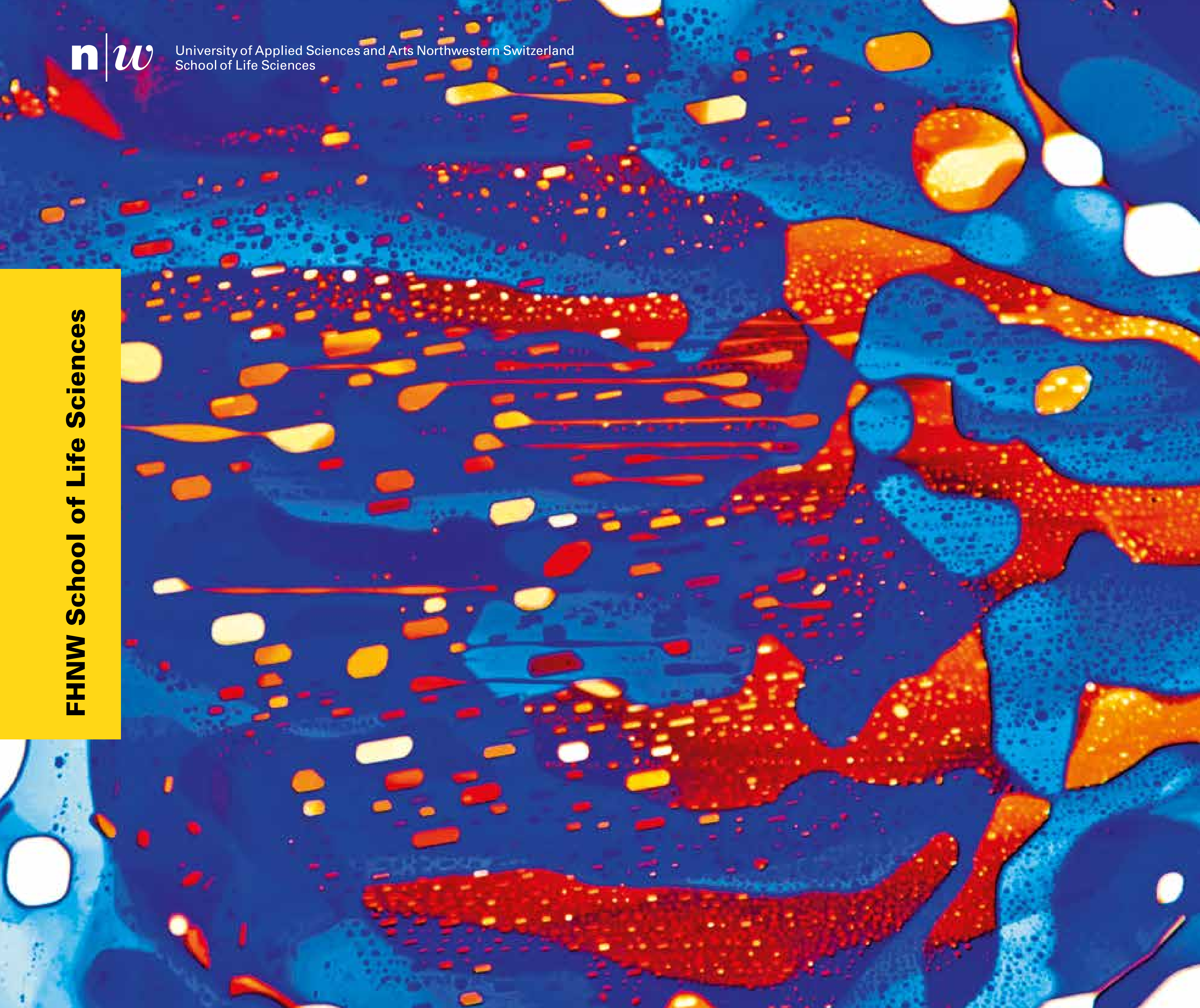
University of Applied Sciences and Arts Northwestern Switzerland
School of Life Sciences

FHNW School of Life Sciences



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A conversation with Falko Schlottig

The FHNW School of Life Sciences (HLS) moved into the new Muttenz campus in 2018. For HLS director Falko Schlottig, the joint campus is a great success both for researchers and for HLS industry partnerships. The new campus promotes interdisciplinary cooperation and provides a foundation for collaborative research projects. The HLS is ready to face the future.

"Our goal is for the HLS to be the obvious first contact for life sciences firms."

Falko Schlottig

What has changed with the opening of Campus Muttenz?

The university has moved the two former locations into one, enabling us to exchange knowledge, experience and ideas better and to take full advantage of our infrastructure for education and research. In 2019 there is a new Bachelor of Science programme structure with new content and new fields of study. At Master's level, the FHNW School of Business and the HLS are introducing a joint Master's degree in medical and business IT.

Can you benefit from synergies?

There are a range of synergies within the HLS as well as across all the faculties in the new campus and this cultural shift will benefit us in the long term. We already have closer teaching cooperation with the FHNW School of Education and the FHNW School of Architecture, Civil Engineering and Geomatics.

Has the campus led to more intensive cooperation with industry?

Yes, we have seen that clearly. Almost every week industry events are held on the new campus, both with HLS partners and run for other organisations. We often combine these with guided tours through our laboratories and technology centres. In this way we are preparing the ground for companies to network even better with us and with each other.

What makes the HLS such a sought-after partner for industry?

Firstly, thanks to cooperation founded on specific expertise and experience across disciplines; we have set up our facilities in such a way that all our laboratories are interconnected, thus improving communication and facilitating projects. Secondly, we have an extensive new process and technology centre on three floors of the building, which enables us to replicate almost all value-added processes in the life science industry in both development and production.

So from idea to packaged product?

Exactly. A typical project for our university today would be: "Can you support us in the formulation, production and packaging of a drug?" We can provide a complete single-source and field-specific solution.

What is the current HLS research goal?

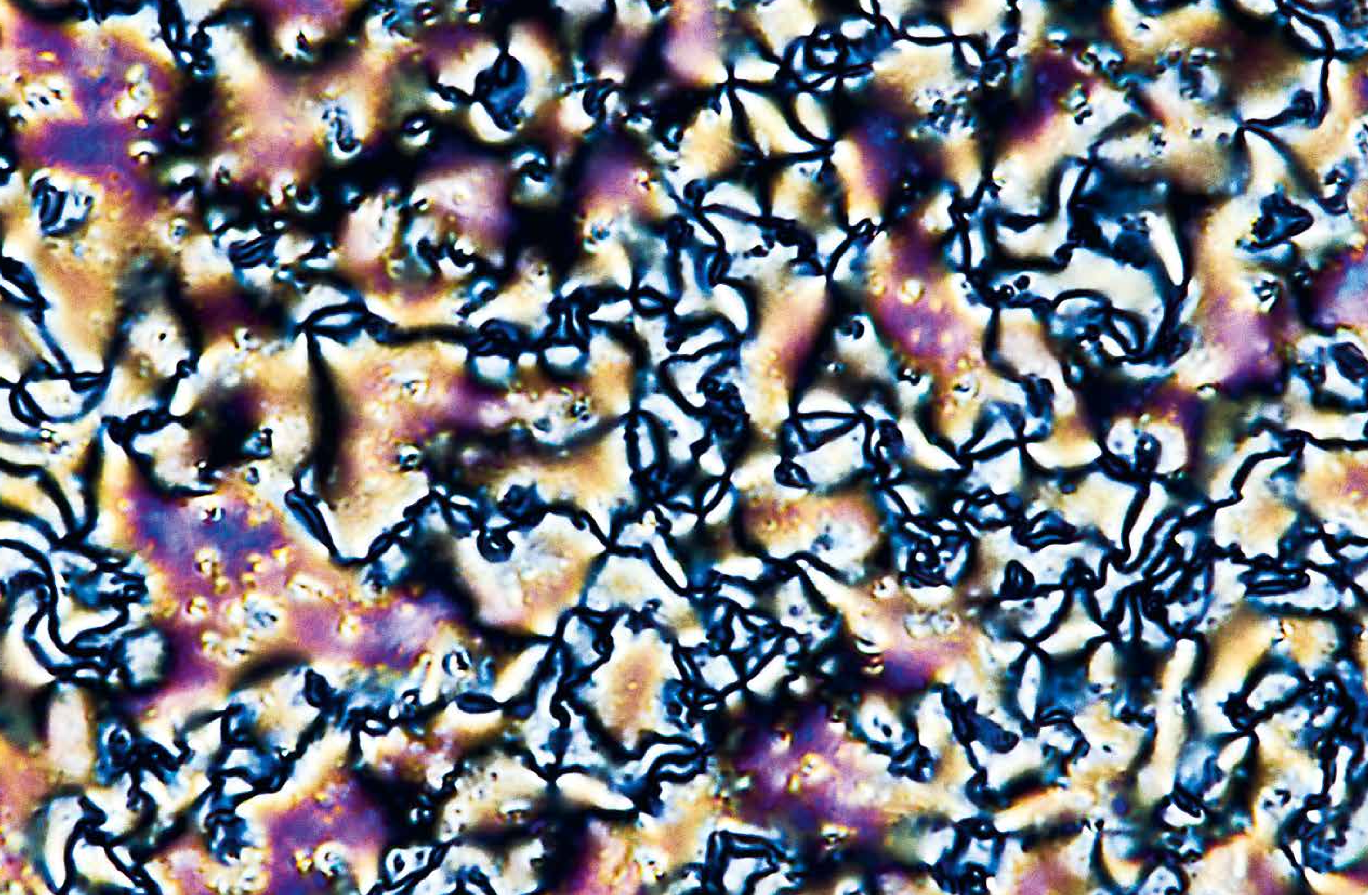
The focus is on developing added value and solutions for, and in collaboration with, industry. This clearly includes driving our own innovative approaches and taking them up to technology transfer or establishing start-ups. More than 700 companies are active in research and production in the northwest Switzerland life sciences sector; we already work with more than 100 of them. Our goal is for the HLS to be the obvious first contact for firms when looking for solutions.

