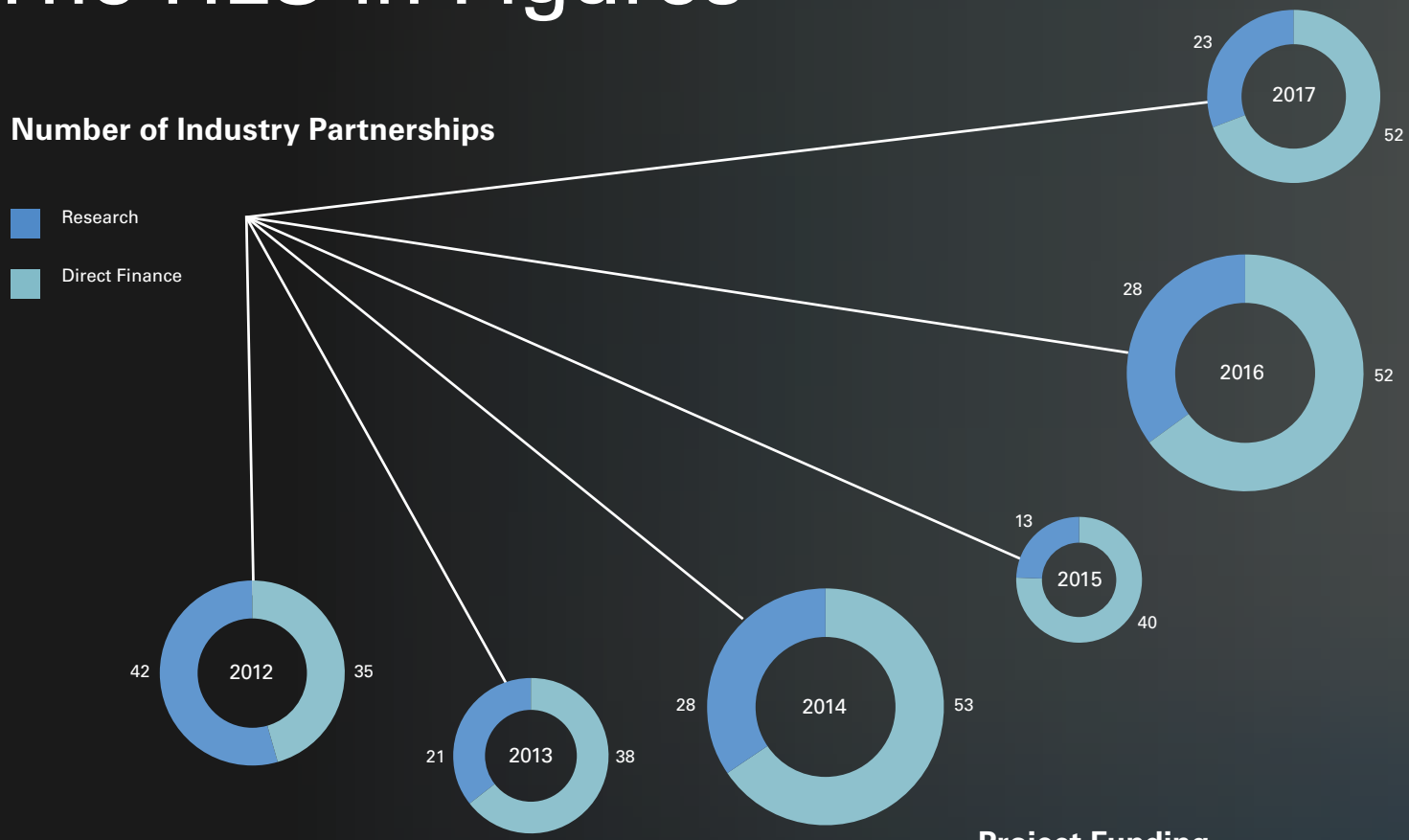
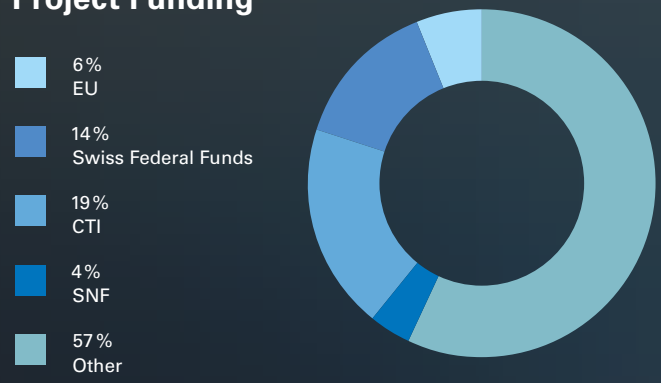
The HLS in Figures

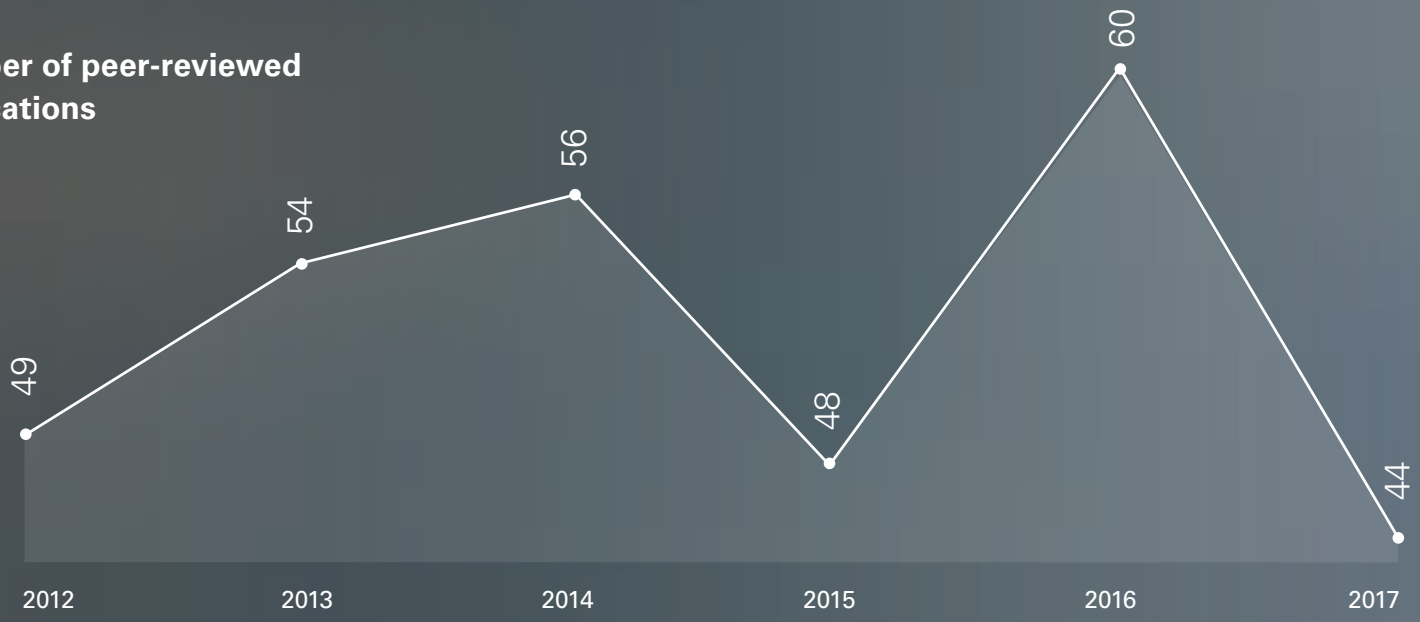
Number of Industry Partnerships



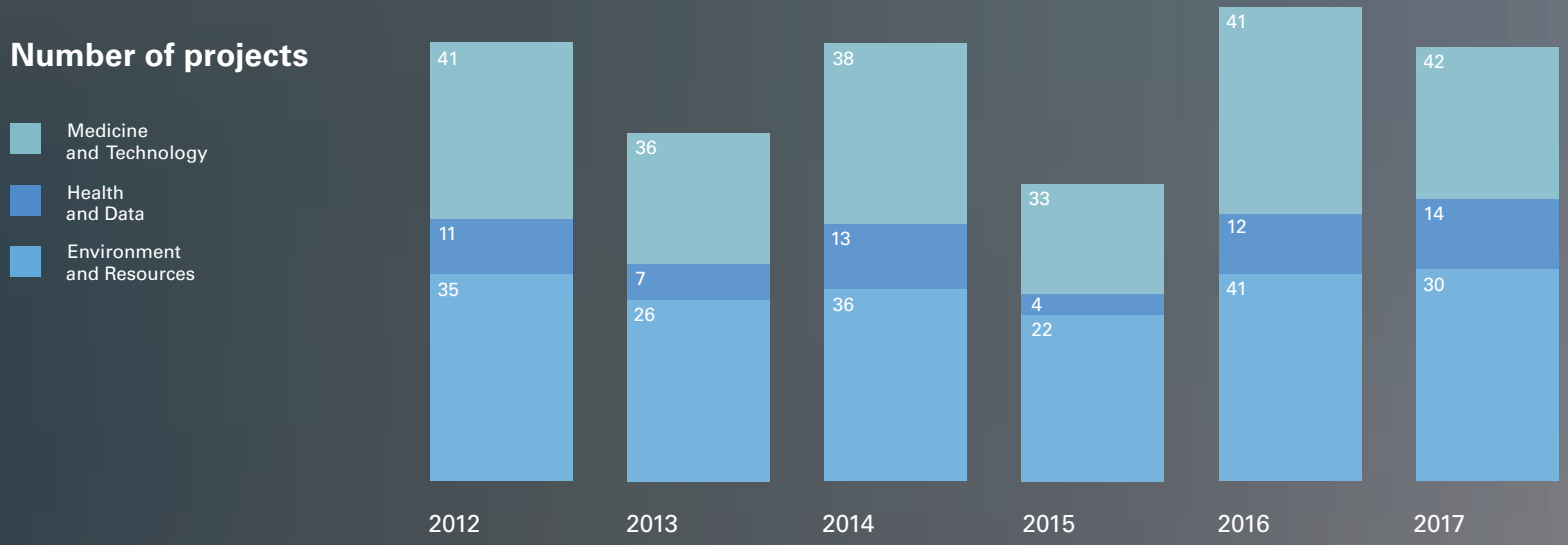
Project Funding



Number of peer-reviewed publications



Number of projects



A conversation with Falko Schlottig

Falko Schlottig has been Director of the FHNW School of Life Sciences (HLS) in Muttenz since 2015. From his appointment he faced a particularly interesting challenge: the new campus project. The two existing HLS sites, Basel and Muttenz, are being merged into a single new building in Muttenz. The new site, together with its strong network in the Life Sciences cluster in North-West Switzerland, will open new opportunities and perspectives for the HLS.

"We do application-oriented research, work closely with industry and can decide flexibly and quickly on technology transfer."

Falko Schlottig

Mr. Schlottig, you became director of the HLS a few years ago. What has impressed you since then?

At the HLS the staff are exceptional: highly qualified, committed and motivated. In terms of infrastructure, it is preparing for the move to the new campus, where we will be visible not only professionally but also literally, thanks to the imposing new building. We have the chance to organise the HLS around technologies, to practise Life Sciences in a focused, interdisciplinary way. In addition, we will have a completely new Process and Technology Centre, where we can map current and future processes in an industrial life science context.

How will working in the new campus building be different?

On one hand, we will be working on a wide range of new technological questions involving the specific skills of all our institutes. We also expect to be able to work more intensively with other FHNW faculties and to tackle common issues, such as our ageing society, together. In addition, we will have an infrastructure there that will enable us to become a meeting point for the surrounding community.

What makes the HLS attractive as a business partner?

We have staff with industrial and project experience, technology-specific as well as interdisciplinary expertise, state-of-the-art infrastructure, and rapid, flexible technology transfer.

What makes the HLS interesting for students?

