

# Faszination Forschung

**TUM Research Highlights**  
Technical University of Munich  
The Science Magazine  
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## Nutrition and Health

**Dietary fiber** – Why it's essential for staying healthy  
**Microbiome** – The ecosystem in our gut  
**Innovative genetics** – How AI is revolutionizing plant breeding

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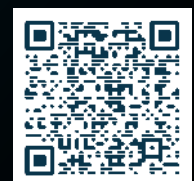
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*Dear TUM friends and associates,*

**The global population is rising at breakneck speed by the size of Erlangen every day, Munich every week and New York every month. At the same time, natural resources are becoming scarcer, we are threatened by the repercussions of climate change and diet-related diseases are on the rise. Consequently, science, business, politics and society are facing pivotal questions that will determine mankind's survival: How can we secure the sustainable production of sufficient quantities of food? And how can we produce food that is tasty and allows people to eat healthily?**

As an active researcher, I have spent the last 25 years studying key molecular questions regarding food quality. In my position as the new President of Technische Universität München, I feel myself all the more committed to the moral obligation to harness research, innovation, education and further training to make strong contributions to identifying relevant solutions. This requires interdisciplinary research approaches along the entire Agriculture > Food > Nutrition chain. Equally, we need a completely new system awareness covering the complex network of effects of biologically relevant substances – from raw materials to the sustainable production of customized food, to its physiological effects and wider questions of lifestyle.

No other university in Germany is as expertly structured as TUM, marshaling the strengths of the TUM School of Life Sciences at the Weihenstephan campus, the TUM Straubing campus for Biotechnology and Sustainability, the engineering sciences including Computer Science at the Garching campus, as well as the strong Medical and Health Sciences in Munich. These strengths are complemented by the technically oriented social, political and business sciences with an interdisciplinary approach.

Based on a selection of focus topics, this issue of Faszination Forschung covers a wide range of topics: From active taste molecules which determine our predilections for certain dishes to the complex metabolic processes in the human body and in coupled ecosystems, including plant and animal breeding, to the technical systems behind sustainable food production.

Professors Hans Hauner, Dirk Haller and Martin Klingenspor are studying the genetic and molecular foundations of met-



abolic processes and their repercussions on diseases such as diabetes, Crohn's disease and obesity. Prof. Michael Schemann is conducting research into the nervous system of the intestines and their malfunctions, which can cause irritable bowel syndrome in humans.

Professors Chris-Carolin Schön, Kurt Hülsbergen and Dr. Franz Xaver Maidl are harnessing innovative approaches to breeding sustainable, future-viable crops. Dr. Mario Jekle is studying the thousands of years old food that is bread. He is drawing on 3D printers to analyze how to bake bread with crispy crusts on the outside and soft and fluffy crumb on the inside. "Vertical farming" is a decidedly innovative approach to plant cultivation. Prof. Ferdinand Ludwig and Dr. Mariana Yordanova are developing multifunctional building facades for this purpose.

Water efficiency and energy efficiency are important ecological and economic factors. Using the example of the brewing process, Dr. Karl Glas has designed a microbial fuel cell that treats wastewater while simultaneously generating electricity. Water is also the subject of the company founders working with TUM graduate Fabian Schlang. They have developed a drinking bottle which imbues water with flavor purely by means of aromas, as a healthy alternative to the usual soft drinks.

I hope you enjoy reading this issue of Faszination Forschung.  
Yours,

Thomas F. Hofmann  
President



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that makes  
you slim?



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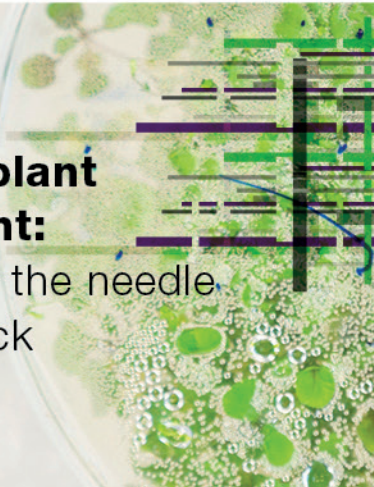
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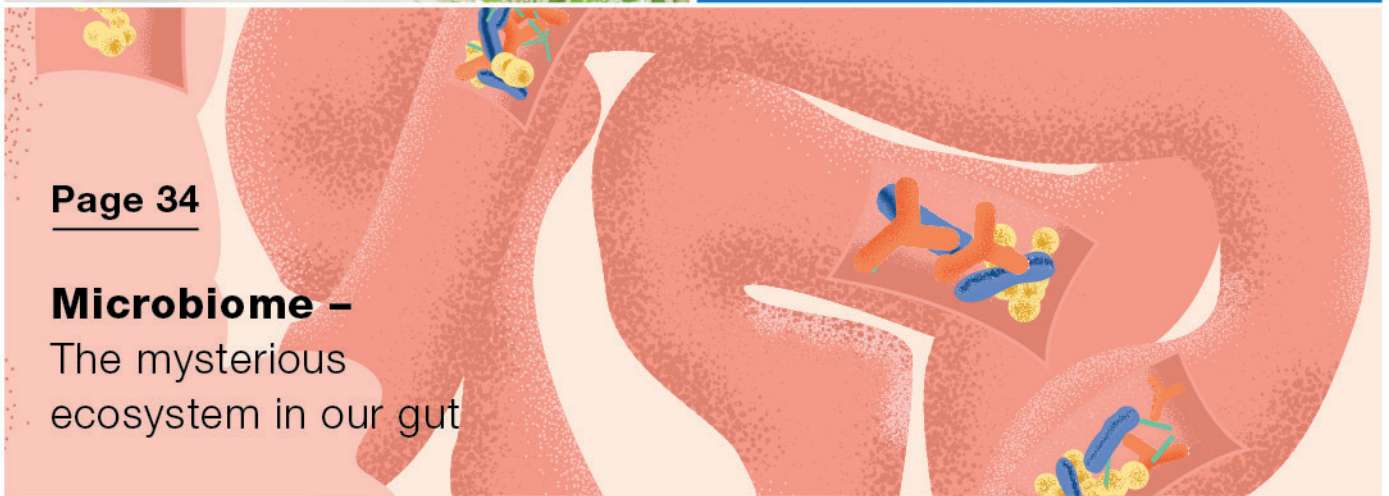
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German edition available as a PDF here:

[www.tum.de/faszination-forschung](http://www.tum.de/faszination-forschung)

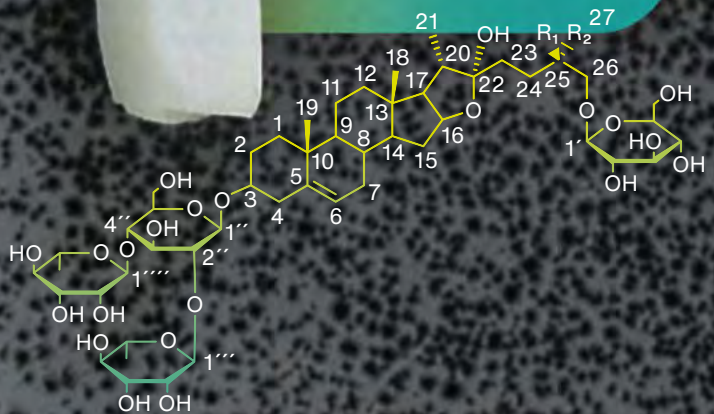
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[www.molekulare-sensorik.de](http://www.molekulare-sensorik.de)

Bitter   
Astringent   
Buttery mouth coating 

**Asparagus contains around 80,000 chemical constituents**, six of them bitter. Prof. Corinna Dawid has tracked them down and identified their chemical structure (example below). Other constituents cause an astringent or – especially at the tips – buttery mouth coating effect reminiscent of melting butter on the tongue.



Picture credit, Graphics: edlundsepp (source: TUM)

# The kaleidoscope of good taste

Some foods contain several dozen chemical substances which determine their taste. Separating them from each other and identifying them is a Sisyphean task to which the team working with food chemist Prof. Corinna Dawid has dedicated itself. The researchers work with a mixture of measuring equipment and human tongues.



**At the end of the day, human perception is what counts.** Trained testers such as doctoral student Sabrina Schalk taste watery solutions of the flavors in different concentrations (see the prepared test tubes, top right). In this way, they can find out the level of dilution at which a bitter substance can be tasted.

**T**he clamp on my nose pinches a bit and makes my voice sound like Donald Duck. “That’s the way it has to be,” says Christoph Hald apologetically, “because we want to eliminate any olfactory stimuli when we’re doing a taste test.” The scene of the action is a sensory booth at the Chair of Molecular Sensory Science in the Weihenstephan Science Center. In front of me, there are two rows of eight tubes each. They are filled with water and all look the same but they contain different concentrations of a bitter substance. “We taste them one after the other, from right to left, from low to high concentrations. Use a pipette to suck up a milliliter, let it roll over the tongue but don’t swallow it and then spit it out!” explains the young scientist who is taking his doctorate at the Institute.

Not so easy but after a few tries, you soon get the hang of it. My job is to compare two liquids in each case. One

contains the bitter substance while the other doesn’t. Only the trial leader knows which is which. The first three dilutions all taste the same, of nothing at all in fact. But from the fourth dilution onwards, one of the two liquids tastes distinctly bitter. This identifies the threshold at which the taste receptors can still just perceive the dissolved bitter substance.

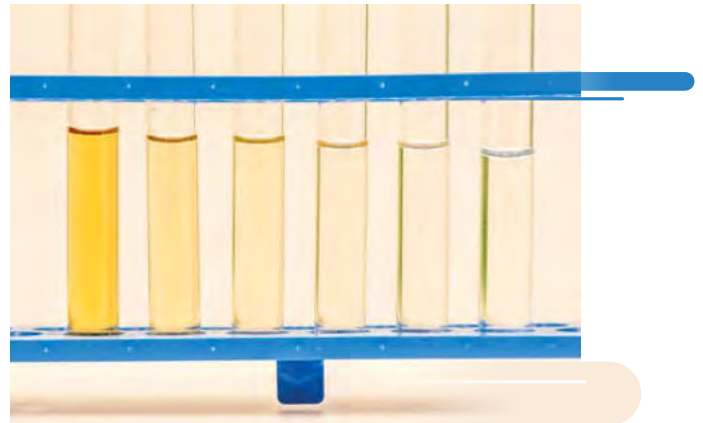
What Christoph Hald has just taught me is run-of-the-mill for him – as it is for his roughly 40 colleagues who are researching the taste of food and beverages as (visiting) academics or doctoral students at the Chair for Food Chemistry and Molecular Sensors. This exercise is an integral part of a clever research concept by the name of sensomics. Developed by food chemists in Munich, it is applied today by researchers and food manufacturers across the globe. What’s special about it is that it combines precise analyses



by high-resolution measuring equipment with the taste perception of human testers. This allows us to take the umpteen thousand substances in red wine, coffee, bread or cheese and identify the precise ones that make up the particular taste of these foodstuffs and beverages. Or to track down disruptive taste notes that make otherwise high-quality dishes inedible.

### **Bitterness is a warning signal**

“If something tastes too bitter, we’re alarmed and prefer not to eat it. Because our body has learned since primeval times that bitter plants are often poisonous. After all, this is how the plant defends itself against enemies wanting to eat it and it can be harmful to us too,” says Corinna Dawid who is a former doctoral student and today the acting successor to Prof. Thomas Hofmann at the Chair for Food Chemistry and Molecular Sensors. Exceptions prove the rule, as the scientist notes: “Not every bitter substance in a plant is poisonous in the concentrations which we absorb, and we appreciate beverages such as coffee and beer or fruit and vegetables such as grapefruit and radicchio precisely because of their bitter note.” In many products, however, a bitter aftertaste is unacceptable – e.g. in pastries, vegetable spreads and synthetic sausages or even in milk



substitutes. These and many more foodstuffs could be enhanced with valuable vegetable proteins of pulses, potatoes or corn – if it wasn’t for this intrusive bitter taste. For example, large volumes of nutritious vegetable proteins occur today as “byproducts”, i.e. as residual products from certain manufacturing processes, which cannot be used for human consumption. Instead they are added to animal feed in low concentrations or serve to produce biogas. ▶

**The lighting in the test booths** is set in such a way that the tester cannot draw any conclusions as to the taste of the solution from its color.





Six times more agricultural land is required to produce animal protein than for vegetable protein.

6x

### The struggle against bitterness

Take the example of rape: In order to extract the coveted cooking oil from the pulses, the ripe seeds are pressed. What's left is the rape cake, which is 30 to 40 percent protein. "Rape protein in combination with other vegetable proteins has an ideal amino acid composition for human nutrition. What's more, its production is sustainable and does not require any additional agricultural land as the plant is cultivated in any case for oil production. For that reason, we should definitely use this source of protein," Corinna Dawid states with conviction. And the fact is that around the world today, six times more land is used for grazing and cultivating animal feed than for producing wheat, fruit and vegetables. Mass livestock husbandry

heightens the struggle for the limited arable land on our planet and their flatulence contributes towards a further rise in gases harmful to the climate. Against this backdrop, it seems to be a matter of urgency to develop more vegetable sources of protein for human consumption.

Byproducts of corn and potato processing such as husks and peelings could also serve as a source of valuable fiber in future. However, this poses the same problem as with rape: the purified oat, wheat and potato fiber contains bitter substances which turn out to spoil the taste. "Thanks to our sensomics concept, we have now found out what those substances are. In contrast to rape protein, here we are dealing with a whole bouquet of different bitter substances. We are now searching for ways of removing them to make the fiber edible," Corinna Dawid explains. If we're successful, these new vegetable fibers might one day be used in pizzas and burgers and make them healthier to eat (see also the article on page 20).



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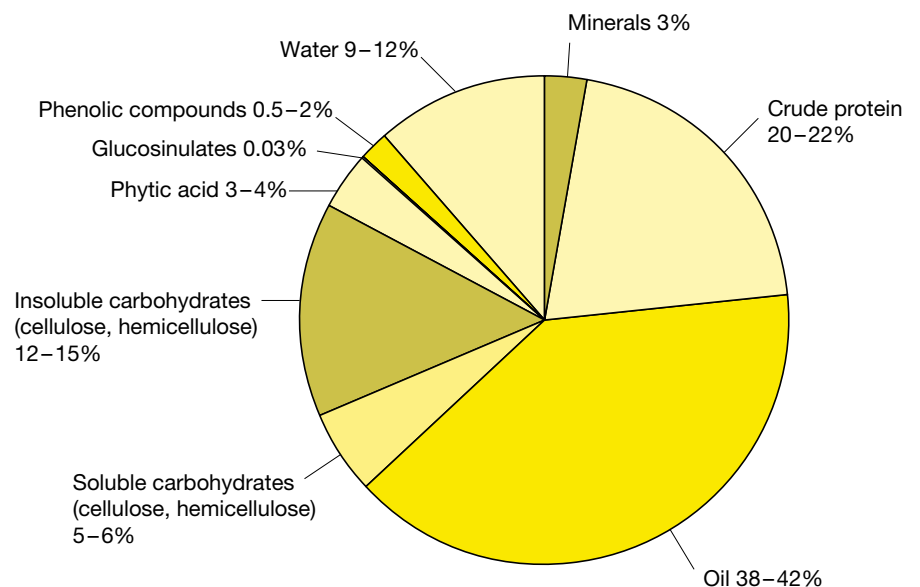
### The sensomics concept

Byproducts such as rape, pea or potato protein might play a significant role in this process. To remove or mask their bitter taste, you first have to know which substances are causing it. Christoph Hald has found the main bitter substance in rape – with a lot of hard work and a decent slice of luck. Because as it turned out, it comes from a single substance by the name of kaempferol 3-O-(2''-O-sinapoyl-β-sophoroside). The doctoral student discovered and identified the compound with the aid of the sensomics concept. He explains the basic principle as follows. “Firstly, the rape protein is cleaned and split into several fragments by means of various solvents – i.e. sub-groups depending on their solubility. Then the solvents are removed, replaced with water and trained testers taste the product in the sensory booth. This way we can identify the groups containing the bitter substances. Then we subject them to further analysis.” Using ever more sensitive methods, the bitter-tasting fragments are further sub-divided, cleaned and tasted again until finally only those extracts remain that contain the substances we are looking for. “In my case, there was only one fragment left at the end. That was pure chance, as in other food, the bitter taste is caused by a variety of ingredients.” ▶

### Of smelling and tasting

Smell and taste contribute equally to the enjoyment of food and drink. The aromas reach our nose and the non-volatile components stimulate the various receptors in our mouth. The first bite or swallow can release further odors which pass over the palate, thus rounding off the overall impression. A few compounds in the right ratios are usually enough to create an unmistakable odor. We recognize butter by just three aromas, while pineapple or strawberry juice require nine and ten, respectively, and beer up to 20 compounds. More complex blends go to make up the aromas of drinks and spirits. Beer contains 17–20 active odorous substances, orange juice and grapefruit juice 22 and 24, respectively. Coffee, red wine and bourbon give off more complex odors with 24 to 27 aromas. The undisputed champions are cognac and brandies, with characteristic bouquets consisting of 36 different components.

**One fifth of freshly harvested rape seed** consists of high-quality protein. After the oil has been pressed out, the protein percentage in the dried rape cake can be up to 40 percent.



## Teamwork between man and machine: The sensomics concept

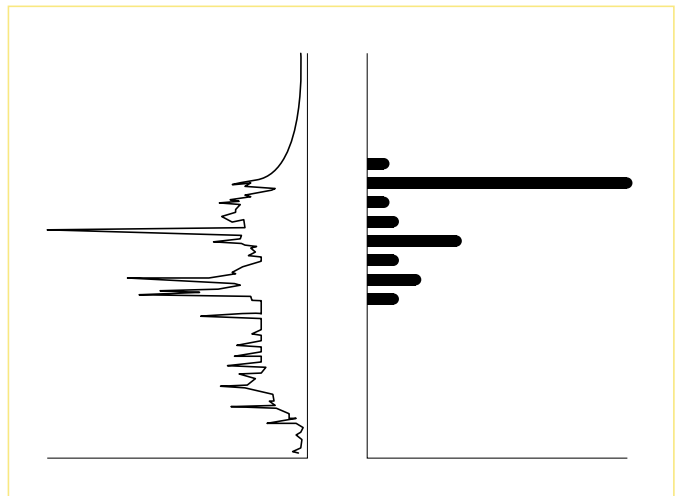
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### Activity-driven fragmentation

A food sample is divided into numerous fragments by means of various solvents. Every fragment undergoes further treatment by high-resolution analytical equipment until all the constituent parts have been separated. Every peak in the curve on the right denotes an individual substance.

At the same time, every fragment is tasted by trained testers in order to track down the constituent parts contributing to the taste. The higher the bar, the more powerful the flavor (bars on the right). Of the umpteen thousand compounds in a foodstuff, typically only a few of them will be of significance for the taste.

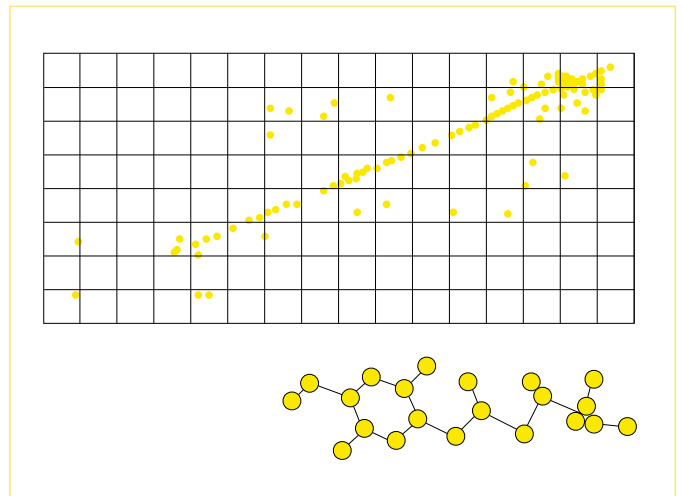


# 2



## Identifying the structure

The challenge now is to identify all the individual compounds tasted by human testers. To do so, the atomic weights are determined in a mass spectrometer (left) and their spatial arrangement defined in the magnetic resonance spectrometer (below).



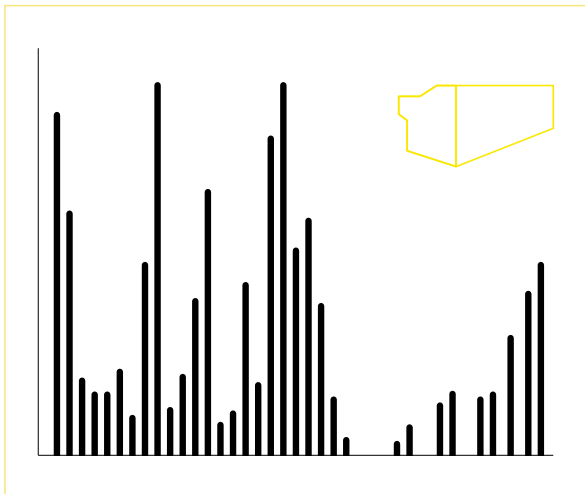
# 3.



Christoph Hald beside a series of appliances which evaporate the solvent from the flavors. It is then replaced by water.

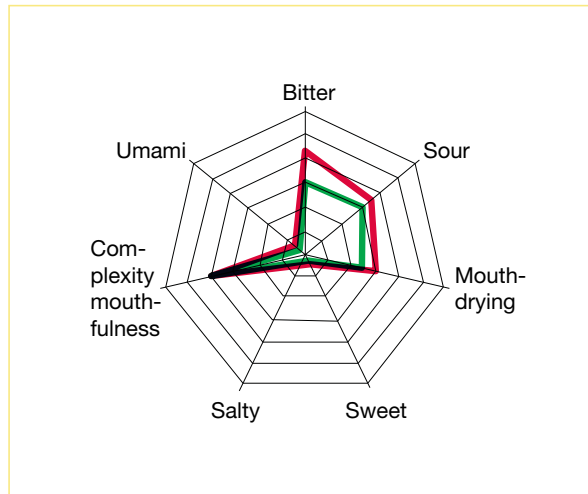
### Quantitative analytics

When all the active taste components have been identified, their natural concentrations and ratios in the food must be determined. This quantification is usually conducted mechanically and demands extremely precise work.



### Recombination experiments

Finally, all the active taste components are combined in their naturally occurring ratios. This recombined product should now exhibit exactly the same taste properties as the genuine food. If the testers are unable to tell the difference between the recombined product and the original, we have pulled it off. But if they can, the search is on for any missing substances or a slightly different composition in the next round.



A test is repeated if the results are too different



Successful recombinant

**Measurement devices such as mass spectrometers and high-performance liquid chromatographs are available for quantitative analyses to employees at the Chair of Food Chemistry and Molecular Sensory Science.**



The principle behind the sensomics concept sounds simple. But applying it requires a huge amount of time and effort in terms of measurement technology. The equipment available in the laboratories for the Chair is suitably impressive, spread over three floors. Various chromatography systems can split minute quantities of a food sample into its constituent parts fully automatically. High resolution mass spectrometers give information on the molecular weights of unknown compounds. In order to reveal the exact structure of substances, there are three nuclear magnetic resonance spectrometers available at the Center for Food Chemistry, operating at 400, 500 and 600 MHz. “These are true high-

end appliances,” Corinna Dawid enthuses. According to the acting head of the Chair, this measurement equipment can even be used to investigate scientific questions beyond taste. “We are interested in metabolism and we want to know what happens to food in our body. How much of it arrives in the liver, how much is secreted in urine? Or we work with biologists to measure phytohormones and other vegetable substances. For example, we’re keen to find out what valuable food ingredients are created through abiotic and biotic stress or to what extent their concentration is affected. The applications are almost limitless.” ▶

*“The production of rape protein doesn’t require any additional agricultural land.”*

Corinna Dawid

### How can the bitter taste be removed from rape protein?



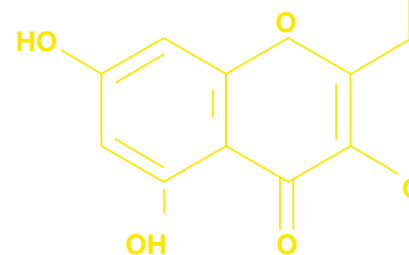
#### Option number 1

We look for bitter blockers which mask the bitter taste, thereby so-to-speak outwitting the sensory cells on our tongue.



#### Option number 2

The technical process of extracting protein also offers opportunities to wholly or partially remove the kaempferol 3-O-(2''-O-sinapoyl-β-sophoroside). The determining factor is that the concentration of the bitter substance in the final product must be below the taste threshold that humans can still perceive.



### Rape with no bitter substances?

And what happens next to the rape protein after the bitter substance has been identified? “There are two ways of getting rid of the bitter taste. On the one hand, we search for rape strains containing fewer kaempferol derivatives or none at all. To do so, we are currently working with geneticists and breeding researchers in Göttingen, Gießen and Bielefeld as part of a program sponsored by the Federal Ministry of Education and Research. On the other, we are collaborating with an industrial partner in Magdeburg to remove the bitter substance in the technical process to extract the protein. In both cases, we must be able to determine the precise concentration of the kaempferol

derivative,” Corinna Dawid explains. The high-resolution analytical equipment is perfectly designed to tackle this task. But even the best measurement equipment has one flaw: it can’t taste. Which means it can’t assess what concentration is relevant to us humans. This crucial job is still being performed by taste testers in sensory booths: from right to left, from low to higher concentrations. Use a pipette to drip a milliliter onto the tongue, but don’t swallow, and then spit it out.

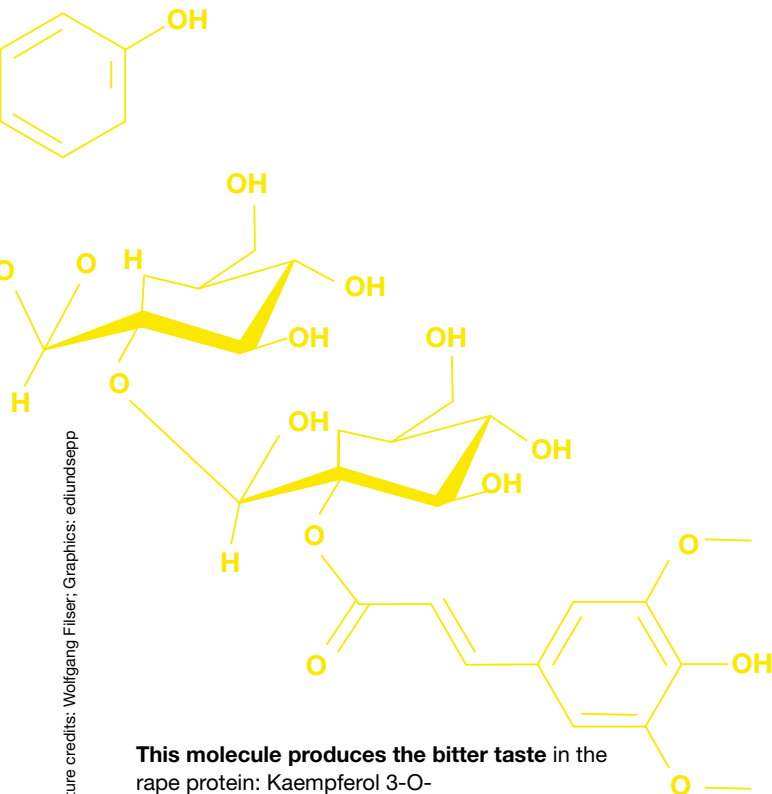
Monika Offenberger





### Option number 3

Plant breeders together with geneticists are looking for rape plants that naturally produce less kaempferol 3-O-(2''-O-sinapoyl-β-sophoroside) or none at all. To do so, hundreds of different strains of rape are planted and their bitter substance content tested. Promising strains can be crossed to form elite breeds.



**This molecule produces the bitter taste** in the rape protein: Kaempferol 3-O-(2''-O-sinapoyl-β-sophoroside)

Picture credits: Wolfgang Filser; Graphics: edlundsepp



**Prof. Corinna Dawid**

After studying food chemistry at the University of Münster, Corinna Dawid started her doctorate while still in Münster with Prof. Thomas Hofmann. In 2007, she followed her doctoral supervisor to the Weihenstephan Science Center at TUM. During a research stay at the University of Bangkok, she played a pivotal role there in setting up the Institute for Molecular Sensors. Back in Munich, she began her habilitation with studies of stress resistance in plants. After Prof. Thomas Hofmann was appointed TU President, Corinna Dawid took over the Chair of Food Chemistry and Molecular Sensory Science as its acting leader. Since then, her research work has focused again on research into taste and smell.

# Variety for water drinkers

**A Munich-based company, air up, is bringing flavor to water – without actually adding any new ingredients. Its founders have developed a bottle with an aroma ring that carries a scent into the mouth in such a way that the brain registers a flavor even though the person is only drinking water.**

“**N**utritional science has taught us that water is a very healthy drink. In the long run, though, it tastes boring,” says Fabian Schlang, the company’s founder, who studied nutritional science and food technology at TUM. Flavored water does exist, but it almost always contains sugar or sweeteners. “By contrast, the bottle we have developed allows a person to drink pure water while still enjoying a flavor experience.” The start-up hopes to offer water drinkers a simple and healthy chance at variation and to make the transition to water easier for those who prefer soft drinks and juices.

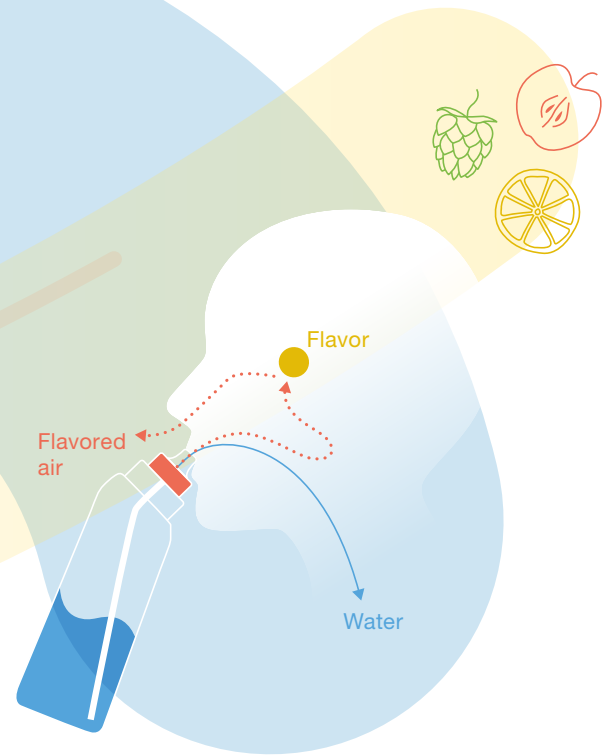
The bottle has a straw-like nozzle onto which the aroma ring is placed. It can be filled up with tap water, either still or carbonated. Five aromas are available at present, from classic apple to lemon and hops. The ring snaps into place in two positions and can be engaged or disengaged depending on whether the user fancies some pure water or a flavorful drink.

