University of Basel

UNI NOVA

University of Basel Research Magazine — N°134 / November 2019

Eye Research

Restoring Vision.

In conversation
School and gender.

Debate
Switzerland in Europe.

Album
Tiger mosquitoes – dangerous?

Essay
Buddha and the early Christians.


Work.
Learn.
Relax.
In der neuen UB Rosental
Mattenstrasse 42 4058 Basel

Team

Contributors to this issue

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1 **Suren Manvelyan** has taken the close-ups of the human eye for this issue's cover page and dossier. His photographs have been published worldwide. The 43-year-old professional photographer from Armenia graduated from Yerevan State University with a PhD in theoretical physics, and also teaches natural science. Pages 1, 4, 14–35

2 **Samanta Siegfried** has worked for various newspapers and magazines as a freelance journalist in Basel, her adopted home, since finishing university and her professional training in Germany in 2017. She interviewed educational researcher Professor Elena Makarova and researchers at the IOB on behalf of UNI NOVA. Pages 8–11, 34–35

3 **Pie Müller** is considered a leading expert in Switzerland on mosquitoes. As a group leader at the Swiss Tropical and Public Health Institute (Swiss TPH), the zoologist and entomologist completed her doctorate this year in medical parasitology at the University of Basel. Pages 40–49

New insights.

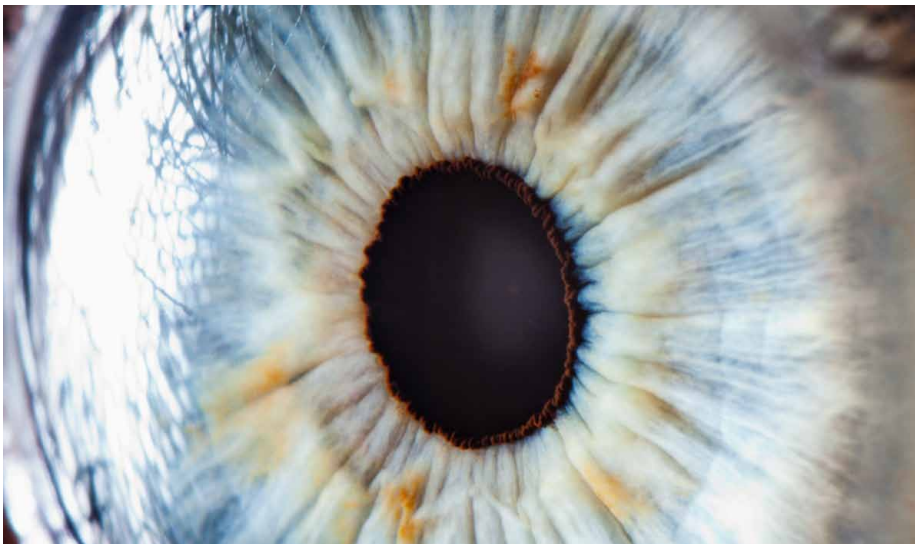
Sight is visual perception: when rays of light hit the eye, various mechanisms convert them into signals that the brain can process. Many of us will experience problems with our eyes at some point in our lives, and some diseases can leave us at risk of losing our sight completely. Many people fear total blindness more than any other condition. After all, the eye is one of our most important sensory organs. It is key to our spatial orientation and consequently to our independence. Glaucoma and cataracts, macular degeneration, retinal diseases, trachoma, and extreme short- and long-sightedness: various eye diseases are becoming more prevalent worldwide, in both the disadvantaged Global South and the aging societies of the Global North.

Two years ago, the University of Basel, University Hospital Basel, and Novartis founded the Institute of Molecular and Clinical Ophthalmology Basel (IOB). Experts conduct basic and applied research, and work on new technologies that will advance understanding of eye diseases and help develop effective therapies in the future. The Institute continues to grow, welcoming new research teams from Switzerland and beyond. As one of the first institutes of its kind worldwide, the IOB will act as a bridge between laboratories and hospitals. Ophthalmology is currently one of the fastest-growing medical disciplines.

In this issue, we present just some of the research projects taking place in Basel, all aiming to better understand the precise mechanisms of sight – and to improve treatment for more and more eye diseases. Read on to discover a wealth of new insights!

Christoph Dieffenbacher,
UNI NOVA editor

For gender equality in schools:
Elena Makarova in conversation, page 8



At the Life Sciences Cluster Basel, the eye is the focus of intensive research – from the laboratory to the hospital.

Dossier

Restoring Vision.

Cover photo
"Your beautiful eyes" is the title given by Armenian photograph Suren Manvelyan to his highly regarded photo series of the human iris.

The tiger mosquito is set to become native to Switzerland. Researchers are closely monitoring its spread, page 40

Imprint

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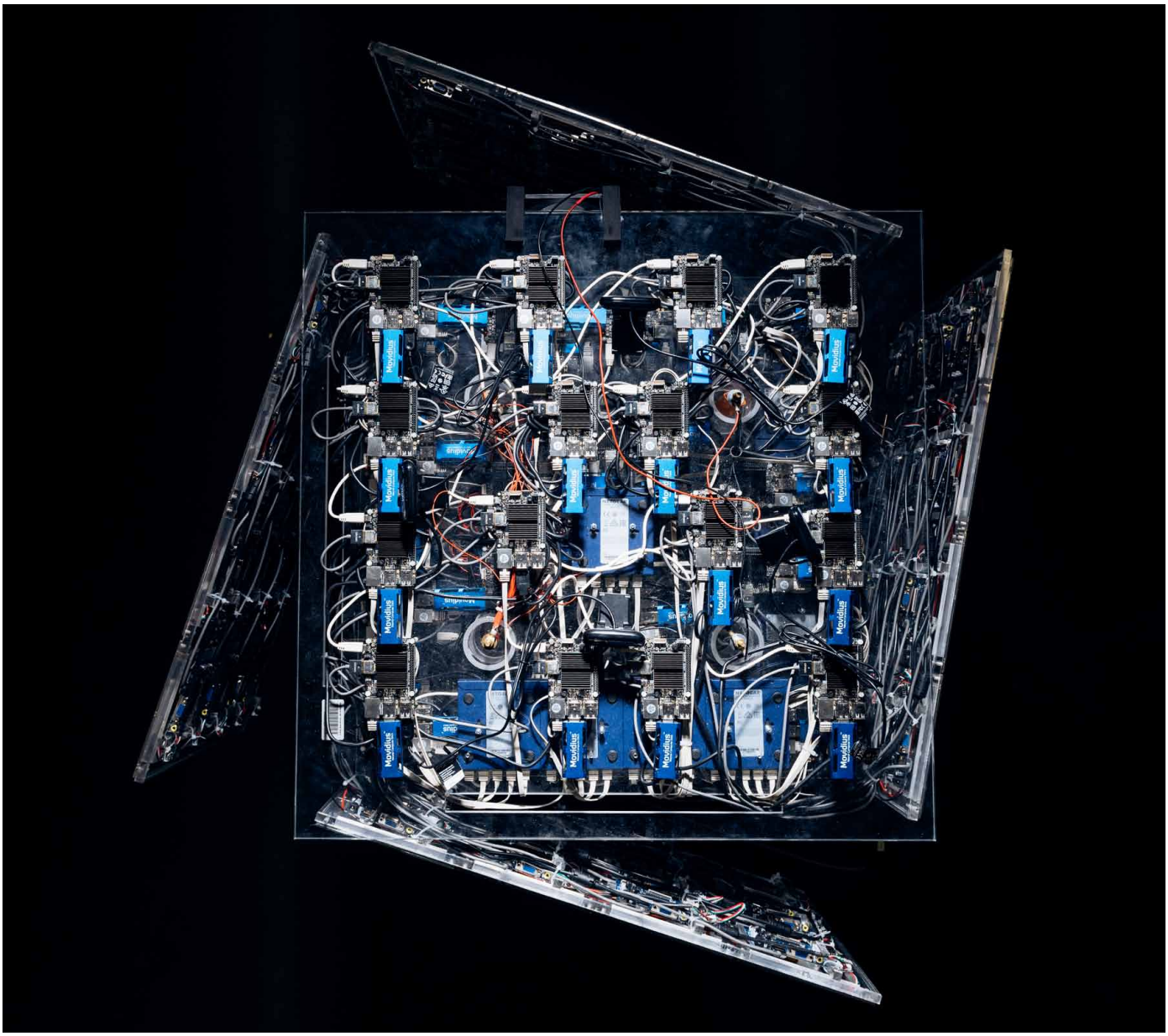
Computing

Understanding abstract technology.



Sixty-six single-board computers, 64 touchscreens, an acrylic case, as well as cables and power supply units: These are the components that make up the cube-shaped µ-Cluster. High-performance computing clusters like this can quickly process large volumes of data, which is why they are used in fields such as the film industry and astrophysics. The clusters are usually hidden away in server rooms, but the µ-Cluster is different: Its aim is to make parallel computing processes visible in real time.

The µ-Cluster began life as the result of a bachelor's thesis in the Department of Mathematics and Computer Science. Thanks to work by the researchers in the High Performance Computing group led by Professor Florina Ciorba, the cluster is now constantly growing and changing. The group also regularly exhibits it at events, such as the Fantasy Basel festival and the university's information day in January 2020. ■

hpc.dmi.unibas.ch

Migration

Hotspots at external borders.

The town of Zarzis in southeast Tunisia is one of the areas from which Tunisian migrants begin their journey to Italy. Zarzis also takes in migrants from Libya, and is home to a cimetière des inconnus – a cemetery for the unknown who wash up, drowned, on the shores of this coastal town. How does a local community deal with the consequences of migration?

In 2015, the EU agreed to support so-called "hotspots" at its external borders with infrastructure measures. An interdisciplinary team led by political scientist Professor Bilgin Ayata and architectural historian Kenny Cupers is investigating the effect of the migration policy on local areas. The researchers have visited places that are rarely a focus for the European public. They traveled from the Tunisian-Libyan border to Sicily and the Greek islands, where the hotspots were set up. ■

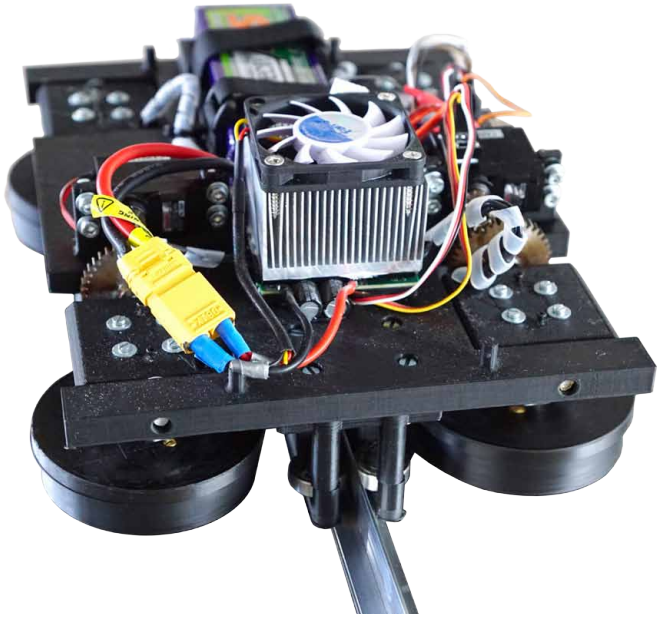
bit.ly/uninova-eu-hotspots

Technology

An innovative magnet array.

This maglev board is the result of an award-winning project by two teenagers. The invention won both the technology category of Germany's federal Jugend Forscht award and a first prize in the European Contest for Young Scientists. The Swiss Nanoscience Institute and the Department of Physics at the University of Basel supported the young researchers as they worked on making the board hover above a metal surface using rotating permanent magnets. One of the two inventors, Alex Korocencev, began a physics degree in September – at the University of Basel. ■

bit.ly/uninova-hoverboard



“The focus should be on the individual, not on their gender.”

How gender-equal is teaching at Swiss schools? Not yet fully, according to a recent study. Educational researcher Elena Makarova also believes that plenty more work is required to establish gender equality in the working world.

Interview: Samanta Siegfried Photo: Basile Bornand

UNI NOVA: Professor Makarova, what do you remember of your own math lessons?
ELENA MAKAROVA: I should start by saying that I went to school in the former Soviet Union. Math and science were highly significant in ensuring the supremacy of the country in the Cold War. Math was strongly emphasized throughout my schooling and we also had lessons in IT and basic programming. I remember being taught by male and female teachers. I enjoyed math and science and always earned good grades. No distinction was made between boys and girls.
UNI NOVA: It sounds like your experience was very different to that of many Swiss women…
MAKAROVA: Yes, compared with Switzerland, the USSR had a coeducational school system much earlier with lessons that involved both sexes equally. In Switzerland, girls used to be sent off to study home economics and were sometimes excluded from science lessons.
UNI NOVA: Is that why we still can’t shake the assumption that boys are better at math than girls?
MAKAROVA: When PISA test results are followed by headlines like “Girls are scared of math”, it perpetuates this assumption linking differences between students to their biological sex, usually unconsciously. Yet, various studies show that this explanation is far too simplistic. In their early school years, girls are often just as good at math as boys, or even better, and don’t lose this advantage until later on. It has also been proven that differences in performance can be balanced out through targeted intervention: For example, one study showed that, after a brief phase of training, girls achieve the same level of spatial attention and mental rotation as boys, who have an initial advantage. This confirms the supposition that gender-specific differences are due to socialization rather than evolutionary biology.
UNI NOVA: So we’re brought up that way?
MAKAROVA: Socialization works on the assumption that differences develop through experience. These experiences are, in turn, closely linked with social expectations imposed by our familial and social environment. Specifically, children notice at an early stage whether they are considered to have a talent for science. This is internalized and affects how they assess their own skills, the topics that interest them, and whether they enjoy the subject. There is also plenty of evidence that motivation plays a significant role in performance. Although most people are born with one unambiguous biological sex, we learn what it means to express being man or woman from parents, sib-

“In their early school years, girls are often just as good at math as boys and don’t lose this advantage until later on.”

Elena Makarova

lings and friends, but also at school, a core sociocultural environment.

UNI NOVA: In one of your latest projects, you examine gender equality in school science books at secondary level II. What were your key findings?

MAKAROVA: For one thing, we identified a linguistic disparity. The teaching materials analyzed feature practically no female protagonists and masculine is used almost exclusively as the generic form; the German uses words such as "Physiker" (male physicist) and "Naturwissenschaftler" (male scientist) not only to describe a singular protagonist but also as the plural, physicists. However, studies show that the generic masculine form triggers stronger mental representations of men than if the male and female nouns are used (e.g. "Physiker und Physikerinnen"), or alternatively a capital I ("PhysikerInnen") or a slash (Physiker/innen). Even if the materials state explicitly that the masculine form is intended to represent all genders, women may be intended, but they are not represented. Language is personification! And the word "Physiker" is the personification of the male gender. Another study, which examined whether gender-neutral language is clunky, showed that it does not impede readability or comprehension of a text. To be honest, I'm astonished that we still need to discuss whether female and male protagonists should be represented equally in language.

UNI NOVA: Did you find other disparities in the teaching materials?

MAKAROVA: Yes, there was also a lack of contemporary female role models. Marie Curie appeared most often, and Lise Meitner got the occasional mention. But that's it. Otherwise, the women shown were predominantly young women practicing a hobby, but not an occupation. In contrast, the men depicted were older and shown to have prestigious jobs such as scientists. To this day, teaching materials perpetuate the stereotypical image of science as a male domain. This is simply outdated. The problem is that when teaching materials are revised, the focus is usually on the subject content. But if we look at their socialization effect, they are maintaining 1960s' gender roles. There's a lot of work to be done.

Elena Makarova
studied special needs education and speech therapy at the National Pedagogical University in Kiev. She then moved to the University of Bern to study educational science along with Slavic and Russian philology, receiving her doctorate from the Faculty of Human Sciences in 2007. From 2003 to 2015, she was a research associate and senior research associate at the Department of Educational Psychology of the University of Bern. After completing her postdoctoral qualification in educational science in 2014, she spent two years at the University of Vienna as Professor of School Education with a special focus on social, cultural, and linguistic diversity. She then became Professor of Educational Science at the Research and Development Institute of the School of Education, University of Applied Sciences and Arts Northwestern Switzerland (FHNW). Since early 2019, she has been working at the University of Basel as Professor of Educational Sciences and Director of the Institute for Educational Sciences.

UNI NOVA: So why haven't these aspects of teaching materials been overhauled?

MAKAROVA: Partly due to a lack of awareness. And it will certainly take considerable effort. In a recent project supported by the Swiss Federal Office for Gender Equality, I worked with two authors to revise their physics textbook. It involved a huge amount of work. There were numerous stipulations: The content had to adhere to the school curriculum, fit in with the topics of the example tasks, and not exceed a particular length. And it wasn't just about showing more female scientists, but about generally incorporating more contemporary contexts and role models within the sciences – including men and scientific teams working and performing research today. In this case, the publisher covered the purely linguistic revisions, something not all publishers are willing to do.

UNI NOVA: As well as offering suitable material, teachers can surely also make an impact in the way they design their lessons. What do you advise your students to do?

MAKAROVA: Yes, the instructional design of a lesson is important. In my seminar on the importance of gender in the socialization and education process, I like to let my students uncover their own, unconscious biases; for example, I use the Implicit Association Test, which was developed at Harvard and tests biases against various social categories that can be linked with stereotypes, such as gender, age, and ethnicity. It's not about saying "Ha, caught you, you're biased!" but about showing that our biases are often unconscious in nature. We can then move on to consider how these biases might influence the teaching process. Feedback is one example of this: Studies have shown that teachers tend to praise girls for their careful work, such as their beautiful handwriting, and boys for their subject knowledge. The way in which feedback is given has a huge influence on how students see themselves.