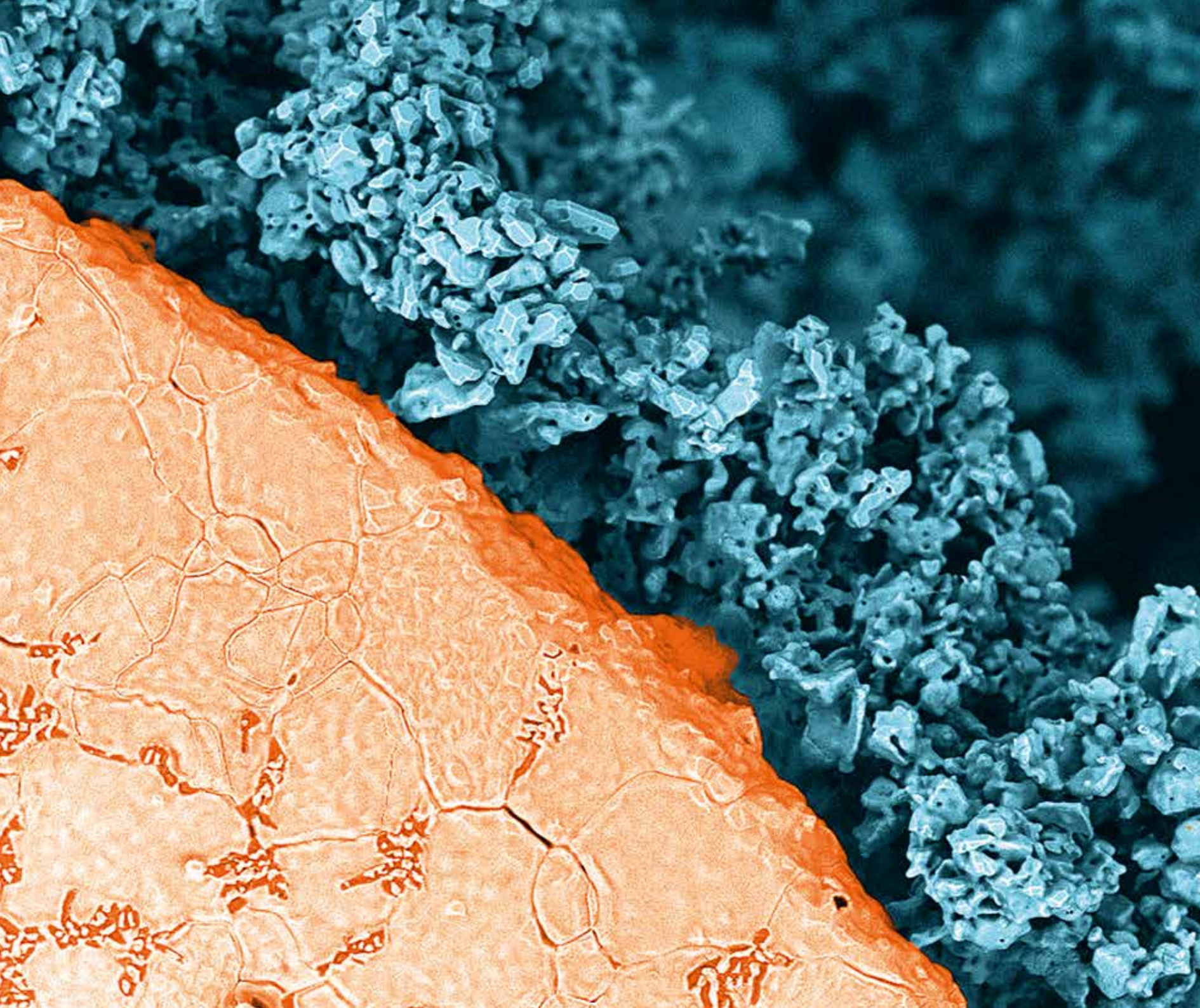
The HLS offers students a very practice-oriented education and we can use our contacts in industry for projects, degrees or postgraduate theses. 80% of bachelor's degrees and all our students' master's theses are carried out in industry. As a consequence our graduates are highly sought-after in industry.

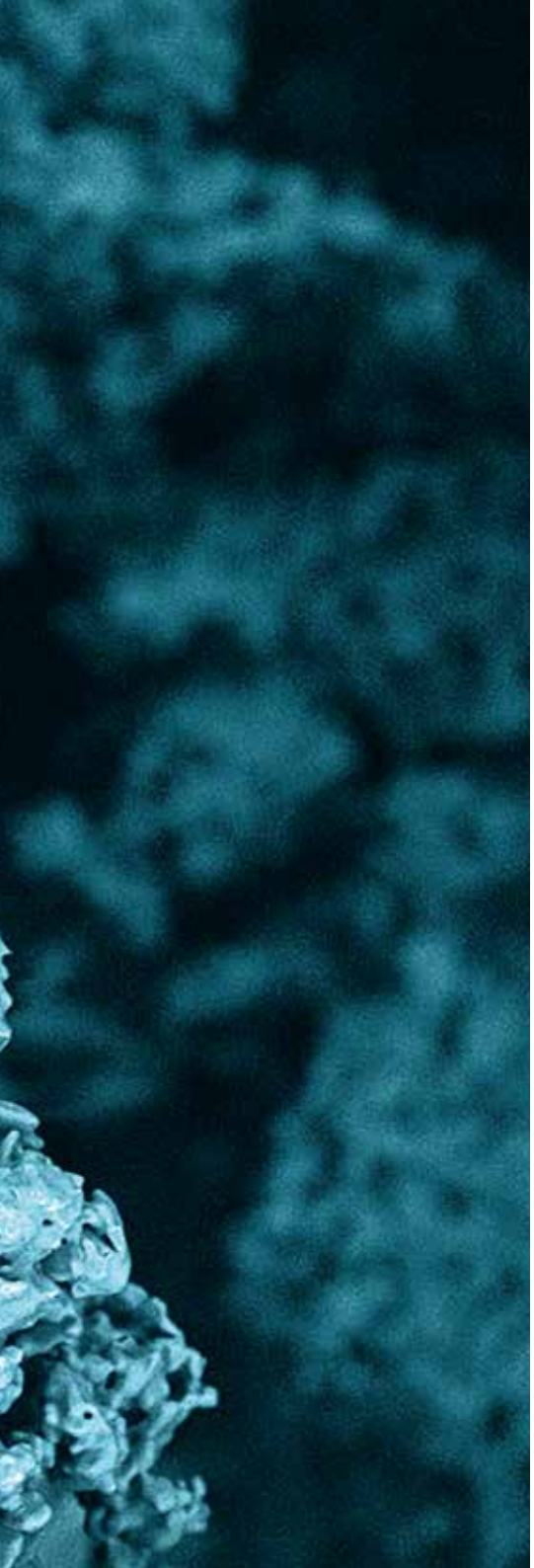
Why should researchers move to the HLS?
Scientists who are truly interested in seeing the results of their practice-oriented research in a product or in product development will find the perfect environment at the HLS.

How does the HLS work with its partners?
Collaboration is organised in different ways. One is direct projects; we are given a research assignment and we work closely with the firm in solving the problem. The second approach is projects with companies, supported by the CTI (the Swiss Commission for Technology and Innovation), to develop new technologies or products. A third possibility is to obtain finance from the various national and international funding boards, from the EU through the Swiss National Science Foundation, to research collaboration grants from foundations.

Will the HLS have an even more international outlook in future?
The FHNW is a locally-oriented institution with an international network and presence. Successful applied research cannot just be carried out locally. You have to see what is being done elsewhere and you need to operate in an international environment to develop in the long term. The overwhelming majority of firms with whom we work operate internationally. If we want to train our students well and if they want to work in a locally situated but internationally oriented organisation, we have to play our part. We are already doing this today by cooperating with several academic institutions in other countries and we want to increase this in the future.

Does knowledge transfer play a role at the HLS?
Knowledge transfer is essential for us. It has two sides: one is cooperation with companies. In order to be successful we must be able to act very quickly and flexibly. Because we are autonomous as a university, we can decide independently what is an advantage. The second aspect is start-up support: we are one of the leaders in this field in northwestern Switzerland and want to expand this culture further.





Medicine and Technology

In almost no other field are there currently such far-reaching changes as in healthcare: innovative measurement technology, mobile sensors, high-precision analytical devices and 3D printing techniques are transforming the healthcare system. Medicine can be customised and patients have more say in their treatment. Researchers at the HLS are therefore developing practical solutions for the digital age. With modern pharmaceutical technology they are driving the development of new drugs and applications.

A race against time

Whether or not a drug helps, depends on more than just its active ingredient. That ingredient first has to get to the place where it needs to work. However, the more targeted new drugs are, the larger and more complex the molecules which have to be developed. As a result, they are often poorly soluble and difficult to get from the gastrointestinal tract into the bloodstream. Therefore the HLS pharmacist Martin Kuentz is working on a reliable lipid-based system to transport poorly soluble drugs in dissolved form in the gastrointestinal tract.

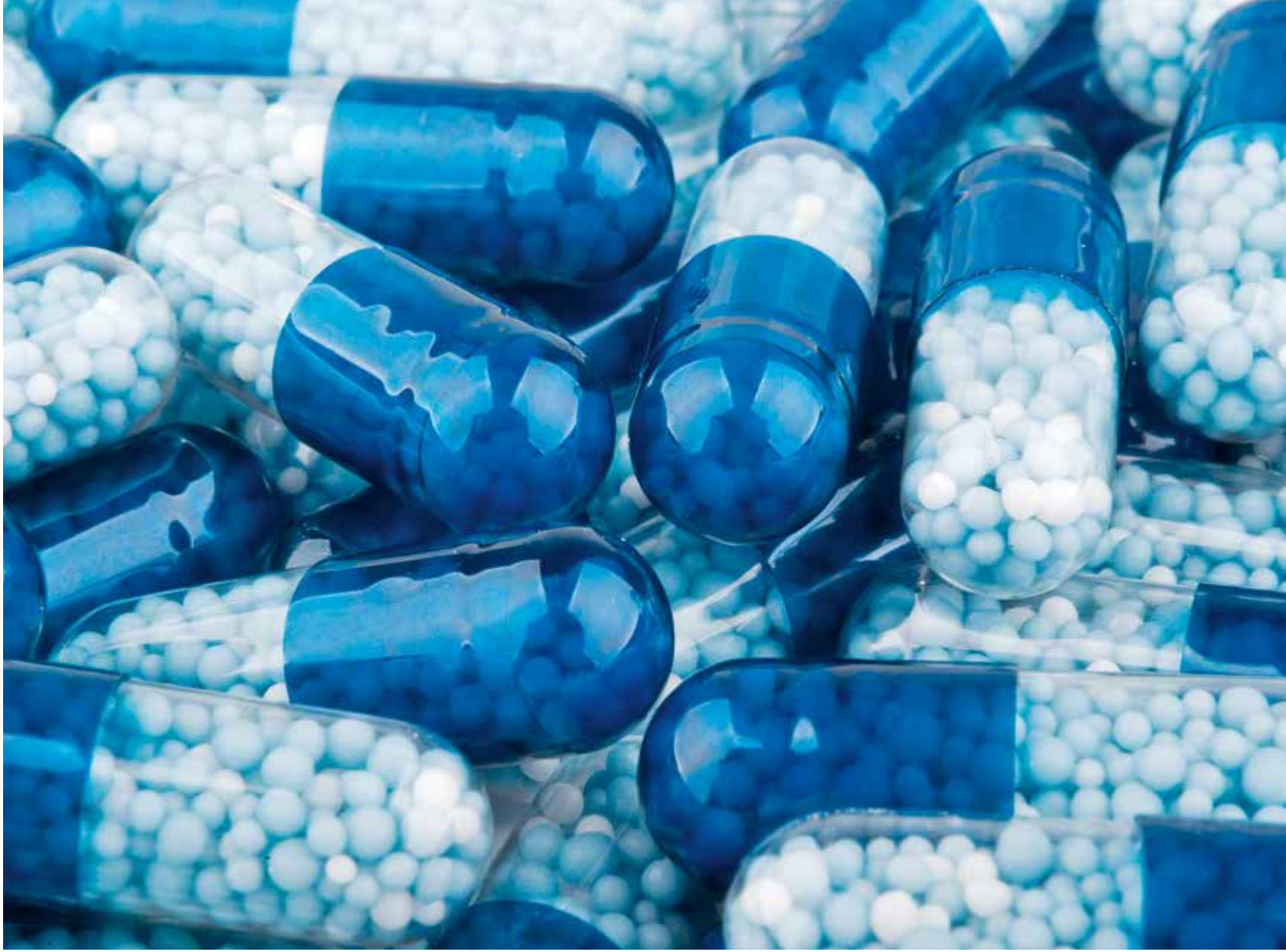
The human body only has about four hours to absorb nutrients, vitamins and drugs from the stomach and small intestine. After that, whatever we ingest reaches the large intestine, where very little is absorbed before being excreted. In order to get as much of the medicine as possible into the blood, active ingredients must be in a dissolved form. With water-soluble molecules such as sugar or vitamin C this is no problem as the body can easily absorb them. However many medicines are poorly soluble in water since they either crystallize or do not mix with water at all. Ibuprofen, an active ingredient in many painkillers, is one example. "Some substances are as poorly soluble as a stone" says Martin Kuentz of the Institute of Pharmaceutical Technology. "What is crystallized in the stomach or intestine is usually lost."

For the last ten years he has been developing new drug formulations at the HLS. Formulations in this case means how medicines are assembled: in addition to the drug itself, medicines contain other components which, for example, increase shelf life or suppress side effects. One of the most important jobs of these components is to ensure absorption of the active ingredient into the bloodstream.

In cooperation with the firm DSM, Kuentz and his research team have developed a new technology which effectively prevents crystallization of the active ingredient. "Designed Lipid Micro Domains" (DLM) absorb active substances like a sponge, except that they are only a few microns across. The micro domains stabilize the drug molecules by keeping them separate; if they get too close the substances crystallize because of their high affinity.