Retronasal olfaction is the name of the process behind the product. While humans perceive smell directly through the nose, scents can also take a detour via the throat, such as the aroma of food. As scents in the mouth are usually associated with food, the brain perceives them as flavors – even if they are only scents carried with water.

*“It was sort of basic research  
for a retronasal drink system.”*

Fabian Schlang, air up founder

The drinks bottle developed by air up uses an aroma ring so that, when the user drinks water, they also inhale scented air. This gives them the impression of drinking flavored water because the scent produces a taste experience in the brain.



Product design students Lena Jüngst and Tim Jäger from the Hochschule für Gestaltung Schwäbisch Gmünd stumbled across this topic quite by chance, and asked themselves: How could a scent be carried directly into a person's mouth to produce the experience of taste? They created a prototype for a bottle that combined water with flavored air. Friends put them in contact with Fabian Schlang, who was looking for a topic for his Master's thesis. Trained as a chef, he leaped at the opportunity. There were many questions to answer: How do people actually drink? How can we achieve a positive taste experience for both small sips and large gulps? What would be the best carrier material for the aroma? What would be the most effective design for the aroma ring? What's more, how do you even measure aroma? "It was sort of basic research for a retronasal drink system," remembers Schlang. His enthusiasm shines through when he talks about how much he benefited from the fact that, at TUM, there was somebody to answer practically every question – someone who knows the topic, can lend a device, or help in some other way. A lot of work went into the bottle's design. It had to ensure that, when the user took a drink, exactly the right amount of air was sucked in, flowed through the aroma ring and mixed with the water. And, despite its sophisticated design, it had to be possible to clean the entire system to ensure flawless hygiene.

The three-strong team were then joined by Jannis Koppitz and Simon Nüesch, both TUM Management and Technology graduates. UnternehmerTUM helped the founders to access the EU's Climate-KIC business accelerator. The company was then awarded an Exist Business Start-Up Grant and moved into the TUM Entrepreneurship Center in Garching. "Being in contact with other start-ups, the TUM network and the Maker Space helped us to develop quickly," recalls Schlang. Investors got on board and put the company in touch with production companies. Since then, air up has moved into offices of its own and – as of the summer of 2019 – has grown to 15 employees. New aromas are currently in the works and additional bottle designs, including models made from glass, are also in the pipeline. The product has been on the market since July 2019 – just three years since the company was founded – and is available online, in supermarkets and in sports stores. Quite obviously, air up has struck a chord: Only a few days after the product's sales launch, many retailers had sold out.

Christine Rüth

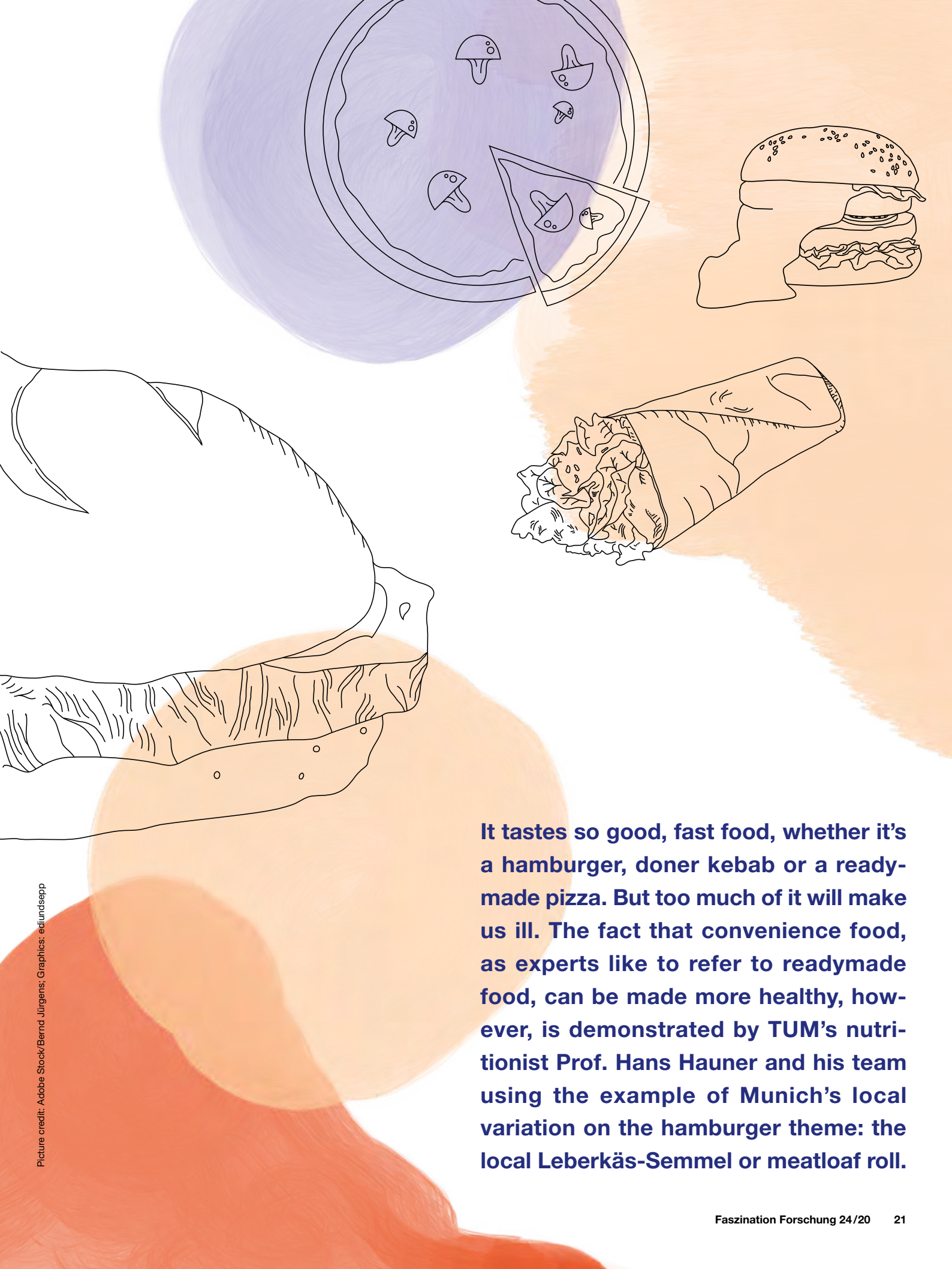
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# Meatloaf roll –

*but a healthy  
one please!*

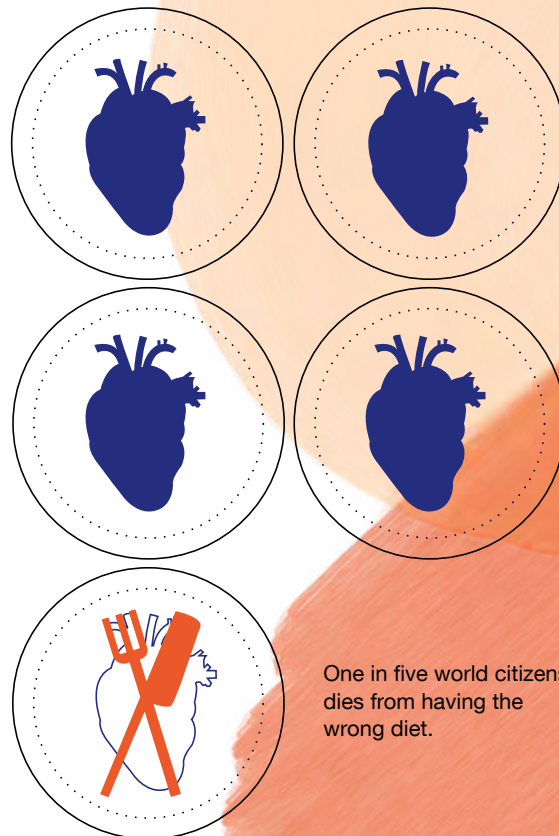


Picture credit: Adobe Stock/Bernd Jürgens; Graphics: edlundsepp

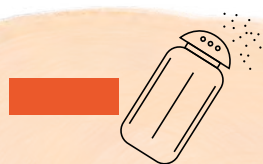
**It tastes so good, fast food, whether it's a hamburger, doner kebab or a ready-made pizza. But too much of it will make us ill. The fact that convenience food, as experts like to refer to readymade food, can be made more healthy, however, is demonstrated by TUM's nutritionist Prof. Hans Hauner and his team using the example of Munich's local variation on the hamburger theme: the local Leberkäs-Semmel or meatloaf roll.**

**B**ad food makes us ill and can even kill us: Every fifth person in the world dies from the consequences of a poor diet. Prof. Hans Hauner has spent more than 30 years advocating for people to change their diets – but so far not nearly enough has happened. Around 20 percent of deaths worldwide can still be attributed to an imbalanced diet, stated the authors of a piece of research when summing up their work in the medical journal “The Lancet” in 2019. Too much salt and too few whole grain products, fruit and vegetables can lead to cardiovascular diseases, diabetes and cancer, causing the deaths of eleven million people every year.

Hans Hauner, Director of the Else Kröner-Fresenius Center for Nutritional Medicine at TUM, has spent his whole career studying the consequences of diet on health, and treats and advises above all grossly obese patients and patients with diabetes (*registration for consultation on 089 28924921*). And he advocates in numerous media articles for people to eat more healthily, e.g. more fiber. Because fiber holds the key. It lowers blood sugar and cholesterol while promoting digestion and a sense of satiety. Fiber prevents arteries from clogging up, reduces the risk of bowel cancer and helps people who are grossly overweight, or obese. Our great grandparents consumed 60 to 100 grams of fiber a day. Today, it should be at least 30 grams according to recommendations issued by the German Nutrition Society, but we only manage around 20 grams on average.



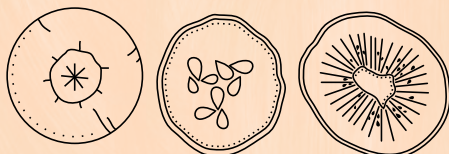
One in five world citizens dies from having the wrong diet.



less salt



more whole grain products



more fruits and vegetables

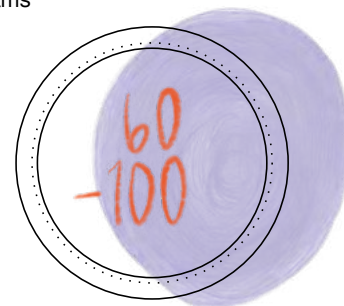
A lot of whole grain bread and pulses would be a good idea as they are particularly rich in fiber. But instead we prefer to eat hamburgers, frozen pizzas and – very popular in Bavaria – meatloaf rolls. Eaten hand-held at snack time, preferably heated up, and served in a white roll of course. “But they don’t contain much fiber,” Hauner states. “The composition of corn seeds is in fact excellent. It’s not just starch but also some fatty acids, protein, a lot of micro nutrients and plenty of fiber. That’s what we need for a healthy diet.” But a lot gets lost in the milling process and further industrial processing, he notes, because we are only interested in the starch. “We make the quality of the raw ingredients worse and create products which are no longer really healthy.” And then you’ve got the meatloaf in the roll. “For that you tend to use what’s left over in the slaughterhouse, a lot of fat, salt and additives to make the whole thing edible.”

But it still tastes good to people, which is why they like to eat meatloaf rolls in spite of all the advice on nutrition. “People find it hard to break old habits,” Hauner says. “A few manage it but the vast majority are unsuccessful.” So Hauner’s idea is that the food that people enjoy eating and consume the most of in Germany must get healthier. Fast food and convenience food, in other words, food that has been industrially prepared and only needs to be heated up. Guided by this principle, Hauner formed the research cluster “enable” together with more than 20 partners; in September 2018, this group, for whom he is the spokesperson, entered the second funding round as one of four research clusters now dominating nutritional research in Germany. Together with epidemiologists, geriatricians, neuroscientists, food chemists, computer scientists and consumer researchers as well as industrial companies, Hauner is investigating the physiological effects of nutrition and particularly connections to diseases such as type 2 diabetes and obesity. And how we can make food better to prevent these diseases caused by poor nutrition.

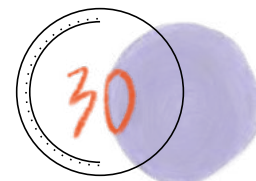
One of the projects is a healthier meatloaf roll. To this end, scientists added fiber to both the roll and the meatloaf, and the latter had its salt content reduced and lean meat added. This resulted in 20 grams of fiber and 30 percent fewer calories per portion. The meatloaf roll was still tasty, as blind tasting with 20 respondents proved. And an analysis of satiety parameters showed that it makes people feel just as full in spite of the fewer calories. ▶

Actual amounts of fiber in grams

two generations ago



recommended amount in 2019

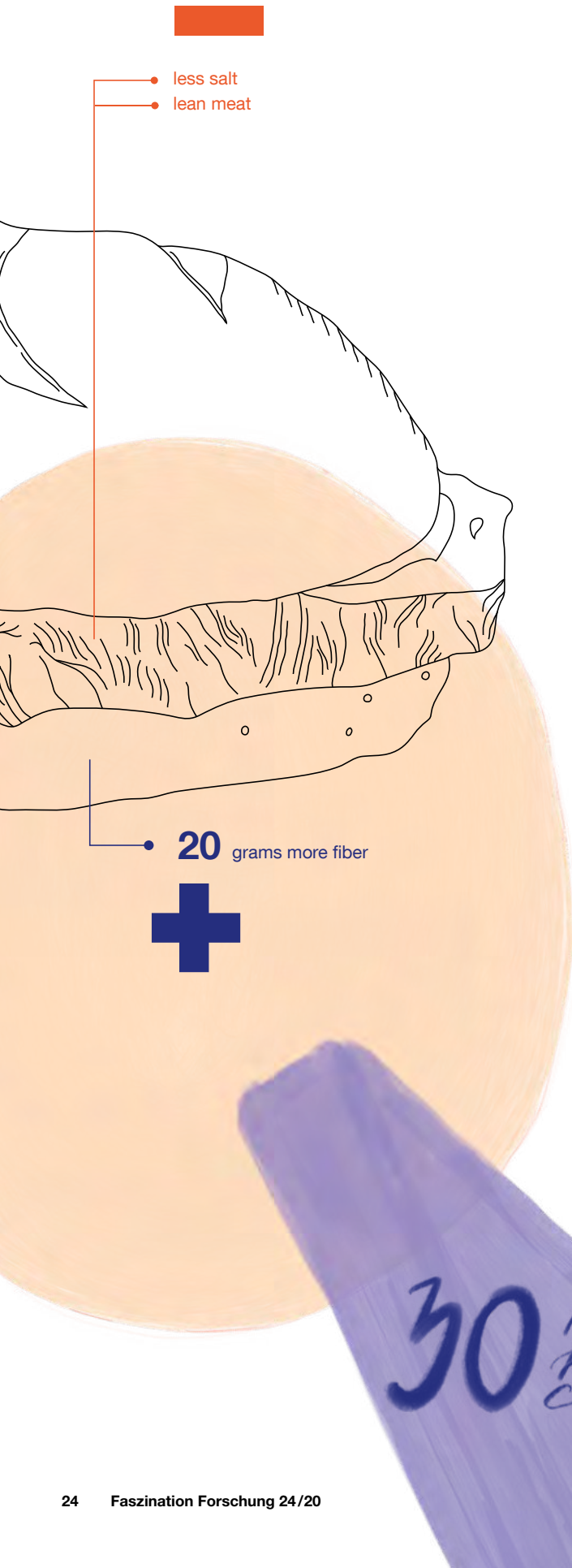


actual amount in 2019



#### What is fiber?

These are largely indigestible elements in food, mostly carbohydrates which mainly occur in vegetable foodstuffs. They are to be found predominantly in cereal, fruit, vegetables, pulses and also in low volumes in milk. Fiber is divided into soluble fiber (such as locust bean gum, guar, pectin and dextrin) and insoluble fiber (e.g. cellulose).



“For us, this shows that even popular convenience products can be made more healthy without compromising enjoyment,” Hauner notes with satisfaction. The next step is to find butchers willing to sell the healthier meatloaf roll. It remains to be seen whether the healthy fast food has any chance on the market in spite of the cost of the ingredients being 10 percent higher. Hauner’s test subjects at least stated they would like to buy the healthier meatloaf roll. In a further study with 120 test subjects, half of them were given a series of fiber-enhanced foods to choose from over a period of twelve weeks, including rolls, packet soups and sausages. The other half ate the same food without any fiber enhancement. “We are still evaluating the results,” Hauner reports, “but it looks as though we can already observe improvements in the blood sugar and blood lipid levels as a result of the fiber in spite of the relatively short period of the study, and the participants accept these products.”

The test subjects came from a sample of the population consisting of 500 persons who were recruited in the first phase and medically categorized: weight, body fat, abdominal girth, cardiovascular system, behavior after a glucose tolerance test, smell and taste testing, predilection for and aversion to certain types of food, etc.

Hauner and his partners now want to observe these 500 persons for several years and, for example, test new dietary concepts with them. In the process, the intention is to examine the effect of various fiber types on the glucose metabolism in order later to develop the best possible products to prevent type 2 diabetes, for example.





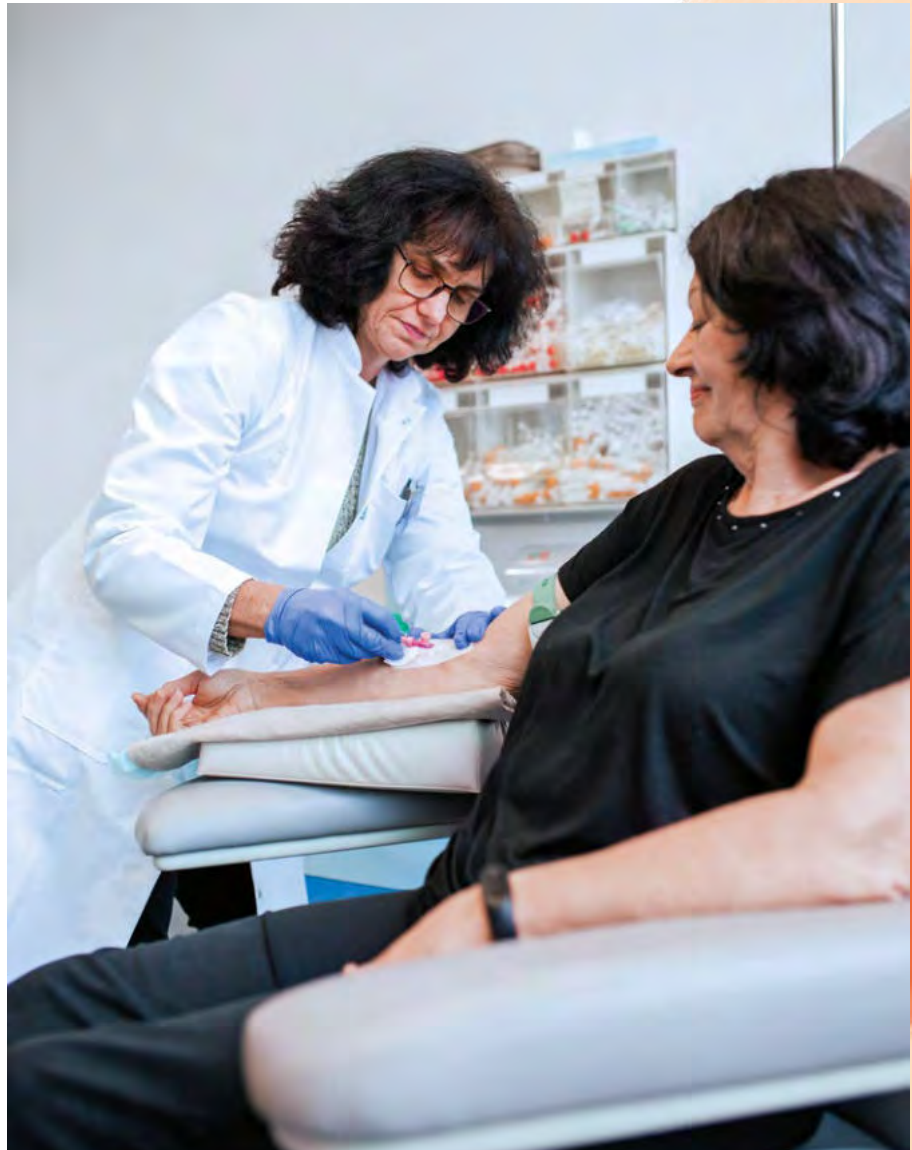
**Hans Hauner and his team** are conducting studies on the effect of eating habits. Here we see a member of his team, Christina Holzapfel, in a consultation with a participant in the LION study.

The researchers are particularly interested in sensory perceptions as people essentially choose their food by how it tastes and not in accordance with abstract health values. As Hauner explains: “If someone doesn’t like fish, I can’t force them to eat it. The question then is: What kind of healthy alternative can I offer them?” And studies in England show that you have to gradually accustom people to eating less sugar or salt. Hauner continues: “Dietary habits are created over many years. I can’t expect someone to change their diet for three weeks and then say: ‘That’s great, I’ll stick with this for the rest of my life’. I have to connect with people in their present situation, and I have to be able to offer them tasty products to improve their diet.” The scientists have therefore incorporated 14 partners from the nutrition industry in the enable cluster. For example, they provide free food for studies and in return they receive

the results of those studies – in the hope that this will give them a better understanding of the nutritionists’ demands. Because as companies, their first focus is on their sales figures and they fear proposals such as the food traffic lights system in which many of their products would not fare well. But Hauner also has sympathy for the companies: “On the one hand, they are criticized for selling so much poor quality food. And on the other, although consumers say they would like to eat healthily, they are not prepared to pay a bit more for it.”

A further project directed particularly at the overweight is LION ([www.enable-cluster.de/lion](http://www.enable-cluster.de/lion)). This stands for “Life-style Intervention” and its aim is to use innovative approaches to successfully manage weight. The nutritionist Dr. Christina Holzapfel and her team are investigating how the metabolism of test subjects responds to different meals and what happens to it when they are losing and maintaining weight. The results of her study are helping to improve and personalize the therapy given to the overweight.

It's not so easy to say what kind of food puts one particular individual at risk (or is of benefit to them). Our diet consists of thousands of ingredients which interact and are received and metabolized differently from one person to another. Whether food makes us sick is also determined by our genes, which, for example, play a major role in type 2 diabetes. Although obesity is the main risk factor for diabetes, only one fat person in three actually becomes diabetic. The rest is down to the genes. Hauner is working with colleagues to find out how dietary components and gene mutations combine to influence the risk of diabetes.





**In various studies**, participants' vital signs – e. g. blood sugar – are used to test how their metabolism reacts to various meals and what happens to it when losing and maintaining weight.

#### The *enable* research cluster

The *enable* research cluster (“enable – healthy food choices in all stages of life”) is one of four research networks in Germany dedicated to nutrition and receives support from the Federal Ministry of Education and Research to the tune of 11.6 million euros. The cluster is developing new ways of giving the population a healthier diet in different phases of life, in pregnancy and early childhood, in their youth, as adults or as senior citizens.

[www.enable-cluster.de](http://www.enable-cluster.de)

The interplay between a complex diet and hereditary disposition makes it hard work to gain insights in the field of dietary research, as Hauner explains. In addition, people in control groups also change their behavior sometimes, as they know that they are taking part in a study on nutrition and they live more healthily. This can blur the difference between the intervention group and the control group. A difficult research field in a scientific world that prefers clear-cut findings. But Hauner is convinced: “What we’re doing here is important for society. Our cluster and the three further research clusters are now leading the way in nutrition research in this country. And we hope that our work will induce policymakers to invest even more. Because, as we say, a poor diet is the most important risk factor for chronic diseases and the population’s sickness burden in Germany.”

■ *Markus Bernards*

“When it comes to nutrition and diet matters, a lot of young people are **pretty clueless**”

**How can we motivate people to eat healthier food? TUM nutritionist Prof. Hans Hauner and his team are adapting their tactics to different age brackets: To address young people, they are relying on social media, for adults, enhanced fast food is on the cards, while 3D printers will help make food more appetizing for senior citizens. A conversation on the difficulty of breaking entrenched habits.**

Link

[www.professoren.tum.de/hauner-hans](http://www.professoren.tum.de/hauner-hans)





**Mr. Hauner, you – and your colleagues – have been encouraging your patients for many years to improve their diets, and you are also appearing quite regularly in the media as an expert on nutrition. But ultimately, not much has changed. Why did you nevertheless fall back on a counseling concept in your major GeliS study – Healthy living in pregnancy?**

**Hans Hauner:** Pregnant women are exposed to a particular risk of overeating. Almost half of the women in Germany put on more weight in pregnancy than is recommended. For a woman of normal weight, this should be 11 to 16 kilos. Putting on more weight increases the risk of gestational diabetes, high blood pressure and birth complications. In a preliminary study to GeliS, we found that professional lifestyle counseling had a clearly positive effect, while there were similar indications in the specialist literature.

**But your study with around 2,300 respondents then showed that the lifestyle counseling had practically no effect.**

**HH:** We were surprised. Maybe our four counseling sessions were not enough. The main difference, though, was that the counseling was held in normal gynecologist practices where there is often little time for relaxed conversations and little experience in lifestyle counseling. We will, however, continue to evaluate the results and follow the weight developments and health status of the children until they reach the age of five. We want to find out how diet and exercise in pregnancy affects the risk of the children becoming overweight at an early age. And in the GeliS study, we were able to establish that at least the weight of the children at birth was slightly lower when the expectant mothers had received lifestyle counseling.



*“Dietary habits are the result of a very long learning process and they are not easy to change.”*

*Hans Hauner*

**Hans Hauner is also offering courses and further training.** In the Institute’s teaching kitchen, for example, students can learn how to cook good, healthy food.

**You are also using counseling with young adults in the enable cluster, although success is looking quite modest – why is this the case?**

**HH:** We are not providing advice in the traditional sense in the form of teaching on nutritional and dietary topics. We wouldn’t be able to reach the young generation like that. The 18-to-25-year-olds are particularly at risk when they leave their families where the parents may have made sure they were eating sensibly. Many of them are pretty clueless in terms of nutrition, and wind up living largely on pizzas and fast food. Together with our computer scientists, we are developing apps in which we can subconsciously convey the message of a sensible diet through a games-led approach. In the Appetite app, users photograph what’s on their plate in front of them, and the other users then assess whether that is healthy food or not. By the way, the assessment of the crowd matches that of the nutrition experts – we tested it. As a further refinement, we are planning a virtual nutrition consultant in order to incorporate users’ current context. The main aim is to register indications of stress. Because under stress, we tend to pay less attention to our diet. We are also considering offering a virtual supermarket where we will include typical products, thereby linking the choice of foods to information on nutrition in a fun and playful manner.



**Young people can be inspired by the Appetite app:** Users take pictures of what they have on their plates in front of them. The community then assesses whether these are healthy, sensible meals or not.

**You are following a different concept for the age bracket of older adults: It's not about trying to change people's behavior but the food instead.**

**HH:** Yes, because dietary habits are the result of a very long learning process and they are not easy to change. At the same time, we have an increased risk of diabetes, cardiovascular diseases and certain cancers in the age bracket from 40 to 65, all of which are heavily influenced by diet. Consequently, we conducted studies in this age group in which we added fiber to various convenience food products such as frozen pizzas, hamburgers and meatloaf rolls and changed other ingredients, thereby improving the health value of these products. We were able to establish that people accept this from a taste perspective and that their blood test results improve at the same time.

**While more and more people tend to overeat, and therefore put on too much weight, around one third of the very senior individuals have the opposite problem: they are undernourished. There have been many demands for those of very advanced age in nursing homes to be given more meat on their plates. Would that be the solution?**

**HH:** It would probably suffice if people of that age ate whatever was on their plate. Older people feel less hungry and thirsty. As a result, they get too little protein and don't drink enough. This means they are in danger of losing muscle mass, becoming fragile and dehydrated.



## But you cannot force people to eat.

**HH:** That's true, but you certainly can make food more attractive. Many people of advanced age experience difficulty swallowing or have serious dental issues. They are not able to eat stringy meat any more. In nursing homes, food is pureed for such individuals. But it looks so unattractive that they don't enjoy eating it. Consequently, in one of our projects, our partners are working on using a 3D printer to restore shape to pureed food so that it looks like attractive food once again. Another group is trying to make protein drinks so tasty that individuals will enjoy drinking them. Together with our computer scientists, our geriatrician partners in Nürnberg have developed a cup with built-in scales which measure the volume imbibed and remind people to hydrate themselves by way of voice messages.

**You recruited and studied more than 500 people in the four age groups in the enable cluster. In view of the variety of foods that interact with each other and our genes, by which the metabolism differs from person to person, isn't that too small a group to obtain meaningful results?**

**HH:** We analyzed these 500 people very carefully with regard to their health status, their eating habits and preferences and their metabolism. We were able to identify major individual differences – we wouldn't have been able to do that to the same depth with 5,000 respondents. I think this gives us a good chance of finding new connections between diet and health. But to do so, various disciplines are working closely together, and the complexity of the subject of nutrition is such that nothing less is required. These are socially highly relevant issues and I really enjoy addressing them.

