FHNW School of Life Sciences

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

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A conversation with Falko Schlottig

During the Corona pandemic, the new FHNW Campus Muttenz had to prove itself under extremely challenging conditions just three years after its inauguration. Falko Schlottig, Director of the FHNW School of Life Sciences (FHNW HLS), draws positive conclusions. With its modern, flexible infrastructure the campus is not only ready for the future, but also ideal for the present.

“The fact that we have come through the Corona period so well and that our university has thrived, is thanks to the outstanding performance of our staff and excellent cooperation with our students.”

Falko Schlottig

Mr Schlottig, an important aim of the new campus development was to enable greater collaboration. Today, three years after the inauguration, has this happened as you imagined at the time?

Throughout the university, various platforms are already running: some are formalised, such as Digital Life Sciences; others have arisen – and are continuously being formed – from informal collaboration across institutes, such as Biofabrication or 3R. So we are certainly on a very good path, but we still have some way to go.

How do these interdisciplinary projects influence the university, and in what direction should it go?

We have been able to set new priorities and sharpen the profile of the university. For example, we are working intensively in the field of digitalisation in life sciences. This starts with IT specific for life sciences based on our expertise in the natural sciences and engineering, moving from there to optimisation and modelling solutions, and on to diagnostics, analytics, medical IT, sustainability, processes and automation. Here too, the focus is on solutions to questions arising from practice. Because we operate at this interface between pure science and practical applications, we can see where we need to strengthen ourselves further as a university. Our open channels of communication, both internally and with colleagues in industry, help in this.

How is the campus perceived by students and researchers?

It has significantly increased the visibility and attractiveness of the university and of its range of services in further education, continuing education and research. Our staff and students are very happy with the campus and especially with the laboratory infrastructure.

What is the significance of the new Process Technology Centre (PTC)?

The PTC is unique for a university. We can reproduce the complete production chain there, from experimental set-up to large scale. This is exciting for the students, whether they are producing antibodies, brewing beer or pressing tablets. They learn technologically relevant processes, not just in a small laboratory but on a scale very close to practice. Also for industry and research institutions, the PTC is a unique selling point of our university, and cooperation has become much more intensive as a result.

What innovations are planned for further and continuing education at the university?

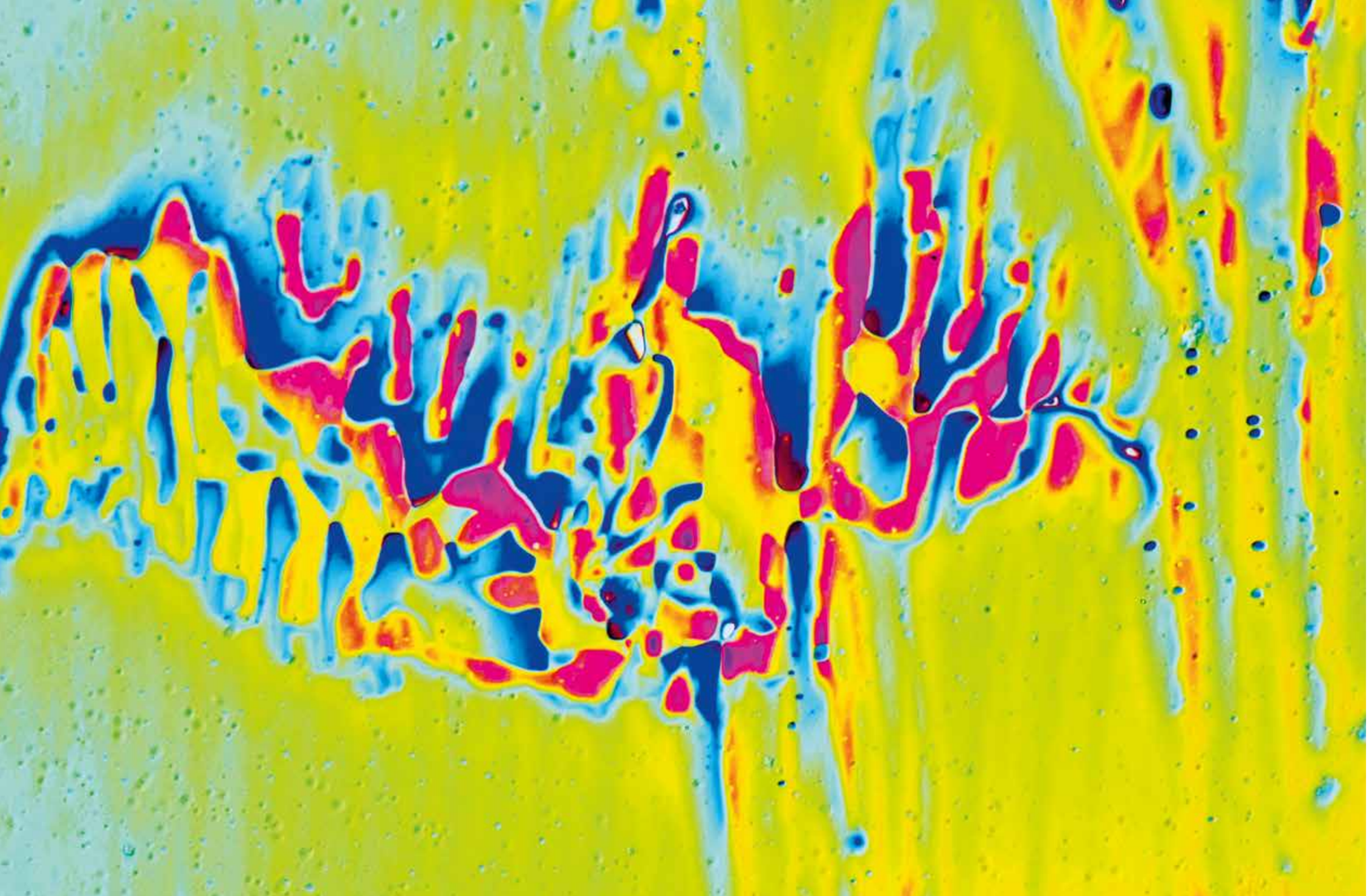
We have developed a new Master’s programme in Medical Informatics, a combination of medical informatics and business IT which was highly successful from the outset. We also constantly develop and update existing courses in the Bachelor’s, Master’s and continuing education programmes. With our advisory board and our industry partners, we are intensively engaged in identifying skills needed for the future and we include those in our education and training programmes.

In the Corona pandemic, does a campus like Muttenz offer advantages?

Having so many modern laboratories in close proximity has helped us enormously in coping with these difficult times. By organising research in two shifts, we were able to continue working without interruption despite the restrictions. It was also possible to run all the student practicals with a shift system and by moving external internships in-house. Importantly, by participating in practicals together our students could maintain contact with their colleagues.

What were the key goals of the university during this time?

To provide the most complete education possible in terms of quality and content, to ensure the health of students and staff and to contribute to society. The fact that we have come through the Corona period so well and that our university has thrived, is thanks to the outstanding performance of our staff and excellent cooperation with our students. Even during the pandemic, we are trying to make everything possible for our students within the limitations of the circumstances. This is only possible with unconventional ideas and with the commitment, passion and hard work of our staff.



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 FHNW HLS are therefore developing practical solutions for the digital age. With modern pharmaceutical technology they are driving the development of new drugs and applications.

De-coding complex diseases

Despite decades of research, many diseases cannot be treated successfully as science still does not fully understand what causes them. This is particularly true for illnesses in which multiple factors interact, such as chronic liver disease or Alzheimer's disease, and which are often diagnosed at advanced stages. Researchers at the FHNW HLS are using elaborate cell culture systems to model these diseases and gain a better understanding of the mechanisms behind them. This ground-breaking work also contributes to a reduction in animal experiments.

"In our models, we can watch human cells develop the characteristics of liver fibrosis or Alzheimer's disease."

Laura Suter-Dick

Some diseases have a single cause, such as the bacterium Vibrio cholerae for cholera. Many others develop via the interaction of several factors, for example genetic predisposition, an unhealthy lifestyle and environmental effects. Since identifying a clear cause is often impossible, such illnesses are called complex diseases and are often difficult to diagnose and treat. Cell biologist Laura Suter-Dick from the Institute for Chemistry and Bioanalytics at the FHNW HLS has dedicated herself to researching these diseases on a cellular level: "Understanding the molecular mechanisms that underlie a complex disease is essential for successful treatment. Various factors can interact and trigger the development of the disease – or they may trigger cellular processes which then cause the disease."

To study such processes, researchers like Suter-Dick work with miniature replicas of organs called 3D models or organoids in which diseases can be simulated. These models contain organ-specific cell types that closely mimic a real organ in their function and layout. In her cell biology and in vitro toxicology laboratory at the FHNW HLS, Suter-Dick is developing sophisticated 3D cell culture systems which she uses, for example, to simulate chronically diseased liver tissue or Alzheimer's disease. The researcher and her team want to use this technology to find markers that could enable early diagnosis and treatment options, as well as to look for ways to prevent the development of the disease altogether. "The earlier you detect a disease, the more effectively you can treat it," says Suter-Dick.