UNI NOVA: I assume, though, that many things happen before they start school. What role do you think parents need to play?

MAKAROVA: Of course, attributing characteristics to a specific gender, and thus to associated gender roles, starts at birth. Parents often adapt the way they dress or play with their child according to its sex. Outside the family, for example in careers guidance, widespread terms like "fireman" and "cleaning lady" signal that certain professions are only suited to one gender. I would therefore also advise parents to expose their own biases and try to introduce their children to a variety of areas and experiences, whatever their gender.

UNI NOVA: So I should send my son to ballet classes?

MAKAROVA: If he wants to go then yes, of course! Encouraging an individual's potential talents and interests should not depend on their sex. But it isn't easy to go

against shared social preconceptions and stereotypes ascribed to a particular gender category. We are all constantly reproducing gender differences as part of the "doing-gender process".

UNI NOVA: What does that mean?

MAKAROVA: If you behave contrary to society's expectations of your gender category, you can expect sanctions. These can be very subtle; you might be told that "you play soccer well for a girl". The subliminal message is that you will never be as good as a boy because, as a female, you do not have the potential to play soccer. This might discourage a girl from developing her interest in the sport. Society and its structure need to change in order to modify the gender preconceptions they disseminate.

UNI NOVA: What are the problems involved?

MAKAROVA: The figures show that even women who study a STEM subject (science, technology, engineering, mathematics) rarely choose a career in the field after graduating. And even if they do, they are far more likely to leave than men. This is partly due to family policies. Just think about the UNICEF study published this summer, which showed Switzerland to be the least family-friendly country in Europe. There is no paternity leave, maternity leave is too short, childcare is too expensive, and so on. Studies show that part-time positions can often be found in "female professions" such as nursing/caring, social care, and education, but definitely not in STEM areas, where it is much more difficult to balance family and work. And so we find ourselves in a vicious circle: Women are overrepresented in stereotypically female part-time jobs, so we ascribe them the characteristics that these jobs require. We say that women are more suited to these jobs. Structural influences are coupled with biological sex, perpetuating biases.

UNI NOVA: So far we have only discussed the negative impact on women. But what about men? They are also subject to certain gender-based expectations.

MAKAROVA: The research projects I have conducted so far have paid less attention to the lack of men in social and educational professions. While we're talking about it, it's interesting to note that studies have shown that men in a gender-atypical working environment tend to be admired and regarded as highly skilled, while women in male-dominated occupations often experience discrimination. Clearly, egalitarian conditions can only be achieved if preconceptions about both genders change. But that won't be easy if we continue to think in terms of binary gender categories.

UNI NOVA: What do you mean?

MAKAROVA: I'll give you an example. Students frequently ask me "what about if we simply reverse the situation and have only women working in IT and only men working in the care sector, for instance?" This is exactly what I don't mean. I mean that young people should not choose their careers based on what they consider to be typically female or male, even if they do it unconsciously. They should all be able to choose a career that reflects their personal interests. From birth onward, the focus should be on the individual, not on ascribing them to a gender. ■

"'You play soccer well for a girl' means: you will never be as good as a boy."

Elena Makarova

New sports building, strategy, and starting grants.

Eucor anniversary

Thirty years of cooperation.

This year marks the 30th anniversary of Eucor, which was founded in 1989 as the European Confederation of Upper Rhine Universities. Since 2013, it has been a European campus run by the universities of Basel, Freiburg, Haute-Alsace, Strasbourg and Karlsruhe (KIT). Within the European research area, Eucor is a unique project that gives thousands of students the opportunity to pursue their studies across borders. Researchers at the universities should also experience cross-border mobility as an everyday reality that helps them to collaborate more easily. ■

eucor-uni.org

Sports campus

Groundbreaking at St. Jakob.

The ceremonial laying of the foundation stone for the new building of the Department of Sport, Exercise, and Health was held in September. The building will be the first university site located in the supporting canton of Basel-Landschaft. Starting in the 2021/2022 winter semester, the department will be able to provide – at one location – the increased space it now requires as a result of growth in sports science, sports medicine, and training science. The new building will accommodate around 600 students and 100 employees. ■

Building together: Councilors Conradin Cramer and Monica Gschwind lay the foundation stone for the new sports building.

Strategy & mission

University development.

This year saw the University Council address two key policy documents: the university's new mission statement and its 2022–2030 strategy. A core aspect of the mission statement is its emphasis on a strong profile as a comprehensive university that brings together innovative faculties of the humanities, social sciences, and natural sciences. The statement also stresses the university's strong regional foundations and its international networks. This identity is also expressed in the new strategy. One of the strategic principles is about expanding the university's collaboration with social, political, and economic actors, and with partner institutions. Other principles focus on efforts to strengthen identification with the university, make it more agile and capitalize on the benefits of its unique location in the three-country region. ■

unibas.ch/strategie

ERC Starting Grants

Funding awarded to Basel researchers.

The European Research Council (ERC) has awarded its coveted Starting Grants to three Basel researchers. Marloes Eeftens, PhD, of the Swiss Tropical and Public Health Institute will spend the next five years researching how pollen affects the heart, breathing, and allergies. Neurobiologist Professor Flavio Donato, PhD, received a grant for his work investigating brain development in early childhood. The third awardee is the new Professor for Data Analytics, Ivan Dokmanić, PhD. The ERC awards its substantial Starting Grants to excellent researchers who are beginning their careers and pursuing innovative ideas in their work. ■

Restoring Vision.

Photos: Suren Manvelyan

Worldwide, people are living longer and consequently the number of eye diseases is increasing – at the same time, research into these diseases is also growing. Basel researchers aim to ensure that their theoretical insights directly benefit patients.

Page 20
The best way to treat hereditary vision conditions is to replace the defective genes.

Page 23
Most eye diseases begin in the retina. Retinal cells can now be artificially cultivated for research purposes.

Page 31
Currently, there is no direct treatment for glaucoma. New drugs are being developed that safeguard retinal ganglion cells.

Advancing vision research.

The development of new treatments for patients suffering from vision impairments worldwide is the focus of a group of research teams at the new Institute for Molecular and Clinical Ophthalmology Basel (IOB), which is affiliated with the University of Basel, helping to enhance the university's international reputation.

Text: Botond Roska and Hendrik Scholl

Vision is precious. In a survey conducted in the United States, asking people what their worst clinical condition would be, blindness topped the list.

Globally, the prevalence of eye diseases continues to rise. A total of 36 million people are blind, and more than 1 billion people experience a significant degree of vision impairment. Many conditions that lead to blindness cannot be treated effectively, or even at all.

The eye is particularly suited for diagnostic and therapeutic exploration owing to its easy accessibility, small volume, internal compartmentalization, stable cell populations, optical transparency for evaluation, and reduced adverse responses to injected therapeutics thanks to the favorable immune situation.

Nevertheless, innovation in ophthalmology has been frustratingly slow. Basic researchers rarely understand the unmet medical need, because they lack the experience of patient feedback. Clinicians are often not sufficiently aware of the latest advances in fundamental research.

A medical dream

The new Institute of Molecular and Clinical Ophthalmology Basel (IOB) was created in 2017 to bridge this gap. At the institute, basic researchers and clinicians work hand in hand daily to develop novel therapies in ophthalmology. A key innovation compared with previous approaches is our focus on cell types rather than tissue.

Different disciplines and technologies are combined including genetics, virology, molecular biology, organoid research, electrophysiology, two-photon imaging and computational tools. Taken together, these methods enable an understanding of the structure and function of the eye and of vision at different stages of processing, as well as the mechanism of eye diseases. We can then develop innovative therapies to slow the progression of vision loss, or to restore vision when it is lost.

Most vision disorders originate in the retina. Restoring sight to the blind by retinal repair has remained the desire of medicine for centuries. Gene replacement or gene editing can, however, now slow down, stop, or even reverse vision loss. The first successful procedures have recently been reported.

The most common causes of blindness in younger people are hereditary retinal dystrophies. Stargardt disease and *retinitis pigmentosa* – a retinal degenerative disease caused by damage to the photoreceptors – begin to harm vision in childhood, and can lead to

Hendrik Scholl
is head of ophthalmology at the Eye Clinic at University Hospital Basel and is co-founder and co-director of the IOB. The professor of ophthalmology was born in Germany in 1969 and specializes in the treatment of retinal diseases.

Botond Roska
is a professor at the Faculty of Medicine of the University of Basel and co-director of the IOB. The neuroscientist was born in Hungary in 1969. His research findings on the visual system and on the restoration of sight are considered to be groundbreaking.

blindness even in early adulthood. *Retinitis pigmentosa* affects nearly 1.5 million people worldwide; one in 8,000 people suffers from Stargardt disease. Both conditions are the focus of translational research at IOB, that is projects that aim to translate preclinical research into practical application in hospitals quickly and efficiently.

The retina as computer

An approach known as optogenetic therapy is currently being developed, for example, to re-sensitize a degenerated retina to visible light. The expression of an optogene encoding a light-activated channel or pump in the remaining inner retinal cells makes them light sensitive, independent of the mutation causing photoreceptor cell loss. The human retina is like a powerful computer that shapes visual perception. At IOB, a computer model of the retina was built that simulates the different pathways that a signal can take through the retina. When adapted to the human retina, this model could allow the prediction of the outcome of eye diseases.

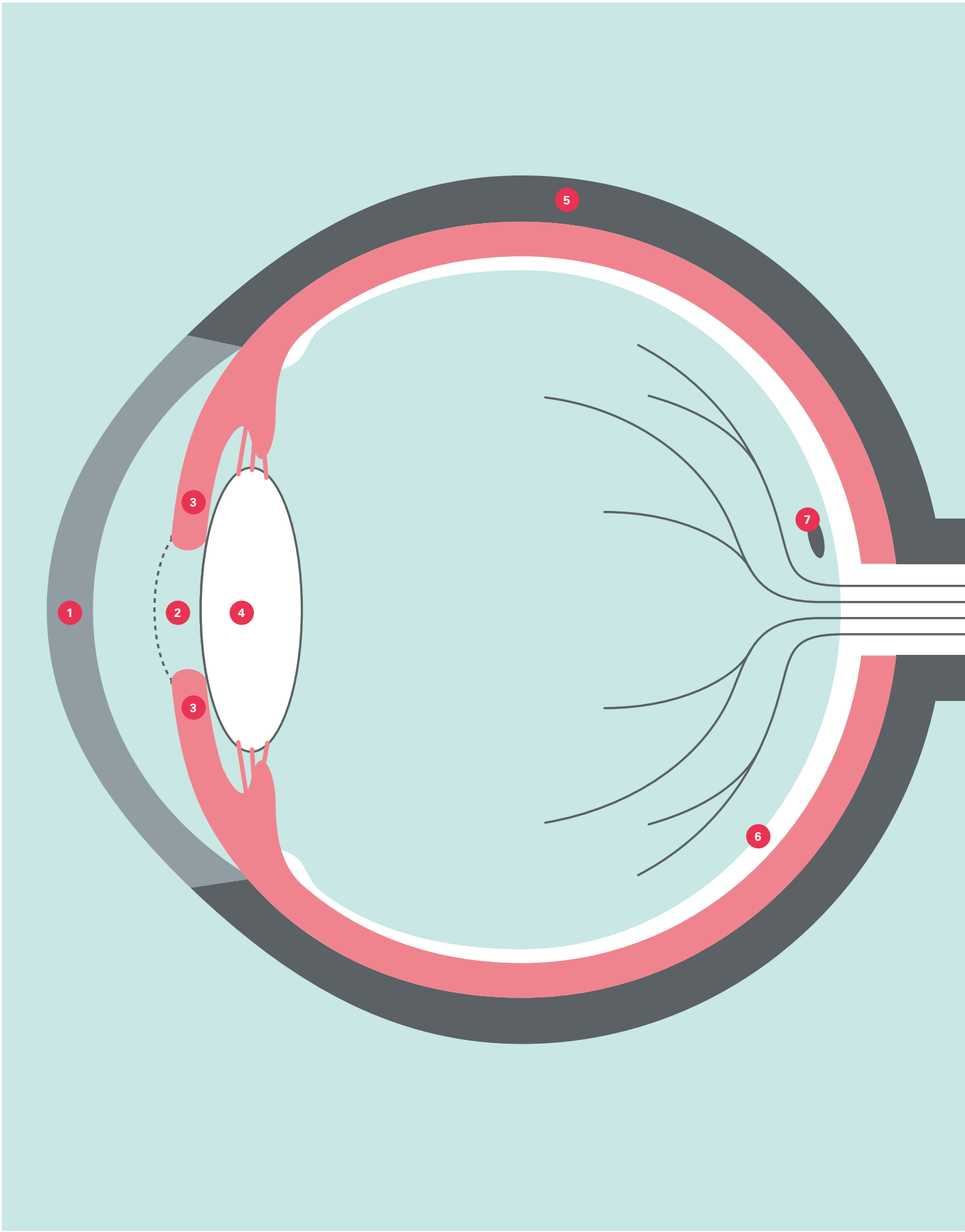
Stem cell technology allows the transformation of patient skin samples into highly organized in vitro retinas with the donor's genetic markers. These human retinal organoids demonstrate many of the cell types that are found in a normal retina of a living human, plus they can form a primitive optic nerve. The effects of mutations on retinal cells can therefore be studied directly in a culture dish. Such organoids can also be used to develop in vitro disease models, e.g. for retinal and macular dystrophies such as Stargardt disease. Now, gene therapies can be developed that can precisely target each of the different cell types with specific vectors. New therapies could soon be tested specifically on patients' own retinal organoids.

If gene therapies do not target specific cell types, it is possible that they will be ineffective or even harmful. Adeno-associated viral (AAV) vectors are the most promising approach for delivering gene therapy into the retina or the brain. The targeted expression to specific cell types, however, still poses challenges. Researchers at IOB have developed a library of 230 AAVs, each with a different synthetic promoter. This AAV vector library allows fast and efficient targeting of expression to neuronal and glial cell types in a variety of species. This is a milestone, both for fundamental science and for gene therapy. AAV vector libraries also allow for cell-type targeting in human retinas to be tested in vitro. This significantly increases the probability that a chosen vector will target the desired cell type in patients in vivo.

A novel "virus stamping" method has also been developed at IOB that allows the efficient study of genes. Here, individual cells in cell cultures, from brain tissue, experimental animals, and organoids can be infected with a virus – or with multiple viruses, either simultaneously or at different time points. Virus stamping allows for the examination of the role of specific genes in clearly defined cells. It is a versatile solution for fundamental biomedical research, and potentially for gene therapy.

Short-sightedness on the increase

Worldwide, and especially in Asia, short-sightedness is increasing rapidly. In some regions, up to 90% of teenagers are affected, compared with 10 to 20% in the Chinese population 60 years ago. The major problem with short-sightedness is not the need to wear glasses, but rather frequent loss of vision via resulting complications, such as myopic macular degeneration, glaucoma, or retinal detachment. Neurodegeneration of the retina such as in dry age-related macular degeneration, diabetic eye disease, retinal dystrophies, and glaucoma currently remains untreatable. In aging societies, such disorders are a leading cause of disability and loss of independent living. At IOB, research therefore also focuses on growth regulation of the eye to address myopia and to expand our understanding of glaucoma. ■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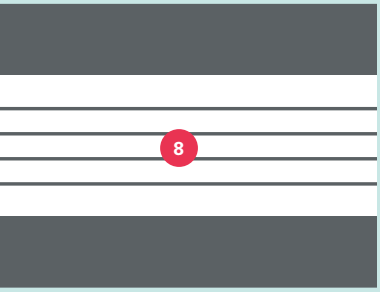
How the eye sees.

When we look at an object, we see it – instantaneously. What sounds simple actually relies on a complex process of multiple coordinated steps. It begins when light from the object we are looking at is reflected. Within fractions of a second, the light reaches our eye, which processes it and passes it on to the brain.



1. Light enters the *cornea.* The cornea is transparent and kept moist by lacrimal fluid. This allows it to refract and focus the light, which then continues its journey through the eye.

2. The light reaches the inner eye via the *pupil.* Although the pupil is also transparent, it looks black because the retina behind it absorbs all the light. Depending on how bright our environment is, the pupil changes size so that more or less light reaches the retina.

3. Our eye color depends on pigment cells in the *iris.* High pigmentation results in brown eyes, while low pigmentation results in blue. Also, muscles in the iris are responsible for changing the size of the pupil.

4. The *lens* lies behind the pupil. It is also transparent, and refracts the light again. Depending on whether the object is close or far away, a muscle contracts or relaxes to alter the shape of the lens. This helps to produce a clear image.

5. The white part of the eye is called the *sclera.* It protects the eyeball and, along with the interocular pressure, is responsible for maintaining the eye's shape. The sclera has nothing directly to do with light that enters the eye. A gap in the sclera provides space for the cornea, the area where light first reaches the eye.

6. Finally, the *retina* perceives the light. This means that photoreceptors transform the light information into electrical impulses that the brain can then process. The rods and cones on the retina allow us to recognize colors and see in different levels of light, for instance.

7. In the center of the retina lies the *macula,* which is about six millimeters in diameter. At the center of the macula, we find a much smaller area where our keenest vision is located – the *fovea centralis.* In photographic terms, the resolution is at its highest here. In daylight, the object we are looking at appears sharpest when it is in the center of our line of sight because the light in our eye falls directly on the fovea centralis.

8. The *optic nerve* receives the electrical signals from the retina and passes them on to the *occipital lobe* in the cerebral cortex. Once there, they can finally be interpreted as images.