■ *The interview was conducted by Markus Bernards*




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**Prof. Hans Hauner**

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As a child, Hans Hauner, who was born in 1955 and grew up in Regensburg, actually wanted to become a missionary. In some ways, nothing has changed, he reckons, as he's spent 30 years of his career trying to convince people to improve their diets. Hauner studied medicine in Regensburg and at TUM and continued his studies at the University of Ulm, qualifying as an internist majoring in endocrinology/diabetology. This was followed by a period as Senior Physician at the German Diabetes Center in Düsseldorf. In 2003, Hans Hauner was appointed to TUM's newly founded Chair for Nutritional Medicine and since then has been active as Director of the Else Kröner-Fresenius Center for Nutritional Medicine.

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*Escherichia coli* are the best-known intestinal bacteria and belong to the family of proteobacteria.

*Bacteroides* are rod-shaped bacteria that can grow without oxygen.

*Bifidobacteria* are lactic acid bacteria from the family of actinobacteria.

*Enterococci* are to be found everywhere and also form part of humans' core microbiome.

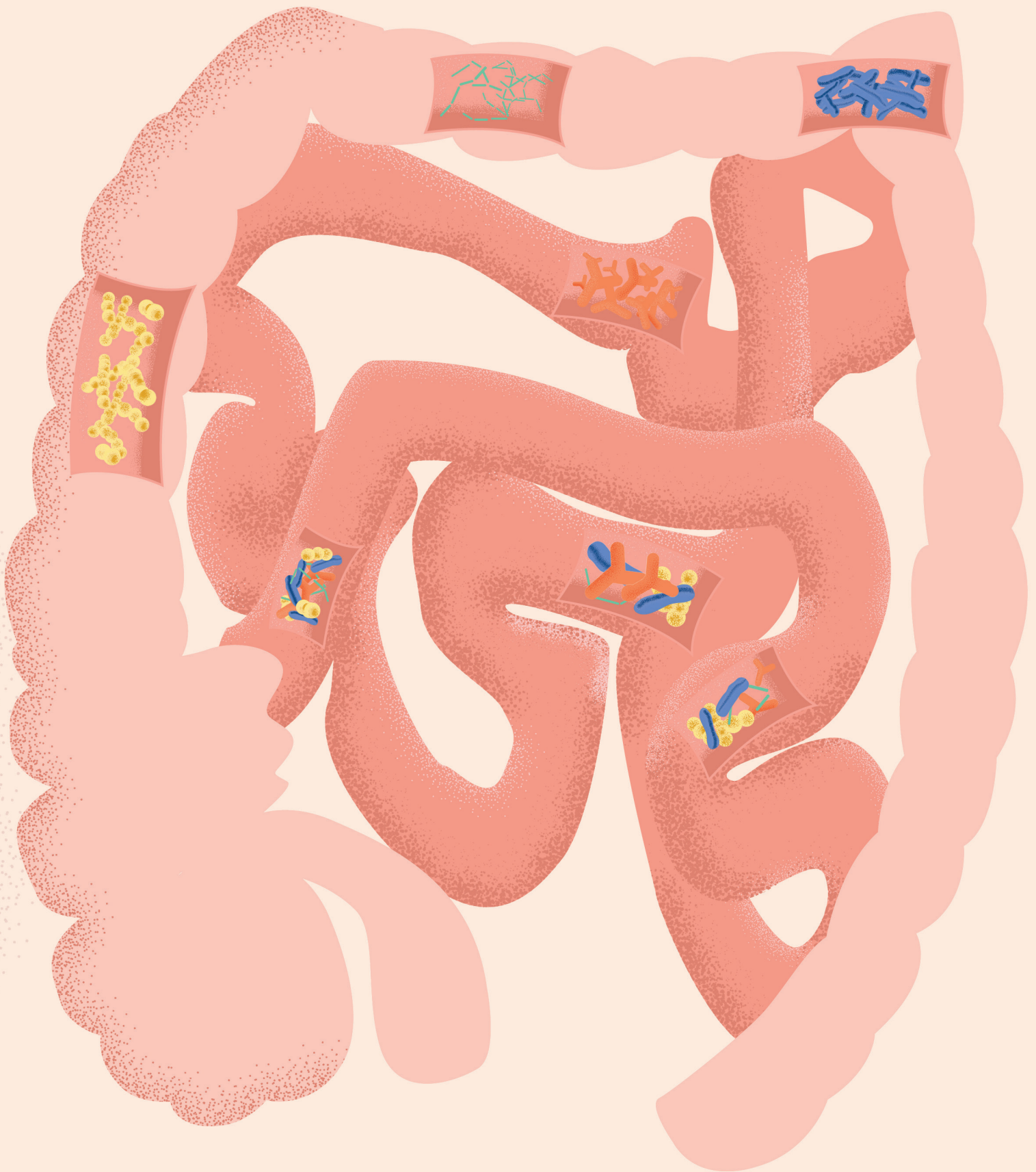
# Microbiome

## – The mysterious ecosystem in our gut

**Fast forward to 2040: A small stool sample will be all it takes to tell if someone is susceptible to certain diseases. You can then take the appropriate preventive action to avoid contracting them, or at least provide better treatment. Unfortunately, however, we have not yet advanced to that stage. But researchers are optimistic that in the next few years, they will be able to detect the characteristic signatures of many diseases in our intestinal bacteria. TUM Professor Dirk Haller and his team are working flat out to achieve it.**

Link

[bflm.wzw.tum.de](https://bflm.wzw.tum.de)



**The human intestines** are populated by a dense network of microorganisms, the microbiome. It is dominated by four phyla of bacteria forming up to 200–300 different species in an average adult. In a healthy human, these are in equilibrium.

**E**ach and every one of us, whether clean or not, is populated by about 100 trillion bacteria – on our skin, in our saliva, behind our ears or in the crook of our arm. Most of these microorganisms, however, are to be found in the intestines, adding up to one kilogram to our weight. Their community, referred to as the microbiome – gut or intestinal flora in somewhat obsolete terms – consists of a blend of bacteria, some physiologically beneficial, and some pathogenic, depending on the family of bacteria to which they belong. Only if the latter are kept under control are human beings healthy, as then the balance is maintained. In that case, their microbiome supplies an entire range of enzymes which help to digest food. It also produces vitamins and short-chain fatty acids. These are important tasks which ensure that food not digested in the small intestine can continue to be exploited regardless of whether we are eating a juicy steak or a bowl of salad.

In addition, researchers are identifying an ever-increasing number of functions performed by the intestinal microbiome. First and foremost, our immune system is apparently existentially dependent on the bacteria. They act as a kind of sparring partner, giving it the confidence to distinguish dangerous pathogens from harmless constituents of our food. After all, the food we partake of contains numerous foreign germs and pathogens. The wall of the intestine must keep them at bay, i.e. erect a barrier, while on the other hand, it must let through the elements in our food containing energy so that they can reach the bloodstream. If something goes wrong here, we run the risk of developing allergies or autoimmune diseases.

#### How many species of bacteria are there in our intestines?


There are around 1,500 species which can populate the intestines. The average European has around 200–300. But a sick person may only have 30–50 (Crohn's disease). And if there are complications after a stem cell transplant (graft-versus-host disease), the microbiome may under certain circumstances shrink to one strain. This is highly dangerous.

#### When the system tips


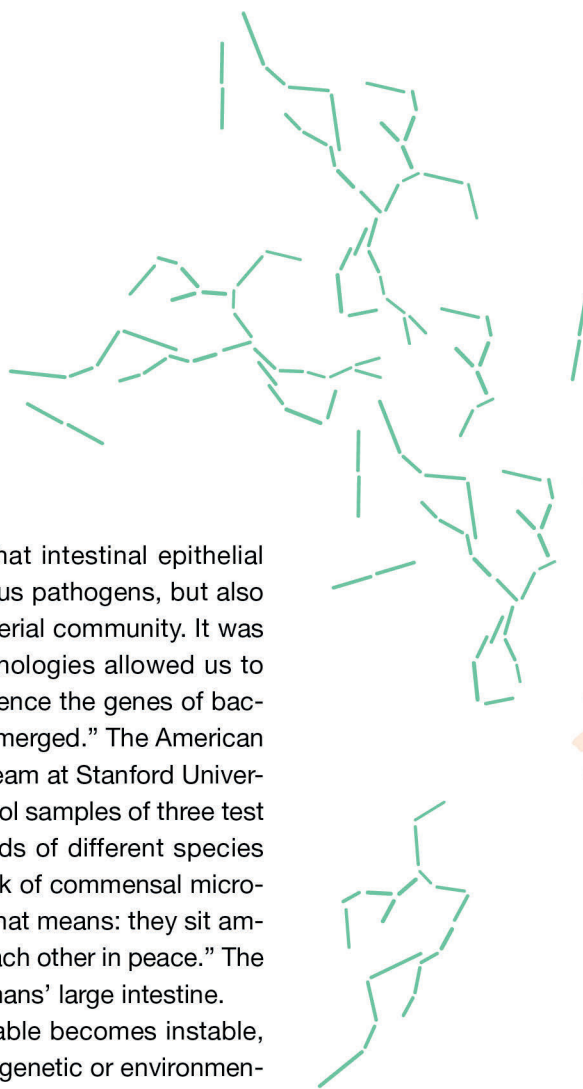
This is precisely the situation that Professor Dirk Haller takes as his starting point. Haller heads up the Chair for Nutrition and Immunology at TUM's Weihenstephan School of Life Sciences, as well as the Institute for Food & Health (ZIEL) which is also located there. Since his Ph.D. thesis, the 51-year-old nutritional scientist and microbiologist has been fascinated by the complex collaboration between the microbiome and its host. "Back then, a good 20 years ago, hardly anyone was interested in the subject," he remembers. "Initially, I myself came from the area of food microbiology, i.e. nutritional science, and we asked ourselves how probiotic bacteria in the gut communicate with us.

*"Today, we are in more or less the same situation with the microbiome as we were 20 years ago with the human genome."*

Dirk Haller



Here we challenged the dogma that intestinal epithelial cells not only perceive the infectious pathogens, but also the harmless members of the bacterial community. It was only around 2005 when new technologies allowed us to quickly and comprehensively sequence the genes of bacteria, that a new field of research emerged.” The American scientist Paul B. Eckburg and his team at Stanford University analyzed the bacteria in the stool samples of three test subjects and realized that hundreds of different species were peacefully coexisting. “We talk of commensal microorganisms,” Haller explains, “and that means: they sit amicably around the table and leave each other in peace.” The table in this case is the food in humans’ large intestine. Sometimes, however, this round table becomes unstable, and certain bacteria – triggered by genetic or environmental factors – gain the upper hand. The system threatens to overturn, resulting in the symbiosis becoming a dysbiosis. Something of this nature can occur, for example, when you take antibiotics, resulting in infections with *Clostridium difficile* bacteria. These spore-forming organisms occupy the niche cleared by the antibiotics and multiply quickly. They produce toxins and frequently cause life-threatening diarrhea. When and how dysbioses cause intestinal diseases and how they can be prevented are among the research topics which Dirk Haller and his team are working on. ▶

Germ-free experimental animals



Crohn's disease sufferers



Average European

**There are around 1,500 species** of bacteria which can populate the intestines; the average European has around 200–300. Crohn's disease patients only have 30–50 left. For experimental purposes, mice are bred entirely free of intestinal bacteria.



In the meantime, the scientist has succeeded in firmly establishing microbiome research in Germany: The German Research Foundation (DFG) has just set up a separate field of research (SFB 1371), with Haller as the spokesperson. “It’s a matter of the functional relevance of the microbiome in the digestive tract,” he says. “We want to find answers to the following questions. When is there a causal link between a change in this microbial ecosystem and an illness? Can this be used for diagnoses? Or for prognoses? Or for therapeutic purposes?”

*“The basic finding has now been confirmed that we all have a completely individual fingerprint in our intestines.”*

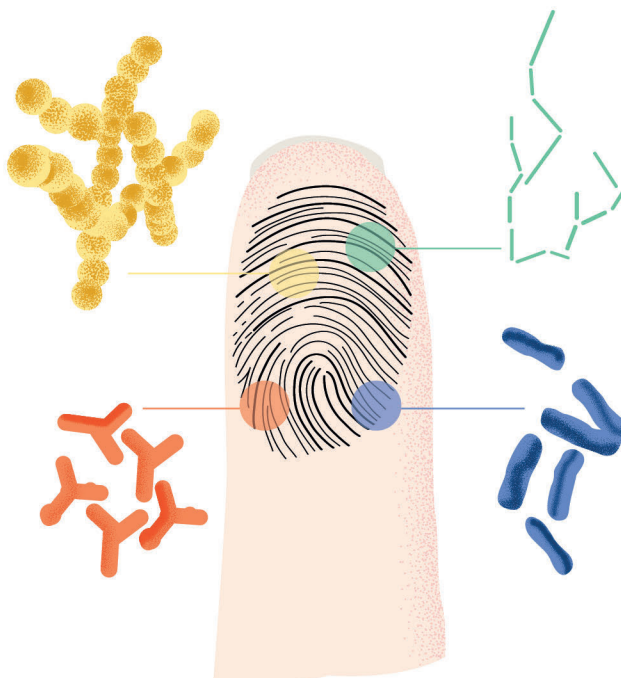
Dirk Haller

#### **New technology has helped the field to flourish**

Researchers are pursuing three strategies to clarify such questions.

- › First, they conduct causal examinations on mice and transfer the insights gained to humans.
- › Second, they analyze the microbial ecosystem in the human gut using high-throughput sequencing technologies.
- › Third, in their studies on humans, they search for interventions which can prevent or treat diseases.

The progress of science in the last 15 years comes to their aid here. Research in this field rapidly picked up pace after 2005, the number of publications shot up and ten years later, the microbiomes of thousands of test subjects had already been analyzed. While this led to a huge increase in data, the analysis on its own was not sufficient to draw conclusions with regard to cause and effect.

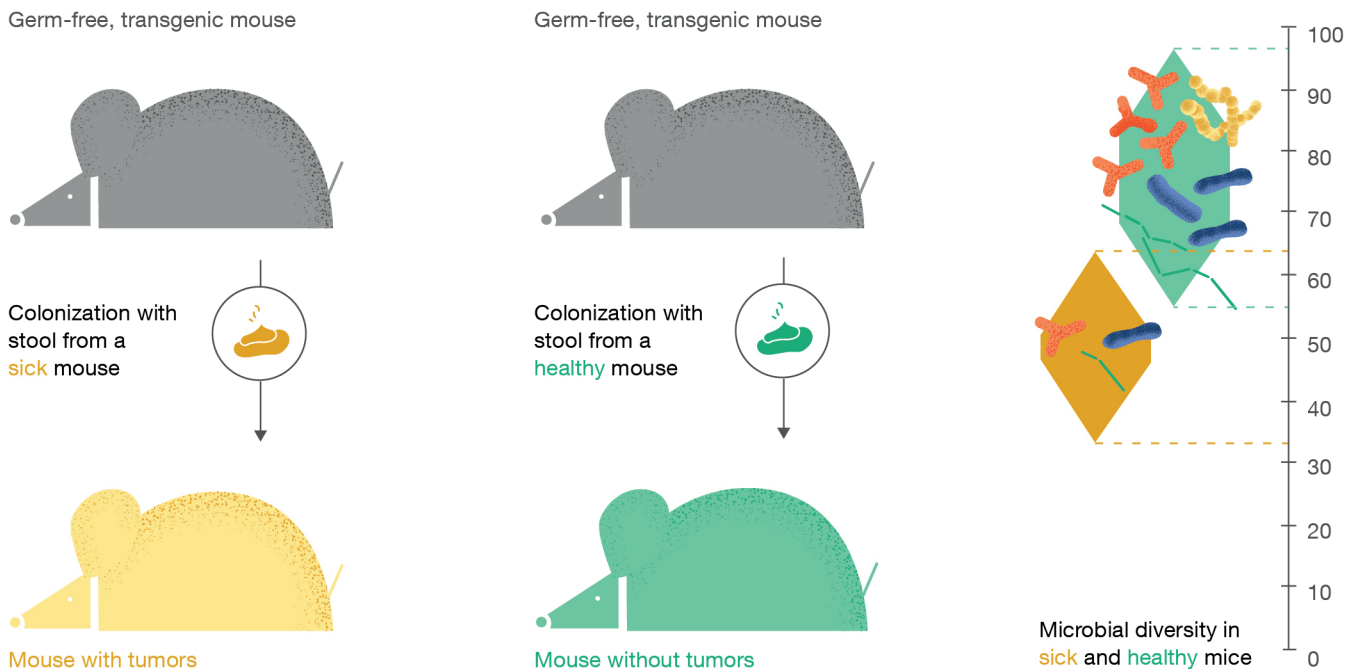


In 2018, for example, a Chinese research group which had examined stool samples of 7,009 persons from 14 districts was amazed by the differences in the bacterial composition between individuals and the major role that lifestyle played. However, they were unable to find what they were primarily looking for, namely a uniform pattern that might point to a general tendency to metabolic disorders such as diabetes. They were only able to detect a regional distribution of individual differences. One central conclusion is that we differ markedly from each other with respect to our microbiomes. The basic finding has now been confirmed that we all have a completely individual fingerprint in our intestines with respect to the composition of the bacteria colony. We can find a large degree of overlap between individuals, but if we look at the level of individual bacterial strains, our microbiomes differ totally. And the differences are so marked that they could even be used forensically, in other words to identify any person by their stool sample. Nevertheless, there are still many more unanswered questions than problems solved. “Today we are in more or less the same situation with the microbiome as we were 20

years ago with the human genome,” Haller says. “Back then, we had high hopes that we would soon be able to recognize every disease genetically. This did not materialize, however. In diagnostic terms, success has been decidedly modest. Although we have a much better understanding now, when it comes to applying our findings, we are still in the starting blocks.” For this reason, he and his colleagues are now leveraging all the opportunities offered by modern analysis and bioinformatics.

**The animal model as a template**

For example, Haller has established his own mouse-breeding center and sterile mouse husbandry at his institute. Around 1,200 mice live in 25 isolators with sterile air and sterile food, in a germ-free environment from birth. They also have no bacteria whatsoever in their gut, i.e. no microbiome, and are ideally suited for researching the effect of certain implanted bacteria or groups of bacteria in their intestines.



**At Dirk Haller’s Institute**, mice are bred in a germ-free environment. As they do not have any intestinal bacteria of their own, they react very specifically to the transfer of stool samples from other mice. For example, it can be shown that certain microbiomes can transmit bowel cancer. The diversity of intestinal bacteria is significantly higher in healthy mice than in sick ones.

**The microbial diversity** in human intestines – symbolized here by colors – has steadily decreased the more people have adopted an industrial lifestyle.



“In order to distinguish which bacterial changes make us susceptible to illness from the heterogeneity and individual diversity of people, we translate this into animal models,” the researcher explains. “For example, we take sterile animals which are genetically susceptible to a disease. If they then do not become ill in spite of their predisposition, this will probably be due to the lack of bacteria.” Conversely, a particular microbiome can make the mice ill if it is transplanted – representing an initial step towards proving causality. Stool transplants both between mice and between man and mouse play a major role in such research. In the past, this procedure was also applied to humans, for example in the treatment of life-threatening *Clostridium difficile* infections. Taking countermeasures with a transplanted, healthy, rich ecosystem was successful in around 90% of patients. Otherwise conventional medicine only has the option of prescribing a further antibiotic. But only 20–30% respond to this treatment.

After a death in the USA following a stool transplant, authorities in the EU are now imposing strict requirements. Fecal transplants are only allowed in human medicine for therapeutic use in accordance with Section 2(1) of the Medicines Act. For applications, the material to be transplanted has to be prepared under the direct, technical supervision of the doctor treating the patient and reported to the responsible state monitoring authorities.

### Are changes to the microbiome cause or effect?

“We and other groups are currently conducting a world-wide search for cause and effect relationships between microbiome and disease,” Dirk Haller explains. “At the moment, many diseases, starting with dementia and autism and on to cirrhosis of the liver, colon cancer, Crohn’s disease, ulcerative colitis and diabetes are being traced back to the microbiome. And these diseases are indeed associated with changes to the microbiome. The question arises, however, as to whether these changes are the cause or are they perhaps only one effect of the disease?” This chicken and egg problem is occupying him and his staff, primarily in the case of chronic intestinal diseases.

It was definitely established that the microbiome is markedly altered in such patients. As this probably also applies to diabetes patients, the Weihenstephan researchers are also collaborating in the Augsburg cohort study KORA.





**Nutritional scientist Dirk Haller** heads the Chair for Nutrition and Immunology at the Weihenstephan School of Life Sciences.

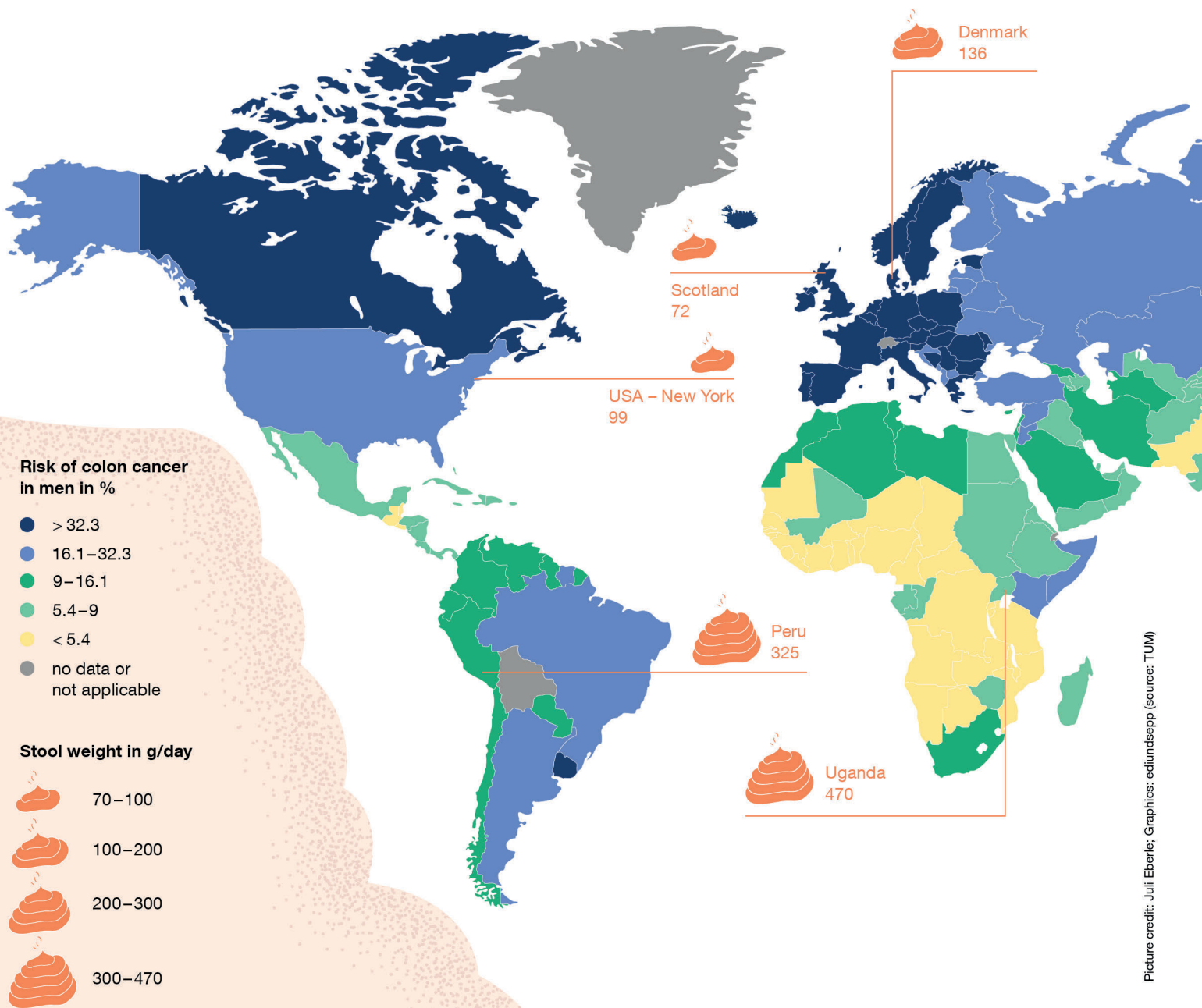
They examined stool samples from 2,500 subjects to find out whether disease signatures for type 2 diabetes can be found. Surprisingly, they found circadian rhythmicity in the microbiome and identified a diagnostically relevant risk profile of arrhythmic bacteria in patients with type 2 diabetes. The scientists analyzed high-throughput sequencing data and applied Artificial Intelligence to identify populations at risk for type 2 diabetes. The key questions for a successful clinical application are the following. Are microbiome signatures capable of predicting the future onset of

disease? And, are we able to change disease-conditioning microbiomes?

While chronic inflammatory intestinal diseases didn't even exist in many still under-industrialized countries until recently, statisticians are now recording a sharp increase. This is exemplified in Hong Kong. "There were no incidences of Crohn's disease there," Dirk Haller says. "But in the last 15 years, the frequency of the disease has shot up, i.e. in precisely the period in which the Hong Kong lifestyle has transitioned from traditional to highly industrialized. ▶

Other epidemiological surveys clearly reveal the following: “Obesity is usually associated with chronic inflammation in the same way as type 2 diabetes. This means modern lifestyle makes us somewhat chronically prone to inflammation even if on a different scale if you compare obesity with Crohn’s disease,” Haller states. “At some point – figuratively speaking – a fuse blows in the system, depending on an individual’s genetic susceptibility, and then the disease escalates.”

The following proposition could be derived from these findings: Industrialized lifestyles entail an altered microbiome, and its interaction with the host’s immune system engenders the disease. Mere statistics, however, are not sufficient to prove causality, and for that reason, a functional understanding of the microbiome needs to complement the computational analyses in order to achieve the next level of knowledge about this complex ecosystem. We need to answer the following questions: What characterizes an individual microbiome and why do patients fall ill? What microbial interaction is able to trigger a chronically inflammatory intestinal disease or even turn it into cancer? And is there a way to counteract this effect therapeutically?



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

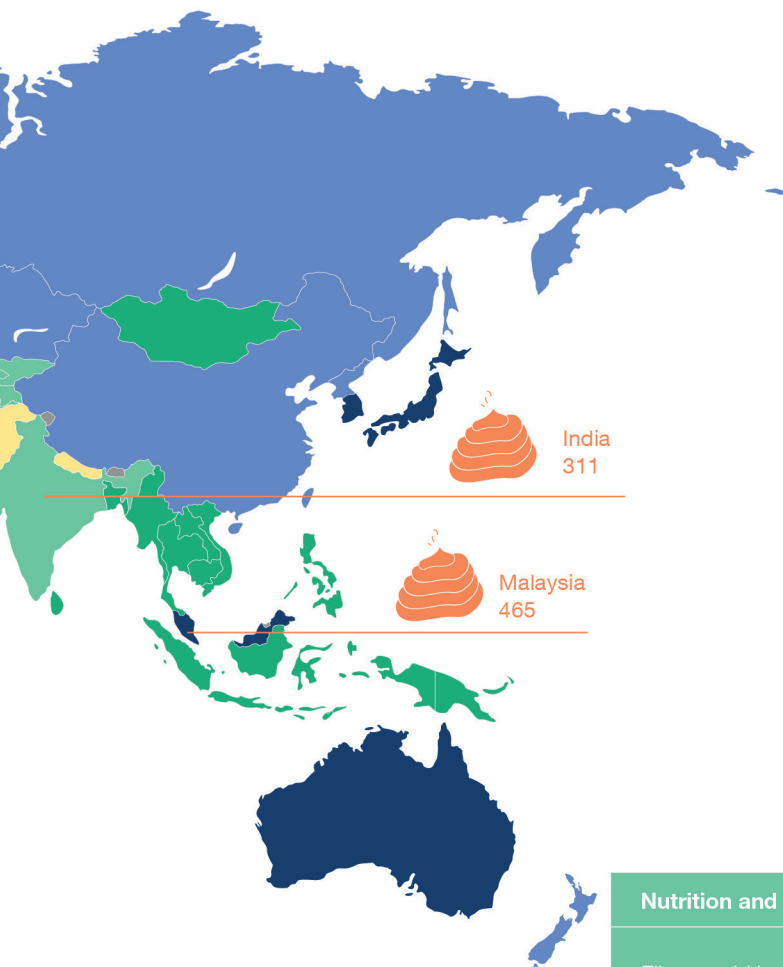
Dirk Haller summarizes the state of play: “There is a lot of correlation, but scarcely any causality. I am convinced it will take another 20 years before we have identified all the causalities and know for sure whether the microbiome is just a symptom or the cause of diseases.” Nevertheless, he sees a bright future for his discipline. “The biology of the microbiome will have a definitive effect on the science of the 21st century, of that I am sure. After this special field of research has finished in twelve years’ time, we want to be able to answer the following question. In which diseases does the microbiome play a role, and in which not, and if it does, what precisely is that role?”