From cell to model

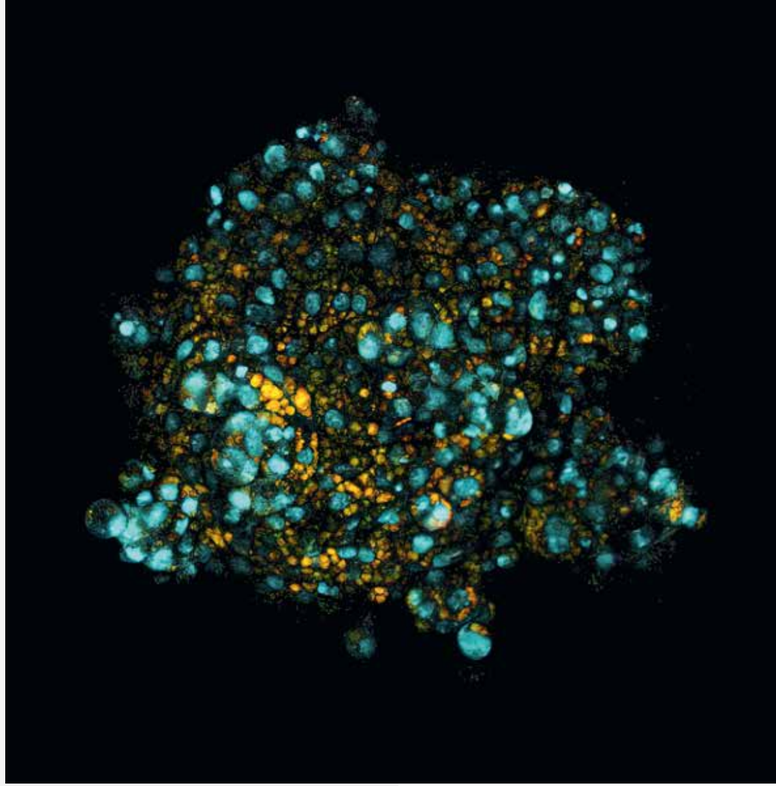
The scientist bases her research on the 3R principle – "replace", "reduce" and "refine" –, a guideline that aims to work responsibly with laboratory animals and to reduce and replace animal experiments. "There is often no need for an animal model," explains Suter-Dick. "If we recreate the physiological architecture of a tissue in the lab, we reproduce its physiological function." Hence the researcher builds her cell systems under specific conditions to resemble the tissue they are designed to imitate. Since real organs need a range of cell types running different processes in order to function, the models also do not consist of just a single cell type. Imitation of the disease under investigation begins during the cell growth phase: if the researcher wants to simulate a disease, the cells are exposed to the causes from the start.

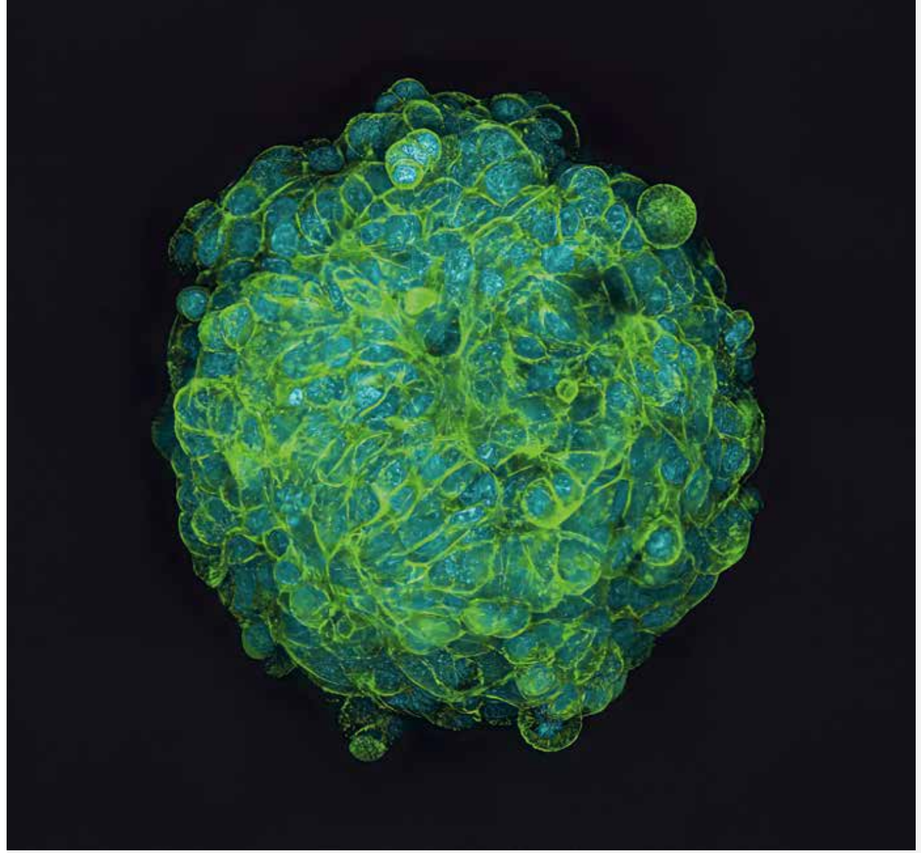
The example of liver disease

A disease model with which Suter-Dick's group has many years of experience is liver fibrosis, a chronic condition that causes pathologically activated cells to deposit collagen fibres. Liver tissue is gradually replaced by connective tissue and the organ becomes scarred. There are many causes, including chronic inflammation from viral infections such as hepatitis C, but also medications or toxins that stress the liver over a long period. For example, prolonged high alcohol consumption can cause a fatty liver, which leads to fibrosis. However, fatty liver can also develop for other reasons and is then referred to as Non-Alcoholic Fatty Liver Disease (NAFLD), which is the most common liver disease in western countries. It can be caused by an undiagnosed metabolic disease or an unhealthy lifestyle, is most common in people who are overweight or obese, and even children are increasingly suffering from it. Fatty liver can lead to liver fibrosis and from there to cirrhosis: the liver stops working and has to be replaced by a transplant. Liver cirrhosis also often leads to liver cancer.

Liver fibrosis in the culture dish

Suter-Dick uses three types of human cells for her liver cell cultures: hepatocytes (the main cells in the liver), Kupffer cells, which are responsible for local immune response, and stellate cells. The latter produce the collagen fibres in a scarring liver and thus play a key role in fibrosis and cirrhosis. Using her culture dish liver models, Suter-Dick is investigating how liver fibrosis develops and which molecular signals the cells display. "After extended treatment with bile acids and other stimuli, our models showed clear signs of fibrosis," the scientist reports. "The cells in the model also released specific liver damage markers called microRNAs. This is significant, as elevated microRNAs, especially





microRNA-122, can also be detected in blood in animal studies and in humans with liver damage." Hence, microRNAs are good candidates for biomarkers that could be relevant not only in vitro, but also in the clinic, opening the way to better diagnosis and therefore enabling earlier treatment.

Using the new single-cell sequencing technology in her models, the researcher also measured which sections of the genetic material are read and transcribed in individual cells. This enabled her to compare the metabolic processes which are particularly active in healthy and fibrotic liver cell cultures. She also observed how cell populations change over the course of the disease. This work should help identify specific approaches for the treatment of liver fibrosis.

Hunting down Alzheimer's

Such new techniques are also urgently needed for Alzheimer's disease. This neurodegenerative dementia condition leads to neuron cell death in the brain, but the mechanisms that cause it are still unclear. However, a hereditary form of Alzheimer's could be linked to genetic mutations. Suter-Dick's team genetically modified neuron precursor cells to show characteristic features of Alzheimer's and were then able to differentiate these cells in cultures. This resulted in mature neurons and astrocytes, two key cell types in the brain. In this process, "healthy" progenitor cells developed into healthy neurons and "diseased" progenitors developed into diseased neurons. "Of course, Alzheimer's disease does not show up in cell culture with memory impairment and other cognitive problems," Suter-Dick explains, "but we see the same biochemical changes that occur in the brains of Alzheimer's sufferers: the formation of beta-amyloid plaques and the alteration and accumulation of tau protein." Disease development in the model takes about six to ten weeks, relatively long for a cell culture process. But this slowness corresponds closely to the chronic progress of the disease in humans.

In the culture dish, diseased and healthy neurons can now be compared. This new approach will be used in a follow-up project to further investigate the basic mechanisms of Alzheimer's disease and related therapeutic approaches. These 3D cell culture systems not only help to reduce the use of animal experiments; they make it possible to model disease processes on human cells and better investigate the development and treatment of those diseases.

Methods and infrastructure

- General cell culture methods
- 3D cell culture models and microfluidic systems (MPS: microphysiological systems)
- Enzymatic, biochemical and immunodetection methods (to determine protein expression)
- Flow cytometry and cell sorting (FACS)
- Imaging, incl. confocal microscopy
- Molecular biological methods, incl. single cell sequencing

Support

- Swiss Center for Applied Human Toxicology Foundation – SCAHT
- Innosuisse
- F. Hoffmann-La Roche AG
- BRIDGE Programme, Swiss National Science Foundation and Innosuisse

Collaboration

- InSphero AG
- CSEM Swiss Center for Electronics and Microtechnology Inc.
- Haute École Arc, HES-SO

Sensor socks instead of plaster casts

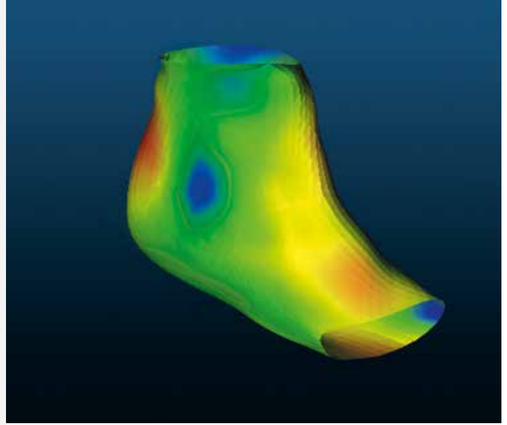
For an orthopaedic splint to fit the patient well, a precise model is critical. In future, the painstaking work of making a plaster cast model will be replaced by measuring textiles. Researchers at the FHNW HLS have developed a prototype sock that measures foot shapes in 3D with millimetric precision, thanks to tiny sensors in the sock which measure magnetic field values. The application only needs a weak magnetic field above the treatment table and the precise shape of the foot in the sock can be acquired in a few seconds.

“Our measuring textiles provide the same data as a plaster cast at the push of a button. And because they are more accurate, they can be used to make better orthoses.”

Joris Pascal

Orthopaedic splints correct joint position, relieve pain and provide stability, but a high level of skill and manual dexterity is required for their manufacture. The orthopaedic technician has to place the patient’s foot in exactly the right position; only by successfully recording this position digitally can a precisely fitting splint be produced. To do this, the technician must hold the foot in the desired position with one hand while with the other hand wrapping it in a plaster bandage. Once the plaster is dry, it is cut open and the inner shape of the cast can be recorded with an optical 3D scanner. This provides a computer model, on the basis of which a patient-specific corrective splint – the orthosis – is made. Researchers at the FHNW HLS have shortened this complex procedure to a simple push of a button: they are developing an electronic networked sock that can record foot position and shape in a matter of seconds. Patients would only need to put on the sock. With the foot correctly positioned, a specialist can trigger the measurement via pedal switch or voice command. Nothing gets wet or dirty, the specialist has both hands free and the outcome is a high-precision model for the orthosis.

