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

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## FHNW School of Life Sciences Research Highlights 2024

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## In conversation with Falko Schlottig

Since 2022, the FHNW School of Life Sciences has focused on deepening its core scientific disciplines, implementing digital tools and renewing its commitment to applied research that matters to industry and government. Prof. Dr. Falko Schlottig, Director of the FHNW School of Life Sciences, comments on key aspects of the school's strategy and vision for 2035.

#### Collaboration is a key driver of innovation

Prof. Dr. Schlottig, what role does collaboration play at the FHNW School of Life Sciences? Universities of Applied Sciences play a unique and important role in Switzerland's education and economy. First, we contribute research expertise and cutting-edge facilities to projects with the private sector and government agencies, helping them address challenges and answer questions. Second, these collaborative research projects offer undergraduate and postgraduate students exciting opportunities to work on real world situations and needs. We adapt our BSc and MSc programmes each year, to reflect changes we see in industry. The success of our school is built on a dynamic interplay between research and education.

Working with others helps us excel. By selecting the right partners to collaborate with, we are more innovative than when we work solo. This philosophy also applies within our school. Our four institutes work together on crossdisciplinary projects. A collaborative approach is needed to solve the challenges of our time.

#### **Technology focus**

Which educational and scientific areas has the FHNW School of Life Sciences identified as a priority?

Our school is moving forward in different areas. We always aim to keep pace with developments in academia and industry.

Digital technologies are now integrated into all our BSc programmes. We're implementing a combination of life sciences and artificial intelligence, data science, digital twins, automation and robotics across our research areas, and defining how staff and students effectively and ethically work with new tools. Future health is a priority topic identified by the FHNW that our school can make important contributions to.

The FHNW School of Life Sciences is moving forward in applied quantum computing. We've established a new research group in this field, and are working closely with Quantum Basel to bring applied research problems to the table (see page 42).

Sustainable chemistry is growing, with a new BSc programme in development. Several of our research projects contribute to the FHNW's zero emission priority and to EU projects. Grassroots efforts initiated by the school's researchers are underway to make our lab operations more sustainable

It's critical to take a step forward in applying biobased technologies and other green methods for producing basic chemicals. This is a need shared across the industry that will require us to be ambitious and work together.

Furthermore, the FHNW School of Life Sciences is strengthening its activities in biotech, medtech, medinformatics, pharmatech, cell biology and diagnostics.

#### Internationalisation

What is the FHNW School of Life Sciences' local and international positioning?

The FHNW School of Life Sciences offers a wealth of international study programmes and opportunities to students. Being well connected to the international environment is our responsibility. Many multinational companies are established in Switzerland and do business around the world. Our MSc programmes in particular need to prepare students for this context. In parallel, Universities of Applied Sciences are at the service of local businesses, cities and cantons. Our staff and students develop many valuable business relationships at the regional level.

Negotiations for Switzerland's reassociation to Horizon Europe are progressing well. Already in 2024, researchers in Switzerland were able to



Prof. Dr. Falko Schlottig leads the FHNW School of Life Sciences.

participate in the ERC Advanced Grants call as beneficiaries. In 2025, Swiss researchers can participate in the calls for the ERC Starting Grant, Synergy Grant and Consolidator Grant. These are all positive signals that the full reassociation of Switzerland to Horizon Europe is around the corner. In the meantime, our researchers have found new ways of making meaningful contributions to European research projects, several of which are showcased in this brochure.

#### Challenges facing us

The pandemic followed by two wars have led to What is the FHNW School of Life Sciences' difficult conditions around the world. How has the vision for 2035? FHNW School of Life Sciences felt this impact? In addition to the collaborative, scientific and For the most part, we are in a very privileged international aspects we've talked about, a key position as a member of a world-leading life element is putting people at the centre. It's our sciences cluster here in Basel. Like others in the staff's enthusiasm and ideas that drive us forward. field, we were affected by changes in the price of We've been lucky to add several new team leaders energy, chemicals and gases, as well as other that bring industry experience and networks with

"In our communities, with industry, for patients and with research peers, the people of the FHNW School of Life Sciences are driving innovation forward."

Falko Schlottig

strains on the supply chain.

We are confronted by uncertainties and changes in industry, finance and society. That's why we aim to develop critical thinking and a sense of self-responsibility in our students. Listening, asking questions in order to propose relevant solutions and not being afraid to make a change. Recognizing that our research is important and has the potential to make a difference in the world.

#### People at the centre

them. Our gender and cultural diversity are increasing, and this brings a greater range of perspectives to our work.

Harnessing our potential means empowering staff. Providing freedom to operate and taking the time to listen to each other. Asking ourselves honestly where we can have the most impact and setting priorities together helps us stay focused. As we embrace new work and its flexibility, we recognise the value of face-to-face conversations and being present for our colleagues and clients. In our communities, with industry, for patients and with research peers, the people of the FHNW School of Life Sciences are driving innovation forward.



# In our communities

Our world is facing unprecedented environmental, agricultural and energy challenges. The FHNW School of Life Sciences actively contributes to developing solutions at the municipal, cantonal, national and international level to foster a high quality of life in our communities.

## Water expertise at the service of our communities

Access to clean drinking water is inequitable worldwide. About 2 billion people live in water-stressed countries. Climate change and population growth are putting pressure on an already critical situation. Water resources are also under strain from the agriculture industry, which uses an estimated 70% of all freshwater worldwide.

Switzerland's expertise in water conservation, management and treatment is internationally recognised. Municipal and cantonal governments as well as industry are contributing to technological advances in understanding wastewater and optimizing its treatment.

At the Institute for Ecopreneurship, three research groups are making significant contributions to local, national and global needs for clean water.

#### Minimising combined sewer overflow

Michael Thomann's team is using online sensors and modelling to exploit existing wastewater collection and treatment infrastructure.

In combined sewer systems, rainwater and wastewater from households are collected together and make their way to wastewater treatment plants. Heavy rainfall can cause these canals to overflow before the water has been treated.

To counter this, Prof. Dr. Michael Thomann's team is participating in the European project StopUP, which aims to reduce pollution in receiving waters. The team is working closely with canton Basel-Landschaft's Office for Industrial Operations (AIB), which is responsible for sewers wastewater treatment plants (WWTP) and landfills

Although AIB monitors the amount of stormwater discharged from their sewers, little is known about its quality and thus the pollution load released into the environment during combined sewer overflow spills. Sewer networks and runoff dynamics are so complex that representative sampling and lab analysis are challenging to implement in everyday operation.

"Online sensors can collect sufficient data points to capture the dynamics of events. We aim to correlate parameters measured with our sensors with toxicologically relevant pollutants such as heavy metals or certain organic compounds" explains Michael Thomann. First sampling campaigns and chemical analyses showed promising results. Ecotoxicology testing is

planned in 2024 to further understand environmental impacts of untreated wet weather runoff The project aligns with the Swiss concept to minimise the ecological impact on receiving waters through integrated management of the sewer network and WWTP, including optimal utilisation of the hydraulic and biochemical capacity of the WWTP. The WWTP Birs uses sequencing batch reactors to treat wastewater. During dry weather, these reactors execute full cleaning cycles. The plant switches into wet weather mode when heavy rainfall is expected, so the reactors can partially treat a greater quantity of water.