The DLM consist of several components, which are combined with the active substance by melt extrusion – a polymer technology process. The product of this method is a solid dispersion, i.e. a mixture of substances which normally do not bond. Polymers have traditionally been used as a dispersant to absorb the active ingredient. However, since

this can lead to the problem of active ingredient crystallization in the drug or later in the gastrointestinal tract, Kuentz and his team now use lipids and an inorganic substrate (aluminium-magnesium silicate) in addition to the polymers. The lipids usually absorb the active ingredient well but during melt extrusion they can also crystallize and thus no longer be used by the active ingredient. "To avoid this, we need the inorganic substrate. This interacts with the lipids to keep their long hydrocarbon chains apart," explains Kuentz. "Since the active ingredient is highly liposoluble, after heating and intensive mixing during melt extrusion its droplets easily make their way into the spaces between the lipid chains." The researchers used a range of analytical methods to establish how well these mechanisms actually work. In addition to spectroscopic techniques such as nuclear resonance



spectrometry and infrared spectroscopy to investigate organic components, they also worked with imaging techniques. They wanted to see whether and to what extent crystalline areas were present in DLM. “The answer to this question lies in a combination of highly specific methods,” says Kuentz. The most important of these is atomic force microscopy (AFM), in which a tiny leaf spring tip scans the sample nanometre by nanometre. The deflection of the spring shows the surface texture of the sample.

"Our aim is to use biotechnology and modern formulation techniques to make pharmaceuticals more readily available to the body; this will create substantial pharmaceutical value."

Martin Kuentz

The hardness of the material can be determined by penetrating the sample with the scanning tip. This is called phase contrast, since the crystalline phases are generally harder than the non-crystalline ones and produce a contrast in the image. However only in combination with other analytical methods such as conventional scanning electron microscopy is it possible to determine whether hard areas in the sample are actually crystalline. Kuentz and his team analysed the chemical composition of the micro domains, using a scanning electron microscope and X-ray diffraction. After the melt extrusion, the active substance is present in the DLM as an amorphous material, i.e. in a solid but not crystalline form. In modern pharmaceutical technology this form has proved to be the best at enabling the absorption of drugs with water-insoluble active substances into the bloodstream via the gastrointestinal tract. "Apart from the fact that the DLM ensure a long enough shelf life of the active ingredients, they remain highly stable as an aqueous dispersion under natural conditions in the stomach and intestine" explains Kuentz. Thus the body can absorb the amorphous active ingredients from the DLM before they are excreted. For Kuentz, the challenge of active substance absorption in the gastrointestinal tract has been achieved: "Once it is absorbed, we have fulfilled our pharmaceutical and technological mission."

Kuentz is clear about the potential of DLM "The drug delivery system we developed is designed for small doses of highly potent drugs but it can also be used for other substances that have a tendency to crystallize". For example he and his team carried out DLM tests on very poorly water-soluble beta carotene, a precursor of vitamin A. Their success in these experiments show that the new technology is not limited to medical applications; dietary supplements could also benefit from it in the future.

Methods
- "Solid dispersion" technology and lipid-based systems

Infrastructure
- Pharmaceutical extruder ("Hot Melt Extrusion")
- "Time Domain" Nuclear Magnetic Resonance Spectroscopy (TD-NMR)

Support
- Industry

Animal experimentation: 3D for 3R

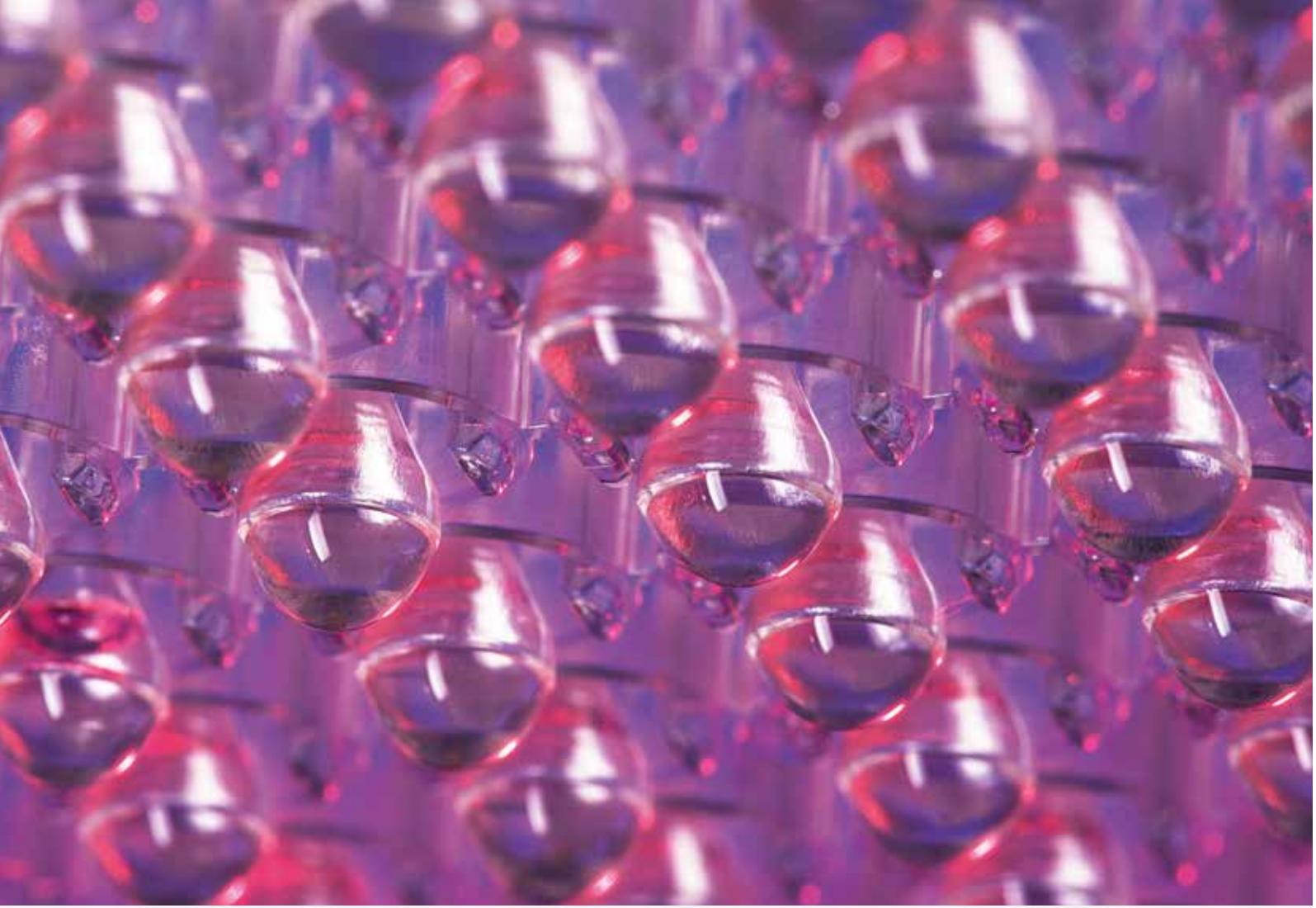
More than 600,000 animals a year are used in experiments in Switzerland alone. Despite tougher animal protection regulations, the number remains high due to ever stricter patient protection requirements: the safety of new drugs must first be proven in animal tests. In order to reduce the number of animal experiments, HLS researchers are working on alternatives such as cellular 3D test systems designed to emulate organs and their function. The HLS team have now established the efficacy of their tests for kidney cells and for disease-altered liver tissue.

A cell is clearly very different from a whole organ. However cell cultures can be used as models for research into cell division, metabolic processes or signal transmission, as well as for testing the effects and risks of new drugs. However, conventional cell cultures are less efficient at showing the influence of structures and environmental interaction. Hence the need for animal experiments. Or perhaps not. According to toxicologist Laura Suter-Dick from the Institute of Chemistry and Bioanalytics, a large number of animal experiments may soon be redundant, replaced by growing tube-shaped 3D kidney cells which imitate the structure of a real kidney.

"If you can already see in an organ-like cell culture that an active substance damages the cells, you do not need an animal experiment anymore," Suter-Dick says. That goal is reached using organoPlateTM cell culture plates to replicate the tiny tubes in the kidney: a gel is introduced along several small parallel channels on the cell culture plate, forming guide tubes on the inner walls of which kidney cells are grown. "This new biochip technology has enabled us to create kidney cells in the form of small tubes, like in a real, healthy kidney, which we can use for tests" says Suter-Dick.

The kidney has an important detoxification function in the body, filtering harmful substances and blood metabolism end products and transferring them to the urine. Due to this filter function, the kidney is heavily exposed to the degradation products of drugs which can permanently damage the small tubes in the kidney. Hence why pharmaceutical companies must test every new drug for its effect on the kidneys and their filter function. Suter-Dick: "There are still areas in toxicology or in pharmacology where animal experiments have to be done however. They cannot be replaced because the regulatory authorities put patient safety first."

Suter-Dick bases her research on the 3R principle: replace, reduce and refine. The aim of this 1959 guideline is the responsible treatment of lab



animals as well as the reduction and replacement of animal experiments. Although animal experiments are subject to very strict regulations in Switzerland and are only approved after examination by cantonal animal experiment commissions, they remain ethically controversial. A majority of the animals are used to investigate the toxicity of new active ingredients in healthy organisms, as required by law before it allows the use of a new drug in humans. About 2% of drugs at the pre-clinical stage and 19% of those in a Phase III trial never get to the market because they cause kidney damage. Failure at such a late development stage means not only a high cost to the pharmaceutical companies but also a senseless use of test animals during the drug development phase. Since most drug-induced kidney damage affects the proximal tubules, Suter-Dick is focusing on these complex structures: “The proximal renal tubule cannot be mimicked in normal cell cultures as it consists of several cell types that form a

tubular structure and perform different tasks". Normal kidney cells have a transport function that allows them to import or export drugs and other substances. Many conventional cell cultures cannot emulate this transport function and can thus seldom be used to test for renal toxicity, leaving no alternative to healthy test animals.

Suter-Dick's work, in collaboration with two research partners from the Netherlands (Radboud University and Mimetas), is funded by the British National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs). Together they have investigated the transport and barrier functions of kidney cells using 3D techniques. Damage to renal cells from substances such as immunosuppressive agent cyclosporin A or virostatic agent tenofovir can be demonstrated by elevated biomarkers in patients' blood or urine. The same biomarkers, usually monitored in the lab, have been tested by Suter-Dick in 3D cell cultures, showing their efficacy with a high throughput system which can test many substances in parallel, saving both time and money.

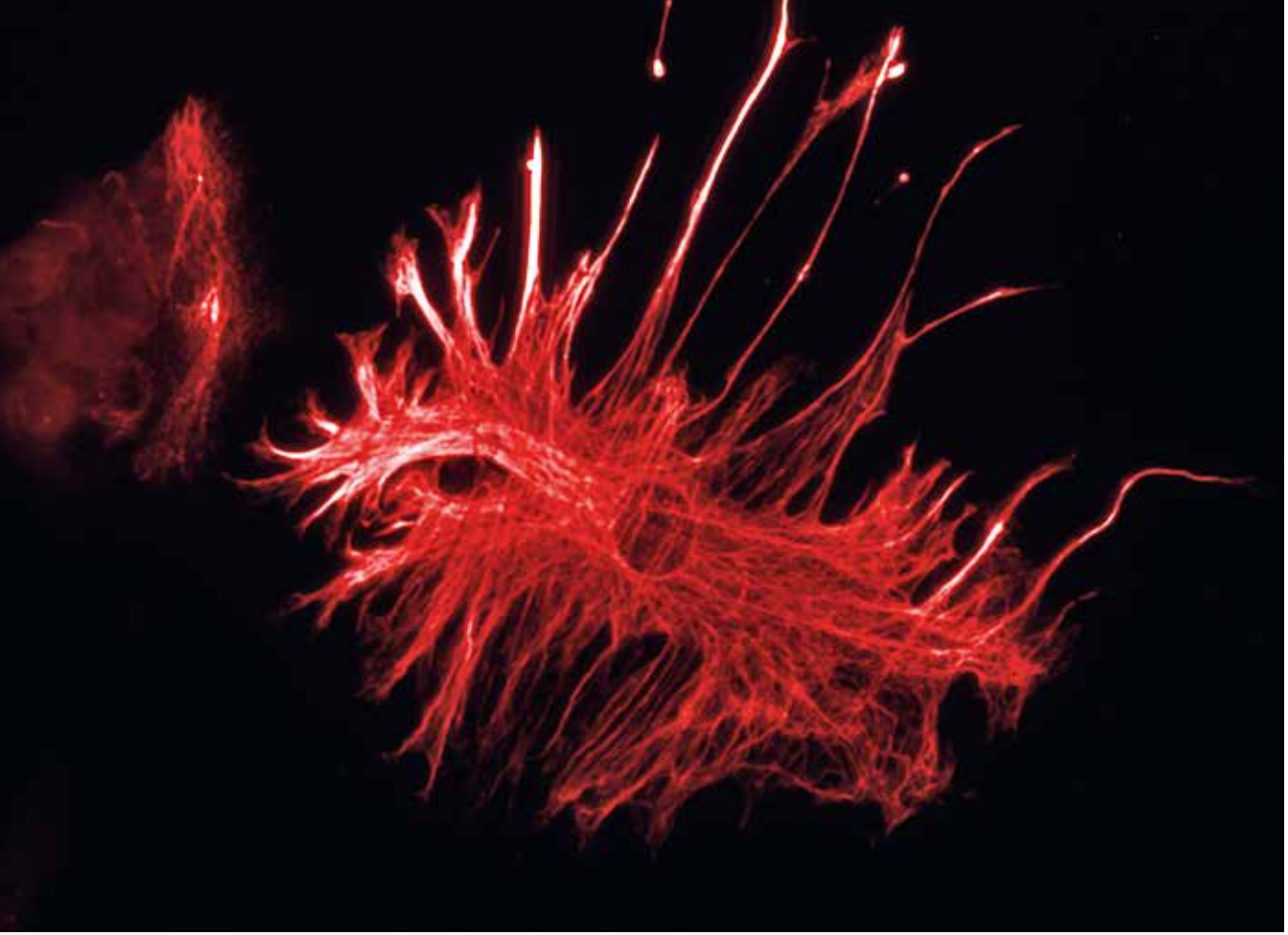
"If an organ-like cell culture already shows that an active ingredient damages the cells, you no longer need an animal experiment."