“Senior orthotist Thomas Ruepp had the idea of an intelligent sock for orthosis production in the early 1990s; together with my FHNW colleague Ralf Schumacher we then patented the integration of sensors into textiles,” says Joris Pascal of the Institute for Medical Engineering and Medical Informatics at the FHNW HLS. But it is only now becoming reality thanks to a successful interdisciplinary project between FHNW electrical engineers and medical technology start-up Bellwald Tec to develop a prototype sock. It enables foot measurement to an accuracy of two to three millimetres within a few seconds, thanks to over a hundred small magnetic sensors incorporated into the sock. With the sock on the foot in a suitable magnetic field, the sensors deliver measured values to an electronic control unit which accurately calculates each sensor’s position. Software uses the resulting point



cloud to reconstruct the foot shape as a digital 3D model which, as in conventional orthosis production, is then sent to a 3D printer to create a splint. It can also be used as a direct template for a computer-designed splint. “We wanted a solution that seamlessly follows orthotists’ usual workflow,” says Pascal. He and his team hope that the intelligent textile will not only make the splint production process easier for everyone involved, but also lead to greater therapeutic success. “A splint that fits well is also worn more regularly,” says the researcher.

The sensor sock is more accurate than a plaster model since, as plaster dries, even small foot movements can change its shape. Moreover, the accuracy of the plaster cast can be affected by cutting, opening and removal, and thus two or three different splints often have to be made in order to eliminate pressure points. However, since health insurance companies pay a lump sum for orthoses, some sufferers do not get a second version for cost reasons and rarely wear their uncomfortable splint. The result can be a permanent deformity, possibly leading to problems walking and an inability to work. On the other hand, if a child’s pointed foot or other joint deformity is corrected early enough, he or she can walk better as an adult. Good orthoses therefore improve quality of life as well as giving economic advantages.

For their prototype, the researchers developed sophisticated electronics and a special communication protocol, with all the sensor chips on a single flexible circuit board and transmitting simultaneously. This avoids a tangle of dozens of individual wires and means that the circuit board can be wound in a spiral and woven into the sock. The weak magnetic field, whose magnitude and direction the sensors measure, is generated with small current-carrying coils located a few centimetres under the foot. In a medical practice, the coils could be positioned under the treatment table, for example.

In practice, the smart sock still has to become more robust so that it can regularly be put on, taken off and washed. This is the team’s follow-up project. “With the foot, we have chosen a body part with a relatively complex shape,” says Pascal. “When the sock is ready for practical use, we could adapt the system for other orthoses and applications, for example, corsets or a smart cap that scans head shapes.”

Methods and infrastructure
- Computer Aided Design (CAD)
- Sensor and electronics development
- Hardware-related software development
- Algorithm development for magnetic tracking
- 3D mapping and modelling of magnetic fields
- Modelling of anatomical shapes
- Electronics laboratory
- Calibrated Helmholtz coil
- 3D scanner, digitiser
- 3D printer

Support
- Bellwald Tec GmbH

Collaboration
- Bellwald Tec GmbH
- Basler Orthopaedics René Ruepp AG

A folding heart model

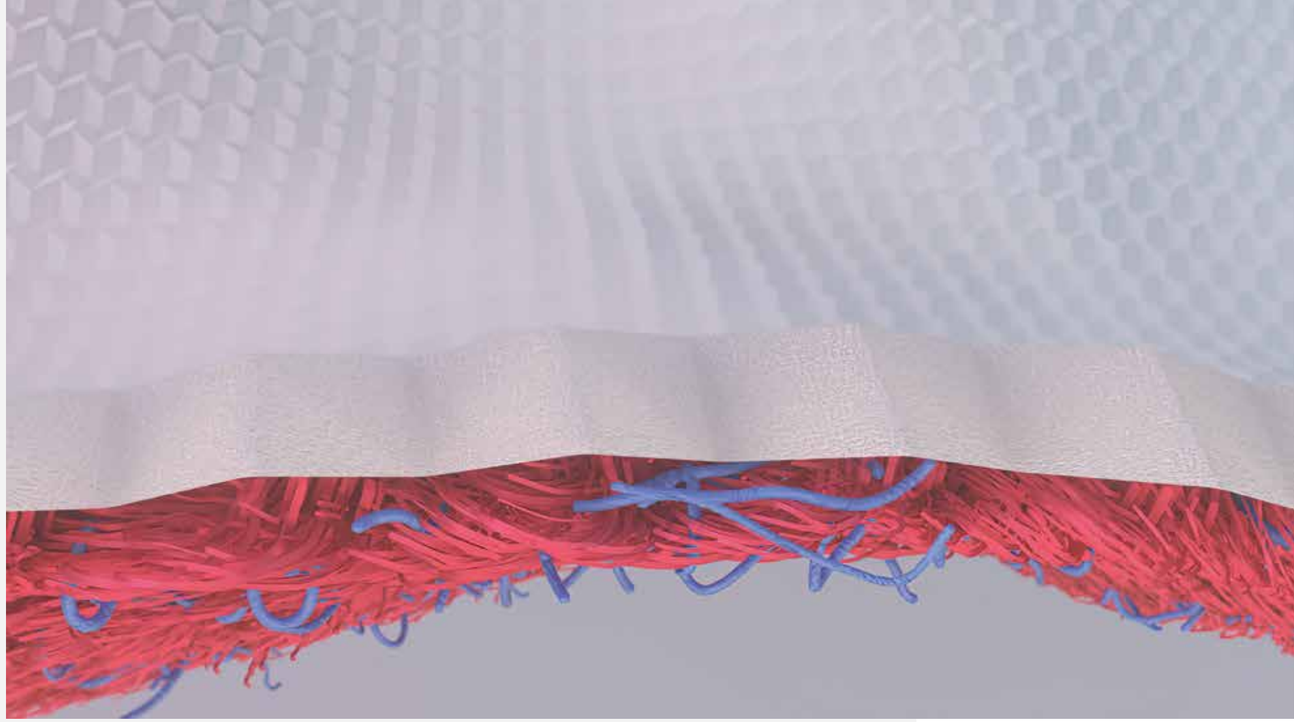
A heart model would be an ideal solution for some drug tests, provided that it could mimic the heartbeat and deliver meaningful results. A research team including the FHNW HLS has now developed an artificial miniature heart that comes very close to this. The basis is a square-shaped paper structure with fishbone-like folding elements that allow it to be compressed and stretched. When coated with heart cells, this origami 'scaffold' contracts and expands in response to tension stimuli – just like a real heart muscle.

To test a drug's efficacy or side effects in the lab, researchers need suitable models, for example of the heart – the organ in the human body with the highest stamina muscle. Heart muscle cells can already be grown in small clusters known as organoids, on which pharmacological substances are tested. However, these are very simple models compared to an anatomic heart, which is a hollow muscle with four chambers that continually contract and expand. To better represent this complex organ, a research group from the FHNW HLS and the University of Basel has developed a miniature heart model that can beat.

In the KOKORO Nano Argovia project funded by the Swiss Nanoscience Institute, the team applies thin layers of living heart cells onto cellulose paper using bioprinting. The pre-folded paper can be compressed and stretched in two dimensions, a little like an accordion. If the printed cells grow and develop properly, the "origami" heart tissue can contract and expand repeatedly, like a heart muscle.

3D printing with cells

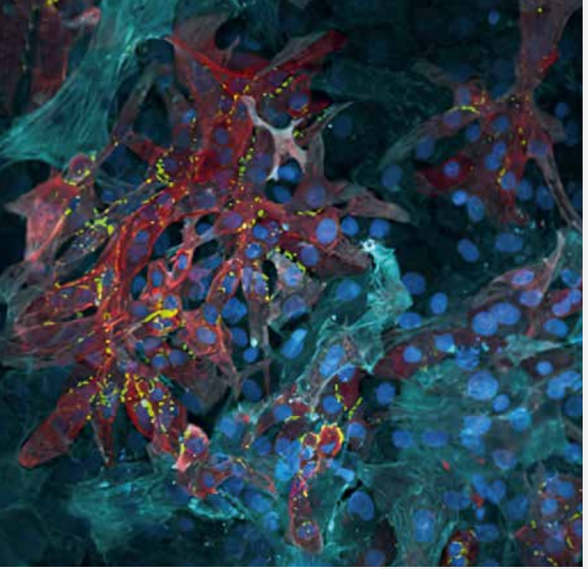
Bioprinting – the technology for manufacturing this heart model – is similar to 3D printing with polymers, but the result is biological tissue. Experts at the University of Basel provided the cell cultures: newborn mouse heart cells, which are not yet fully mature and can still proliferate. In order for them to be printed like polymers, they must first be embedded in hydrogel – a gelatine-like substance made of water and a strong mesh of hydrophilic fibres that swell up in it. For the heart model hydrogel, the researchers used collagen fibres also found in gelatine. "Our hydrogel has about the same consistency as jelly," says Maurizio Gullo from the Institute for Medical Engineering and Medical Informatics at the FHNW HLS. "Even when we add cells, the gel can still be pressed through a thin nozzle, giving us a fine filament that we use to print a layer of cells line by line and layer by layer on our paper scaffold." Using this technique, Gullo's team first printed a thin layer of heart muscle cells, then a second layer with vascular cells. They supply the muscle cells with nutrients and remove harmful

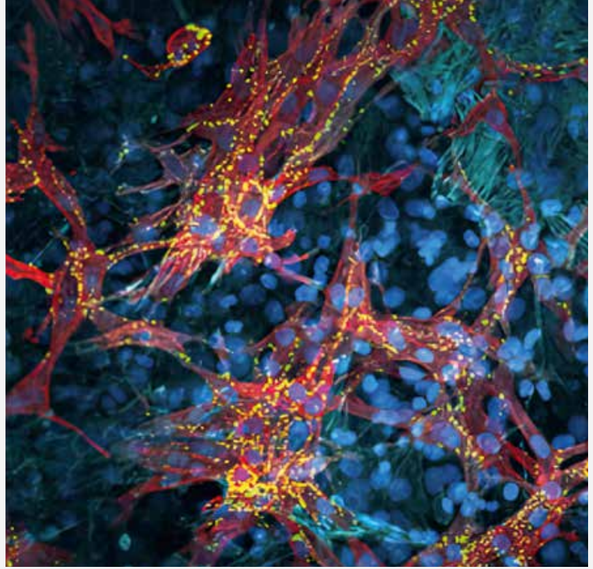


metabolic products. Each heart model contains several million cells and the surface measures one square centimetre; it is thus slightly larger than the cross-section of a mouse heart.