"Our hypothesis is that it's probably beneficial to perform a shorter treatment, even if that treatment is a bit less effective, than having untreated water spill over" says Michael Thomann. "Modelling will help us understand how we could further increase the inflow to the WWTP during rainy weather without unduly compromising treatment efficiency."

"Water guality information is key in an integrated management of sewer networks, wastewater treatment plants and receiving waters" says Gerhard Koch, Head of Technology and Deputy Head of AIB Birs. "The FHNW helps us understand this aspect better and take it into account in our plant operation."



Research associate Bartosz Kawecki cleans sensors installed at the wastewater treatment plant Birs.

**Communities:** Kanton Basel-Landschaft: Europe Water system: Municipal wastewater Partners: 11 partners Funding: EU Horizon 101060428, SBFI 22.00128



#### Prof. Dr. Michael Thomann

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### How well do industrial companies know their wastewaters?

A tool developed by Miriam Langer's team is helping industry better answer this question.

The metal, pharmaceutical, chemical, cleaning and waste management industries all need to understand their wastewater and comply with environmental norms. While chemical analyses can indicate the presence and concentration of targeted substances, they cannot predict the responses of organisms or cells to a combination of these substances. Nor do chemical analyses reveal whether unknown substances, residues and metabolites are present if they are not specifically searched for.

Taking inspiration from gaps identified in an industry workshop, Prof. Dr. Miriam Langer and Research Associate Dr. Xenia Klaus first collected national and international knowledge about industrial wastewater screening with bioassays. To answer the challenges that companies face, they came up with the idea to create a panel of biological tests. Their tool, ABIScreen, combines a time-efficient biodegradation test with a battery of robust, broad-based bioassays, including toxicity to the bacteria in the wastewater treatment plant, and effects on luminous bacteria, daphnia and algae. If desired, an Ames-test can be included to determine whether substances in the wastewater have mutagenic potential.

ABIScreen is currently being deployed in five Swiss cantons. Companies collect samples of

their wastewater from a combined waste stream or a sub-stream of interest. The flasks are picked up by the Institute for Ecopreneurship and analysed in its labs, with the cost covered by the Federal Office for the Environment and the Swiss cantons involved in the project. Langer's team provides a readout of key parameters in a comprehensible report, which the company can use to both treat and prevent problems – or in many cases, confirm the success of their wastewater treatment performance.

Since the project began in 2023, over 50 companies have participated. They value the information they receive about their wastewater, the confidentiality of the process and the ability to take matters into their own hands. Some have requested follow-up screening of sub-streams so they can zero in on specific issues. The contact between members of Langer's team and industry helps stimulate dialogue.

"We're very happy with what we've achieved" says Klaus. "Companies have realised that performing bioassays is not as long, complex or expensive as they might think, and it complements chemical analysis nicely. The project is encouraging them to measure more often and check that their treatment processes are working."

Industry clients and government agencies agree. "In future, ABIScreen could help us to identify critical substances in our wastewater more easily and eliminate them at source wherever possible" says Christine Wegmann from dsm-firmenich.

"The combination of degradability tests and bioassays in ABIScreen enables a holistic characterisation of a specific wastewater in addition to chemical analyses and simultaneous evaluation of the company's own wastewater treatment. Tracing toxic and non-biodegradable substances in wastewater back to their source helps companies to find out about the required state-of-the-art techniques and therefore represents added value" says Saskia Zimmermann-Steffens, Water Division, Federal Office for the Environment.

In the next phase of the project, Langer's team will publish anonymous biotest results in a database accessible to participating companies, allowing them to compare metrics within their industry sector. The database is expected to go live in 2025, with a detailed analysis of combined results by 2026.

As more companies see value in these tests and the volume of testing increases, the FHNW School of Life Sciences plans to transfer the

knowhow to private sector labs, helping them expand their service offerings.

"This project truly illustrates the value of the FHNW's applied research expertise for Swiss industry and government, and is an active contribution to future good water quality" says Langer.

Community: Switzerland (Cantons AG, BL, GE, VD, ZH) Water system: Industrial wastewater Financing/Support: Federal Office for the Environment (FOEN) Switzerland, Cantons of Argau, Basellandschaft, Geneva, Vaud and Zurich Partners: Verband Schweizer Abwasser- und Gewässerschutzfachleute



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Technical specialist Patrik Eckert takes wastewater samples for the FHNW Institute for Ecopreneurship.

#### A systemic approach to safe water

Maryna Peter and her project team are preventing disease through handwashing technology, behavioural science, effective management and long-term relationships



School children in a primary school in Maiduguri, Borno State, Nigeria use a Gravit'eau handwashing system.

Over 45% of primary health care facilities and 50% of schools in low-and middle-income countries do not have access to handwashing facilities, basic hygiene and water supply systems necessary to prevent disease transmission. In response to this challenge, Dr. Maryna Peter and her team at the Institute for Ecopreneurship answered a call from the Swiss Agency for Development and Cooperation with a project called Hands4Health. The project proposes an approach to support water, sanitation and hygiene (WASH) systems that reduce diarrhoea among children at schools and prevent transmission of infections in health care facilities.

Coming from a background in environmental engineering, Peter is the inventor of a gravitydriven membrane technology that filters water and removes pathogenic microorganisms. It can be used for treating drinking water, but also to recycle water. Gravit'eau systems use this technology for handwashing, reusing the same

water for several weeks before it is replaced. By providing a source of water for handwashing only, the technology helps conserve drinking water, which is important during emergencies and in water-scarce areas. Peter's not-for-profit association Gravit'eau offers the design under open access to communities, who learn to produce the system themselves with the support of association members. When Peter joined the FHNW School of Life Sciences, she not only brought this technological legacy with her, but also the vision to deploy it using a systemic approach.

The Hands4Health project she leads jointly with her WASH team is active in Mali, Burkina Faso, Nigeria and Palestine. The consortium is composed of researchers from the FHNW, the Swiss Tropical and Public Health Institute, École Polytechnique Fédérale de Lausanne and the Palestinian Polytechnic University. Alongside them are non-governmental organisations Terre

des hommes. Cesvi and Skat Foundation, as well as private sector partners Ranas and Martin Systems. The team works closely with local governments and community representatives, focusing on improving water, sanitation and hygiene services at off-grid schools and health care facilities located in conflict-affected areas.

The first step is developing a shared understanding of the context-specific challenges and defining a common goal to work toward. "Each situation is different, and it's crucial to engage local stakeholders at the outset so that we can prioritise the needs effectively and sustainably and understand the barriers" says Peter. "NGOs like our partners Terre des hommes and Cesvi have long-standing relationships with communities, local governments, schools and health care facilities and help us build trust."

A key partner of the project, Ranas, is contributing their model of behaviour change to

understand motivators for and barriers to handwashing in school children and health care facility staff. Factors such as risk perceptions, attitudes, norms and values, abilities and self-regulation are important drivers of behaviour. For each country, behavioural factors that can improve consistency of handwashing practices were identified. Corresponding behaviour change activities can then be selected from activity catalogues that are prepared within the project, specifically targeted to the schools' and health care facilities' contexts Peter's team is contributing overall project leadership as well as hardware interventions, monitoring technologies and impact evaluation. They are evaluating sensors for the handwashing stations that measure water level, and supporting NGOs and authorities in establishing effective monitoring processes using Kobo-based data collection apps linked to dashboards. Finally,

they offer simple how-to guides for planning

"Our goal is broad public dissemination of a systemic approach to communities and NGOs, so they can test and implement it to increase sustainability and impact of their WASH programmes."

