uni wissen

02 2012

The research magazine of the University of Freiburg | www.wissen.uni-freiburg.de

Cappuccino, Fries, and Romance

Consumer culture and urban lifestyle in China

Compute and care: Sociologists analyze the use of modern technology in emergency medicine

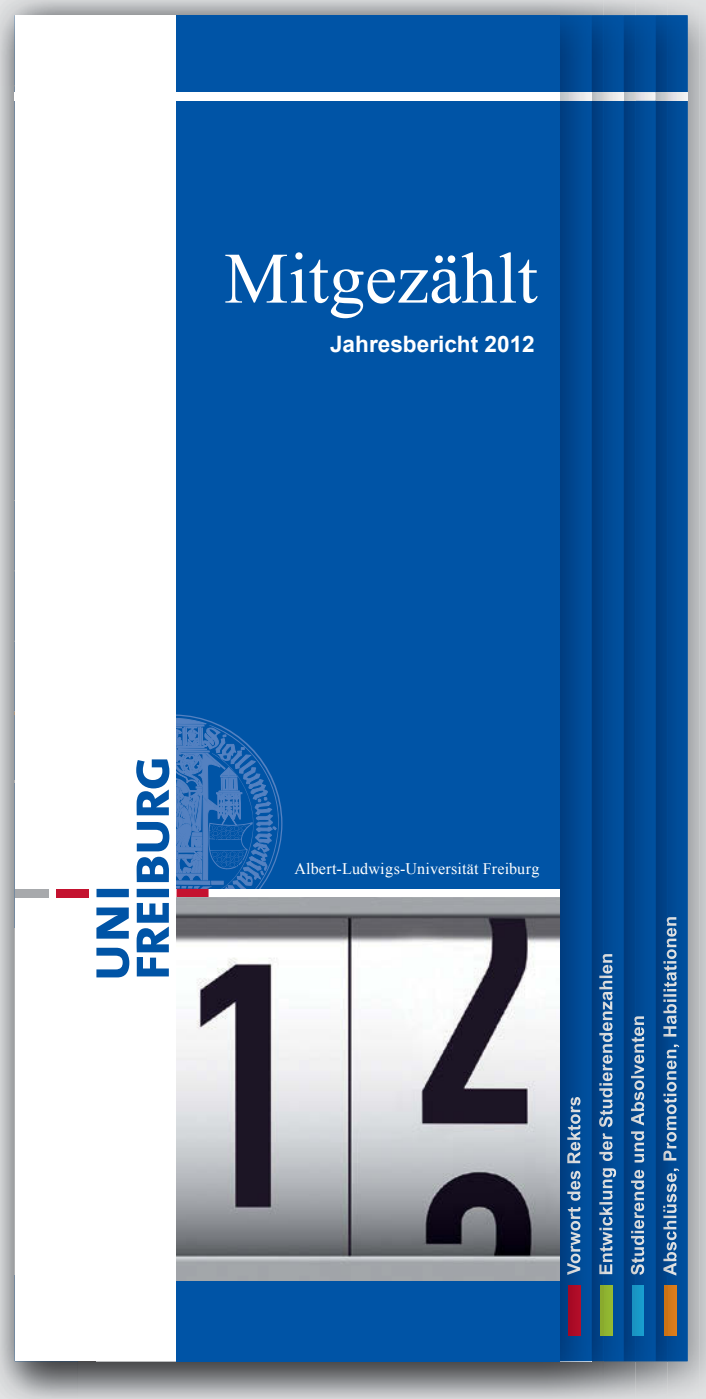
Capture and comprehend: Computer scientists teach computers to find objects on videos

Cleave and cultivate: Biochemists enable plants to supply themselves with nitrogen

UNI FREIBURG

Yearly Report 2012: The Numbers Stand for People

The positive development of the University of Freiburg cannot be represented by means of numbers alone, because the numbers stand for people and their achievements. All the same, the university would like to give you an idea of these developments in compact form. The detachable yearly report presents data and facts from the past year (1 Oct. 2011 – 30 Sept. 2012)



Read the yearly report here:
www.uni-freiburg.de/go/jahresbericht_2012

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Neuronal networks on a microelectrode array with 60 electrodes, with which scientists record the activity of the networks simultaneously. At the top of the picture is the objective of the microscope, and on the sides two glass capillary microelectrodes measure the membrane potential of the neurons. Photo: IMTEK/Müller

Playing with Nerve Fire

The Neuroscientist Ulrich Egert Is Studying Artificial Nerve Networks in Order to Understand the Rules Governing Their Interactions

by Eva Opitz

"We know that the neurons communicate with one another in their own distinct way, but unfortunately we hardly know anything at all about what they talk to each other about"

The precise way in which the nerve cells in our brains present, process, and pass on information is a secret that neuroscientists are particularly eager to unravel. "We know that the neurons communicate with one another in their own distinct way," says Prof. Dr. Ulrich Egert from the Laboratory for Biomicrotechnology at the Faculty of Engineering of the University of Freiburg, "but unfortunately we hardly know anything at all about what they talk to each other about." Egert is co-director of the new Cluster of Excellence BrainLinks–BrainTools. Scientists at the University of Freiburg's center for neurotechnology from the fields of biology, medicine, microsystems engineering, and computer science are investigating the function of the human brain and developing systems to communicate with it directly: interfaces that enable patients to control technical devices over their nervous system and implants that produce their own energy, identify changes in brain activity, and step in to counteract them.

A Host of Forces Acting in Concert

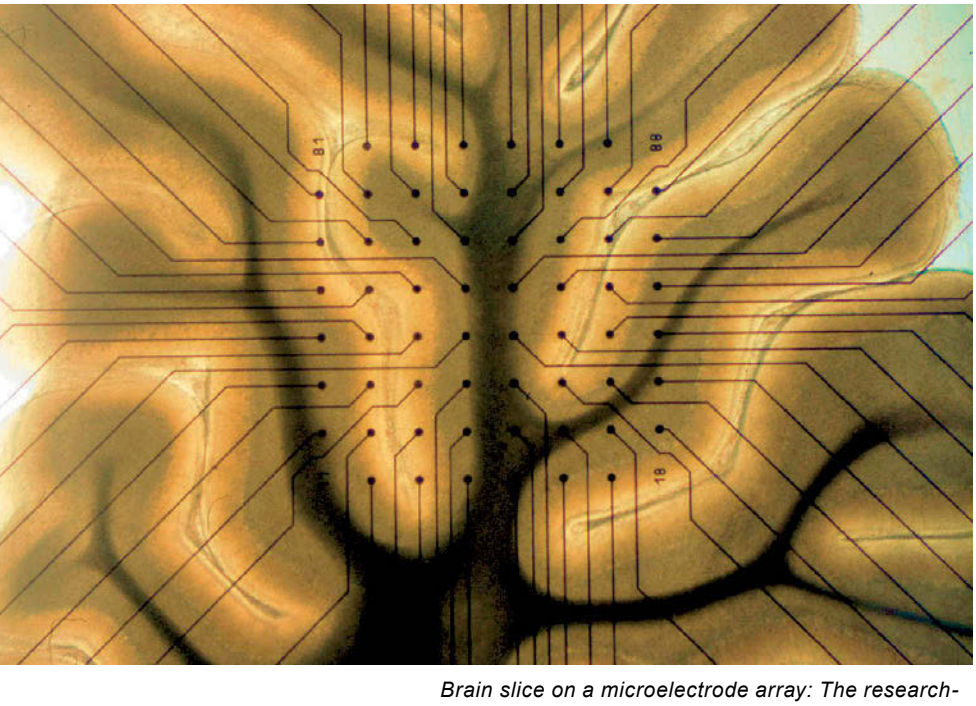
What the close to 100 million nerve cells of the human brain have in common are the dynamics of their individual activity. These dynamics, most of which have already been described in detail, are based on changes in voltage above the cell membrane, which creates a nerve impulse that is also referred to as an action potential or spike. The difficulty, explains Egert, lies in proceeding from the relatively well-understood biophysics of the individual cell to networks at different spatial levels: "We can measure the spikes of individual neurons using electrodes, but we don't see what the networks make out of them." A mere three cells is all it would take to make up a small network, and the next larger-sized network would consist of maybe 300 nerve cells. In the case of three cells, it is a straightforward affair to observe the transmission of stimuli over the so-called axons, cable-like conduction systems, to the synapses, the points of transmission between individual neurons. Unfortunately for neuroscientists, however, the behavior of a small network reveals only little about that of a much larger network.

The brain can contain up to 10,000 synapses for every pyramidal cell, the most common type of nerve cell in the cerebral cortex. This means that the influence of one nerve cell on the next is much different in a large network than it is in a network in which each cell only has one connection to two other individual cells. "The individual cell exhibits a completely different type of behavior in this large network," says Egert. "The larger the network becomes, the less I can assume that all of the cells in it behave in the same way." Different types of cells enter the picture: Some have an inhibiting effect, others have a stimulating effect, and still others belong to one of many subtypes. The system is complicated further by incoming impulses from outside, from the cortex, and from other parts of the brain as well as by local feedback. To make things even more confusing, the next cell translates the spike into a current signal that looks completely different from the action potential of the source cell. Hence, there is hardly any knowledge to be gained by studying the form of the spike. "The important thing then is the temporal sequence of the spikes," says Egert. "In other words, I need a device that tells me which cell fired when."

Scientists are responding to this challenge by first breaking the system down into smaller units. One approach involves observing the electrophysiological activity, i.e., the activity of the action potential, of cell cultures with approximately

"We concentrate initially on basic properties in order to study how the general rules of neural networks function"

25,000 nerve cells and measuring the interaction between the cells. This complicated undertaking can be achieved with the help of so-called microelectrode arrays, which can be used to study active networks. Up to 1,000 external contact points are connected to micrometer-sized measuring points in the middle of the square receptacles, which are only a few centimeters in size. Each measuring point corresponds to an electrode that has contact with one or more neurons. Their signal is picked up by an amplifier. "We need a good sample of neurons that we can measure simultaneously," says Egert. "The arrays give us a high spatial and temporal resolution." The scientists then observe the network to determine what forces are unleashed in it. "The neurons in the arrays spontaneously form groups and create local centers," says Egert. "The role of the structure for the function is unclear. In the human brain, for instance, we have layers in which there are various types of cells, which are in turn located at very precise levels." However, the example of bird brains illustrates that high performance is possible even without layered neurons.

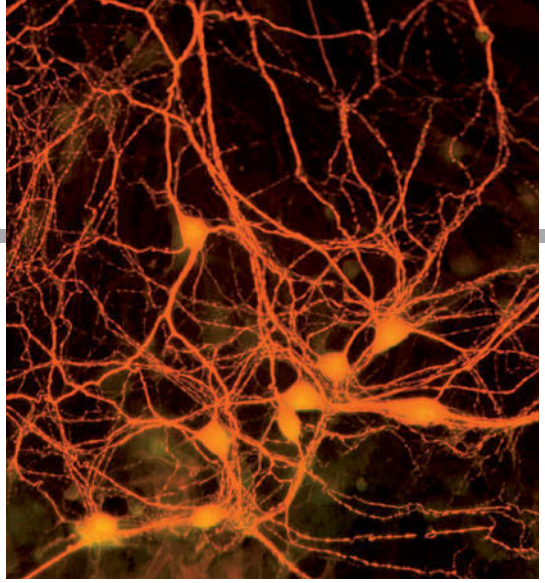


Brain slice on a microelectrode array: The researchers stimulate various areas and measure the reaction of the nerve cells.