Fine-tuning

The foldable paper for the heart model was made by industry partner Omya from biocompatible cellulose fibres, to make it as cell-compatible as possible. It looks like typical square origami paper and was pre-folded by machine at the FHNW HLS into fine structures only a few hundred micrometres in size. The researchers coated the folded paper structures with hydrogel for structural stability and printed them with the hydrogel cell layers. "With the paper as a structural support, we were able to use a slightly softer hydrogel for printing," explains project partner Joachim Köser from the Institute for Chemistry and Bioanalytics at the FHNW HLS. "For the cells to develop well, the gel has to be as soft as an embryonic mouse heart. If it is too stiff, they don't get enough nutrients, waste products don't disperse fast enough, and they suffocate." Köser and his team have therefore developed available





hydrogels into a new product that meets the requirements of the heart model. In addition to gel stiffness, they also analysed the optimal density and length of the hydrogel fibres. The final criterion was price. "If 3D print-based heart tissue can ever be used to treat heart patients in the future, it should be affordable," says Köser.

Active and aligned

In this project the research team has shown that the origami-based heart model principle works: thanks to the protective hydrogel coating, the paper scaffold does not dissolve, and it is compatible with the cells. The two different cell layers – muscle and vascular – are also compatible. The researchers succeeded in finding a hydrogel and nutrient solution in which both cell types thrive: "We dyed the cells in viability tests and analysed the different factors they released," Gullo explains. "This allowed us to confirm that the cells are surviving and are sufficiently active." However, this is not enough, he adds: "It is important that the cells feel comfortable, since after application, they still have to mature: they have to differentiate and become functional."

The vascular cells, for example, form a network while the muscle cells develop the protein structures they need for contraction: actin and myosin fibres. In this context, the paper scaffold has a third purpose in addition to its folding and support functions: its cellulose fibres provide the cells with a structure. "By aligning the muscle cells along the paper fibres, we enable the muscle fibres to contract directionally later," explains Köser. "We have strengthened this effect by structuring the hydrogels in such a way that the cells can align themselves with them. To this end, we gave the hydrogels linear structures."

"Thanks to origami folding, our heart model is more than just a collection of cells. We can make it beat and observe how different stimuli change the heartbeat."

Maurizio Gullo

Successful interaction

In order for the muscles to function like real muscle fibres, they have to synchronise with each other during maturation. Only then can they all contract together in response to an impulse. Moreover, they have to exert enough force while doing it. To test this, the researchers at the University of Basel stimulated the cells with electrical impulses and measured the voltage needed to trigger a contraction. The smaller this value, the stronger the muscle cells. "In a real heart muscle, the nervous system triggers the heartbeat; this is not possible in the model," explains Gullo. "Nevertheless, in our model the impulse is transmitted in the same way as in the heart: it is transferred from one muscle cell to the next in a kind of domino effect, and one row of cells contracts after the other."

Gullo and Köser are pleased with the outcome: "Our heart model really 'beats'. The cells contract synchronously and directionally in response to stimulation." Other researchers can now use the model to study the effect of drugs on the heart, not just at the cellular level but also in functional terms. For example, they will learn whether the model heartbeat changes when a drug is added.

Looking forward, the research team hopes for a second possible application: with a different base structure than paper, the heart model could be developed into a patch that replaces scarred tissue with the patient's own cells after a heart attack. In this case, too, the newly attached heart muscle cells would follow the contraction of the neighbouring cells, helping the still healthy tissue to beat and thus reducing the risk of a second heart attack.

Methods and infrastructure
- Cell culture laboratory
- Chemistry laboratory
- Bioprinting (RegenHU 3D Discovery)
- Hydrogel chemistry
- Rheometry
- Soft lithography (impression)
- Mechanical paper folding

Support
- Swiss Nanoscience Institute (Nano Argovia project KOKORO A14.07)

Collaboration
- Omya AG
- University of Basel

Well packaged for the large intestine

Tablets or capsules usually release their active ingredients in the stomach or small intestine. If the effect of the drug is needed in the large intestine, this is clearly a disadvantage – the drug is absorbed too early into the bloodstream or acts in the wrong place. Researchers at the FHNW HLS have therefore developed a method of embedding active substances in a framework of dietary fibres. This framework can reach the large intestine intact, at which point large intestine bacteria break down the fibres, releasing the active ingredient exactly where it is needed.

Chronic inflammatory bowel diseases such as Crohn's disease and ulcerative colitis are common - around 20,000 people are affected in Switzerland alone. Despite their suffering, therapy options are limited. Standard treatments include anti-inflammatory drugs such as cortisone or the salicylic acid derivative mesalazine, as well as liquid diets. These are designed to give patients the necessary nutritional intake despite disease-related pain, diarrhoea and loss of appetite, but even so, the disease can often only be partially or temporarily halted.

Biochemist Georg Lipps from the Institute for Chemistry and Bioanalytics at the FHNW HLS is convinced that if drugs could act at the inflammation site itself, treatment could be more successful. In colitis, and to some extent in Crohn's disease, the target site is the large intestine. However, before a drug can get there, it has to pass through the five-metre-long small intestine. It is here that many medicines dissolve so that the intestinal mucosa can absorb the active ingredients. But of course, this also affects medicines that are actually supposed to reach the large intestine. On their long journey through the small intestine, they are removed too early.

Bacteria as helpers

A team led by Lipps and Georgios Imanidis from the Institute for Pharma Technology has discovered a packaging material that 'smuggles' active substances past the small intestine's digestive enzymes and into the colon. They had this brilliant idea while browsing through scientific journals, where they read that colon bacteria break down the dietary fibre xyloglucan. The human body cannot digest these plant cell wall fibres, but our gut bacteria feed on them. By breaking down the fibres in the large intestine, they release metabolic products that we can use. The small intestine on the other hand has almost no bacteria. Lipps assumed that a xyloglucan-based tablet could therefore reach the large intestine intact, only decomposing once there. "Up to now, a pH-based approach has been used," the biochemist explains. "Medicines are given a coating that is insoluble in acid, but which dissolves at neutral to mildly alkaline pH. Tablets should thus disintegrate in the lower small intestine, but the pH of the gastrointestinal tract varies both between people and within the same person, depending on food and physiological conditions. Therefore with this method, where the tablet actually dissolves varies considerably, and the administration of the drug is neither reproducible nor efficient."

To test whether an active substance embedded in xyloglucan reaches the large intestine, the researchers led by Imanidis produced two different tablets at the FHNW HLS Process Technology Centre: one with the active substance mesalazine and a control with caffeine. To do this, they pre-processed the polysaccharide xyloglucan fibres, mixed them with the active or control substance and then pressed the tablets. "Pressing creates a coherent polysaccharide scaffold which encloses the active substance," explains Imanidis. "Only when bacteria break down the scaffold is the mesalazine released." Imanidis' team also sealed the tablets with a polymethacrylate film that protects them from stomach acid. "When the tablet enters the neutral environment of the small intestine after going through the stomach, this first protective layer gradually dissolves," says Imanidis. "The key is that once it is gone, the xyloglucan matrix takes over the protection role so that no active ingredient is released before the end of the small intestine. When the tablet enters the large intestine, the bacteria go to work."

After producing the tablets, the researchers tested active ingredient release in a three-stage experiment funded by the BRIDGE programme of the Swiss National Science Foundation and Innosuisse. First, they simulated conditions in the large intestine by exposing the tablets to an enzyme that breaks down xyloglucan. Next, instead of the enzyme, they used bacteria that control the digestion, such as Bacteroides ovatus. Finally, they followed the passage of the tablets through the digestive tract in pigs by analysing concentrations of mesalazine and caffeine in continuous blood and stool samples. "The active ingredient mesalazine is well absorbed in the small intestine but hardly at all in the large intestine," explains Lipps. "If the tablet only releases mesalazine in the large intestine, the amount of active substance in the blood circulation will therefore be low, and this is exactly what we observed. The caffeine control on the other hand can also reach the systemic blood circulation from the colon. Since only caffeine was detectable in the blood, the protective dietary fibre shell functions exactly as we had hoped and only dissolves in the colon. Stool samples confirm this result."

In addition to therapeutic use in intestinal disease, xyloglucan tablets are suitable for other applications. For example, they could transport specific nutrients into the large intestine that have a positive effect on intestinal flora and thus also prevent inflammation.