Maryna Peter

improvements to water systems, maintaining water tanks and chlorinating water.

"This project is not only about getting scientific results" says Peter. "Our goal is broad public dissemination of a systemic approach to communities and NGOs, so they can test and implement it to increase the sustainability and impact of their WASH programmes."

Since 2021, Hands4Health has worked in 26 schools and 24 health care facilities, with additional implementations planned in 24 health care facilities and 26 schools by the end of 2024, reaching nearly 100,000 people.

Communities: Health care facilities and schools in Mali, Burkina Faso, Nigeria and Palestine Water and sanitation systems: Recycling water for handwashing; Chlorination; Rehabilitation of infrastructure; Behaviour change; Digitalised monitoring and impact evaluation Partners: 10 partners Funding: Swiss Agency for Development and Cooperation - Transform 2020



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## Let the sun shine in

Ensuring sustainability of new photovoltaic materials

#### Perovskites - Did you know?

Perovskite is a mineral composed of calcium titanium oxide. Its crystal structure has inspired the development of a class of materials, also called perovskites, which feature two positively charged ions and three negatively charged ions.

Perovskite solar cells (PSCs) contain compounds with the perovskite structure, most often methylammonium lead halides. They offer a high absorption coefficient coupled with simplicity and low production cost. Incorporation of carbon electrodes in PSCs can further improve their sustainability, using fewer critical raw materials. However, there are also voices expressing concerns about environmental compatibility due to their lead content, which is low but present.

Perovskite solar cells can be printed as thin. flexible films for applications in buildings, vehicles and electronic devices. In tandem perovskite cells, a perovskite cell is layered on top of a traditional silicon cell, which significantly boosts its energy conversion. PSCs can also be used alone to power small vehicles such as drones. As solar panel size. location and energy needs vary, PSCs can provide new options to help diversify the solar market and meet clean energy targets.

Net zero by 2050 – this goal is at the heart of the EU's Green Deal. To achieve it, the deployment of solar photovoltaic technologies must be scaled up exponentially. New materials offer a leap forward in the capacity of solar panels to absorb and convert energy, but it's important not to lose sight of sustainability considerations relating to their production, use and end of life.

Dr. Markus Lenz and his team at the Institute for Ecopreneurship are leading the charge in investigating the sustainability of new photovoltaic materials. Specializing in the circular economy of metals and minerals, they are participating in two EU Horizon projects, namely Nexus and Pearl, to examine if perovskites can be safely used in the next generation of solar panels. In parallel, they are working on recycling perovskites so that they will not become a waste problem in the future.

Perovskite cells contain minimal amounts of lead, with a protective layer of glass or plastic designed to contain it. Lenz's team is conducting outdoor leaching tests to determine if the cells are hermetic. To do this, they installed several perovskite panels on the roof of the FHNW School of Life Sciences in Muttenz that are exposed to real-life weather conditions. Temperature, light, moisture and wind vary throughout the year, and the panels are subject to more extreme weather

events such as hail. Metal quantification tests performed on rainwater samples collected from the panels have shown very low predicted environmental concentrations, comparable to those permitted in drinking water. Within the Nexus project, further facilities are now being installed in Bolzano and Valencia to ensure that perovskites can be safely operated under different climate conditions. "We currently see little reason to be concerned about the possible environmental impacts of lead during the use phase" says Lenz.

But what if the cell were to be damaged? To find out. Lenz's team simulates more extreme weather events in a controlled environment. In the Pearl project, they expose perovskite modules to higher UV radiation, create defects (holes) using a laser, and look at whether bacteria could damage protective plastic layers.

And when the modules reach their end of life? Recovery and recycling of critical minerals is key to solidifying an independent European supply chain and ensuring sustainability of solar and battery power. Using their expertise in hydrometallic recovery, Lenz's team has demonstrated for the first time how water alone is sufficient to recover pure lead iodide (PbI2) from perovskites.



Lenz's team conducts outdoor leaching tests to assess the safety of perovskite photovoltaic panels installed on the roof of the FHNW Campus in Muttenz.

The recovered lead iodide can be used to produce new perovskite materials, while the old cells are no longer considered hazardous waste, a win-win situation.

Innovative solar firms participating in the Nexus and Pearl projects are grateful for the environmental fate testing and material recycling done by Lenz's team.

Oxford PV, who set a world record in energy conversion of 28.6% for their commercialsized perovskite-on-silicon tandem solar cell in January 2024, is working toward a target of >30% for module power conversion efficiency in the Nexus project.

Saule Technologies, who is participating in the Pearl project, specialises in printing perovskite solar cells on thin, flexible substrates at low temperatures.

"In the past decade, perovskite PV has gone from a lab curiosity to a powerhouse with the

"We're providing scientific facts that can help manage possible risks of perovskites, determine their environmental and socially acceptability and facilitate their adoption." Markus Lenz

potential to democratise clean energy. At Saule Technologies, we recognise the urgency of the climate crisis and are committed to harnessing this technology responsibly, minimising environmental impacts at every stage of development and production. Through the PEARL project we are gaining crucial insights, ensuring a sustainable future for the clean energy coming from our perovskite PV technology" says Dr. Konrad Wojciechowski, Chief Science Officer at Saule.

"Our role is neither to engage in greenwashing, nor to generate alarmism" says Lenz. "In these projects, we're providing scientific facts that can help manage possible risks of perovskites, determine their environmental and social acceptability and facilitate their adoption. We also hope our methods contribute to scaling-up and broadly deploying recycling processes for critical minerals."

#### Community: Europe Financing / Support:

Nexus: Horizon Europe (GA 101075330) and SERI (22.00314) Pearl: Horizon Europe (GA 101122283) and SERI (23.00383)

#### Partners:

Nexus: 12 partners including Oxford PV Pearl: 10 partners including Saule



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## In the mix

Combining biochar and compost to rehabilitate degraded soils

#### **Biochar - Did you know?**

Biochar is a form of charcoal obtained by thermally decomposing biomass at temperatures between 400 and 700 °C without oxygen, a process known as pyrolysis. Over 2500 years ago, Amazonians used a similar process of smouldering agricultural waste, bones, broken pottery and other organic matter to create highly fertile Terra preta, which means dark earth in Portuguese. Today, most biochar is produced from woody and grassy biowastes.

Pyrolysis of biomass results not only in the production of solid biochar but also in biofuel and syngas. Plants producing biochar may use the syngas they generate to fuel pyrolysis.

Biochar can provide stable carbon in soil for hundreds to thousands of years. Its porosity helps soil retain water, nutrients and organic matter. It can also reduce nitrous oxide ( $N_2O$ ) emissions during composting, which helps counter greenhouse gas emissions. If you have a vegetable patch in your garden or flowers on your balcony, you know the benefits of using compost to maintain or increase the quality of your soil. Materials added to soil to improve its chemical, physical and/or biological properties are called soil amendments. One soil amendment generating substantial interest is biochar, a form of charcoal obtained from biomass.