Simulation on the Computer

Thus, when neuroscientists use computers to simulate such networks, they initially ignore the geometry. "There are various ways of building such neural networks," says Egert. "We begin by concentrating on basic properties in order to study how the general rules of neural networks function, which we can then simulate in a realistic way on the computer." When the simulations are successful, they serve as the starting point for new experiments. However, in order to create realistic simulations it is necessary to have a large mass of concrete data that must be determined by way of experiments. What biophysical properties should the neurons have, which frequency should the stimulation be set at, where exactly should it be applied and in which phase, and how often and how long should the network be stimulated?

The researchers are also investigating how an incoming stimulus spreads in the various network architectures. If it spreads evenly over the entire brain from a single point, the nerve cells in a particular area fire simultaneously and use up their resources all at once, much like in the case of an epileptic seizure. "We need areas that differ from one another, that react to different kinds of excitation, that have a certain amount of robustness, and whose nerve cells do not use up



Detail of a cell culture that has been colored with antibodies against a neuron-specific protein. The image shows the cell bodies as thick "knots" and the neuronal networks connecting them. Several non-neuronal cells are barely visible in the background.

all of their resources immediately." This corresponds closely to the situation that can be found in clustered networks. The activity of the neurons in an artificial network of this kind can be designed in a simulation to be functionally similar to a biological network. "It looks as if we were replacing one chaos with another," says Egert, "but that is not the case." On the contrary, the various paths of excitation in the electrode array can be precisely traced and even influenced.

Epilepsy research provides the neuroscientists access to the biological networks in the brains of mammals. Epileptic areas of the brain undergo restructurings that change the neural networks permanently. Mesial temporal lobe epilepsy, which occurs in the hippocampus, often cannot be treated adequately with drugs. Surgeons therefore often remove the tissue in order to prevent an excitation from occurring. The scientists initially failed in their attempt to simulate the excitation in a brain slice of a modified section of the hippocampus. "We didn't succeed in causing epilepsy in the tissue section." In further experiments with epileptic mice, however, they discovered that various sub-networks with incorrectly functioning interactions in the hippocampus and in the so-called entorhinal cortex react with one another in a feedback loop.

"We do not yet know precisely how this leads to epilepsy, but we find it systematically and only in epileptic animals," says Egert. The scientists found similar processes in cell cultures: spontaneous transitions between normal and extremely strong activity, like in the epileptic system. "We are now asking ourselves what these two processes have in common and whether we can repair them. We have found a new approach for intervening, but we are not yet certain whether it will be successful." In collaboration with Prof. Dr. Oliver Paul and Dr. Patrick Ruther from the Department of Microsystems Engineering, the neuroscientists have defined new microelectrodes for simultaneously collecting data on different areas of the entorhinal cortex and the hippocampus. "But at the same time we are working with our cell cultures, in which we can stimulate the individual nerve cells and modify the networks without too much effort. Here we have entirely different possibilities for accessing and manipulating the samples than we do in experiments on animals."

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SURPRISING SCIENCE

On the Internet platform Surprising Science, Prof. Dr. Carola Haas from the Freiburg University Medical Center, who collaborates with Prof. Dr. Egert at the Cluster of Excellence BrainLinks–BrainTools, explains her fundamental medical research on epilepsy, to which microsystems engineering is making important contributions.

http://www.surprising-science.de/en/specials/the-brain-and-technology/epilepsy-in-a-model/

Prof. Dr. Ulrich Egert *studied biology in Tübingen and Durham, England. He wrote his dissertation on the development of thin-film electrode arrays and their use in neurophysiology at the Natural and Medical Sciences Institute of the University of Tübingen. In 2005 he completed his habilitation at the Faculty of Biology of the University of Freiburg. In 2008 he established the Laboratory for Biomicrotechnology, which has 15 employees today. He also serves as coordinator of "Bernstein Focus: Neurotechnology Freiburg/Tübingen," a priority project funded by the Federal Ministry of Education and Research, as director of the Bernstein Center Freiburg, and as co-director of the new Cluster of Excellence BrainLinks–BrainTools. He and his colleagues are working on reaching a better understanding of the foundations of activity dynamics in neuronal networks and clarifying their relation to diseases of the nervous system and their treatment.*

Taking Technology's Pulse

The Sociologist Stefan Kaufmann Is Analyzing the Opportunities and Dangers of Technical Progress in the Emergency Medical Care of Accident Victims

by Holger Lühmann

Simulated airplane crash: The rescue crew receives quick and reliable information on free capacities at nearby hospitals. This speeds up the process of distributing the injured among the hospitals.

"Our study focuses on the functionality of new technologies in emergency medicine and their suitability for daily use"

Ultrasonic devices analyze organic tissue, cardiographs check the patients' heart rates, magnetic resonance imaging tomographs scan their bodies: The use of modern computer technology has improved medical diagnostics and brought health care a huge step forward. Now new technologies are also finding their way into the area of emergency care. A handheld computer equipped with Internet-based software has the potential to revolutionize immediate rescue operations at large-scale accidents. However, the use of the device also harbors risks. A team of sociologists led by Prof. Dr. Stefan Kaufmann from the University of Freiburg is conducting a field study on the professional and societal consequences of advances in medical technology.

Emergency at the Frankfurt Airport: A passenger machine has collided with a smaller jet while landing. Next to the wreck lie injured passengers. Debris is strewn about, complicating the rescue work. Firefighters are freeing the victims with welding equipment and angle grinders. In addition to brute force, however, sensitive technology is also in use: The rescue workers are carrying so-called personal digital assistants (PDAs), tiny Internet-enabled computers the size of a pocket calculator that can be used to quickly measure and store data on patients, such as their pulse, breathing, and the severity of their injury. The devices transfer the data instantly to the commander of operations. Information concerning the situation at the scene of the accident can thus be collected at a central location faster than ever before.

Drill with 1,000 Participants

Not everything goes off without a hitch, because the instrument is new and the emergency personnel are not yet used to it. However, mistakes in entering the data don't have any negative consequences – at least not yet. "The airplane accident was only a simulated catastrophe scenario," explains Stefan Kaufmann. "More than 1,000 firefighters, paramedics, and amateur actors participated in this emergency drill, making it the largest ever." It was the first big drill to be conducted within the context of the research project "Sofortrettung bei Großunfall – SOGRO" (Instant Rescue in Large-Scale Accidents), which was launched in 2009 to explore new strategies in emergency medical care for accident victims. "Our study focuses on the functionality of new technologies in emergency medicine and their suitability for daily use," says Kaufmann, one of the partners in the project, which is being coordinated by the German Red Cross in Frankfurt. "We sociologists are concentrating particularly on the changes that take place at the rescue and command levels during large-scale disasters." In early 2012 the researchers conducted a somewhat smaller emergency drill in a Frankfurt sports hall involving the collapse of a grandstand.

Frankfurt rescue services, paramedics, firefighters, and hospitals practiced for a real emergency at the two drills and tested the modern handheld computers. Kaufmann observed the two staged emergency operations together with his colleagues Nils Ellebrecht and Markus Jenki and a team of students. In order to capture the action at the drills, the team installed stationary cameras at strategically important points. For the second emergency drill, Kaufmann also gave six of his assistants helmets with attached video cameras in order to record the reactions and instructions of the persons in charge of the operation. The SOGRO project was commissioned by the German Federal Ministry of Education and Research and is being followed closely all over the world due to its methodologically innovative approach of including both sociologists and experts on emergency medical care. “The drills were observed by representatives from Singapore, Israel, and the United States,” reports Kaufmann.

“We need to bear in mind the possibility of an unexpected defect in the handheld computers and the danger of a broken Internet connection”

These handheld computers are designed to ensure that all information on an accident is collected as quickly as possible at a central location.

The study is an excellent example of the practical applications sociology has to offer. “The video recordings help us to analyze behavioral patterns in rescue service personnel,” explains Kaufmann. “One of our findings is that while the handheld computers do lead to a faster appraisal of the situation, they cause delays in the flow of work in other areas. We still need to solve such resultant problems of new technologies.” The use of the PDAs is a big help from a methodological standpoint, as it allows Kaufmann to use the data from the situation appraisal system for the analysis. The handheld computers provide useful research material, such as the time of entry of patient data, and they can thus be used to meticulously track down errors or bottlenecks in the work flow. The goal is to improve efficiency, because in rescue operations a single second less or more can mean the difference between life and death.

The Test Phase is Underway

Now that the two drills are over with, the researchers are subjecting the PDAs to a test phase. Several ambulances in Frankfurt are already equipped with the device. If a large-scale accident with many injuries occurs, the rescue teams are ready to use the Internet-based system immediately. In the case of a real emergency, the system is not only designed to improve the flow of work at the scene of the accident but also to speed up the process of distributing the

Rescue crews and firefighters have already tested the handheld computers during two large-scale drills with hundreds of participants in Frankfurt.

injured among nearby hospitals. The rescue coordination center can compare the data on the victims to the capacities of hospitals in the surrounding area directly from the scene of the accident. "The advantage is that the hospitals continually feed information about their capacities into the network," says Kaufmann. "This allows the rescue teams to quickly determine where which victims can be admitted and where they can't." Despite these advantages for the appraisal of the situation and the coordination of tasks at the scene of the accident, Kaufmann views several aspects of the technology with a critical eye: "We need to bear in mind the possibility of an unexpected defect in the handheld computers and the danger of a broken Internet connection."

However, several aspects of previous rescue practices remain unchanged: The rescue teams still separate the victims into groups depending on how urgently they need treatment. The injured are given color-coded markings, red marks signifying a severe injury and green a light injury. But instead of cards providing information on injuries, signs of life, or drugs that have already been administered, the patients will now receive armbands with a memory chip. "The chip contains all of the patient's data and can be read and written on at all further transport stations and at the hospital," explains Kaufmann. In this way, subsequent teams will be able to determine more easily how urgently the patients need to be transported to the hospital and treated. "The previous procedure with cards often proved to be inefficient. In addition, the entries were sometimes unreadable due to rain or hectic writing." Kaufmann is thus in favor of the new data recording system. However, he also warns that "initial analyses indicate that the sorting of victims is not error-free even with the help of the PDAs. For instance, the rescue teams occasionally classified uninjured persons as severely injured, which distorted the situation appraisal." The decisive factor is still qualified personnel, as Kaufmann stresses.

Due to the large amount of data, precise findings are not expected until after the completion of SOGRO in the spring of 2013. Afterwards, Kaufmann intends to continue concentrating on questions of civil security research. In 2009, he was already involved in the establishment of the "Centre for Security and Society," an interdisciplinary network of jurists, sociologists, computer scientists, and scientists from further disciplines at the University of Freiburg who are planning innovative projects in the area of civil security. "This is a field of research in which there is still a lot of work to do," says Kaufmann. "Questions of security were largely informed by military concerns up until the political transformation processes of the 1990s. Now that the Cold War is over, we need to start focusing more of our efforts on civil security."

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Prof. Dr. Stefan Kaufmann
Kaufmann has served as adjunct professor at the Institute of Sociology of the University of Freiburg since April 2012. Upon completion of his studies in Freiburg and Berlin, he began his academic career in 1997 at the University of Freiburg collaborative research center "Identities and Alterities." After the project ended in 2002, the sociologist taught and conducted research at other institutions – for instance at ETH Zurich, Switzerland, on a scholarship from the German Research Foundation and later as a fellow at the Center for Interdisciplinary Research in Bielefeld. Kaufmann has headed several research projects on civil security since 2007 and was involved in the establishment of the Freiburg Centre for Security and Society in summer 2009. The interdisciplinary network addresses questions of civil security.

