Researchers demonstrate in their lab how digital twins make communication more robust.** The lab's digital twin is updated in real time through continuous LiDAR scans. Any objects or movements detected by the LiDAR are replicated in digital space. The network simulation analyzes how the change affects the transmission paths and commands the handover to the other base station if necessary.

Picture credit: A. Heddergott; Graphics: ediundsepp (source: TUM)



Further participants, not shown in the picture:

Prof. Gerhard Kramer
Chair of Communications Engineering

Prof. Holger Boche
Chair of Theoretical Information Technology

Prof. Wolfgang Utschick
Professorship of Signal Processing Methods

Prof. Georg Carle
Chair of Network Architectures and Services

Picture credit: A. Heddergott

Participants in the 6G Future Lab

Prof. Klaus Diepold
Chair of Data Processing

PD Carmen Mas Machuca
Chair of Communication Networks

Prof. Georg Sigl
Chair of Security in Information Technology

Prof. Jörg Ott
Chair of Connected Mobility

To ensure that the connection between the base station and the device (a cell phone, for example) does not drop completely if an obstacle blocks the way, the communication must immediately be transferred to another base station. Today, this type of handover occurs whenever a cell phone detects that its network signal is too weak. This requires constant monitoring of signal strength.

The team under Prof. Wolfgang Kellerer and Prof. Eckehard Steinbach believes it would be simpler if the cell phone always knew what its environment looked like and the location of potential obstacles. This applies in particular to indoor settings such as factories, storage facilities and other similar premises. In such cases, the cell phone could switch to another base station, thereby reducing outage time. Enabling this requires sensors like cameras or LiDAR, which sweep the room and generate an electronic image of it – a digital twin. Then, using image processing and artificial intelligence, a computer can identify obstacles and provide appropriate commands in real time.

This has already yielded success in a prototype model, with the handover rate cut by 45% and outage time down 10%. The next step will be to generate the digital twin faster and with greater precision, and to incorporate moving objects into these scenarios.

A dedicated TUM network

At present, the primary focus is defining and developing new, refined algorithms that can make the 6G network a success. However, the hardware involved is also subject to new requirements. Using higher frequencies requires smaller radio cells, which in turn means more – albeit smaller – antennae. Sensors will also be needed to constantly monitor and connect all signals, and the interfaces between systems must also be coordinated. Last but not least, these technologies will need batteries capable of operating for decades and drawing energy from their surroundings, such as by using temperature differences, light or the communication network itself.

In principle, the 6G Future Lab has not been set up for the purpose of hardware development. Nevertheless, Wolfgang Kellerer has plans for a dedicated network on the TUM main campus. “We don’t want to become a mobile service provider,” he says. “But we want to be able to precisely measure and test all the components, their effects and how they interact.” ■ *Brigitte Röthlein*

On the Road to the **Super-Battery**

Link
www.frm2.tum.de

A research team led by TUM has taken an in-depth look at the internal workings of batteries during charging and discharging. Their findings may help optimize charging processes.

When an electric car is being charged, the charge indicator moves quickly at first, but then much more slowly at the end. “It’s like putting things into a closet: In the beginning it’s easy, but finding available space gets more difficult as the closet fills up,” says Dr. Anatoliy Senyshyn from TUM’s Research Neutron Source Heinz Maier-Leibnitz (FRM II).

The internal structure of a battery both before and after the charging process is already known. Led by the Heinz Maier-Leibnitz Zentrum (MLZ) at TUM, a research team has now observed for the first time a battery’s lithium distribution during the entire charging and discharging process with the materials science diffractometer STRESS-SPEC. They then verified the measurements using the high-resolution powder diffractometer SPODI.

Distribution of lithium ions is crucial

Lithium ions move from the cathode to the anode during charging, and in the reverse direction when discharging. In their investigations, the researchers ascertained that the distribution of the lithium constantly changes during charging and discharging. “When the lithium is unevenly distributed, the exchange of lithium between the anode and the cathode doesn’t work at a hundred percent in the parts of the battery where too much or too little lithium is present. However, an even distribution of lithium increases performance,” says Senyshyn.

More exact, smaller, better

The researchers succeeded in capturing the uneven distribution of lithium in a battery with high-resolution images: In order to obtain a view of the entire battery, they investigated one small partial volume after another and put these individual images together to form an overall picture.

With the help of the Helmholtz Association’s DESY (“Deutsches Elektronen-Synchrotron”) and the European Synchrotron Radiation Facility ESRF, it was possible to select partial volumes with dimensions on the order of micrometers. As a result, the researchers discovered that the lithium is distributed unevenly not only along the electrode layers, but also perpendicular to the layers.

Rapid charging vs. range

The effects observed may help in long-term development of rechargeable batteries, for example for electric cars, says Senyshyn: “The distribution of the lithium can influence many battery properties. Once we have these better under control, we’ll be able to significantly improve the performance of batteries in the future.”

■ *Elene Mamaladze (TUM)*

Picture credit: Andreas Heddergott

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Masthead

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Note on photos
Some of the photos printed in this issue were taken during the Covid-19 pandemic. During all photo shoots the protection and hygiene rules in force at the time were observed.

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