In the Agrocomposit project conducted as part of the European Joint Programme on Agricultural Soil Management (EJP SOIL), scientists from the Institute for Ecopreneurship and Agroscope are collaborating with researchers and practitioners in Norway and Hungary to combine biochar with composting of different types of biowaste. They are testing the potential of composite soil amendments to rehabilitate degraded soils, increase nitrogen use efficiency along the entire value chain and reduce greenhouse gas emissions.

In Switzerland, FHNW researchers are cocomposting biochar with anaerobically digested green waste and the organic fraction of municipal solid waste from an anaerobic digestion plant. In Norway, researchers are combining aquaculture biowaste with biochar, while in Hungary, a mixture of sewage sludge and biochar is being investigated. First, the team is producing composite soil amendments from different biowastes and with varying biochar concentrations in the lab, and testing these mixtures in pot experiments on wheat and maize plants. They are measuring the level of nutrients, carbon, trace metals and polycyclic aromatic hydrocarbon (PAH) in the composites themselves, in the different types of soils they are applied to and in the crops. These results will be compared to pots that contain no amendments, digested waste only, biochar only and traditional mineral fertilisers.

Next, the team will apply its findings outdoors in large-scale field tests, to quantify the potential of the composite soil amendments to improve degraded soils at specific sites. They will determine which composite amendments help enhance soil properties to support agroecological functions, including increased carbon content and improved water-holding capacity.

"Field tests are challenging, with a large number of variables that can't be fully controlled, but they are essential to translating lab results into application. We are excited to generate new insights into biowaste valorisation routes for healthier agroecosystems in Europe through the application of biochar-compost composites in real-world situations" says Gross.



Thomas Gross uses a drum composter to generate a new composite soil amendment that includes biochar, anaerobically digested green waste and the organic fraction of municipal solid waste.

Finding promising composite soil amendments is not the only aim. The project collaborates with several full-scale biowaste treatment facilities and farms in Switzerland and Europe to explore environmentally and economically sound biowaste valorisation. To quantify the environmental footprint, Gross' team is conducting substance flow and lifecycle analysis to calculate environmental impacts from resource use and emissions along the biowaste value chain. Combined with ecotoxicological assessments conducted by other consortium partners, this will provide a solid basis to determine if there are risks for soil health and crop safety, and whether the addition of biochar to compost is justified in terms of yield, environmental impacts and economic costs.

Agricultural and environmental agencies require this type of data to establish regulations and provide sound guidance to farmers. The Swiss Federal Office of the Environment is calling "Ultimately, we hope to help close resource cycles, reduce the dependency on non-renewable fertilisers, and provide new solutions to rehabilitate degraded soils." Thomas Gross

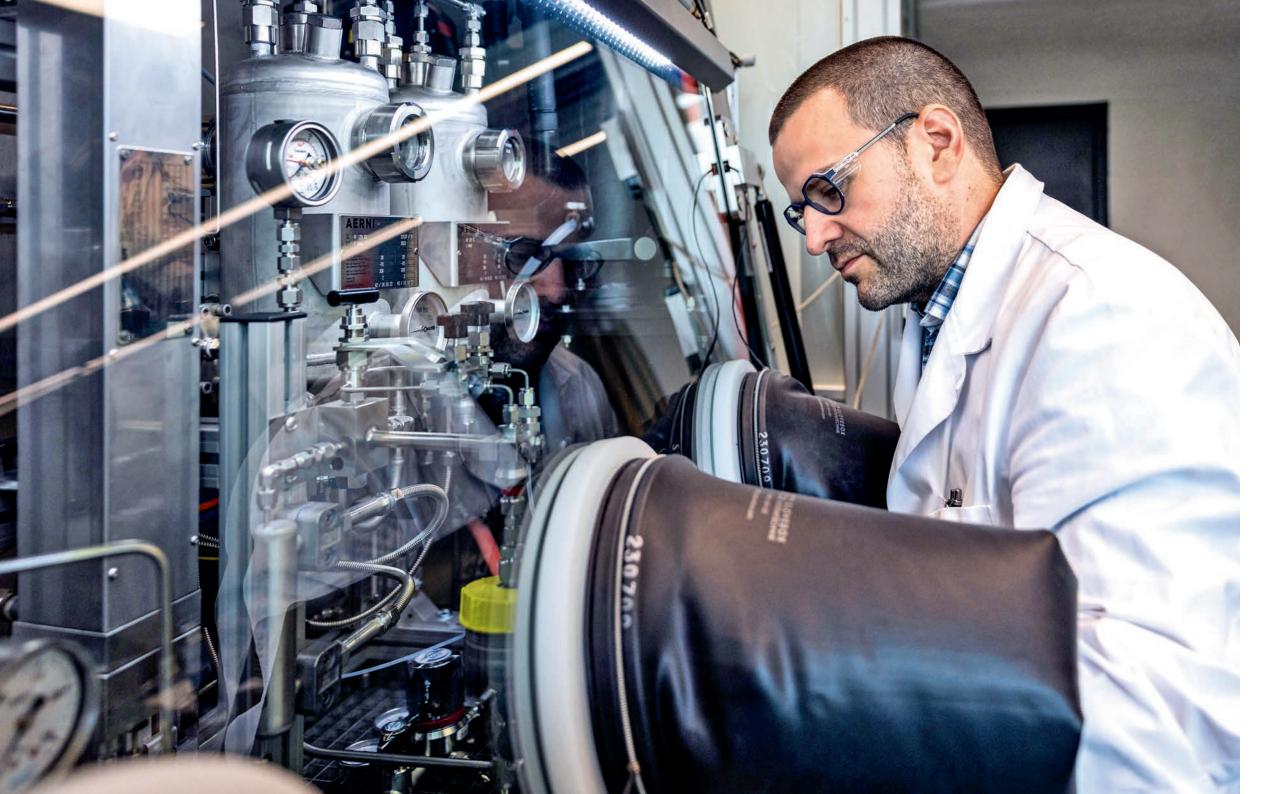
for more knowledge from research before biochar can be recommended for use in Swiss soils, particularly with regard to the effects on soil organisms. Concerns regarding biochar have been formulated in the following fact sheet: Biochar in Swiss agriculture - risks and opportunities for soil and climate [in German: Pflanzenkohle in der Schweizer Landwirtschaft – Risiken und Chancen für Boden und Klima].

At the intersection of biowaste valorisation, agriculture and bioenergy, this project can help generate knowledge about the safety and efficacy of combining biochar with compost, and in the long run, contribute to driving the Swiss bioeconomy. "Ultimately, we hope to help close resource cycles, reduce the dependency on non-renewable fertilisers and provide new solutions to rehabilitate degraded soils" says Thomas Gross. Community: Switzerland, Europe Financing / Support: SNSF 31SL30\_214524 Partners: Agroscope; Budapest University of Technology and Economics; Norwegian Institute of Bioeconomy Research; Institute for Soil Sciences of Hungary



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# Trusted partner for industry

Swiss companies of all sizes seek us out as a trusted partner for applied research. With a key role in the Basel cluster, our competences and stateof-the-art facilities are an asset for both big pharma and SMEs. Innosuisse project financing is available for firms who collaborate with us to bring their ideas toward the market.