Methods and infrastructure

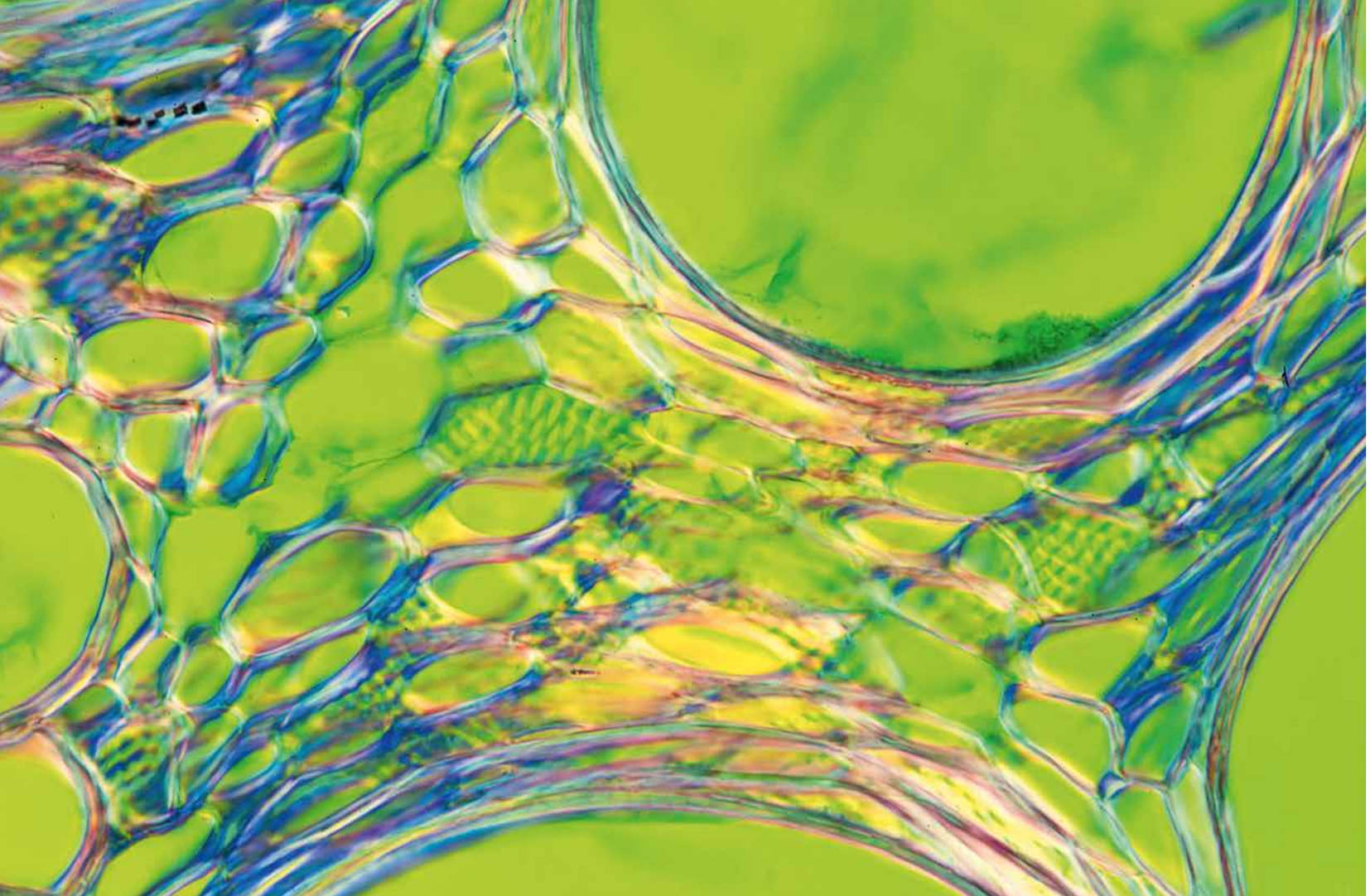
- Fluid bed granulation
- Tabletting by eccentric press
- Drum coating
- Detection of xyloglucanase activity (viscometer, UV/VIS spectroscopy)
- Cultivation and analysis of the microbiome (anaerobic box)
- In vitro dissolution test USP II/release
- Pre-clinical in vivo test
- Chemical analysis of plasma and faeces samples by LC-MS/MS

Support

- FreeNovation, Novartis
- BRIDGE Programme, Swiss National Science Foundation and Innosuisse

Collaboration

- Vetsuisse Faculty University of Zurich



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, FHNW 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.

The best of both worlds

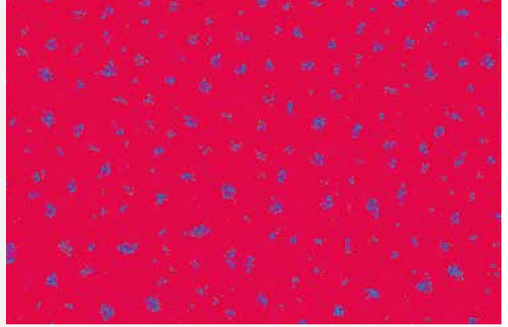
Paint on a wall should not only be nice to look at: it must be easy to apply, durable, prevent algae and mould and help maintain a good indoor climate. The key to this is the binder, which holds all the components of a paint together. Researchers at the FHNW HLS have developed a new molecular link between the building blocks of two conventional paint binders. The result is a new binder that combines the advantages of its two source components to produce versatile wall and façade paints without biocides.

House façades should look fresh, be attractive in the long term and not be vulnerable to microorganisms. To this end, most façade paints contain biocides, but these are washed off into the groundwater during storms, endangering water and soil organisms as well as our health. "Silicate paint is different," says Michel Ledeur, head of the research laboratory at vanBaerle, a cooperation partner of the FHNW HLS. "Silicate paint does not require biocides or solvents and looks almost as good as new even after decades. A good example of this is the façade of the historic town hall in Schwyz; it has been there since 1891." But because silicate paint only adheres to a few substrates, vanBaerle wanted to combine its advantages with those of emulsion paints – a well-known type of paint widely used on walls. Hence the company developed a new binder in collaboration with the Institute for Chemistry and Bioanalytics (ICB) at the FHNW HLS.

"Thanks to the molecular adapter we have developed, there is now a paint binder that consists of mineral and organic polymers simultaneously."

Uwe Pieles

"The binder combines the various components into paint," explains Ledeur. "It ensures that colour pigments, thickeners, defoamers, dispersants, fillers and water blend into a single mass that you buy as paint in the DIY store." In silicate paints, the binder is based on potassium silicate. Dispersion paints on the other hand contain an organic binder – often acrylic-based, as with artists' paints. The binder plays a key role in determining the properties of the two types of paint, as Ledeur explains. "The secret behind silicate paint is that it cleans itself by losing a few micrometres through abrasion every month. Nevertheless, it adheres very well because it bonds with the substrate through a chemical reaction. Moreover, it is insensitive to sunlight, and rainwater simply rolls off it." Dispersion paint, on the other hand, scores with versatility and user-friendliness: it can have a wider range of colours since, unlike silicate paints, organic pigments can be added to it. In addition, emulsion paint adheres to a wide variety of surfaces, it is less brittle and easier to apply.



To get the best features of both types however, you cannot just mix them because their binders do not work together. "Mixing acrylic binder and commercial silicate binder gives an uneven mixture of glass chips and plastic," says nanoscientist Uwe Pieles from the ICB. Although Pieles' team showed that a specially developed silicate increases compatibility with the acrylic binder, there was still no direct bond between the silicate and acrylic molecules. The researchers at the FHNW HLS created this missing bond in collaboration with vanBaerle's research and development department. "You have to think of it as an adapter that links the silicate and acrylic polymers both physically and chemically," Pieles explains. "When we add it to the silicate-acrylic binder mixture and look at it under the electron microscope, we see a homogeneous material in which the silicate molecules are evenly surrounded by acrylic polymers thanks to the adapter bonds."

The researchers ran a series of practical tests to investigate whether the new hybrid binder really combines the positive properties of its two basic components. For example, they wanted to see how well the hybrid binder adheres to different surfaces; to do this, they painted it on test surfaces and exposed it to wind and weather for several days. "Our new organo-mineral binder performed as well as silicate paint on mineral glass surfaces and even better than emulsion when applied to organic paint," says Ledeur. The hybrid binder can therefore be used on almost any substrate, whether plaster, brick or even directly on top of an old coat of paint. Just like silicate paint, however, it needs time to cure in order to achieve its best adhesive properties. Once it is completely dry, it no longer absorbs water, even when a test panel is submerged for three days. As the research team has demonstrated in electron microscope images, the silicate content in the hybrid binder also means it penetrates into painted surfaces, making the finish very durable. In addition, paints with the hybrid binder can absorb and release moisture from the air in a similar way to silicate paint, allowing walls to breathe and preventing mould. A final advantage is that the high pH value of the hybrid binder counteracts the growth of microorganisms, making biocides unnecessary.

Ledeur calculates that it will take at least another year before paint with the new binder is launched on the market, since manufacturers first have to develop suitable formulations and test their colours. But the breakthrough has been achieved: a hybrid binder created for durable, environmentally-friendly and safe paints for exterior walls and interiors.

Methods and infrastructure
- Chemical laboratories
- Synthesis equipment
- Electron microscopy
- Headspace GC-MS for the determination of volatile components
- Thermogravimetry

Support
- Innosuisse

Collaboration
- vanBaerle AG

Supramolecular engineering of enzymes

Enzymes are biocatalysts: they accelerate chemical reactions in organisms. They are widely used in industry, for example to produce food or medicines cheaply and without harming the environment. Without using genetic modification, researchers at the FHNW HLS have improved enzymes' properties by embedding them in nanometre-sized organosilicate particles and have now adapted their process for special 'promiscuous' enzymes. The positive results of this work open the way to exciting industrial applications.

Enzymes are sensitive: if you remove them from their natural environment they often no longer function normally, making industrial applications problematic. Hence, given that firms want to use enzymes to catalyse chemical processes that do not occur in nature, there was considerable interest in 2016 when Patrick Shahgaldian from the FHNW HLS overcame this hurdle. He presented a method to embed enzymes in nanoparticles and thus protect them, for example from the damaging influence of heat or acids.

"Precisely tuning the nanoenvironment of enzymes enables their use in industrial applications."

Patrick Shahgaldian

Processing whey

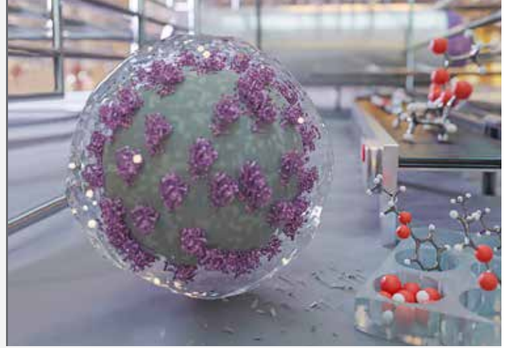
These nanoparticle-stabilised enzymes should enable, among other things, the efficient extraction of valuable substances from whey, a by-product of cheese production. That is the goal of the EU-funded INGREEN research project, in which Shahgaldian's team at the Institute for Chemistry and Bioanalytics is involved. The researcher has also co-founded the spin-off INOFEA to market his technology.

"We now know that the technology can do more than just protect sensitive enzymes," says Shahgaldian. "We can also use it to change the properties of the embedded enzymes." Shahgaldian and his team have now demonstrated this with 'promiscuous' enzymes.

'Promiscuous' is normally used in the sense of 'sexually permissive', but when biotechnologists refer to 'promiscuous enzymes', they mean something else: these biocatalysts accelerate the transformation of not just one but a whole range of substances. That would be highly advantageous for a variety of technological applications; but there is a drawback.