Have HLS research fields changed in the last two to three years?

Yes. We analyse which way industry is developing and expand or create the relevant expertise.

What questions will HLS researchers address in the coming years?

We will continue to be involved in every aspect of the life sciences sector. A current example is questions relating to data science: what is real, what will become reality and what is just academic hype? What does data science mean for life sciences development and production processes? Can machine learning be applied in the development of biotechnology-controlled processes? What does data science really mean for personalised medicine? How is it implemented? What do business models in the highly regulated pharmaceutical and medical technology environment look like? How will the hospitals of the future be organised? How does IT interface with classical chemical-pharmaceutical, medical-technical and bioanalytical trades? Who is driving development? What does that require from our education programmes? How can all this be brought together to create real added value in the end? With the expertise, experience, interdisciplinary approach and proximity between departments at our university, we are in an excellent position. We have many of the departments necessary in-house and a lot of exciting work ahead of us.



Medicine and Technology

Healthcare and the treatment of diseases are currently undergoing significant changes. 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.

Robot assistance in the laboratory

A great many experiments are required before a medicinal substance can become a finished drug. Researchers must find the best combination of stabilisers and other additives and test whether a drug always works as intended. This process can be facilitated with an HLS robot system which enables reliable studies to be done on highly sensitive biomolecules. A newly developed software tool provides a clear overview of the results of individual experiments, thus accelerating the search for the optimal drug formulation.

Drugs, whether as tablets or other dosage forms, contain not only active pharmaceutical ingredients but also various additives to ensure that the active substances remain stable and that the intended dose is released at the right place in the body. These additives differ according to the drug. In order to find out which formulation best achieves the desired medicinal effect, thousands of tests are necessary. "It is not enough to produce different additive combinations," explains Oliver Germershaus from the HLS Institute for Pharma Technology. "We also have to analyse those formulation candidates chemically and assess their shelf life, which means: storing them for long periods of time and then testing them. Many of these steps are still done manually; the process is vulnerable to errors and it takes a long time, especially for biological agents." In order to automate the production of different formulations as well as the sample preparation, the HLS researchers have adapted a commercial robot platform for this special purpose in a project funded by the FHNW Foundation and in collaboration with Hamilton Bonaduz AG.

Glass not plastic

The biggest challenge of the project was the biological agents themselves: biomolecules degrade over time. They are less stable and are more sensitive than conventional active ingredients, for instance when they come into contact with air. "Conventional laboratory robots work with plastic vessels," says Germershaus. "However, these are not completely airtight. If samples are stored for shelf life studies, air can get in and may affect drug stability. Moreover, substances can leach out of the plastic and influence the efficacy of the drug." HLS researchers modified the robot and replaced the plastic containers with glass ones, which do not react with the drug, are airtight and can be sealed, ensuring more reliable test results.

The research team used a monoclonal antibody, i.e. an artificially produced biomolecule, as a test system. Different concentrations of six different additives, such as stabilisers and buffers to regulate acidity, were used for the formulation. A total of 324 different combinations were produced by the laboratory robot. "The robot has several advantages,"

says Germershaus. "It is about one and a half times faster than humans, can produce the formulations very reliably and does exactly what it was programmed for. In addition, the robot has a clean-air hood to filter the air and remove particles and microorganisms, enabling it to produce the formulations under sterile conditions."

IT meets pharma technology

The research team did a great deal of the work on the computer. Due to the many possible test substance formulations, this programming was very time-consuming and only feasible with the help of researchers from the Institute for Medical Engineering and Medical Informatics at the HLS. First, they had to adapt the robot and clearly define its new tasks for each step, such as: go to this location with the pipette, take one millilitre of the active substance solution, go to the next location and mix again.

Germershaus believes that despite extensive process automation, the laboratory robot cannot completely replace humans: "Humans see an experiment with all their senses. A robot works systematically but not necessarily efficiently. A human notices this immediately, but an automatic mechanism only checks the things it has been programmed for."

Chemical analysis also relies on that combination of human expertise and IT efficiency. "Using statistical test design, we were able to reduce the 324 formulations produced by the robot to just 40 in the analysis phase and still find an ideal combination," says Germershaus. His team stored the 40 formulation candidates at two different temperatures and analysed their effectiveness at four different points in time, meaning that the researchers still analysed 320 different samples using a variety of methods. For this purpose, they developed a new software tool that provides a clear visual presentation of the test results.

The researchers see potential for further automation in future. The robot and its algorithms could take on sampling and analysis for example, as well as the interpretation of the analysis results. However, it will probably be some time before the entire formulation process is fully automated.

Methods

- Automated liquid handling for the production of formulation candidates
- Stability studies according to ICH Q1
- Physical-chemical analysis of biological agents
- Peptide mapping
- Aseptic production
- Databases
- Visualisation of complex analytical data

Infrastructure

- Size exclusion chromatography
- Ion exchange chromatography
- Flow microscopy
- Liquid handling platform
- SDS polyacrylamide gel electrophoresis
- Liquid chromatography with tandem mass spectrometry (LC-MS/MS)

Support

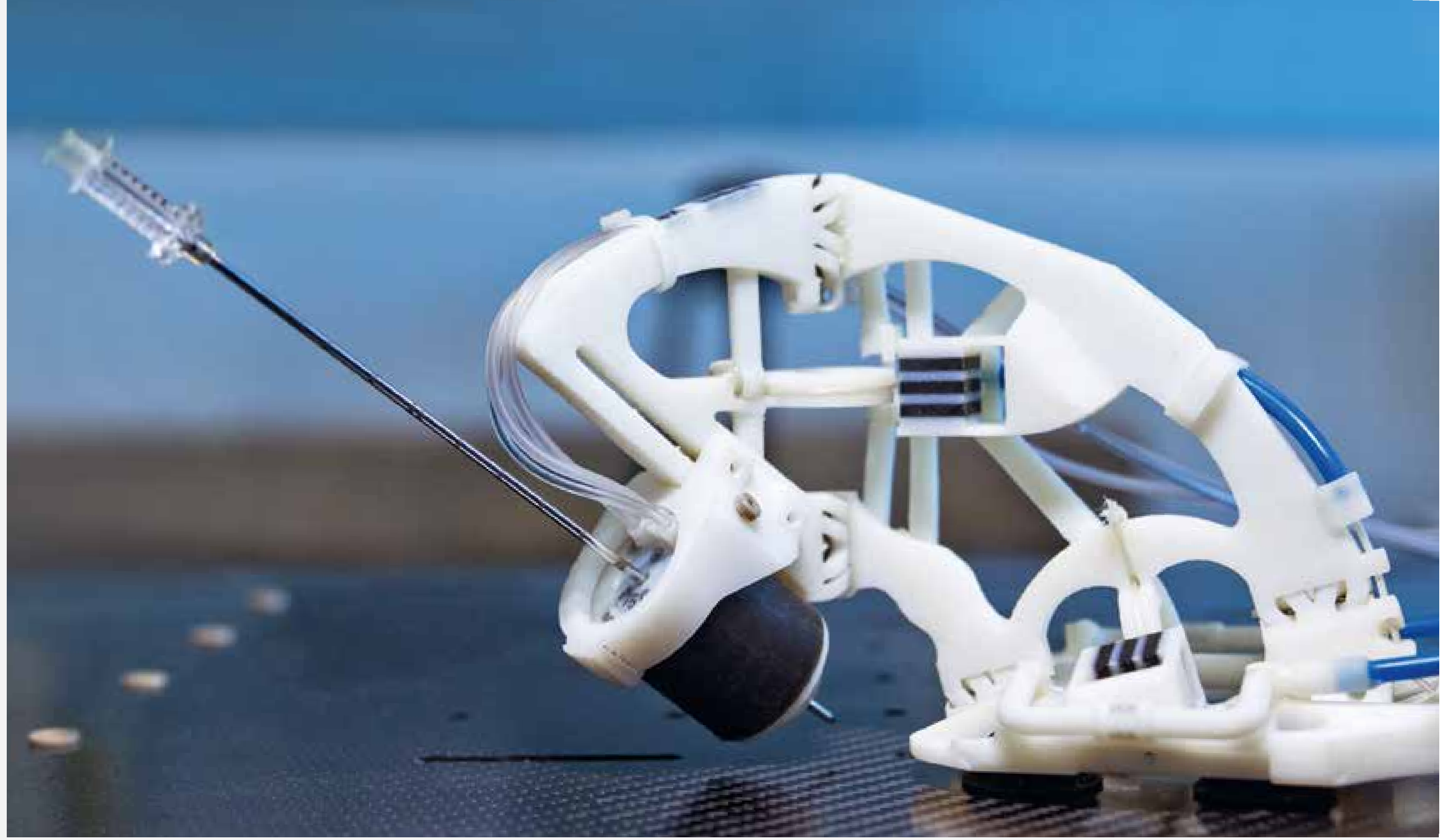
- FHNW Foundation

Collaboration

- Hamilton Bonaduz AG
- Institute for Medical Engineering and Medical Informatics (HLS FHNW)
- Institute for Chemistry and Bioanalytics (HLS FHNW)

Radiation protection with robotics

Minimally invasive surgical procedures such as tissue removal from internal organs or tumour treatments are often performed with radiology imaging, leading to radiation exposure of both patients and medical staff. To avoid this, HLS researchers working in a multinational project are developing a robotic drive system to place needles precisely in the body. The system is not only highly innovative but is also an important step forward in the development of 3D titanium alloy printing.



"With a force feedback robot, interventional radiologists will feel as if they are guiding the needle themselves but without being exposed to X-rays."
Michael de Wild

The Institute for Medical Engineering and Medical Informatics (IM²) laboratory has row after row of 3D printers. Layer by layer, they create metal or ceramic implants to support healing bones. In an international research collaboration, Michael de Wild and his team are now applying their 3D printing expertise to robotics. "We are developing a robotic support system that can help with image-controlled surgical procedures," says the researcher. "For example, when taking tissue samples, doctors have to insert biopsy needles with millimetric precision into the organ or area to be examined. Using medical imaging such as computer tomography (CT), they can see where the needle is and, if necessary, correct its position. With the planned robotic system, the needle can be controlled remotely and observed on the monitor while the patient is lying in the CT scanner. This not only improves the precision of tissue extraction but is also suitable for interventional tumour radiology or for localised drug treatment, such as pain therapy with image control."