## **Biologics – a new generation** of medicines that require new solutions

Biologics have established their place as a new generation of medicines that provide more targeted treatment options for cancer, autoimmune diseases, metabolic diseases and genetic disorders.

Today, biologic modalities such as antibody-drug conjugates, bispecific proteins and cell and gene therapies have opened up even more avenues, yet they present unique challenges in biopharmaceutical production. Meanwhile, some established biologics are moving from clinical to home settings, where patients can administer them themselves. This creates novel considerations for biologics storage, injection and alternative delivery routes.

Two teams at the Institute for Pharma Technology and Biotechnology are collaborating with industry to find solutions to new challenges across the entire biomanufacturing process, from cell line development to culture, purification, formulation, fill, finish and quality assurance of technical and preclinical trial material.



Endress + Hauser, a leading provider of Raman systems, is implementing calibration models developed at the Institute for Pharma Technology and Biotechnology.

Cell culture

Mammalian host cell lines such as Chinese Hamster Ovary (CHO) or Human Embryonic Kidney (HEK) cells act as living factories to produce biologics. Understanding what is happening inside the bioreactor during different stages of cell culture is key to obtaining high yields.

Raman spectroscopy, including analysers, probes and software, can enable real-time analysis of nutrients, metabolites, product quality and cell viability, helping manufacturers gain control of the process and make decisions about when to feed the culture. However, its wide-scale implementation is currently limited by calibration model development, which requires labour-intensive and time-consuming experimental setups as well as complex IT infrastructure.

In an Innosuisse project called Raman Ready. researchers from the Institute for Pharma Technology and Biotechnology are developing

ready-to-use calibration models for Raman spectroscopy in bioprocesses.

"By combining Raman technology with machine learning expertise, we aim to create versatile and accurate models that are applicable for a wide range of biologics and processes" says Prof. Dr. Thomas Villiger, Group Leader, Bioprocess Technology.

The project's implementation partner, Endress + Hauser, is a leading provider of Raman systems who believes in the importance of delivering high-quality sensors to its clients.

"We are confident that the work we are doing with the FHNW will help make Raman systems more accessible to our clients and broaden the application of this powerful technology" says Lukas Jegge, Senior Sales Engineer at Endress + Hauser.

Doctoral researcher Sherin Panikulam performs chromatography to purify biologics, and analyses whether host cell proteins remain after purification.

#### **Purification of antibodies**

After production, biologic modalities such as antibodies produced from a host cell need to be separated from the culture medium in which they were grown. Centrifugation, membrane filtration and protein affinity chromatography are the most common steps to capture and purify the target biologics. However, small amounts of protein impurities, known as host cell proteins (HCPs), may remain after chromatography and can cause concerns for product quality, safety and/or efficacy.

In a large-scale study conducted with Novartis, Sherin Panikulam from Villiger's team analysed 23 biologics after affinity chromatography. The goal was to find out what types of HCPs remained and understand why they had been captured along with the biologics, to better guide process development

Of the 449 HCPs identified, most were captured along with fewer than 3 biologics. However, some HCPs remained identified in many biologics. Using protein network analysis, Panikulam showed that protein-protein interaction is an additional mechanism for HCP co-elution, resulting in failure to remove them by chromatography.

"Our findings may help to guide host cell line development, for example knockdown or knockout of the primary binding partner in the CHO cell line. We also hope that new purification strategies can be developed to prevent certain host-cell proteins from bringing their friends to the party and being captured with target biologics" says Panikulam.

"Nowadays, we need a better knowledge of residual impurities remaining in biologics. These results are key to understanding how HCPs behave during the purification process of a drug, and support process development in case a problematic HCP is spotted" says Nicolas Lebesgue, Principal Scientist in Analytical Characterization at Novartis.



Doctoral researcher Julia Müller develops new continuous purification strategies for viral vectors used in gene therapy.

"Continuous chromatography offers great promise for achieving higher yields in gene therapy manufacturing, while increasing sustainability and reducing costs." Thomas Müller-Späth, CEO, YMC



#### **Purification of gene therapeutics**

In gene therapy, a repair DNA sequence is packaged inside a viral vector, also called a capsid, that delivers the DNA to the nucleus of a cell. Manufacturing gene therapeutics is complex and time consuming, as the traditional production process requires three plasmids, growth of host HEK cells, introduction of the three plasmids into HEK cells, production by the HEK cells of viral capsids that contain the therapeutic DNA sequence, and separation of capsids from the material used to produce them.

Not all viral vectors produced contain the therapeutic DNA. After production in HEK cells, about 50-80% of capsids are empty. Capture and polishing chromatography steps are used to obtain 80-90% full capsids and to ensure therapeutic efficacy. Purification processes for viral vectors are not as well established or standardised as those for antibodies, especially at

larger scale. This is a critical bottleneck to making gene therapies more affordable and available.

In a project with YMC, a leading developer of chromatographic stationary phases and purification equipment, Julia Müller from Villiger's lab is working on continuous purification strategies for adeno-associated viral vectors (AAVs).

"Instead of capturing AAVs on a single column and losing some during loading, we are using twin columns to transfer the flow-through from the first column to the second, giving AAVs a second chance to be captured" says Müller. Afterwards, the first column is emptied and reintegrated into the process, picking up the baton when the second column is full, and so on until everything has been purified. Continuous purification not only captures more AAVs - it also uses less material and energy than batch purification and is easier to characterise for quality assurance.

Similarly, during polishing to separate full and empty AAVs, the purest fraction of full AAVs (centre cut) is extracted from the first column, while partially pure side cuts containing both empty and full AAVs are recycled on a second column, resulting in increased yield of full AAVs without compromising purity.

"The results generated by the FHNW demonstrate that continuous chromatography offers great promise for achieving higher yields in gene therapy manufacturing, while increasing sustainability and reducing costs" says Thomas Müller-Späth, CEO of YMC.

#### **Biologics drug product formulation**

Biologics can become destabilised by conditions during transport, storage, and handling, which can lead to loss of efficacy or unwanted immune reactions. With biologics administration moving from the doctor's office to the home, patients are becoming part of the cold chain and sharing responsibility for consistent refrigeration and proper handling of their biologics.

To prevent damage to their structure, biologics are formulated with surfactants, amphiphilic molecules composed of a hydrophilic head and a hydrophobic tail. Surfactants prevent biologics aggregation by blocking their adsorption at air-water interfaces encountered during manufacturing, storage, transport and use. Only three surfactants are currently used in commercial biologics formulation, and they face challenges when it comes to degradation.

In a project conducted in collaboration with

Surfactants, which have a hydrophilic head and hydrophobic tail, are used in biologics formulation to prevent aggregation.

Novartis, Prof. Dr. Oliver Gemershaus and his team helped assess 40 new potential surfactants, including existing molecules and novel surfactants synthesised by Novartis. They first examined biophysical properties of the candidates, followed by their ability to prevent agitation-induced aggregation when formulated with different types of biologics including a disordered protein, a fragment antigen binding region, monoclonal antibodies and a fusion protein. Most importantly, the chemical and enzymatic degradation propensity of the new surfactants was investigated.