Like left and right hand

This drawback is due to the fact that some substances occur in two forms. Such substances are known as enantiomers and the two forms differ in their chemical structure like a person's left hand differs from their right. The two enantiomers contain the same number of atoms but can differ in essential properties. For example, one enantiomer may have a healing effect in the body and thus be a medicine, while the other may harm the body; or one enantiomer is biodegradable in landfills while the other pollutes the environment.



Specialised enzymes are often enantioselective: they ensure that only one enantiomer is produced, i.e. the one with the desired properties. But when promiscuous enzymes catalyse chemical reactions, the result is often a mixture of enantiomers.

The FHNW HLS researchers used three promiscuous enzymes discovered and characterised by collaborators from the Consejo Superior de Investigaciones Científicas (CSIS), a Spanish agency for research and technological development. Two of the enzymes came from microorganisms living in a polluted marine area off Sicily. The third was supplied by microbes from Lake Arreo in northern Spain. All three are esterases, enzymes which are often used for industrial applications: they can break down dozens of esters into their starting substances, but if an ester occurs in two enantiomeric forms, the natural enzymes do not distinguish between the two.

However, after the researchers bound the enzymes to silicate nanoparticles and coated them with protective organosilicate shells, they behaved differently. Some of the resulting biocatalyst nanoparticles were 100 per cent enantioselective, converting only one of the two enantiomeric forms of the respective ester.

Moreover, embedding in nanoparticles improved another essential property of the enzymes studied. Without protection, they lost their catalytic abilities in liquids containing 40% of the common organic solvent acetonitrile. Integrated in nanoparticles on the other hand, their catalytic activity in the same solution continued.

A strategy with broad applications

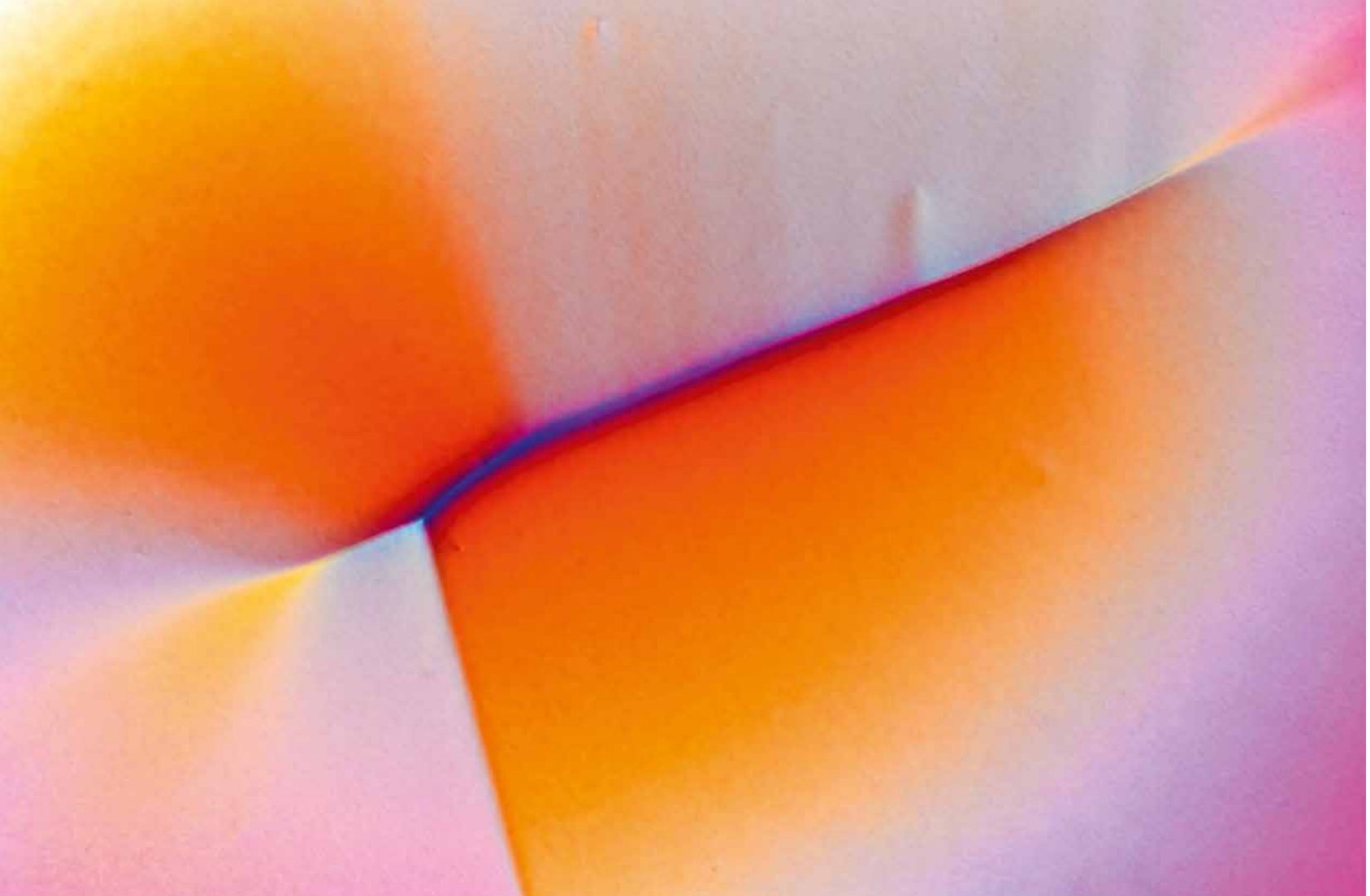
"We have thus developed a technique that allows us to improve both the enantioselectivity and the stability of some promiscuous enzymes in organic solvents," Shahgaldian concludes. "We expect this approach to be applicable to a wide range of promiscuous enzymes." The use of the resulting biocatalyst particles may be attractive for industrial processes since their production is inexpensive and requires little energy.

The properties of biocatalysts can also be improved with genetic engineering, for example to change the sequence of amino acids in the natural enzyme, but many consumers reject the use of genetic engineering in sectors such as the food industry. This breakthrough by the researchers at FHNW HLS offers a promising alternative.

Methods and infrastructure
- Nanosynthesis
- Bioconjugation
- Biocatalysis
- Synthesis laboratory
- Electron microscopy
- Atomic force microscopy
- Gas chromatography
- HPLC

Support
- EU Horizon 2020 funding programme

Collaboration
- Spanish Superior Council for Scientific Research (CSIS)
- Bangor University, UK



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 FHNW HLS, with its focus on information technology and processing, helps people deal with and benefit from the ever-increasing flood of data.

Antibodies with AI

Our immune system is vulnerable to viruses. Vaccinations can train it, but developing a vaccine takes time, especially if different variants are circulating and the vaccine needs to protect against them all. A team at the FHNW HLS is therefore using artificial intelligence to search the immune system in mice for antibodies which are particularly effective against several virus variants simultaneously. These antibodies, for example against the dengue virus, could guide vaccine design.

A small bite is enough: every year, several hundred million people contract dengue virus from mosquitos. Not all get ill, but many develop flu-like symptoms with high fever. In some countries in Asia and Latin America, dengue fever is one of the main causes of severe illness and death, and those who have had the fever can get it again – several times. "There are different dengue virus variants called serotypes," explains scientist Enkelejda Miho from the aiHealthLab at the FHNW HLS. "If you have been infected by one variant, your immune system is only trained to fight that particular serotype, i.e., it has antibodies to help fight it. But this does not normally protect you from other variants, making it difficult to develop an effective dengue vaccine." The only existing vaccine has limited use, there are no specific drugs, and dengue viruses and their vector mosquitoes continue to spread. Therefore Miho's team are using artificial intelligence to search for antibodies that protect against different virus variants at the same time.

"Our computational analyses allow us to find, among billions of possible antibodies, the ones that are effective against different variants of a specific pathogen."

Enkelejda Miho

Antibodies are protein complexes produced by specialised immune cells known as B cells. "They are like small 'Y's with two tentacles that bind the pathogens," says Miho. "The pairs of arms come in countless variants, so each antibody can only dock with specific particles, for example one dengue virus serotype. We are looking for special antibodies that catch more dengue variants; these antibodies exist, but they are rare." To find them, Miho and her team sequenced the B cell genome from mice that had been immunised against dengue. This B cell genetic material includes the genes that provide the blueprint for the antibodies.

Each B cell usually produces only one antibody variant and thus only contains the blueprint for one antibody. However, this blueprint is spread over five different genes, some of which influence how the arm pair is formed while others are a template for the trunk part of the antibody. This makes it hard to determine antibody sequences, since older methods give gene sequences of all the cells analysed, without distinguishing which sequences come from which cell. "We would have got a mixed up jigsaw puzzle of different antibody sections from all the B cells we examined and would not have known which belonged together," says Miho. "Fortunately, we can use single-cell sequencing at the FHNW HLS. With this modern method, the genome of each B cell is read separately. We get all the genes for one antibody together and thus the complete gene sequence for the whole antibody."

Since Miho and her team obtained several million gene sequences from each mouse, the next step was to take advantage of computers' ability to recognise patterns in huge amounts of data. Each mouse had been immunised with a variant of the dengue virus, while a control group was unimmunised; hence the researchers could use a computer to find the gene sequences for antibodies produced in response to immunisation. This is possible because during an infection or after a vaccination, B cells whose antibodies match the invading pathogens proliferate. "We can therefore tell the computer that those gene sequences belong to anti-dengue antibodies that occur more frequently in immunised mice," Miho explains. "However, it can also be that an antibody is rare but binds particularly well

to dengue particles. That's why we programmed our analytical approaches to combine different machine learning models."

To complement machine learning, the research team also used network analysis to assess similarities between the various mouse antibodies: the more similar two antibodies are, the closer together they are represented in the network. "When a mouse or human has an infection, we see structures in the network that look like a dandelion," says Miho. "There are dense nodes of multiple antibody sequences that are all very alike." When reacting to a pathogen, the immune system tries to optimise its defences by creating new, slightly modified versions of the antibodies that have already been able to dock with the pathogen. This is how the "flowers" in the network are created, whose centres – the hubs – contain promising antibody variants.

Once the computer has identified an antibody which the analyses indicate could be effective against different dengue serotypes, the researchers have to test it in the lab. They multiply the B cell that produces this antibody and check whether it in fact binds to all dengue variants. If it does, it can be used to develop a treatment or a better vaccine. The search for a vaccine is still complex, but this preliminary computer work could save a lot of research effort in the lab.