Brigitte Röthlein



**Prof. Dirk Haller**

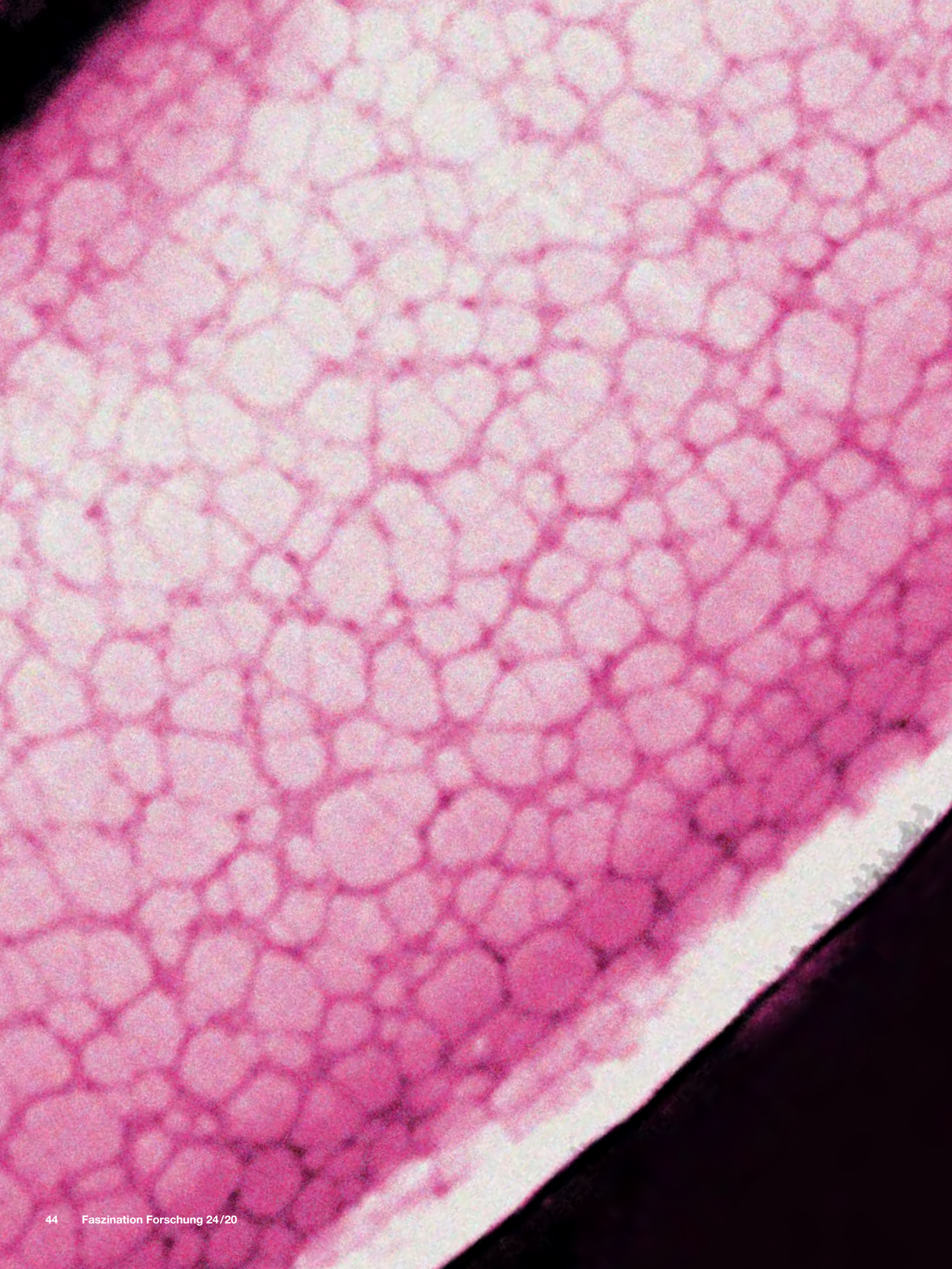
The researcher was born in 1968 and studied food technology and nutritional science at the University of Hohenheim, obtaining a degree in both. Haller then took a doctorate in microbiology and immunology on the subject of “Modulation of the immune response of non-pathogenic bacteria”. After staging posts with Nestlé in Lausanne and at the University of North Carolina, he returned to TUM with an Emmy-Noether group funded by the German Research Foundation where he has held the Chair for Nutrition and Immunology at the Weihenstephan School of Life Sciences since 2008.



**Nutrition and the microbiome**

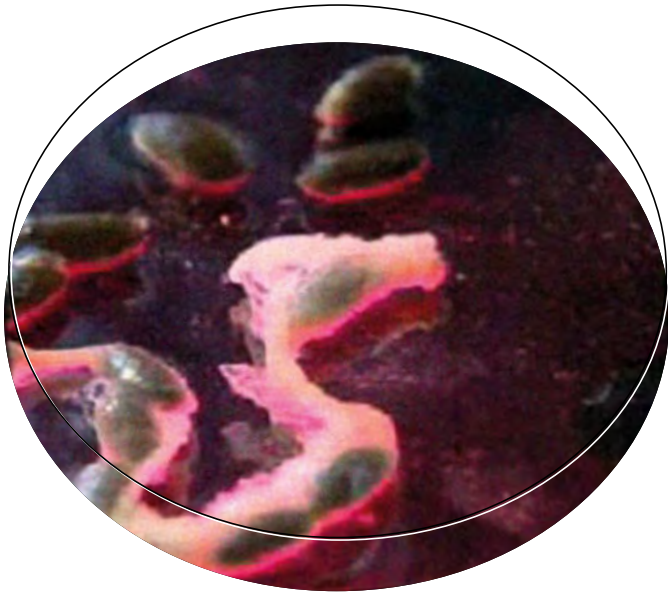
Fiber could be one key to a rich microbiome and intestinal health. Central Africans, for example, have an extremely fiber-rich diet. They eat around 70 grams of fiber per day. In Central Europe, we consume around 10-20 grams a day.





# The intestines have their own “brain”

Prof. Michael Schemann has spent almost his entire career in research studying the “little brain in the gut” which autonomously controls the movements of our intestines. New methods from his working group have helped to finally identify the cause of some organic intestinal diseases. The challenge now is to turn these findings into benefits for patients.



An intestinal specimen is capable of moving outside the body. It performs regular muscle contractions, which researchers refer to as the “peristaltic reflex”. This enables the intestine to move contents distally in a coordinated fashion (see fig. above and below).

**T**he man has an urgent need to get some more ideas off his chest. Michael Schemann holds the Chair of Human Biology at TUM Weihenstephan and is one of this country’s rare experts on an organ whose ideally silent performance we all have a decided appreciation for, but which we otherwise regard as somewhat unseemly: the intestines. Or to state it more accurately: Schemann conducts research into the intestines’ nervous system (officially called the enteric nervous system), the “little brain in the gut” – although the scientist puts great emphasis on the quotation marks.

After all, it is obvious that the intestines can’t think. Pain, emotions, intelligence – all the preserve of the large brain in our head. And we only feel pain in our gut if certain centers in the brain receive so many signals from the sensory pathways leading from the intestines that they make us aware of pain. But by strictly scientific criteria, the intestines also have their own small brain, he states.

You need proof? Schemann jumps up and hurries to his PC screen. He shows a film of a kind of sea cucumber twisting around in a petri dish and constantly contracting in different places. We are viewing a highly magnified, isolated intestinal specimen – and one that is clearly very much alive. Specimens, sections of animal or human intestines – whether the large or small intestine – can be preserved in culture for at least a week and perform their peristaltic movements there day and night with which they otherwise slowly carry chunks of food through the organism, from front to back and from top to bottom.

### **Uniquely autonomous organ**

No other human organ can perform such autonomous movements when separated from the rest of the body and left to its own devices, as Schemann emphasizes. If you were to cut the nerve pathways from the heart, diaphragm or skeletal muscles to the spinal cord and brain, all activity would cease, he explains. But even in the smallest intestinal specimen – held in isolation – an autonomous nervous system continues to direct its movements. Schemann informs us instructively that a nervous system acting autonomously like this is called a brain in biology. Anatomically, the “little brain in the gut” is distributed across several nerve plexuses.

Schemann’s group has developed new methods which enable the network to be identified for the first time. For many years, scientists were unable to access stimulus and information pathways in human intestines. It was not possible to capture the weak electrical signals from the “intestinal brain” with electrodes as is possible with many peripheral nerves and in the brain. “The network of nerves in the intestines is very delicate, and above all, the cells are in constant motion – which is not the case in the brain. You can’t get near them with electrodes, they quickly break off,” the scientist explains.



### Making cells shine

Neuroimaging renders the work of nerve cells visible. Each activity is associated with a change in voltage. By using special voltage-sensitive dyes – the color of which changes in a flash – it is possible to view this process in ultra-slow motion and high magnification. This reveals which nerve cells are active and when.

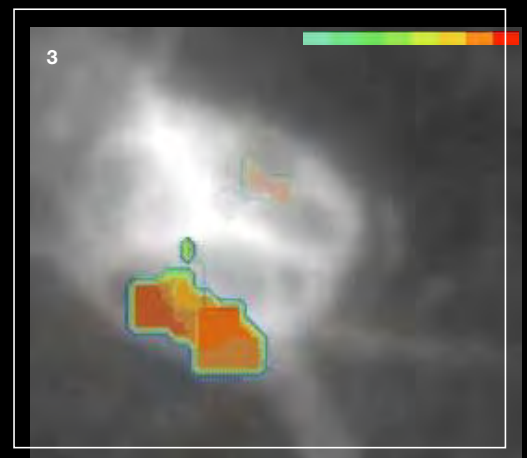
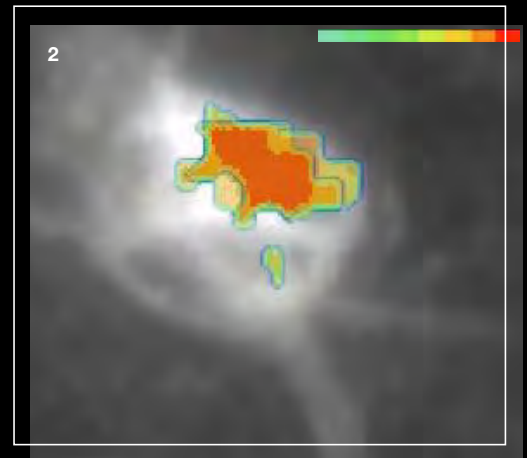
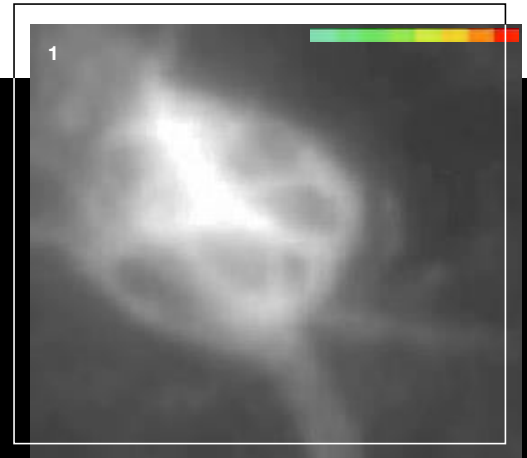
At the end of the 1990s, his staff developed an alternative. They adapted the method of neuroimaging in such a way that it could also be used in the intestines. To do so, the scientists place special dyes on the nerve cell membranes, the color of which changes in a flash if the voltage changes. The change of color when the nerve is stimulated only lasts a few milliseconds and can only be detected by the human eye at ultra slow motion and high magnification. Consequently, a high-resolution camera is used to film the experiments.

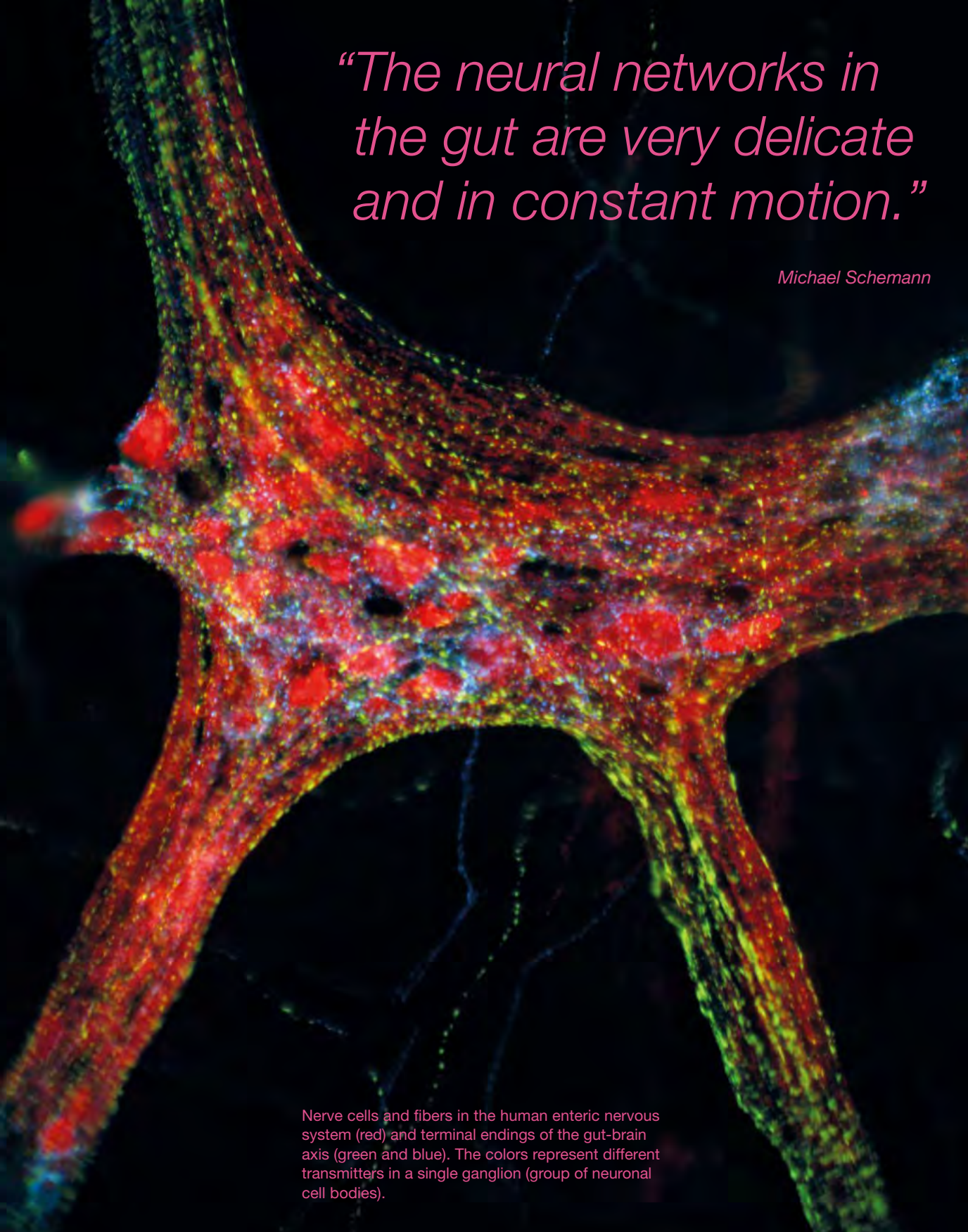
### Understanding intestinal disorders such as irritable bowel syndrome

Drawing on such methods, Schemann's group was also the first to identify the foundations for understanding intestinal disorders which are clearly related to malfunctions in the "little brain in the gut" – e.g. irritable bowel syndrome. According to estimates, ten percent of the population in this country experience puzzling, intermittent over- or under-activity in the intestines: diarrhea or constipation. Inflammation is not the cause. But what are the reasons? There is a lack of diagnosis and causal treatment.

In 2009, Schemann's team succeeded for the first time in proving that false stimuli in the enteric nervous system play a key role in this syndrome. If you bring nerves in the "intestinal brain" into contact with substances secreted from the mucosa of irritable bowel syndrome patients, this triggers a whole storm of action potentials. And indeed, we can see the occasional red flash in the videos which Schemann now calls up on the monitor. "Every red flash reflects the activation of a single nerve cell," the researcher explains. However, if the mucosal supernatants originate from healthy people, the enteric nervous system remains calm and quiet. ▶

Picture credits: Michael Schemann





*“The neural networks in the gut are very delicate and in constant motion.”*

*Michael Schemann*

Nerve cells and fibers in the human enteric nervous system (red) and terminal endings of the gut-brain axis (green and blue). The colors represent different transmitters in a single ganglion (group of neuronal cell bodies).



The search has also been narrowed down to a few possible miscreants. The neurotransmitter serotonin, the immunomodulator histamine and above all some digestive enzymes that break down protein, so-called proteases, which can stimulate nerve cells via their own receptors, occur in such volumes in patients with irritable bowel syndrome that they lead to permanent overactivity of the “little brain in the gut”. These are scientific findings that have attracted worldwide attention. However, concerted interdisciplinary cooperation is now required to ensure that we capitalize on this breakthrough. “We must combine the clinical data of many patients with such physiological tests on biopsies and intestinal specimens; then we will have a chance of developing reliable diagnostic markers and effective drugs against the disease,” Schemann believes. But as he also points out, “It will be up to others to do that work.” In less than three years, Schemann will be retiring. But as we said, the man is in a hurry to get some more ideas off his chest.

■ *Bernhard Epping*



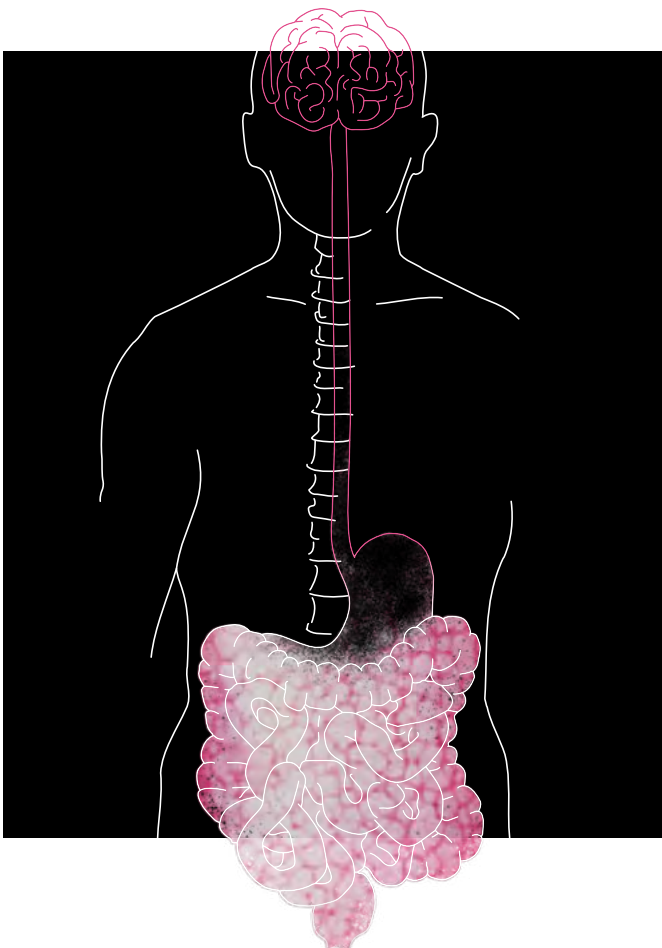

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#### Prof. Michael Schemann

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Michael Schemann was born in Cologne in 1956. Identifying as a genuine native of the Rhineland, he studied agricultural biology in Stuttgart-Hohenheim – and obtained his doctorate there in 1985. As from 1989, this was followed by three postdoc years at the Ohio State University in Columbus, Ohio, USA. It was then and there that Schemann encountered the guru of research into the enteric nervous system: Jackie Wood. His habilitation in Hohenheim in 1990 was followed by two years at the MPI for Physiological and Clinical Research in Bad Nauheim, and in 1994 Schemann moved on to the University of Veterinary Medicine Hannover. Since 2002, he has held the Chair for Human Biology at TUM in Weihenstephan. Michael Schemann has won numerous prizes for his work. He is married and has one daughter.

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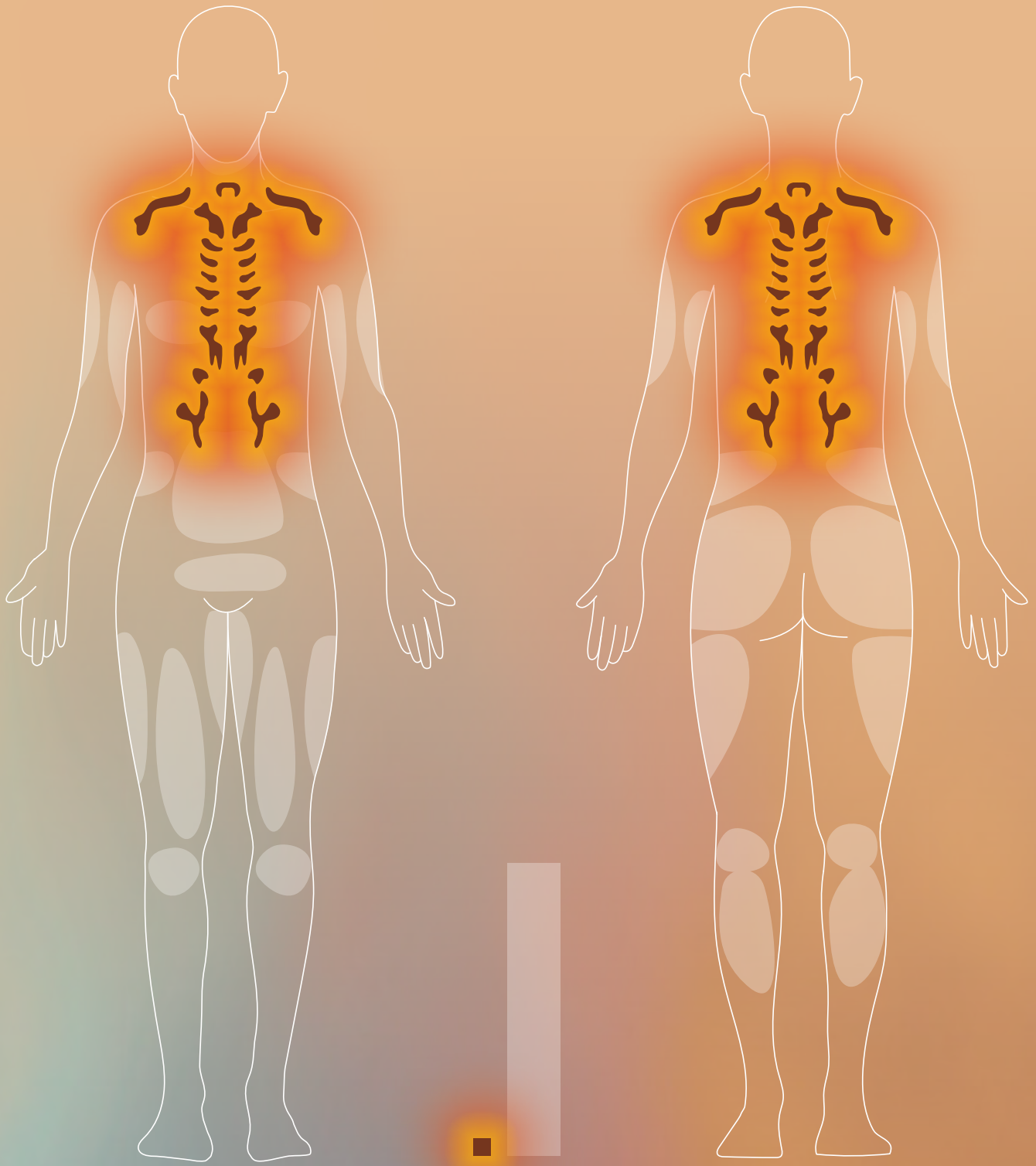
The autonomous “little brain in the gut” is connected to the brain in the head via the spinal cord as well as the vagus and pelvic nerves, and can exchange information.

Link

[go.tum.de/671324](https://go.tum.de/671324)

# The fat that makes you slim?

**Brown adipose tissue can produce heat without making our teeth chatter. But this natural “thermal jacket” has a further use: It tells the brain when we’ve had enough to eat. Does this offer a new approach to the treatment of overweight and obesity?**



**Humans have an average of 300 grams of brown adipose tissue.** This tissue is to be found on the neck, collar bones, along the spine and near the kidneys. In contrast to white fat, of which a normal male adult has around 15 kilos, this brown tissue makes an active contribution towards generating heat.

**A**fter feasting comes the hot flush. When the pork roast has been polished off, the last drops of sauce licked from the spoon and the final crumbs of cake consumed, most people start to feel warm. Because eating also means work for our bodies. But that is apparently not the only reason. The second seems to be our brown adipose tissue. This special type of fat can heat up the organism without making our teeth chatter. With this function, it acts like a thermal jacket. It's thanks to brown fat, for example, that small rodents foray out in search of food even when temperatures are far below zero and still maintain their body temperature. For a long time, scientists assumed that only babies and small mammals possess this special kind of fat. But that is not the case. "Almost 20 years ago, it was discovered that adults also still have small deposits of

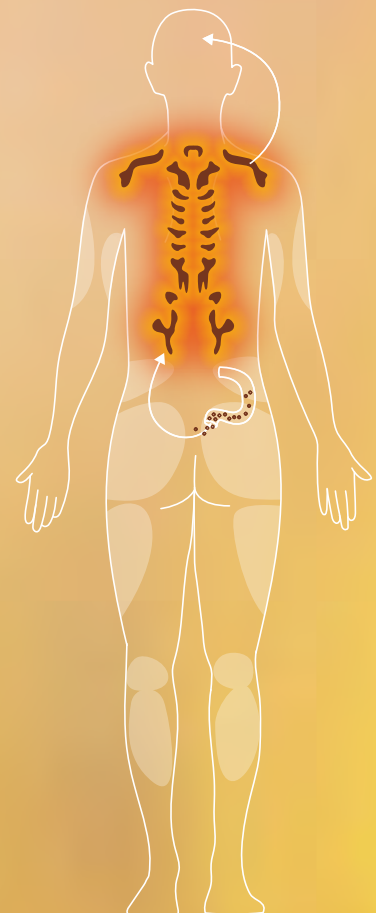
brown adipose tissue," explains Prof. Martin Klingenspor from the Chair for Molecular Nutritional Medicine at TUM's Else Kröner-Fresenius Center.

Initially, the decisive clues did not come from researchers studying the human metabolism, but oncologists looking for metastases in their patients. In this nuclear medicine process, radioactively marked glucose molecules are injected into the bloodstream. As cancer cells have a special predilection for sugar, they consume particularly large amounts of these energy-rich compounds. This can be detected with so-called PET-CT scans.

Doctors noticed that it was always the same regions which lit up in their images even with very different patients. In the neck area, above the collar bones and along the spine, occasionally around the kidneys. Could so many patients really have developed tumors in exactly the same places? That seemed unlikely. In 2009, three studies established beyond doubt that these tissues were active brown adipose tissue.

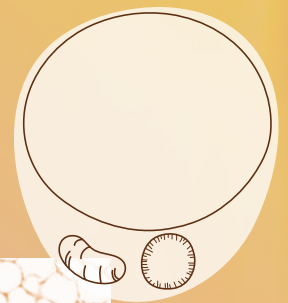
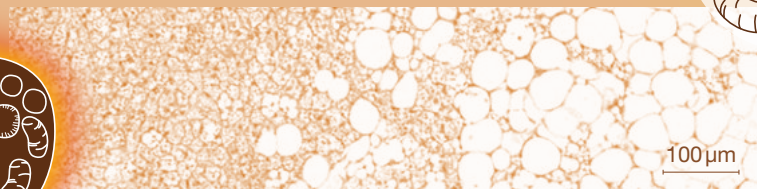


**What Martin Klingenspor and his team discovered:** During a meal, the cells of the duodenum produce the hormone secretin. It circulates through the bloodstream, docks onto receptors on brown fat cells and activates them: the tissue heats up. Special nerve cells in the brain register this rise in temperature, and trigger a feeling of satiety.



*“The brown adipose tissue plays a central role in the communication between the gut and the brain.”*

Martin Klingenspor



In a white fat cell (right), the lipid droplet in which the fat is stored takes up almost the whole cell. Brown fat cells (left) have several lipid droplets that store less fat and also many mitochondria which are responsible for the high metabolic activity of these cells.

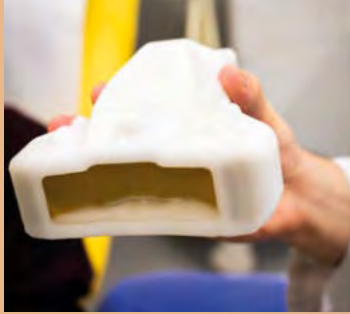
### Overweight individuals have scarcely any brown adipose tissue

Older people or individuals suffering from diabetes or obesity had less or even no more brown adipose tissue that could be activated. It hasn't been clarified yet whether there is a causal connection or the loss is only a side effect of the disease. But since this discovery, there have been an increasing number of clues indicating that this thermal jacket also plays a very important role in our energy metabolism. Martin Klingenspor is driven by the following question: Can brown fat perhaps help to treat diabetes or obesity?

To understand how that might be possible, we first have to know that brown adipose tissue not only looks different but also has different tasks to white adipose tissue. Our body stores energy in this white adipose tissue for times when food is scarce. An average adult man carries about 15 kilos of white adipose tissue around with him, mainly in the abdomen, legs and hips.

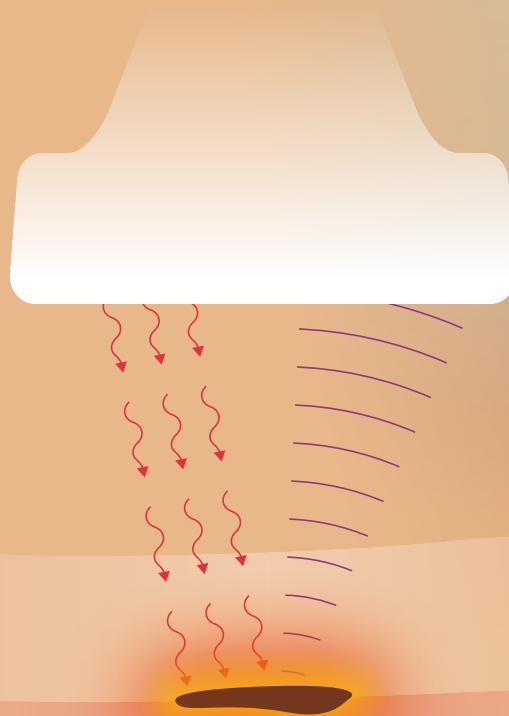
Brown fat, on the other hand, is much rarer, as every one of us has no more than an estimated 300 grams of such tissue. It is activated by cold when neural pathways in the brown adipose tissue leading from the brain release increasing quantities of the neurotransmitter noradrenalin. As a result of this stimulus, the cells begin to absorb and break down fatty acids and glucose as fuel from the blood. In contrast to all other tissues, however, the mitochondria, our cellular power plants, do not produce the molecule adenosine triphosphate (ATP), the universal source of energy. Instead, the energy is released directly in the form of heat. The blood heats up as a result and with it the whole body. Scientists refer to this process as thermogenesis, a specialist discipline of brown adipose tissue. If we spend time in a cold environment, our energy metabolism rises considerably as a result. Slender and slim from freezing? Possibly. But not pleasant. ▶

Thanks to an invention by Prof. Vasilis Ntziachristos, researchers can now more easily make brown adipose tissue visible.



#### Laser and ultrasound in a single device

In “multispectral, optoacoustic tomography” developed by Ntziachristos, infrared laser pulses are beamed into the tissue. They heat it up locally, thereby generating ultrasonic waves that are shown on the computer as images.