Collecting knowledge to combat eye diseases.

Researchers in Basel are investigating treatments for various eye diseases. Botond Roska is focusing on the retina through a series of experiments as well as exploring potential gene therapies.

Text:
Martin Hicklin

At the back of everyone's retina, in the middle of the so-called "yellow spot" *(macula lutea)*, lies a pit measuring just one and a half millimeters across. This *fovea centralis* is packed with 150,000 color-sensitive cones per square millimeter – and the signals they detect are converted, processed and relayed to the brain via the optical nerve. Damage to this site, which is responsible for high-acuity vision, makes daily tasks such as reading impossible, and there is nothing glasses can do to help.

"Those one and half millimeters are enough to keep half of the cerebrum busy," says Botond Roska, Director of the Molecular Center at the Institute of Molecular and Clinical Ophthalmology Basel (IOB), emphasizing what a fascinating and miraculous role the retina plays. His mission is to understand what exactly goes on there with the aim of preventing blindness and giving affected individuals their eyesight back.

Born in Hungary in 1969, Roska already had the retina in mind when he came from Harvard to the Friedrich Miescher Institute in Basel in 2005. Meanwhile, his research group has conducted experiments to investigate the thin lining of the eye. For example, they have shown that the retina works like a biocomputer and that cells can adopt different roles. They also revealed the complex structure of the circuitry.

A new era in sight?

If Roska had not injured his hand in an accident, he might have become a famous cellist. But he was forced instead to swap his musical career for a degree in medicine. At Berkeley and Harvard, he would ultimately turn his attention to neurobiology and the retina in particular. Numerous awards – including, most recently, the Louis-Jeantet Prize for Medicine in spring 2019 – are a testament to his reputation as a leading retinal researcher. In Hendrik Scholl, Director of the Clinical Center at the IOB, Roska has found an ideal partner and friend.

Indeed, it appears that the two researchers and their colleagues have opened the door to a whole new era in ophthalmology. Progress seems to be coming in giant leaps right now. In 2018, for example, researchers succeeded for the first time in keeping a deceased donor's retina in "incredibly good condition" for a whole day. Using fine electrodes, they were able to listen to the electrical murmur of the cells – a real turning point in this field of research. Now, they understand how to keep sections of a retina in working condition for up to 14 weeks and even how to restore a retina's photosensitivity "optogenetically", using smuggled-in genes. "This works remarkably well," says Roska.

Access to viable retinas has also made it possible to examine the individual genes of the roughly 100 different cell types that work together there and to record which of them is being read and controlling the building of proteins. Known as "single-cell transcriptomics," this process involves huge computing power and provides new insights into the development and function of the retina as an "image pro-

cessor". It also allows researchers to localize and map genetic defects.

Replacement of defective genes

Roska's enthusiasm shines through as he discusses these newly acquired abilities to grow artificial retinas and to carry out tests on "organoids" of this kind. Stem cells can now be made to differentiate in the retina in a process that uses skin cells as its starting material and coaxes them into converting back into pluripotent stem cells. In a suitable environment, these cells then grow into retinal organoids. These days, it is even possible to regrow a specific patient's retina in the lab, with all its defects and peculiarities – providing an ideal basis for personalized medicine. Now, high-throughput techniques can also be used to test active substances on any number of organoids.

The best way to treat hereditary vision conditions, such as those that fall into the category of *retinitis pigmentosa*, is to replace the defective genes. This relies on gene vectors that can transport a working replacement into the defunct cells. The best candidates are "adeno-associated viruses" (AAVs), which only multiply in the presence of adenoviruses, do not cause disease, and barely trigger an immune response. "We were working with AAVs back when none of the major players were talking about them," says Roska.

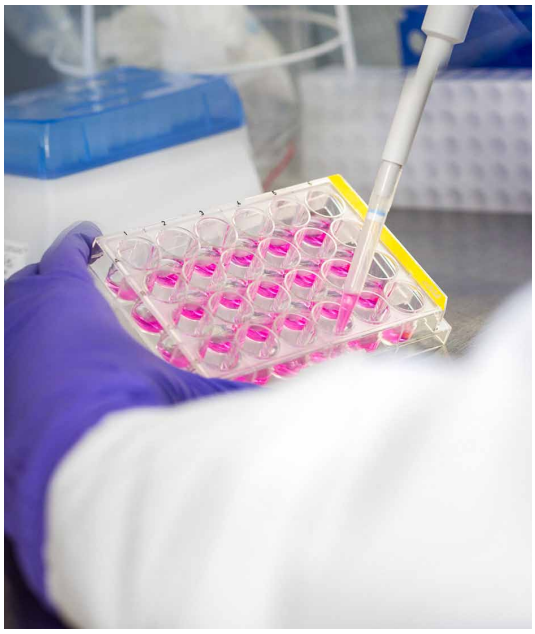
Today, the vectors are a highly sought-after commodity, and IOB recently led the publication of a library of 230 AAVs that are suitable for various cells and could be used for gene therapy. In collaboration with ETH Zurich's Department of Biosystems Science and Engineering (D-BSSE) in Basel, the researchers developed a method whereby viruses are attached to magnetic nanoparticles, allowing them to be transported to the desired location more efficiently. In the case of Stargardt disease, in which only one letter of the genetic material is changed, there are plans for a precise "editorial" intervention.

Vision through the roof of the skull

One AAV vector from Roska's lab is currently being used for the optogenetic treatment of advanced *retinitis pigmentosa* in a clinical trial in collaboration with GenSight Biologics in Paris. Running since 2018, this trial aims to restore some of the patients' lost color sensitivity and to give the retina a genetic upgrade. Those receiving the treatment wear a pair of light-amplifying glasses.

"There are 30 people working in my group, and they have thousands of different ideas," says Roska. For example, researchers are considering how to make cells light-sensitive at an intermediate point on the way to the cerebrum in the event of a total failure of the optical nerve. This would allow visual information to be transported to the brain through the roof of the skull instead of the eye. It would also be conceivable to equip people with infrared sight.

"70 percent of my research focuses on basic principles, while the other 30 percent is clinically oriented," says the researcher, adding that his work always looks at possible applications and how these can be translated into patient benefit. Growing insights may also pave the way for the treatment of widespread conditions such as age-related macular degeneration. ■



It is possible to examine the individual genes of the roughly 100 different cell types in the retina.

New retinal tissue from skin samples.

To better understand certain eye diseases, researchers are recreating human retinas in the lab. To accomplish this, they create tissue cultures known as organoids from human skin and blood cells.

Text: Christoph Dieffenbacher

Magdalena Renner
conducts research into retinal organoids as head of a team at the Institute of Molecular and Clinical Ophthalmology Basel (IOB). In her previous work, the molecular biologist recreated miniature brains.

The young Austrian molecular biologist Magdalena Renner specializes in organoids – tiny organs comprising a small number of cells artificially grown in culture from reprogrammed stem cells. For her doctoral research in Vienna, Renner worked with brain organoids, creating miniature brains from a handful of cells and studying how they develop.

Now, Renner leads a team at the Institute of Molecular and Clinical Ophthalmology Basel (IOB) devoted to retinal organoids. The goal of her work, which straddles basic and applied research, is to better understand various eye diseases. Her team has already succeeded in engineering relatively highly organized forms of human retinal tissue in the lab.

Complex nerve tissue

The retina, a multi-layered membrane lining the inside wall of the eye, is anything but a simple organ. It is a highly complex tissue structure "with a variety of cell types performing a variety of functions, arranged in no less than five different layers," explains Renner. Or, to be precise, three layers of cell bodies and two intermediate layers that contain synapses among the nerve cells. In organoids, as in the human retina, photoreceptors are located in the outer layer. In the human body, photoreceptors capture incoming light signals and transmit them to the brain in the form of neural impulses.

This complex structure also makes the retina (Latin for "net") highly sensitive – it is where most eye diseases originate. The most common diseases, some of which are hereditary, include age-related macular degeneration, diabetic retinopathy, vascular occlusions and retinal detachment. Renner highlights the retina's fragility with an example: "failure of a single gene in the photoreceptors is enough to make a person blind." Accordingly, many researchers believe that modeling the development of the retina and possible genetic mutations associated with certain diseases in the laboratory would be a major step toward new treatments.

"Our retinal organoids resemble three-dimensional miniature organs with an appearance and structure very close to those of actual retinas," the researcher explains in her lab. The tiny structures only reach a size of around 2 by 2 millimeters before they stop growing. They contain similar cell types with functions that are related or identical to those of fully fledged retinal tissue. Renner explains: "We generally begin with a donor cell from a small skin biopsy, or – a less invasive option – a blood sample. Donor

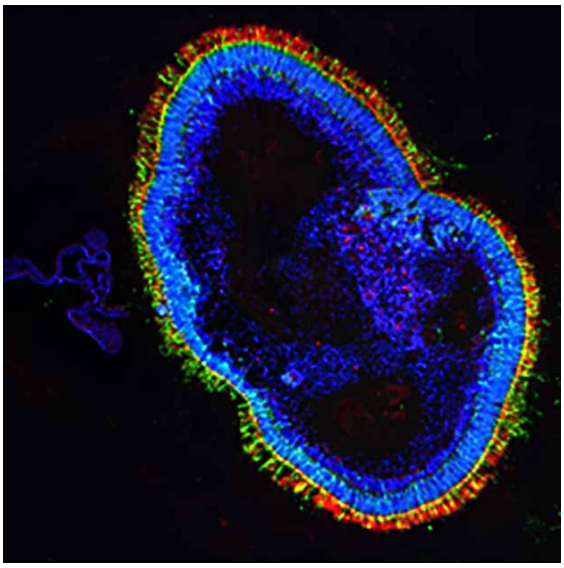
cells are reprogrammed into what are known as induced pluripotent stem cells using a method that has only been known for around twelve years." These stem cells, which can differentiate into any kind of body cell, are then encouraged to multiply.

The eye as part of the brain

Renner recalls how much the early results of her research surprised even her: "The process that the stem cells go through in the laboratory culture very closely mirrors the natural development of retinal cells in human embryos." To begin with, the retinal cells develop as general brain cells, before subsequently specializing. "Obviously," Renner remarks. "The eye is in fact a part of the brain." At various points during the development process, the researchers separated organoids into individual cells, which they then dissolved in order to sequence the RNA of 60,000 individual cells. This enabled them to determine which genes were expressed in the various cell types. Their goal is to come as close as possible to mature retinal cells.

Aside from the cell cultures, Renner's team also studies retinas from organ donors, analyzing them in terms of gene expression and comparing them against the lab-grown organoids. They found that a majority of the known genes associated with inherited retinal degeneration are expressed by particular cell types. "This is an important finding, as we want to treat the cells immediately affected by a mutation first," Renner explains.

How difficult is it to recreate human retinas in culture? The main problem, according to Renner, is that the maturation process takes over 30 weeks – a huge investment in terms of time and effort. It also means the team has to plan its experiments a very long time in advance – and exercise a great deal of patience. One as-yet unsolved problem is that not all cells of the same type result in viable organoids.



Fluorescence image: Cross-section of an organoid; cell nuclei are blue, photoreceptor rods are green and the photoreceptors' photosensitive antennae are red.

Mouse model a poor substitute

In any case, there is still a long way to go before it will be possible to repair parts of the retina with custom-grown tissue, or cure eye diseases in humans. Unlike the cornea, the retina cannot simply be transplanted. Researchers are therefore exploring a different approach, in which cells operating defectively due to a hereditary mutation are supplied with a correct copy of the gene to restore their functionality. This is achieved by packaging the appropriate sections of the retinal gene into viruses that are then injected into the ocular fundus – a therapeutic approach that is very easy to test in organoids. According to Renner, this method is promising as the eye is largely overlooked by the immune system, meaning it will not immediately seek to fight off the intruding virus.

Possible applications of this method or other therapies resulting from organoid research would still have to be tested on animals, Renner points out. The mouse model widely used in eye research laboratories, however, has a major drawback in this regard: "Mice have very poor eyesight, as their retina is built quite differently to that of humans." At the center of our retina is the fovea, a region equipped with special photoreceptors that play a key role in color recognition and focus. Mice lack this region. Aside from humans, the fovea is only found in a few primate species, so it is unlikely that tests on animals can be eliminated altogether, Renner says. Nevertheless, she hopes that most of the necessary testing can one day be performed on organoids instead. ■

Eyesight thanks to gene therapy.

Stargardt disease is a hereditary condition that leads to the loss of sharp vision at a young age. In Basel, scientists and clinicians are working together to develop a gene therapy treatment for the disease. The method is expected to be available for clinical trials within a few years.

Text: Yvonne Vahlensieck

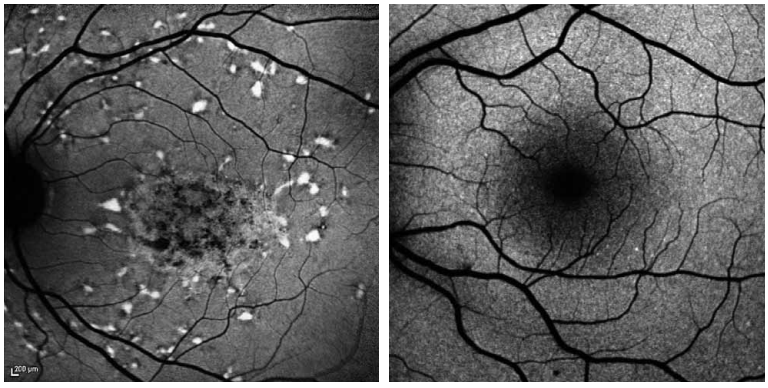
The yellow spot on the retina, also known as the macula, measures just six millimeters across – and yet it plays an incredibly important role as the center of sharply focused vision. Without this, we would only see a blurred outline of our surroundings. "Sharp vision is something we rely on constantly, especially in modern society," explains Professor Hendrik Scholl, Co-Director of the Institute of Molecular and Clinical Ophthalmology Basel (IOB). "We use it to look at our cell phones, work on computers and recognize peoples' faces in social interactions." Retinal diseases that damage the macula therefore lead to a considerable reduction in quality of life.

A genetic defect with serious consequences

One such condition is the hereditary Stargardt disease, which typically has its onset in adolescence and quickly leads to the complete loss of visual acuity. Those affected retain some degree of mobility, but they can neither read nor make out detailed aspects of their surroundings. Although the disease is still considered incurable, that might be about to change: Scholl and his colleagues at the IOB are working on a gene therapy treatment aimed at halting the progressive loss of visual acuity and thereby preserving sharp vision.

The IOB chose Stargardt disease as one of its research focuses for several reasons: "Especially as this affects young people, it is a disease that deserves serious attention – even though it only occurs in one out of 8,000 individuals," says Scholl, who also hopes that the findings from this project will lead to advances in the treatment of other, related diseases. For example, these include age-related macular degeneration, which affects around a fifth of people over 65 and, in industrialized nations, represents the most common cause of blindness in the elderly.

It is, furthermore, of great advantage that the genetic basis of Stargardt disease is well known.



Accumulation of toxic substances: the retina of a patient with Stargardt disease (left) and a healthy specimen (right).

"Retinal diseases can be caused by mutations in many different genes and, so far, more than 200 of these genes have been identified," says the geneticist Professor Carlo Rivolta, who was appointed professor at the IOB in 2019. "Stargardt disease, however, mainly results from mutations in only a single gene, the ABCA4 gene." People who carry one defective and one intact copy of the gene are not affected. Only when a child receives a non-functioning copy from each parent will it develop the disease. Consequently, the mode of inheritance is recessive.

Targeted defect repair

The function of the *ABCA4* gene is also well known: It encodes a protein that removes the degradation products of Vitamin A produced during the visual process. If the retinal cells are unable to produce this transporter because of a gene defect, these degradation products accumulate underneath the retina and lead to damage to the macula. "In theory, it should be sufficient to restore the function of this single gene to achieve a positive effect," explains Rivolta.

"Stargardt disease mainly results from mutations in only a single gene."

Carlo Rivolta, geneticist

Therefore, the researchers are working on a way to correct the defective gene directly in the cells. They are trying to pack a nucleotide sequence that specifically recognizes the mutated site into a virus that is harmless to humans and then inject it directly under the retina of the patients. The virus transports the nucleotide sequence into the target cells. Enzymes coupled to the nucleotides are then directed to the mutated site where they activate cellular repair mechanisms that lead to the targeted correction of the defective gene.

A drug recently approved in the USA for the treatment of early childhood blindness demonstrates the potential of gene therapy in the treatment of diseases of the visual system. Furthermore, previous studies reveal that the effect of such therapies can last for many years – long-term observations of the patients treated will in time show whether the therapy lasts a lifetime.

Faster path from the laboratory to the hospital

Another goal of Professor Scholl is to accelerate the translation of basic science into clinical applications: The innovative methods developed by research groups at the IOB can contribute to this. For example, it is now possible to use tiny skin samples from patients to cultivate small cell clusters with a composition matching that of retinal tissue. These so-called "organoids" allow the scientists to test the gene therapy treatment in a petri dish. "This not only reduces the number of animal experiments, but also enables us to reach the stage of clinical trials faster," says Scholl.

In parallel, other groups are analyzing the toxicity of this treatment and establishing methods of tracking its effects. At this rate of progress, Scholl believes that a clinical gene therapy trial for Stargardt disease could realistically start within the next five years, and he is already recruiting suitable patients from across Europe.

Yet, Scholl cautions against unduly high expectations: "Complete restoration of sharply focused vision almost certainly cannot be achieved using gene therapy, as many of the retinal cells are unfortunately damaged beyond repair." Nevertheless, the researcher is optimistic that the treatment will yield substantial improvements in patients' eyesight. And if this method proves successful, the distant future could see affected children receive preventive gene therapy at a young age in order to preserve visual function. ■

Cell type atlas is an eye-opener.