Complex 3D-printed designs

The SPIRITS project (Smart Printed Interactive Robots for Interventional Therapy and Surgery) involves the HLS as well as companies, clinics and universities from Austria, France, Germany and Switzerland. The HLS team is constructing the motor to move the needle forward in the body. To enable safe operation of this actuator in the operating theatre, it is driven by compressed air. "What's special is the way the drive structure functions," explains de Wild. "The biopsy needle is mounted in the centre of a cylindrical grid structure surrounded by four to five channels. Unlike ordinary materials, this grid structure expands transversely to the direction of pull, so when pressure inside the cylinder is increased, the structure expands along the longitudinal axis and drives the needle forward." The HLS researchers achieve this through the auxetic geometry of the lattice. "We raise the pressure in the cylinder with four to five of the small balloons that are used in cardiac surgery to expand stents to their final size to keep blood vessels open," says de Wild. "However, because the auxetic structure is only extended by fractions of a millimetre, the process needs to be repeated several times per second. The needle moves forward using a clamping system in very small steps, similar to a caterpillar."

This geometry is too complex and fragile for conventional manufacturing processes but not for 3D printing. IM² at the HLS is one of the few institutes in the world that can 3D print such fine metallic structures as the drive cylinder. The researchers use titanium powder for the cylinder, applied in a thin layer to a printing platform, then fuse the areas which will form the structure. "We use a fiber laser that melts an area of around 100 micrometres in diameter with up to 200 Watts," says the researcher.

Temperature management is key

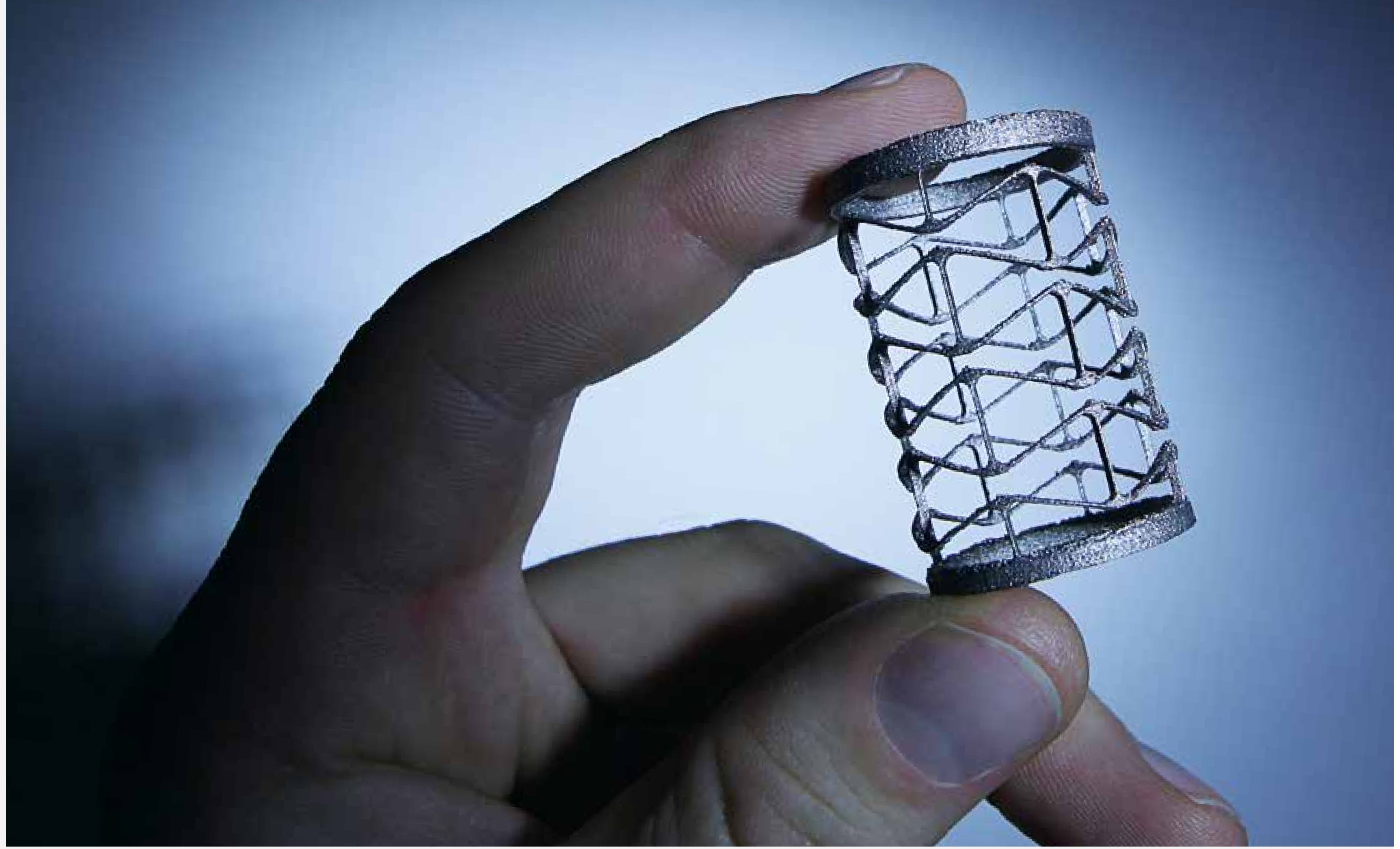
Such energy densities require special designs, explains de Wild: "If the layer below or beside the laser target area is not melted, the gas between the particles acts as an insulator. The titanium then becomes too hot, even evaporating as a result of the laser beam, or causing stress or deformations in the manufactured object. Components are anchored to the building platform with struts so that heat can be conducted away. We therefore specifically add support structures to the final design that not only give mechanical stability during 3D printing but also dissipate the heat."

Prior to manufacturing, the researchers did extensive calculations to customise the localised laser energy, taking into account the material and shape of the object. For each of the thousands of points in the design, this heat calculation simulates how well heat can conduct through the structure and supports and calculates with how much energy and for how long the laser should stay on each point. Using this exhaustive construction and process plan, the 3D printer then produces a structure a few centimetres in size from thousands of layers over a period of several hours.

The human touch

Despite state-of-the-art 3D printing technology, finishing is currently still done by hand. The researchers first take the structure off the printing platform and remove the slender supports. This requires a delicate touch to avoid damaging the fragile structure. Then they smooth the surface using electro-polishing, mechanical polishing, chemical etching or sandblasting.

Finally, the researchers subject the structures to various tests. In static mechanical tests, they pull them apart and measure how strong and elastic they are. In dynamic tests, they analyse fatigue after thousands or millions of load cycles; improvements from all these tests are incorporated in the surgical robot prototypes. On completion of the 2020 project, medical technology companies in the three countries area around Basel should complete the product development and bring it to market; a spin-off is also an option for de Wild. He and his team are already investigating alternatives to pure titanium such as the nickel-titanium alloy Nitinol; the shape memory alloy is up to five times more elastic and the first auxetic structures made of Nitinol have already been printed.



Methods

- Computer Aided Design (CAD)
- Freeform modelling
- Material and process development for metallic 3D printing
- Mechanical, chemical and electrochemical surface treatment

Infrastructure

- 3D printing technologies: selective laser melting for metals, particularly titanium alloys
- Metallographic laboratory (SEM & EDX incl. in-situ mechanical testing and Ion Milling System for sample preparation, µCT, confocal microscopy, X-ray diffractometer)
- Mechanical test laboratory (static testing incl. climate chamber and video extensometer, dynamic fatigue measurement incl. tracking, uniaxial torsion testing, optical 3D scanner, tribology)
- Dynamic scanning calorimetry

Support

- Cantons of Basel-Stadt, Basel-Landschaft and Aargau
- Swiss Confederation
- Baur SA Sauges
- States of Baden-Württemberg and Rheinland-Pfalz
- Region Grand Est
- European Regional Development Fund (EFRE)
- INTERREG Oberrhein programme of the EFRE

Collaboration

- Kantonsspital Baselland
- Sensoptic SA
- École polytechnique fédérale de Lausanne (EPFL)
- Furtwangen University, DE
- Heidelberg University, DE
- Mainz University, DE
- HelpTech GmbH, DE
- iSYS Medizintechnik GmbH, AT
- INSA Strasbourg, FR
- Alsace Biovalley, FR
- Axilum Robotics, FR
- SAES Getters S.p.A, IT

Brushing your teeth without detergents

Enzyme-based toothpaste uses less aggressive chemical substances than normal toothpaste, enabling gentler oral hygiene. The complex action of the enzymes it contains is linked to one of the body's own protection mechanisms. However, enzymes are sensitive and do not keep for a long time, resulting in, until now, a shorter shelf life for the toothpaste. Researchers at the Institute for Chemistry and Bioanalytics have optimised the composition of an enzyme toothpaste so that their industrial partner has been able to launch an effective, chemically stable and long-lasting product on the market.

Reading the ingredients lists of some toothpastes feels like being in a chemistry lab: the well-known fluoride and menthol, antibacterial agents such as triclosan, preservatives, colouring and a substance called sodium lauryl sulphate, or SLS for short. Chemically speaking, SLS is a detergent, killing bacteria and ensuring foaming when brushing teeth.

But SLS has fallen out of favour, being said to irritate the oral mucosa and cause aphthae. Hence, like other manufacturers of dental care products, the Swiss firm Curaden looked for an alternative. In cooperation with the HLS, various enzyme-based toothpastes were developed.