This handheld device, placed on the skin, can measure the oxygen content in the underlying veins, thereby detecting increased activity.

### Brown fat signals: satiated

Martin Klingenspor has discovered a further path by which brown adipose tissue can be activated: food intake itself. At a molecular level, this works as follows: Shortly after the beginning of a meal, the cells of the duodenum produce the hormone secretin. This stimulates the pancreas to change the pH level in the gut in such a way that the digestive enzymes can work to optimal effect. But that's not all.

Secretin circulates through the bloodstream, docks onto receptors on brown fat cells and activates them. The mitochondria work to their fullest capacity, and the tissue heats up. Special nerve cells in the brain register this rise in temperature, thereby prompting a feeling of satiation. "The brown adipose tissue plays a central role in the communication between the gut and the brain," Martin Klingenspor explains.

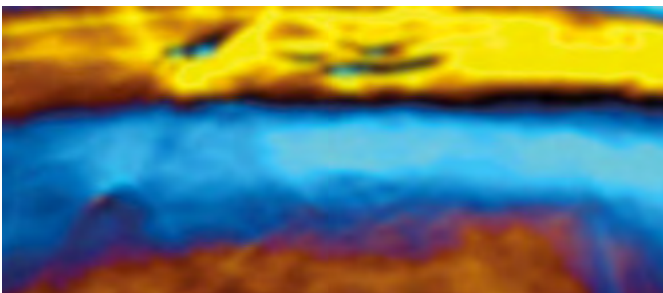
Exactly how the brain registers the activation of the brown adipose tissue is still to be researched. "Our pet hypothesis is that its activation first heats up the blood and then direct-

ly warms the brain," states the metabolism researcher. Two further approaches, however, are also conceivable, he concedes. On the one hand, it is possible that after activation, the brown adipose tissue releases its own neurotransmitters, called batokines, into the blood which reach the brain through the bloodstream. On the other, so-called afferent nerve fibers could transmit the information from the brown adipose tissue to the brain. "We're conducting our first experiments in the lab right now in order to confirm or disprove this theory," the scientist reports.

Through his discovery, the biologist has somewhat shifted the discussion of the significance of brown adipose tissue. Previously, everything had revolved around the question of whether the small amount of this tissue could in any way be sufficient to significantly alter the energy management of an organism by its activation. But since it has become known that it is involved in triggering feelings of satiation, it is now clear that large amounts may not even be needed. ▶

*"Our pet hypothesis is that this activation first heats up the blood and then directly warms the brain."*

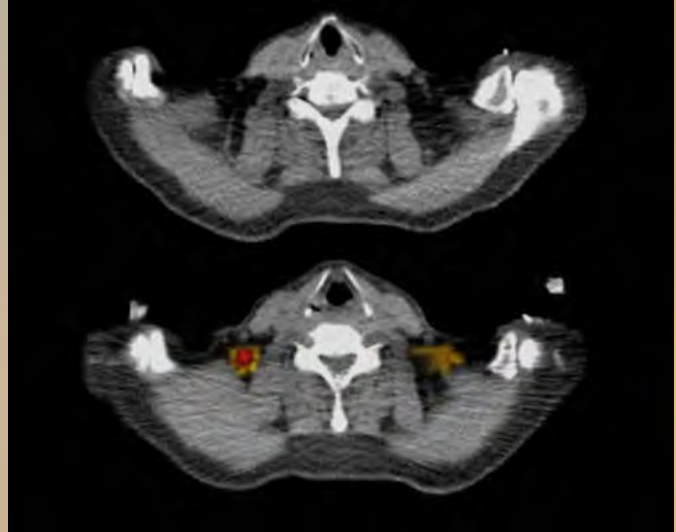
*Martin Klingenspor*



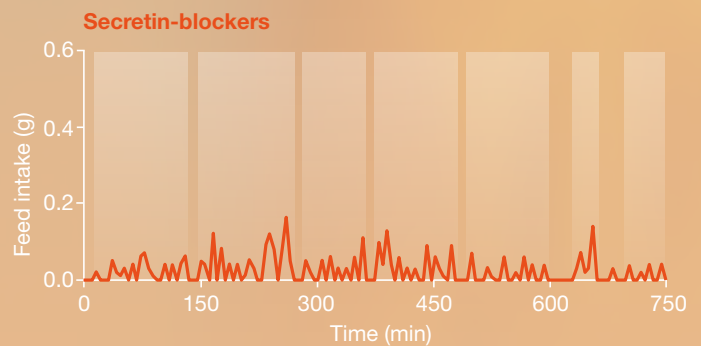
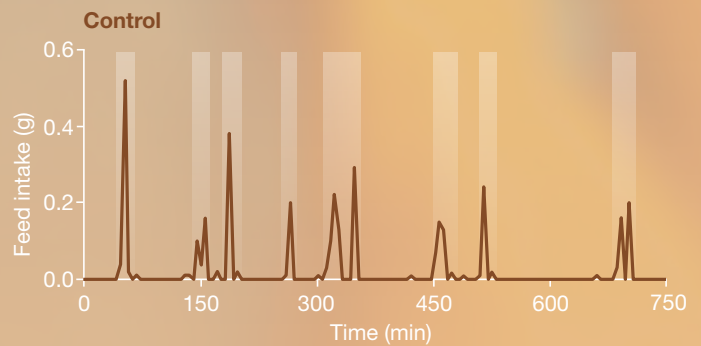
The ultrasonic images thereby created, shown here in false colors, indicate the brown fat layer.



The effect of secretin on the cellular respiration of brown fat cells is examined in a respirometer.



The increased absorption of glucose by the brown adipose tissue, stimulated by secretin, can be shown by modern imaging technologies (above without, below with).



**Mice did not become slimmer**

In mice, secretin affects the number, size and length of meals. The total energy intake, however, remains the same. If the effect of the secretin is blocked by an antibody, the mice eat significantly larger portions but in fewer meals. These are marked here by the lightly shaded areas. We can see that the rodents take in exactly the same level of energy as they did before.

Could a secretin pill that makes you feel satiated soon be on the market as a new slimming aid? No, it's not that simple. Nocturnally active, mice eat around ten times per night. Secretin certainly affects the number, size and length of these "meals". The long-term energy intake remains unchanged, however. When the effect of secretin was blocked by means of an antibody, the eating habits of the mice changed. They ate significantly larger portions in altogether

fewer sessions. The result, however, was that in the course of the whole day, their energy intake was exactly the same as before.

The reason is that from an evolutionary perspective, the regulation of our energy reserves has a major impact on our survival. "That is why there's more than one mechanism controlling the balance between energy intake and consumption," Martin Klingenspor explains. "There are multiple



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**Prof. Martin Klingenspor**

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Klingenspor studied biology at the Philipps University in Marburg. In 1994, the scientist obtained his doctorate in the field of animal physiology. After a research stay at the Lipid Research Laboratory in Los Angeles, USA, Martin Klingenspor returned to Marburg and became Assistant Professor for Animal Physiology. His habilitation followed in the same discipline in 2001. Klingenspor remained in Marburg for a further five years before moving on to TUM as Professor of Molecular Nutritional Medicine in 2007. The aim of his research is to find out how the body establishes a balance between food intake and energy consumption.

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back-up systems just as with any technical system. And we have to expect our body to resist any intervention.” That means if we consume more energy by activating our brown adipose tissue, we may also feel hungrier and eat more.

This research may also be advanced thanks to an invention by Vasilis Ntziachristos, Professor for Biological Imaging at TUM. He has developed so-called multispectral, opto-acoustic tomography, a kind of ultrasound with laser light. Thanks to this method, researchers can now make brown adipose tissue visible without relying on a biopsy or radioactively labeled substances. Initial tests on mice and humans have shown promising results.

Martin Klingenspor now wants to find out what happens when secretin receptors in the brown adipose tissue are deactivated. This can quite easily be accomplished in mice by genetic engineering. “The metabolic activities in mice and humans are very similar, and we can derive genuinely good information from the mouse model for humans and make faster progress,” the biologist explains. In such a mouse, you would not expect secretin to trigger any further feeling of satiation.

**A miracle pill is still a distant prospect**

He is also tracking down further activators of the brown adipose tissue. For example, Klingenspor intends to investigate the influence of the adrenocorticotrophic hormone ACTH. So far, ACTH is known to stimulate the release of the stress hormone cortisol. But brown fat cells also have numerous ACTH receptors. What’s their purpose? Hopefully, that will be revealed in the next few years.

In spite of all the groundbreaking innovations, we cannot expect a miracle pill for metabolic diseases anytime soon. “So far there have only been a few pharmacological therapies for obesity, and none of them relies solely on one drug,” Martin Klingenspor says. People should still change their lifestyle, eat more healthily and play more sport in order to keep their weight in check. But it looks as if brown adipose tissue may be able to support this process.

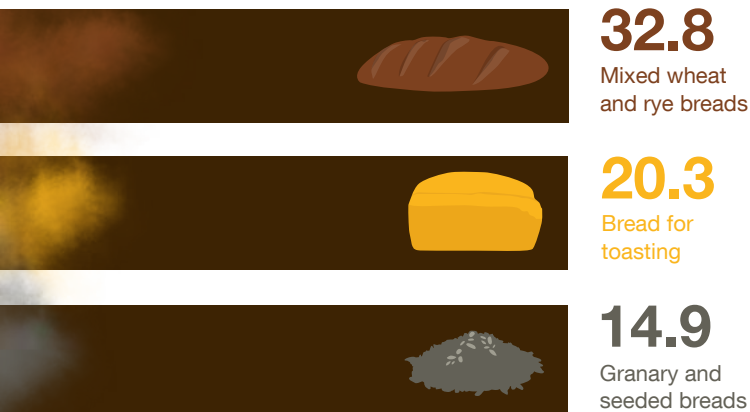
■ Claudia Doyle

*“We will be able to produce  
baked goods with com-  
pletely new characteristics.”*

*Mario Jekle*



The most popular bread types in Germany in percent (in 2017)



# Bread from the printer

**What gives bread its bite? What are the processes that create a crunchy crust and lend a loaf its soft crumb? Using a 3D printer, TUM researchers are unlocking the secrets of baking bread and paving the way for fast, flexible production in the future.**

**F**or thousands of years, man has baked bread. And there are thousands of different recipes and methods of doing so. They are all based on combining water and flour – starch and proteins – before fermenting the mixture and heating it in an oven. This transforms the dough into a fragrant loaf with a soft crumb and crunchy crust. But why does this happen?

“To this day, we still do not fully understand the complex processes involved in baking,” says Dr. Mario Jekle of the Chair of Brewing and Beverage Technology at TUM, which is headed by Prof. Thomas Becker. Several dozen parameters influence the outcome – including the composition and particle size of the ingredients, the ability of the proteins to polymerize and the volume of water added, as well as process parameters such as the temperature of the oven.

In their laboratory at the TUM School of Life Sciences, Jekle and his team examine the interactions between these factors. “To do this, it is important not to bake under standardized conditions; instead, we have to decouple the processes,” emphasizes food technologist Jekle. “In a conventional oven, this isn’t possible. That’s why we use 3D printing technology.”

At the moment, the new process is only capable of baking small bread rolls hardly larger than a sugar cube. Nothing in this process, however, is left to chance: Every ingredient is chemically analyzed and weighed before being kneaded with water into a sort of dough in a miniature mixer. The printer then turns this dough into bread – without using yeast or any other leavening agent and without waiting a long time for the bread to rise.



The researchers have been working to investigate the printability of dough and optimize the process for three years. “Applying the dough evenly represented a major challenge: The tough, elastic mass of flour and water needs to be squeezed through a funnel, the deposition, without the narrow opening of barely a millimeter wide becoming blocked,” explains Jekle, the Head of the Chair’s Cereal Technology and Process Engineering research group.

Over time, the researchers have perfected the system. As the print head whizzes back and forth, it produces thin threads of dough, placing new threads beside the last, until an area of 1 square centimeter has been covered. A laser beam then scans the layer of dough, with its heat ensuring that the proteins combine and create a stable structure. Once this “transformation” is complete, the print head places the next layer on top – leaving spaces for pores to form. After 5 minutes, the bread cube is finished. The researchers have already printed hundreds of these miniature bread rolls.



**To date, the 3D printer** has only baked very small bread rolls; however, it makes it possible to guarantee the same baking conditions each time and decouple the individual processes. Mario Jekle (in the background) and his team have optimized the process.



**The characteristics of a loaf of bread** depend on its ingredients, the ability of the proteins to form networks, and the baking temperature. Jekle and his team analyze crust and crumb at their bread research lab.

Every cube is different and contains different proportions of starch and proteins, different pore sizes, and are heated to a greater or lesser degree to create the crusts and crumb. Jekle's team measures the compressive strength, moisture loss, weight and porosity of each cube. The samples are sent to the TUM Chair of Food Chemistry and Molecular Sensory Science for analysis of their fragrance and taste. Joining forces, the research teams now hope to examine the extent to which porosity and flavor release are interrelated. Jekle plans to use the results to develop a mathematical model that can depict the baking process. Simulations will enable the examination of issues such as how a bakery can achieve the best results with the lowest energy input, as Jekle explains: "To do this, we need to model how much heat is required for the structure to stabilize."



The 3D printing technique also opens up new possibilities in terms of product development: "In a few years, there will be bread printers for domestic use and small bakeries, as well as for clinics that need to comply with dietary requirements," predicts Jekle. "We will be able to produce baked goods with completely new characteristics – with soft exteriors and crunchy pieces of crust on the inside, with or without certain proteins. Production in 3D printers makes it possible to adapt to the customer's wishes quickly and easily."

■ *Monika Weiner*

Link

[www.bina.wzw.tum.de](http://www.bina.wzw.tum.de)



# Enjoying apples without regrets

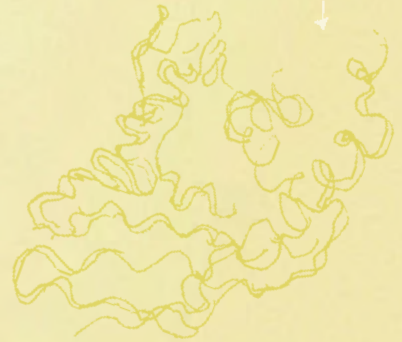


Deep-frozen samples of newly bred apples such as these form the basis of the analyses in Wilfried Schwab's laboratory.

Mat d 1  
23.9.17



Mat d 1



Picture credits: Magdalena Jooss, Arne Dierend;  
Graphics: eclundsepp

**In Germany, the average person eats almost 20 kilos of apples every year – and they're expected to be as crunchy, rosy-red and sweet as possible. More and more individuals, however, are allergic to fruit. In response to this situation, a team of researchers headed by Wilfried Schwab, Professor of Biotechnology of Natural Products at TUM, are working on a project to breed "allergy-friendly" apple varieties. If all goes well, consumers could find these varieties in stores by 2025.**



The samples come from Osnabrück. Prof. Werner Dierend, right, from Osnabrück University of Applied Sciences, shows how he selects the best apple trees and registers them on the computer for further breeding.



Prof. Dr. Werner Dierend



Mal d 1

No, there won't be apples to sample today. Emilia Romer briefly lifts up pieces of apple, chopped up into small bits and vacuum-packed in plastic film. "These are our investigation objects," she says, before immediately placing the sample back in the deep freezer. The designation P 98 10.10.2018 was barely visible on the packaging. "What you saw was an apple sample from tree 98, harvested on October 10, 2018," explains Romer. Researchers examining the biotechnology of natural substances at TUM on its Weihenstephan campus are searching for apple varieties that allergy sufferers will also be able to enjoy. Sample P 98 is one of hundreds that doctoral students Emilia Romer and Soraya Chebib are analyzing to determine the precise concentrations of a specific group of proteins known as Mal d 1 proteins. New varieties of apples suitable for allergy sufferers need to contain as little of these proteins as possible, as they are the main cause of apple allergies in Central and Northern Europe. Almost five percent of German adults suffer from such food allergies. Even the very first bite into a piece of fruit or vegetable entails the risk of itching and rapid swelling of the lips, tongue and mucous membrane of the mouth. Thankfully, highly dangerous reactions culminating in anaphylactic shock are rare.

### Completely allergen-free is not feasible

So, will the first allergen-free apples soon be on the markets? Wait a minute, not quite. Project leader Prof. Wilfried Schwab promptly warns against overly grandiose pronouncements: "We can't promise allergen-free produce. There will, however, be 'allergy-friendly' apple varieties." The research has not reached that stage yet, though, and the scientists are keeping their cards close to their chest. What they will disclose, however, is that such apples could be available in selected stores by 2025. This work is enabled by a joint project financed by the Federal Ministry of Food and Agriculture in which TUM experts are contributing the analytics. The samples are exclusively delivered by post – from Osnabrück University of Applied Sciences (HS OS) in northern Germany.

Prof. Werner Dierend, holder of the Chair for Fruit Growing and Processing, remembers that, back in 2002, fruit farmers from the Züchtungsinitiative Niederelbe association (ZIN) asked whether he could help them with new apple varieties. ZIN is an association comprising 170 apple producers and wholesalers. A number of its members had identified a need to refresh and rejuvenate the market.



### Image-boosting new varieties

“Customers want crunchy, juicy apples,” as Dierend emphasizes. What’s more, he tells us, the most common apple varieties in Germany, Jonagold and Elstar, are no longer exactly the crunchiest. Generally speaking, the apple specialist explains, new apple breeds are announced every 15 to 20 years – for marketing and image reasons, but also because years of cultivation of varieties tends to lower the quality levels. With this in mind, in 2003, Dierend launched a breeding program together with the ZIN association. The objectives? Fresh, crunchy apple varieties suitable for cultivation in northern Germany, high yields and as pathogen-resistant as possible. And all in one apple variety, if you please.

The technique to achieve this is tried and tested. By way of controlled pollination the researchers from Osnabrück University of Applied Sciences and ZIN cross selected va-

rieties whose descendants are to combine the desired characteristics of both parents. The university’s contacts from all corners of the world helped to source suitable parent varieties. Selecting the best apple trees is crucial for the subsequent F1 generation. Year after year, the apple breeders evaluate flavor, resistance and yields. In total, the program is working on around 300 crossing batches. The new varieties stand in long rows in trial fields at ZIN and the HS OS. In 2016, the breeders were able to submit an application for protection for the first new apple variety to the Federal Plant Variety Office (BSA).

Initially, the topic of allergies had not been on their radar screen at all. “It was only in 2012, when we first learned that people at TUM can measure significant apple allergens, that we included this aspect in our program straight away,” explains Dierend. ▶

*“When we learned that researchers at TUM are able to measure significant apple allergens, we included that in our program straight away.”*

Werner Dierend

The Züchtungsinitiative Niederelbe’s selection field is used to grow low-allergen apples. The best of an initial stock of trees (at bottom of image) are selected, while the others are cleared out. In the end, this leaves the mother trees for the new varieties (top center of image).



### From white strawberries to apples

Wilfried Schwab also first became involved in allergen research by a lateral route, when he had initially started tweaking aromatic substances and pigments in fruits at TUM in 2003. It was the work of biochemist Prof. Cecilia Emanuelsson at Lund University in Sweden that first prompted him to track down allergens. Starting in 2004, Emanuelsson's research group discovered that some varieties of white strawberry contain very small amounts of a protein called Fra a 1 (the name of which is derived from the scientific name for garden strawberries, *Fragaria ananassa*). They also noted that patients with strawberry allergies were often better able to tolerate white varieties – not because of the lack of pigment but due to the low levels of Fra a 1. Today, this protein is seen as the most significant allergen in strawberries. At the same time, it is a member of a family of allergens with relatives in many other plants including tomatoes, plums and cherries. Its equivalent in birch pollen is called Bet v 1 (for *Betula verrucosa*, commonly known as weeping birch). The protein in apples is Mal d 1 (for *Malus domestica*, domestic apple trees). The function of proteins in plants is just as unclear as the question of why some people's immune systems react to the members of this family of proteins in particular. The high degree of similarity between these proteins explains

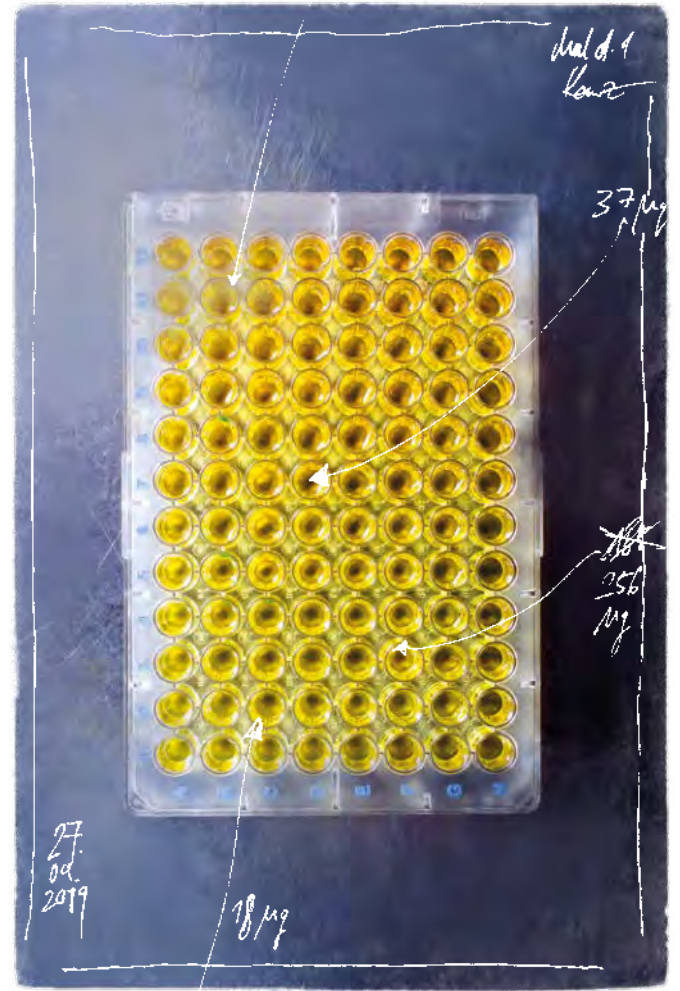
the frequent cross-reactions in food allergy sufferers. According to the current hypothesis, if a person in Central and Northern Europe has a corresponding disposition, there is a high risk they will develop a sensitization to Bet v 1 in birch pollen. From there, it is just a short step to cross-reactions with food allergies. As a result, 50 to 75 percent of the individuals suffering from birch pollen allergies in Central and Northern Europe are also allergic to apples and other fruits.

Schwab's research group has had an antibody against allergens such as Fra a 1 at hand since 2012, which it used to develop measurement methods for the entire protein group – known as ELISA (enzyme-linked immunosorbent assay). Several years ago, his team was thereby able to demonstrate that strawberries and tomato varieties differed tremendously in terms of their allergen content. This opened the door to the notion of using plant breeding to search for varieties with the lowest level of allergens possible. The project to develop "allergy-friendly" apples is one of the first to attempt to implement the concept. Since 2016, ZIN, HS OS and TUM have collaborated on the project to breed low-allergen apples, drawing on funds provided by the Federal Ministry of Food and Agriculture. Ever since, sample after sample has arrived at Romer and Chebib's lab.

The analytical work is conducted in Wilfried Schwab's laboratory in Freising. The tests examine the level of allergens the apple samples still contain.



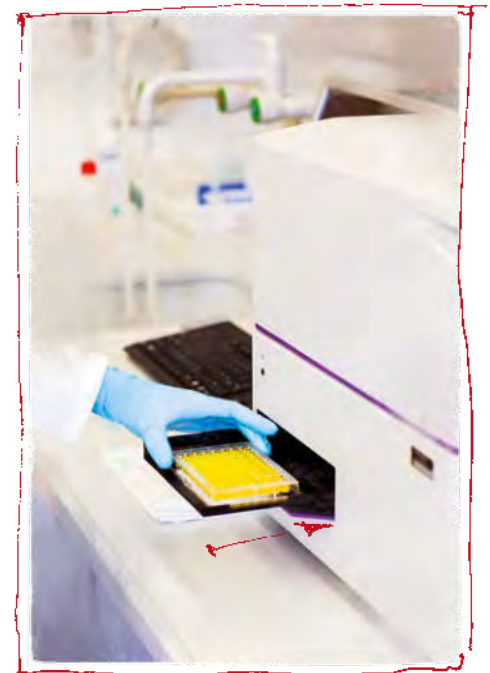
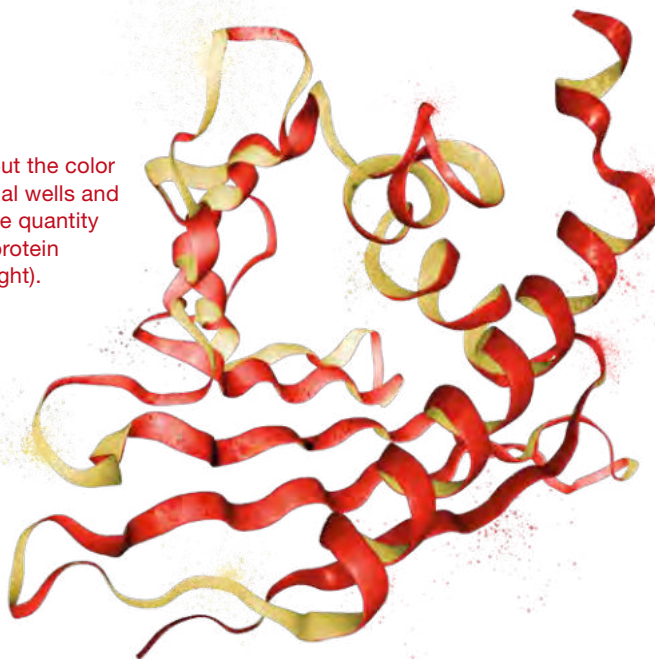
Protein Mal d 1 is then inserted in the 96 wells in micro-titer plates. The researchers then pipette extracts from the apple samples and an antibody that binds to Mal d 1.



**Predatory competition on the titer plate**

The two researchers use standard microtiter plates for their analyses. To begin with, they always insert the same, precisely defined quantity of high-purity Mal d 1 proteins in each of the 96 wells in the microtiter plate. The researchers then pipette extracts from the apple samples and an antibody that binds to Mal d 1. The antibody binds with both the Mal d 1 proteins on the plate and the proteins from the apple. This continues until a balance is reached. ▶

The machine reads out the color values in the individual wells and thereby calculates the quantity of allergen Mal d 1 (protein structure shown at right).



Graphics: ecludnsepp (based on a model in: C Seutter von Loetzen et al. (2012) NGL viewer. www.rcsb.org/structure/2LPX)  
Picture credits: Magdalena Jooss



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**Prof. Wilfried Schwab**

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Wilfried Schwab is Professor of Biotechnology of Natural Products at TUM in Weihenstephan. Born in Franconia in 1961, he studied food chemistry at the University of Würzburg and was awarded his doctorate in 1989. Following a year at the Institute of Biological Chemistry at Washington State University in Pullman, USA, Schwab spent three years working for Hoechst AG and AgrEvo in Frankfurt. He returned to the University of Würzburg in 1994 and qualified as a professor in 1999. In 2003, Wilfried Schwab accepted an endowed professorship at TUM, and some five years later, the university made his professorship permanent. While Schwab does not rule out resorting to genetic engineering in plant breeding, he advocates first using and selecting the aspects available in the current diversity of fruit and vegetable varieties. Wilfried Schwab is married and has two children.

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*Krusallergene*

Once new varieties have been admitted to the national list, allergy-friendly apples could be available in selected stores as from 2025.

*“We can’t promise allergen-free produce. But there will be ‘allergy-friendly’ apple varieties.”*

*Wilfried Schwab*

### **Tests on subject groups**

It doesn’t take a genius to predict the people who might be suitable candidates to test some of the latter apples. Wilfried Schwab, however, continues to warn against oversimplification. He asserts that we know the Mal d 1 content does not allow us to draw definitive conclusions on the allergic reaction risks in each individual case. This is because there are dozens of protein variants related to Mal d 1, which can often appear in different quantities in different varieties of apple. It is also apparent that patients can experience very individual reactions to only specific variants. The antibody test in the TUM lab generally records all variants as a total value – but does not say anything about the proportions in which the different variants appear.