The team identified 2 finalists that offered comparable or better biologics stabilisation and significantly less surfactant degradation compared to existing formulations.

"It was crucial to have the expertise of FNHW at our disposal when selecting the above alternative surfactants" says Karoline Bechtold-Peters, Director Science & Technology at Novartis.

"We will continue to explore new surfactants together."

Capabilities at the Institute for Pharma Technology and Biotechnology have been beneficial in two other projects with Novartis: Micro downscale models to evaluate the freeze-thaw stability of biological agents; as well as Physical assessment and models to evaluate the silicone oil depletion activity of biological agents. Both are essential for products in pre-filled syringes.

"Early downscale models and simulations enable speed to first-in-human and help accelerate the development timeline" says Bechtold-Peters.



PhD student llias Amara produces artificial reference particles using two photo polymerisation.

Scientific assistant Yasmin Grether conducts tests in the FHNW's Process Technology Center, where companies can develop new fill finish formats and protocols.

#### Packaging and administration

Once biologics have been formulated and characterised, they undergo fill finish, which involves transferring the biologic drug substance to a sterile vial or syringe, stoppering, inspection and labelling. Some biologics are lyophilised before stoppering to increase their stability. The Process Technology Center at the FHNW Campus Muttenz features a cleanroom where companies can develop new fill finish protocols, fill reference samples or manufacture biologics for preclinical trials. Increasingly, biologics are becoming available for patients to administer at home using pre-filled syringes, autoinjectors or patch pumps. These products offer patients convenience and autonomy, and are designed to help overcome needle

phobia and incorrect administration.

Pre-filled syringes contain the right dosage, and the patient can control the injection speed. Autoinjectors are semi-automatic, with a button to

#### **Particle characterisation**

After biologics have been produced, purified and formulated, they undergo quality assurance to ensure they meet established standards for injectable drug formulations, including limits of visible and subvisible particles.

Particles typically range from nanometers to hundreds of micrometers. They may be extrinsic to the normal manufacturing process, for example cellulose fibers from cleaning processes. They can also be intrinsic, having emanated from normal manufacturing processes or the container closure system, or they may be inherent, originating from formulation excipients or the active ingredient, for example expected aggregates or hazes.

Calibration of instruments used for sizing and counting such particles is done with perfectly spherical reference particles that offer high optical contrast. Intrinsic protein particles, on the

other hand, pose a challenge for instruments due to their irregular shape and translucent nature.

To address this, Germershaus' group fabricated irregularly shaped particles representative of subvisible and visible particles, in a collaboration project with Roche. Created by two photo polymerisation (2PP) printing, these artificial particles may serve as new reference material mimicking the morphological, optical and physical properties of protein particles.

In their study, they compared the new reference material to currently used polystyrene spheres, standard particles from the National Institute of Standards and Technology and actual protein particles generated by exposing monoclonal antibodies to various stresses.

"We are currently working towards broad evaluation of the suitability of the protein-like particle standards we developed with stakeholders in the pharmaceutical industry, with the

ultimate goal of harmonising subvisible and visible protein particle characterisation across laboratories and organisations" says Germershaus.



start the injection, a hidden needle protected by a safety cover and audible clicks that indicate when the injection is complete. Patch pumps and other wearable devices are the newest, most advanced options for biologics self-administration. The latest devices feature innovations to reconstitute lyophilised biologics and enable delivery of larger volumes by subcutaneous infusion.

Germershaus' team is collaborating with companies from the pharma, packaging and device sectors focusing on the development of new injection devices. The subcutaneous delivery of larger volumes is currently an important topic. Studies range from investigation of the compatibility of devices (e.g. patch pumps) with biologic drug products, to filling of novel packaging formats (e.g. cartridges) under aseptic conditions. Filling can be performed manually or automatically in batch sizes from single digit unit numbers up to 1000 units per hour.

#### Financing / Support:

Raman Ready: Innosuisse 114.286 IP-LS Development of a Mobile Dosing Pump for the Administration of Biologics: 25721.1 PFLS-LS Partners: Endress + Hauser, Novartis, Roche, YMC ChromaCon, Sensile Medical AG



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# **Overcoming frontiers in brain medicine**

Our brain is protected by a layer of tightly woven endothelial cells that line the brain's blood vessels, called the blood-brain barrier. These cells block foreign agents such as pathogens from entering our body's command centre. At the same time, nutrients that the brain needs are allowed to pass, via a process called receptor-mediated transcytosis (RMT). Receptors on the surface of endothelial cells recognise and bind to nutrients, and carry them into the brain.

The barrier also prevents some therapeutics from reaching disease targets in the brain. Medicines that can successfully enter the brain include anesthetics, antidepressants and antipsychotics. A great need remains however for therapies to treat Alzheimer's, ALS, Parkinson's, brain cancers and more. Biologic drugs could offer hope, but strategies must be devised to sneak these large molecules past the barrier using RMT.

Teams at the Institute of Chemistry and Bioanalytics are working on engineering nanomedicines that can enter the brain, as well as new models of the blood-brain barrier that can be used by pharmaceutical companies to test whether medicines can cross.

#### **Big hopes for nanomolecules**

Nano-engineered shield for enzyme replacement therapy could help it reach targets in the brain

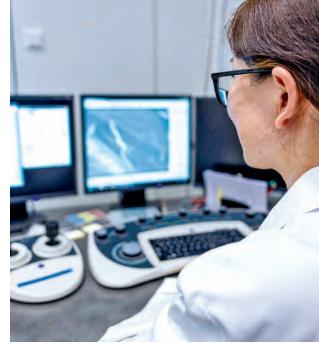
Enzymes are proteins that speed up chemical reactions in cells. They break down food and toxins in our digestive system and liver, and help DNA unwind during cell division and replication for example. Beyond their role in our bodies, their properties as catalysts make them interesting as a greener alternative to chemical catalysts for chemical reactions.

In 2016, scientists at the Institute for Chemistry and Bioanalytics developed an innovative method to engineer enzymes inside nanoparticles, making them more resilient for applications in biocatalysis. They spun off the company Inofea, focused on providing solutions for stable, active and pure enzymes for chemical reactions and production processes.

Enzymes can also act as therapeutics, in Shahqaldian's team is seeking to overcome cases when the body is not producing enough on this problem by designing an outer enzyme shield its own. Building on their enzyme engineering that will not only protect the enzymes, but more technology, Prof. Dr. Patrick Shahqaldian and his importantly, bind to receptors on the blood-brain team developed nano-architectures to protect barrier to allow transport across it. sensitive enzyme therapeutics from degradation "By decorating the enzymes with structures in the body (e.g. intestinal tract). The team that the brain's endothelial cells recognise designed an organic-inorganic hybrid that enables and bind to, it may be possible to deliver enzymes enzymes to stay alive and reach their targets in to the brain. We hope our approach will contribute to new treatments for lysosomal storage the gut. This can significantly reduce the pill diseases affecting central nervous system burden for patients. For the therapeutic applications of the shielding technology, Shahgaldian targets" says Shahgaldian.

spun off Perseo Pharma in 2019. The firm is currently conducting preclinical testing of four digestive therapies, as well as investigating if a similar approach could be used to deliver a cocktail of enzymes that prevents metabolic activity in cancer cells.