Laura Suter-Dick

In another project, rather than a healthy, normal cell system the toxicologist has developed a liver disease model in the petri dish. The aim is to avoid rats and mice being exposed to a particularly hard group of experiments: they are bred as mutants with specific diseases or the disease is chemically induced to obtain very accurate understanding of clinically relevant diseases. Such "models" are necessary to see the effect of new drugs on the exact symptoms for which they have been developed. However, since many metabolic processes work differently in animals from humans, the significance of those experiments can be limited. There is still no effective animal model that realistically replicates common liver fibrosis — a late stage of chronic liver disease. Despite that, thousands of rats and mice used as test animals for liver fibrosis suffer every year.

These animal experiments last a long time and add significantly to the pharmaceutical companies' high costs of developing new active ingredients. The firms are thus stepping up the search for alternative ways to test liver fibrosis drugs in vitro. Cell culture experiments make it relatively easy to work with human tissue, increasing the relevance of the findings for patients. However, normal cell cultures cannot emulate the disease pattern of liver fibrosis, since it produces three types of cells which must be activated one after the other in order to form its fibrous scar-like tissue. A further complication is that liver fibrosis can only be induced by the constant effect of a harmful substance, which takes more than two weeks in the laboratory.

In a CTI project, Suter-Dick in collaboration with the Swiss company InSphero, has developed a 0.3mm diameter spherical cell culture model which contains all three cell types needed for the formation of liver fibrosis. "The hardest thing was to activate and combine the different cell types so that they function together correctly," the scientist says. Her experiments have provided the first evidence that the 3D liver fibrosis model works and can be used by firms and other researchers. The next step will show whether it is possible to prevent the activation of the liver cells and therefore to develop potential remedies for fibrosis.



Methods
Cell cultures with primary cells and cell lines, organ-on-a-chip technology, microfluid systems, InSphero hanging drop technology, viability assays, Impedance measurements, gene expression analysis, cell staining (histology), immunofluorescence, confocal microscopy

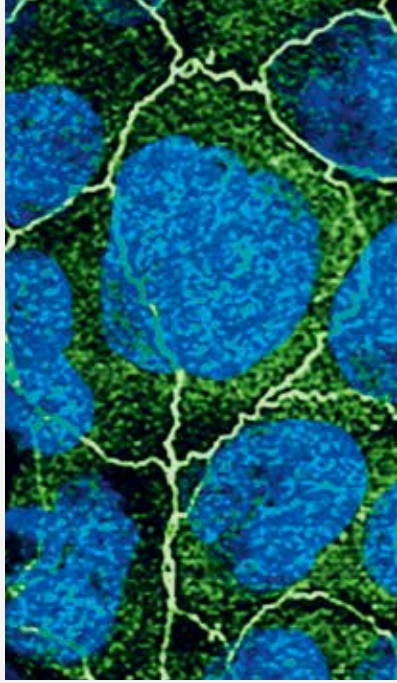
Infrastructure
- Cell culture accessories, including microfluidic systems (U-cup, Minucells, own apparatus) and bioprinting
- 3D-cultures: organoplates (mimetas), micro-tissue (InSphero), Transwell systems, microencapsulated alginate spheres
- Analytical methods: western blot, ELISA, receptor interaction (Flex station), qPCR (Corbett rotor)
- Functional tests: cell respiration (seahorse) and cell growth (xCelligence) microscopy, including confocal microscopes

Support
NC3Rs, CTI

Collaboration
Mimetas B.V. Leiden, Netherlands
Radboud University, Netherlands
InSphero AG Schlieren
SCAHT Basel

Beer: good health!

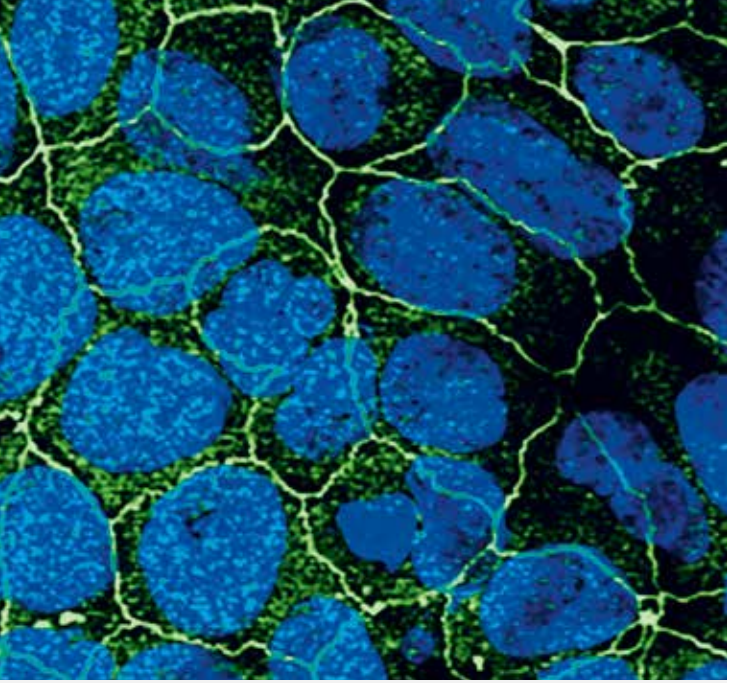
Beer is one of our most important drinks, both economically and culturally: the Swiss drank over 460 million litres of beer in 2015. It isn't often said that beer is good for you but the hops which give beer its distinctive taste have a positive effect on health. Researchers at the HLS have discovered that prenyl flavonoids in hops stabilize the gut wall and can counteract some illnesses.



Almost no other organ in the human body carries out so many different tasks simultaneously as the intestine: as well as digesting food and absorbing nutrients, the intestine regulates the water balance in the body and makes hormones and neurotransmitters. However it also has a fundamental protective function: the intestinal barrier stops the toxins and bacteria we consume from entering the bloodstream. This protection is compromised by diseases such as Crohn's disease or food intolerances. "If there's a malfunction in the intestinal barrier, the so-called Leaky Gut Syndrome, the tight junctions are impaired. These are membrane proteins that hold cells in the intestinal mucosa together. In a healthy body, they prevent potentially harmful substances from entering the blood stream" explains Veronika Butterweck from the Institute for Pharmaceutical Technology at the HLS.

Working with German researchers, she has demonstrated that certain ingredients in hops improve the stability of the intestinal barrier. The impetus for the research came from an Austrian research partner, the Paracelsus Medical University in Salzburg. Scientists there have proven that there are substances in hops which stimulate growth in certain damaged nerve cells. These substances are called prenyl flavonoids, also known for their oestrogenic, antioxidant, anti-cancer and anti-inflammatory properties. "For the first time, we have shown that certain prenyl flavonoids have a protective and even a regenerative effect on the tight junctions in the intestinal wall" Butterweck says.

Butterweck's team first developed a cell culture model from cancerous colon cells, so-called "Caco-2" cells. She says of the advantages of this experiment: "We sowed the cells on a porous membrane and surrounded them with medium. The resulting dense cell layer enabled us to access intestinal cells from the outside, which is not possible in a real intestine." To monitor the tight junctions, the researchers measured the electrical resistance between membranes of adjoining cells using electrodes on the inner and outer sides of the intestinal cells. "The tighter these tight junctions are, the higher the resistance," says Butterweck. "We compromised the cells with the TNF-α inflammatory marker at the



points which are damaged by inflammatory diseases such as Crohn's disease. The TNF-α loosens these tight junctions and the resistance falls."

In order to look into the influence of hops on tight junctions in the intestinal wall, the researchers tested four different prenyl flavonoids. To demonstrate the repair effect, they treated the Caco-2 model with TNF-α for 24 hours. As Butterweck expected, resistance across the intestinal mucosa cells decreased. The cells were then treated with the hop components for 72 hours. "One of the substances, 8-prenylnaringenin, significantly increased the resistance between the electrodes," says Butterweck. "The tight junctions became denser and regenerated."

Butterweck demonstrated the preventative effect not only for 8-prenylnaringenin but also for the structurally similar 6-prenylnaringenin. After pre-treating cells with the prenyl flavonoids for one hour, adding TNF-α had a much smaller effect on them: resistance between the electrodes decreased by significantly less.

"Now we want to find out what mechanism causes this and whether a natural hop extract has a similar effect," says Butterweck. Prenyl flavonoid content varies considerably between beer types. Dark American ale, porter and British stout contain significantly more prenyl naringenins than lager or wheat beer for example.

For Butterweck, such research projects are relevant to real life: "The concept of healthy ingredients is already established with probiotics, which contain bacteria that produce low molecular weight substances to seal tight junctions. A health drink could be developed which is enriched with these prenyl flavonoids." The current booming beer market could benefit from this research: a 'healthy' reputation would do the traditional beverage no harm at all.

Methods
- Cell culture (Caco-2 cells)
- TEER value online calculation
- Immuno-histological staining and evaluation using fluorescence microscopy

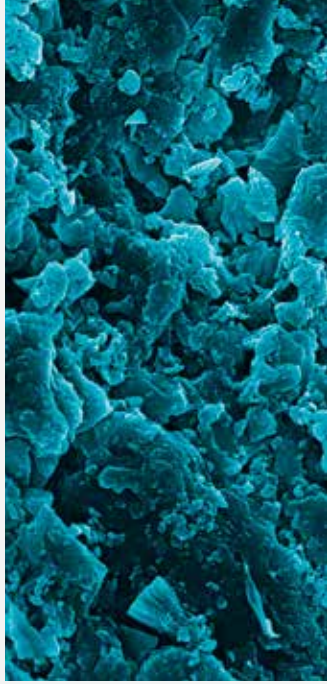
Infrastructure
- CellZscope (online monitoring of the TEER value possible)
- Fluorescence microscopy (live cell imaging and confocal microscopy)

Support

HLS research fees

Collaboration
- Weihenstephan Straubing Science Centre / Germany
- Paracelsus Medical University, Salzburg / Austria

Nanotechnology in cleanrooms



Medicines must be produced in sterile conditions. Industry and research organisations use hydrogen peroxide for disinfection and sterilization but the extremely reactive oxidizing agent must not come into contact with humans, reagents and products. Therefore researchers at the Institute of Chemistry and Bioanalytics working with Skan AG have developed a catalyst system to break down hydrogen peroxide more efficiently. The nanotechnology-based manufacturing process is simple and scalable.

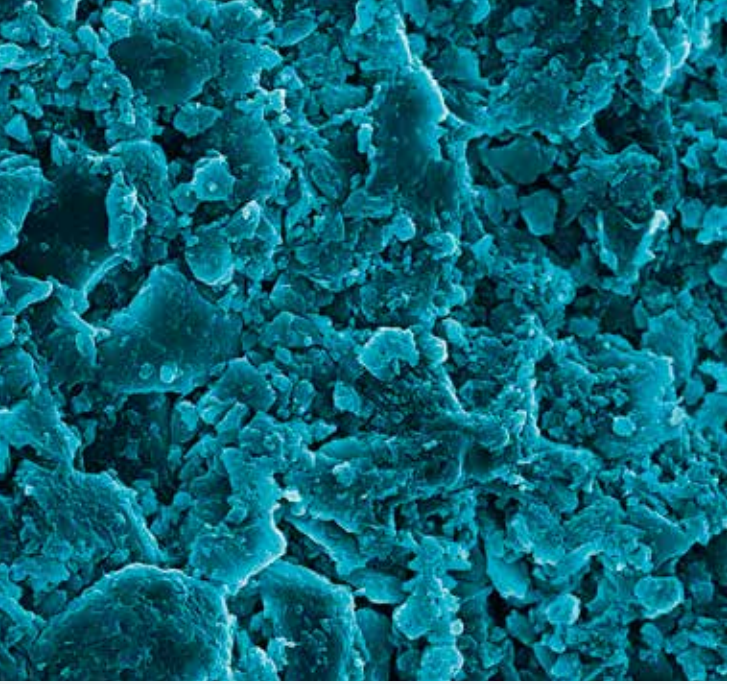
«Within four years, we were able to put an energy efficient solution onto the market which is substantially cheaper than previous processes.»