Recognition 2.0

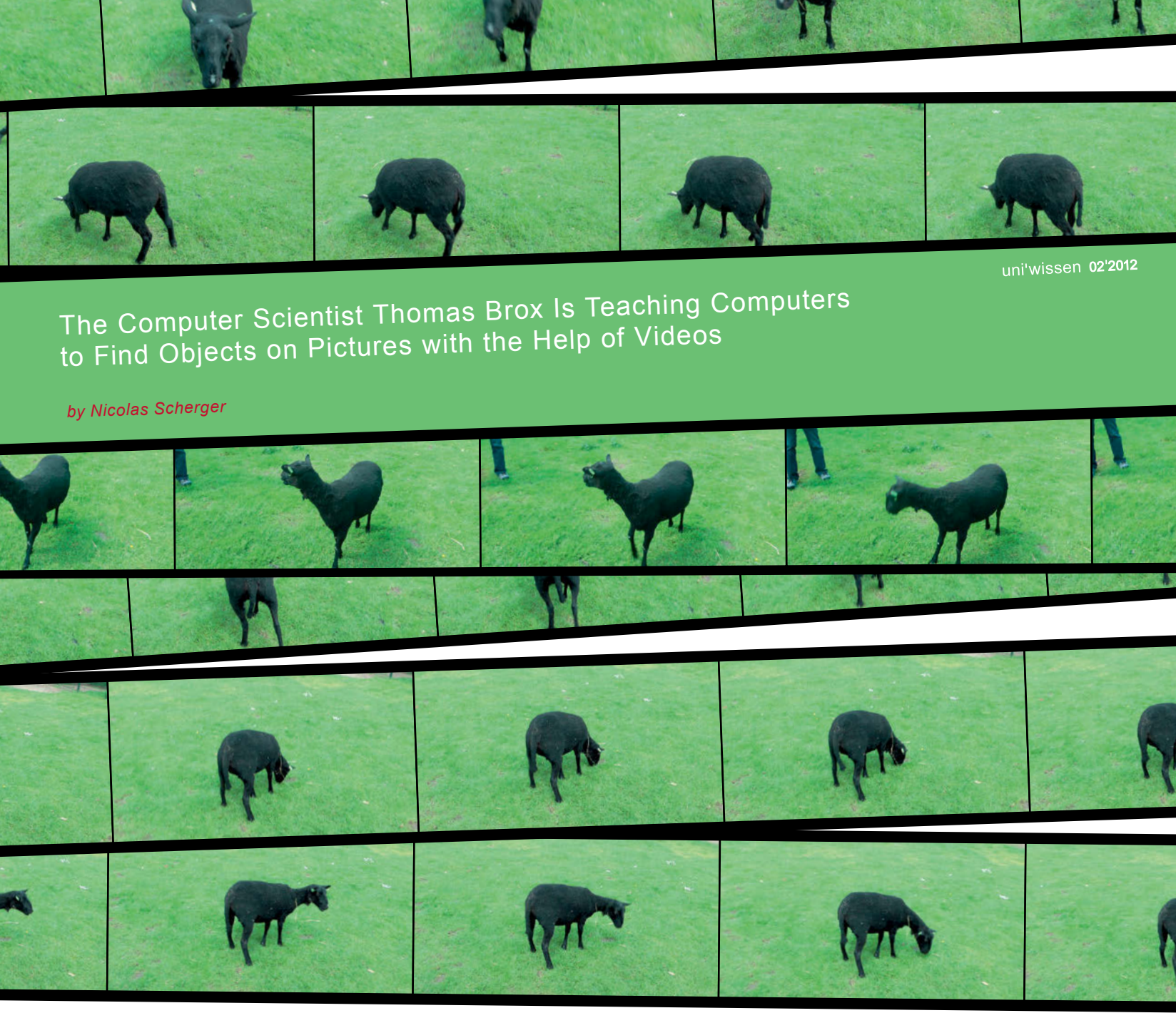
Observed from different perspectives: Videos provide the computer with a wealth of image data that show the variations of an object. This allows it to learn, for instance, what a sheep looks like – and to acquire the ability to find sheep on other pictures.

When we see dachshunds, Dobermans, or Great Danes, we know right away: They're all dogs – no matter what perspective we see them from and no matter whether they are eating, sleeping, or fetching a stick. Computers do not have this knowledge. For them pictures are nothing other than a long chain of numbers composed of points with various color values. Prof. Dr. Thomas Brox from the Department of Computer Science of the University of Freiburg wants to teach computers to grasp the meaning of these abstract data: "The goal is an automatic learning process in which computers find objects on pictures and improve their search independently."

In order for a computer to recognize objects, it has to be able to come to grips with their variations on two different levels. To take the example

The Computer Scientist Thomas Brox Is Teaching Computers to Find Objects on Pictures with the Help of Videos

by Nicolas Scherger



of humans: Our appearance changes depending on what clothes we're wearing or what perspective one views us from, and when several people are in the same picture the diversity of appearances becomes completely confusing. In order to recognize humans with any degree of reliability, the computer must be able to distinguish between these variations. "It can't memorize all of the possibilities, because this would involve too many training examples," says Brox. Instead, the computer has to learn how to abstract from particulars: "It has to find features that are common to all humans," meaning typical structures and forms, such as the head and shoulders.

The idea of teaching computers to recognize features that are characteristic of particular classes of objects – humans, cars, dogs, potted plants – is by no means new. Up until now, however, scientists have trained computers by marking objects on individual images with so-called annotations, for instance a frame and the remark that there is a dog inside it. The computer recog-

> "On videos the computer has an easier time segmenting objects or separating them from the background"

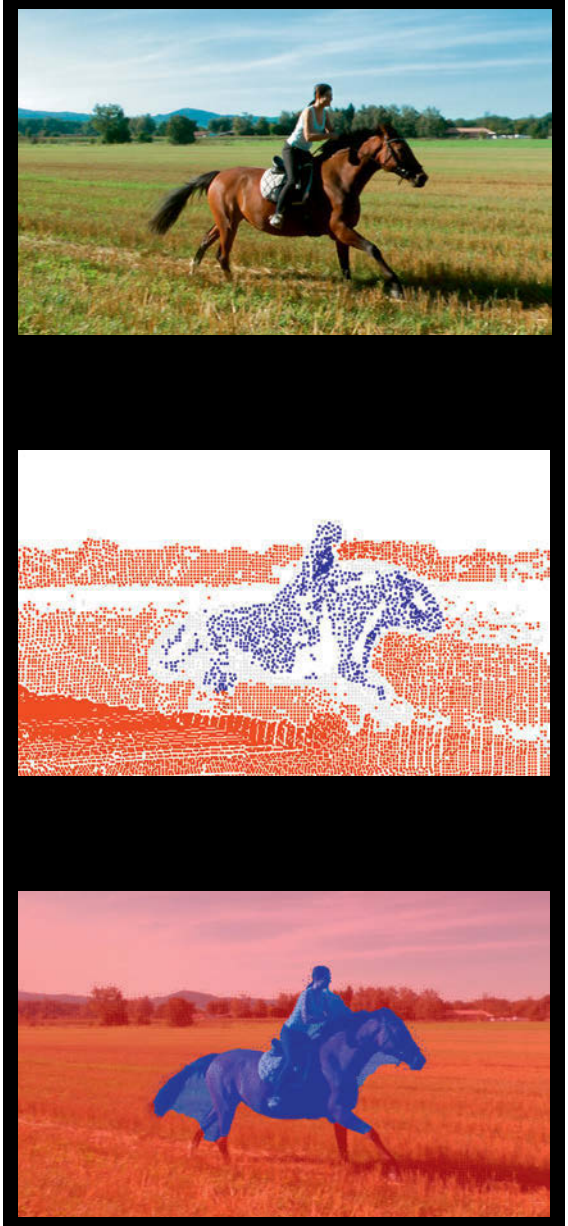
nizes the forms and structures that describe the dog on the basis of the edges inside the frame, at which the color in the picture changes. This method has disadvantages, says Brox: "The manual effort for the annotations is high, and the computer learns only what it has been provided

with." Instead, Brox wants to teach computers how to acquire new knowledge on their own in order to automate the learning process and reduce the number of necessary annotations.

Finding Points that Move in Similar Ways

In order to achieve this, he does not use static images but films. "On videos the computer has an easier time segmenting objects or separating them from the background," says Brox. He developed a method of analysis that has the computer find all of the points in the video that move in similar ways – for instance a rider on a horse. "That is a clear indication that these points differ from the rest of the pictures." Humans, animals, and vehicles move on their own. In the case of stationary objects, such as a piece of furniture, Brox creates the illusion of movement by moving the video camera around the object, enabling a three-dimensional reconstruction. The computer then compresses the segmentation: "It also assigns all points that it could not locate previously to the object or the background with the help of color information." In this way, the computer can separate the object from the background without needing to be shown a frame telling it where something relevant is located. All Brox has to do is let the computer know what class the object shown on the video belongs to.

In addition, a video is composed of two dozen images per second. Since the object, for example a car, looks slightly different on each image due to the movement, the computer already learns a large number of variations just from watching the film. "Furthermore, it's also clear that the reason for this variety is not that the cars in question are different. That is important information for the learning," says Brox. The computer scientist has solved the first part of the learning process: The computer recognizes variations of, for instance, the same cars on the ba-



The computer separates the rider on a video (top) from the background by assigning the points that move in a similar way to the same object (middle). It adds the remaining points with the help of color information. In this way, every point on the image is assigned either to the rider or the background (bottom, overlaid on original image)

"If we only used YouTube, the computer would develop an Internet-centric view of the world that doesn't adequately reflect the real world"

sis of the video analysis. Now Brox is working on the second step: teaching the computer to compare several films and find similarities – such as images showing different cars from the same perspective. The computer can lay these images on top of one another. "Then it can determine what forms and structures are common to all cars and develop a general description of the class of 'cars.'"

Independent Collection of Training Data

This provides a basis that enables the computer to identify variations of cars that it was previously unfamiliar with on other videos. Since it already knows the class, it shouldn't need to be told that a car is on the film anymore – in other words, it can get along without annotations. The new variations present an opportunity for the computer to expand its knowledge: It compares them with those it has already leaned, refines the abstract description of the class, and thus becomes better at finding examples of it in the future. In this way, the scientists aim to initiate a learning process in which the computer collects most of its own training data and develops its ability to recognize objects on pictures autonomously. In order to get this process underway, all the scientists need to do is provide the computer initial information on the class it is supposed to learn. "The ideal thing would be to just give the computer pictures in which it finds similarities, allowing it to form the categories itself and acquire a nice representation of the world," says Brox. "This works with humans, but for computers we have to simplify the problem."

In the future, computers that can recognize objects on pictures could be used among other things to optimize driver assistance systems in cars or help robots to orient themselves better in their environment. In order to make the technology practicable for such applications, however, the scientists will need to accelerate the process: Currently, the computer needs around a second to search an image and up to two minutes to complete the learning process. "Real time is not absolutely necessary for the learning process, but it is for the recognition of objects. After all, a robot shouldn't have to stop all the time to think."

Thomas Brox is regarded as a pioneer in the field with his research approach. "At conferences I notice that other scientists are finding the idea of working with films for image recognition more and more attractive." The computer scientist and his research group film most of the training videos for the computer themselves: cars, sheep, dogs, and soon humans. In order to capture an object from all sides, he walks around it once while filming. The resolution is high, the examples of the class are representative. These are things most Internet videos can't offer. "At the end of the learning process it is wise to show the computer a couple of YouTube videos, which usually contain non-standard examples of objects, in order to obtain new variations," says Brox. "If we only used YouTube, the computer would develop an Internet-centric view of the world that doesn't adequately reflect the real world."