"Typically, you look for antibodies by testing the B cells of immunised mice directly in the lab, rather than sequencing their genome," Miho explains. "This means choosing some B cells and seeing if they produce antibodies against the target molecule, for example a specific protein of the dengue virus. This is very time-consuming and only a limited number of cells can be tested at a time, not to mention the risk of missing the best-binding and rarest antibodies." However, with their new approach, Miho's research group has already found more than 20 potential antibodies that bind dengue variants.

The specific antibodies can be used for more than just vaccine design. Another potential application is to treat people who already have dengue. "For this, the mouse antibodies would first have to be converted into antibodies similar to those of humans," says Miho. "The biological and computer techniques for this are well-established. Most importantly, you have to change the trunk parts of the antibodies; they are the regions which interact most strongly with the body's cells and the rest of the immune system. You leave the arm pair sections that bind to the virus so that the antibodies retain their effectiveness against the dengue variants." Antibodies produced in this way would be suitable for use in humans and could then support the immune response, especially in severe dengue fever. Once patients are injected with them, their immune system can use them like the body's own antibodies to defend itself against the virus. The special antibodies would bring a key advantage, just as with a vaccination: a single dose would be effective against the various dengue serotypes.

In future, the search process and computer models developed by the aiHealthLab team will also be used to search for antibodies for other infectious diseases, especially pathogens with different variants.

Methods and infrastructure
- Single cell sequencing
- Binding assays
- Antibody expression
- Machine learning

Support
- Wellcome Trust, UK (Innovator Award 215840/Z/19/Z)

Collaboration
- Institut Pasteur, FR

Home Diagnostics Made Easy

SARS-CoV-2 coronavirus infections can already be detected at home. But until now, home detection of the different virus infection stages or of vaccination effectiveness has been impossible. That is why researchers at the FHNW HLS are developing a new type of self-administered test in a nationwide cooperation project. The new self-administered corona test only needs a little saliva and shows the result within a quarter of an hour. This simple method is an important step on the way out of the pandemic.

"Our test covers the whole diagnostic spectrum, from infection to vaccination response to whether someone has had COVID-19 in the last few months."

Frank Dieterle

Everyone wants a return to normality. A key element of achieving that is simple, inexpensive corona tests which deliver fast, reliable results. This is the only way to find out who is infected or perhaps already immune, but so far, people can only test themselves for acute Coronavirus infection. The DAVINCI consortium of eight partners from Swiss universities and industry want to change this. In a project funded by the Botnar Research Centre for Child Health, chemist Frank Dieterle from the Institute for Chemistry and Bioanalytics is working with the consortium to develop a saliva test that can be carried out at home and that detects both active infection and immunity to the virus.

"So far, saliva has only played a minor role as a diagnostic body fluid," says Dieterle, "yet it is a real all-rounder. It not only helps with digestion, but also forms the first line of defence against pathogens that enter through the mouth or nose. "When the immune system comes into contact with a pathogen, it creates antibodies that can fight that pathogen and prevent a second infection. These antibodies circulate in the blood, but small numbers are also released into our saliva.

We need alternatives

"Until now the gold standard for detecting active coronavirus infections has been PCR tests," Dieterle explains. Polymerase Chain Reaction is a very sensitive and safe laboratory method that can detect SARS-CoV-2 virus genes from a nasopharyngeal swab, or a saliva sample. Another test method that uses nasal or throat swabs is the antigen test, which reacts to virus components such as proteins and is also used to detect active infections. These antigen tests give results after only a few minutes and are suitable for access control in care facilities, hospitals or airports; however, they are less sensitive. A third type is the blood antibody test, which does not detect early active infection but only whether someone has had contact with the virus or has been vaccinated. It shows how strong the body's immune response is and is therefore suitable for checking after vaccination. All three common test methods have one disadvantage: to get a reliable result, professional staff are needed for the swabs, analyses or for taking blood samples.

You do not have to be an expert

Dieterle and the DAVINCI consortium researchers now have a solution: a saliva testing device that looks like a fever thermometer. The new instrument is single use and is mainly aimed at non-specialists who want to know quickly whether they are infected with the SARS-CoV-2 virus or whether their vaccination still protects them. This is done with a double test which simultaneously detects antibodies against the virus and viral antigens, and which can be easily carried out at home. "It was essential for us that the device works safely in all situations and is as foolproof as possible," says Dieterle. "That's why we chose the easy-to-use lateral flow test method, which is also used in pregnancy tests and to detect drugs." For the new double test, simply open a flap, spit into a small chamber and seal the flap again. The saliva is automatically transferred to two hidden test strips that contain reagents to detect the antibodies and antigens. If a red line is shown on the test device after 15 minutes, the result is positive. There is a second control line to show whether the test has functioned correctly.

The FHNW HLS developed the test set-up for production and identified the reagents. The research team, led by the Swiss Tropical and Public Health Institute Swiss TPH, then collected saliva samples from study participants at several COVID testing stations. The studies should be completed by the end of 2021 so that applications for approval in the USA and Europe can be submitted in 2022 and large-scale production of the test devices can start. In parallel, the DAVINCI consortium is developing an app that facilitates test result evaluation and that can be linked to national COVID tracing apps. In future, the test procedure is to be expanded as a platform technology for other infectious agents to enable quick, easy and reliable home diagnosis.

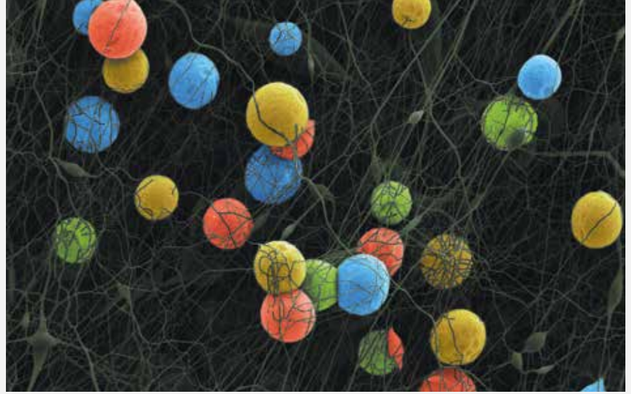
Methods and infrastructure
- Lateral flow immunoassays
- ELISA
- Antibody immobilisation
- Antigen immobilisation
- Assay optimisation
- Biacore and Octet measurement systems for label-free interaction measurement
- Spotters for antibodies and antigens
- Assembly lines for lateral flow tests

Support
- Botnar Research Centre for Child Health

Collaboration
- SwissTropical and Public Health Institute SwissTPH
- University of Basel
- ETH Zurich
- CSEM Swiss Center for Electronics and Microtechnology Inc.
- BioInitials GmbH
- Effectum Medical AG
- Hemex AG

Double protection for new teeth

Dental implants often lead to inflammation of the surrounding tissue, endangering gums and bone and - if untreated - resulting in loss of the implant and bone resorption. Researchers at the FHNW HLS have developed small capsules to be administered directly to the inflammation site, with antibiotics for the infection and plant extracts with a regenerative effect. Moreover, by embedding the capsules in a mesh of fine peptide fibres, the healing process is structurally supported.



"There was a very good synergy with our industry partner credentis AG; thanks to the excellent collaboration, clinical observations could be combined with the latest research results."

Franziska Koch

An inflamed tooth bed is extremely unpleasant: the jaw hurts, gums recede and the process can even spread from the gums to the bone. It is particularly common for a tooth bed to become inflamed if an implant has replaced the original tooth; experts refer to this as peri-implantitis. In severe cases, the implant can become loose or even fall out, resulting in time-consuming and expensive follow-up treatment. In Switzerland and Germany, more than 700,000 dental implants are fitted every year; as they become more common, so do cases of peri-implantitis. Successful therapy is difficult, as Franziska Koch from the Institute for Pharma Technology at FHNW HLS explains: "On one hand, you want to regenerate the bone and the surrounding soft tissue but on the other, there is a high density of bacteria in the mouth, which makes regenerative therapy difficult without antibiotics." With her team and the project partner Credentis, Koch has therefore developed a preparation that helps diseased tissue to heal while at the same time fighting the pro-inflammatory bacteria with antibiotics. In contrast to standard therapies with systemic or local antibiotics however, it has a targeted use of antibiotics with continuous low doses and the ability to combine different preparations. This reduces the risk of side effects, limits the development of antibiotic resistance and increases treatment efficiency.

The basis for the researchers' product is peptides – short sections of protein that can bind to water and that self-assemble into a fibrous structure. The resulting peptide hydrogel can stimulate damaged tissue to regenerate. "The fibrous matrix provides anchor points for cells from healthy neighbouring tissue," says Koch. "This allows them to attach, re-align and proliferate." In this process, the peptide hydrogel mimics the natural extracellular matrix that surrounds our cells and thus new tissue grows in the inflamed area around the implant. Like the extracellular matrix, the gel can bind proteins in the blood such as fibronectin; the cells then attach to this and are anchored. "The key issue however, is that the inflammation-causing bacteria form a biofilm on the implant, which prevents healing," says Koch. Biofilms are highly adhesive systems of microorganisms. To combat them, the researchers have developed tiny capsules made of biodegradable lactic acid compounds called polylactides, which they fill with antibiotics and add to the peptide hydrogel. For peri-implantitis treatment, the hydrogel-capsule mixture could be injected into the inflamed pocket. The antibiotics then diffuse out of the capsules and through the gel, so that they are released continuously for several days directly at the inflammation site. Meanwhile, the polylactide capsules are broken down by enzymes in the oral cavity. The technique is also suitable for the treatment of periodontitis, an inflammation of the tooth bed unrelated to implants.

The researchers used the clean room in the FHNW HLS Process Technology Center to produce the nano- or micrometre-sized capsules. Using liquid chromatography, they analysed how the antibiotics were released from the capsules and then carried out in vitro antimicrobial tests to investigate the effectiveness of the antibiotics released. To do this, they grew a bacterial layer on agar plates with typical inflammation-associated oral bacterial species such as Streptococcus mutans. They then placed their nanocapsule preparation in the centre and observed how an inhibition zone slowly spread out: an ever-widening circle of killed bacteria following the diffusion profile of the antibiotics. For quantitative evaluation, the researchers also treated the bacteria with special dyes so that the living ones glowed green and the dead ones red.