For the first time ever, researchers at the University of Basel have been able to show in detail that retinal tissue grown from induced pluripotent stem cells provides a suitable model for drug research. Key to this breakthrough was close collaboration between the Institute of Molecular and Clinical Ophthalmology Basel and University Hospital Basel.

Text: Samuel Schlaefli

Hereditary eye conditions such as Stargardt disease or *retinitis pigmentosa* were long considered incurable blinding diseases. Both diseases affect the retina, a very thin layer of nerve tissue at the back of the eyeball whose millions of light-sensing cells convert light into electrical impulses that are sent to the brain, where we perceive them as vision. Hereditary retinal diseases often emerge in childhood or adolescence and can, in the worst cases, lead to total blindness.

Lack of experimental models

Research into the causes of such hereditary eye conditions has remained challenging, as has the development of effective therapies. "In the life sciences, mice are a standard model for studying eye disease, but they have many limitations," explains Dr. Cameron Cowan, senior researcher at the Institute of Molecular and Clinical Ophthalmology Basel (IOB). One reason is that mice lack a fovea, the central portion of the retina that is responsible for human high-acuity vision and is affected first in many eye conditions. Alternatively, retinal tissue donated from post-mortem patients would be a preferred specimen for laboratory testing. However, such tissue is hard to come by, with only about 120 potentially suitable donations made in Switzerland each year, while slow collection procedures leave the available tissue unhealthy.

Against this background, researchers have been working on a new model for several years now: Human cells obtained from various types of tissue, including blood, hair roots and skin, can be reprogrammed in a laboratory to grow into the desired organs, so-called organoids. This method is based on the trailblazing research of Japanese scientist Shin'ya Yamanaka, who was the first to successfully produce induced pluripotent stem cells in a laboratory. This won him the 2012 Nobel Prize in Medicine. Retinal tissue, too, can be produced by reprogramming stem cells. "Until now, the use of retinal organoids has been plagued with a great deal of uncertainty," Cowan explains. "We had no way of knowing whether they would develop as in humans, or under what circumstances this retinal tissue could provide a suitable model."

"We miniaturize the output of a video projector so that the image size corresponds exactly to that of the retina."

Cameron Cowan, retinal researcher

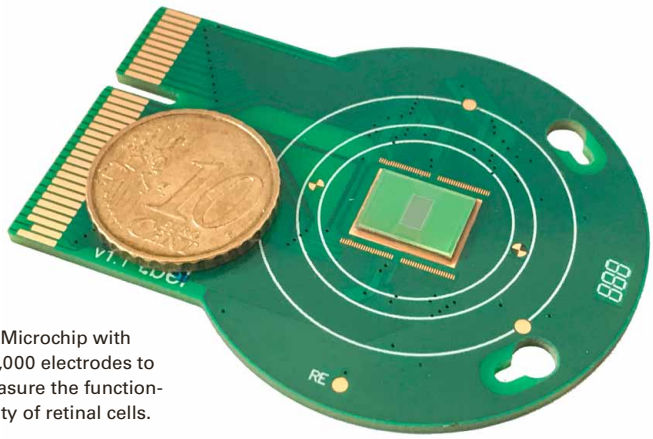
To find an answer, it was necessary to characterize the human retina in greater depth than ever before. Success, here, depends above all on the quality of the tissue used. Tissue from donor organs, however, deteriorates rapidly after the operation even if oxygen is artificially supplied. "We were able to reduce the time the tissue spends without oxygen from an average of eight hours to five minutes," says Cowan. "This would not have been possible without close collaboration with the clinicians at the hospital."

Establishing tissue quality

Assessing the condition of this unique tissue required a further innovation: Colleagues at the Department of Biosystems Science and Engineering at ETH Zurich developed a special microelectrode array, just a few square millimeters in size but packed with 26,000 electrodes, to measure cell function. In this process, ganglion cells in the retina are artificially oxygenated and placed adjacent to the electrodes. The photoreceptors are then stimulated by light, which they convert into electrical signals that are transmitted to the retinal ganglion cells. Electrical impulses from ganglion cells, intended for the visual centers of the brain, are intercepted by the electrodes. "To replicate the retinal input in the laboratory, we miniaturize the output of a video projector so that the image size corresponds exactly to that of the retina," says Cowan. The researchers were able to measure the responses of thousands of retinal cells with the aid of the microelectrode array and confirmed the results through repeated light stimulation. "Nobody had ever measured such activity from post-mortem human retinal tissue," he says with pride.

Based on tissue proven to be of high quality, the team of researchers has created a cell-type-specific "Gene Expression Atlas" for the human retina. This involved sequencing the RNA of approximately 100,000 single cells from different regions of the retina and assigning genetic "barcodes" to them. For the first time ever, the cell-type-specific transcriptome of the healthy human retina has been made possible, i.e. the sequencing of the RNA contained in its cells. This is relevant because the RNA is responsible for gene expression, in other words, triggering specific genetic programs. What was largely unknown was the types of retinal cells in which many disease-associated genes are expressed, and under what circumstances and from what stage this expression is paralleled in organoid cells.

Using their Gene Expression Atlas for the healthy human retina, the scientists are now able to precisely characterize the cell tissue of the retinal organoids grown in the laboratory. This was achieved by measuring the gene expression of approximately 50,000 organoid cells at six points in time over their 38-week growth period. "We were able to demonstrate that our lab-grown retinal organoids developed fully ex vivo and that they developed in much the same way as in humans and with the same gene expression patterns." The correspondence was found to extend to the cell-type-specific expression of genes linked to particular eye conditions.



Microchip with 26,000 electrodes to measure the functionality of retinal cells.

Paving the way for personalized medicine

Cowan is convinced that this model holds enormous potential for the development of new treatment approaches: "In the past, we'd often make assumptions about which cell types expressed the genes responsible for a particular disease. Today, we're able to pinpoint them through gene expression analysis." By way of example, he adds that assumptions made in developing new gene therapies for Stargardt disease about the distribution of mutated genes in tissue have now been shown to be inadequate.

Moreover, the newly developed methods and the organoid model are in keeping with the overall trend in the life sciences and pharmaceutical industry toward personalized medicine. For instance, Cowan considers that, in the future, a patient suffering from a rare eye condition might well have an organoid grown in a laboratory from cellular material taken from their own body. Such organoids would make it possible to test alternative treatments, with the most promising option then chosen for the patient. In addition, thousands of active ingredients could be serially tested on thousands of organoids with no need for donor organs, and the probability of the results being transferable to humans would be far higher than if the mouse model were used. ■

Treating glaucoma.

Text: David Herrmann

Among people over 50, one in 50 will suffer from glaucoma, which can lead to a loss of vision if left untreated. The Eye Clinic at the University Hospital Basel has been making major contributions to research into the condition.

Many glaucoma sufferers are unaware that they are going blind. As the condition progresses, retinal ganglion cells become irreversibly damaged and gradually die. A person with glaucoma will typically still see clearly in the center of their visual field whereas their peripheral vision will constantly deteriorate, ultimately leading to total blindness.

While high eye pressure is the main risk factor for glaucoma, two in five sufferers have normal eye pressure. In such cases, the condition is often due to poor blood circulation. This type of glaucoma was the long-standing research focus of Professor Josef Flammer, previous head of the Eye Clinic at the University Hospital Basel. Since Professor Flammer's retirement six years ago, it is Professor Konstantin Gugleta, senior attending physician at the Eye Clinic, who has been advancing glaucoma research. His work has centered on new treatment approaches.

Konstantin Gugleta is senior attending physician at the University Hospital Basel's Eye Clinic and specializes in ophthalmology research into glaucoma.

Ginkgo and antioxidants are effective

Demographic developments mean that glaucoma research is growing in relevance. Swiss society is increasingly aging, and the older a person is, the higher their risk of glaucoma: From two percent of people over 50, the incidence of the condition rises to five to eight percent in people over 70. From a medical perspective, this translates into an urgent demand for new forms of treatment.

Most current approaches to treatment of normal-pressure glaucoma use insights and empirical knowledge from alternative medicine. Small-scale clinical studies have found that ginkgo and antioxidants contained in foodstuffs such as dark chocolate, green tea or red wine help protect retinal ganglion cells. Conventional treatments are aimed mainly at lowering eye pressure and regulating blood pressure. The drugs used can have serious side effects, however. As yet, there is no form of treatment that targets the root cause of the disease. With his own research, Gugleta aspires to close this gap and help develop drugs that safeguard retinal ganglion cells.

As a fundamental first step, he is working to understand what causes these cells to die, expecting his findings to provide some initial clues as to how these cells could be kept alive. He is placing great hope in

While some growth factors are known, the picture is far from complete.

the collaboration with the Institute of Molecular and Clinical Ophthalmology Basel (IOB), a center of excellence that combines fundamental and clinical research.

Down a blind alley and out again

Gugleta is an ophthalmologist with a background in clinical research. In his postdoctoral research, he began trying to find new approaches to glaucoma treatment. At the time, he had high hopes for a then novel procedure for measuring blood flow in the eyes of patients. Using a computer-aided method, blood vessels in the fundus, or back of the eye, were filmed while the eye was being exposed to different stimuli. This made it possible to determine not only how blood circulation in the eye responds to different stimuli but also what long-term effects this has on the optic nerve and consequently on eyesight.

The assumption was that this approach, which involved following patients over a number of years, would prove a link between deteriorating circulation and an increasing loss of nerve cells or visual field. The results were disappointing, however, with statistical analysis revealing no clear correlation between datasets. One explanation for this could be that processes occuring in optic nerve cells are significantly influenced by additional factors.

Focus on growth factors

For Gugleta, the way to overcome this impasse is to collaborate with the IOB, whose technological and human resources offer him entirely new opportunities. It has been known for some time that the survival of any nerve cell, and by implication the optic nerve, depends on so-called growth factors. It could be that growth factors are no longer present in glaucoma patients, causing the cells to die. Gugleta is currently laying the groundwork for a new research project. The plan is to identify and understand these growth processes via a multistage approach involving complex examinations of the relevant biochemical and molecular genetic processes both in the laboratory and in vivo.

First, he plans to investigate how retina-like structures grown from stem cells respond to exposure to different growth factors. Such organoids are being grown in Petri dishes as part of an IOB project. This involves researchers adding different external growth factors and examining how the cells react. The idea is to determine which factors cause cells to die faster and which protect them.

Experiments on pigs' eyes

The findings will then provide a starting point for the second stage, where pigs' eyes will be examined. The organs will be collected immediately after slaughter and taken from the slaughterhouse to a laboratory. Here, the challenge is to find effective ways to keep the organ and its cells alive for long enough so that all the necessary tests can be carried out. The retinal ganglion cells contained in the pigs' eyes will also be tested for the presence of sought-after growth factors.

While some growth factors are known, the picture is far from complete. For this reason, the findings are to be expanded through in vivo experiments on monkeys. The researchers want to identify the RNA responsible for vital signaling between cells and to determine its protein structure.

The ultimate goal is to develop new drugs that tackle the root cause of glaucoma and protect retinal ganglion cells. In this way, Gugleta hopes to contribute to the treatment of eye diseases and so help people maintain a high quality of life in older age. ■

Macular degeneration: no cure in sight.

Text: Samanta Siegfried

Ghislaine Traber
is senior physician at the University Hospital Basel's Eye Clinic and a member of the Institute of Molecular and Clinical Ophthalmology Basel (IOB).

Christian Prünte
is Medical Director of the Eye Clinic at University Hospital Basel and Head of the Department of Ophthalmology at Kantonsspital Baselland in Liestal. He also works at the IOB.

Age-related macular degeneration is the most common cause of visual impairment in old age and is currently untreatable in the majority of cases. Researchers at the Institute of Molecular and Clinical Ophthalmology Basel (IOB) are investigating why this is such a complex disease.

For most of their lives, people needn't give a second thought to age-related macular degeneration (AMD). The disease only affects three percent of the population just before retirement age, but this figure rises to one in three among those aged 75 or over. It is therefore regarded as the most common cause of visual impairment in old age – and the older the population gets, the more prevalent the condition becomes. Treatments are available. However, the prospect of a cure remains elusive to this day, despite the efforts of numerous researchers.

How can that be the case? Professor Christian Prünte, medical director of the Eye Clinic at University Hospital Basel, explains: "AMD occurs for a multitude of reasons, which are not yet fully understood. So far, it hasn't been possible to define one central factor, but rather a variety of different risk factors. This complicates the course of disease significantly." For example, the known risk factors include smoking, unhealthy eating habits and exposure to light – and research has shown that various genetic factors may also play a key role.

When tiles look warped

As its name suggests, the disease attacks the macula – an area at the very back of the eye that is also known as the "yellow spot". This is responsible for the high-acuity vision that allows us to recognize fine details. Although everything we look at directly is depicted there, patients usually only become aware of the disease's effects at a relatively late stage. This is to do with the fact that the condition often only affects one eye initially, with the other eye compensating for any vision loss. In many cases, it is only when the disease crosses over to the second eye that patients complain of visual impairment. "Most people notice it while reading or because their vision is blurred when they look at people from a distance," Prünte explains.

Yet, if AMD transitions to a wet form at a later stage of the disease, the patient experiences different effects: "In many cases, they can no longer perceive straight lines. For example, doorframes or tiles in the bathroom start to look warped." The wet form causes swelling and deformation of the macula, which can lead to distorted vision and, in the worst cases, to blindness. Unlike the dry form, however, it only affects some ten percent of AMD sufferers. And, most importantly, it is treatable: If you inject a drug directly into the eye every few weeks, the loss of vision can be slowed down and sometimes even counteracted.

Underlying genetic defect remains unclear

Dry AMD, on the other hand, does not result in total blindness – although the loss of vision can be severe and may lead to considerable limitations in everyday life. To this day, this form presents a number of challenges for both physicians and researchers. Although there have been promising approaches that fared well in initial trials, Prünte says that "they didn't prove sufficiently effective in the pivotal studies."

Researchers at the Institute of Molecular and Clinical Ophthalmology Basel (IOB) are continuously testing new drugs, but they are also exploring approaches based on the principles of gene therapy. This involves using viral vectors to smuggle the corrected DNA into the cell where the defective gene resides in order to replace it.

Although promising gene therapy research is currently underway into another eye condition, known as Stargardt disease, the procedure for AMD is more complex: "The main problem is that, of all the patients studied so far, none have been found to

exhibit a single genetic defect that triggers the disease," says Prünte. "There are usually various genetic factors involved – and until you know which gene is responsible, you can't replace it."

Ultrasound with light

Another of the researchers studying age-related macular degeneration is Dr. Ghislaine Traber, a senior physician at the Eye Clinic in Basel. Like Prünte, Traber is responsible for clinical research – and she is currently involved in an observational study seeking to improve the assessment of disease progression. "There are many things we still don't know, such as why the disease remains at an early stage in some AMD patients but moves to an advanced stage in others – or why the wet form appears in some patients as the disease progresses," says Traber.

Known as the Pinnacle Study, this research project centers around an imaging technique based on so-called optical coherence tomography. This is vaguely comparable to an ultrasound scan, except that it uses light instead of sound to visualize the retina. Traber specializes in this field, having worked intensively on medical imaging of the eye and visual pathway at the Eye Clinic, University Hospital Zurich: "The layers of the retina are shown in high resolution, potentially revealing initial pathological processes in the early stages of AMD."

One aim of the Pinnacle Study is to explore whether, even in the early stages, imaging can reveal certain retinal biomarkers that provide information about disease progression. In addition, patients will also undergo genetic testing in order to identify risk factors of disease progression. As well as the IOB in Basel, the study has participating centers in Europe and the USA. In total, 400 patients are to be recruited within a year and then observed over a period of three years.

Therapies are a long way off

At the Eye Clinic in Basel, 50 patients are to be incorporated into the study, all of whom must be aged over 55 and suffering from early-stage AMD. Once the Ethics Committee gives the green light, patient recruitment will begin. Summarizing the main objectives of the study, Traber says: "Knowing where the disease's origins lie provides new insights for research and eventually also for potential therapies."

For the time being, however, the ophthalmologist Christian Prünte offers little hope for those affected: "It will undoubtedly be a very long time before we find the first approaches to curing AMD." ■

Music, landscape, and thrills.

At music festivals, bands perform their songs while the setting – stage, tents, lighting and sounds – brings the landscape to life. Cultural anthropologists study the everyday lives of people by participating in different activities. In late summer, they took a field trip to a music festival in eastern Switzerland.

Photo: Victoria Heim

Theres Inauen and Michel Massmünster lecture at the Center for Cultural Studies and European Ethnology and have an interest in experimental research formats. Theres Inauen researches cultural policy in Switzerland, while Michel Massmünster focuses on night and infrastructures. As part of a field trip, they spent three days and nights with students at the "Sur le Lac" music festival in Eggersriet, St. Gallen.

1 As participant observers, researchers examine everyday events not from a bird's-eye perspective, but rather by immersing themselves in the experience and reflecting upon it. Ethnography results from the to-and-fro between proximity and distance.
2 At festivals, many different bodies gather in a confined space. They move, dance, drink, flirt and hang out. In doing so, they reproduce norms, behave according to expectations and negotiate the socially possible.
3 The infrastructure of tents, lamps, bars, stages, sound backdrops and lighting opens up and defines a space for action. Materialities shape visitors' feelings and experiences.
4 When the sun goes down, in the transition from day to night, the festival is given a temporal ordering. Together with other events, it lends a rhythm to the year for both visitors and helpers.
5 Who eats falafel, who eats sausage; who drinks wine and who chooses coffee with schnapps? Who wears a leather jacket, rubber boots or a festival T-shirt? Through their clothing and food choices, festivalgoers position themselves, indicate the groups to which they belong and distance themselves from others. They experience themselves both as individuals and as a crowd.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Europe and us.