"Our oral flora consists of 700 different species of bacteria. There are no good and bad species, only the wrong oral hygiene. Our research is doing something about it."
Michel-Angelo Sciotti

Michel-Angelo Sciotti, a molecular biologist in the Institute for Chemistry and Bioanalytics at the HLS, co-developed and tested the enzyme toothpaste. Describing the challenge, he says: "The enzyme system is much more complex than the chemical mechanism in conventional toothpaste. Enzymes are part of a biological system and are more or less stable depending on environmental conditions; their activity when brushing teeth depends on various factors." These include the bacteria naturally living in the oral cavity, brushing duration, how soon afterwards the mouth is rinsed and how long the tube has been open. This makes enzymes difficult to use in oral hygiene products.

Nevertheless, enzyme toothpaste has one big advantage: it triggers active substances that are already present in our mouth, either created by oral mucosa cells or by saliva, and it produces others that enhance the cleaning effect. It also preserves the mouth's microbiological balance. Sciotti says: "There are 700 different species of bacteria in the oral cavity. Our diet and lifestyle make some of them problematic since at some point they can cause tooth decay or periodontitis. We must curb their excessive growth."

This is where enzyme toothpaste comes in. Unlike ordinary toothpaste, which acts like a detergent and breaks down all microorganisms, it cleans more gently and leaves your own protective bacteria

in your mouth. This makes the toothpaste much more effective.

In the development phase the research team tested two enzymes: glucose oxidase and lactoperoxidase. While not attacking bacteria themselves, during brushing they form two active ingredients: hydrogen peroxide and hypothiocyanite. Hypothiocyanite is formed by lactoperoxidase from thiocyanate, which is present in saliva; it mainly attacks germs that enter the oral cavity from the environment. However, evolution and dietary changes have led to the development of bacteria which live in the body and cause tooth decay and periodontal disease. A different remedy is required for these, for example the antibacterial hydrogen peroxide, which is already produced in small amounts by oral mucosa cells. When brushing teeth with enzyme toothpaste, it is produced from sugar and oxygen with the aid of glucose oxidase. "In the same way bees give honey its antibacterial effect," says Sciotti.

Although the active ingredients, hydrogen peroxide and hypothiocyanite, are effective against caries bacteria, they are very unstable and thus cannot simply be added to toothpaste. Rather, they must be freshly produced in the oral cavity with each brushing, making it difficult to regulate the toothpaste enzyme system. Moreover, the enzymes must stimulate the formation of hydrogen peroxide and hypothiocyanite rapidly, since you usually only brush for a few minutes and then rinse your mouth, causing the active ingredients to disappear again. In order to solve this problem, Sciotti and his team have refined the formula of the toothpaste several times.

Sciotti explains that initial results were surprising. "We used to think that the enzymes were unstable. Then we saw that the system was not airtight and hydrogen peroxide was being formed during the mixing process and was decomposing the enzymes in the tube. To prevent this, we had to add an exact level of antioxidants so that the production of hydrogen peroxide was only triggered by brushing, but happened as soon as brushing started."

The researchers developed a preclinical study test procedure specifically for this project. In the lab they blended bacterial cultures with toothpaste for ten minutes and left the mixtures on a growth medium overnight. They then counted how many bacteria had survived contact with the toothpaste.

During testing Sciotti and his team discovered a peculiarity of the interaction between the two enzymes. "The toothpaste which contained both glucose oxidase and lactoperoxidase had no effect on Streptococcus mutans bacteria," says Sciotti. "It seems that all the hydrogen peroxide produced was used up to form hypothiocyanite." In contrast, toothpaste containing only glucose oxidase was highly effective against these caries-causing bacteria. In use, it produces a certain amount of hypothiocyanite from lactoperoxidase in our saliva, but the excess unconverted hydrogen peroxide remains and has a strong antibacterial effect against Streptococcus mutans. Thus, this single enzyme formulation ultimately combines the effects of hypothiocyanite and hydrogen peroxide. By not adding lactoperoxidase, Sciotti also reduced production costs and increased the stability of the toothpaste.

As well as ongoing long-term studies, the researcher is also working with Curaden on other innovative products for oral hygiene.

Methods
- Enzyme systems, enzyme kinetics
- Stability and stress studies
- Enzyme immobilisation
- Oral microbiology, Streptococcus mutans
- Microculture-based antibacterial assays
- Short exposure antibacterial assays
- Preclinical and clinical studies
- Toothpaste formulation

Infrastructure
- Plate reader spectrophotometer
- Microbiology laboratory safety level 2
- Glove box workstation

Support
- Innosuisse

Collaboration
- Curaden AG
- Centre for Dentistry at University Hospital Zurich

A water filter for emergencies

Clean drinking water is a luxury. In many parts of the world water is polluted and full of harmful bacteria; the problem is particularly acute during humanitarian crises, such as in refugee camps. A simple short-term solution is a domestic water filter. There are many different types on the market, but their quality varies widely, so HLS researchers tested filters in three disaster areas. Working with the local population, they have made suggestions for product improvements.

"As a research institute, we can help aid organisations invest in products that work well and reliably in specific situations."
Maryna Peter

Drought, floods or military devastation can all deprive people of access to a functioning clean water system, leading to humanitarian crises that aid agencies try to alleviate. But often there is neither time nor money to install entire water supply systems quickly. Household filters are an alternative way to supply clean water in the short-term and have been used for many years with varying degrees of success. Maryna Peter and her team at the Institute for Ecopreneurship have therefore been commissioned by the Humanitarian Innovation Fund to investigate which filters work best in humanitarian emergencies.

In the joint project with Caritas Switzerland, Eawag and the Italian aid organisation Cesvi, the HLS researchers tested five pre-selected commercially available household filters. They wanted to know how easy the filters were to assemble and use, how robust they were and whether they reliably removed germs from the water.

"First we tested the filters here in the HLS laboratories," explains environmental engineer Peter. "They were then distributed to families living in refugee camps in Somalia, in rural areas in Kenya and in the West Bank. These families live in small households, often with their animals. In some places, the groundwater has a high salt content, in others, wells cannot be built for political reasons. Attempts are made to collect rainwater, but this stored water is of poor quality and household filters could help."

Household filters usually consist of two buckets, the upper containing a filter to remove bacteria and other microorganisms, the lower one to collect the clean water. Such a small, practical filter system can easily fit on a table. Peter and her team tested different models of ceramic and membrane filters, both of which work on the same principle, with small pores that trap bacteria when the water flows through. However, ceramic filters break more easily and have to be cleaned by hand whereas membrane filters should not be touched and have backwashing mechanisms.

The researchers tested three ceramic filters and two membrane filters – 150 filters each in Kenya and the West Bank and 120 in Somalia. Every family that wanted to could take part and the filter type was assigned at random. A special feature of the study was that each household was allowed to test a second filter after the first four months. Peter explains: "Many needy people in developing countries do not dare criticise anything; they are afraid that they will then no longer receive humanitarian aid or are very reluctant to criticise because of their culture. By trying out two filters, they found it easier to compare the advantages and disadvantages and to criticise. That worked very well."

The researchers analysed the filters' technical performance – their actual microbiological cleaning effect – at low cost on-site test stations. They found that the filters worked better in the lab than in practice. Water quality was certainly improved but not by as much as the manufacturers expected. Working with Eawag, the researchers developed a simple test for use in crisis regions, to enable aid organisations to see for themselves whether the filters work properly under real-life conditions.

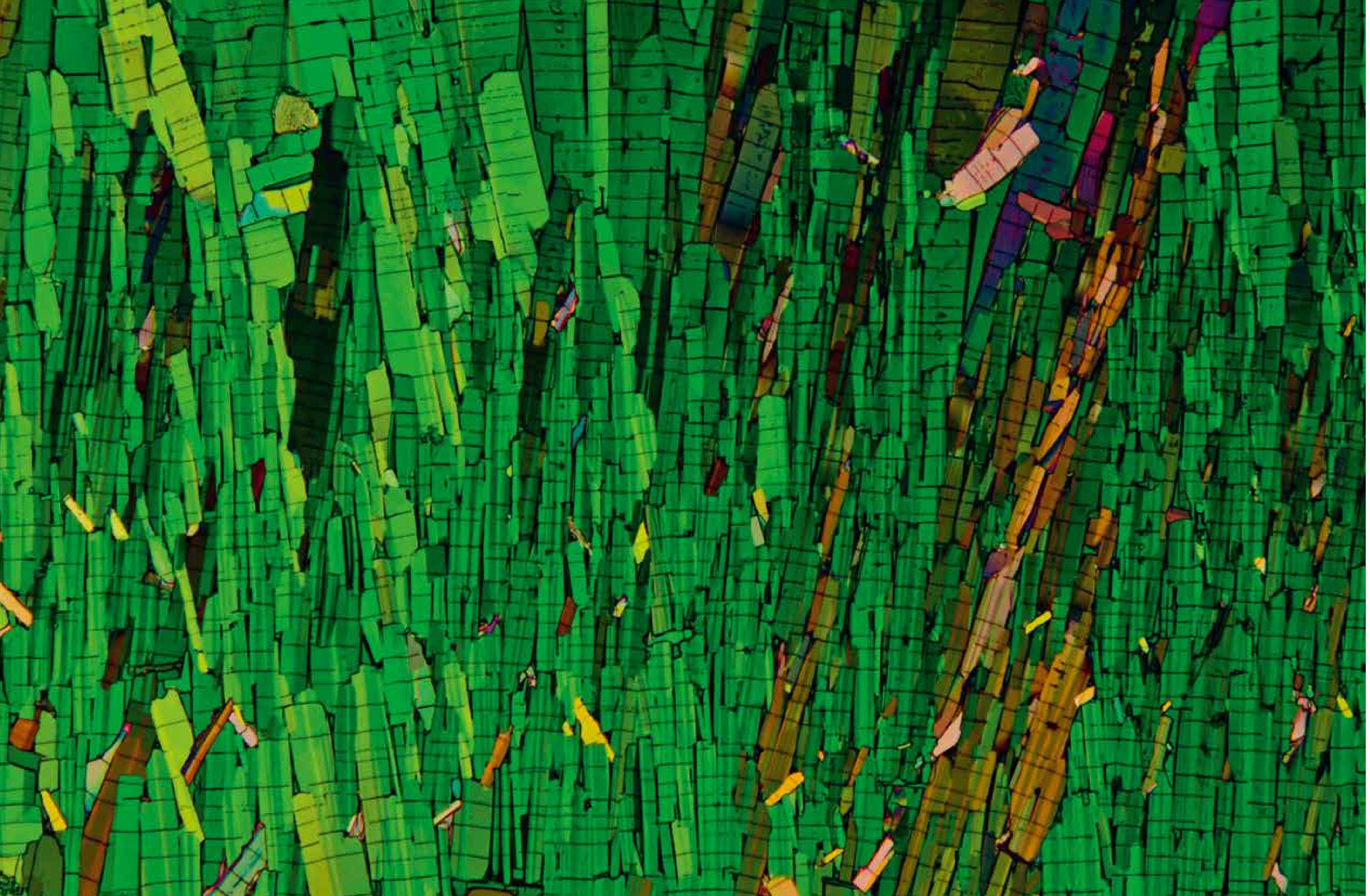
In addition to testing the filters' performance, the researchers were interested in whether families could install a filter by themselves and use it regularly. They therefore filmed several documentaries and ran video interviews, giving people the chance to talk about their experiences and make suggestions for improving the filters. Of all the products examined, the best was found to be one of the ceramic filters. Nevertheless, although all the filters worked well technically, the research revealed that there is still room for improvement in the design. At three co-design workshops, the researchers and the users therefore developed ideas together on how to improve the filters. This could be done very simply, for example by using lids to stop insects getting into the water or fitting tougher hoses to protect against rats. "Only by running field tests could we see which products are both accepted and suitable," says Peter. "As a research institute, we can help aid organisations invest in products that work well and reliably in specific situations." The findings from this multinational project show how important household filters, their further development and practical test methods are for people in crisis regions.