Uwe Pieles

In the pharmaceutical industry, product purity is everything. To ensure this quality, strict conditions must be met during production, packaging and analysis; micro-organisms and germs must not come into contact with pharmaceutical products. In cleanroom environments therefore, both industry and research use so-called containments: isolators and workbenches, separated from the ambient air by filter systems which can be decontaminated automatically. For their disinfection and sterilization, pharmacists and food technicians use evaporated hydrogen peroxide. The H_2O_2 molecule is a very reactive oxidant due to an oxygen-oxygen single bond; it reliably destroys bacteria and other microorganisms. There is a catch though: hydrogen peroxide reacts just as quickly with other organic substances, including active ingredients in medicines. To avoid this, an insulator must not contain any hydrogen peroxide when in use.

The traditional method of removing hydrogen peroxide from the isolator is by ventilation with large quantities of sterile air. In order not to simply discharge this air and hydrogen peroxide mix into the environment, it is circulated in a closed system through a catalyst which converts the remaining hydrogen peroxide into harmless water and oxygen. However, conventional catalysts do not work efficiently unless the air is warm and a powerful fan is needed to overcome the high pressure differential of about 1100 Pascals and penetrate the catalyst. These temperature and pressure criteria increase energy consumption and therefore costs.

In order to reduce air volume, energy costs and time, a team of researchers led by Uwe Pieles at the Institute of Chemistry and Bioanalytics (ICB), in collaboration with the market leader in insulators, Skan AG, have developed a more effective technology. In a project funded by the Swiss Nanoscience Institute and the Commission for



Technology and Innovation, the new process could be on the market within four years.

Pieles and his team have succeeded by using nanotechnology. Instead of applying the catalyst on a solid support material as before, the researchers coated porous ceramic spheres with a layer of metallic nanoparticles and the catalyst. The porosity of the carrier material creates an enormous surface area and thus much more capacity for catalysis. For example, a 50 x 50 cm module with the new technology achieves a surface area of about one hundred soccer fields. "The layer can only be a few nanometers thick, otherwise the pores would become clogged. However, it cannot be too thin, or sufficient catalysis does not take place" explains the director of the ICB, Gerhard Grundler. The exhaust air penetrates from the insulator into the pores; the large surface area guarantees a high hydrogen peroxide decomposition rate.

In order to find the right catalyst, researchers analysed and tested various materials using computer simulations. During simulated ageing experiments for example, the research team found a metal compound that can be used for more than ten years. "A good catalyst does not wear out with time because it is not involved in the reaction but only mediates between the reagent and the product," says Grundler. In addition to the search for the right catalyst, the HLS researchers also solved the problem of packing the material as closely as possible into a catalyst module. As a result, they were able to reduce the pressure at which the exhaust air is forced through the catalyst by 80%

Finding the right combination of catalyst, carrier material and packing density makes the higher efficiency possible. Grundler explains: "The highly efficient catalyst allows us to circulate the air: we extract the air from the isolator and after catalysis it is sent back. The heat thus remains in the building and is not wasted." This makes the catalyst process independent of a complex ventilation system and the insulator can be used much more flexibly.

Methods
- Proof of concept studies

Infrastructure
- FHNW analytical equipment and chemical laboratories
- SKAN isolator systems and catalyst test system
- SKAN catalyst production

Support
- CTI, SNI

Collaboration
- SKAN AG
- University of Basel ("Swiss Nanoscience Institute")

3D printed implants

The 3D printer is a catalyst for industry 4.0. Researchers at the Institute of Medical and Analytical Technology are demonstrating that it is also opening up entirely new directions for implantology. They are developing the complete process chain, from implant design, to manufacturing, to quality management of 3D printed implants. The research groups are testing the potential of a wide range of materials and developing new production techniques; their vision is that in the not too distant future doctors will design implants in the hospital.

"Wherever patient-specific bony structures are involved, physicians will be able to use 3D-printed implants in the future, and in some cases they are already doing so."

Erik Schkommodau

3D printers are revolutionising production technology. They enable the large-scale production of objects with significantly more complex three-dimensional structures than is possible with conventional production methods. At the HLS, Erik Schkommodau and Ralf Schumacher are making sure that medical technology also benefits from these advances. For them, the advantages of 3D printing for implantology are clear. Schkommodau, the head of the Institute for Medical and Analytical Technology, explains: "In future, and in some cases already today, doctors can create 3D-printed implants for patient-specific bony structures, for example in the face. We have been working on this technology for about 15 years. Ralf Schumacher, who heads the HLS spin-off Mimedis in addition to his teaching and research activities in the field of 3D printing and medicine, has a clear vision: "We want to develop 3D printing systems which doctors can use to design implants themselves in the clinic." To this end the two researchers are developing complete processes, from the implant design software, through to production and quality management. This vital work goes hand in hand with their research into new materials for the next generation of implants.

Applications in the human body place high demands on materials: they must not be toxic or otherwise harmful, they need to be very strong where necessary and in some cases should also interact with the body, e.g. dissolve over time or allow bone cells to grow through them. To meet these requirements, HLS researchers are working with both metals and ceramic materials.

Titanium and its alloys have been the state of the art in implantology for many years. Over the last three years the Institute has established a quality management system for the manufacture of implants using 3D printers, according to EU guidelines. External medical technology firms can thus outsource implant production to the HLS and audit

them as a supplier. The HLS laboratories can provide these firms with special implants and help to cure patients with complex bone defects.

One printing process for metallic implants is Selective Laser Melting. The printer holds a layer of metal powder a few microns thick, which is melted by a laser at predetermined points. "In this way, the bone structure, its pores and hence its biomechanical properties can be replicated very precisely. It is also possible to give an implant different elastic properties" explains Schumacher. "Artificial joint sockets can be modelled in such a way that they are dense near the joint gap and open-pore near the bone. Bone cells can then grow through the pores, strengthening the anchoring of the implant."

In addition to traditional implant materials, the scientists are researching NiTinol, an alloy containing nickel. Not only is it more flexible than conventional titanium alloys, it also has good mechanical damping properties and has form memory. The HLS researchers have even succeeded in maintaining this form memory at body temperature: 3D printed NiTinol forms can be changed at low temperatures so that they can easily be introduced into the body; they then resume their original shape when heated in the body.

Ceramic implants that break down in the body are also being investigated. However, they are not bonded with a laser but rather with a chemical binding agent which is applied by a print head to the powder layer. The ceramics used, hydroxylapatite and tricalcium phosphate, make up the bulk of the extracellular matrix of the bone and give it its strength. However, bone also contains biopolymers such as collagen which give it flexibility. These are difficult to add to the artificial production process, since the ceramics are brittle after printing and being baked in an oven at 1200 to 1400 degrees Celsius. Working with the Paul Scherrer Institute, the researchers are taking a different approach, using crystalline nanoparticles instead of biopolymers; the print head applies these nanoparticles with the binder. First results have shown a very promising stabilization of the implants.

With all the different materials and the need to establish quality management systems for them, the HLS researchers are taking ambitious steps into the future: "Standard printers are rather limited and we do not have the range of possibilities we need. Therefore we are now developing our own printers."

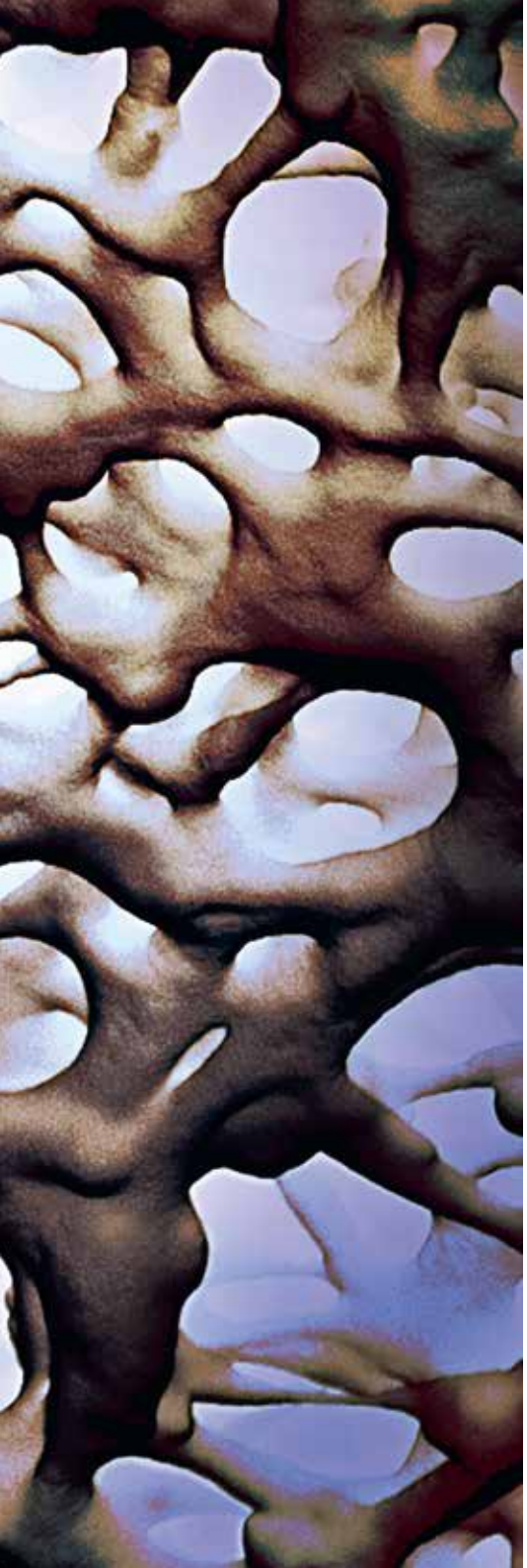
Methods
- Computer Aided Design (CAD)
- Free-form surface modelling
- Material and process development for 3D printing
- Antibacterial tests
- Electrochemical surface treatment

Infrastructure
- 3D printing technologies: MultiJet Printing for Plastics, Selective Laser Melting for Metals, Binder-in-Bed Printing for Bioceramics, Fused Deposit Modelling, Bio-Plotter
- Metallographic laboratory (SEM, EDX, µ-CT, confocal microscopy)
- Mechanical test laboratory (tribology, hydropulser, tracking, optical 3D scanner)
- Plasma cleaner
- Dynamic differential calorimetry

Support

EU, SNSF, CTI, FHNW Foundation

Collaboration
- University Hospital of Basel
- Cantonal Hospital of Basel-Land
- Cantonal Hospital of Aarau
- Cantonal Hospital of Baden
- Paul Scherrer Institute
- University Hospital Cluj-Napoca, Romania
- Industry



Environment and Resources

In Switzerland, natural resource management is critical due to the lack of raw materials, necessitating a sustainable approach to the environment. In a key HLS research area, researchers are therefore developing environmentally friendly production technologies as well as new methods for waste decontamination, processing and regeneration. They are analysing the effects of chemicals on microorganisms and their human and environmental consequences.

Using bacteria against crude oil spills

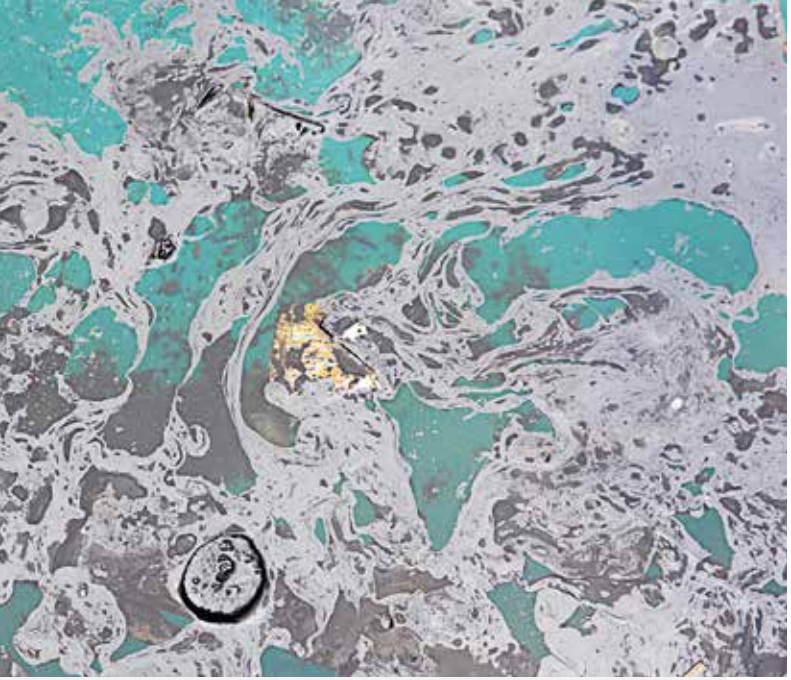
Crude oil spills are one of the greatest risks to the industrialised world. Oil spills in the sea are not only difficult to contain but also highly resistant to natural decomposition. HLS researchers have taken up the fight. As part of the EU Kill Spill project, they are working with more than 30 partners from science and industry, developing biotechnology techniques to clean up oil-polluted waters.