What should the relationship between Switzerland and the European Union (EU) look like in future? A lawyer and an economist give their views on the current state of play.

Switzerland's relationship with the EU is nearly always right at the top of the agenda for the Swiss Government and civil service – and therefore very often at the forefront of public debate. What interests me most is the legal framework – that is to say, the bilateral law – that governs this relationship. It has its origins in the 1950s and 1960s, when Switzerland first concluded international agreements with the then European Communities – the EU was not created until much later – on issues like trade in clocks and watches. Incidentally, this is an agreement that still works extremely well. Over time, more and more agreements on different subjects were added. There is now a large, multifaceted, but complex network of bilateral law governing the legal relationship between Switzerland and the EU. This is a unique arrangement not replicated for any other EU non-member state.

In this country we like to refer to Switzerland as an "exceptional case", for which only special rules are good enough. From outside, however, things look a little different. Switzerland is one of many countries with which the EU has agreements. In their eyes, there are definitely parallels to be drawn between different agreements and states – in commercial law, for instance. A number of countries have concluded agreements with the EU that allow their nationals and businesses to access the EU's large single market (and vice versa). Today, the EU speaks of an enlarged single market in which not only its own member states, but certain other states can participate to some extent. The closest ties are with Liechtenstein, Iceland and Norway, which together with the EU states form the European Economic Area (EEA). Here, practically all the EU's single market rules apply. Andorra, Monaco and San Marino are also mapping out a comprehensive legal relationship with the EU single market. Although Switzerland is not involved in all aspects of the single market through bilateral law, in certain areas it is very close to it. Next come other countries like Turkey and Ukraine. Finally, the draft EU withdrawal agreement for the United Kingdom and Northern Ireland envisaged that the EU's single market rules would continue to apply during a transition period.

Christa Tobler
has been Professor of European Law at the University of Basel's Institute for European Global Studies since 2005. Since 2007 she has also been a professor at the University of Leiden (NL). She works on various areas of European Union law, specializing in two areas: issues relating to equal rights and discrimination, and the legal relationship between Switzerland and the EU.

This wider development, which goes well beyond Switzerland, is the reason for the negotiations that are now taking place between Switzerland and the EU to set new rules in selected bilateral economic agreements, under the heading of what is being termed a framework agreement or institutional agreement. These negotiations are motivated by the EU's concern that the same rules should apply to all participants in the enlarged single market – not just to provide legal certainty, but to ensure fairness. The issue is still unresolved. In my opinion, how this debate unfolds will be crucial for the future relationship between Switzerland and the EU. It is also important for the public, given that it will define fundamental aspects of Switzerland's relationship with the EU, its most politically and economically important neighbor. Yet the subject matter is really quite complex. For academia, that is something of a boon, as many interesting questions of practical importance arise. In my case, findings from this work will feed into a document designed to make factual information on the issue available to the public in a form that most people can understand. The "Tobler/Beglinger Guide to the Institutional Agreement between Switzerland and the EU" will be updated on a regular basis and is freely available online (brevier.eur-charts.eu). ■

As an economist, I regard the European Union as *one* institution supporting economic and political integration in Europe. Central to this process are interactions within society, the economy and politics.

Economic integration within the EU comprises the reciprocal opening up of markets (in goods, services, labor and capital) between EU member countries. As exchange increases within the resulting single market, this allows for better allocation of scarce resources and what we economists call an increase in efficiency – through specialization, for example. While prosperity increases within the EU and its members, economic integration also leads to restructuring, producing winners and losers within individual countries. It is important to recognize that the selective opening up of markets to non-EU members, such as Switzerland, implies an element of disadvantage, as their operators face discrimination. It is therefore not surprising that those countries should be looking for solutions to facilitate access for their businesses and citizens through accession or special agreements.

Political integration within the EU involves member countries handing over freedoms and powers to shape economic policy to EU bodies in Frankfurt, Brussels and Strasbourg. In external trade policy (goods and services) this is a direct consequence of the economic integration that the EU is pursuing. However, that is not true of other areas of economic policy such as fiscal, monetary, social, environmental or labor market policy. Here, the question arises as to whether and, if so, to what extent the sovereignty of member states should be restricted in the interests of efficiency, and why in the EU we see a tendency to push political integration too far. This is exemplified by the euro, which has removed a key adjustment mechanism (the exchange rate) from the system as a whole and deprived individual countries of an important tool for regulating the economic cycle (monetary and interest rate policy).

As an academic, I enjoy the privilege of contributing to this development through analyses that use economic theories to produce interesting new findings. For example, I applied the "theory of contestable markets" to the EU's decision-making system as reformed by the Lisbon treaty. Together with Herbert Grubel, I reached the conclusion that centralization in the EU is not being curbed because entry barriers for citizens are too high. And 15 years ago, Beat Spirig and I showed that Switzerland's decision not to join the EU can be seen as entirely rational based on the "theory of irreversible investment under uncertainty". Joining would involve substantial accession costs (especially because of the limits that it would place on Switzerland's system of direct democracy), a high degree of uncertainty (with regard to the future development of the EU) and high costs in the event of withdrawal (consider the Brexit negotiations).

When it comes to the framework agreement that is currently being debated, economic theory highlights one benefit that is often overlooked in this discussion, namely, the arbitration panel, which would reduce uncertainty and parties' room for maneuver, especially in the case of the more powerful partner. Given the EU's limited capacity for reform, it is ultimately both rewarding and, in my view, important to think about alternatives to the EU in Europe and the systems competition that goes with that. ■

Rolf Weder
has been Professor of International Trade and European Integration at the University of Basel since 2000 and Dean of the Faculty of Business and Economics since 1 August 2019. His research deals with the effects of globalization and regional integration between countries. He also looks at the implications for economic policy and business, particularly in the context of the relationship between Switzerland and the EU.

Photos: Christian Flierl
Text: Reto Caluori

Tiger mosquito on the increase.

At first, the spread of the Asian tiger mosquito was limited to Ticino. Now, however, it is colonizing more and more new regions in Switzerland. The Asian tiger mosquito (Aedes albopictus) is an invasive mosquito species that originates from Southeast Asia. It has adapted perfectly to its new environment and is starting to establish itself here.

This striped mosquito poses a problem, as it bites even during the day and can transmit tropical diseases. Although the latter has not yet happened in Switzerland, it is reason enough to monitor and control the mosquito's spread.

The current populations are offspring from individuals that were introduced into Italy from the USA in 1990s. In Europe, the tiger mosquito has primarily been transported passively in vehicles along the main traffic axes and has come to colonize large parts of the Mediterranean basin, even crossing the Alps. In 2015, its presence was also confirmed in Basel.

Since then, researchers from the Swiss Tropical and Public Health Institute (Swiss TPH) have been monitoring its spread in the region. "We have found tiger mosquitos in various locations," says Dr. Pie Müller, who leads the monitoring project. DNA analyses will show whether these are newly introduced individuals or come from populations that have overwintered here.

Although it's unlikely that the tiger mosquito will be prevented from gaining a foothold, the researchers' aim is to keep the populations as small as possible. To this end, they are studying aspects of the mosquitos' behavior, such as their flying abilities. This will make it possible to estimate how far the insects are able to spread without the aid of transportation.

To give them an idea of the prevalence and distribution of the tiger mosquito, the researchers place containers with water in which the female mosquitos lay their eggs.

Each trap contains a strip of wood sticking out of the water for eggs to be deposited on. The containers are collected every two weeks. On the pieces of wood, there are now rows of dark eggs that were laid on the water surface at different times (right).

Potential breeding grounds are located along transport routes, which play a key role in the spread of the tiger mosquito. Since the Basel region is a hub for international goods transport by road and rail, researchers like Martin Gschwind and Freya Pappert from the Swiss TPH (pictured here) monitor these locations very closely.


TIGER


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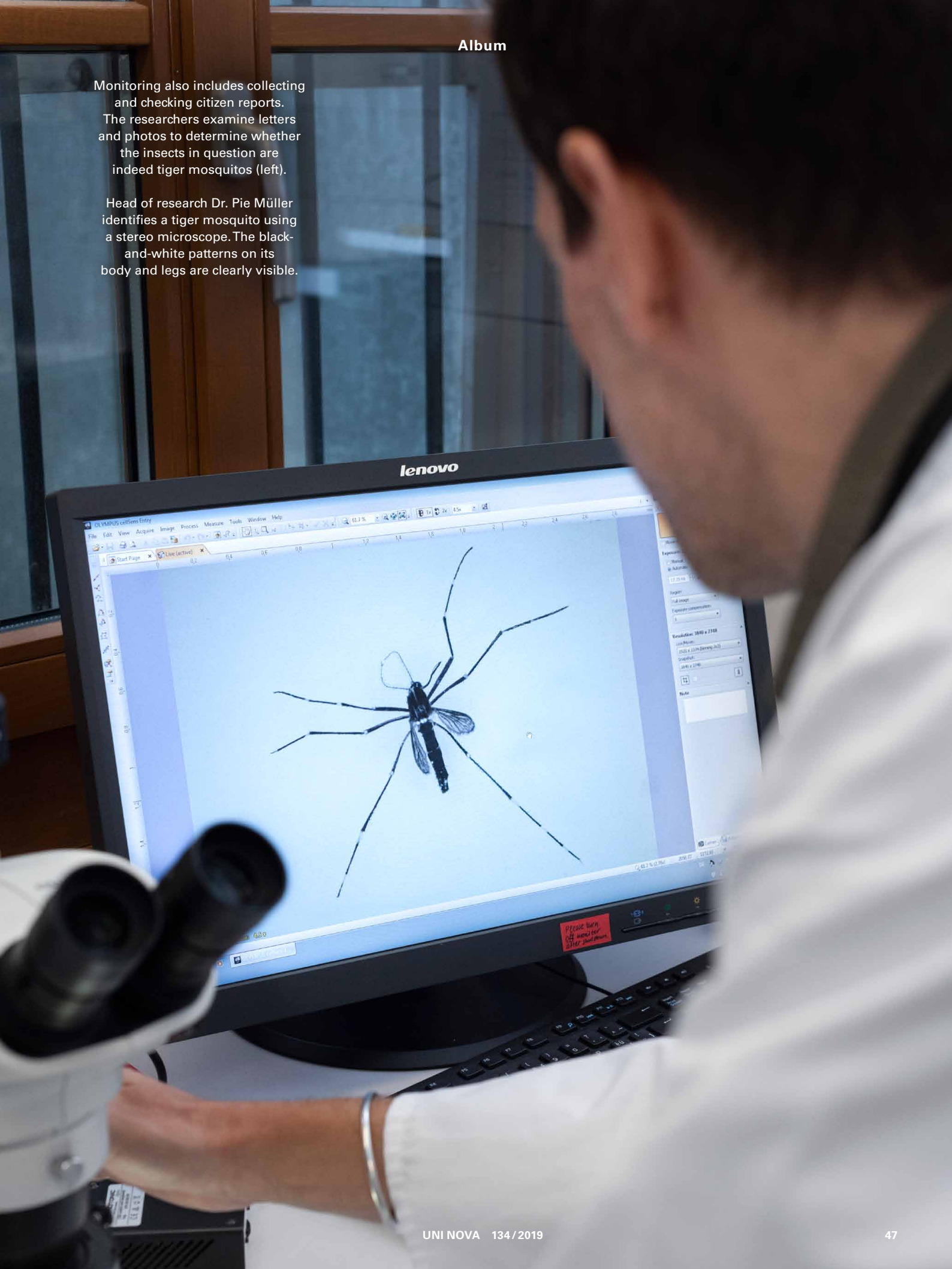
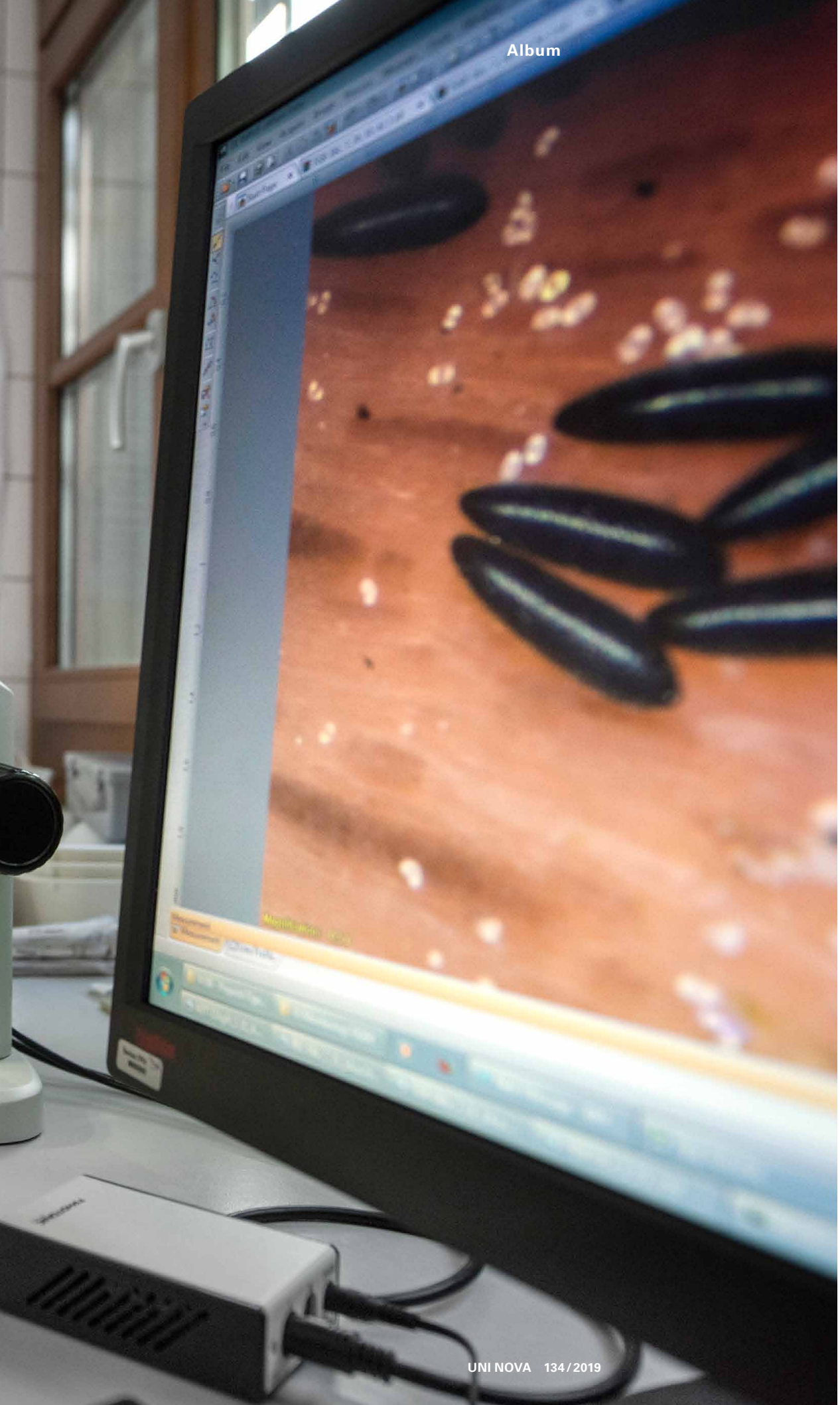
Monitoring also includes collecting and checking citizen reports. The researchers examine letters and photos to determine whether the insects in question are indeed tiger mosquitos (left).

Head of research Dr. Pie Müller identifies a tiger mosquito using a stereo microscope. The black-and-white patterns on its body and legs are clearly visible.



In the laboratory, the eggs on the wooden strips are also counted. Using mass spectrometry, it is possible to determine whether the eggs come from a tiger mosquito.



Pie Müller
is a research group leader at the Swiss TPH and a lecturer at the University of Basel. His main research interest is the biology of mosquitos, and developing and implementing new methods of surveillance and control. He is the Swiss principal investigator for TIGER, a trinational network that surveys the Asian tiger mosquito in the Upper Rhine region.

tiger-platform.eu

Combating bacteria with viruses.

Text: Yvonne Vahlensieck

As viruses that specialize in attacking bacteria, phages promise huge potential for the treatment of infections. Scientists in Basel are searching the natural world for new species of phages that can help them identify vulnerabilities in bacteria.

Alexander Harms is project leader in Professor Urs Jenal's research group at the University of Basel's Biozentrum.

When the microbiologist Dr. Alexander Harms from the Biozentrum at the University of Basel needs new materials for his research, he simply goes down to the Rhine, a sewage treatment plant or a nearby park. There, he collects samples that are teeming with the subject of his experiments. These bacteriophages are viruses that penetrate bacterial cells and multiply inside them, killing the bacteria in the process. As such, they are considered a new wonder weapon in the fight against infections – especially as a growing number of pathogens are developing resistance to antibiotics.

A return to old ideas

Actually, this is not an entirely new approach. Around 100 years ago, ingenious doctors successfully used bacteriophages to combat bacterial infections. With the discovery of antibiotics, however, the method soon vanished into obscurity in most places. Phages continued to serve as an important model system for molecular biology research before finally falling out of use altogether in the 1980s. "Whereas research has advanced steadily in other areas, phage research has skipped a generation," explains Harms. He finds this extremely regrettable, especially considering that the Biozentrum was once a world leader in this area. Indeed, the Basel-based professor of microbiology Werner Arber received the Nobel Prize in 1978 for research projects in which phages played a vital role.