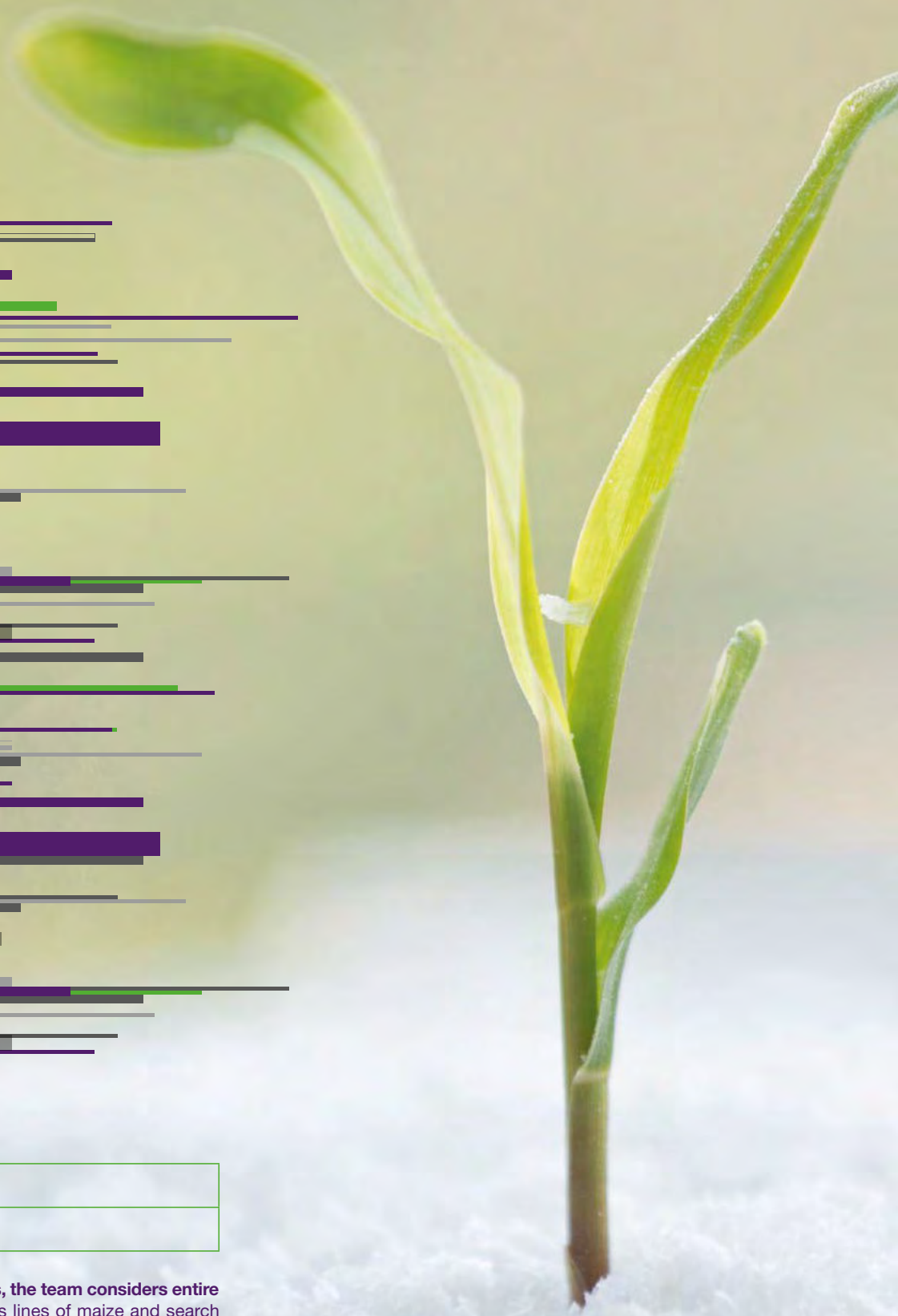
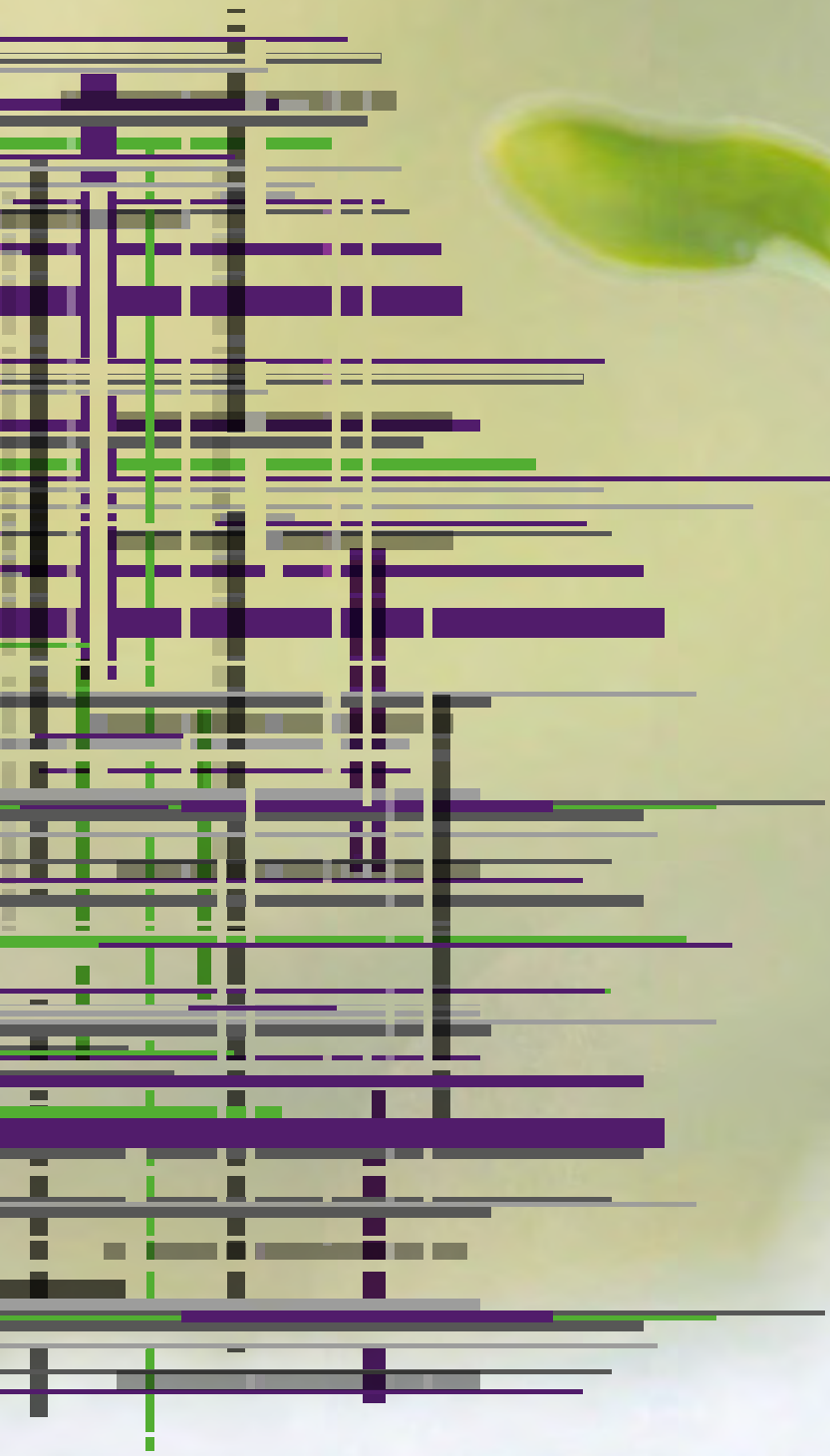
The final stage of the project is therefore testing on subject groups; since 2018, these subjects have regularly attended the Allergy Center at Berlin’s Charité hospital (Prof. Karl-Christian Bergmann) to eat apples from the breeding project with a low Mal d 1 content. The subjects are asked to eat 30 grams of apple and note down whether they experience allergic reactions and, if so, how severely. If the first sample is tolerated, they retry with 100 grams and record the results once again. This data will show which new apple varieties are the most “allergy-friendly” for as many allergy sufferers as possible.

That is to say, in Northern and Central Europe. That’s because a separate research project would have to be carried out for Southern Europe. The whole protein group of Mal d 1 & co. is not of any major significance for food allergies in that region. The assumed reason for this? Birch trees are fairly rare in Spain and Italy, so there is no incidence of initial sensitivity to birch pollen and subsequent cross-reaction to Mal d 1 & co. While there are also many people with food allergies in Southern Europe, they are responding to different proteins. That, however, is a story for another day.

*Bernhard Epping*

The decisive factor: The more Mal d 1 an apple sample contains, the more antibodies attach to these molecules. In the end, a color reaction quantifies the number of remaining antibodies. In this way, the researchers are able to calculate how much Mal d 1 an apple contains. All this involves painstaking manual input – pipetting and washing, buffering and coloring. “Each titer plate takes us several hours to process and allows us to analyze twelve samples,” reports Chebib. The last step is quite fast, with a machine reading the color values of all 96 wells on the plate and the computer converting everything and reporting: The sample from tree P 98, collected on 10.10.2018, contains ... well, so what exactly?

No, the researchers are not ready to disclose any precise findings just yet. They do offer an overall insight, however, namely that the variability in the new varieties is enormous. The values recorded can differ by a factor of 400 – to put this in context, this means that while some might contain 40 micrograms of Mal d 1 per gram of fresh apple, others may contain as little as 0.1 micrograms.



Link

[plantbreeding.wzw.tum.de](http://plantbreeding.wzw.tum.de)

**Rather than analyzing individual genes, the team considers entire DNA profiles.** They compare numerous lines of maize and search their profiles for patterns to which beneficial characteristics can be assigned.



# Intelligent plant improvement: Searching for the needle in the haystack

The genes responsible for different characteristics of plants make up a complicated puzzle that, to date, researchers have had little success solving. Prof. Chris-Carolin Schön's interdisciplinary team at the TUM School of Life Sciences in Weihenstephan is using machine learning methods to analyze millions of combinations. This is an effort to find the best genes for particularly efficient, productive maize plants.

**A**re you looking for a stylish ceiling light for your living room? Perhaps you're interested in e-bikes, smartphones or exciting audiobooks? For every search request a user makes, their web browser lists a wide selection of suitable products, often accompanied by the note: "Customers who viewed this item also bought ...". The recommended items are usually exceptionally well suited to the user's preferences. This is enabled by collecting millions and millions of search requests and comparing them with Internet users' personal details – from their shoe size and place of residence to their last holiday destination. Mathematical algorithms search in this gigantic data pool for prominent associations and make use of recurring patterns. This makes it possible to research and influence customers' buying behavior.

"We work with similar mathematical models to forecast the characteristics of future plant varieties," explains Chris-Carolin Schön. The Professor of Plant Breeding conducts research on key crops, such as maize and sunflower, at the TUM School of Life Sciences in Weihenstephan. "We want them to thrive and produce high yields, also in an era of climate change," emphasizes Schön. "We need robust varieties adapted to the respective climate to secure food supplies for a growing global population and, in doing so, to keep the use of water, energy and agrochemicals as low as possible."

Maize is one of the world's most important crops for the production of food, animal feed and fuel. Cultivating maize in Europe entails certain challenges.

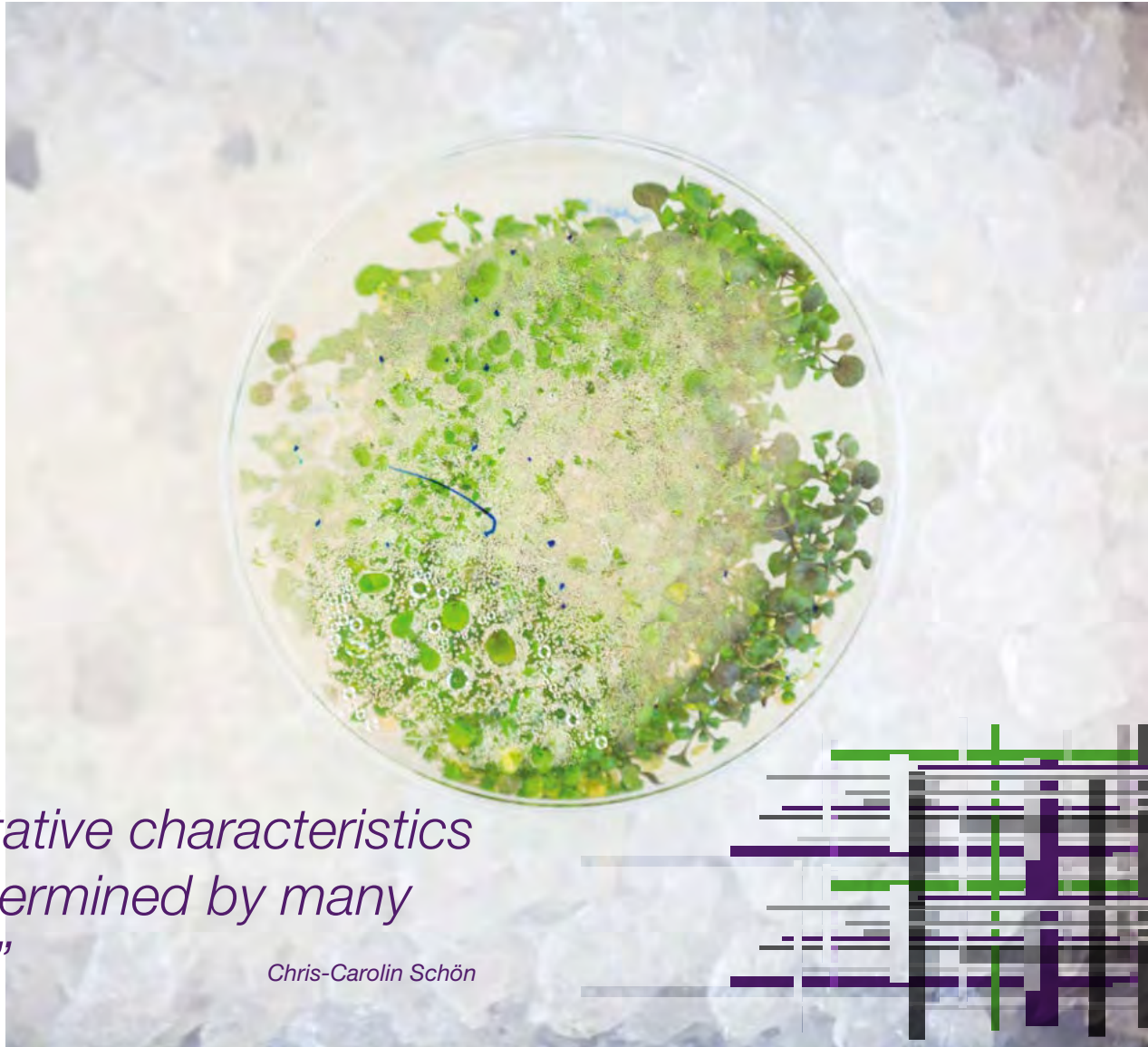


**Starting from regionally adapted maize landraces, the researchers have produced almost a thousand lines for genetic analysis.**

**When analyzing young plants, the team measures cold tolerance and early development of each maize line – important characteristics for environmentally friendly cultivation.**







*“Quantitative characteristics are determined by many genes.”*

*Chris-Carolin Schön*

**Chris-Carolin Schön and her team** not only analyze maize but also other important crops, such as rye and sunflower.

Picture credit: Tom Freudenberg/TUM; Graphics: edlundsepp

Maize is planted late in spring and develops slowly due to high temperature requirements, bearing the risk of soil erosion, nutrient depletion and the need for herbicide treatment. In addition, young maize plants can easily become overrun by wild herbs, which necessitates the use of herbicides. “We can address these challenges with new, cold-tolerant varieties that develop more quickly at the beginning of the vegetation period and allow farmers to plant earlier,” explains Chris-Carolin Schön.

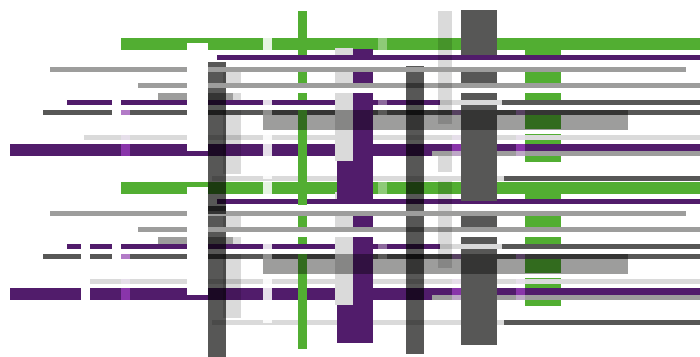
The geneticist points out that this work also relates to changing the flowering time: “To avoid drought stress over the summer months, the plants should flower early – but not too early, because that would have serious impacts on yield. Finding the optimum is complicated.” ▶



The development of young plants, their robustness, their flowering time and their yield are typical quantitative characteristics. This means the trait values follow a continuous distribution and it is difficult to distinguish between slow and fast development, robust or fragile plants, early or late flowering, high or lower yield. However, it remains unclear which genetic factors control the manifestation of these characteristics. “We are increasingly coming to realize that quantitative characteristics are determined by a very high number of genes in complex interactions. This is why, instead of analyzing individual genes, we analyze entire DNA profiles. We’re comparing the profiles of as many different maize lines as possible, looking for patterns to which we can assign beneficial characteristics,” explains Chris-Carolin Schön.

When it comes to characterizing plant traits, the same principle applies as in forecasting customer preferences: the larger the dataset, the more precise the predictions. In the course of their work, the scientists started with three maize landraces to produce almost a thousand lines. Leaf samples from each of these lines were sent to a specialized German laboratory that produced extensive DNA profiles. “We now know the genetic makeup at 600,000 positions along the genome of each and every line,” explains Armin Hölker. The doctoral student became familiar with plant breeding methods during his Master’s thesis. He now works on genetic data in Chris-Carolin Schön’s laboratory to identify the optimal model for predicting the genetic values of maize lines.

“The task is to predict what contribution each individual genetic component can make to the crop’s yield or to other relevant characteristics,” outlines Armin Hölker. To make this prediction, he not only needs DNA profiles but also measurements on the phenotype of as many maize lines as possible. For this reason, a total of over 80,000 plants has been planted from all these genetically characterized maize lines at TUM’s research station in Roggenstein.



Similar trials have been implemented at ten other sites from northern Germany to northern Spain. Once the seeds germinated, Armin Hölker and his colleagues had their hands full, as he explains: “We measured the cold tolerance and early development of young plants as well as further agronomic characteristics such as flowering time, maturity, yield and maximum plant height.”

This comprehensive set of measurement data, combined with the associated DNA profiles for every maize line, formed the data matrix for Hölker’s statistical model. He uses statistical methods to identify which DNA profiles are associated with high yields, faster development of young plants, and other quantitative characteristics. The doctoral student refers to this process as “training”. This is because the model “learns” from comparing genetic data with the phenotypic data obtained from field experiments and matches them as precisely as possible. In the next step, the model has to examine the DNA profiles of maize lines with unknown phenotypes. This is precisely the objective of the task: The intelligent prediction model should make the need for trait measurements, an expensive and time-consuming task, obsolete. “This means that, in future, we will be able to examine thousands of unknown maize lines using only their genetic data to see whether they could lead to new maize varieties better suited to their environment. This will save time and money,” explains Armin Hölker. ▶

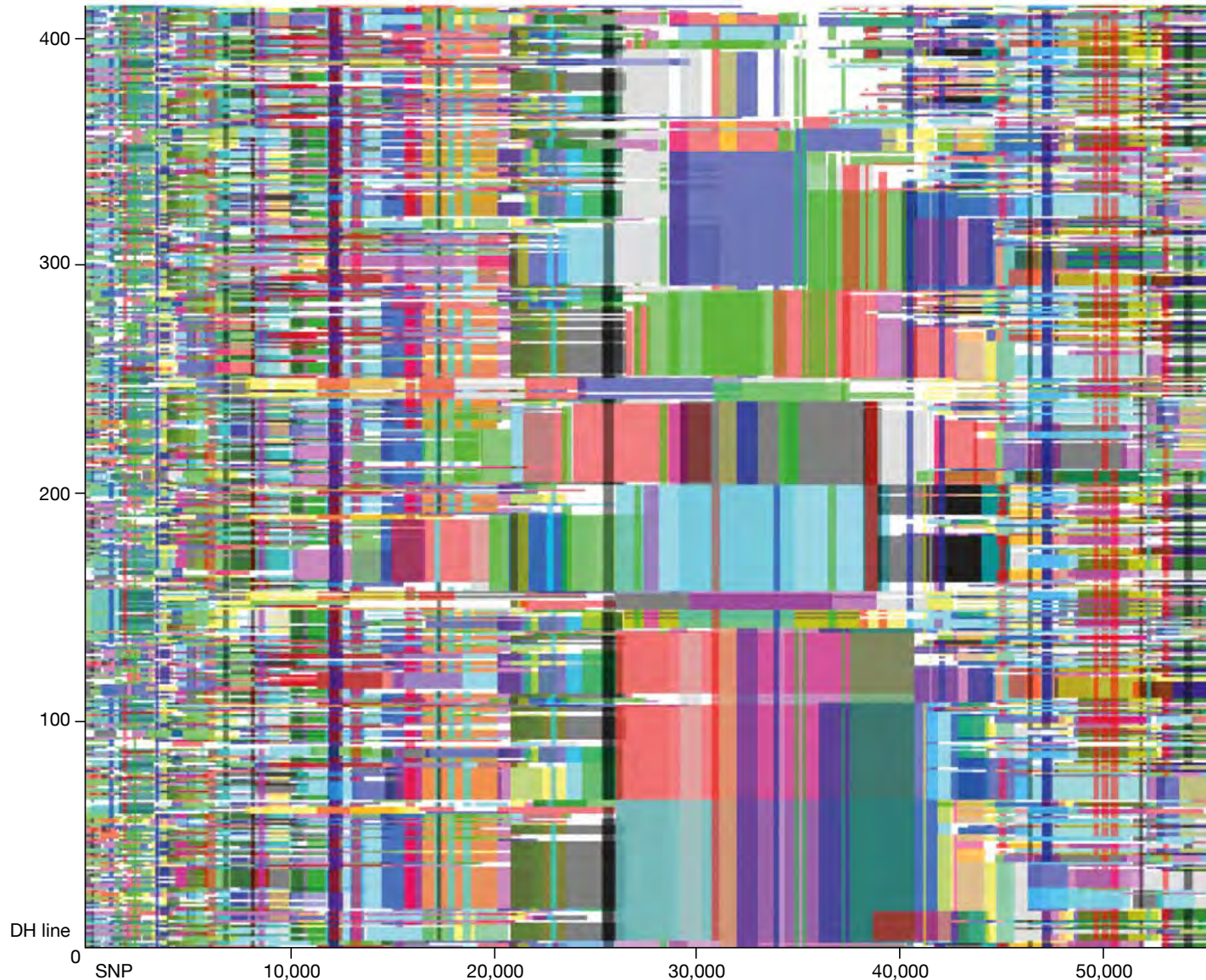
◀ **At TUM’s Roggenstein research station,** more than 80,000 plants were planted to check the appearance of each of almost 1,000 genetically characterized maize lines.

### Genomic selection: Overall picture at a glance

The maize genome consists of 2.3 billion DNA compounds known as nucleotides distributed over ten chromosomes. Only a fraction of these nucleotides form the coding units we call genes. The vast majority do not have any coding function, at least from what is known to date.

Nevertheless, these nucleotides can also be used to predict specific plant characteristics. Their overall combination and sequence forms a specific pattern in every maize line that separates it from all others. The image below depicts more than 70,000 genomic markers (horizontal axis) from a maize landrace represented by 409 individual lines (vertical axis) and shows chromosome 1 (in total, maize has 10 chromosomes).

If the nucleotide pattern of a particularly productive or drought-tolerant maize line has been identified, it is highly probable that plants with a similar pattern will be similarly productive or drought-tolerant. Consequently, these patterns alone make it possible to detect lines that possess the desired characteristics when selecting among a high number of plants with unknown phenotypes. The benefits of this process – known as genomic selection – are clear: It allows us to differentiate between productive and less productive plants and to select the more useful strains without the need to assess their appearance in field experiments.



The extensive training dataset of DNA profiles and phenotypic measurements is not only suited to predicting the genetic value of plants. “The great thing about it is that the same data can also help us to shed light on the genetic mechanisms underlying specific characteristics,” says Chris-Carolin Schön. “We regard maize as a model plant and work on fundamental questions that also arise with other crops: How do plants cope with drought stress? Do drought-resistant plants also grow well under optimal conditions and produce high yields?”

The insight we gain from this is of interest to all plant breeders – whether they’re on the search for new varieties of sugar beet, wheat or sunflower.” Of course, the TUM researcher adds, new plant varieties will not be able to stop climate change. Nevertheless, she believes it is immensely important to develop new varieties for sustainable production: “If we can reduce the input of nutrients, agricultural chemicals, energy and water, we’ll have made a big step forward!”

■ *Monika Offenberger*



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#### **Prof. Chris-Carolin Schön**

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Schön studied agricultural sciences at the University of Hohenheim and was awarded her Master’s degree by Oregon State University, USA, in 1990. In 1993, she received her doctorate from the University of Hohenheim and subsequently served as Coordinator for New Technologies at KWS SAAT SE. From 1996 to 2007, Schön was active as Director of the State Plant Breeding Institute at the University of Hohenheim, where she also completed her habilitation in plant breeding. She has also worked as a visiting researcher at the Molecular Plant Breeding CRC in Adelaide, Australia. Chris-Carolin Schön has held a full professorship in plant breeding at TUM since 2007; she was offered a chair at the University for Natural Resources and Life Sciences (BOKU), Vienna in 2009 and at Heinrich Heine University (HHU), Düsseldorf in 2015.

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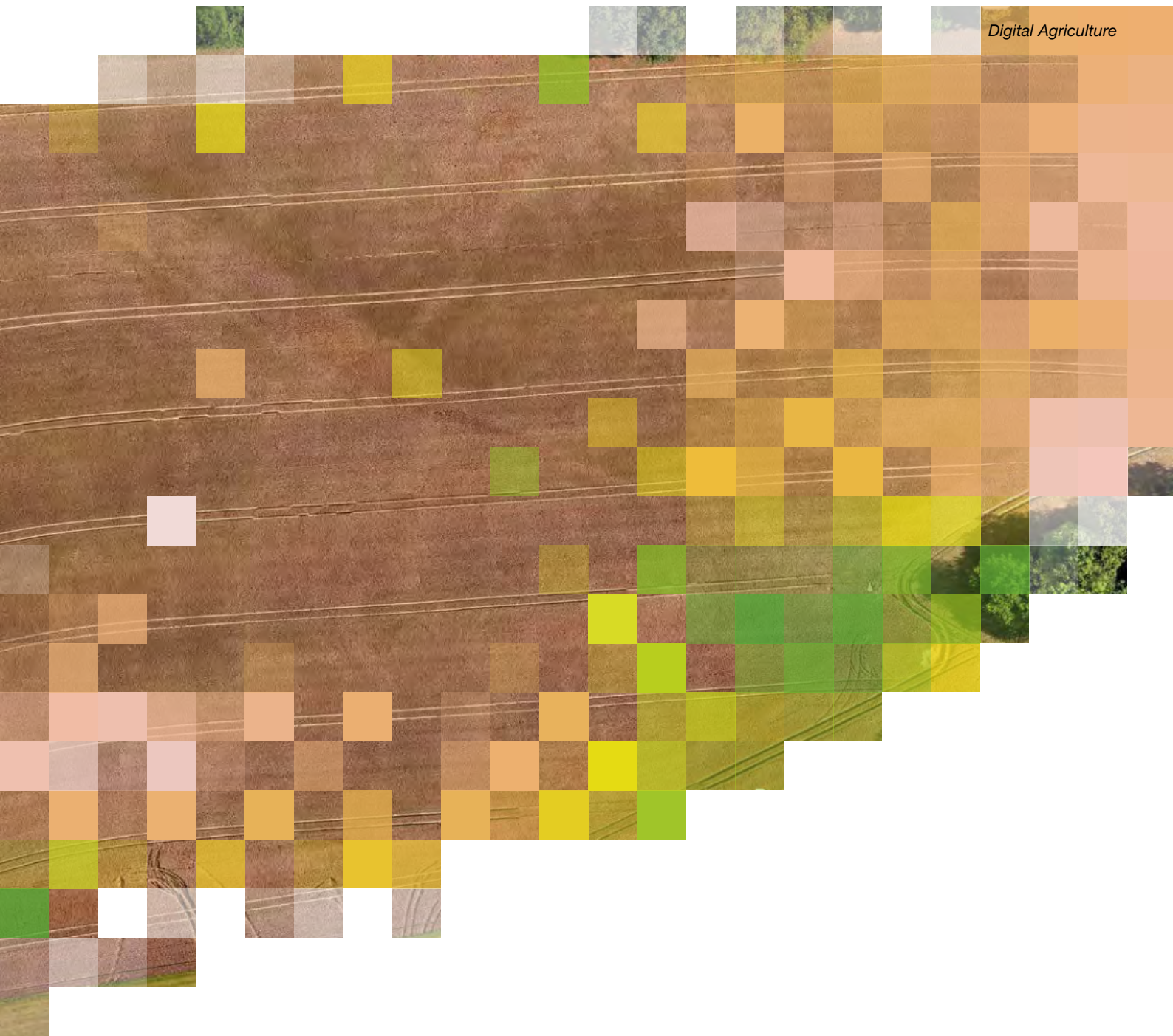
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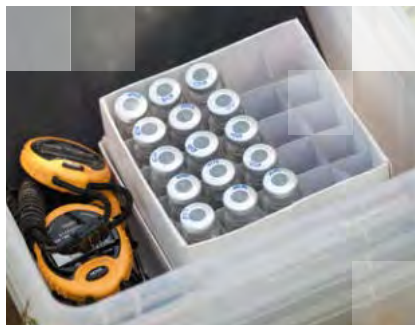
# Protecting groundwater

without compro-  
mising yields

**The Bergfeld** – a 13 ha (130,000 m<sup>2</sup>) strip of farmland at TUM's Roggenstein research station. The image shown is a yield map that depicts the different yield zones within the strip in 10 x 10 m resolution. Data was collected using sensors.