The EU Kill Spill project is an international network of research organisations and businesses which is playing a key role in dealing with crude oil catastrophes. This includes developing new technologies to solve several problems at once: the first aim is to contain oil spills more effectively or spread them more thinly, thereby aiding breakdown. Secondly, the breakdown process itself will be improved. Finally, the group are developing new environmental decontamination methods.

Given that the project is based on the self-cleaning abilities of the sea, researchers are concentrating on biotechnology solutions. Ocean microorganisms, especially bacteria, can break down tar and long-chain hydrocarbons from crude oil. This is the focus of the HLS team led by Philippe Corvini at the Institute for Ecopreneurship, and Patrick Shahgaldian and his colleagues at the Institute of Chemistry and Bioanalytics. The team are developing porous silica particles (SiO_2) that provide bacteria with the additional nutrients they need to break down the oil. Up to now microorganisms have taken too long to do this and were therefore unsuitable for targeted cleaning of contaminated waters; mechanical methods such as floating booms were used. However, since these cannot absorb small quantities of oil, a thin film always remained. Solving this problem is one of the aims of the Kill Spill project.

Even the floating oil itself stops the bacteria breaking down the crude. The hydrocarbons in it are hydrophobic, adhering to one another, repelling water and accumulating in the floating mass. To counteract this, a Kill Spill team from Northern Ireland is working on a method of dispersing the oil by making the molecules more accessible to bacteria. However the microorganisms cannot break down the oil fast enough as the process is chemically limited. Corvini compares the problem to eating: "It's like people, who need meat and vegetables. Bacteria require the right proportions of carbon, nitrogen and phosphorus in order to reproduce." Crude oil consists mainly of hydrocarbons; bacteria thrive when nitrogen and phosphorus are added.

The problem with these "bacteria food supplements" is that they are diluted by the sea. This is caused by diffusion, as in still water, but is augmented



by waves and currents. Corvini and Shahgaldian have designed a method using porous silica nanoparticles to release the required elements only when they are absorbed by the bacteria. Corvini explains the function of these tiny spheres, which consist of the same elements as glass: "highly water-repellent molecules are anchored to the surface of the silica particles, which are loaded with nitrogen and phosphorus. These hydrophobic molecules close the pores of the silica particles in water. Like oil, these structures are hydrophobic, hence they accumulate on oil slicks. The pores open, releasing nitrogen and phosphorus precisely where the bacteria break down the oil."

Since the silica spheres are so small they can be sprayed as a powder on to the oil spill from a helicopter or a ship. Although nitrogen and phosphorus have been used in the past to stimulate bacterial oil breakdown they had to be dissolved in vegetable oil. The new HLS process eliminates that additional pollution: the dry powder does without solvents or additional contamination. The researchers have already produced a kilogram of the bacterial nutrients and the next step is to scale-up the process; Corvini needs a hundred kilograms for the planned trials. He says: "Initial results are very encouraging and we are now going to do further tests near Athens." Corvinis's team are evaluating large-scale production and are upbeat about the chances of a successful spin-off.

Methods
- Chemical synthesis
- Bacterial cultures
- Breakdown tests
- Liquid-liquid extraction
- Gas chromatography

Infrastructure
- GC-MS
- SEM
- Incubators
- OxiTop

Support
- EU FP7

Collaboration
- Technical University of Crete
- Environmental Protection Engineering (EPE)

Bacterial super-resistance decoded

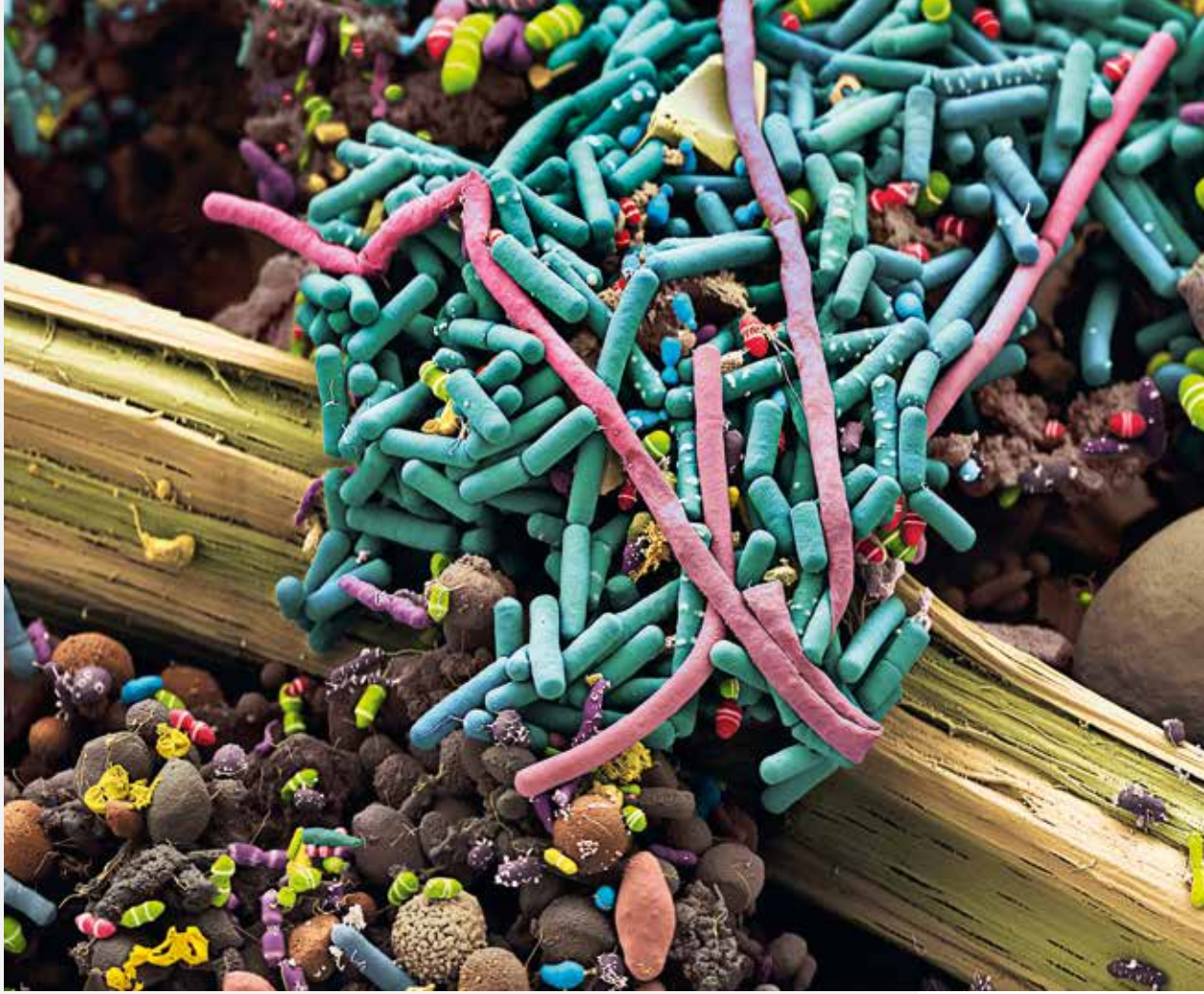
Scientists and politicians agree: antibiotic-resistant bacteria are a major challenge for medicine, both now and in the future. The World Health Organization estimates that by 2050 more people will die as a result of infection by multi-resistant bacteria than from cancer. A team of researchers at the HLS have shed light on a particularly alarming mechanism by which bacteria not only survive antibiotics but even use them as nutrition.

"The extraordinary thing is that the bacteria gain energy by fighting the antibiotic."

Philippe Corvini

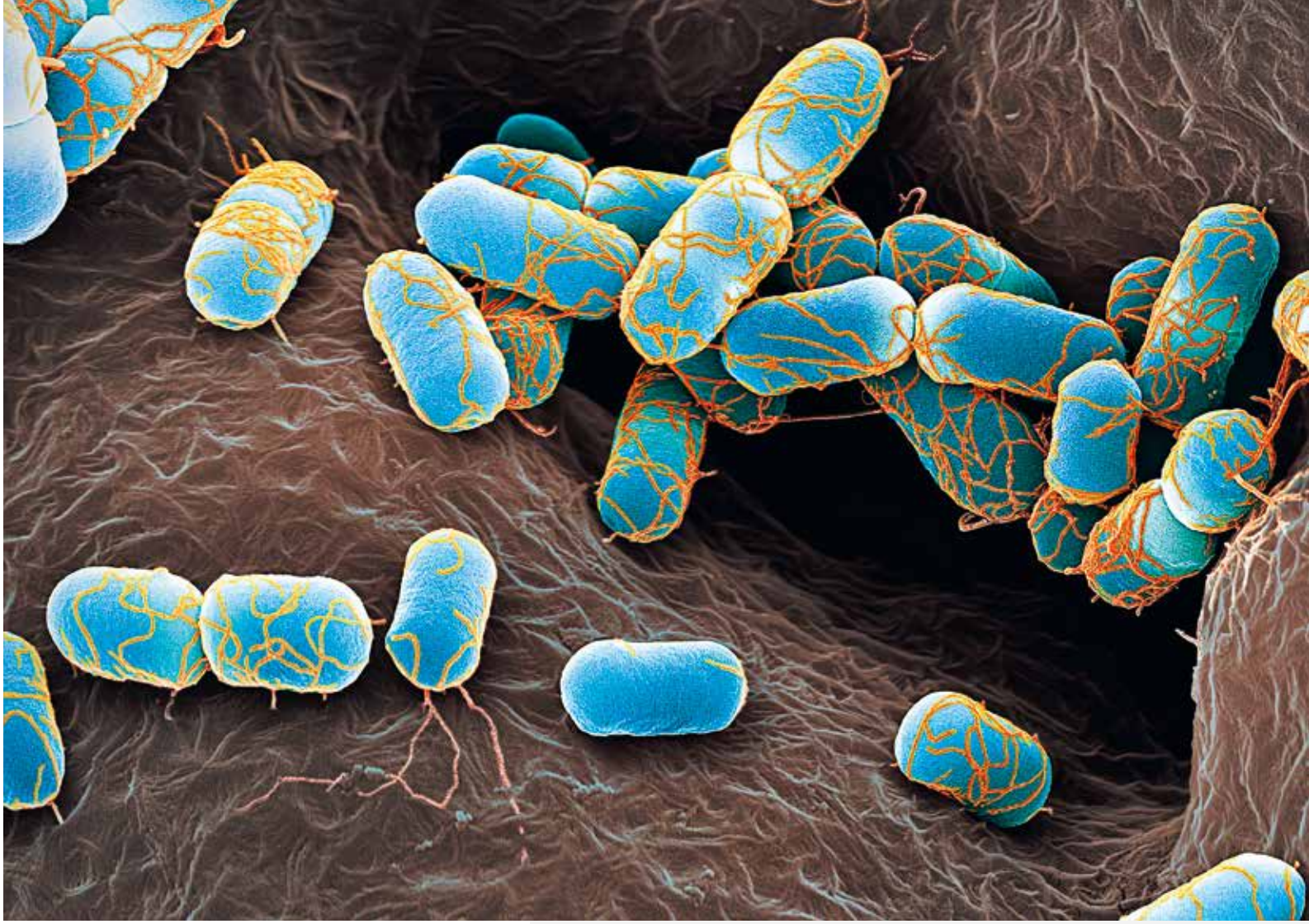
Sulphonamides are among the oldest synthetic antibiotics and have been used for over 70 years. They interfere with folic acid metabolism by blocking the formation of tetrahydrofolic acid, which bacteria need for DNA synthesis. However sulphonamides do not harm human cells; we absorb folic acid as a vitamin in our food. Various sulphonamides have been used in human medicine, for example against urinary tract infections; in veterinary medicine they are used against parasites. "About 20,000 tonnes of sulphonamides reach the environment every year" reports Philippe Corvini of the Institute for Ecopreneurship at the HLS, who is leading several projects looking at sulphonamide resistant bacteria. He explains: "The first step to the environment is the sewage treatment plant. The sludge there contains large quantities of bacteria which break down the organic pollutant input, i.e. hydrocarbons. Sulphonamides enter the sewage treatment plant at low concentrations — they are present but not effective. This allows bacteria to adapt to them perfectly". Corvini's research team have shown this by cultivating bacteria from sewage treatment plants in a nutrient medium and adding different sulphonamides. A few years ago, they were able to detect sulphonamide resistant bacterial cultures. The bacteria are not only resistant however; they can also feed on sulphonamides and metabolize them completely to carbon dioxide. "So the bacteria are doubly resistant to the antibiotic" Corvini concludes. "We call these cases super-resistance." In cases of antibiotic resistance which scientists have dealt with up to now, resistant bacteria enzymes have led either to small structural changes in antibiotics or are themselves no longer antibiotic-sensitive.