The tests included antibiotics commonly used to treat dental bed infections such as doxycycline and ciprofloxacin. "We set up a platform technology," Koch says. "This means that in practice, the gel can be equipped with specially combined capsules for each application, with different antibiotics in different doses." Plant extracts that support the healing process or that prevent biofilm formation can also be incorporated into the capsules. The nanocapsules are thus also suitable for preventative gels in dental practices. They can be inserted with the implant, thus avoiding the painful inflammation in the first place.

Methods and infrastructure
- Scanning electron microscopy
- HPLC
- Production of capsules by "solid in oil in water emulsion" (SOW) method
- Various antimicrobial assays, e.g. live-dead staining, growth kinetics, agar diffusion assay
- Cell culture techniques with various primary human cells
- Various cell-based assays on growth, production of extracellular matrix proteins, metabolic activity, and differentiation
- Class C clean room
- Cell culture laboratory
- Microbiology laboratory safety level 2

Support
- Swiss Nanoscience Institute (Nano Argovia project PERIONANO A14.15)

Collaboration
- High-Tech Research Centre University of Basel
- credentis AG

Summary Reports

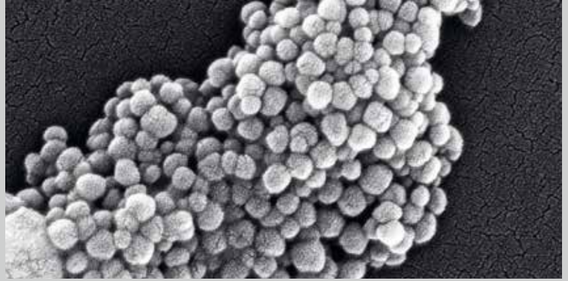
A helping hand for diabetic foot

Diabetes is very common in our society, often because of an unhealthy lifestyle with a high-calorie diet and too little exercise. While many consequences of the disease can be treated with medicine and changes in behaviour, diabetic foot is a dreaded late symptom. With diabetes, blood capillaries have a limited blood flow, so even small injuries do not heal well. When bacteria get into the wound, it often becomes inflamed, becoming larger and deeper until both the skin and the tissue underneath are affected. Over time, tissue can die and in severe cases part of the leg must be amputated.

Until now, there has been no approved therapy apart from cleaning the wound regularly and changing the dressings. Swiss start-up Topadur Pharma AG wants to change that with a new drug substance. "TOP-N53 increases blood flow in the wound and can even trigger the formation of new blood vessels, thereby promoting healing," says pharmaceutical technologist Georgios Imanidis from the FHNW HLS. The researcher and his team are working with Topadur Pharma to develop the formulation of the drug: "Our job is to put the active ingredient into a form that can be applied to the wound." To do this, they are testing different application modalities and measuring how much active ingredient penetrates into the tissue. Ideally, the active ingredient should be dissolved and gradually enter the wound tissue over several days. The final drug product must allow the tissue to breathe, otherwise fluid accumulates in the wound and can be a haven for bacteria. It must also be well tolerated when applied under a dressing and be suitable for home care, as it needs to be applied as part of regular wound care: patients should not need to visit a clinic to use the treatment. A cream or ointment formulation is not ideal, so the researchers have incorporated the active ingredient into a hydrogel made from cellulose derivatives, starch,

liquid co-solvents and water, which combine to form a gel-like structure. "Because its consistency can be adapted, the hydrogel is suitable for very different types of wounds," explains the scientist. "For dry wounds it's slightly thinner than honey, for weeping wounds it's more like a jelly."

Testing should be complete by the end of the year, by which time the research group aim to identify the best solution for delivering the active substance into the wound. TOP-N53 will then undergo a clinical trial.



New energy storage concept

Storing several hundred kilowatt-hours of electricity needs either a lot of lithium-ion batteries or a single redox-flow battery with two large, liquid-filled tanks. Potential advantages of redox flow technology are low-cost, large-scale storage, an almost unlimited lifetime and no risk of fire but this potential has still not been fulfilled.

To change this, FHNW HLS researchers in cooperation with CSEM, Muttenz, and Aigys AG, Rheinfelden, are investigating a new concept. The liquids used in the usual redox flow batteries have two disadvantages: they contain the toxic heavy metal vanadium, and, due to the low solubility of vanadium compounds, each litre of liquid cannot store much energy.

In a project funded by the Swiss Nanoscience Institute, researchers led by chemist Marcus Waser therefore focused on more readily available iron compounds and on liquids – known as dispersions – in which these compounds are suspended as nanoparticles. They showed that working redox flow batteries can indeed be produced in this way.

Personalised treatment for autoimmune patients

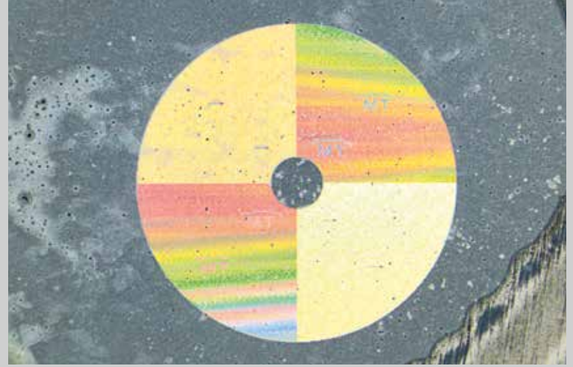
Autoimmune diseases such as lupus are hard to treat. The difficulty in making a diagnosis is, among other things, due to overlapping symptoms and a multitude of laboratory test results. FHNW HLS researchers have therefore developed a prototype clinical decision support system for hospitals. It uses artificial intelligence that can recognise patterns in the genetic, biomedical and clinical data of autoimmune patients, compares them with data from other patients and makes predictions. The results are integrated in software used by doctors to better diagnose patients and select a personalised therapy based on the individual patient disease status.

Start assistance for clean drinking water

Lake Victoria is known for its diversity of plants and animals, and people living in the surrounding villages use it primarily as a drinking water reservoir. But the idyll is deceptive: the water is dirty and often contaminated with bacteria and parasites. With support from the Symphasis Foundation and the Georg Fischer Clean Water Foundation, a team of Swiss researchers has therefore installed several “drinking water kiosks” that filter water from the lake to provide clean water for the population. The Prix Eco award-winning project was developed jointly by FHNW HLS researcher Maryna Peter and Eawag in Switzerland, and Africa Water Solutions and the Nalwire Technical Institute in Uganda.

The lake is several kilometres from some of the villages, so the water is pumped to the drinking water kiosks using solar power. The lake water is collected in a tank, usually located near a school, then filtered through membranes using only gravity. Schoolchildren receive the clean water free of charge while others pay only a very small amount for it. To ensure that plant operation is truly sustainable, local people take care of maintenance, and in future the plant should be self-supporting, even if filter membranes need to be changed or repairs are necessary. This is made possible by selling the water and by the extremely long life of the filter membranes: thanks to the low water flow pressure, the membranes can be used for up to ten years without needing a rinse cycle. Even if a biofilm forms on the membranes from bacteria and other material in the lake, the filter remains permeable to water.

Initial surveys by the researchers have shown that almost two-thirds of the local population now drink the clean water, resulting in fewer cases of diarrhoea. More water kiosks are soon to be built in the surrounding villages.



Using cherry stones and sewage sludge to combat trace substances in wastewater

Activated carbon filters are an effective means of controlling micropollutants in wastewater. However, the manufacture of activated carbon leads to high CO_2 emissions. As part of the EU's Horizon 2020 funding programme, researchers from the FHNW HLS have investigated whether activated carbon can also be obtained from natural waste materials such as cherry stones and sewage sludge, and whether it is as effective as traditionally produced activated carbon. Initial results from a pilot plant in Altenrhein are promising.

Protection against fakes

Anyone getting a dental prosthesis expects a high-quality product; dental implant manufacturers therefore have elaborate and expensive quality control systems. Imitators offering products superficially very similar in appearance may be less concerned about this, however, and use less suitable materials and production processes. In the worst case, the consequence for patients is that the implant has to be replaced, hence a method is needed to quickly and clearly distinguish originals from fakes.

FHNW HLS scientists have developed such a method in the SwissHolo project, working with research partners CSEM and Thommen Medical AG. The key to the new technology is an ultra-hard steel device to stamp identification marks into implants or abutments. An abutment is the central structure connecting the root replacement with the visible crown. The implant as well as the abutment are made of titanium, a light metal which does not cause allergies, and which integrates well into the body.

These embossed marks could be coloured holograms or visible elements such as logos or a Unique Device Identification. It is also possible to record hidden information that is only visible under special laser light.

The base of the stamp has recurring micro- or nanostructures, which are transferred to the heated titanium implant or abutment when pressure is applied. Incident light is diffracted by these structures, creating new light waves which overlap to form patterns or give the appearance of colours. Such diffractive structural colours can also be seen in nature, for example on peacock feathers and butterfly wings. The advantage of this marking method is that there is no need for coatings or other additional materials that can age or cause the body to react adversely.

The FHNW HLS project team led by Michael de Wild determined the optimal conditions for embossing implant surfaces and demonstrated that, even after being used 5,000 times, the new stamp is still effective enough to mark implants and abutments with a coloured hologram.

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FHNW University of Applied Sciences and Arts Northwestern Switzerland

The FHNW University of Applied Sciences and Arts Northwestern Switzerland is a leading education and research institution with strong links to the surrounding region. It is one of the most innovative universities of applied sciences in Switzerland. The FHNW comprises nine schools covering the following fields: Applied Psychology, Architecture, Civil Engineering and Geomatics, Art and Design, Business, Education, Life Sciences, Music, Social Work and Technology. More than 13,100 students are enrolled at the FHNW campuses in the cantons of Aargau, Basel-Land, Basel-Stadt and Solothurn. Around 1,300 lecturers teach 29 bachelor's and 18 master's degree courses as well as a range of practical and market-focused continuing education programmes. FHNW graduates are highly sought-after specialists. Application-oriented research and development has an equally high priority at the FHNW. With national and international partners from industry, business, culture, government and institutes, the FHNW runs research projects and is an active participant in European research programmes. The FHNW supports the transfer of expertise and technology to firms and institutions: in 2020, application-oriented research and development included 1,291 research projects and 359 service projects.

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