The next frontier for Shahgaldian and his team is another difficult environment for medicines: the brain. This time, they're working on solutions for lysosomal storage diseases (LSD), a large group of metabolic disorders caused by enzyme deficiencies in the lysosome. About 50-70% of LSDs affect the central nervous system. Enzyme replacement therapies can help address some of these conditions, but unfortunately they do not cross the blood-brain barrier.



Research associate Congyu Wu performs scanning electron microscopy to characterise nanomolecules designed to bind to the blood-brain barrier.

Another strategy that the team may explore in the future is the design of nanoparticles for intranasal administration. Nose to brain is a promising route that avoids some challenges associated with the blood-brain barrier and for which nanomolecules are particularly suited.

#### Financing / Support: Swiss Nanoscience Institute Partners: Perseo Pharma



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#### Testing brain medicines in the fast lane

New *in vitro* model of the blood-brain barrier helps pharma identify promising candidates



Research associate Floriana Burgio seeds brain microvascular endothelial cells in an OrganoPlate-3 lane (Mimetas) to create a model of the blood-brain barrier.

model exhibits functional transferrin receptormediated uptake and transcytosis."

The project was conducted in collaboration with UCB Pharma Belgium, a leader in medicines for neurological, immune and rare diseases.

"The FHNW's model of the BBB represents a great step forward towards testing the ability of potential drug candidates to enter the brain. In the end, such a model can improve preclinical testing of future medicines from both an efficacy but also a safety point of view" says Rainer Class, Associate Director of *In vitro* ADME, UCB Pharma.

"Not only did this project enable us to develop a model that UCB Pharma Belgium can use as part of their drug screening process; it also allowed the FHNW School of Life Sciences to break new ground in designing *in vitro* models with induced pluripotent stem cells, propelled by the latest microfluidic technologies" says group leader Prof. Dr. Laura Suter Dick. "The FHNW's model of the blood-brain barrier represents a great step forward towards testing the ability of potential drug candidates to enter the brain."

Rainer Class, Associate Director of In vitro ADME, UCB Pharma.

Partners: UCB Pharma Belgium



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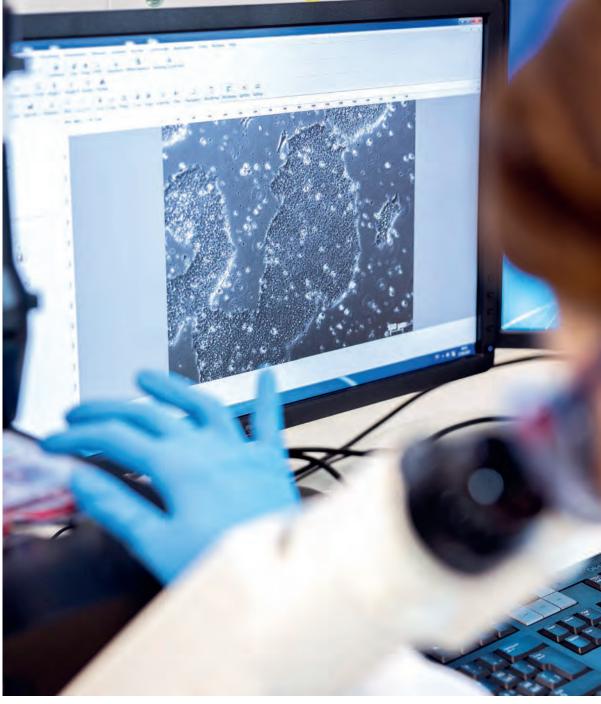
The need for brain therapeutics is great, and many pharmaceutical companies are developing drugs. To test these novel medicines, clinically relevant models that measure their ability to cross the blood-brain barrier are needed.

*In vitro* models are cells grown inside a special device that mimics how an organ, or part of it, functions. Prof. Dr. Laura Suter-Dick's team at the Institute for Chemistry and Bioanalytics has deep expertise in developing liver models to test the safety of new medicines, while reducing and replacing the need to use animals for example.

Backed by this strong foundation in advanced *in vitro* models and new approach methodologies (NAMs), postdoctoral researcher Dr. Floriana Burgio from Suter-Dick's cell biology group, in collaboration with scientists from UCB Pharma Belgium, set out to create a model of the bloodbrain barrier using induced pluripotent stem cells (iPSC). These immature cells can be differentiated into any cell type, making them versatile for research.

The model implemented by Dr. Burgio features a single cell type: brain microvascular endothelial cells (BMEC) derived from iPSC. She grew the model in an OrganoPlate® (Mimetas) and conducted tests to confirm that it mimics barrier tightness. The model features a top channel with endothelial cells, a middle channel with extra-cellular matrix, and an empty bottom channel. Test molecules are perfused into the top channel; those that bind and pass are collected in the bottom channel. The system is compatible with automated fluid handling and allows the evaluation of 40 chips simultaneously.

"When tested in our BBB model, we showed that a molecule which binds to the transferrin receptor has an 11-fold increase in crossing the barrier compared to a control molecule that does not bind" says Burgio. "This established that our



Burgio assesses if the induced pluripotent stem cells are dense enough to start differentiation into brain microvascular endothelial cells.

## Safety first!

Andreas Zogg brings chemical engineering companies and students together to make shared advances in process safety

"The process safety models developed by FHNW are enabling safer, more energy efficient reactions that produce high quality surfactants. We look forward to applying the models to scale up production in our facilities" Roland Borner, Schärer & Schläpfer AG

#### Managing ethoxylation - Did you know?

Ethoxylation is a chemical reaction of ethylene oxide with an alcohol, acid or triglyceride oil. The reaction is performed to produce surfactants, which are used in laundry detergents, surface cleaners, cosmetics, agricultural products, textiles and paint.

Performing ethoxylation as a continuous reaction is more sustainable and cost-effective than running it as a batch reaction, but the explosive nature of ethylene oxide requires mastery of reaction safety.

Properly managing and scaling up hazardous continuous reactions includes:

- reaction calorimetry: measuring heat released from the reaction, determining heat and gas removal requirements to control the reaction.
- thermal decomposition: knowing the temperature at which a substance chemically decomposes.
- explosion pressure: measuring the reaction's pressure to determine its risk of explosion.
- pressure relief: providing a mechanism in the reactor to release excess pressure.

Prof. Dr. Andreas Zogg has a passion for process safety. He joined the FHNW School of Life Sciences in 2018 after serving as Safety expert at Novartis, and Process development chemist at F. Hoffmann – La Roche and Ciba SC for several years. Now he leads the process development group at the FHNW's Process Technology Center. He is founder and president of the association Miniplant 4.0.

"Three drivers of innovation in today's Swiss chemical industry are safety, sustainability and quality" says Zogg. "If you ask me, safety always comes first!"

Many chemical reactions performed to produce ingredients for detergents and cosmetics pose a danger of fire and explosion. Transitioning from batch or semi-batch reactions to continuous flow chemistry can provide safety advantages.

Second, as companies look to reduce their energy consumption, they see the opportunity to conduct some reactions in continuous mode to avoid costly energy peaks. This is creating a demand for continuous reactor systems deployed at smaller, decentralised production sites.

Finally, as the price of chemicals manufactured in Switzerland is high, their quality must be a differentiating factor. Scaling up flow chemistry helps promote the fine chemicals sector nationally.