In light of the antibiotic crisis, interest in phage research has seen a renaissance in recent years. "Thanks to a whole host of new techniques, such as rapid genome sequencing, researchers have realized just how many unknown species of phages are out there waiting to be discovered," says Harms. Every drop of water and every speck of soil contains thousands upon thousands of phages – including, in all likelihood, some with the potential to neutralize dangerous bacteria using mechanisms that are still unknown to science.

Targeting dormant bacteria

This precisely is the basic premise of Harms' research project: From his samples, he isolates phages that can kill off pathogens such as *Salmonella, E. coli or Staphylococcus.* Then, he selects the most promising specimens for more rigorous analysis using the latest techniques in molecularbiology, as well as many of the classical methods that the Biozentrum helped develop decades earlier. His aim: to determine what tricks the phages use to eliminate the bacteria and which genes are involved.

Harms is particularly interested in bacteria that evade treatment with antibiotics by temporarily lapsing into a sort of deep sleep. These so-called persister cells are thought to be responsible for chronic infections such as cystitis and pneumonia in patients suffering from cystic fibrosis. Despite repeated courses of antibiotics, these chronic infections never fully disappear. Rather, they flare up time after time and can even prove fatal in the worst cases. With this in mind, Harms is specifically looking for phages that can attack bacteria in their dormant state: "We then want to identify the genes that help phages destroy persister cells."

Aiming to construct new phages

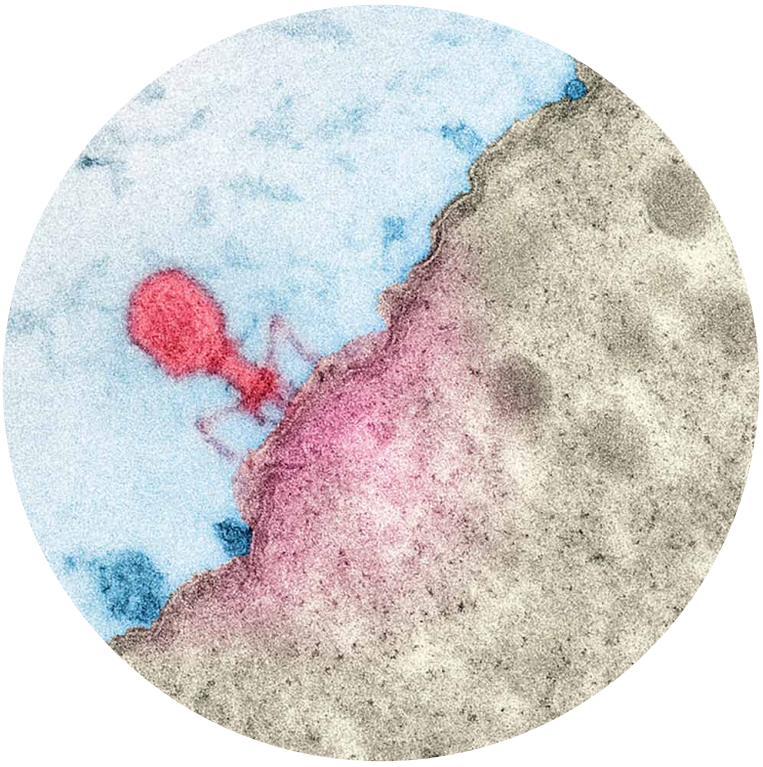
This systematic approach is very different from classical phage therapy, which has recently been the subject of frequent media coverage. In the classical method, physicians scour water samples from sewage treatment plants, for example, for a phage that just happens to attack the precise bacterium with which a patient is infected. After being multiplied, this phage is often administered to the patient under time pressure without thorough analysis of its mode of action. Harms has concerns about this approach: "The problem is that everything is very empirical. You don't know exactly what's going on between the phages and bacteria in the patient's body or why it works in some cases but not in others."

The researcher therefore plans to gradually amass a whole arsenal of phage genes and to use these to build tailor-made phages based on a number of well-known basic types. For example, the phages could be specifically geared toward combating chronic diseases, in which case they would benefit not only single individuals but also larger groups of patients suffering from the disease. Harms also hopes that the insights derived from his analyses will feed into the targeted development of other antibacterial drugs.

No problems with resistance

The use of phages offers another key advantage over antibiotic therapy. Experts believe there is little risk of bacteria developing lasting resistance to phages, and even if the bacteria develop mechanisms to defend themselves, the phages will adapt to these mechanisms very quickly. After all, they've been one step ahead in this evolutionary arms race for millions of years. "Bacteria evolve very quickly. But there's something that evolves even faster, and that's phages," says Harms. He would also like to arm his custom-built phages to attack bacteria at several vulnerable sites at once, reducing the risk that bacteria could escape the phages by means of a simple adaptation. There's also little chance of dangerous side effects, as experience has so far shown phages to be harmless to humans.

Like many researchers around the globe, Harms is confident that there are numerous potential discoveries lurking in the world of phages – a world that a group of high-school students had the chance to discover for themselves this summer as part of the "Basel Summer Science Academy." After collecting samples from the Rhine, they isolated phages that Harms now plans to characterize in greater detail. There's a chance that one of these specimens will contain an undiscovered gene – which may one day help restore patients with serious infections to full health. ■



A bacteriophage (red) infects and kills a bacterium.

Montages at the boundary between art and politics.

Text: Ylenia Sartorel

German artist John Heartfield used photomontages to shine a critical light on social issues in interwar Germany. Now, an art historian in Basel has re-examined his work.

During the interwar period, the artist John Heartfield (1891–1968) created numerous political photomontages that were regularly printed in popular illustrated magazines such as the widely circulated *Arbeiter-Illustrierte-Zeitung* (AIZ). To this day, one of his most well-known works remains *The meaning of the Hitler salute,* in which the *Führer* is shown reaching up as if to accept money from an oversized man standing behind him.

Under the magnifying glass

Heartfield's photomontages, which have in the past been studied mainly from the perspective of art history and aesthetics, recently became the subject of an interdisciplinary examination by art historian and sociologist Vera Chiquet. Her lines of inquiry ranged from the role of Heartfield's work in society to the techniques used in his creations. Besides her sociological interest, Chiquet's expertise as an art historian stood her in good stead for the project: using a special lamp and a magnifying class, she scoured the AIZ originals for clues as to how they were made.

Heartfield, who was forced to flee Nazi Germany in 1933, and lived in the GDR from 1950 onwards, is regarded as the inventor of political photomontage. His sensitivity as an artist led him to pay close attention to the events unfolding around him – and use them in his work. In this way, he made an important contribution to the use of image manipulation to stimulate reflection. "Despite the harrowing times he was living in, he did all this with humor, gallows humor – it was his way of coping with the tribulations of the interwar years," the researcher explains.

A reaction to propaganda

Two crucial aspects on which Heartfield's work depended were the ease with which it could be reproduced, and the widespread dissemination of photography – a key feature of contemporary media at that time. In the years leading up to 1939, photography and painting were intimately connected as visual mediums, Chiquet explains. Photographs were rarely published in their original form – as a rule, they were enhanced manually first: advertising photography, for instance, went through an extensive retouching process.

Heartfield borrowed this technique from the field of advertising in his own work, but he always did so with critical intent. According to Chiquet, his photomontages and collages should be interpreted as a reaction to the propaganda of the European dictatorships of the time – the fascist regime in Italy in particular made frequent use of photomontages in which certain themes were depicted in a highly exaggerated manner.

The number of discrete elements that make up Heartfield's images is not necessarily apparent at first glance – the individual photographs seem to blend into each other. It is only when looking at the resulting ensemble that viewers realize that they are in fact looking at a montage. "Heartfield's intention was never to deceive anyone – he wanted to encourage his audience to reflect on how it consumed media, and critically examine this process," says Chiquet. The aim of his photomontages was precisely to highlight the technique's potential for deception. To make this abundantly clear, his images were always accompanied by the subtitle: "Photomontage: John Heartfield".

The aesthetics of advertising

Advertising as a link between art and the mass media: The technique of drawing the viewer's attention first and foremost to the image is a key feature of advertising – both then and now. This process of capturing and retaining viewers' attention was described as a "clever trap" by the German philosopher Walter Benjamin. "The deceptiveness of first appearances is something that Heartfield's work has in common with advertising – except that Heartfield's goal was to expose the deceit of billboards and propaganda, and the intentions behind them," says Chiquet.

The particular aesthetics of Heartfield's montages never arose from a desire to create intricate works of art, but rather to appeal to a broad readership. "His creations are by no means complex collages that require a great deal of effort to absorb – much of the content is accessible at a glance," Chiquet explains.

Chiquet's research focuses primarily on Heartfield's publications in one of Germany's most widely read popular magazines of the time. The AIZ, run by communist publisher and editor Willi Münzenberg, was published from 1921 to 1933 in Berlin, and from 1933 to 1938 in exile in Prague. In its time, it was viewed as a groundbreaking publication for its extensive use of images and pictorial narratives. The magazine's popularity can be attributed in large measure to Heartfield, with numerous readers cutting out his illustrations to hang as posters.

Fake news in the interwar years

"I am fascinated by the extraordinary degree to which different areas – politics, everyday life, advertising, art, technology – were intertwined in the mass media of this period," says Chiquet, currently a researcher at the University of Basel's Digital Humanities Lab. Heartfield's images do not just deal with political issues – they also incorporate contemporary advertising culture and (photography) techniques, she explains. To interpret his creations, the knowledge that they are montages is crucial.

Even if a particular image as a whole does not reflect reality, the elements that comprise it do. Their place in the collage gives them a new context, subverting their original significance. This shows that the phenomenon of fake news was already an issue in interwar Germany and elsewhere: fabricated stories were disseminated by recourse to calculated manipulation in pursuit of a given (political) aim – just like today. ■

Graphic design and advertisement: AIZ front page by John Heartfield (1933) and FLIT advert (1929).

Breathing air reveals diseases.

Text: Martin Hicklin

A person's exhalation reveals their personal metabolic profile. Researchers at the University Children's Hospital Basel (UKBB) are investigating how this information can be used to diagnose and monitor particular illnesses.

Unbelievable but true: A single puff of breath contains large amounts of information that could potentially be used to diagnose and treat illnesses, namely tiny but measurable traces of volatile substances. Such chemical "breath prints" have the potential to provide insights that otherwise could be derived only from blood or urine or would be altogether elusive. For instance, it can reveal how our body breaks down and converts substances, how our lungs work and what differentiates us from others in terms of our metabolism. Exhaled air contains typical telltale signs of microbial lodgers, which in future could indicate illnesses such as pneumonia.

Breath profiles could be used for noninvasive disease monitoring. The procedure is as easy as breathing: Instead of being repeatedly pricked with needles to have blood samples taken, patients need only to blow into a little tube. This is a blessing, especially when treating children. In comparison to diagnostics using blood or urine, breath analysis needs no sample preparation. The fact that the information sought is then available nearly immediately makes the method particularly attractive from a clinical perspective.

Airborne information

The final step, however, has yet to be taken: The treasure trove of information hidden in exhaled air still needs to be unlocked and reliably interpreted. Among the trailblazers is Professor Pablo Sinues, Botnar Research Professor of Pediatric Environmental Medicine and member of the Department of Biomedical Engineering at the University of Basel. A pioneer of mass spectrometry analysis of volatile organic compounds in exhaled air, the 42-year-old Spaniard has been involved in developing the necessary high-sensitivity apparatus from an early stage: "We are trying to develop new tools and methods to address unmet clinical needs like for example rapid and accurate diagnosis and therapeutic monitoring." Sinues, who studied chemistry and mechanical engineering, is convinced that this surprisingly underexplored field has a bright future. Basel offers him privileged opportunities in that the University Children's Hospital Basel allows him and his team to conduct first-hand research with young patients while maintaining close contact with the attending physicians.

Pablo Sinues is Botnar Research Professor of Pediatric Environmental Medicine at the University of Basel and works at the University Children's Hospital Basel (UKBB). He is also a member of the Department of Biomedical Engineering at the University of Basel.

As sensitive as a dog's nose

Analyzing exhaled air is quite challenging. The tools used need to be sufficiently sensitive and specimens have to be fed into the measuring device in the right form and in real time. Basel recently saw the arrival of a combination of equipment that is sensitive enough to detect molecules of relevant organic compounds and is ready for clinical use.

Sinues was already involved in developing such highly sensitive apparatus as a visiting doctoral student at Yale University, working in the former laboratory of Professor John B. Fenn, who was awarded the Nobel Prize in chemistry in 2002 for his contributions to mass spectrometry. Eight years ago, Sinues moved to ETH Zurich, where he continued to develop these technologies and conduct pilot clinical trials. After completing his postdoctoral thesis in 2015,

Sinues, a co-holder of two relevant patents, became Botnar Research Professor at the University of Basel two years ago.

At the heart of the apparatus, which was recently installed at the University Children's Hospital Basel, is a specialized device. It prepares the exhaled breath in real time, enabling the commercially available high resolution mass spectrometry device to distinguish downstream minimal traces of substances, measured in parts per trillion, according to their molecular weight. Only a dog's nose has the same extremely high level of sensitivity.

"Breath prints" displayed as tracings

A "breath print" takes the form of peaks in the mass spectrum, representing the presence of specific substances in breath. Because the technique is real-time, the presence of such molecules is monitored on the fly. Thousands of substances may be present, which leads to a mountain of data. For the method to work, exhaled molecules need to be electrically charged or ionized. This is achieved by combining the exhaled breath and an electrospray. Accordingly, the method is known as secondary electrospray ionization with high-resolution mass spectrometry, or SESI-HRMS. Sinues was involved in developing the device that is fundamental to the method. The device is currently marketed under the name SUPER SESI by a former postdoctoral researcher of Sinues at ETH Zurich and produced by a company founded in Spain.

The challenge now is to prove conclusively that measurements obtained are repeatable and reproducible. This means developing standard procedures for routine use of breath analysis. In this connection, Sinues, along with other researchers, published a seminal technical paper in the spring of 2019. Meanwhile, the repository of data such as mass spectrometry peaks and associated information is growing with each puff of breath analyzed and is waiting to be interpreted.

15 minutes instead of 48 hours

According to Sinues, SESI breath analysis will also find applications in therapeutic drug monitoring where the correct dosage is difficult to determine. Drugs used to treat epilepsy or cancer, for instance, have a narrow therapeutic window, that is, the margins separating ineffective, effective and toxic dosages are very small, not to mention the wide variability from patient to patient. To enable safe, personalized treatment, series of blood samples need to be taken. Sinues is currently working to replace the use of needles with noninvasive breath analysis, which would be a huge relief, especially for children. Instantaneous results also represent an unbeatable advantage, with no need to wait for news from a laboratory. The aim of making life easier for younger patients is very much in keeping with the ethos of the Basel-based Botnar Foundation, which focuses on issues in child health and has funded the apparatus.

To speed things up, Sinues co-founded the start-up "Deep Breath Initiative", which aims to bring together international research in this field to make it accessible to the wider healthcare system. This start-up is supported by the University of Basel with the Innovation Space. A further project is being conducted jointly with the University Hospital Zurich and ETH Zurich, which form part of the Zurich "Exhalomics research consortium". Its goal is to use breath analysis to diagnose pneumonia and even distinguish its causative agents based on their waste products. If this is achieved, then diagnostic results will become available within 15 minutes – today the wait is 48 hours and can result in serious complications for patients. ■

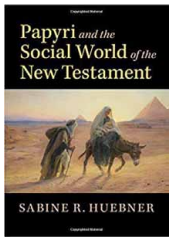
This special apparatus prepares the exhaled breath so that a mass spectrometry device can distinguish minimal traces of substances. (Image: UKBB)

Social Psychology

Decision-making and coin tosses.

To reach a good decision, we usually want to know as much as possible about the available options. Too much information, however, is not always more helpful. It can cause us to delay decision-making or even make an inferior choice. This was the subject of a study carried out by Maria Douneva, a doctoral student at the Faculty of Psychology. She found that a person who tosses a coin to help make a decision will not necessarily do what the outcome of the toss suggests but is less likely to want additional information.

In five online experiments involving different scenarios and samples, Douneva presented a total of 997 participants with binary options; for instance as to whether or not to renew an employee's contract or which of two charitable organizations to donate money to. After making a preliminary decision, some of the participants were shown a virtual coin toss suggesting one of the options. The final decision was theirs, however. While participants were rarely influenced by the coin toss in their final choice after they had made a preliminary decision, those who had seen the coin toss felt less of a need for additional information than those in the control group. For instance, they were less likely to request further information about the employee whose contract was up for renewal and spent less time on the website of the charity to which they ended up making the donation. According to Douneva, the results of the experiments demonstrate a potential way of counteracting blocks and procrastination in decision-making. ■



Early Christians

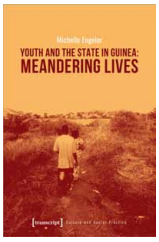
Family life 2000 years ago

In this book, Sabine R. Huebner explores the world of the protagonists of the New Testament and the early Christians using the rich papyrological evidence from Roman Egypt. In so doing she provides unparalleled insights into the everyday lives of the non-elite population in an area quite similar to neighboring Judaea-Palestine.

Among the questions Huebner addresses: What were the daily concerns and difficulties experienced by a carpenter's family or by a shepherd looking after his flocks? How did the average man or woman experience a Roman census? What obstacles did women living in a patriarchal society face in private, in public, and in the early Church? Given the flight of Jesus' family into Egypt, how mobile were the lower classes, what was their understanding of geography, and what costs and dangers were associated with travel?