Together with researchers from Switzerland, Portugal and Germany, Corvini's group have now clarified how sulphamethoxazole — an active ingredient for urinary tract infections and pulmonary infections — is broken down in sewage treatment plants.

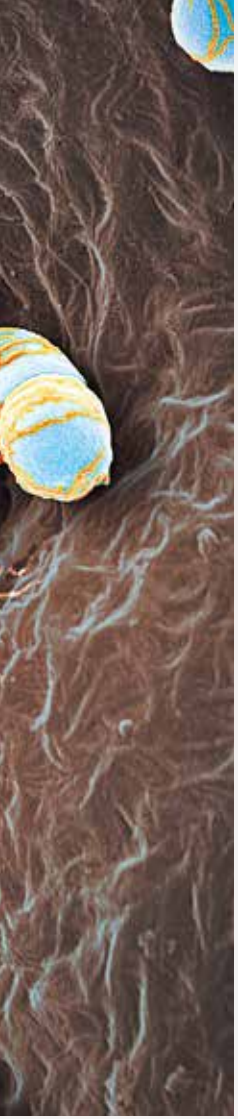


Corvini and his team first had to collect activated sludge from sewage treatment plants. From the resulting resistant bacteria, the researchers then transferred genes which encode decomposition enzymes into coliform bacteria and fed them with sulphamethoxazole. "We were not only able to characterize the intermediate products of the decomposition, but also to identify three genes and the enzymes they encoded" says Corvini. The first two enzymes — a flavin reductase and a monooxygenase — form an enzyme system. For its the next reaction the flavin reductase takes a pair of electrons from an energy source in the body. The resulting electrons are transferred to another enzyme, monooxygenase, which the sulphamethoxazole hydroxylates with oxygen and breaks up. After an abiotic reduction, the starting material for the third enzyme, another monooxygenase, is formed. This converts the intermediate into trihydroxybenzene, which the bacteria use as food and convert to CO_2. "The extraordinary thing about the process is that the bacteria gain energy and small molecules to boost their fight against the antibiotic. Usually the opposite is true and resistance costs the bacteria energy. It could be a completely new resistance mechanism" Corvini said. This understanding of the breakdown mechanism is also the basis for industrial applications. Corvini adds "By understanding these mechanisms on a molecular level, we can look at new sulphonamides from a different angle. In future, it may be possible to predict whether these new sulphonamides are easier to break down or more stable"

According to Corvini, the newly explained breakdown mechanism is critical: "We are worried: our experiments suggest that this process is not limited to this one antibiotic. Studies of other sulphonamides reveal exactly the same spectrum of degradation products and the molecular structure of other sulphonamides is also vulnerable to the first reaction in the degradation process." This first hydroxylation reaction is a key step in breaking down sulphonamides, as the HLS researchers have shown.



Corvini and his team are now investigating whether bacteria are resistant to and can break down other antibiotics. To this end, they take samples from the in- and outflows of wastewater treatment plants, add them to the antibiotics and measure the residual concentration of active ingredients in the wastewater bacterial cultures. These monitoring studies have enabled Corvini's team to track bacteria that are super-resistant to sulphamethoxazole. "We are working on five different sewage treatment plants in different locations and, most importantly, with different sewage treatment processes. We want to find out whether some processes are better at preventing the spread of antibiotic resistance than others." In addition to the research at sewage treatment plants, the researchers are also studying soil samples to see whether this super-resistance has reached the environment. There are two vital



questions about the link between resistance and the ability to break down antibiotics: “On one hand we want to know if the bacteria can only break down sulphonamides if they are already resistant. This would mean that the bacteria can evolve, so that after several generations they produce precisely those enzymes which break down antibiotics. The second question is: if a bacterium can feed on an antibiotic whilst having a resistance gene for it, does the bacterium’s ability to metabolise it lead to a more rapid spread of resistance genes?” The researchers have already found the first evidence of this link between resistance and the ability to break down antibiotics.

The fact that super-resistant bacteria can break down antibiotics may however be useful in the future. Knowing the precise molecular structure of the enzymes means that they can be manufactured using biotechnology and thus used deliberately to break down the antibiotics. This would prevent resistance being passed on to disease-causing bacteria. This enzyme-based process would probably be too expensive for conventional sewage treatment but Corvini believes that targeted applications are feasible: “You have to consider the benefits for society, for industry and for the environment. You could treat badly affected industrial waste water using this technology.”

Methods
- Cell cultures
- Resting cells
- DNA extraction
- Genome sequencing, quantitative PCR
- Proteome analysis
- Radio analysis and classical mass spectrometry
- Enzyme testing
- Digestion by trypsin

Infrastructure
- HPLC-MS
- HPLC radio detector
- Illumina Miseq NGS
- qPCR
- MALDI

Support
EU FP7, SNF, Porto University, EAWAG

Collaboration
EAWAG, RWTH Aachen,
MPI Magdeburg, ICTP

Health and Data

The raw material of today's world is information. As with traditional raw materials, this must be obtained and processed if it is to be used in a meaningful way. The right algorithms and search strategies combined with customised data processing enable the visualisation of workflow characteristics, individual behaviour and connections. The HLS, with its focus on information technology and processing, helps people deal with and benefit from the ever-increasing flood of data.

Measuring the knee

The knee is one of the largest and most important joints which, if damaged, can be replaced by an implant. Alex Ringenbach from the HLS has written software that can create an individual 3D model of femur and tibia bones from magnetic resonance images. This algorithm speeds up the making of precise patient-specific templates that enable surgeons to position and fit new knee implants more easily and accurately.

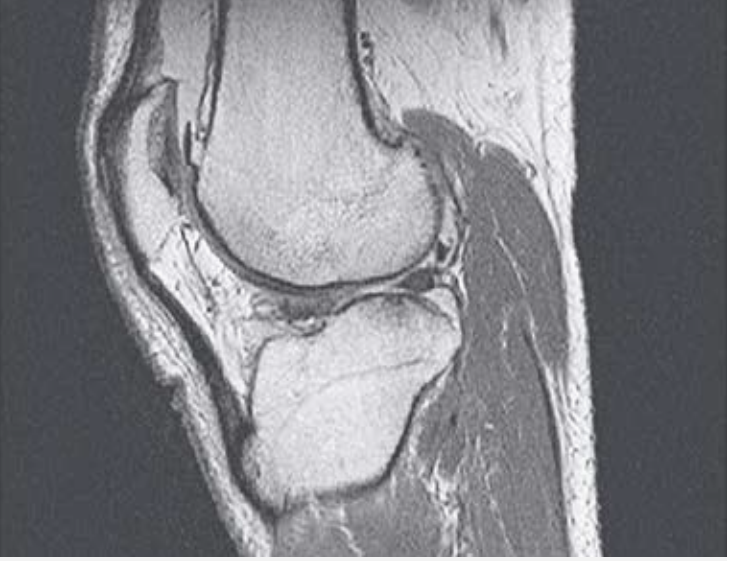
"For a prosthetic knee implant, the geometry of the knee must be recorded from image data. This takes only ten seconds with our algorithm — compared to five hours previously."

Alex Ringenbach

Fitting knee implants has been standard surgery for years. However even today, it still requires extensive planning due to anatomical differences between patients. An implant is an artificial object that must fit into a living system, the body. No two knees are the same and thus implants have to be positioned differently in each operation. In order to fit them accurately and ensure good joint function, surgeons today often use cutting templates. These attach to the femur and tibia and guide the surgeon when cutting through the bone to which the implant is to be fixed. To make these templates, a precise virtual 3D model is needed; Alex Ringenbach from the Institute of Medical and Analytical Technology creates this from Magnetic Resonance Images (MRI). For him, the advantage of this new method is clear: "In the past these templates were done by hand, which takes about five hours. We have written an algorithm that does the same job in less than ten seconds." On this project Ringenbach is working with the firm Medivation AG in Brug, which integrates the segmentation algorithm into a planning tool for the production of templates.

There are several steps before the program generates the 3D blueprint for the cutting template. The main job of the algorithm is segmentation: the software must decide whether a point in an MRI image is bone, cartilage or other body tissue — a classic problem of machine image recognition, as Ringenbach explains: "It is much easier for a human being than a computer because we have prior knowledge. We know what the shape of the bone looks like and can complete our image of it in our head. We therefore also know what is bone and what is other tissue. From the signal data alone, which the MRI shows as shades of gray, this cannot be determined."

Consequently the research team uses the Active Shape Model. From section images that a surgeon has segmented manually the software learns the shape of the bone and what the area near the



bone surface probably looks like. From ten to twenty sets of data the researcher creates a bone model on the computer. This includes average shape, shape variation, information on the area around the bone and our prior knowledge. With this a picture can be reliably segmented.

In order to segment an image data set the model with the prior knowledge is applied: image values are put into the model, compared with the original, and the position and the shape of the model are adapted accordingly. "You have to be creative to find the right model parameters and to perfect the segmentation process," says Ringenbach. Another challenge is the MRI examination itself: "Each patient lies in a different position in the MRI machine, which means that the bones are in a different part of the image, so there is no standard positioning system." For the model, mathematical methods, the individual MRI datasets and the measured "average bones" must be harmonised as closely as possible. This process, which enables comparison of different data sets, is called registration and is the most time-consuming part of creating the 3D model. Due to the complicated mathematics it can take up to several days but it only needs to be done once.

Since signals are not standardized, data from different MRI machines often vary greatly. Hence there are also wide differences in the maximum intensity of individual image points — as in photos with different contrast levels. The new algorithm is programmed so that it can correct these variations in individual sectional images.

Ringenbach considers the effort invested to be justified: "Knee implants often involve elderly people whose bones are fragile and have signs of wear such as spurs. If the templates do not fit exactly, they slip." Ringenbach's partner, Medivation AG, has developed a planning instrument with the algorithms to produce cutting blocks for the first successful operations. Further applications for the software are in development.

Methods

- Manual segmentation of MRI reference data
- Registration of segmented surface data
- Formation of statistical shape models (for femur and tibia)
- Analysis of tissue texture in MRI data
- Model development by incorporating texture classifiers
- Model development by incorporating registration algorithms
- Performance optimization by incorporating range limits

Infrastructure

Computer, programming language C ++

Support

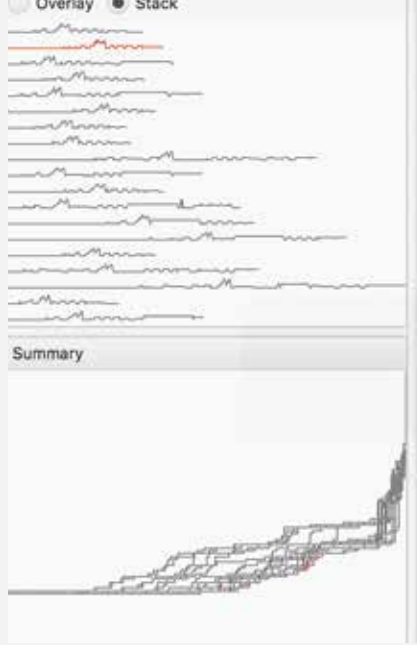
FörderstiftungTechnopark Aargau, Research Fund Canton Aargau

Collaboration

Medivation AG

Tracking the patterns

Imaging with computer tomography and magnetic resonance tomography is an integral part of modern medicine. In 2014, Swiss radiologists did more than 800,000 CT scans and more than half a million MRIs and the trend is growing. The equipment used contributes significantly to electricity consumption in hospitals. Researchers at the HLS are developing an evaluation program to make these examinations cheaper and more ecological.



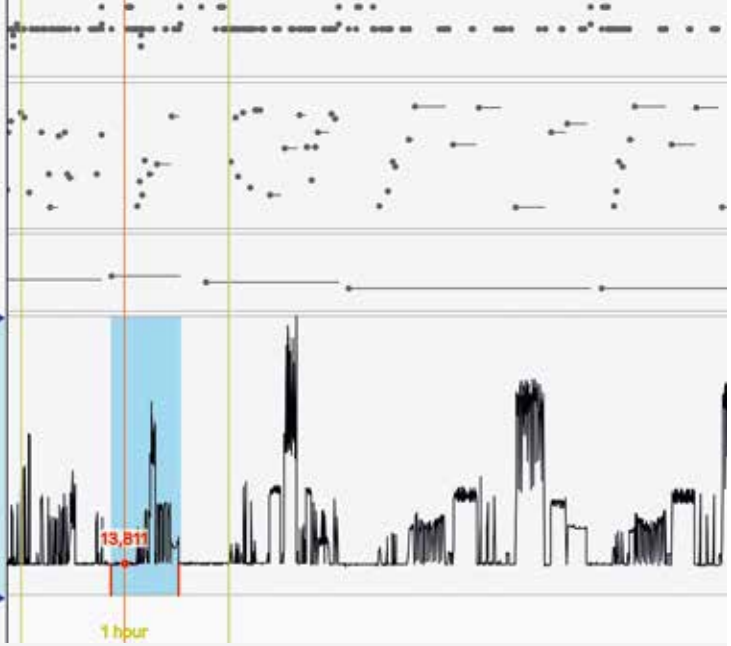
Dominique Brodbeck and Markus Degen from the Institute of Medical and Analytical Technology already have experience on research projects outside the natural sciences. For example, they developed software for hospital managers to trace patient movements between examinations. The data is used to plan future infrastructure and help improve daily routines in both the clinic and administration.