Methods
- Flow cytometry
- Simple low-cost field methods for water quality analysis using bacterial plating (Nissui Compact Dry Plates) as well as turbidity, oxygen and conductivity analyses
- Automated monitoring of water use and flow using Solinst Pressure Dataloggers
- Mobile phone-based data collection and questionnaires
- Human centered design (e.g. co-design workshop)

Infrastructure
- Low cost field laboratories established for the analysis of filter integrity, recontamination and microbial regrowth using plating methods for Enterococci, Escherichia coli and total coliforms

Support
- Humanitarian Innovation Fund

Collaboration
- Caritas Switzerland
- Eawag
- Cesvi, IT
- Italian Agency for Development Cooperation (AICS)
- Palestine Polytechnic University
- Jomo Kenyatta University of Agriculture and Technology, KE
- Elrha's Humanitarian Innovation Fund, UK

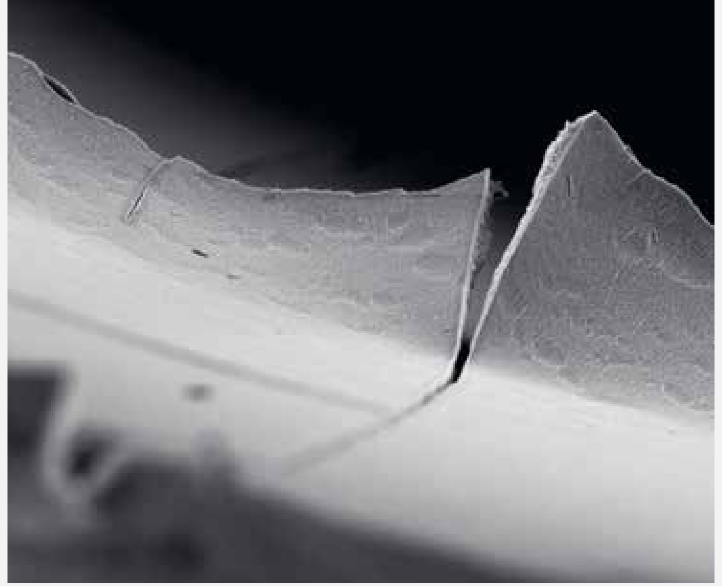


Environment and Resources

In Switzerland, natural resource management is critical due to the lack of raw materials, necessitating a sustainable approach to the environment. In a key research area, HLS scientists 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.

Tailor-made membranes

Economic efficiency and environmental protection are often perceived as conflicting goals. Nevertheless, research shows that they can be combined if scarce resources are used efficiently or if raw materials are recovered. In the case of phosphorus, researchers at the HLS are already on the way to achieving this with the help of a multi-layer membrane that can be customised for specific objectives. In laboratory tests they have recovered 90 per cent of the phosphorus from acid waste solutions. The new technology will be used to extract phosphorus from sewage sludge.



"The Layer-by-Layer membrane has outstanding potential for cleaning waste streams and recovering raw materials."
Kirsten Remmen

As a country with limited natural resources, Switzerland depends on imports of raw materials. This reliance can be offset by recovering raw materials from waste products such as the sludge produced during water treatment in sewage plants. In addition to phosphorus, this sludge also contains large quantities of metals and heavy metals. Since phosphorus is economically vital as a basic component of fertilisers, its recovery from sewage sludge will be compulsory in Switzerland from 2026. However, many existing recycling technologies are still expensive or inefficient. The engineer Kirsten Remmen from the Institute for Ecopreneurship at the HLS has now developed an improved method for phosphorus recovery by nanofiltration using a modified layered membrane.

Nanofiltration is a well-known technology applied in the pharmaceutical and food industries. Unlike microfiltration and ultrafiltration, in which pore size determines which particles pass through the membrane, nanofiltration uses the charge of the ions. "Nanofiltration membranes are charged, enabling them to differentiate between polyvalent and monovalent charged ions," says Remmen. "Monovalent ions can pass through the membrane but polyvalent ions are retained."

"Before conducting the nanofiltration, sewage sludge must pass a multi-stage process in which metals, heavy metals and phosphorus, among other things, are dissolved using acid," explains the researcher. After that, individual components are separated using one of several possible technologies. "In Switzerland liquid–liquid extraction is applied, although nanofiltration could be used as the final purification stage to further improve the quality of the product." The problem is that commercially available nanofiltration membranes are not very efficient at sewage sludge phosphorus recovery.

Nanofiltration should retain metals and only allow the important phosphorus to pass through the membrane. In order to achieve this, Remmen and her team have modified the nanofiltration membrane properties layer by layer (LbL), in particular the charge. "Unlike most conventional negatively charged nanofiltration membranes, an LbL membrane can be charged positively; in this way we can also vary the charge strength," explains the engineer. The more positive the charge of the LbL membrane, the more metals it retains.

The researchers coated a hollow fibre membrane with charged polymer polyelectrolytes, some with positive and some with negative charges. Plus and minus layers are applied alternately, together forming a so-called bi-layer. "By altering the type and number of the bilayers, I can change the properties of the membrane and hence its filtering properties," explains Remmen. The big advantage of this membrane is the many parameters that can be individually adjusted and adapted to specific applications, such as the solution concentration or the polyelectrolytes used.

Remmen and her team have run laboratory tests on the LbL membrane's suitability for phosphorus recovery. Their experiment with an acidic model solution showed that the membrane allows permeation of 90 per cent of the phosphorus, which can then be processed for fertiliser, while unwanted metals were retained by the membrane. The researcher is pleased with this success: "There is still no satisfactory solution on the market. The LbL membrane has great potential for decontaminating acidic waste flows and recovering raw materials. Phosphorus is just one example."

Another advantage points to the future use of LbL membranes: the flow rate in Remmen's phosphorus recovery experiments was 16 times higher than conventional nanofiltration membranes, making this technology attractive for industry. Due to the acidic, viscous and highly osmotic leachate from sewage sludge, conventional membranes require either high pressure to force the liquid through the membrane or a great deal of time, both of which add to the expense. These high costs are one reason why recovery from acid waste products is not more widespread; until now it has been cheaper to neutralise and dispose of the acid. With the LbL membrane, smaller systems can be used for recovery, thus reducing the investment necessary. Remmen is convinced of the potential of customised LbL membrane technology; she and her team are working to make it suitable for industrial use and are developing a prototype with Pentair.

Methods
- Nanofiltration
- Layer-by-Layer modification

Infrastructure
- Inductively coupled plasma optical emission spectrometry (ICP-OES)
- Inductively coupled plasma mass spectrometry (ICP-MS)
- Scanning electron microscope (SEM)

Support
- Swiss National Science Foundation
- Innosuisse
- EU H2020

Collaboration
- RWTH Aachen University, DE
- Delft University of Technology, NL
- Pentair plc, UK
- Sandvik AB, SE
- IVL Swedish Environmental Research Institute

500°C and potassium

Sewage sludge produced during waste water purification contains not only biomass and pollutants but also precipitated phosphorus. By law, starting in 2026 this important component of fertilisers must be recovered, making Switzerland less dependent on phosphorus imports. In this context, HLS researchers are using pyrolysis to turn sewage sludge directly into fertiliser. This oxygen-free thermal process produces high-quality fertilisers, can easily be integrated into existing sewage treatment plants and will shortly begin a pilot phase.

"The project aims to integrate the process as a component in existing sewage sludge treatment systems in order to achieve the broadest possible implementation."
Thomas Wintgens

There are several reasons why Swiss farmers are not allowed to put sewage sludge on their fields: it is contaminated with persistent chemicals, pharmaceutical residues and toxic heavy metals, which seep into the ground and threaten water habitats. Therefore, thermal sewage sludge recycling via incineration is now standard. The disadvantage of this is that the phosphorus contained in the sludge, which has great agricultural value as a fertiliser, is lost.