**The more fertilizer, the better? This is rarely a good idea. Good harvests depend on different factors and too much nitrogen fertilizer can contaminate groundwater. Prof. Kurt-Jürgen Hülsbergen and Dr. Franz-Xaver Maidl from TUM School of Life Sciences in Weihenstephan have set themselves the goal of giving farmers the digital tools to determine optimal fertilizer quantities. In doing so, the TUM researchers are making it possible to achieve good yields without polluting groundwater with excess nitrate.**



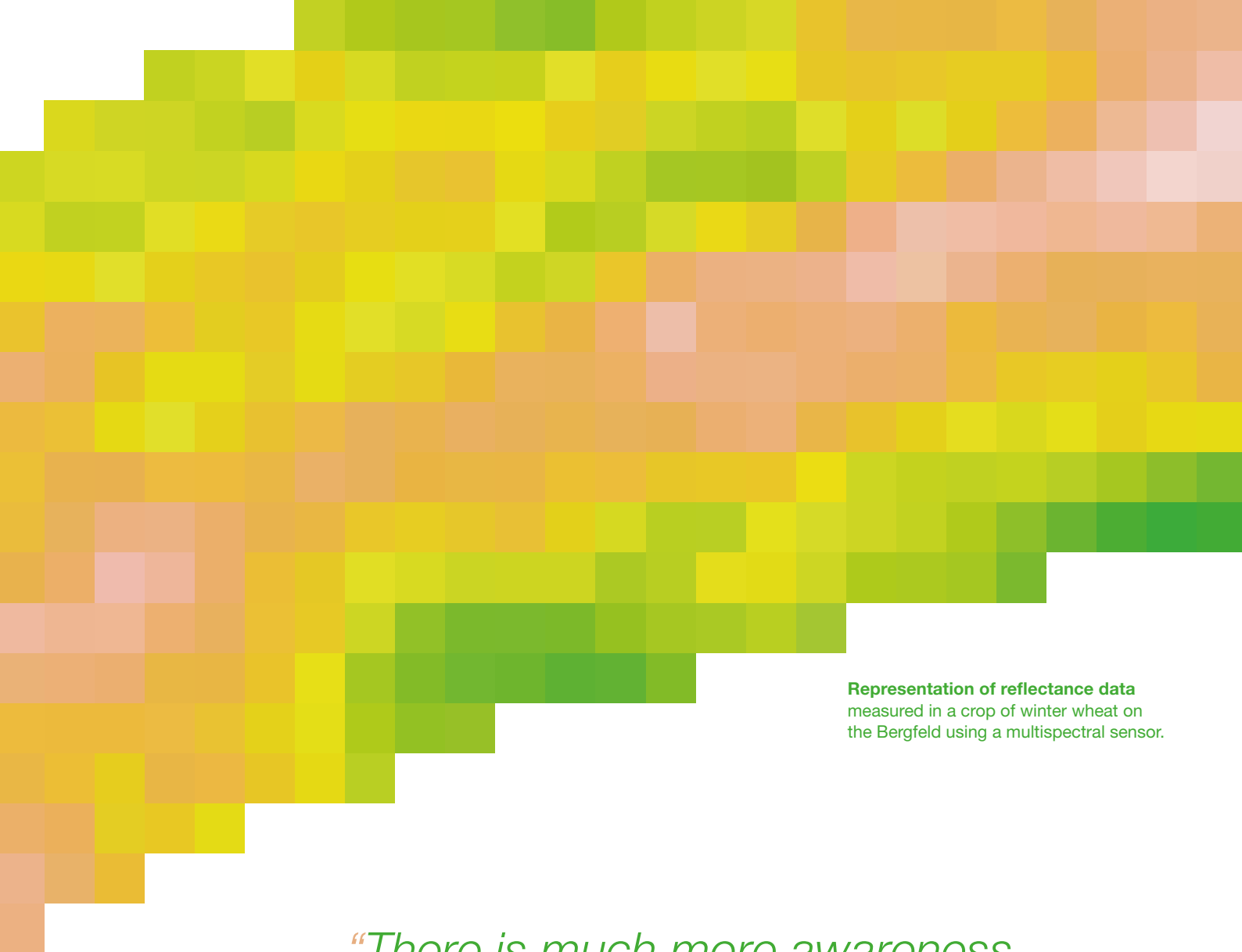
The **respiration chamber**, which is placed over the soil, measures the quantities of nitrous oxide emitted by the soil. The pump (right) is used to fill test tubes (above) that are then analyzed in the lab.



**Y**ou could say they're working in the eye of the storm. Kurt-Jürgen Hülsbergen and Franz-Xaver Maidl are researching the efficient use of nitrogen in agriculture – a highly topical field of research. In June 2018, the European Court of Justice censured Germany for breaching the EU Nitrates Directive. This obligates countries to comply with a limit of 50 mg per liter of groundwater. Since 2008, however, at least 16.9% of measurement sites in Germany have failed to meet this limit each year. High nitrate concentrations in groundwater are mostly caused by agriculture.

While Germany has reviewed and amended its Fertilizer Ordinance, it is apparent that this legislation will not suffice. Hülsbergen holds the Chair of Organic Agriculture and Agronomy at the School of Life Sciences in Weihenstephan. The agronomist has worked on the topic of nitrogen management in agriculture for more than 20 years. This includes developing the REPRO model – a digital system to analyze, evaluate and optimize nutrient and energy flows.





**Representation of reflectance data** measured in a crop of winter wheat on the Bergfeld using a multispectral sensor.

*“There is much more awareness of the importance of nitrogen efficiency now, but that wasn’t always the case.”*

*Kurt-Jürgen Hülsbergen*

Professor Hülsbergen and his team collect data on parameters such as utilized agricultural area, crop yields, animal husbandry, soil quality and the use of mineral fertilizer and liquid manure; using this data, they develop models of nutrient cycles that – in the case of nitrogen – highlight surpluses and deficits and indicate potential areas of improvement. For example, the amount of mineral fertilizer used should be adjusted accordingly if liquid manure has been applied, as this means less additional nitrogen fertilizer is needed.

The algorithms used for analysis contain the knowledge gathered from years of field experiments. How do the type and quantity of fertilizer and the timing of its application affect yields and product quality? How much nitrogen is lost to the air or seeps into the water? What influence do soil properties and weather conditions have on nitrogen turnover in the soil? “Looking back, I’m happy that we persevered with the topic of nitrogen management for so many years,” says Hülsbergen. “There is much more awareness of the importance of nitrogen efficiency now, but that wasn’t always the case.”

### An online tool for digital nutrient management

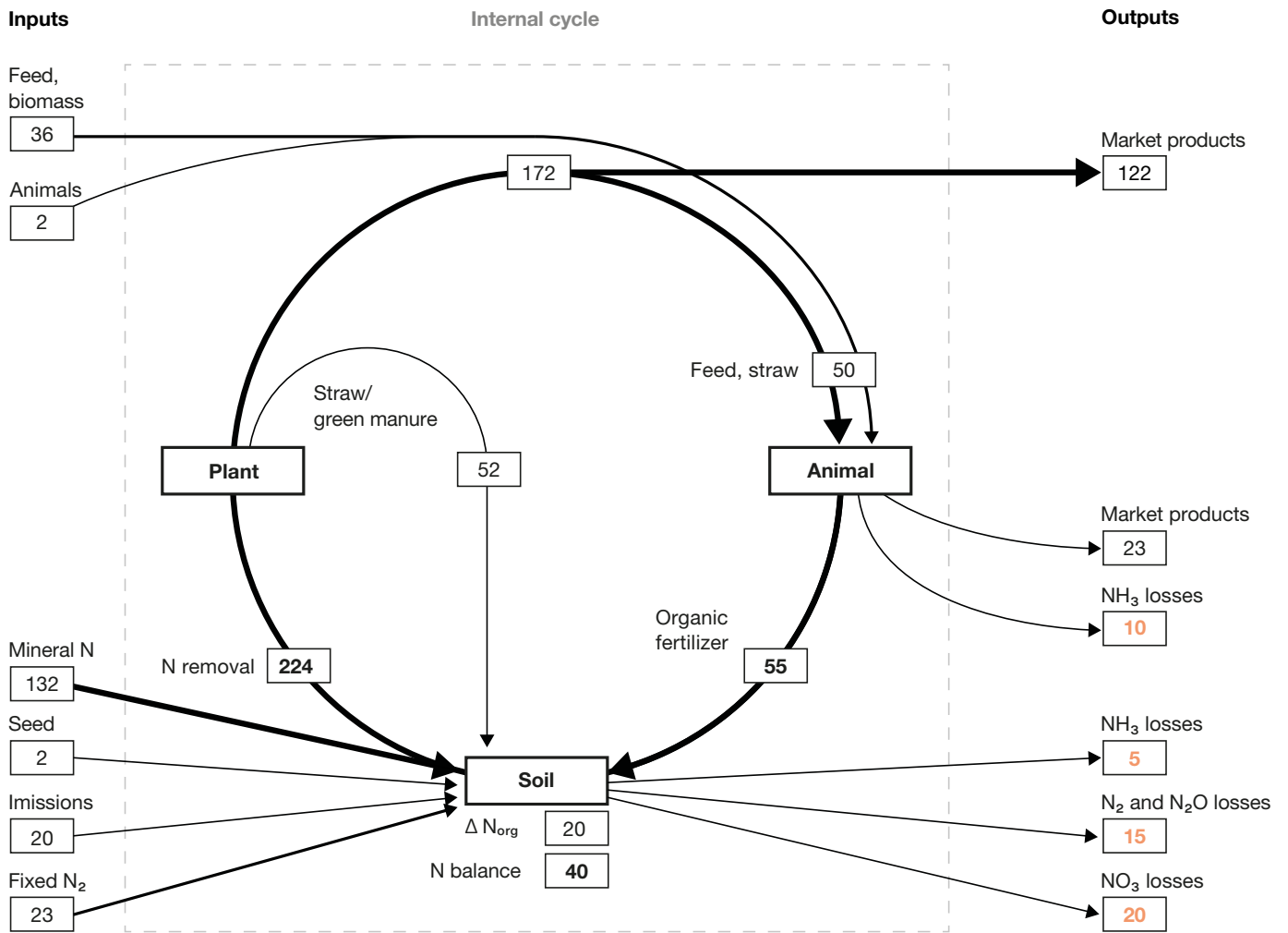
Advances in sensor technology also benefit the REPRO model. Digitalization in agriculture and the adoption of precision farming methods – methods taking differences within individual fields into account – mean more data will be available. This requires new IT solutions to integrate data from many different sources into one overall system. REPRO is currently being developed further as a nutrient management system called Web-Man. This digital tool is now ready to be put into practice. The researchers hope that specially trained farmers and farm advisors will use the tool to analyze their farms and develop optimization measures. It has been designed to be used on both organic and conventional farms. This work is being funded by the German Federal Environmental Foundation (DBU) and the Federal Office for Agriculture and Food (BLE).

As well as calculating nutrient cycles, Web-Man also contains powerful data analysis algorithms that generate information to assist with decision-making. It provides advice to the user and makes specific optimization suggestions. At present, however, the tool is still a prototype that Hülshberger and his team of specialists use to advise farmers. “We can’t just hand farmers the results and leave them to it,” says Professor Hülshberger. IT specialists at the university are, however, currently developing automatic decision-making algorithms based on expert knowledge and artificial intelligence. Other computer scientists are working together with agricultural experts to create user-friendly, self-explanatory user interfaces to ensure that users can use the finished tool without needing assistance from scientists.



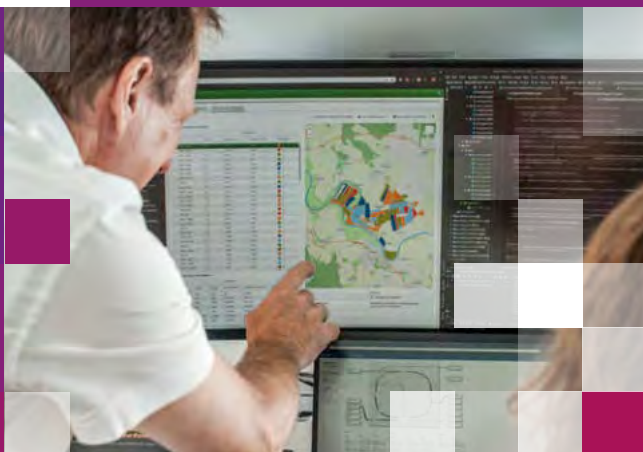
To keep the soil data in their database up to date at all times, the researchers regularly collect soil samples using a small auger. The soil cores are then analyzed.





**Above:** The nitrogen cycle on a farm, calculated with the REPRO model: The figures represent the volume of nitrogen in kilograms per hectare per year. Figures in red are areas needing improvement.

**Below:** Kurt-Jürgen Hülsbergen demonstrates the digital Web-Man tool. The pixelated image represents the nitrogen footprint of the Bergfeld at Roggenstein in 2018.

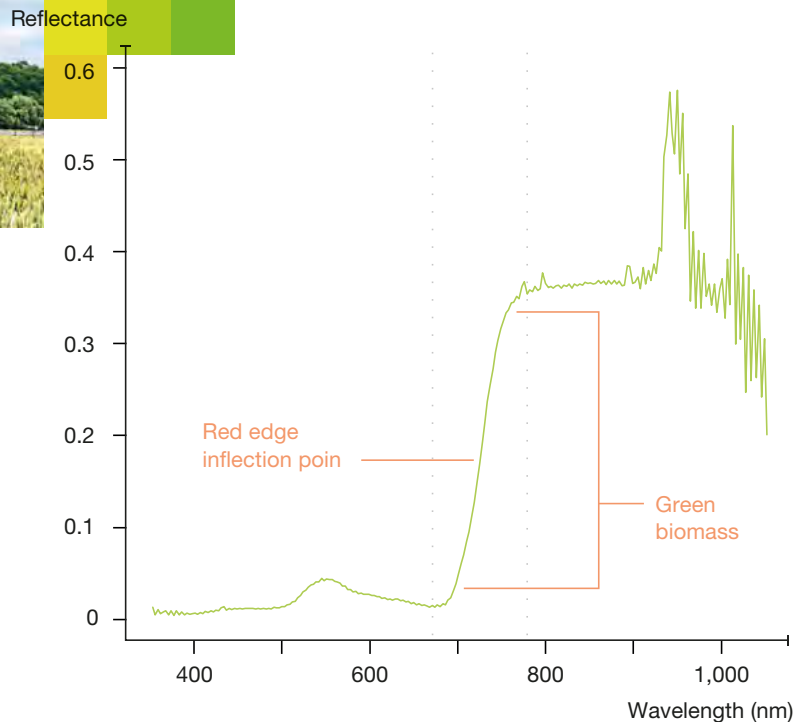


*“We can’t just hand farmers the results and leave them to it.”*

Kurt-Jürgen Hülsbergen



**Measurement at the front, fertilization at the back:** Sensors mounted on the frame on the front of the tractor record reflectance values; the computer analyzes these in real time and uses the values to control the rear-mounted fertilizer spreader with pinpoint accuracy. At right is the reflectance spectrum of a crop plant.

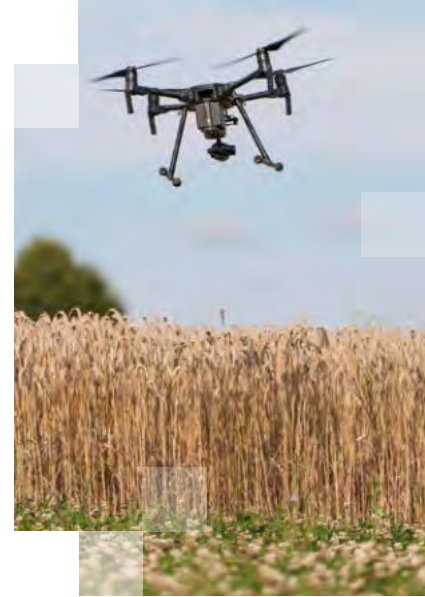


#### How sensors determine plant fertilizer requirements

Commercial sensors for fertilization according to crop requirements measure the light reflected by the plants. They use only two to four wavelengths and are suitable for only a limited number of crops. Maidl hopes to expand the technology for use with other crops, such as maize, and to include other plant properties. Each plant has a different reflectance spectrum, which changes as it grows and is also dependent on the weather and the time of day. Different wavelengths make it possible to record different plant properties. Maidl's multi-spectral sensor measures 220 different wavelengths and precisely records the properties required for different crops, times of day and weather conditions. This sensor was developed using spectral measurements from a wide range of trial plots. In addition, crop biomass and yield measurements are taken in the field and crop nitrogen content determined in the laboratory; the protein content in the kernel is also analyzed for cereal crops. Over the years, he has compiled an enormous treasure trove of data. By examining the correlation between different spectral measurements and plant analyses, Maidl can derive a fingerprint for the respective crop and the parameter in question. This is then used to develop fertilizer algorithms.

#### Save nitrogen using precision farming

Parallel to developing Web-Man, HÜlsbergen's colleague Franz-Xaver Maidl is researching efficient nitrogen usage with sensors according to the principle of "Ask the plant what it needs". Sensors directly measure the nitrogen nutrition status of plants, which is then used to calculate the optimal quantity of fertilizer – taking into account the plant's growth stage, soil quality and the desired product quality. This technology is now being integrated in Web-Man. This process is based on the reflectance behavior of plants. Plants absorb visible light for photosynthesis and strongly reflect light in the near-infrared spectral range at longer wavelengths. If spectrally resolved measurements of the reflected light are taken, different wavelengths return different reflectance values. These reflectance curves then allow researchers to compute specific parameters, such as the amount of biomass or nitrogen intake.



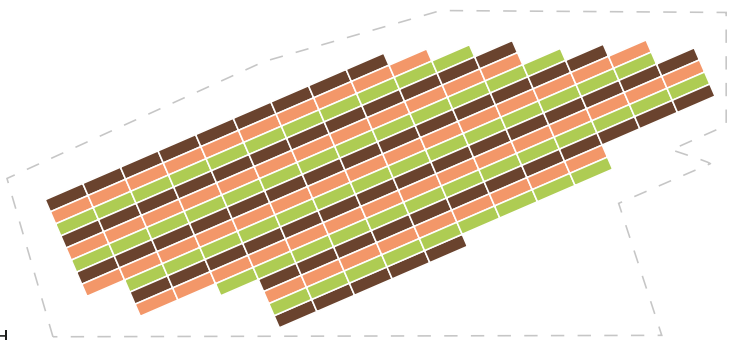
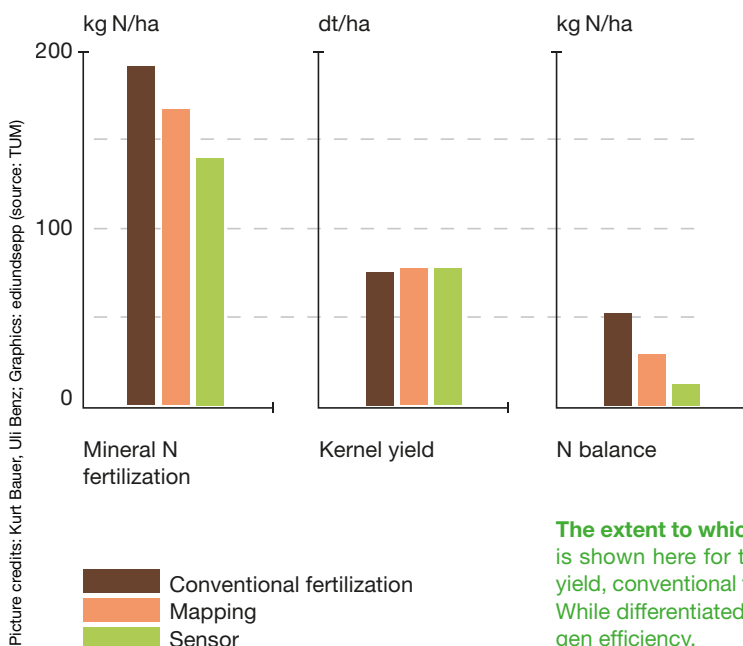
Farmers have already started using this technology, mostly using satellite measurements. Maidl's solution, on the other hand, is far more direct – specifically, a system mounted on a tractor coupled with the fertilizer system. This method is far more precise – also because measurement and fertilization coincide. In a single pass, the system measures plant nitrogen content, calculates in real time the correct quantity of fertilizer, and delivers this quantity with pinpoint accuracy.

This process opens the door for much more precise fertilizer application than has been the case to date. At present, farmers generally calculate the quantity of fertilizer for a field based on the average yield and average soil quality. In reality, however, soil properties, yield potential and fertilizer requirements also vary within a single field. Consequently, crops in areas with properties that deviate from the average values for the field either receive too much or too little fertilizer. Excess nitrogen remains in the soil, accumulates over years and, at some point, is discharged into the environment, such as groundwater. Sensor-assisted fertilization can prevent this. Trials conducted with winter barley at TUM's Roggenstein research station produced the same yields with almost a quarter less nitrogen. The scientists achieved similar results using winter wheat and winter rape.

**Flying drones over a field** is also an effective way of recording yields. Drones can carry sensors with an optical or thermal imaging camera.

### Sensor measurements give farmers peace of mind

The methods used by the researchers in Weihenstephan have also impressed farmers themselves, for example in the Hohenthann research project in the Landshut district. The region is home to numerous intensive livestock holdings; due to the high volumes of liquid manure this involves, the region is battling rising nitrate levels in groundwater. Hülshberger and Maidl analyzed nitrogen flows in farms that are typical for the region. They identified where and why nitrates were leaching into groundwater and derived groundwater protection measures, such as the timing of liquid manure applications and modifying animal feed. Field experiments testing fertilization using sensor data have also been conducted; this proved to be effective at increasing nitrogen efficiency. The measurements showed that soils that had been fertilised for years with manure had high nitrogen levels. In these areas, the application of additional fertilizers needs to be reduced significantly in order to comply with nitrate limits.



**The extent to which the Web-Man digital tool can improve nitrogen efficiency** in the field is shown here for the Bergfeld at Roggenstein. The comparison shows that, for the same yield, conventional fertilization uses the most fertilizer and leaves the most nitrogen in the soil. While differentiated fertilization is better, fertilization using sensor data has the highest nitrogen efficiency.

*“With appropriate fertilizer algorithms, farmers can maintain yields and society would benefit from good water quality.”*

*Kurt-Jürgen Hülsbergen*

The Bergfeld at Roggenstein is shown again here. The colors represent crop nitrogen uptake in 2018.

### Optimizing crop rotations

Many organic farmers face a very different problem: they use organic fertilizers such as liquid and solid manure but do not use nitrogen from mineral fertilizers. Organic guidelines also limit the number of animals per hectare of agricultural land. This means nitrogen is a scarce resource, which often limits yields. It is therefore crucial that farmers use the nutrient efficiently. Leguminous crops – plants such as red clover, lucerne and soybeans – are therefore

an important tool as they can add nitrogen to the soil via atmospheric nitrogen fixation. It then undergoes mineralization processes that make it available for subsequent crops. Some of the nitrogen is bound in soil organic matter over the long term. The speed of this process depends on soil quality and weather conditions. Plants, on the other hand, take up different amounts of nitrogen during different growth stages. The challenge is, therefore, to coordinate crop rotation and organic fertilization so that, taking into account soil processes, crops always receive an optimal supply of nutrients. There are currently no models that depict these processes or that include suitable fertilization algorithms for organic farming. Hülsbergen and Maidl hope to integrate this as an additional module in Web-Man.



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### Dr. Franz-Xaver Maidl

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When he isn't researching at TUM, Franz-Xaver Maidl runs the family farm in Lower Bavaria. "The farm is, in a way, also an experimental station," he says. He claims he can tell straight away which methods might be relevant to farmers and can be implemented in practice: "It can be difficult to see how scientific research could be applied in the field, this is only possible if you have a lot of contact with farmers." Maidl is a man in demand in his community. Many turn to him for advice, currently in relation to revisions to the Fertiliser Ordinance.

Maidl studied agricultural sciences at TUM and did his doctorate on nitrogen dynamics. A research project at the German Aerospace Center (DLR) aimed at recording the nutrition status of plants using measurements from aircraft attracted his attention and led him to his current research topic of fertilization according to crop requirements using sensor measurements. A system he developed and patented is available on the market in the Isaria and Crop Sense sensors.

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**Prof. Kurt-Jürgen Hülsbergen**

Hülsbergen grew up on a farm in the Magdeburger Börde and studied agricultural sciences at the University of Halle-Wittenberg. After being awarded his doctorate in 1990, he helped establish organic agriculture as an area of study at the university. Hülsbergen qualified as a professor in 2002 and, in 2003, was appointed to the Chair of Organic Agriculture and Agronomy at the TUM School of Life Sciences in Weihenstephan.

Moving to Freising, the researcher also switched to agriculture with a completely different structure: “In Bavaria, the average field size is 1.8 hectares; at home, there are fields of 50 to 150 hectares. One field there is many times the size of an entire farm here.” Hülsbergen lives in the Hallertau, the world’s largest contiguous hop-growing area – so work is just outside his front door: “Nitrates are a hugely important issue for hops.”

### Protecting groundwater using nutrient management

The researchers are motivated by the idea that “our work can minimize the amount of nitrogen used and reduce environmental contamination,” explains Hülsbergen. “With appropriate fertilizer algorithms, farmers can maintain yields and society would benefit from good water quality.” Taking this one step further, the fertilizer algorithms could be used to optimize drinking water quality instead of crop yields. The model can simulate these scenarios and calculate expected yield reductions. It would then be possible to derive potential compensation for farmers.

The next generation of farmers might even take these concepts for granted. Maidl and Hülsbergen are doing their best to make this happen by engaging heavily in teaching. “Today, many people study agricultural sciences because they want to make the world a better place with the help of modern technologies,” says Hülsbergen. “That’s ideal for us, because we want to make students enthusiastic about environmentally friendly farming. Digitalization and precision farming are important and innovative ways of achieving this.”

*Christine Rüth*

### Nitrogen in agriculture

Plants need nitrogen to grow and can only absorb it in certain forms – mainly as ammonium or nitrate. Mineral fertilizers make nitrogen directly available to plants in a form they can quickly absorb. In liquid and solid manure, and compost, organic nitrogen predominates. It remains in the soil for years or even decades as it is slowly mineralized. Leguminous crops capture nitrogen from the air, hold it in the soil and thus make it available for subsequent crops. If too much organic nitrogen is present, such as from liquid manure, this can remain in the soil for decades. The excess nitrogen can then seep into groundwater, rivers and lakes. It is therefore a threat to ecosystems and potable water. Liquid manure emits ammonia, which disperses in the air and thereby “fertilizes” areas where this is not desirable. As a result, nitrogen also contributes to loss of biodiversity. Specific turnover processes also cause nitrogen to be emitted as nitrous oxide. This is a highly potent greenhouse gas and is therefore critical even in very small quantities.



Graphics: edlundsapp





# “Vertical farming is a child of the Silicon Valley high-tech world”

Is cultivating plants indoors an opportunity to protect the world against famine – or just another fashionable, inner-city gimmick? We discussed aspects beyond the technical parameters with cultural and social anthropologist Dr. Mascha Gugganig.

Link

[www.mcts.tum.de/people/mascha-gugganig](http://www.mcts.tum.de/people/mascha-gugganig)

### Dr. Gugganig, what exactly is vertical farming?

**Mascha Gugganig:** The term is very widely used and different people associate it with entirely different things. I make a distinction between three types. First is a sort of black box, as Dickson Despommier, who is regarded as the founder of the movement, strongly advocated in his 2010 book "The Vertical Farm". It is, ostensibly, a fully controlled cultivation system, independent of external factors. Secondly, there is the semi-controlled system. This involves growing crops in vertically stacked racks, on vertically inclined surfaces or in other integrated structures in which environmental factors can be controlled. And the third type is the adaptive system. In this case, energy efficiency is at the forefront – so it might involve using previously wasted energy flows, such as waste heat from cold storage, to promote plant growth. These systems are often fully or partially integrated into existing structures, such as buildings.

### What are the benefits of vertical farming compared with conventional cultivation methods?

**MG:** There are several. For one, it allows year-round, high-density production without weather-related crop failures. Pesticides, herbicides and fertilizers are superfluous, though ongoing studies are currently examining just how free from pests these systems can actually be in reality. They require 70 to 95 percent less water than conventional cultivation and reduce transport distances to urban consumers. Vertical farming is also considered an opportunity to return spaces to nature. That is too simplistic, however, as it does not represent a path away from the monocultures we have at present. Ultimately, vertical farming achieves exactly the same thing, but in enclosed spaces.

### What are the drawbacks?

**MG:** The issue of how energy-efficient and cost-efficient such systems are remains contentious to date. Many start-ups in the sector have already been forced to fold. Except for Japan, where the state provides financing, the money in the sector is primarily derived from Silicon Valley. Major investors have discovered the food industry as a potential playground. Which raises the question: How sustainable is this?

### What are the origins of vertical farming?

**MG:** In 2010, microbiologist Dickson Despommier from Columbia University proposed cultivating crops in multi-story buildings. The subtitle of his book – "Feeding the world in the 21st century" – also helped to create a degree of hype around vertical farming in the years since. From a technical perspective, this new form of food production is based on the accomplishments of the greenhouse industry and also of the cannabis industry. It is a child of the Silicon Valley high-tech world. In actual fact, vertical farming has nothing to do with conventional agriculture.





### So vertical farming won't be the answer to the global food issue?

**MG:** No, but your question is also problematic, as it suggests there might be “one” answer to “the” global food issue. To date, the closed systems are only suitable for growing lettuce, tomatoes and herbs. While they can also be used to grow cereals, this would not be sustainable from an economic perspective. The marketing slogan of “feeding the world” was a mistake – as many people in the sector agree. In this context, the flurry of excitement revolving around the new technology wasn't justified. Today, vertical farming is also criticized as a yuppie trend, with affluent urbanites using it to cultivate basil or arugula. ▶



## How have consumers accepted the new method?

**MG:** Approaches aiming to encourage a more in-depth discourse around the issue do exist already. Together with an industry partner from Holland and the European Food Information Council (EUFIC), we developed a citizen participation forum in 2017 and used it to approach visitors at Deutsches Museum in Munich and the Science Museum in London. In many cases, this resulted in what I call an educational moment. People didn't just exchange views about vertical farming but also discussed the agricultural system in general. Is vertical farming really so much more artificial and technical than our current agriculture? Where do our lettuce and tomatoes come from? Vast quantities of fruit and vegetables are grown in distant greenhouses. Most people have no idea of what goes on there. Are these greenhouses better or worse than vertical farming?



## What influence do consumers have on vertical farming?

**MG:** Apart from a few exceptions, there is more of an interest in selling vertical farming products than in democratizing vertical farming, that is to say, encouraging a wider public discourse on the topic. There are certain aspects of democratization, such as the trend of establishing city food councils. These councils address the issue of how food production in cities can be made more attractive and more accessible. I do believe, however, that science, industry and politics need to make a sincere effort to bring this issue that concerns our future more into the public. While vertical farming is still very much in its infancy, it certainly holds a great deal of potential. One niche, for example, could be to use such controlled production methods to create a buffer in times of increasingly volatile weather. This should entail dialoging with the agricultural sector, which, however, is still quite a rare occurrence.

Interview by Karsten Werth

There are four different methods of growing plants.



### Dr. Mascha Gugganig

As a cultural and social anthropologist, Gugganig focuses on scientific and technological research in the field of food, agriculture and the environment. Since 2016, Gugganig has worked as a postdoctoral researcher at TUM in the Innovation, Society and Public Policy research group at the Munich Center for Technology in Society (MCTS). As part of the pan-European EIT Food consortium, an innovation initiative launched by the EU, she headed the "Cultivating Engagement" project, which addressed citizen participation in the context of vertical farming, among other issues. Her current research project looks at sustainable agriculture in the EU, and the use of innovation and technology.

Sunlight



### 1 Outdoor farming

Outdoor gardens or agricultural land with natural light and water

Sunlight



### 2 Greenhouse

Cultivation in a greenhouse with artificial irrigation. Artificial lighting is also used in many cases.