The current project also focuses on optimising hospital operation. Together with a software developer, the two researchers have created a computer program that shows the energy consumption of imaging examinations in hospitals. The focus is on radiological departments, whose MRI and CT devices consume a million kilowatt hours per year – the equivalent of around 250 households.

Brodbeck speaks of two reasons for the "GreenRad" project, run in cooperation with Basel University Hospital: "One is economic: with ever more equipment and rising prices, electricity bills in radiology are soaring. The other is an ethical drive to reduce CO_2 footprints and with them, damage to the environment."

However in order to cut the bills, electricity consumption is not the only factor. The maximum power capacity must also be paid for and that depends on how much total power the hospital uses at one time. "In order to reduce energy consumption, you have to be able to say how much energy is used by one machine per time unit, per examination and in standby," explains Brodbeck. "It is not enough to just look at the current curve. That is why we use different data sources."

In addition to electricity consumption, the scientists also collect operation data from the cooling system, activity records for each machine, as well as clinical data on the type of examinations. GreenRad can correlate and present these data quickly and interactively, allowing users to monitor energy consumption patterns and to determine their frequency and characteristics. IT engineer Degen sees this approach as fundamentally different compared to conventional handling of large amounts of data: "Data mining is usually used with correlation algorithms to find patterns automatically. We use humans as a recognition algorithm;



people not computers recognise recurring processes and patterns. Our thesis is that there are many questions where only people can make sound decisions. We present the data on a plate and provide the software tools." In order for the data to end up on that plate however, a considerable effort is required, says Degen: "The data isn't consistent at all at first, either in time or in content: it must be aligned." Once this has been done, the data must be visualised in such a way that the relevant information can be extracted. Brodbeck describes the requirements of the program: "It must be interactive and visually clear so that you can find information quickly if you have an idea."

The system test in Basel already revealed energy consumption trends: in standby mode, a machine consumes constant current, just like a TV. During an examination, power consumption rises to peak level from less than a second up to a few minutes. Here, Degen sees improvement potential: "A high-level control system could synchronize all machine operations of less than one second so that high current consumption occurs in series and not in parallel." This could significantly reduce the maximum power capacity needed.

GreenRad's key ability to make patterns visible comes to the fore when reducing total electricity consumption and thus the CO_2 footprint. Degen cites an example: "We counted up to twenty calibration sequences during CT scans. This could probably be reduced." He is sure that the program has even wider potential: the researchers used their software to test the log files of computer programs. Because they wrote the program, they can determine all variables and data types themselves. As a result, there are virtually no limits to the possible applications.

Methods
- Exploratory Data Analysis
- Interactive Visualization
- In-Memory Processing

Infrastructure
- Software tools for data processing and correlation (in some cases developed in-house)
- Modern software development environment with version management system, automated creation and tests on our own server systems

Collaboration
- University Hospital of Basel, Radiology & Nuclear Medicine Clinic

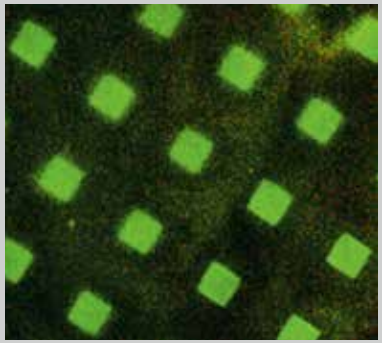
Summary reports

Metabolic disorders in newborn babies

Since the 1960s newborn babies have been screened for congenital metabolic disorders. Researchers at the Institute of Chemistry and Bioanalysis at the HLS are working to improve the laboratory methods used for this screening. Up to now, midwives have put a drop of blood from the baby's heel on filter paper for the Dry Blood Spot test. A central laboratory then tests the sample for signs of disease. One to three millimetre diameter discs are cut out of the filter paper with a punch, from which the blood is then extracted with a solvent. However the automated punching process is liable to errors, since the tiny discs can fly off and land in the extraction vessel of another sample and thus no longer be assigned to the baby.

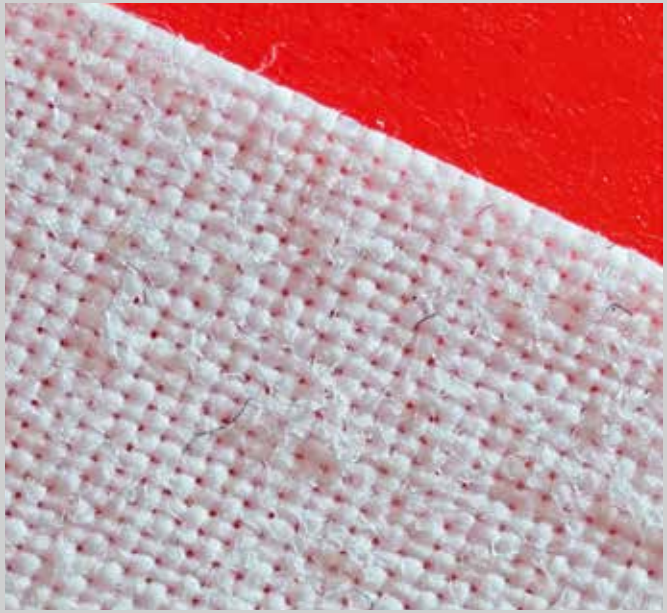
The research group of chemist Götz Schlotterbeck have solved this problem in cooperation with the firm CAMAG and Zurich Children's Hospital. They analyse the sample directly on the filter paper using an extraction unit; this is a device that can detach the sample directly from the paper with a solvent, thereby eliminating the unreliability of the punching process. Schlotterbeck adapted the idea from an earlier thin film chromatography project: "The thin-film MS interface, which we developed with CAMAG about ten years ago, could transfer a sample directly

from a thin-film plate to a mass spectrometer. That interface is relatively similar to the technology for newborn screening."
The chemist is not only looking at sample extraction but also wants to refine the analytical method and improve sample transfer to the analysis machine. "With mass spectrometry we can measure approximately fifty different chemical substances for neonatal screening in a cycle time of only two minutes whilst simultaneously making the analysis results more reliable."



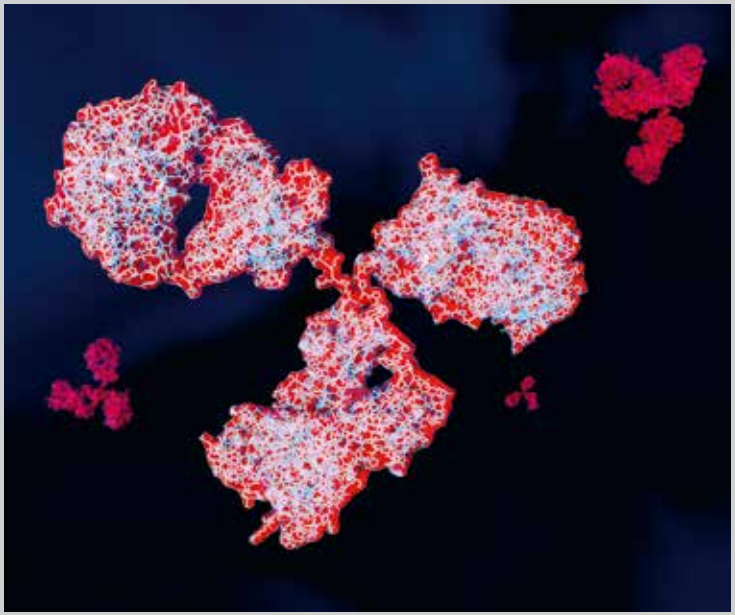
Flow Reactor Enzymes

Flow reactors enable continuous chemical reaction processes. The drawback is that catalysts with the required reaction product are washed out of the reactor and lost. To prevent this loss, HLS researchers have developed a reversible method of anchoring enzymes, i.e. biological catalysts, on a membrane. This has the advantage that, unlike previously, the membrane does not need to be changed when the enzyme is no longer active.



Silk protects both on and under the skin

Silk has high tensile strength, is very water absorbent and thanks to its proteins is a biological product which is easily tolerated by the body. HLS researchers can encapsulate individual synthetic fibres with silk proteins, thus making the advantages of silk available for functional clothing. They have also managed to encapsulate active pharmaceutical ingredients in silk so that they can be implanted under the skin and released slowly, extending their effectiveness for months.



A rapid test for immunosuppressant

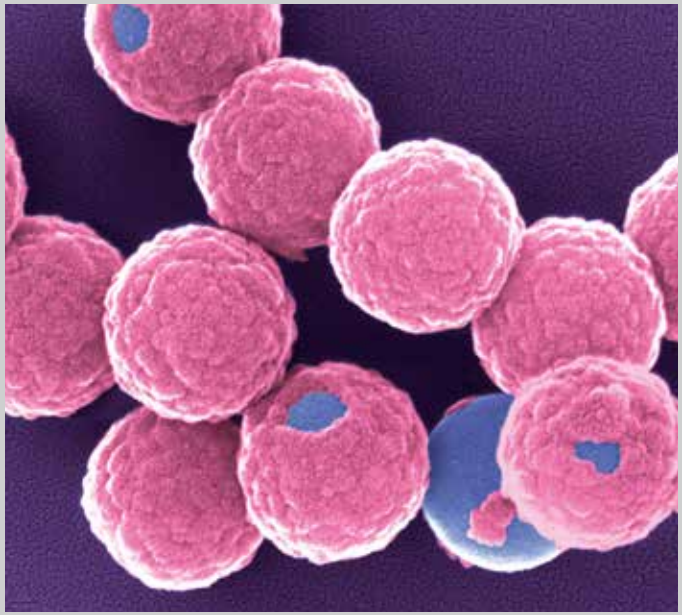
To prevent rejection of donor organs after transplants, patients have to take medicines to suppress the immune system for the rest of their lives. These immunosuppressants only work correctly at a certain concentration in the blood. Up to now, this level had to be monitored by a doctor. As part of an interdisciplinary CTI project, researchers at the HLS are currently developing a rapid test so that in future patients will be able to measure their own medication levels.

Over 500 Swiss people had a heart, lung, liver or kidney transplant in 2014 alone. Since the body's immune system sees a donor organ as alien, it fights it. In the worst cases there is a rejection reaction and the patient may die. To prevent this, patients receive immunosuppressants — medicines that inhibit the immune system — which must be precisely prescribed and checked by the doctor. Daniel Gygax's team at the Institute of Chemistry and Bioanalysis have therefore been working on a rapid test for two such drugs — Tacrolimus and Ciclosporin. In future, patients will be able to measure their blood immunosuppressant levels in comfort at home, without having to go to the trouble of an outpatient visit every time. The rapid test is being developed by a CTI project led by Gygax, with an interdisciplinary team of chemists, doctors, IT specialists, Bühlmann Laboratories AG and Dorner Health IT Solutions. In order that the test is understood and adopted by patients, Gygax has also brought in psychologists and industrial designers.

The system consists of an applicator for taking blood samples – of which there is already a prototype – and a container where the patient tests the sample. The latter has a test strip with different analysis reagents. "We use antibodies to determine the level of immunosuppressants and their degradation products. The antibodies are chemically combined with gold or plastic particles," explains Gygax. "A test strip in the container changes colour depending on the concentration. For some substances though, the discolouration is too faint so we need to use fluorescent markers." Gygax is enthusiastic about the fact that a mobile phone can be used for the evaluation: "This means that a patient can send their own data to the hospital".

Saffron petals help wounds to heal

Saffron is one of the most expensive spices in the world, obtained from the autumn flowers of the saffron crocus (Crocus sativus). Each flower usually produces only three stigmas, which are picked by hand and dried at a low temperature. Around 150,000 flowers are needed for one kilogram of pure saffron. Although the petals also contain many valuable natural substances, up to now they have been thrown away. HLS researchers therefore developed a method for extracting those valuable ingredients from saffron petals. This Accelerated Solvent Extraction used several different solvents, the extracts of which were then analysed for their components using HPLC. The flower extracts were tested on cell-based wound healing models: human skin cells which are artificially damaged in the laboratory. Treating the cells with the extract improved healing and produced more VEGF growth factor, which ensures that wounds heal faster. These findings could lead to the development of an innovative natural product.



A soft silane layer protects enzymes

Enzymes are biocatalysts which reduce the energy needed for chemical reactions. They have very specific functions but are not very stable. HLS researchers have solved this problem by binding enzymes to silica nanoparticles which cover them with organosilanes - silicon oxide with functional organic groups. This silane layer is arranged perfectly around the enzyme to protect the biocatalyst from high temperatures and aggressive chemicals without stopping catalysis.

Some of our partners

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