Prof. Dr. Thomas Brox *has served as professor for pattern recognition and image processing at the Department of Computer Science of the University of Freiburg since 2010. He studied computer engineering at the University of Mannheim and earned his doctorate in computer science at the University of Saarland in 2005. He then continued his research as a member of the Computer Vision Group at the University of Bonn and taught at the Dresden University of Technology from 2007 to 2008. After two years of research activity in the Computer Vision Group at the University of California, Berkeley, USA, he accepted a position as professor in Freiburg. His main research interests include the visual understanding of computers, three-dimensional reconstructions, and the automated and intelligent analysis of spatially and temporally resolved microscopic images.*

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Nitrogen from Roots

Biochemist Oliver Einsle's Research on Enzymes Has the Potential to Reduce the Environmental Impact of Agriculture

by Annette Kollefrath-Persch

Soon a thing of the past? Nitrogen fertilizer would be made superfluous if plants could produce enough of the nutrient on their own.

They are small, their names sound complicated – and they are important for the environment: the enzymes nitrogenase and nitrous-oxide reductase. In nature they occur in highly specialized microorganisms. Nitrogenase is used to convert nitrogen (N_2) into a fixed form, making it available for plants whose growth is dependent on N_2. Nitrogen is one of the fundamental building blocks of life and accounts for almost 80 percent of the air we breathe. On account of its stability, however, the gas molecule is very difficult to cleave through chemical means and is thus a scarce resource in industrial agriculture. Farmers therefore use synthetic nitrogen fertilizer to support the growth of their crops. When produced using the so-called Haber–Bosch process, synthetic nitrogen fertilizer uses up roughly one percent of all globally produced energy at current production volumes.

The enzyme nitrous-oxide reductase, on the other hand, cleaves the environmentally harmful gas nitrous oxide (N_2O), also known as laughing gas, which is created among other things by soil bacteria during the decomposition of nitrogenous fertilizer – a process in which large amounts of N_2O are released from fertilized crop land. N_2O contributes to the depletion of the ozone layer and to the greenhouse effect and is probably the most critical gas for the fate of the climate in the 21st century. In addition, it also remains intact in the atmosphere for 120 years. Since natural nitrogen is not available in sufficient amounts, farmers use more industrial fertilizer for their crops, thus releasing even more N_2O. Prof. Dr. Oliver Einsle, a biochemist at the University of Freiburg, is tackling this environmental problem in his research: He is studying the enzymes nitrogenase and nitrous-oxide reductase in order to find a natural alternative to synthetic fertilizer on the one hand and to enable the decomposition of environmentally harmful compounds on the other. “That would be a fundamental step forward,” says the researcher.

> “We first need to reach a complete understanding of the basic properties and functions of the enzymes, even if this is a time-consuming endeavor”

Solution from nature: The roots of leguminous plants, such as peas, beans, or soybeans, possess special bacteria that fix nitrogen from the atmosphere. These plants thus grow well even in poor soil.

In his project "N-ABLE," funded by the European Research Council and the German Research Foundation, Einsle and his team will be reconstructing the complex and highly oxygen-sensitive enzyme systems in model organisms in the coming years. This has never been achieved before, neither in biological nor in chemical research: "We first need to reach a complete understanding of the basic properties and functions of the enzymes, even if this is a time-consuming endeavor." Einsle is concentrating his efforts on a solution suggested by nature: Leguminous plants – such as peas, beans, or soybeans – associate with a particular type of soil bacteria, rhizobia. The plant forms a special organ on its root for these bacteria. The organ protects the microorganisms from oxygen (O_2), which is harmful for them, and provides them with the nutrients they need to go about the laborious process of nitrogen fixation. Rhizobia possess the enzyme nitrogenase and capture N_2 from the atmosphere. This reliable source of nitrogen is why leguminous plants are particularly rich in protein and thrive even in poor soil with low nitrogen content.

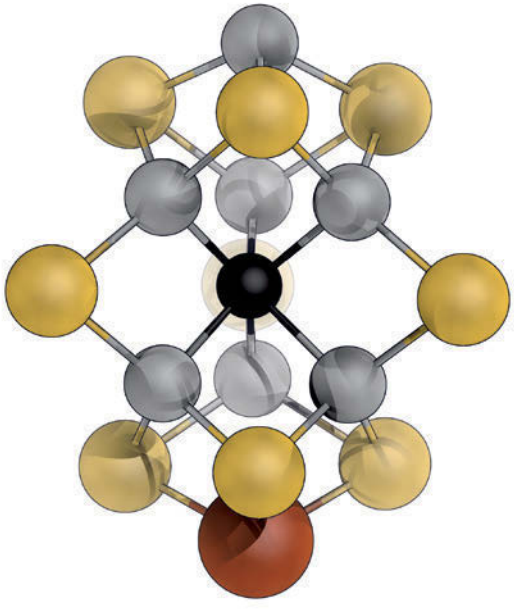
"We place the bacteria under evolutionary pressure and tell them what to do for us"

After studying this symbiosis in the laboratory, the Freiburg biochemist aims to extend it to other plants in agricultural practice, enabling them to take up bacteria with the enzyme nitrogenase in their roots and provide themselves with sufficient N_2. This would make industrial fertilizer superfluous. "We are creating chemical systems that fulfill important metabolic tasks and bringing them to organisms that otherwise would not have this ability," explains Einsle. He stresses that the potential for this method is not limited to the edible parts of crop plants.

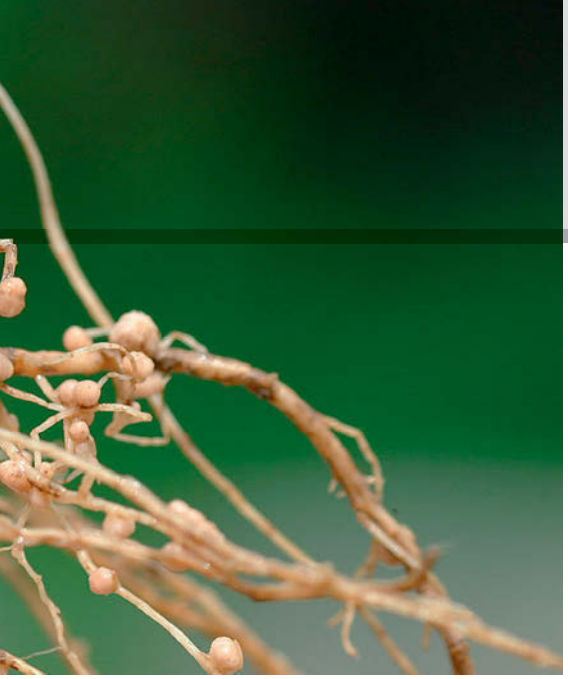
Switching Individual Components On and Off

As an initial step, Einsle and his team analyzed the enzyme in detail in order to understand the foundations of the function of nitrogenase. In the process, they explained the precise structure of its complex metal center, in which the chemical activation of N_2 takes place. Einsle reported these findings in two articles published in the renowned journal *Science*. The second step will involve determining which processes each of the individual components of the metal center are responsible for. Then the researchers will reassemble the enzyme in a model bacterium step by step and switch the individual components on and off as a test: Only in this way can Einsle find out which parts of the system engage with each other during the cleavage of N_2 and how they do so.

"In the end we will have to optimize the stability of the system," explains the biochemist, because the oxygen sensitivity of the bacteria and their enzyme nitrogenase is a big problem. Legu-



The researchers analyzed the enzyme nitrogenase in order to understand its function. They found out that its metal center, at which the chemical activation of nitrogen takes place, is composed of iron atoms (gray), sulfur atoms (yellow), a molybdenum atom (brown), and a carbon atom (black).



minous plants build a protective environment for the bacteria in their roots by nature. In order to reduce the bacteria's dependency on this environment, the scientists are counting on another solution: directed evolution. "We place the bacteria under evolutionary pressure," says Einsle, "and tell them what to do for us." On culture plates, the scientist is growing numerous bacteria that can only cover their need for nitrogen by producing nitrogenase. An advantage of this method is that bacteria have short generation times. Einsle then adds a small amount of O_2, damaging the nitrogenase and thus preventing further growth. Eventually, however, mutations start taking place that can enable one or two out of every million bacteria to continue growing anyway, because their modified nitrogenase is more tolerant of oxygen. At this point, the biochemist understands and possesses a bacterium that can do exactly what he wanted it to do. Now he just needs to introduce this bacteria into higher organisms, because the ultimate goal is to enable this process to take place in plants. Einsle knows that this is a big challenge: "It will be an exciting journey that will lead us far into uncharted territory."

Future Microorganisms Will Break Down Harmful Gases

Einsle has another reason to be optimistic: The goal of his research project "N-ABLE" is not just to give plants the ability to supply themselves with N_2, thus obviating the need for industrial fertilizer. In addition, the Freiburg researcher wants to produce modified bacteria that break down the harmful N_2O gas before it is released into the atmosphere. Laughing gas is released even without synthetic fertilizer – for instance by industrial plants and through geological processes. Einsle thus plans to use the same method of directed evolution he has developed for nitrogenase to analyze the process of nitrous-oxide reductase. The ultimate goal is to use this enzyme to produce modified bacteria that N_2O can use as a source of energy. The bacteria would then break down the gases from the air.

"The topic has attracted the attention of various organizations and many political bodies," explains Einsle. Among other things, he is receiving a starting grant from the European Research Council worth 1.64 million euros in the next five years. In addition, the International Panel on Climate Change of the United Nations recently called on scientists to find a solution to these problems at a conference on global climate change.

Prof. Dr. Oliver Einsle *studied biology in Constance and earned his PhD in biochemistry and biophysics at the Max Planck Institute of Biochemistry (MPIB) in Martinsried. After a year as a postdoctoral researcher at the MPIB, he worked from 2001 to 2002 at the California Institute of Technology in Pasadena, USA. From 2003 to 2008 he had a position as junior professor of protein crystallography at the University of Göttingen. Since 2008 he has served as professor of biochemistry at the Faculty of Chemistry, Pharmacy, and Earth Sciences of the University of Freiburg. Einsle is a member of the Cluster of Excellence BIOSS Centre for Biological Signalling Studies of the University of Freiburg and the American Chemical Society. His main research interests are the structure and function of membrane proteins and metalloproteins. Photo: Seeger*

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Small Coffee, Big Effect

The Sinologist Lena Henningsen is Studying Contemporary Consumer Culture in Chinese Cities

by Rimma Gerenstein

Frappuccino, salted caramel mocha, iced latte: The American chain Starbucks serves coffee specialties designed to convey the atmosphere of the modern and elegant "West." Photo: suttonIs/Flickr

The first McDonald's restaurants in China were popular places for rendezvous for years after they opened. Today children and older people are the most common customers. Photo: BYTE RIDER/Flickr

Exquisite, an exquisite machine," the sales clerk assures a married couple eying a coffee machine. In the store across the way, two young women cast yearning looks at a sweater from the collection of a French designer – if only cashmere weren't so expensive. Just a few meters further along is a long succession of restaurants, bookstores, jewelers, nail studios, cosmetic salons, and electronics stores. The shoppers are accompanied on their shopping tour by piped-in music and the constant drone of voices.

With more than 1,000 stores, 20,000 employees, and 230 elevators, the Golden Resources Shopping Mall in Beijing is one of the largest malls in the world – a temple of consumerism the size of 70 football fields. Men and women laden with shopping bags? Negative. Most people spend their time strolling from display window to display window and killing time at chain restaurants like McDonald's or Starbucks. "They might not spend a lot of money at the mega-mall, but they do consume," says Dr. Lena Henningsen. "They take part in practices of everyday life and enjoy the atmosphere, the luxury, and the glamour of expensive and sought-after products."