Artificial lighting and irrigation



Sunlight



### 3 Indoor farming

Indoor farming – in recent times, food has also come to be cultivated in enclosed spaces within buildings. This method requires artificial lighting and irrigation.

Artificial lighting and irrigation



Sunlight

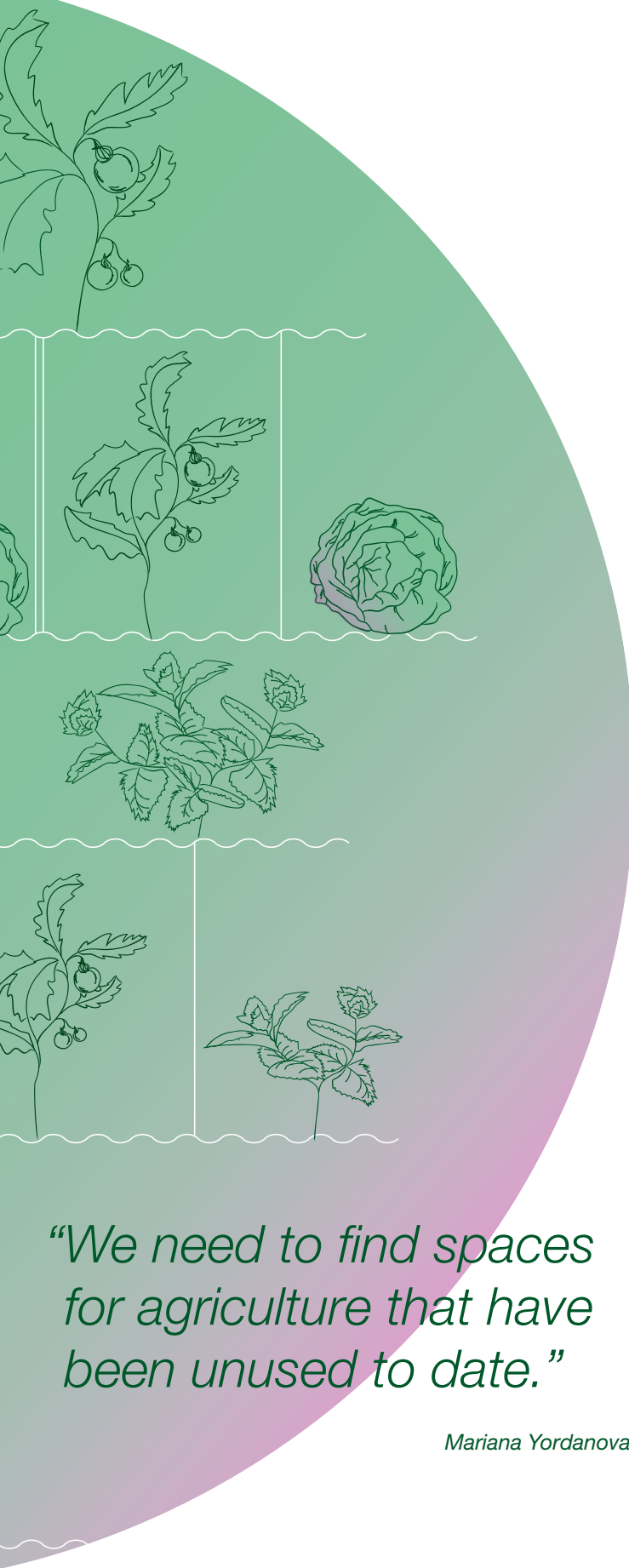


### 4 Agricultural lighting facade

Vertical farming involves growing plants behind the windows of residential and office buildings. They receive light from outside but require artificial irrigation.

Artificial lighting and irrigation





# Multifunctional facades:

## Light systems and food production

**In cities, space is at a premium. A new concept now makes it possible to use the space behind windows and facades for more than just one purpose, namely for esthetic building lighting and for raising fresh vegetables.**

**C**ities around the world are growing – and so are their demands for food. The average German citizen consumes almost 100 kilos of fresh vegetables per year. Supplying a city of one million residents means sourcing 100,000 tons of produce per year, which often entails transporting produce over hundreds of miles.

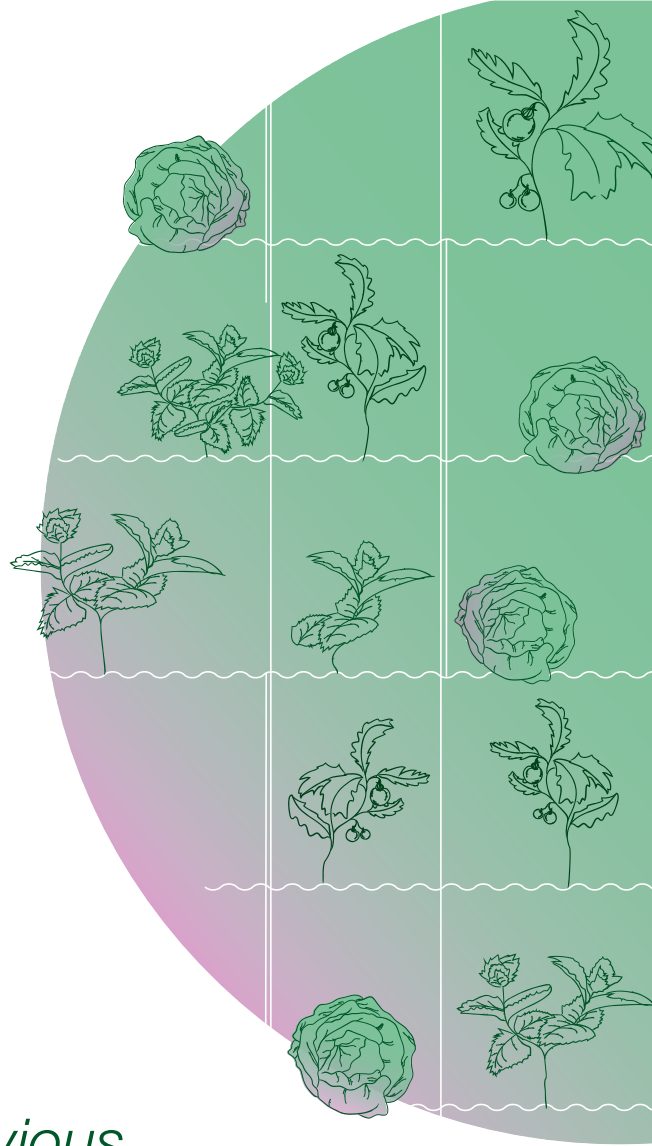
“It seems quite obvious to cultivate produce where the consumers are,” says Ferdinand Ludwig, Professor for Green Technologies in Landscape Architecture at TUM. “It would save both transport costs and energy, while at the same time, consumers would benefit from freshly harvested produce.” In other words, a genuine win-win situation.

But where will all this freshly grown produce come from? “Our Agricultural Lighting Facade project started with precisely that question,” remembers his colleague, Dr. Mariana Yordanova. “In cities, space is at a premium and expensive. We need to find spaces for agriculture that have been unused to date. And so we came across the idea of windows. Business premises, offices and administrative buildings have millions of them.”

In the course of her doctoral thesis, the architect and climate designer performed truly pioneering work. Existing approaches in “vertical farming” were restricted to the mass production of plants in specially constructed, multi-story and mostly windowless buildings. This calls for space and energy for lighting and air conditioning. “By contrast, our new concept integrates vegetable cultivation in different building types and harnesses natural light as much as possible,” emphasizes Yordanova. “Consequently, when additional lighting is required it is kept to a minimum and can be used simultaneously as esthetic facade lighting, which is also perceived as a clear indicator of urbanity and modernity in our cities.”

*“We need to find spaces for agriculture that have been unused to date.”*

*Mariana Yordanova*



But can standard facade lighting really be sufficient to promote the growth of plants? The TUM's Gewächshauslaborzentrum – a greenhouse conservatory in Dürnast near Weihenstephan – offered Ludwig and Yordanova the perfect conditions for their experiments and the support of horticultural researchers. Over the course of several months, they experimented with different hydroponic systems, temperatures, light spectra, luminous intensities and lettuce varieties.

*“It would seem quite obvious to cultivate produce where the actual consumers are.”*

*Ferdinand Ludwig*

The team of architects now hopes to apply these findings in developing a market-ready system that will allow the space behind window facades to be used to cultivate vegetables. The system will be made up of narrow, space-saving racks that can be stacked up to the ceiling and enable functional, low-maintenance irrigation. Its integrated lighting system, which automatically activates only when natural light is insufficient, creates a comfortable indoor climate. At the same time, the researchers want to examine which and how many of a building's windows would be suitable for “greening”. A key factor is ensuring that the rooms' users find the view of the illuminated plants agreeable and esthetically pleasing. “The design will be another key focus,” as Yordanova emphasizes. “The racks should feature a linear, clear-cut and functional design and become an integral component of the facade structure.”

It is also important that the facade-mounted gardens are easy to care for and maintain. As illumination and irrigation are automated, planting and harvesting are the only tasks left for people to do. In the case of residential buildings, this could be the residents themselves, while in office buildings, it could be employees or canteen staff, and in supermarkets, where lettuce could thrive behind the shop windows, it could be the customers.

“The concept is certainly future viable and sustainable,” summarizes Ludwig, who researches interdisciplinary solutions at the interface of natural sciences, engineering, landscape architecture and urban planning. “Over the long term, we will have to find new spaces for food production in order to feed a growing global population – and glass facades and window facades are exceptionally well suited to this.”

*Monika Weiner*

# On the road to brewing self- sufficiency







**Dr. Karl Glas and his working group are experts in water management in breweries and food producing companies. From designing the chemical and biological properties of water to solving complex purity issues, they are searching for the optimization potential inherent to these companies and their processing operations. Currently, their aim is to help small and medium-sized breweries to clean their wastewater self-sufficiently with the aid of microbial fuel cells. The fall of 2019 saw the first pilot system in the brewery and beverage industry in the whole of Germany go into operation at a major German brewery.**

Link

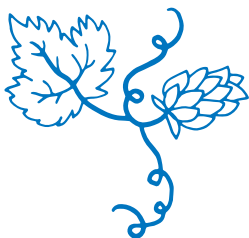
[www.molekulare-sensorik.de/index.php?id=55](http://www.molekulare-sensorik.de/index.php?id=55)



**In the face of rising costs,** the pressure on breweries to use power and water more efficiently is also on the rise and with it interest in innovative solutions.



**W**ater is not just water. There is probably no-one who knows that better than Karl Glas, Head of the Water Technology working group (AGW) at the Chair for Food Chemistry and Molecular Sensors at TUM in Freising. Whether as a raw material for production or as process water and wastewater in the food and beverage industry, water can exhibit a large variety of properties.

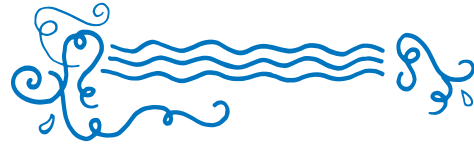


#### **Which water is it to be?**

“We are talking about water design,” Glas says and asks: “How can I design my water in such a way that it is pristinely clean or precisely matches the requirements of a certain application? That is the core element of our work. In the food and beverage industry, the water must be sterile and other substances already in the water or introduced into the water during operations such as pesticides, lime, copper, disinfectants, etc. must be removed.” In this context, the AGW is researching innovative solutions in sensor technology, filtration and disinfection. Process water in the brewing industry, the specialist area of Karl Glas, occurs in various physical states in the plant: as hot water, cold water or steam – in every state, it must be of drinking water quality and be processed accordingly.

In addition, water is an important factor when it comes to the cost-effectiveness of facilities and their impact on the environment. “Industry still has a lot of opportunities to save H<sub>2</sub>O and CO<sub>2</sub>,” Glas emphasizes. Born in Augsburg, the man is steeped in practical experience. About himself and water, he says: “Actually, I did study brewing but I’m not your typical brewer, the kind you maybe imagine dressed in Lederhosen with a beer in one hand. Water as such is more important to me. Water is exciting because it’s scientific, technical, political and cultural. Water is always interesting, and the chemistry of water is no easy matter – thank goodness, otherwise we’d have nothing to research!”

*“Industry still has a lot of opportunities to save H<sub>2</sub>O and CO<sub>2</sub>.”* Karl Glas



### **At the interface between water, energy and the environment**

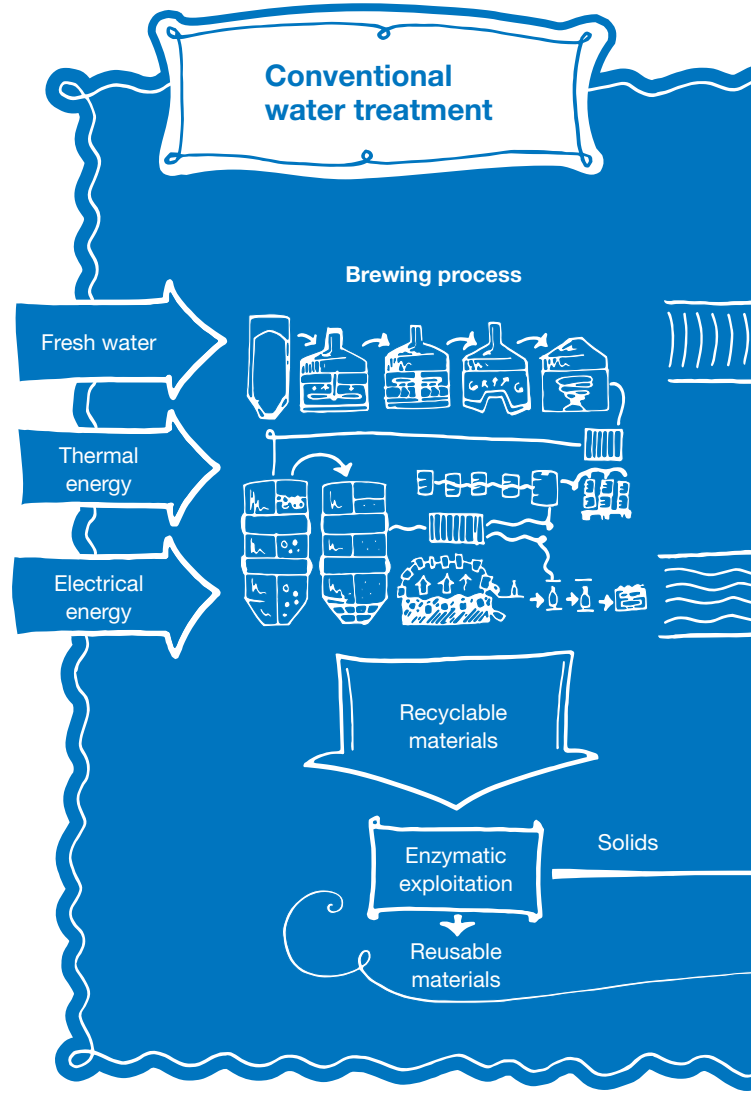
AGW takes the interface between water, energy and the environment in the food and beverage industry as its starting point. The scope of its research comprises the development of new techniques for treating drinking water and wastewater, the system and process-driven management of energy and material flows, as well as issues of microbiology and hygiene. It employs methods for simulating chemical-physical processes, analyzing new materials or abstracting and modeling system and process structures. The chemical and biological quality of the water is of fundamental importance in brewing beer. There is not a single stage in the brewing process not affected by the composition of the water. As breweries and beverage companies draw their untreated water either from public water grids or their own wells, its treatment must meet both statutory and brewing criteria. For example, the parameters of water hardness and alkalinity differ considerably from each other, in some cases due to geographical and geological factors.



**Karl Glas with the innovative wastewater cleaning pilot plant** developed in collaboration with TU Freiberg and commissioned in October 2019.

**The brewing industry is aiming to become more efficient**

Glas is very well networked within the brewing industry, not least due to his longstanding consultancy work. For example, the two-day “Weihestephan Seminar for Water Technology” organized by his working group offers a forum every year for promoting dialog between scientists and companies on developments in water technology. The brewing industry in Germany is a cost-driven business with tight profit margins. Small to medium-sized companies comprise 90 percent of the industry, and they are dependent on fossil fuels and the external procurement of electricity. A volatile energy market, rising energy and raw material prices as well as growing interest on the part of consumers in ecologically sustainable products – these are the challenges facing the industry today. Consequently, the pressure to use energy and water more efficiently is rising, and with it the industry’s interest in innovative solutions. Even in the most modern plants, for example, every liter of beer produced generates two liters of wastewater. Glas forecasts that as soon as water becomes noticeably more expensive, German beer brewers will also attempt to treat their entire wastewater in such a way that it can be returned to the production cycle.

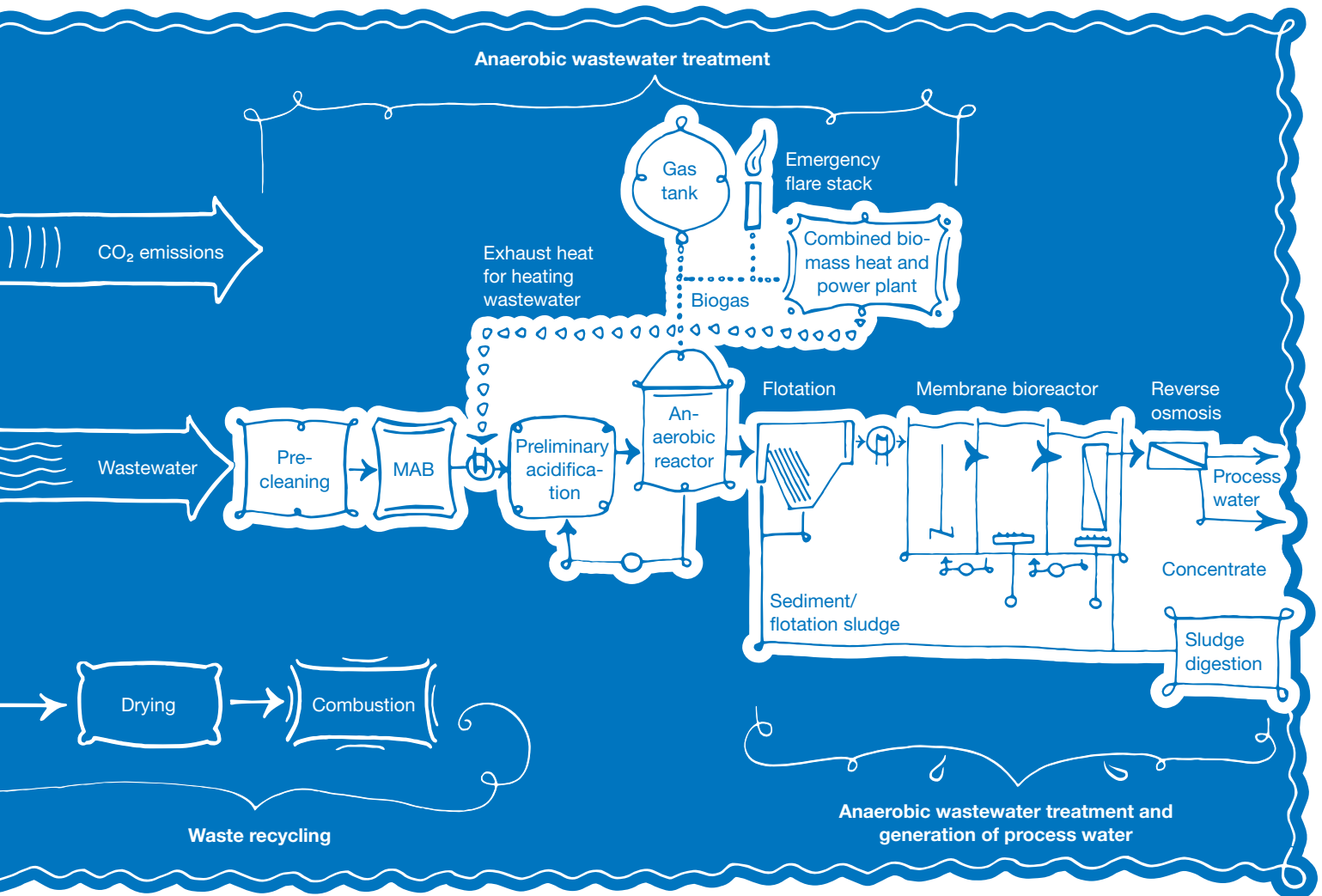


**Focus on small and medium-sized companies**

The AGW is currently developing a modeling and simulation tool with a TUM partner that facilitates a standardized, overarching analysis and forecast of the energy and media

consumptions of process chains. Beverage producers and systems manufacturers are thus to be given, for the first time, an integrated tool for tapping previously concealed potential for savings. The quest for self-sufficiency was the starting point for Glas and his working group for this and other running projects. In a feasibility study (“BrauTark”), they previously studied the energy and material flows of a brewery. The researchers identified the potential of the flows, examined the options behind the use of energy and then revealed ways of replacing conventional sources of energy with renewables.

“Brewing is energy-intensive,” Glas reminds us. “When you brew beer, you start by boiling the beer wort. That costs no small amount of energy. In the case of smaller breweries, they are naturally not as efficient as large ones in which



production runs continuously. A typical small brewery only has one or two brewing days a week, which means it always has to re-heat the mash. In most instances, these facilities cannot afford to build a wastewater treatment plant.” Such companies have mixing and equalization tanks in which the impurity and freight peaks and pH levels of the water are equalized before the wastewater is discharged to the municipality. Frequently, a heavy polluter surcharge has to be paid. In this way, the wastewater also becomes a cost factor. “Self-sufficient plants would alleviate the problem. For example, a small or medium-sized company could produce one CO<sub>2</sub>-free batch from Monday to Wednesday and take its time over the next few days to break down its wastewater by means of a fuel cell and even generate electricity in the process,” Glas explains. ▶



**Every liter of beer generates two liters of wastewater.** To date, large breweries have cleaned wastewater in anaerobic reactors (i.e. systems operating without oxygen) with biogas extraction. The current “Brew-Cell” project replaces the section in white, illustrated above, with a fuel cell.

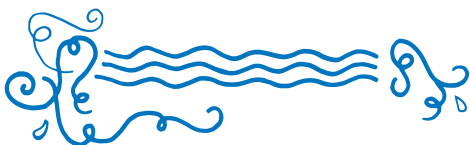
### **Brew-Cell: New prospects for integrating energy**

Wastewater treatment with the simultaneous generation of electrical energy through the use of microbial fuel cells (MFC) is now set to open up new prospects for the industry. To date, large companies have usually cleaned their wastewater in anaerobic reactors (i.e. systems that operate without oxygen) with biogas extraction. The current “Brew-Cell” project shows how the whole operation can be accomplished on a smaller scale with fuel cells. It is sponsored by the Federal Ministry for Economic Affairs and Energy in its Central SME Innovation Program.

First, researchers selected suitable wastewater flows for the microorganisms, and then conducted basic experiments on a laboratory scale with various designs of MFC. Are “the little helpers”, as Glas calls them, unable to tolerate certain disinfectants? Is the wastewater “fatty” enough for them? Good results are only obtained if the design is right. At the same time, the AGW has developed software on the basis of a mathematical model which helps with decisions on design, process set-up and operation at optimum points of the plant. From this, they derived a concept for incorporating the MFCs into the brewery’s power management. ▶

*“Water is exciting because it’s scientific, it’s technical, it’s political, it’s cultural.”*

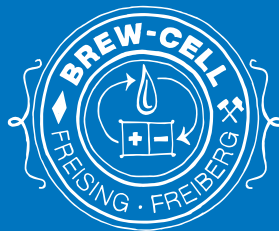
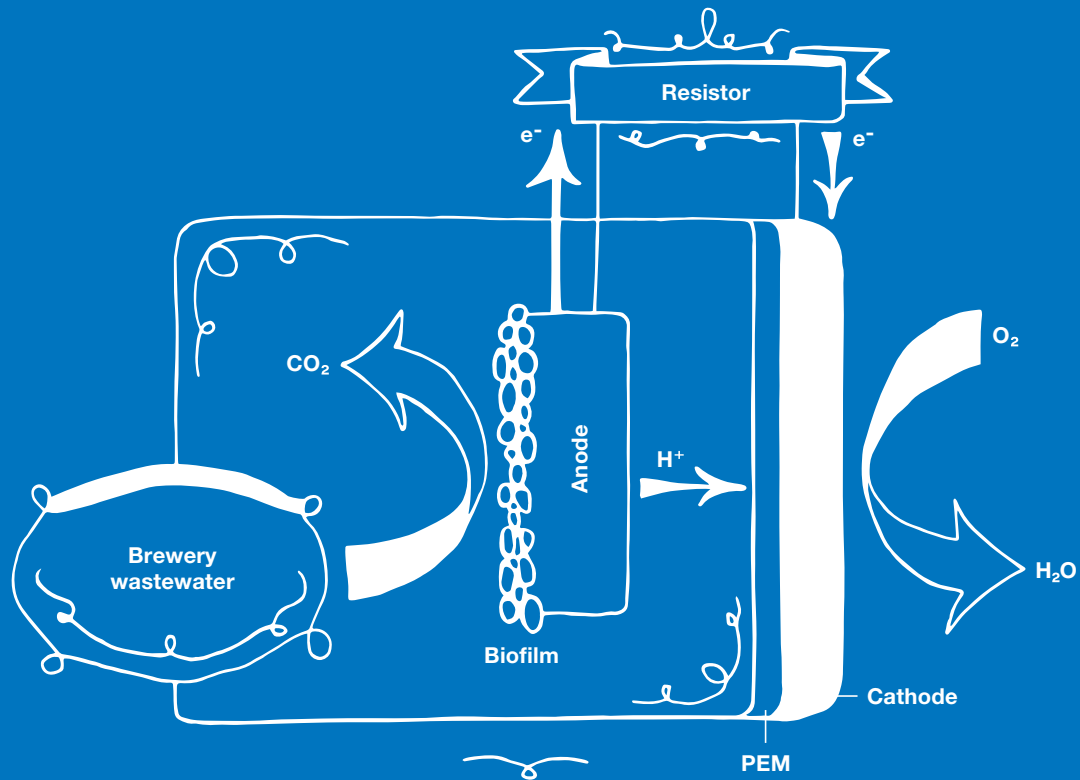
*Karl Glas*





Picture credit: Stefan Hopf; Graphics: edlundsapp

**Already successfully trialed** in the laboratory on a one-liter scale, tests are now starting in the 100-liter pilot plant. The details for managing the process of wastewater treatment are now being tested out.



#### The Brew-Cell concept

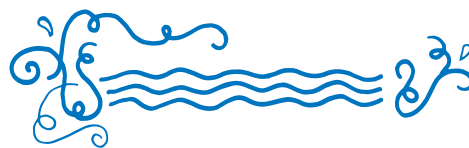
The use of fuel cells to clean wastewater represents a completely new approach. It enables the cleaning of wastewater while generating electricity at the same time. Exoelectrogenic bacteria have the ability to exploit organic substances in the wastewater and to transfer the electrons gained as a result to an electrode. The biofilm on the anode oxidizes a substrate which releases electrons and protons. Electrons are transferred to the anode and flow on to the cathode via an external resistor. In the presence of the protons previously gained, ( $H^+$ ) oxygen is reduced to water.





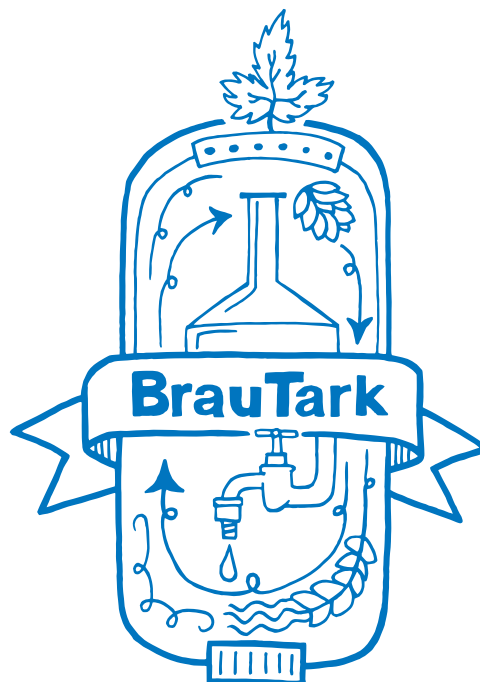
**Dr. Karl Glas**

Karl Glas studied brewing and beverage technology at TUM and obtained his doctorate with distinction in 1988 on the subject of brewery wastewater constituents. Shortly thereafter, he headed the “Special and Environmental Analytics” Department at the Research Center Weihenstephan for Brewing and Food Quality. From 2006 to 2014, Glas was active as the Scientific Director of the Competence Pool Weihenstephan, and between 2010 and 2015 Head of Science/Research at the Bavarian Research Foundation in Munich. Since 2014, he has been in his current post of Head of the Water Technology Working Group at the Chair for Food Chemistry and Molecular Sensors at TUM, and full-time since 2015. Karl Glas has advised brewing and beverage industry companies in matters revolving around water and the environment both nationwide and internationally for 30 years.



By using different control concepts, it was also possible to determine the particular effects on the process behavior. “We started working with fuel cells a good two years ago. We experimented with prototypes on a one-liter scale in the laboratory. A pilot scheme magnified by a factor of 100 then went into operation in a large brewery in Germany in the fall of 2019.” By studying the parameters, the aim is to gain insights into the further upscaling of such systems and their implementation in other areas of industry. There are still a lot of details to be clarified on this road to self-sufficient breweries. The pilot plant run by the researchers from Freising will help to generate valuable experience.

■ *Karsten Werth*



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## Masthead

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Women and men have equal rights under Article 3(2) of the German Basic Law. All words and job titles of one gender in this magazine relate to women and men in equal measure.

Nothing is so perfect that  
you can't improve it.

Whether down under or down your street, our ideas make life more convenient, more practical and safer. Because as one of the world's leading specialty chemicals companies, we lend products their special properties. For instance, adhesives get their adhesive power, washing detergents their washing power and lightweight designs their lightweight components from us. But above all, our customers get creative solutions from us – for better products that ultimately you love to buy.

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[www.better-with-evonik.com](http://www.better-with-evonik.com)



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