The Environmental Technology Group at the HLS Institute for Ecopreneurship, in cooperation with industry and research groups, has developed a technology that makes sewage sludge suitable for agricultural use. "The project aims to integrate the process as a component in existing sewage sludge treatment systems in order to achieve the broadest possible implementation," says Thomas Wintgens, head of the group. The companies and research institutions involved in the project have practical experience covering the entire value chain from the sewage treatment plant to agricultural fertiliser use.

High temperatures destroy organic pollutants

Central to this innovative process is pyrolysis. Like combustion, pyrolysis is a method of breaking down organic compounds at high temperatures but with an important difference, as project manager Anders Nättorp explains: "During combustion, a surplus of oxygen is added so that carbon is completely converted into CO_2. In contrast, with pyrolysis we add very little oxygen in order to obtain different thermal transformation products. This is a reductive process." The new process also has a combustion stage that completely converts every single organic component. Operating temperatures above 500 degrees Celsius not only destroy the organic pollutants but also evaporate heavy metals, which can then be isolated from the exhaust gases.

The research consortium already possesses experience using this technology with industrial and municipal waste. Although preliminary studies showed that the concept is also well suited for treating dried sewage sludge, the scientists had to overcome another challenge: plants could not absorb phosphorus from the pyrolysis ash very well. "Pyrolysis produces different mineral phosphorus compounds, some of which are so stable that even citric acid secreted by some plant roots cannot dissolve them," says Nättorp.

Potassium turns pyrolysis sludge into fertiliser

The researchers overcame this by adding potassium compounds to the pyrolysis, leading to the formation of mineral compounds more easily absorbed by plants. "With pyrolysis fertiliser we achieved 90 per cent agronomic efficiency in experiments," reports Nättorp. "The plants grew almost as well with the new fertiliser as those that received the same amount of conventional phosphorus fertiliser. The research association has patented the process and has already given a name to the fertiliser: Pyrophos.

Before the sewage sludge ash can be marketed as a fertiliser, a final process step is needed for effective agricultural use. This concerns both the exact composition of the fertiliser and its form. Fertilisers for dry spreading have standard granule sizes and contain different components depending on the crop, especially potassium, nitrogen and phosphorus. With potassium as an additional pyrolysis reagent, the Pyrophos fertiliser provides two of the three most important plant nutrient requirements. If additional nitrogen is needed, it can simply be added.

Circular economy at the sewage treatment plant

As a test site for the Pyrophos process the researchers used the Altenrhein wastewater treatment plant, where sewage sludge from 300,000 inhabitants and food waste is digested and dried. It currently supplies the nearby cement industry with dry sludge as fuel, so the phosphorus is embedded in cement and lost. The Pyrophos consortium is now analysing whether this plant is suitable for a first implementation of the new process. "So far we have produced on a kilogram scale," says Wintgens, "but we are now increasing to the tonne scale. Our aim is to show that our process can recover phosphorus economically and at a significantly smaller plant size than conventional sewage sludge treatment."

Methods
- Calcination
- Wet chemistry (aqua regia and other digestions)

Infrastructure
- X-ray powder diffraction (XRD)
- Inductively coupled plasma optical emission spectrometry (ICP-OES)
- Inductively coupled plasma mass spectrometry (ICP-MS)

Support
- Innosuisse

Collaboration
- Altenrhein wastewater association
- CTU Clean Technology Universe AG
- Landor fenaco cooperative society
- Research Institute of Organic Agriculture (FiBL)

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.

Made to measure treatment

HLS researchers, in collaboration with firms in the Swiss medical sector, have developed a way to measure nutrients in the blood quickly and easily without the need to visit a doctor. Just a few microlitres of a blood sample taken at home are enough to analyse 20 different substances. The results are sent to a mobile phone app to identify and help counteract nutrient deficiencies. The companies involved in the project are already using the new process successfully, leading to infrastructure investment and new jobs.

Personalised medicine is on everyone's lips. It uses data from blood samples and stool analyses, from fitness trackers and patient questionnaires, with the goal of tailor-made medical treatment for each patient instead of standardised textbook therapy. The philosophy is that each person is an individual with very different habits, genetic data and microbiomes – the microorganisms that colonise them. These differences affect not only whether someone gets certain diseases but also how the body processes vitamins, trace elements and other nutrients. Thus general recommendations, such as on dietary supplements, may be ineffective since they are not tailored to the individual. This could soon change. In an industrial partnership with Baze Labs AG and Swiss Analysis AG, HLS researchers have developed a method for measuring vitamins, amino acids, trace elements and omega-3 fatty acids in a single drop of blood.

"The big challenge was to build a robust analytical system, using a small amount of blood, that is fast, valid and cost-effective."

Götz Schlotterbeck

The process is simple: having received a painfree blood collection kit by post, people collect a drop of blood at home and send it to the laboratory – as often as they want. A few days later they receive an analysis via the app and a recommendation as to which nutrients they need more of. "Vitamins and trace elements play an important role in the prevention of diseases and a healthy lifestyle,"explains Götz Schlotterbeck from the Institute for Chemistry and Bioanalytics at the HLS. "Many people feel the need to check them regularly."

Schlotterbeck and his team helped the Swiss companies to develop the analysis method and program the equipment. The biggest challenge for the researchers was the tiny amount of blood available for analysis. "Unlike with conventional blood samples we're only working with a few microlitres," says Schlotterbeck. "One microlitre is 0.001 millilitres and it is not easy to get a robust and valid analysis from this small quantity, even with modern systems."

Schlotterbeck and his team first investigated a solution using dried blood. Like with a blood glucose test, clients would need to prick their finger, collect a drop of blood on a card and send it back. However, this method was not as painless as they wanted.

Since the partner firm Baze initially focused on the American market, the opportunity arose for a different blood collection method: a US-approved device the size of a small computer mouse. "The device uses microneedles to draw very a small amount of blood from the upper arm totally painlessly. Customers send the device with the liquid blood back to Baze's US site, where samples are preserved for transport then sent to Switzerland," says the researcher. Swiss Analysis uses three analytical methods developed by Schlotterbeck's team to determine the 20 nutrients.

"It was vital to find out which substances had the physicochemical properties to be successfully analysed in combination," recalls the researcher. The main goal was cost efficiency; methods should be not only robust and valid but also fast. "Speed is key in analytical chemistry," stresses Schlotterbeck. The more you can combine, the shorter the overall analysis time. This is important financially too, because determining nutrients individually as before was too expensive to be realistic for regular private healthcare use.

The complete analysis of eight vitamins, six trace elements, four amino acids and two omega fatty acids now takes less than a day. The evaluation of the results is then sent to the client via an app, co-developed by the FHNW Institute for Information Systems, along with advice on suitable dietary supplements.

Although this service is not yet available in Switzerland, the Innosuisse-supported project has already had a positive effect on the Swiss economy. In order to meet consumers' needs, both firms involved in the project have not only invested in technical infrastructure but have also created jobs. The methods developed and tested at the HLS were transferred to Baze and Swiss Analysis. The HLS researchers are now working with another Swiss firm to develop a new method – to analyse proteins.

Methods
- Individualised assessment of micronutrient status
- Fitness and nutrition markers in blood samples
- Minimally invasive blood analysis with micro-quantity samples
- Multiple Reaction Monitoring (MRM) methods

Infrastructure
- High-performance liquid chromatography coupled with triple quadrupole mass spectrometer (LC-MS/MS multiplex)
- Gas chromatography with single quadrupole mass spectrometer (GC-MS)
- Inductively coupled plasma mass spectrometry (ICP-MS)

Support
- Innosuisse

Collaboration
- Baze Labs AG
- Swiss Analysis AG
- Biognosys AG

Rehabilitation with virtual trees

Every year about 16,000 people in Switzerland suffer a stroke. Many lose arm or leg movement as a result and the length of time taken for even small improvements is highly discouraging. To help these patients, HLS researchers together with their partners have developed a tracker app focused on arm movement rehabilitation. The app's sophisticated reward system motivates patients and helps them with targeted exercises.

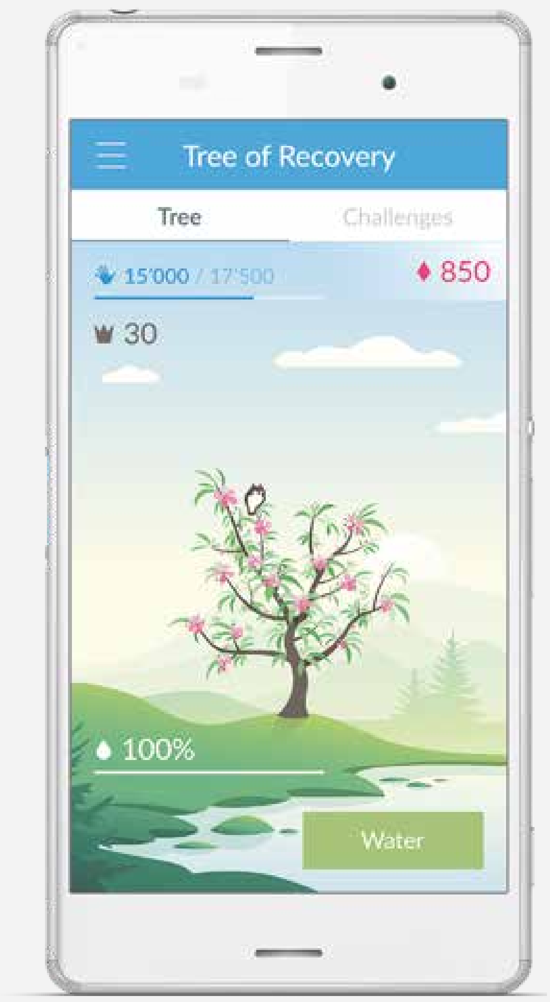
"Motivation and intensity are crucial for stroke rehabilitation. This is where we come in."
Denise Baumann

Many people lose their independence after a stroke, often being unable to walk, grasp anything or even bring a fork up to their mouth. The reason for this is a hemiparesis or hemiplegia and is particularly evident in the arms. A team led by Denise Baumann from the HLS Institute for Medical Engineering and Medical Informatics, along with partners from industry and research, have been working to help patients recover hand and arm function.