The Freiburg junior professor in Sinology is researching contemporary consumer culture in Chinese cities like Shanghai, Beijing, and Nanjing. The attractions include coffee specialties from American chains and overpriced noodle soups from a Japanese company. Such products are particularly popular with consumers, because "the buyers know what to expect and the producers know what to offer in terms of price and quality." The Sinologist also investigates popular novels, widely read blogs, and several popular Korean and Taiwanese television series and films. The consumer landscape in these large cities is paradoxical, says Henningsen. Although people are becoming more affluent, the social safety net is still not well developed, and many people do not have retirement or health insurance. As a result, the products at the shopping malls often remain unsold, because many people have to save their money. "Most Chinese only spend a lot of money on a few select things: a car, a home, education for their children, and – out of necessity – the doctor."

"Most Chinese only spend a lot of money on a few select things"

The researcher has chosen a mixture of methods from literary theory and ethnology. She combines readings and interpretations of cultural texts with interviews she conducted with visitors of chain restaurants in China. Why do they come here? How do they spend their time here? What do they like to order? "I'm not interested in what the people eat or drink. I want to know what it says about their cultural self-image when they assert: 'Starbuck's has my favorite coffee.'"

A Space for Rendezvous

Modern coffee specialties and fast food have established themselves as trend products almost all over the world in the past 20 years. In the urban chaos of China, however, the chains that sell them have a special significance: "They are regarded as romantic locations," explains the researcher. In the novel *The First Intimate Touch*, for instance, a bestseller in both Taiwan and China, the author Cai Zhiheng tells the love story of two students who meet for their first rendezvous at a McDonald's. According to Lena Henningsen, the book illustrates a phenomenon that began to change the forms of social expression available to young adults in late 1990s China. The private sphere was narrowly constricted in the People's Republic in those years: Students shared a dorm room with several fellow students, and young

Harry Potter and an imitation: Plagiarized copies of the series of novels were among the best-selling books on the Chinese black market when the first film adaptations hit the cinemas and ignited a Harry Potter boom.

people with jobs generally lived with their parents. Most cities didn't yet have a coffeehouse culture with drinks and snacks at affordable prices, and restaurants were much too expensive for young people. And in the booths at Karaoke bars, the operators themselves provided the ladies for their patrons. "McDonald's was not just popular because of the food but because the chain provided a new space in which young people could escape from the influence of their parents."

The book does not provide a completely accurate representation of reality, says Henningsen, but it does play an important role: "Fictional texts serve as a kind of guidebook that helps readers to orient themselves in the jungle of consumer society." They provide knowledge about the products, define their role in everyday life, and show what one can do with them and how one can interpret this use for one's own identity. "To a large extent, the popular books explore the phenomena of modern consumer culture. They convey an urban lifestyle that includes international brands as well as features of upscale Chinese consumer culture and elements of so-called

"Fictional texts serve as a kind of guidebook that helps readers to orient themselves in the jungle of consumer society"

high culture" – da Vinci and Shakespeare side by side with Rolex, red wine, and Chinese tea. In addition, although the fast food chain McDonald's has now become primarily a meeting place for the elderly and a place for children's birthdays, it is still seen as the embodiment of the American way of life. "Many Chinese now know that the food at McDonald's is unhealthy, but parents still go there with their children because it also provides something of an educational experience," says Henningsen.

A few years ago, the cool hipsters all began congregating at Starbuck's. The coffeehouses serve innumerable coffee specialties and offer the added attraction of comfortable armchairs and oversized sofas. Henningsen has observed that many of the people who patronize the coffeehouses work in the creative industries, from authors to graphic designers. They enjoy reliable Internet access and can work more or less in peace at Starbucks, because not everyone can afford this exclusive atmosphere. The coffee of the day costs the equivalent of around two euros – half the price of a bowl of noodle soup at the snack bar around the corner. Oftentimes the patrons only order a small coffee, but it has a big effect: The consumer goods serve as a kind of cultural bridge to the modern and elegant "West," says the Sinologist. "The people see themselves

as part of a global group. They say to themselves: Even though I'm sitting here in a city whose name no one knows in the USA, I can pretend I'm drinking my Frappuccino on Broadway in New York." The fact that their "favorite coffee" is actually called an iced latte or a salted caramel mocha doesn't bother them in the slightest. Henningsen has found out that people tend to use generic names like "iced coffee" in guestbook entries, and this didn't change after Chinese stores started giving out brochures in which the correct names of the products were translated and explained.

Books on the Black Market

Living a certain lifestyle and being part of a modern group are also factors that resonate in the consumption of popular literature in China. In her research, Henningsen didn't confine her inquiry to the bestseller lists. "Numbers are very easy to manipulate. You never know whether the people really read the books with the highest circulation. After all, almost all of us have the telephone book lying around at home." Instead, she uses other sources to get a reliable impression of what people read: She asks her students, who regularly take language study trips to China, to take a look at what's being offered on the black market and bring her back the top-selling titles. When Henningsen was working on her dissertation several years ago, the most popular black-market titles were above all genuine and plagiarized Harry Potter books. Sales of the fantasy series went through the roof when the first film adaptation hit the cinemas – a prime example of multimedia marketing. Henningsen studied all manner of plagiarized copies of the series, from amateur translations produced at lightning speed to adaptations in which the protagonist has adventures at culturally significant places in China.

Today one of the best-selling authors is Han Han. The literary star compiled a list of 48 titles circulating under his name that he did not write. Several of these plagiarized books have even made their way into Chinese libraries. The young author is a master of self-marketing. In his blog, one of the most widely read in China, he stylizes himself as a rebel, using vulgar language, writing that he has chosen a Japanese porn star as his idol, entering into races as a professional race-car driver, and criticizing the educational system of the People's Republic of China. "Han Han is no dissident, but he is seen as an outspoken personality who is not afraid to say what he thinks in current political and social debates. The readers also consume this feeling of freedom when they buy his books."

Dr. Lena Henningsen *studied Sinology, musicology, and political science at Humboldt University in Berlin, Nanjing Normal University in China, and the University of Heidelberg. From 2004 to 2012 she worked as a lecturer at the Institute of Chinese Studies at the University of Heidelberg. In 2008 she completed her dissertation in Heidelberg, part of which was on plagiarized Harry Potter novels. Since 2012 Henningsen has served as a junior professor at the Institute of Sinology of the University of Freiburg. Her research interests include 20th and 21st century popular literature in China, contemporary Chinese consumer culture, and Chinese music. Photo: Kunz*

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Enjoy your meal: Young mice need to ingest sufficient glucosinolates to strengthen the immune defense in the intestines – for instance by eating broccoli. Photos: Ben, CUKMEN, Pakhnyushchyy (all Fotolia)

Broccoli Strengthens the Immune

Freiburg Researchers Have Discovered that the Immune System Only Develops Correctly with the Help of Certain Substances from Cabbages

by Jürgen Schickinger

Caring mouse mothers would do well to feed their offspring broccoli rather than cheese. Although the milk product might have an attractive scent and taste delicious, in contrast to plants from the cabbage family it does not contain any glucosinolates. Mice need these plant chemicals in order for certain immune cells in their intestines to develop into lymphocyte clusters, where they guard against infections and chronic inflammatory diseases. Young mice deprived of broccoli risk contracting such diseases. That is the result of research conducted by Prof. Dr. Andreas Diefenbach and his doctoral candidate Elina Kiss. The two scientists have both received prestigious awards for their findings.

Scientists who conduct experiments on mice typically have more lofty goals. “I think that these plant components are also biologically active in humans,” says Diefenbach, who conducts his research at the Institute of Medical Microbiology and Hygiene of the Freiburg University Medical Center and the Cluster of Excellence BIOSS Centre for Biological Signalling Studies of the University of Freiburg. Glucosinolates are believed to be most important during childhood. In baby mice they have the strongest effect from around the tenth day to the eighth week of life. “However, glucosinolates are also contained in mother’s milk,” explains Diefenback. Human and mouse mothers should thus not scorn broccoli, at least while they are nursing their offspring. Those who aren’t fond of broccoli can also eat Brussels sprouts or any of several other vegetables in the cabbage family that contain large amounts of glucosinolates. For the project NutrImmune, Diefenbach has been awarded a Starting Grant worth 1.5 million euros from the European Research Council (ERC). “It wasn’t even our intention to investigate the influence of

System

nutrients on the immune system in the intestines," says the scientist. He only wanted to find out how lymphoid tissue inducer (LTi) cells develop and which molecules they control.

"It wasn't even our intention to investigate the influence of nutrients on the immune system in the intestines"

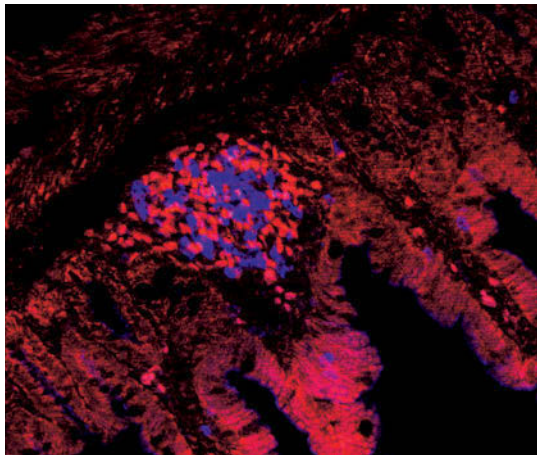
Without Follicles, Infections Are Lethal

LTi cells are a subfamily of the innate lymphoid cells (ILC). After birth, LTi cells develop into various lyphoid cell clusters. They initially form cryptopatches that are located primarily in the small intestines. These accumulations of cells lie at the foot of the crypts, the indentations between two intestinal villi. Then the LTi cells attract other immune cells – B cells, which produce antibodies. This makes the cryptopatch into a follicle: The mouse is now protected against enteropathogens and enterohemorrhagic bacteria. "They always cause lethal infections in mice without follicles," explains Diefenbach. Even in healthy humans and animals, enteropathogens sometimes cause severe, occasionally even lethal, diarrhea. Hemorrhagic bacteria such as EHEC (enterohemorrhagic E. coli) can also lead to lethal kidney damage.

In the case of severe infections, the germs force themselves through the intestinal epithelium. This unicellular layer separates the intestinal mucous membrane from the intestines themselves. Once under the intestinal epithelium, the germs cause inflammations. "We want to prevent this," says Diefenbach. However, it is still unclear how LTi cells, which belong to the innate

Infants are provided with glucosinolates through mother's milk. The Freiburg researchers suspect that these plant chemicals influence the development of the innate immune system in the intestines in mice as well as in humans. Photo: Molin/Fotolia

immune system, identify "enemies." The more well-known adaptive immune system doesn't learn how to distinguish the body's own bacteria from foreign bacteria until after birth. Through contact with the outside world, countless specific antigen receptors develop in the course of time which T cells in the adaptive immune system can use to identify potential invaders. The LTi cells do not have such detection receptors at their disposal. "However, we know more about how they fend off pathogens," says Diefenbach.



Various types of immune cells collect in the crypts, the indentations between two intestinal villi (red: LTi cells; blue: B cells) and form follicles. The follicles protect mice from infections and chronic-inflammatory diseases.

LTi cells produce soluble factors, including interleukin 22 (IL-22), which causes the cells of the intestinal epithelium to form proteins that can be used to combat germs. T cells also release IL-22. In their case, the aryl hydrocarbon receptor (AhR) boosts the production of the factor.