This volume gives a better understanding of the structural, social, and cultural conditions under which figures from the New Testament lived. ■

Sabine Huebner: Papyri and the Social World of the New Testament. Cambridge University Press 2019
206 pages, GBP 24.99



Ethnography

Youth and the State in Guinea

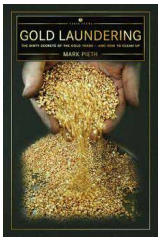
The majority of books discussing youths in African contexts emphasize young people living in urban spaces of major cities. This research monograph, on the other hand, is based on extensive fieldwork among young people living in the Guéckédou borderland, a remote space between coastal and savannah West Africa, approximately 700 kilometers southeast of Conakry, Guinea's capital.

It understands "youth" as a socially constructed category mirrored in the meandering lives of young men and women who explore various avenues to social status and political participation.

Against that background, Michelle Engeler focuses on youth-state relations by discussing different youth groups.

Importantly, this study takes a broader historical view on the Guéckédou borderland to make sense of these contemporary dynamics of youth-state relations and also provides crucial insights into processes of identity formation, generational relations and political transformation. ■

Michelle Engeler. Youth and the State in Guinea: Meandering Lives. Transcript 2019
204 pages, EUR 39.99



Gold Industry

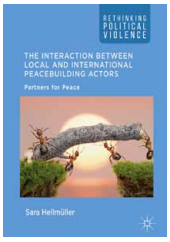
Major power Switzerland

In this eye-opening book, Mark Pieth gives an in-depth insight into how the global gold market works, what role Switzerland plays in it, where the hidden abuses lie and how human rights in the gold industry can be protected in a credible way.

This hard-hitting, exclusively researched depiction of a key area of economic policy takes us both to the glittering world of gold refining and to the world's worst mining regions. Mark Pieth illuminates the historical roots of the gold trade before turning his attention to today's supply chains, from mines to refineries and clandestine intermediaries to consumers: central banks, investors, jewellers and watchmakers. He reveals some of the horrific problems caused by gold mining that still receive little attention due to a lack of binding regulations: severe environmental destruction, forced labour and human trafficking, land grabbing, stolen assets and money laundering.

Switzerland is not only a major power in the financial sector and commodity market: Switzerland is also a leader in global gold trading. But while the EU, for example, has recently turned existing OECD guidelines into binding law, Switzerland continues to rely on voluntary self-regulation. ■

Mark Pieth: Gold Laundering. The Dirty Secrets of the Gold Trade - And How to Clean Up. Salis Verlag, Zurich 2019
304 pages, CHF 18



Rethinking Political Violence

Partners for Peace

The Democratic Republic of the Congo (DRC) has been the theater of local and international peacebuilding for two decades. Yet, peace has not taken hold. In her book *Partners for Peace,* Sara Hellmüller explores the reasons for this ongoing state of turmoil. Based on rich empirical data, she locates the answer in the interaction between local and international peacebuilding actors.

Focusing on the case study of Ituri in the Democratic Republic of Congo, the book analyzes the relationships between local and international peacebuilding actors over the long term and assesses ways to overcome the obstacles to more cooperative partnerships. Focusing on perceptions, the book nuances existing definitions of war, peacebuilding and peace and allows for a more comprehensive understanding of conflict contexts.

Thereby, the book contributes to the literature on peacebuilding effectiveness and makes concrete suggestions for translating these findings into practice, both in the DRC and beyond. ■

Sara Hellmüller: The Interaction Between Local and International Peacebuilding Actors – Partners for Peace. Palgrave Macmillan, Cham 2018
233 pages, GBP 40.00

Buddha and the early Christians.

Did Indian Buddhism influence early Christians in the Middle East? There is evidence that suggests so.

Text: Stephan Peter Bumbacher

In 1938, a perfectly preserved Indian ivory female figurine, presumably of the goddess Lakshmi, was discovered in Pompeii, a city that was destroyed by an eruption of Mount Vesuvius in 79 AD. How did this figurine come to be in Italy? Roman coins continue to be found all over southern India and even in Kashmir. Who brought them to India? Long-distance trade and cultural links are not a modern phenomenon. For instance, the Romans in their heyday controlled trade around and across the Mediterranean, maintained scheduled sea links with India from the 1st to 4th centuries AD and even kept a number of local trading posts, for instance in Muziris (present-day Cranganore), Poduke (Arikamedu) and Comari (Kumari). As early as the 1st century AD, the historian Strabo mentions South East Asian goods being imported to Rome via what is now Sri Lanka.

Cultural exchange can, however, also be brought about by war. As early as 325 BC, roughly a century after the Buddha's death, Alexander the Great with his army and accompanying scientists reached the River Indus. Arrian notes that Alexander, who had been tutored by the philosopher Aristotle, engaged in a debate with Brahman *gymnosophistai,* or naked philosophers, who were considered akin to the Greek Cynics. Greek influence is also visible in Gandharan art, and the Indo-Greek king Menander (c. 130–100 BC), under his Indian name of Milinda, takes center stage in the Buddhist text *Milindapañha.*

It is a legitimate question to ask whether, by the same token, religious concepts could have come to the West in the mental luggage of merchants and caravaneers or the kitbags of soldiers returning home. After all, the *Philosophoumenos,* a work written around 230 AD by the Father of the Church Hippolytus, contains specific information about the Brahmans' religious beliefs that implies knowledge of the Indian *Upanishads* (or possibly a Greek translation thereof). Around that time, Church Father Clement of Alexandria mentions Brahmans and Sarmans (i.e. *shramanas,* or ascetics) in his work Stromateis: "Some, too, of the Indians obey the precepts of Boútta (Buddha), whom, on account of his extraordinary sanctity, they have raised to divine honors." This means that by the beginning of the 3rd century at the very latest, Christian intellectuals had some knowledge of Indian religions. That knowledge could have reached the West not only by sea, but also via the Silk Road, which ran from Luoyang in China to Antioch near the Mediterranean Sea and on to the port of Tyre. It was along this route that Buddhism spread eastward into China in the 1st century AD or earlier.

Is it possible that Buddhist beliefs or themes were orally relayed across language barriers, traveled as far as Palestine and found their way into the New Testament? Some researchers think so. The following discusses two examples chosen from various relevant texts.

Among the world's known religions, Buddhism and Christianity are unique in possessing narratives that talk about their respective founders being tested by a seductive evil power: In the early Hīnayāna scriptures, Māra, the evil one, makes an appearance, endeavoring to lead Gautama (Buddha) astray. First, Māra tries to steer Buddha away from asceticism. Later, he does everything in his might to prevent Buddha from attaining enlightenment. Finally, the demon tries to persuade Buddha, by now an old man, to enter Nirvāṇa prematurely, which Buddha declines. The later Mahāyāna scriptures give a more elaborate

Stephan Peter Bumbacher is Professor of Chinese Studies and Comparative Religion at the University of Tübingen. Until earlier this year, he taught Comparative Religion with a focus on Asian religions at the University of Basel and Classical Chinese studies at the University of Zurich. He is currently reconstructing the writings of the Chinese Philosopher Zhuangzi (3rd century BC) and preparing a critical edition. Another of his research interests is the cognitive and anthropological roots of religions and their interactions.

account of the temptation: Māra makes three attempts to keep Gautama from achieving enlightenment through meditation. He begins by assailing Gautama with a demonic army; next, he mobilizes the forces of nature; and, finally, his three daughters use all their powers of seduction. Gautama, of course, resists all these temptations.

A parallel in substance is found in the New Testament, where the devil tempts Jesus. Mark the Evangelist devotes only one sentence to the temptation of Christ and John does not mention it at all; whereas in both Matthew's and Luke's accounts Jesus is tempted in the desert after a long fast, with the devil challenging him to turn stones into bread. Two more episodes follow: Jesus is taken to the highest point of the Temple and told to throw himself down from it; since, as the Son of God, angels would break his fall. Later, on a very high mountain, he is shown and offered all the kingdoms of the world on condition that he submit to the devil and worship him. Jesus resists these temptations, too.

For all the dissimilarities between the Buddhist and Christian stories, they have some elements in common: Both religions' founders are led into temptation in remote places and enter into dialogue with their tempters. In both cases, the tempter is the "ruler" of the world. Also, both Buddha and Jesus have yet to step into public life. While neither text is directly based on the other, there is a thematic analogy: If Gautama had yielded to temptation, he would have been cheated out of enlightenment and ultimately his teaching. If Jesus had given in, he would not have fulfilled his mission.

Another parallel can be drawn between the miracle stories of Buddha and Jesus walking on water. An ancient text, the Mahāvagga section of the Vinaya Pitaka, talks about a flood: Buddha is walking on the water, alone and in meditation. Kassapa, an adherent of a different religious tradition, worries about Buddha and, together with a like-minded group, sets out in a boat to reach him. When he does, he asks: "Is it you, great ascetic?" Buddha answers in the affirmative and enters the boat. Kassapa is said to have converted to Buddha's teachings on account of this miracle. In the Gospel of Matthew, Jesus is praying by himself on the mountain when his disciples, who are in a boat on the Sea of Galilee, run into trouble. They suddenly see a figure walking on the water, but fail to recognize Jesus and take him for a ghost. Jesus addresses them, identifies himself and steps into the boat. Then the wind dies down. Here the doubting disciples' faith is strengthened.

There are obvious differences between the Buddhist and Christian stories: Buddha is only seemingly in distress, whereas Jesus' disciples are in actual danger. The boat is carrying adherents of another tradition in the former case and Jesus' own followers in the latter. Yet, there are clear commonalities, too: Both protagonists are in a remote place and engrossed in some form of mental activity (meditation or prayer); both are walking on turbulent waters. Both stories switch their point of view from the master to the disciples in the boat, who are astonished or afraid. Both Buddha and Jesus reveal their identities and board the boat. Also, in both cases, the faith of the followers is transformed.

It is conceivable that the Buddhist versions served as a model for the Christian one, but was modified in accordance with Christian requirements and incorporated into the context of the New Testament in such a way that its origin was obscured. We may therefore assume that religions have typically evolved not in isolation, but through an interplay of mutual interpretation, appropriation and rejection, shaped by religious imagery, historical events and changing economic and political conditions. ■

"Religions have typically evolved not in isolation, but through an interplay of mutual interpretation, appropriation and rejection."

Stephan Peter Bumbacher

A participant observer.

Text: Christoph Dieffenbacher Photo: Andreas Zimmermann

Housed in the labyrinthine old building next to the Museum der Kulturen Basel, her office is not easy to find – I climb a steep flight of wooden stairs, continue through low doorways and low-ceilinged rooms, and past a green-tiled stove before finally meeting her at the end of a side corridor: Just back from maternity leave, anthropologist Rita Kesselring is committed to delving into everyday life in southern Africa. Her postdoctoral thesis focuses on a very unique kind of working environment: copper extraction in the town of Solwezi in northwestern Zambia, one of the world's poorest countries. This is the rough and rugged world of mining, where workers use heavy machinery to extract copper and gold from the ground.

Life in a copper town

"Of course it's a typically male subject," the researcher says with a laugh, "and that's probably why it fascinates me." She adds that mining in southern Africa, one of the most important regions for the supply of raw materials, has been a subject of anthropological research for almost a century. Kesselring is now investigating developments that have taken place in the industry since the most recent privatization wave of the late 1990s. She observes, for instance, that although Zambia has seen numerous new mines sunk and equipped with the latest technology, the local environment is still being heavily polluted and human rights are still being breached. She also says: "Even though the mines require fewer workers than they used to, people are still moving into town from the countryside in search of work." The walls and desk of her small and somewhat dark office are covered with maps that show the urban settlement pattern and infrastructure. Kesselring points out that, for instance, whites – mostly senior managers – live in fenced-in houses whereas blacks live in mud huts with inadequate water supply and polluted air. Every day, blasting causes ground vibrations. "The urban structures that emerged after the latest commodity boom are reminiscent of segregated towns in apartheid South Africa," she says. In addition to local daily life, she is examining the various stages of the copper supply chain, from mining to the customer via transport and trade.

She paid repeated visits to Solwezi, living in the settlements for a total of 14 months and visiting open-pit and underground mines. She spent hours talking to the people living and working in the town. This came to an abrupt halt when the mine management broke off all contact with her: "The moment I started asking questions about business links with Switzerland, that was the end of our conversations." Such connections were not to be disclosed, and the anthropologist's attention was no longer welcome. This did not, however, deter her from investigating the background and the reasons for the sudden reticence: "This is also part of the research question."

Switzerland is the world's largest trade hub for raw materials from southern Africa, with most metal traded in the country. "Far too little is known about Switzerland's role in international commodity trade," says Kesselring, adding that the sector is largely unregulated in Switzerland, although relevant proposals have been made in the meantime. Viewed from that perspective, she says, there is an obvious political component to her work on the Zambian copper town. She is involved in anti-globalization organizations, preferably the smaller kind, because she finds larger organizations less conducive to fruitful discussion and exchange.

"Research brings responsibility"

For a previous research project, she lived in Cape Town for two years, visiting and interviewing black people in poverty-ridden housing areas on a daily basis. She wanted to learn, among other things, about their experiences of the apartheid era and about the long-term implications: How were people coping with their physical and mental suffering, such as the pain of losing loved ones? The researcher says that those affected remain deeply traumatized. Closely following the everyday lives of a particular group is a well-established method in social anthropology, known as "participant observation". "I could learn more this way than if I had simply interviewed people," Kesselring explains. "What was more of a problem was that many people found themselves reliving past events, which sometimes put emotional stress on me, too."

Gaining insight, publishing findings and developing academic theories are important to this researcher, who remarks that being an academic, as opposed to a journalist, gives her the opportunity to stay with a subject over a longer period and take an in-depth look, for instance zeroing in on "everyday inequalities," as she puts it. She says that she is always aware of the great debt she owes to the people she researches. And she adds: "As far as I'm concerned, research brings responsibility with it, for example a responsibility to ask myself how the object under study relates to the world I live in."

Yoga on the golf course

Recalling her time in southern Africa, the anthropologist says that, as a young woman, she found it easy to establish a

Social anthropologist Rita Kesselring examines both the legacy of apartheid and mining in southern Africa. For her field research, she often travels alone to townships and inhospitable mining towns.

Rita Kesselring was born in 1981 and grew up in Frauenfeld in the Swiss canton of Thurgau. She is a postdoctoral researcher and senior lecturer at the University of Basel's Institute of Social Anthropology. She studied social anthropology, English studies and international law in Zurich and Cape Town, obtaining her doctorate from Basel in 2013. Having first undertaken research on apartheid victims and their demands for reparations, she is currently examining raw material extraction and commodity trading in southern Africa and Switzerland. Kesselring has been a visiting researcher at the University of Connecticut and Princeton University and has carried out extensive field studies in South Africa and Zambia. Based in Grenzach-Wyhlen, Germany, she is married to an anthropologist and is mother to a young daughter.

rapport with people. Asked whether it was dangerous for a woman on her own to venture into unfamiliar areas, she replies: "Not really, although there were a few difficult situations. For example, in South Africa, I was advised against living in black neighborhoods as a white person. And still, I was often given protection and support by women I was talking to, for example grandmothers looking after their grandchildren." She practiced martial arts so that she could defend herself in an emergency. And she explains that doing yoga exercises on the fenced-in golf course in Solwezi prompted conversations with managers, which in turn led to some initial interviews.

Kesselring still keeps fit, jogging or hiking when she finds the time. After leaving school, she had originally wanted to study sports science, as a keen athlete, but this plan was sadly thwarted by an accident. Then an extended trip to Zimbabwe sparked her interest in anthropology: "At first, I really struggled to understand many aspects of local everyday life, which seemed mostly alien to me." That experience was effectively her entry into the academic discipline she ended up choosing. She is already looking forward to her next research trips, accompanied this time by her husband and their young child. ■

Alumna at work: Tanja Dietrich

From biology to communications.

Interview: Bettina Volz-Tobler

Tanja Dietrich studied biology at the University of Basel. Today, she is communications director at Basel Zoo and owner of a communications agency specializing in online marketing and consulting for small and medium-sized enterprises and associations.

Tanja Dietrich

UNI NOVA: Tanja Dietrich, what made you want to study biology?

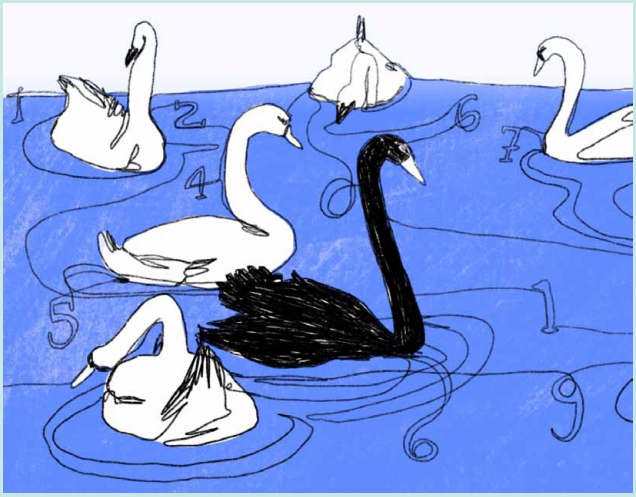
TANJA DIETRICH: Animals have fascinated me since childhood. At the time, the only animals we could keep were a cat and two guinea pigs, so I turned to books and started accumulating knowledge about all kinds of animals. I was something of a walking animal encyclopedia as a child. So it was an obvious choice for me to enroll in the Biology I course, as it was called then. Unlike Biology II, with its focus on cell biology, it included classes on vertebrate biology and systematics. The program as I knew it no longer exists.

UNI NOVA: You've been head of communications at Basel Zoo for 15 years. You also run your own communications agency. How did you end up on this particular career path?