The success of the Innosuisse-funded ISEAR project (Integrated System for the Encouragement of Arm Rehabilitation) is based on a special fitness wristband and mobile phone app. Medical technology engineer Baumann explains: "In the first phase of rehabilitation, patients realise that their physical abilities do not recover spontaneously; in the subsequent chronic phase, some abilities even decline further from lack of use of the impaired body part. That's where we come in."

Patients need to be encouraged to move their arms, because even uncoordinated movements help create new nerve cell connections to take on lost functions. Experts call this adaptability of the brain 'neuroplasticity'. The effect is intensified by repeated controlled movements, so after a stroke, patients receive intensive physiotherapy at the clinic and an exercise programme at home. "Two factors are important for successful home training: intensity and motivation," says Baumann.

Even healthy people know the positive effect of a wrist pedometer. The arm rehabilitation tracker, developed by the firm yband therapy AG, is based on the same principle. Like a pedometer, it has acceleration and position sensors, the data from which enable it to calculate the number of steps using an algorithm developed at the HLS. The partner team at the ETH Zurich developed an algorithm for detecting arm activity and both algorithms are stored in the wristband's microcontroller, along with the parameters recorded. They are synchronised via Bluetooth and evaluated with the associated 'ArysMe' app, which Baumann and her team at the HLS have programmed for iOS and Android.



"The greatest challenge was to recognise and quantify the movements correctly: which signals or signal sequences count as real movements, what patterns do they form and how often are they repeated? These data are the basis of the reward system," reports Baumann.

The 'Tree of Recovery' virtual reward system is based on an idea by two undergraduates at Zurich University of the Arts (ZHdK). The Tree of Recovery is visible as a small tree in the app and only grows if someone has been active. As soon as predefined daily goals have been achieved or exercises have been performed correctly, the system gives virtual badges as a reward. These can be converted into virtual water for your Tree of Recovery so you can see your progress.

At the beginning the app shows only a few green hills and a little stream. The Recovery Tree starts as a seedling which gets bigger and bigger and, if it is watered regularly, eventually fills the whole screen. With more progress, leaves and blossom grow and animals appear; however, if the patient neglects their training, the tree stays the same size but dries out. This visual feedback is designed to motivate patients to continue working to improve their motor skills and achieve their individual daily goal, calculated by the tracker based on average arm activity. There are also other tasks that have to be done in order to water the tree. "Three minutes a day of intensive arm activity is such a task," says Baumann. The tracker recognises the movements and classes them as intensive or less intensive.

Stored exercises can be practised; for example, the physiotherapist reaches for an object or brings it accurately up to the mouth and the patient imitates this as well as they can. The exercise is stored as a motion template in the tracker; the app monitors the real movement patterns and compares them with the recorded template; if an exercise is performed correctly, the virtual reward helps the recovery tree to grow. In addition, physiotherapy specialists can use the professional 'Arys pro' app to compare arm movement data and better assess individual progress. To further motivate patients, a vibrating reminder function is built into the wristband which prompts them to train.

“Working with industry and other universities on this project has been both challenging and enriching.”

Denise Baumann

These and other functions are currently being investigated in a clinical study with patients at the University Hospital Zurich. The researchers are interested in whether patients cope well with the app and tracker, whether arm function is regained and if the app lacks any functions. They hope their work will help as many patients as possible find their way back to independence.

Methods

- Analysis and processing of inertial measurement signals
- Measurement signal-based activity and movement characterisation
- Dynamic time warping
- Development of applications for mobile devices

Infrastructure

- Inertial measurement units
- Tools for hardware related software development
- Software tools for signal and data processing
- Software development environment and versioning system incl. automated tests

Support

- Innosuisse

Collaboration

- yband therapy AG
- ETH Zurich
- Zurich University of the Arts ZHdK
- University Hospital Zurich

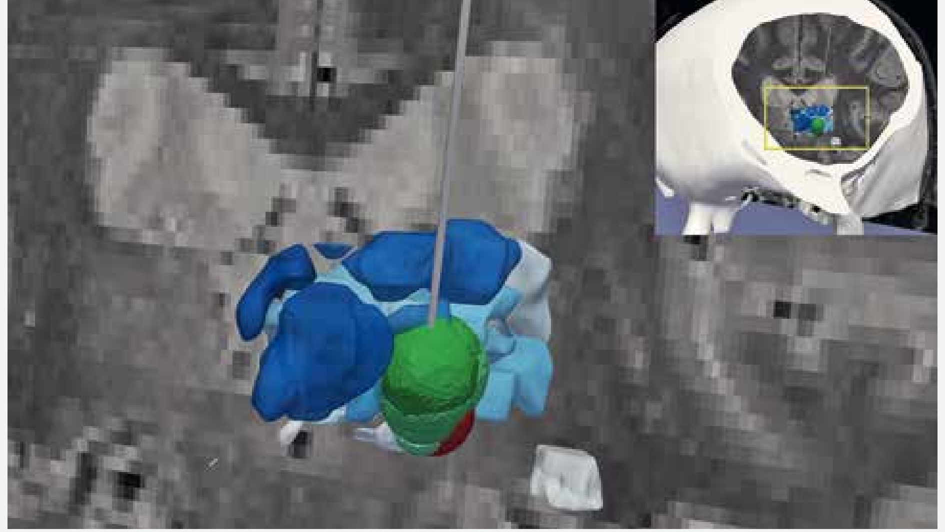
Using data to cope with tremors

HLS researchers have developed a method to make deep brain stimulation in Parkinson's disease even more precise and thus more effective. Deep brain stimulation, in which an electrode is implanted in the patient's brain, is a treatment for the symptoms of tremor and rigidity. The positioning of the electrode in the brain affects the level of improvement in the symptoms. The HLS's data-supported imaging method can identify the best stimulation location more reliably, enabling better intervention planning.

Parkinson's patients suffer from uncontrolled movement disorders such as tremors of the extremities and muscle stiffness, caused by dying nerve cells in the basal ganglia, an area of the midbrain that controls motor function. At present there is no cure. One treatment that can alleviate the symptoms of Parkinson's disease is deep brain stimulation. It works in a similar way to cardiac pacemaker therapy, replacing the defective function of the damaged cells with electrical impulses transmitted from an electrode to an area in the brain a few millimetres in size. The challenge is to implant the electrode in exactly the right place in the brain. Imaging techniques such as magnetic resonance imaging (MRI) and computer tomography (CT) can help, but the images do not show exactly where stimulation is needed. Simone Hemm-Ode from the HLS Institute for Medical Engineering and Medical Informatics (IM²) and her team have developed 'Improvement Maps', a method for measuring symptom variations during deep brain stimulation and visualising the data obtained on CT and MRI images.

"Using Improvement Maps in the operating theatre, it is possible to identify the region in the brain where electrical stimulation triggers the greatest improvement," explains the researcher. "It can also help to avoid areas of the brain where stimulation causes adverse effects such as speech disorders."

Around 200,000 people worldwide have already been treated with deep brain stimulation, including in Switzerland. The procedure involves drilling a small hole in the skull and pushing a needle-thin test electrode down to the basal ganglia in the brain. There, the neuronal activity is measured: electrical signals originating from nerve cells, which are different for each brain region and thus facilitate orientation in the brain during surgery. When reaching the region of interest, it is stimulated several times with a very weak electrical current. The patient is awake during the procedure because the therapeutic effects cannot be observed under general anaesthesia. Some of the stimulation improvements can be seen immediately according to Hemm-Ode: "For example if the patient's hand trembles at rest, when the stimulation begins the shaking decreases and ideally, is finally completely suppressed by the weak electrical stimuli."



Until now, doctors wrote down information about stimulation during the operation: the location of the electrode in the brain, how deep it was inserted, the current used to stimulate the brain region, its effect on symptoms and any side effects. The Improvement Map makes all this information visible digitally on individual layered images taken from previous MRI scans. Brain structures such as the basal ganglia can be seen in shades of blue and there are a range of fields on a red/green colour scale. The darker the green, the greater the improvement in symptoms such as tremor, whereas red shows where adverse effects have occurred. The two areas can overlap. Acceleration sensors attached to the arm during the examination provide information on how severe the tremor or rigidity is.

"The aim is to use all this information to find the best possible point for long-term electrical stimulation," explains Ashesh Shah, postdoctoral fellow at IM². The smaller the brain area stimulated, the fewer the adverse effects. In addition, the electrical current required is lower, extending the battery life of the stimulator. Like a pacemaker, this battery is implanted under the skin and is connected to the electrode via a thin cable. Replacing it necessitates a small operation, hence extending battery life means less disruption for the patient.

The HLS researchers developed the Improvement Maps with a team from the University of Linköping in Sweden and the Clermont-Ferrand University Hospital in France, using clinical study data from patients with Essential Tremor or Parkinson's disease. After the operation, they used this data to create 3D simulation models which, for each patient, show the precise location in the brain where stimulation brings the greatest improvement. The next step for the team is to make this visualisation available during surgery in real time.