LTi cells also have the AhR. What role does it play in them? In order to find the answer to this question, Diefenbach's PhD candidate Elina Kiss from the Spemann Graduate School of Biology and Medicine (SGBM) of the University of Freiburg switched off the receptor in her mice: The level of IL-22 decreased, and there was a hundredfold drop in the amount of LTi cells. "We didn't see any more patches and follicles under the microscope," says Kiss. Hence, the aryl hydrocarbon receptor is crucial. But what substances stimulate the receptor in LTi cells? Dioxin, the most well-known binding partner of the AhR, is toxic and thus does not come into consideration. "Since we are working on the digestive tract, nutrients struck us as the most interesting candidates," explains Kiss. A review of the literature led to the discovery that the aryl hydrocarbon receptor has a binding site for plant substances that glucosinolates can dock onto. Kiss could not simply feed her mice these substances exclusively, because they would not have survived it in the long run. The solution was a mouse diet: Kiss gave half of her animals food in which the glucosinolates had been industrially removed but which contained all other essential nutrients. These mice ended up looking like those without the AhR – they had very few LTi cells, hardly any IL-22, no follicles. The mice that received glucosinolates, on the other hand, developed in a completely normal way. "We were surprised to find out that the entire system is so dependent on AhR and glucosinolates," says the Finn. When she came to Freiburg in 2008, she was familiar with molecular biological techniques, but she was new to immunological re-

"Since we are working on the digestive tract, nutrients struck us as the most interesting candidates"

search. She can be proud of her work: Her findings were published in the renowned journal *Science*, and she also received the 10,000 euro Barbara Hobom Prize for her research.

Andreas Diefenbach is also satisfied with the results: "We found the molecular connection of the AhR and nutrients to the LTi cells and follicles." Stated in the simplest of terms: Broccoli plus AhR equals more LTi cells and follicles that produce IL-22, which in turn enables the intestinal epithelium to produce antimicrobial proteins. The aryl hydrocarbon receptor presumably also strengthens the barrier function of the intestinal epithelium. It lowers the risk of infections by sealing off this barrier layer and preventing germs from the intestines from entering. In addition, the LTi cells probably regulate the stem cells of the intestinal epithelium. Like the LTi follicles, they are located in the crypts. From there they control the regeneration of the layer, which renews itself completely every two days. Glucosinolates could potentially even improve the regeneration over the AhR. This would make it possible to keep centers of inflammation at bay in the case of chronic-inflammatory intestinal diseases like Crohn's disease.

Sautéing Is Better Than Cooking

That is one of Diefenbach's long-term goals: "After all, we are also doctors and want patients to profit from our research." However, several questions are still awaiting an answer: What signals influence the epithelial cells? How much broccoli or Brussels sprouts is enough? "We used amounts that correspond to those that humans take in with food," says the scientist. But do humans react to broccoli in exactly the same way as mice? What amount could lead to undesired effects, and what amount are people willing to eat? Andreas Diefenbach does not yet have answers to these questions, but he does have a tip: It is better to sauté vegetables from the cabbage family for a short time than to cook them in water for a long time. This way they don't lose many of the precious glucosinolates.

Elina Kiss *studied biology with an emphasis on biochemistry in Turku, Finland, and has conducted research at the Spemann Graduate School of Biology and Medicine (SGBM) of the University of Freiburg since 2008. For her work on the development and function of particular immune cells in the intestines, the LTi cells, she received the Barbara-Hobom Prize in 2011. The prize is awarded each year to promising young scientists by the Freiburg Cluster of Excellence BIOSS Centre for Biological Signalling Studies. She is almost finished with her doctoral dissertation. Afterwards, Elina Kiss plans to continue her work in the research group of Prof. Dr. Diefenbach.*

Prof. Dr. Andreas Diefenbach *studied medicine in Erlangen, where he earned his PhD at the Institute of Clinical Microbiology and Immunology. He then conducted research in the USA, first at the University of California, Berkeley, at the Department of Molecular and Cell Biology. Starting in 2003 Diefenbach worked at the New York University Medical Center as an assistant professor in the fields of immunology and pathology. In 2005 he returned to Germany and accepted a chair in Freiburg. He serves as deputy director of the Institute of Medical Microbiology and Hygiene of the Freiburg University Medical Center and heads a research group devoted to inborn immunity and the immunology of biological boundary layers like the intestinal epithelium and skin.*

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Barking up the Right Tree

The Materials Scientist Marie-Pierre Laborie Is Developing Bio-Based Plastics to Keep Your Living Room Warm in Winter

by Felix Austen

Natural insulation: Bark is a protective layer, and one of its functions is to protect trees against the cold. Freiburg materials scientists are transferring this strategy to architecture – they are using components of bark to develop bio-based plastics that can serve as insulating material.
Photo: Spalek

At the very beginning, humans lived in caves, making their home out of that which gave them the most protection with the least work. Then they began to design their own dwellings: animal skins stretched over a wooden frame became a tent, stacked tree branches a hut. It wasn't until much later that humans began using steel, glass, and plastics to build their homes, making tents into office complexes, wooden huts into skyscrapers. The change that is now upon us seems at first thought to be a step back – away from plastics, which are packed into walls as foam to keep houses warm in the winter. In the future, this function will again be fulfilled by a material that might initially seem obsolete: wood.

A research team at the University of Freiburg led by Prof. Dr. Marie-Pierre Laborie is working on the project "BioFoamBark." The project partners include the Institute of Forest Utilization and Work Science, the Freiburg Materials Research Center (FMF), and other scientists from universities and companies throughout Europe. The goal is to develop foams for insulating homes out of substances from tree bark. The project is being supported by the Agency for Renewable Resources with funds from the German Federal Ministry of Food, Agriculture, and Consumer Protection.

Getting More from Wood

There are many good reasons to replace conventional synthetic insulating materials with their competitors from nature: Wood is a resource that is readily available and that is used by industry on a large scale. An estimated twelve million cubic meters of bark are converted into biofuel each year in Europe alone. "But it's possible to get even more from the complex and versatile material wood than to simply process it into wood chips or biofuel and then burn it directly," says Laborie. "We go to the companies that pro-

cess wood and see whether we can produce something worthwhile from the waste." The processing of byproducts like bark is another link in the value chain of wood – and is thus financially attractive for the industry.

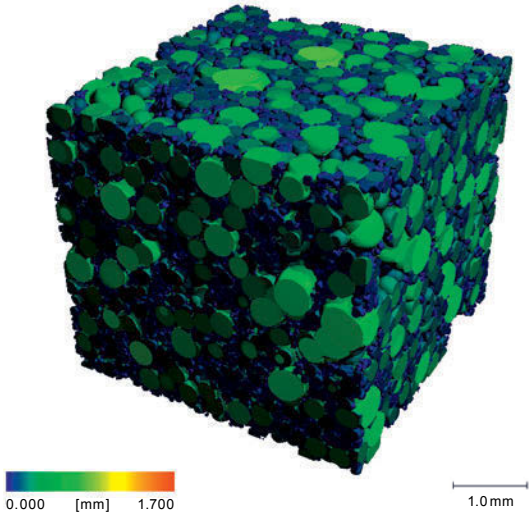
"We go to the companies that process wood and see whether we can produce something worthwhile from the waste"

As far as insulating properties are concerned, biofoams can stand comparison with conventional foams. In a study conducted by a group of scientists including Laborie, it was shown that foams made of tannin, a compound found in tree bark, insulates every bit as well as synthetic insulating material. They achieve a thermal conductivity of 0.033 watts per meter Kelvin. This means that at a temperature difference of one degree Celsius, one ten-centimeter thick square meter of wall made of this material allows 0.33 joules of energy per second to pass from inside to outside. Typical insulating material used today reaches a value of 0.035 watts per meter Kelvin. As a comparison: Concrete allows around 2.3 watts per meter Kelvin to pass through, 70 times as much.

Foam As a Life Saver

Another advantage of the foam is its flame resistance – a potentially life-saving factor in a house. In addition, if one wishes to insulate an existing house there's no need to tear down the facade in order to apply the insulating material. The foam can be injected directly into hollow spaces in the walls, where it self-inflates to fill the empty space: All one needs to do is set off the chemical reaction that leads to the creation of the foam, and it does the rest on its own. The biofoam will even be useful after it is no longer needed as an insulating material: It will be converted into biofuel – a further goal of the project. Last but not least, it is also environmentally friendly since it replaces synthetic foams produced with the limited resource petroleum.

The idea of producing insulating foams from bark is not new. It is based on research on organic tanning agents, the tannins. The distinguishing feature of tannins is that they bond with proteins upon contact and change their properties, dehydrating them and making them resistant to decomposition by microorganisms and heat. This explains the properties of the insulating foams they can be used to produce. However, there are many different kinds of tannins. The



The micro-tomographic image (left) shows the inner structure of the foam being developed by the teams of Marie-Pierre Laborie, Prof Dr. Antonio Pizzi, and Prof. Dr. Alain Celzard, Université de Lorraine, France, as well as Milan Šernek, University of Ljubljana, Slovenia (right). Since the microstructure can be manipulated, the researchers can influence properties of the foam like thermal insulation, sound absorption, and stability. Image: b-cube AG, Switzerland; Photo: Kunz

"There's an excellent tradition in tree research at the faculty, and the university is also very competent in polymer sciences"

ones that have been studied most extensively so far are those extracted from the tropical woods mimosis and quebracho. The production of foams made of these tannins has been studied exhaustively. The problem is that these plant species are relatively rare even in the tropics. It would be possible to produce a maximum of only 220,000 tons of this type of tannin per year – much too little to be of any relevance for industrial applications. Laborie is thus taking a closer look at tannins found in pine and spruce trees. There is a large supply of these trees all around the world, and they are thus important for the timber industry.

A Professorship Receives a New Emphasis

Vegetable-based polymers, the material used to produce bio-based plastics, is a new topic for the Faculty of Forest and Environmental Sciences of the University of Freiburg. Research at the faculty previously focused more on macroscopic observation of trees, for instance growth behavior. Laborie's first task was to give the Chair for Forest Utilization a new emphasis. When she arrived at the institute, the laboratories were not adequately equipped for the research she wanted to conduct. Since then a lab at the institute has been renovated from the ground up for her analytical research. Laborie also received workspaces in labs at the Institute of Inorganic and Analytical Chemistry and at the FMF, of which she is an active member. "That is a great help, but it's only a temporary solution for the growing research group," says the materials scientist. "However, I'm confident that we will soon receive the labs we need." Laborie's goal for the professorship is to close the gap between forest and materials sciences: "I see Freiburg as the ideal location to develop a program of this kind. There's an excellent tradition in tree research at the faculty, and the university is also very competent in polymer sciences," she says. "I was thus very happy to come here. And the students here are fantastic."

Equipping this field of research with the necessary capacities is a good idea, as bio-based plastics can be used to produce much more than just insulating material. Cellulose nanofibers, for instance, which are also found in plants, possess outstanding optical characteristics and can be arranged to form complex structures. Light sensors are just one of many possible applications for this technology. In addition, Laborie contributed a feasibility study to the development of the world's first passenger jet built out of carbon-fiber-reinforced plastic: the Boeing 787, also known as the "Dreamliner."