DIETRICH: For my thesis on an aspect of vision in fish, I worked at Basel Zoo and the Swiss Tropical and Public Health Institute. After graduating, I worked part-time at the zoo and part-time as Director of Education and Interpretation at Museum.BL. At the same time, I was engaged in voluntary conservation work. When Basel Zoo created the post of communications Director in 2004, they asked me. In parallel, my volunteer work was growing and led to more and more inquiries from small associations and organizations. I decided then to found my own agency, specializing in online marketing consulting. I give advice to small businesses, institutions and associations that want to raise their profile and gain new clients. I show them how to use online content to attract visitors and turn them into clients.

UNI NOVA: What's your most vivid memory from your time at university?

DIETRICH: I would say the medical parasitology classes at the Swiss Tropical and Public Health Institute with those great big jars filled with all kinds of parasitic worms, but most of all Professor David Senn and his classes, which were always packed out. His enthusiasm for his subject bubbled over and he would often illustrate his points with spontaneous drawings on the board. His classes left a lasting impression on a whole generation of biology students. He still organizes a dinner every year for "Sennians" to meet and compare notes. ■



AlumniActuarialScience

New alumni association created.

Text:
Jolanda Bucher
Illustration:
Annina Burkhard

Actuarial science has been taught at the University of Basel for 80 years now. This makes the program one of the oldest German-language courses in the field. This year's anniversary event included the launch of the actuarial science alumni association.

On 6 February 1939, the University of Basel introduced actuarial science as a separate examination subject. And 80 years later to the day, the alumni association AlumniActuarialScience was formed. Around 90 alumni, students, university staff and guests with an interest in the program took part in the anniversary celebrations at the Old University. Knowledge and information transfer were a central theme of the event. Two students presented their recently concluded master's projects to the specialist audience. During the drinks reception and subsequent meal for the body's new members, old acquaintances were refreshed and new contacts forged – an all-round success for the launch of the new alumni organization.

Giving something back

Plans for the new association include a yearly meeting on 6 February in collaboration with the Master's Program in Actuarial Science and an alumni group in Zurich. The purpose of the alumni organization is to support friendships, networking and contact with sponsors and industry, besides promoting teaching and research in the field of actuarial science at the University of Basel. The driving force behind the initiative is a sense of connection to the university – for alumni, it is a way of giving something back.

Before they reached Australia, the inhabitants of the Old World believed that all swans were white. This conviction was unshakeable – all the empirical evidence appeared to back it up. When Dutch explorers spotted the first black swan in western Australia in 1697, this belief was turned on its head: something previously thought to be impossible had occurred. Since then, the expression "black swan" has been used as a metaphor for a highly unlikely event with major repercussions, often causing existing theories to be revised or expanded.

Black swans aplenty

In practice, actuaries encounter numerous black swans, which have momentous effects on trends in the financial and insurance markets. The extraordinary success of Google and Amazon, the attacks of September 11, the global banking and financial crisis of 2008, the 2011 nuclear disaster in Fukushima or the meteoric rise of the World Wide Web in the 1990s are all examples of these extremely rare events with far-reaching consequences.

One of the key tasks of actuarial science is assessing the likelihood of black swans, their impact on the financial and insurance markets, and the opportunities and risks they present. Doing so enables the vast implications of these events to be taken into account in the calculation of insolvency probabilities, risk-based premiums and appropriate claim reserves – and thereby at least partially managed. Actuaries therefore not only contribute to the ongoing success of the insurance and banking industries but also play a significant role in the proper functioning of social security systems and positive economic development. ■

Anniversary

UniBall turns 20.

Once a year, the University of Basel hosts an evening of dancing with two shows, two dance floors, a live band and a DJ. In 2020, the traditional UniBall will celebrate its 20th anniversary. As always, students, teaching staff, employees, and friends of the university are invited to dance the night away. The 2020 UniBall takes place on 25 April at the Kronenmattsaal in Binningen. The doors will open and drinks will be served from 7 pm. The ball begins at 8 pm. ■

Social Media

Increased activity.

AlumniBasel has been boosting its presence on social media channels such as Facebook and LinkedIn, and is now also using new communication channels such as Instagram. Our motto remains: Find us, join us, follow us – and like us! ■

Collaboration

Discounted entry to Lucerne Festival.

AlumniBasel members can now buy discounted tickets to selected concerts at the Lucerne Festival, which takes place by Lake Lucerne. The AlumniNews newsletter provides details of relevant events in the concert hall at the Lucerne Culture and Congress Centre (KKL) and how to buy tickets. Founded in 1938, the Lucerne Festival is one of the most renowned classical music festivals and attracts famous artists and symphony orchestras from all around the world. ■

Students help refugees: the "Offener Hörsaal" team. (Photo: Anaïs Steiner)

Annual Giving 2019

Supporting "Offener Hörsaal".

Text: Annalena Durrer and Timo Posselt

Money collected through this year's Annual Giving will be donated to the "Offener Hörsaal" association at the University of Basel.

The "Offener Hörsaal" (Open Lecture Auditorium) student association helps refugees like Mehmet (35) to access university education. In Iran, Mehmet was well on his way to becoming a doctor but had to flee the country for political reasons six months before completing his medical studies. The "Offener Hörsaal" project enabled him to attend classes as an auditor and to complete a German course at the Language Center. He was accompanied by "buddies", volunteers studying the same combination of subjects.

When he came to the University of Basel, Mehmet discovered a love of chemistry, but had to overcome many obstacles before he could join a regular study program. He had to complete a *Matura* equivalence test because his Iranian educational qualifications were only partially recognized. He could not afford the expensive preparatory courses, so "Offener Hörsaal" put him in touch with student volunteers who helped him study for the test. Mehmet began his bachelor's program in chemistry in fall 2018.

Volunteers from "Offener Hörsaal" help introduce people to the University of Basel via the auditor program and to make contact with students. They also help them to register for study programs and find grants and scholarships. So far, almost 70 refugees have attended classes as auditors and taken part in German courses at the Language Center.

Yet, only seven students have entered a regular study program so far. The greatest obstacle is usually that non-Swiss educational qualifications are not recognized by the university. "Offener Hörsaal" also relies on financial support in its fight for equal opportunities. It hopes that donations from University of Basel alumni will enable even more refugees to join study programs in the future. ■

offener-hoersaal.ch

Letter from Washington, D.C.

An economist against inequality.

Pia Schneider has worked at the World Bank since 2004. For the last three years, she has held a position as lead economist for health issues. She graduated in economics from the University of Basel in 1993, and holds a PhD in health economics from the London School of Hygiene and Tropical Medicine.

I have spent the last 15 years working at the World Bank as an economist specializing in health matters. The core mission of the World Bank, which was established in 1944, is fighting poverty and inequality. Our goal for 2030 is to limit extreme poverty to three percent of the global population, and increase the prosperity of the world's poorest 40 percent. The World Bank supports developing and middle-income economies with low-interest loans and technical assistance. This gives me a privileged insight into the workings of health systems and the socio-economic, financial and political circumstances of different countries. As a result of our analyses and funding programs, we are in dialogue with governments and involved in their decision-making – a fascinating experience.

These days, I work mostly in eastern and southern Africa, the Gulf states and Europe. We recently carried out an analysis of the health systems of Namibia and Saudi Arabia. Governments generally take our work very seriously, and often incorporate our recommendations into their programs. According to the latest edition of the World Bank's "Human Capital Index", more than half of the world's children are unable to realize their full potential because governments are not investing enough in education and health. In Europe, I am leading a study on the migration of healthcare professionals from the western Balkans to the EU and Switzerland. The labor market in the health sector is a truly global one – in the Gulf states around 90 percent of doctors and nurses are recruited from abroad in the private sector.

I wanted to work in different countries after university, so my first job in 1994 was as a delegate at the ICRC, for which I spent six months in South Africa and six months in what was then Zaire. After a short project in Basel and an internship in the administrative department of a hospital in Portland (Oregon), I worked for an insurance company and a consulting firm in the US, where I was involved in designing a pilot health insurance scheme for impoverished Rwandans on behalf of the health ministry in Kigali.

In 2004, I applied for a position at the World Bank, and was hired as an economist in the Europe unit. At that time, the reforms in eastern Europe for new accession countries were a key issue, as was the economic crisis and the resulting fallout in 2008/09. I led two evaluations on this issue in the World Bank's Independent Evaluation Group: one on youth unemployment and another on health financing. My topmost priority is providing more people from low income groups with better access to high-quality medical care. That is why I do what I do. ■

International career: Dr. Pia Schneider supports governments in shaping their health systems. (Photo: Beth Payne)

Jan Pieter Abrahams has been a professor at the Biozentrum of the University of Basel since 2015, leading a research group that develops new approaches to high-resolution bioimaging. The group investigates the three-dimensional structure of proteins in order to gain a better understanding of their role and significance in biological processes.

Photo: Andreas Zimmermann

Jan Pieter Abrahams

The Magic Mountain, 4321, and *Game Changer.*

"Why am I here?" – "Because it was likely that I'd be here."

As an avid reader, I've chosen three books: Thomas Mann's *The Magic Mountain,* Paul Auster's *4 3 2 1* and *Game Changer* by Matthew Sadler and Natasha Regan. Together, these reflect my scientific understanding of life. I take the view that the functions of life, although they appear to follow a linear path, can only be understood as probability-weighted interference between all of the possible forks in the road. "Why am I here?" – "Because it was likely that I'd be here."

In *The Magic Mountain,* a young Hans Castorp ends up in a sanatorium after paying someone a visit, and appears to be suffering from tuberculosis. He stays until he decides he is cured – having matured into a thinking man after years of discussions with fellow patients. These often revolve around science: "What was life? It was ... a fever of matter, which accompanied the process of ceaseless decay and repair of protein molecules that were too impossibly ingenious in structure." These were incredibly astute observations given it would be some 35 years before the first protein structures were identified.

4 3 2 1 tells the story of four parallel lives that Archie Ferguson could have lived and whose individual courses are shaped by random events. In three of them, he dies prematurely in unusual circumstances. For me, this book is a reflection of quantum mechanics, which describes observed reality as the random breakdown of an evolving superposition of many branched states into one individual state – in contrast to Mann's linear plot line.

Game Changer is not a novel but rather a description of the computer program AlphaZero, which taught itself to play chess in the space of a few hours. The software would win every game against world champion Magnus Carlsen. Whereas other chess software calculates as many variations as possible in order to select the one with the best possible result, AlphaZero views a chess position as a huge collection of branched states. It selects the position that gives it the greatest potential to search for as many good follow-up moves as possible. Based on this strategy, AlphaFold recently outperformed other tools at predicting protein structures. This could probably also be used to explain the evolution of stable protein structures – such as Mann's "impossibly ingenious" protein molecules. ■

unibas.ch/aktuell

A selection of events. November–December 2019

November 11, 5–6:30 pm

Artificial Photosynthesis Mechanisms and Materials Optimization from First Principles

Dreyfus Lecture by Prof. Emily A. Carter, University of California, who discusses insights into (photo)electrocatalysis and the virtuous cycle of artificial photosynthesis to generate energy from sunlight, water, and carbon dioxide to synthesize the fuels for future generations. Carter is a theoretical and computational chemist whose work combines quantum mechanics, solid-state physics, and applied mathematics.

Department of Chemistry, Large Lecture Hall, St. Johanns-Ring 19, Basel

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November 18, 6:15–8 pm

"Creatures of Their Times": Time Life Books, Pictorial Excess, and the Power of the Series

Lecture by Vanessa Schwarz, University of Southern California, who sketches the history of the Time Life book series, arguing not only that magazines shaped photobooks but also specifically considers the question of "time management" in the Time Life series, asking how layout, narrative, and the sheer volume of images, often originally taken and used to represent the present, eventually became images of the past.

Old University, Rheinsprung 9, Basel

November 25, 6:15–8 pm

Presence & Absence. Photography and the Aesthetics of Historical Return and Disappearance

Lecture by Lorena Rizzo, University of Basel, who looks at late 19th and early 20th century Cape colonial prison photography. A special focus will be given to the problem of the ancestral, using the portraits of Kgosi Galeshewe, a late 19th century Bathlaping political leader and prisoner, to ask how photographs configure and mediate the presence and absence of the dead.

Old University, Rheinsprung 9, Basel

November 25, 6–8 pm

The Logistics City: Infrastructure, Circulation and the Making of Settler Colonial Jurisdiction

Lecture by Deborah Cowen, University of Toronto, who investigates the contested formation of cities and settler state jurisdiction in North America through imperial infrastructure. She explores how the making of 'national infrastructure' holds together seemingly disparate archives of Indigenous dispossession and genocide, of the transatlantic slave trade, and of unfree migrant racial labor regimes.

Kollegienhaus, Regenzzimmer 111, Petersplatz 1, Basel

December 5–6

Swiss TPH Winter Symposium 2019

The topic of this year's winter symposium is "Climate Change and Health: Risks, Adaptation, Resilience and Co-benefits". Climate change will affect global health in many different ways. Adaptation strategies will be sorely needed to prevent major negative health consequences. The symposium offers a rich and intellectually stimulating program of talks, discussions, and debates on cutting-edge research and case studies from various world regions.

swisstph.ch/events

Congress Center Basel, Messeplatz 21, Basel

December 10, 6–8 pm

Regionalism in the Rural and Remote

Mason White, University of Toronto, will consider rural and remote regions in the wake of urbanization. White will focus on Canada as a case study of conflict within various contemporary rural and remote conditions. From transformations of Inuit communities in the Arctic, to ghosts of former coastal villages in Newfoundland, to resources towns in the Northwest Territories.

Kollegienhaus, Mehrzweckraum 035, Petersplatz 1, Basel

December 4, 6:15–7:45 pm

Antimodern Receptivities. Refuting Capital´s Modernism

Lecture by Kerstin Stakemeier, Academy of Fine Arts Nuremburg, in collaboration with the Art History Department of the University of Basel and in context of the exhibition "Circular Flow".

Kunstmuseum Basel | Gegenwart, St. Alban-Rheinweg 60, Basel

December 11, 4–6 pm

Traveling Sounds: Lilian Alan and the Invention of Dub Poetry

Lecture by Sabine Kim, Mainz University, who discusses dub poetry as revolutionary sound that has traveled from Jamaica to the UK, the USA, and Canada. In her talk, Kim will focus on dub poet Lillian Allen, whose work tells us about entangled postcolonial histories and Canada's little-known role in economic imperialism in the Caribbean.

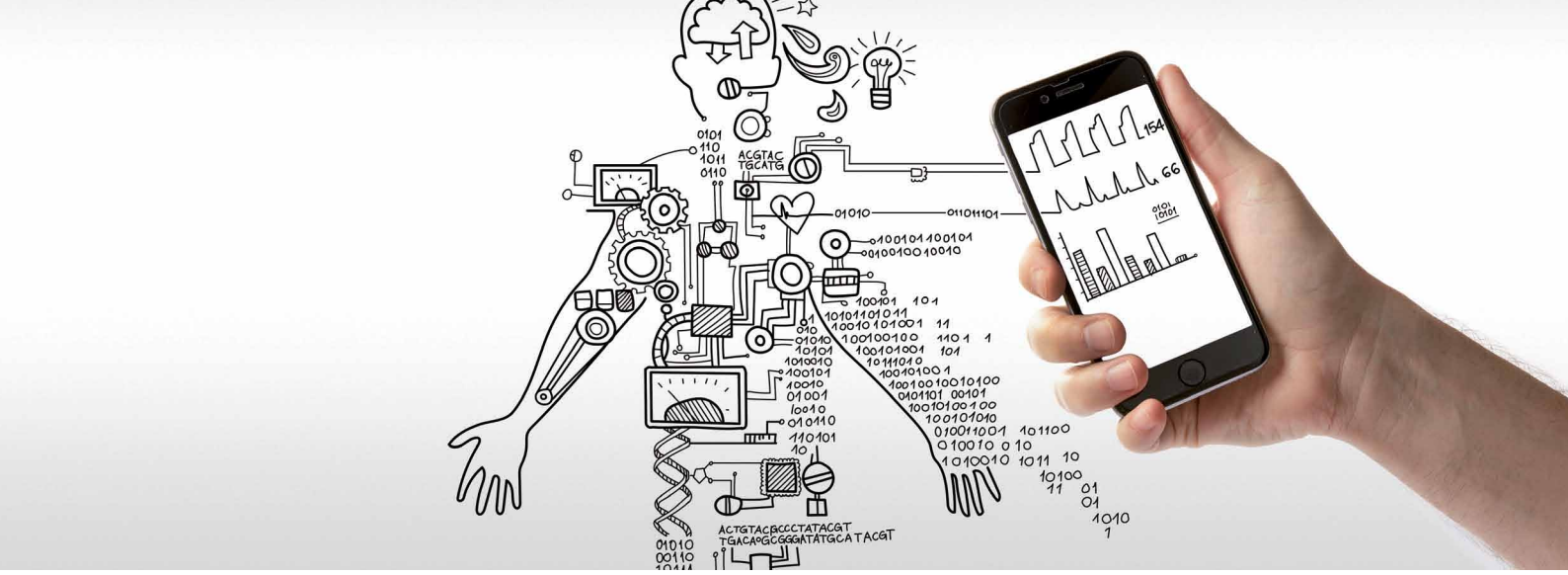
Vesalianum, Vesalgasse 1, Basel

December 18, 4–6 pm

Sounding Out the Modernist Short Story

Tom Vandevelde, Katholieke Universiteit Leuven, explores the peculiar intersection of sound, perspective, and the epiphany in modernist short fiction by Woolf, Joyce, and Sinclair, suggesting they may benefit from a "listening to", rather than a "looking at".

Vesalianum, Vesalgasse 1, Basel



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