Methods
- Intraoperative quantitative tremor and rigidity evaluation
- Acceleration sensor recording and analysis
- Surgical planning
- Patient-specific brain models of the thalamic region
- Patient-specific electric field simulations
- 3D data analysis
- 2D and 3D patient-specific data visualisation

Infrastructure
- Acceleration sensors
- Acceleration sensor platform for symptom evaluation
- 3D printed biocompatible sensor housing
- Data acquisition software
- Stereotactic frame
- X-ray systems
- Brainlab 'iPlan' surgical planning software and expert tool
- Matlab for data analysis
- Paraview for visualisation

Support
- Swiss National Science Foundation
- SATW Germaine de Staël

Collaboration
- University Hospital Basel
- University Hospital Bern
- University Hospital Clermont-Ferrand, FR
- Linköping University, SE

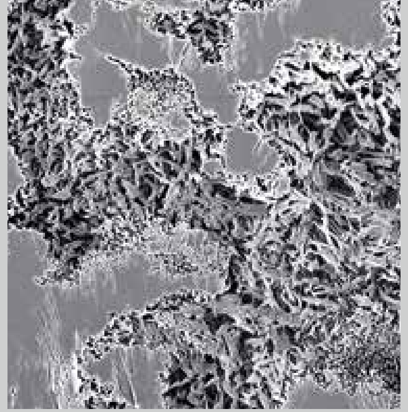
Summary Reports

A knockout blow for knockout drops: a rapid test for nightclubs

Abuse of butyric acid derivatives in Swiss nightclubs is on the rise: low doses of gamma hydroxybutyrate (GHB) and gamma butyrolactone (GBL) give a feeling of euphoria and have names such as Fantasy, Liquid Ecstasy or Blue Nitro in the club scene. The main problem however is not voluntary consumption. "These substances are particularly dangerous because they are put into other people's drinks as knockout drops – so-called 'date rape' drugs. They lead first to dizziness and nausea and in less than half an hour they cause a coma," reports HLS biochemist Eric Kübler. After waking up, victims usually remember nothing at all. To help prevent this, Kübler, his research group and industry experts are developing a rapid test that shows in seconds whether a drink has been laced with the dangerous chemicals.

The research team discovered how to detect these substances chemically in a previous project. "We found that an enzyme test was most suitable," says Kübler. Transferring this method from the lab to the bar requires the test to be practical, clear and cheap. The solution is an inconspicuous strip of filter paper, impregnated with the chemical test system and attached to a plastic holder. If a drink contains GHB or GBL, the test strip dipped in it turns dark purple in seconds, making it easy for people to check drinks themselves.

The chemical test system consists of five substances, of which three, the enzymes, are still produced on a laboratory scale; the HLS's new process technology centre will be used to scale-up production for larger quantities. Kübler: "We can produce enough enzymes there even if the complete product is ready for the market and produced on an industrial scale." In-house production not only keeps costs down but was important for the development process, as the researcher explains: "A big challenge was that alcohol and sweet or sour mixers trigger background reactions that can also cause the test strip to turn purple; the enzymes must act rapidly but must not give false positives. That's why we tested several variants of the enzymes, all of which we had to produce first." The researchers are currently testing the shelf life of the first industrially produced batch. The 'dip&read' test strips will soon be available free of charge at bars and clubs in the same way as ear plugs at concerts.



A gentler way to produce lactic acid

Lactic acid preserves food and is the basis of sustainable and biodegradable plastics. It is still mainly obtained via a biotechnology process which uses chemicals that have to be removed again later. HLS researchers have developed an alternative: using a membrane process, they isolate and purify lactic acid directly, sustainably and without additional chemicals.

Tablets: ice cold, bone dry and lightning fast

Researchers from the HLS Institute for Pharma Technology, in cooperation with Rohrer AG in Möhlin, have developed a new manufacturing process for tablets that dissolve in the mouth in a few seconds – without any additional liquid. This is not only practical but also makes it easier for people who have problems swallowing to take medication. The tablet can dissolve so quickly because of how it is produced: it is freeze-dried and has a very porous structure. Water in the saliva can therefore penetrate immediately, dissolve the tablet and release its active ingredients.

In the Innosuisse-sponsored project, the HLS researchers developed a system where tablets are formed directly in the final packaging. Rohrer built a laboratory-scale prototype machine which fills the blister pack cavities, first with a solid mixture and then with a liquid containing active ingredients and auxiliary substances. The damp mass is frozen with liquid nitrogen before a vacuum pump extracts the water from the tablet. It is vital that the ice does not melt but goes straight to a vapour; if not the tablets clump and cannot dissolve as quickly.

The researchers systematically refined the mix ratio, temperature and vacuum strength so that the tablets can be removed from the pack undamaged and will dissolve in the mouth within ten seconds, with no unpleasant sensation. Compared to conventional freeze-drying, which often takes a day or more, the HLS team have reduced the drying process to a few hours. They have already tested the patented process for active ingredients such as insulin, ibuprofen and vitamin C.

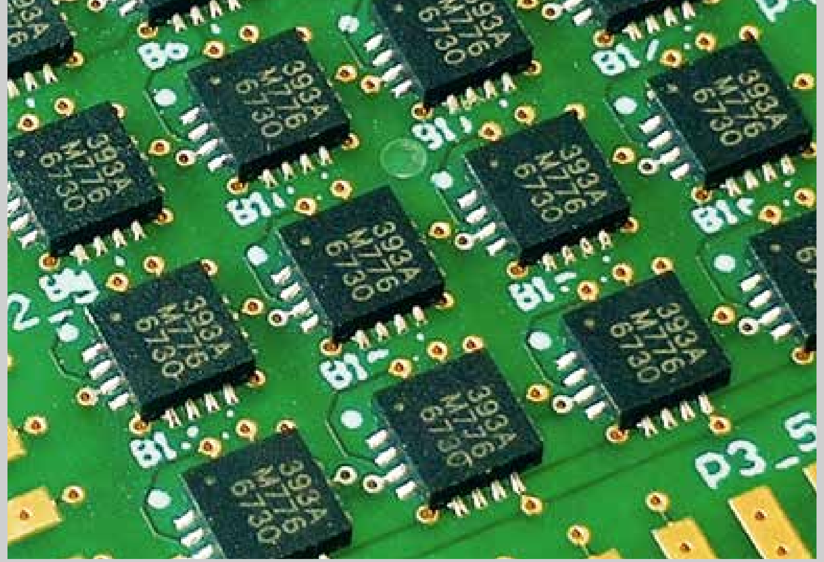
Inspired by camel blood

Targeted medical diagnostics and treatments using antibodies are an established alternative to conventional drugs. Researchers from the Institute for Chemistry and Bioanalytics have tested a new class of 'Sybody' antibodies which were developed in Markus Seeger's research laboratory at the University of Zurich and which are derived from camels. These fragments are one-tenth the size of conventional antibodies and have several advantages that make them good candidates for immunological diagnostics or disease treatment.

Antibodies are proteins which an organism uses to defend itself against foreign agents such as bacteria. The function principle is simple: bacteria and other extraneous entities have molecules on their surface called antigens, which have a characteristic shape. The immune system forms specific antibodies against these structures that fit their form exactly and dock to them. This selectivity, as well as the fact that they cause few side effects, is what makes antibodies so interesting for medicine. They are already used in the treatment of rheumatism, cancer and multiple sclerosis for example and as a vaccine against infectious diseases.

Coupled with a radionuclide, they make tumour cells or inflammation visible.

Antibodies have a characteristic Y-shape consisting of several small fragments called domains. The outermost part of the Y is critical for the high degree of selectivity of the antibodies, which means they only dock to certain antigens. "This protein – the small, exactly fitting part of the antibodies – is sufficient by itself for binding to the corresponding surface structures," explains Daniel Gygax, biochemist at the HLS. Gygax and his team used biophysical methods to characterise the camel antibody fragments modified by Seeger's research group. In particular, the researchers investigated how quickly these Sybodies bind antigens and when the binding releases. They chose Sybodies because their selective fragment consists only of a polypeptide chain and can thus be produced in bacteria easily and quickly. Due to their size, the small Sybodies have other advantages: they enter tissues faster, and are metabolised faster.



New functionalities in MRI scanners

Modern magnetic resonance imaging (MRI) scanners have a static magnetic field 60,000 times stronger than that of the Earth. The imaging process is based on small deviations in this field. These 'magnetic field gradients' are used to locate and measure resonance signals, making it possible to determine the composition of structures in the human body.

Researchers at the Institute for Medical Engineering and Medical Informatics have developed a method using nine sensors to measure these magnetic field gradients extremely precisely. The result is a real time 3D map showing the strength and orientation of the gradients inside the MRI tube at each individual measured point.

This new procedure greatly expands the range of MRI applications. The magnetic field sensors are only a few micrometres in size so they can be mounted on ECG electrodes or in surgical tools to track their position in the MRI tube in real time. The concept can also characterise gradient quality: the system is fast enough to detect fields lasting milliseconds, which can help quality control and the characterisation of new magnet designs.

New sources of Scandium

Scandium, like most scarce things, is highly valuable. The element belongs to the group of rare earth metals and has key applications; for example, it is used in fuel cells and alloyed with aluminium it strengthens aircraft structures. Scandium is only found as an accompanying element in ores mined outside Europe, but it is also contained in waste from the European chemical industry. As part of the EU SCALE project, HLS researchers are investigating how this rare element can be extracted from waste streams using membrane filtration. An efficient recovery technology could contribute to an independent European supply of scandium and thus provide security for important economic sectors.

Some of our Partners

Switzerland

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International

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Contacts

School of Life Sciences
Prof. Dr. Falko Schlottig
Director
Hofackerstrasse 30
CH-4132 Muttenz
+41 61 228 55 71
info.lifesciences@fhnw.ch

Institute for Medical Engineering and Medical Informatics
Prof. Dr. Erik Schkommodau
Head of Institute
+41 61 228 54 19
erik.schkommodau@fhnw.ch

Institute for Chemistry and Bioanalytics
Prof. Dr. Sebastian Wendeborn
Head of Institute
+41 61 228 55 45
sebastian.wendeborn@fhnw.ch

Institute for Pharma Technology
Prof. Dr. Georgios Imanidis
Head of Institute
+41 61 228 56 36
georgios.imanidis@fhnw.ch

Institute for Ecopreneurship
Prof. Dr. Philippe Corvini
Head of Institute
+41 61 228 54 85
philippe.corvini@fhnw.ch

Learn more about the FHNW School of Life Sciences at **www.fhnw.ch/lifesciences/en** or on our social media channels:

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FHNW University of Applied Sciences and Arts
Northwestern Switzerland
School of Life Sciences
Hofackerstrasse 30
CH-4132 Muttenz
Switzerland

T +41 61 228 55 77
info.lifesciences@fhnw.ch
www.fhnw.ch/lifesciences