Prof. Dr. Marie-Pierre Laborie *completed her master's degree in engineering at the École Nationale Supérieure des Technologies et Industries du Bois in Épinal, France. In 2002 she earned her PhD in wood science and forest products at Virginia Polytechnic and State University, USA, and then accepted a position at Washington State University, USA. During a research sabbatical she completed her habilitation in materials and process engineering at the Grenoble Institute of Technology, France. Since November 2009 Laborie has served as professor for forest biomaterials at the University of Freiburg. In November 2012 the Fraunhofer Gesellschaft awarded her and her colleagues Prof. Dr. Antonio Pizzi and Prof. Dr. Alain Celzard from the Université de Lorraine in France the distinction of German High-Tech Champion in the category "Green Buildings."*
Photo: Kunz

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Thale cress is the most important model plant for geneticists. The large specimens of the plant on the photo have developed normally, the small ones have not – they are missing a gene that protects a part of their stem cells from differentiating into specialized cell types. Photo: Kunz

Stem Cells Help Plants Sprout

The Developmental Biologist Thomas Laux Is Decoding Genetic Mechanisms That Explain How Plants Grow and Mature

by Hinnerk Feldwisch-Drentrup

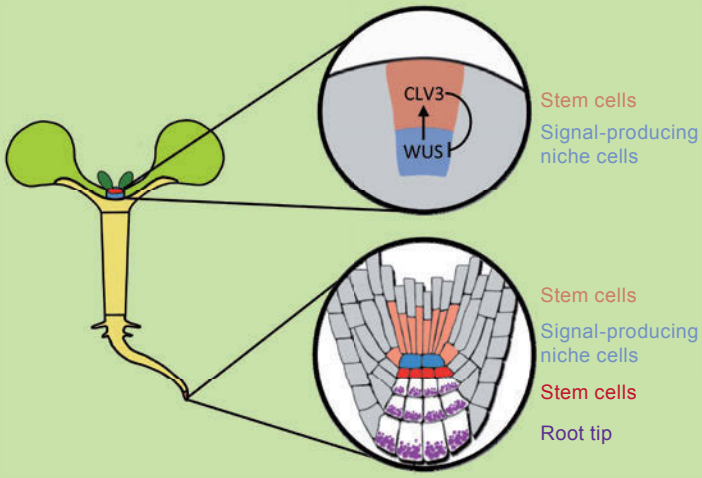
The fertilization of an egg cell triggers a genetic program that causes the organism to grow and prepares it for the adverse conditions of the environment. Stem cells play an integral role in this process, not only during the embryonic stage but throughout the entire life of the organism. They are the generalists in the world of cells: They can transform themselves into other types of cells to form organs or take the place of damaged cells. Doctors and patients are thus pinning their hopes on stem cell therapies for the treatment of diseases like Parkinson's or impairments like paraplegia. The Freiburg biologist Prof. Dr. Thomas Laux has shown that stem cells are not unique to humans and animals, but that they are also present in special niches in plants, where they are regulated by the neighboring cells. In the course of a plant's life, which in the case of certain trees may last longer than a thousand years, the stem cells enable the plant to grow roots under the earth and develop branches, leaves, and blossoms.

"Somatic embryogenesis enables breeders to preserve particular varieties in a precise state"

Only 20 years ago, the mechanisms plants use to keep growing and form new organs over long stretches of time were entirely unknown. Laux wanted to use the experience he had gained writing his dissertation on the biochemistry of animals to solve this mystery. "The prevalent belief at that time was that plants don't have any special stem cells – which would be astonishing when one considers their capacity for growth," says Laux. He chose the inconspicuous plant *Arabidopsis thaliana*, also known as thale cress. It is regarded as a weed but has enjoyed great success in science as a model organism: Thale cress reproduces rapidly, is easy to grow, and has very few genes.

A Niche for Stem Cells

If plants actually do possess stem cells, they must be located in the meristems. These tissues give rise to new organs, such as blossoms, leaves, stems, and roots. They are thus located at the tip of the roots and shoots as well as in the stem. In order to determine which genes regulate the stem cells, Laux asked himself how plants would develop if they could not form or maintain any stem cells due to a genetic defect. By studying classical experiments described in the literature, Laux discovered that the first two leaves generated by a meristem grow without the help of the stem cells, which aren't activated until the plant has produced additional leaf primordia. Laux thus reasoned that the plant could not control this second step without stem cells and would instead revert repeatedly to the original program and grow two leaves. He found that there actually are mutated versions of thale cress that behave in this manner. These plants are missing a gene that protects a part of their stem cells from differentiating into special cell types. Laux' team named the gene WUSCHEL after the disheveled outward appearance of the mutated plant – in German, "wuschelig" means shaggy or fuzzy.



In plants stem cell niches are located in the shoot and in the root, in trees also in the trunk. In the stem cell niches, neighboring niche cells form WUSCHEL signals (WUS) that prevent the stem cells from specializing. At the same time, stem cells form the factor CLAVATA3 (CLV3), which prevents too many new stem cells from forming. Cells at the tip of the root protect the stem cells from damage.

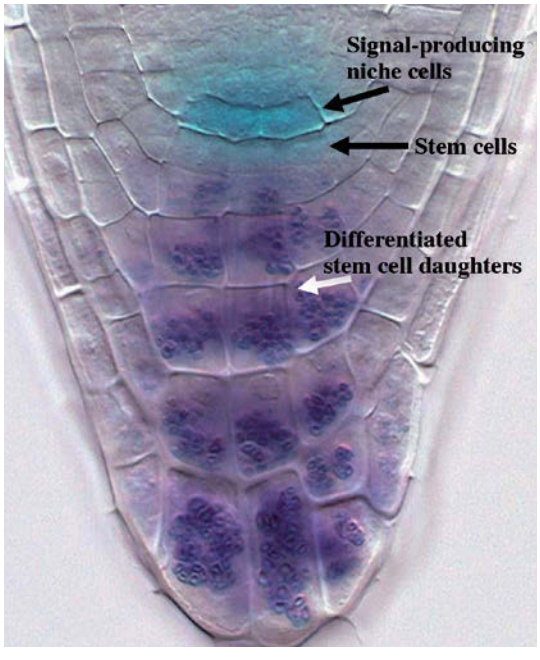
nowned journal *Nature*, his team demonstrated that genes similar to WUSCHEL and CLAVATA3 are active in the root, although the structure of the meristems located there differs greatly from those in the shoot. Other research groups discovered that this is also the case in the third meristem of plants, which is responsible for causing the stem to grow in thickness. Similar regulatory mechanisms are active in animal stem cells; the difference lies solely in the participating molecules. "That is astounding when one considers that the evolutionary course of animals diverged from that of plants at the unicellular stage, where there were not yet any stem cell niches."

"If all we see is that the plant is not doing well after we have manipulated a genetic switch, we do not yet comprehend the underlying relations"

As Laux found out, the neighboring cells of the stem cells use the WUSCHEL gene to produce a transcription factor that influences the transcription rate of other genes. It prevents stem cells from specializing and continuing to divide. Even the daughter cells that stay in the niche remain stem cells. "The remaining daughter cells that leave the stem cell niche no longer receive the WUSCHEL signals," says Laux. "Instead, other messengers cause them to differentiate into specialized cell types." These daughter cells divide several more times before finally finding their place in a leaf, a root, or the stem, where they fulfill their specific function. Thus, much as in animals their fate is determined by signal substances from the surrounding area of stem cells. However, whereas animal stem cells can only form cells for a specific type of tissue – stem cells in the brain of an adult animal, for instance, can only produce specialized brain cells – plant stem cells can still reconstruct any organ even after many years. In humans, this ability is limited to the embryonic stage.

Laux and his team devoted their first experiments to the shoot, in which the gene CLAVATA3 acts the role of WUSCHEL's antagonist. "The messengers produced by WUSCHEL and CLAVATA3 are in balance in healthy plants," says Laux. "In this way they keep the amount of stem cells constant." In a study published in the re-

The Freiburg scientist and his research team also discovered that genes related to WUSCHEL lead the way in the creation of the embryo as well. When the fertilized egg cell divides, the em-



The stem cell niche of the root under a microscope: The cells colored in turquoise maintain the stem cells located below them by means of WUSCHEL signals. The specialized daughter cells of the stem cells in the root tip are visible in the violet-colored starch granules.

bryonic axis takes shape, with the future shoot cells on the one side and the root cells on the other. If the WUSCHEL-like genes WOX8 and WOX9 are missing, the hormone auxin will not be distributed correctly in the embryo, and only an unstructured cell cluster will be created. "Embryo cells are similar to the stem cells – neither of them is specialized yet at this point," says Laux, "and it is thus possible that the original purpose of WUSCHEL was to develop embryos."

Fundamental Research for High-Yield Forests

On the basis of their previous studies, Laux and his team are now working on applications for growing plants by way of embryogenesis rather than through the traditional method of fertilization. In order to do this, the scientists use either active stem cells or sleeping stem cells, which only awaken in trees if the trunk snaps. If they are provided with nutrients and special hormones, these stem cells begin to develop into embryos – much as some plants develop from offshoots of a parent plant. The new embryos can then be planted.

"There are various reasons why it is interesting to avoid sexual reproduction, in which the genetic information of the mother and father are mixed," says Laux. "Somatic embryogenesis enables breeders to preserve particular varieties in a precise state." One promising effect of this is known as heterosis: "When one crosses two different pure-breed parents, the mixed-breed daughter generation can be particularly bountiful. However, the precise reason for this is one of the great secrets of plant science." When the following generation reproduces by way of sexual reproduction, the effect is cancelled out. As increasing the yield of crops is an important goal in many parts of the world, somatic embryogenesis is seen as a promising approach in plant breeding.

From Freiburg to China

The Freiburg biologists are cooperating with a team from the Chinese University of Nanjing that is studying trees. Their knowledge and their experience with the model plant *Arabidopsis* is a valuable addition to the project: Somatic embryogenesis is actually difficult to achieve in trees, but the biologists can stimulate the trees to produce more stem cells and embryos with WUSCHEL. At the same time, the research group is studying how plants can better protect themselves against heavy metals in the ground, which damage the stem cell niches in the roots. "This is a very ambitious project. The various signal substances in the root all combine to make up a big puzzle that we do not yet completely understand."

Through the use of modern methods of analysis like life imaging, which makes metabolic processes visible, the scientists are attempting to identify the various pieces of the puzzle and shed light on the system as a whole. "One stumbling block is that the WUSCHEL factors also influence a host of other genes," says Laux. "The relationships are complex since we can always only study one factor that makes a relatively small contribution to the overall system. If all we see is that the plant is not doing well after we have manipulated a genetic switch, we do not yet comprehend the underlying relations. We are thus using many different molecular genetic and mathematical instruments in order to understand each switch one at a time and to unravel the mystery of how plants develop."

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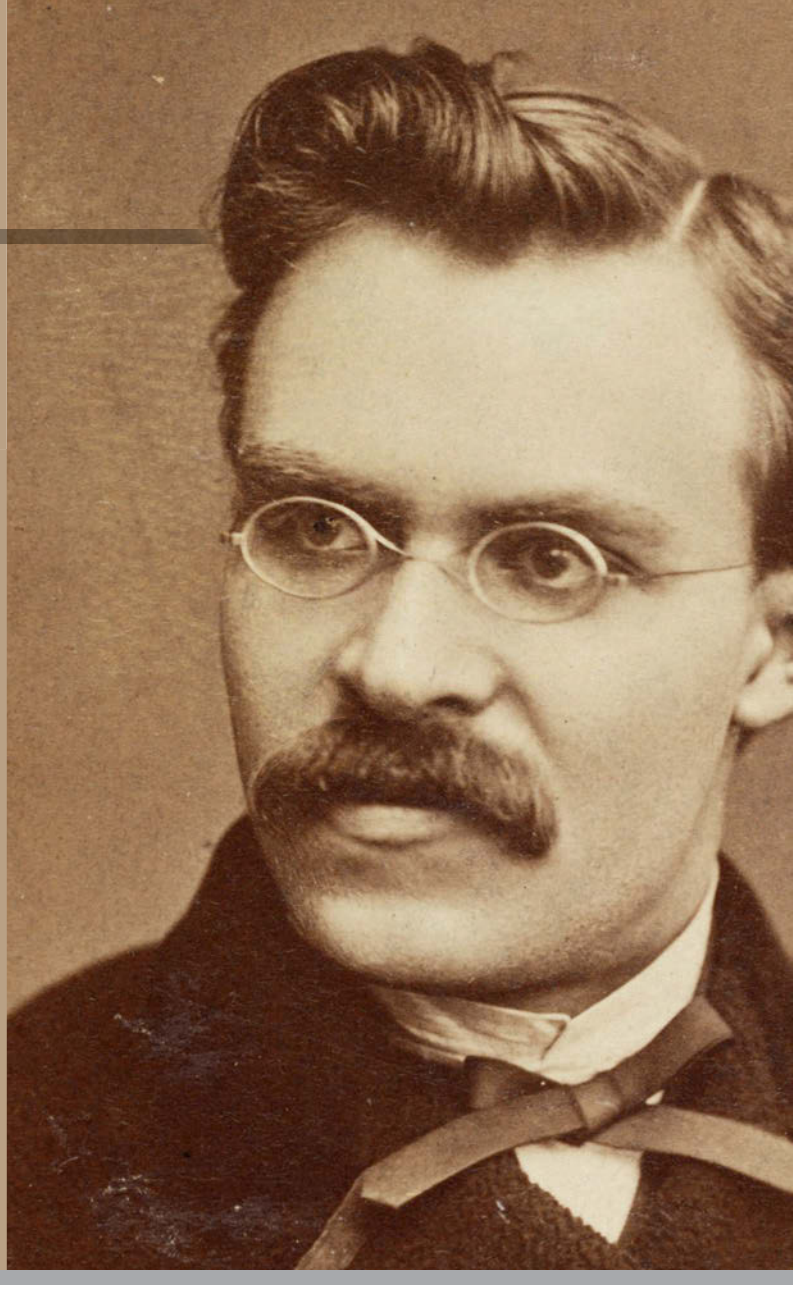
Prof. Dr. Thomas Laux *studied biology in Erlangen and earned his doctorate in biochemistry. After a period conducting research in Los Angeles, USA, and Munich, he earned his habilitation at the University of Tübingen. A year later he accepted a position as professor in molecular genetics and biotechnology of plants at the University of Freiburg. From 2008 to 2011 he was a fellow at the Freiburg Institute for Advanced Studies (FRIAS). He is a member of the Cluster of Excellence BIOSS Centre for Biological Signalling Studies of the University of Freiburg. Together with partners in Strasbourg, France, and Basel, Switzerland, Laux coordinates the trinational degree program Biotechnology and is involved in the Trinational Institute of Plant Research, established in 2011 with funding from the European Union. His research interests include developmental biology and the biotechnology of plants. Laux studies how cellular signals control stem cells and embryonic development and the ways in which they can be artificially influenced.*

Great Thinker, New Perspective



University of Freiburg Researchers Are Preparing an Indispensible Commentary for Future Research on Friedrich Nietzsche

by Stephanie Streif

Nietzsche is dead. He died in 1900. But the works of the great thinker live on – and have inspired generations of scholars. All the more astounding that there is still no comprehensive commentary to his complete works that elucidates his writings and places them in their context. After all, Nietzsche is relevant for a wide range of disciplines: His writings touch on aspects of literature as well as anthropology, art, history, psychology, physiology, and especially philosophy. However, such a diverse body of work is difficult to produce without inspiration from outside, even though Nietzsche stylized himself long before his mental collapse in 1889 as a gigantic philosophical monolith who created everything out of his own inner self.

In order to afford a look behind the scenes and bring the reader closer to Nietzsche, his work, and his impact, the Heidelberg Academy of Sciences and Humanities resolved to commission an interdisciplinary general commentary. The large-scale project is being coordinated at the University of Freiburg. It was initiated with the creation of two full-time positions in 2008 and is set to run for 15 years. The first two volumes were published in October 2012, with the next two to follow in 2013. A third of the work will then be complete. An initial evaluation report described the work the team has accomplished so far as excellent: “The commentary produced thus far offers an abundance of new insights into Nietzsche’s writings, their texture, and their sources,” praises the report.

> “It seems as if the great ideological battles over Nietzsche have been fought out. The time was ripe”

But why did we have to wait so long for a comprehensive commentary of Nietzsche’s work? “It seems as if the great ideological battles over Nietzsche have been fought out. The time was ripe,”

"Nietzsche certainly did receive inspiration from other authors, and this made it necessary to consider numerous sources from the 19th century"

Friedrich Nietzsche was a master at concealing his sources. Now commentators in Freiburg are tracking down the sources of the philosopher's inspirations. Photo: Klassik Stiftung Weimar

says Andreas Urs Sommer, adjunct professor of philosophy at the University of Freiburg and one of the commentators – along with Jochen Schmidt and Barbara Neymeyr. Group leader Schmidt served as chair in modern German literature at the University of Freiburg until 2004, Neymeyr is a professor in the same field. Neymeyr believes that the reason why Nietzsche was interpreted differently again and again in the past is because "his exceedingly erratic, aphoristic thinking seduced many of his readers to construct an entire ideology out of individual quotes." Nietzsche was appropriated time and again by the proponents of various ideologies – from National Socialists to Marxists and feminists.

Another stumbling block was the manipulative way in which Nietzsche's sister Elisabeth and her willing helpers at the Nietzsche Archive in Weimar dealt with his literary remains. After all, they were the ones responsible for tampering with Nietzsche's unpublished manuscripts and piecing together *The Will to Power*. This work was translated into numerous languages and was regarded by many interpreters, including the philosopher Martin Heidegger, as the quintessence of Nietzsche's philosophy, because it concretized and simplified his experimental thinking. However, the fact that too much importance was attached to his literary remains over the course of decades is also a result of Nietzsche's self-stylization: He always told his readers that his most important works were still unfinished. The commentary currently being prepared in Freiburg has now declared Nietzsche's literary remains to be of minor significance.

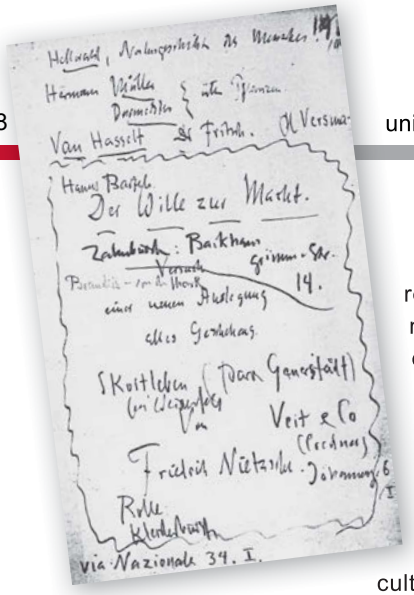
A Master at Concealing His Sources

Each commentator participating in the project has his or her own area of specialization: While Sommer is concentrating on the late writings from 1888 on, Neymeyr is responsible for the *Untimely Meditations*, a work influenced by the philosopher Arthur Schopenhauer, and Schmidt, an expert on Greek antiquity, is working on the early work *The Birth of Tragedy*. Interdisciplinary work is unavoidable. Nietzsche claimed again and again throughout his life that he hardly read anything, but that was simply not true. "Nietzsche certainly did receive inspiration from other authors, and this made it necessary to consider numerous sources from the 19th century," says Neymeyr. The philosopher was a master at concealing his sources. From time to time he would name his references, but usually he did not. A good example of this practice is the third part of the *Untimely Meditations* on "Schopenhauer as Educator." Although Nietzsche mentions the name of Schopenhauer many times here, he only speaks of Schopenhauer's treatise *On University Philosophy* explicitly at two points, says Neymeyr, "but a direct comparison of the two works reveals that Nietzsche takes important elements from Schopenhauer, even argumentation structures."

Polemic against the Zeitgeist

Nietzsche reworked the thoughts of others repeatedly and adapted them to fit his own philosophy – even the viewpoints of his adversaries: "In his late works in particular, he explicitly declares the authors to whom he is most indebted to be his avowed enemies," explains Sommer. In order to avoid being associated with them, he conceals his sources or dissociates himself from them with fierce polemic – a simple and effective way of positioning himself against the predominant zeitgeist. In his last writings, for instance, he construes the history of Judaism and Christianity as one of decline, falling back on Old Testament historian Julius Wellhausen's theory of the emergence of Judaism as a process of "denaturing." Whereas Wellhausen argued that Christianity had been able to reverse this development, Nietzsche contested that it had actually increased the "denaturing." However, Nietzsche does not mention Wellhausen at all in his works. This source was unknown until it was brought to light by the Freiburg commentators – along with a multitude of other sources. "You have to have a detective's nose to sniff out things like this."

The commentators found important clues as to how Nietzsche used his sources at the philosopher's private library in Weimar, which was digitalized for the commentary project. An examination of this library taught the trio a lot about the way in which Nietzsche worked, which – according to Sommer – was extremely selective: "He usually only read what he could use. In many books, only a couple of chapters or 20, 30 pages have his notes in the margin." As far as his own



Erratic thinker: Nietzsche evidently later used this draft of the title page of The Will to Power *from the year 1885 or 1886 as a reference and shopping list. Image: Wikipedia Commons*

readers were concerned, however, he demanded again and again that they "ruminate" on his books very carefully. Nietzsche was thirsty for recognition and approval. This is also one of the reasons why he wrote so much about his role models – such as the composer Richard Wagner, whom he first idolized and later polemicized against, not least in order to stylize himself as the real cultural innovator. But the commentary has now unveiled another Nietzsche. This discovery met with irritation even within the research team: "I don't view Nietzsche as a representative of any kind of grand philosophical system anymore," says Sommer. "He is more interesting to me when he remains experimental."

This does nothing to change Nietzsche's status as an important albeit ambivalent philosophical figure. Neymeyr values Nietzsche's distance from all systems and his spontaneous, aphoristically pithy style. "This can also stimulate our own thought processes and enable us to break out of thought routines." Thus, Nietzsche remains compelling – with and through the commentary, which will take on fundamental significance as a reference work for an appropriate appraisal of his writings.

Prof. Dr. Barbara Neymeyr *studied German literature, philosophy, Latin, and education at the University of Münster, earned her PhD with a dissertation on the philosophy of Arthur Schopenhauer, and completed her habilitation project in 2000 on the Austrian author Robert Musil. In 2006 she accepted a position as adjunct professor. She has served as a commentator for the Heidelberg Academy of Sciences and Humanities research project Nietzsche Commentary since 2008. Neymeyr has long been fascinated by the creative links between philosophy and literature, an interest reflected among other things in her co-editing of a two-volume cultural history of Stoicism. Her principle areas of research include 18th through 20th century German literature and 19th century philosophy.*

Prof. Dr. Andreas Urs Sommer *studied philosophy, ecclesiastical and dogmatic history, and German literature, before going on to earn his doctorate in 1998 at the University of Basel, Switzerland, with a historical commentary on the philosophy of Nietzsche's* Antichrist. *The next stage of his career included stints at Princeton University, USA, and at the Department of Philosophy of the University of Greifswald, where he completed his habilitation in 2004. Sommer has served as a commentator for the Heidelberg Academy of Sciences and Humanities research project Nietzsche Commentary since 2008 and as adjunct professor of philosophy at the University of Freiburg since 2011. His research interests include the history of late antique, early modern, enlightenment, and modern philosophy. He is also interested in the theoretical underpinnings of writings on the history of philosophy, skepticism and Stoicism, the philosophy or religion and history, ethics, and Friedrich Nietzsche.*

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Masthead

uni'wissen, the research magazine
of the University of Freiburg, is published twice yearly.

Publisher
Albert-Ludwigs-Universität Freiburg,
Rector Prof. Dr. Hans-Jochen Schiewer

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Print Run
10,000 copies

English Translation
Dr. David Heyde

Photos
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Cover photo: Kunz

Conception, Design, Production
qu-int. | marken | medien | kommunikation
Alter Zollhof, Freiburg
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Phone: +49 (0)761 28288-16
Fax: +49 (0)761 28288-66
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Printing and Production
Hofmann Druck, Emmendingen

Distribution
Office of Public Relations

Yearly Subscription Price
6 euros
uni'wissen is available free of charge
for students and employees of the university.

ISSN 2194-8054

uni'wissen is available online at
www.wissen.uni-freiburg.de.

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