Zogg is addressing all three elements in an Innosuisse project called Simulation-based safety concept for the scale-up of safety-related demanding continuous processes, performed in collaboration with MSc students from the FHNW School of Life Sciences and industry partners.

Zogg's team is contributing a model to scale up a continuous ethoxylation reaction and determine when an explosion is likely to occur. The initial model is built on data in scientific literature about thermodynamics and reaction kinetics, combined with small-scale differential scanning calorimetry (DSC) measurements collected in the FHNW's Process Technology Center explosion reactor.

To determine when the ethoxylation reaction is likely to cause an explosion, Zogg's team modelled two scenarios and performed them within a unique explosion reactor, using the resulting vapor liquid equilibrium data to refine their model. Although they had modelled a maximum explosion pressure of 12 bar, the reaction was performed up to 20 bar before exploding.

Furthermore, Zogg's team conceptualised the basic design of the continuous ethoxylation plant. including a comprehensive risk analysis (HAZOP).

Finally, they performed the flow reaction in a safety glove box that they designed specifically for this purpose. The box provides a nitrogen

atmosphere, monitors oxygen and ethylene oxide the pharma and chemical industry. The goal is to levels and features an integrated safety washer to enable direct scale-up from lab to production destroy ethylene oxide steam leakage. volumes Fluitec, a designer and manufacturer of

reaction systems, is contributing a small-scale continuous reaction calorimeter to the project This specialised device, which sits inside the safety glove box, measures the heat released from the reaction. The real-time data collected using Fluitec's device is used to adjust the FHNW's process model.

"Deploying our flow calorimeter in an experimental setting and contributing to new models for flow chemistry scale-up provides valuable insights about how the calorimeter performs at small and production scale" says says Marlies Moser, Fluitec.

The FHNW's model, strengthened by data collected by Fluitec's calorimeter, will be applied by the project's implementation partner, Schärer & Schläpfer AG, a producer of surfactants for



Master students This Zahnd and Benedikt Brönnimann gain direct experience in modelling and managing hazardous processes in collaboration with industry partners

"The process safety models developed by the FHNW are enabling safer, more energy efficient reactions that produce high quality surfactants. We look forward to applying the models to scale up production in our facilities" says Roland Borner, Schärer & Schläpfer AG.

In addition to industrial innovation, the project provides hands-on educational opportunities. Two part-time MSc students. This Zahnd and Benedikt Brönnimann, are working on the Innosuisse project while completing their Master's in Chemical Engineering. BSc students in chemical engineering also carry out a portion of the work. The FHNW's Miniplant facility, including its unique explosion reactor for testing the thermal process safety of explosive reactions, provides students with direct experience in hazardous process

modelling and management.

"Especially for students at the Master's level, it enables them to deepen their knowledge in real-life settings before they graduate and fully transition to industry" says Zogg. "At the same time, it allows us to advance knowledge on how to safely scale-up flow chemistry processes to promote their adoption by industry."

Partners: Fluitec; Schärer & Schläpfer AG Financing / Support : Innosuisse project 62273.1 IP-ENG



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# Progress for patients

Healthcare is progressing from the clinic to the home, and from generalised treatments to personalised medicine. A deeper understanding of the human body, disease and health, coupled with technological breakthroughs and intelligent use of data, are providing new options for patients and medical professionals.

## **Navigating the brain**

Intelligent electromagnetic navigation system for precise implantation of deep brain stimulation electrodes

#### Deep brain stimulation - Did you know?

In the late 1980s, a French breakthrough in neurosurgery, deep brain stimulation (DBS), opened new avenues for the treatment of movement disorders. DBS involves the implantation of electrodes and tiny neurostimulators in the brain. These devices send signals to specific targets in the motor regions, to help alleviate motor symptoms.

DBS was approved by the FDA in 1997 for the treatment of Parkison's Disease and essential tremor. It is now also used to treat dystonia, some obsessive-compulsive disorders, epilepsy and chronic pain. It may be combined with taking medicines, or offer an alternative to them.

The success of deep brain stimulation (DBS) depends on precision, both in positioning the electrodes and stimulating specific brain regions. Currently, pre-operative imaging and stereotactic techniques are the gold standard for the insertion of DBS electrodes into the brain, but they do not offer tracking during surgery.

Céline Vergne, who is completing a PhD at the Institute for Medical Engineering and Medical Informatics with a joint enrolment at the Universities of Basel and Strasbourg, has developed an electromagnetic navigation system aiming at the precise tracking of electrodes during their implantation. "The chip integrated into the stimulation device, coupled with our visualisation system, will allow surgeons to see the angle and position of the DBS electrode" says Vergne.

She first integrated a tiny magnetometer into the electrode. Less than 1 mm across, the magnetic sensor can be detected by generating low magnetic fields and using a tracking algorithm to determine its position. Prof. Dr. Joris Pascal's team contributed to the sensor's development, while Prof. Dr. Simone Hemm's team was responsible for the system set-up and testing in the surgical environment. In collaboration with the University of Strasbourg, Vergne is investigating machine learning algorithms to optimise the sensor's tracking performance.

Vergne then set out to ensure the compatibility of her prototype with the surgical environment. In the operating lab at the FHNW School of Life Sciences in Muttenz, she recreated a DBS surgical set-up using a head phantom inside a stereotactic headset. For the electromagnetic navigation system, called ManaDBS, she added a system control unit, a magnetic field generator and a sensor interface unit connected to the DBS lead.

Electromagnetic perturbations from the magnetic field can throw off tracking. To address this, Vergne applied a new tracking principle to limit electromagnetic disturbances and ensure correct tracking of the electrode.

Implantation trials on an eggplant simulating brain tissue were performed in a recreated DBS surgical setup. This gave an initial idea of the sensor's performance. The final step before transfer to the clinical environment is user-friendly software to visualise tracking in the operating room.

The system will then be tested at the University Hospital Basel during a surgical dress rehearsal. This environment can simulate the compatibility of the technology with the unique DBS operating theatre, helping translate the prototype to the clinic.

If successful, a team of neurosurgeons at the University of Basel will test the technology in patients. Ultimately, the system may go through

medical device approvals, led by a producer of neurosurgical or navigation instruments. "It's very exciting to have three fields coming together in this project: electronics, computer science and neuroscience" says Vergne. "This multidisciplinary approach and collaboration with partners are driving innovation forward." "This electromagnetic navigation system is a promising tool for the localisation of the DBS electrodes. We are hopeful that it will be integrated into the surgical procedure and bring advantages for both patients and medical teams" says Dr. Ethan Taub, Neurosurgeon at the University Hospital Basel and external expert of the project.



Céline Vergne tests her electromagnetic navigation system for localisation of electrodes in the brain, using a head phantom inside a stereotactic headset.

Patients / Target Groups: Parkinson's disease, essential tremor, dystonia, epilepsy, chronic pain Partners and PhD Co-Directors: University of Basel: Prof. Dr. med. Raphael Guzman, Chairman, Department of Neurosurgery Université de Strasbourg: Prof. Dr. Morgan Madec, Simulation and electronics systems Financing / Support: SNSF project grant 204448



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## **Stepping up 3D printing of** orthopaedic insoles

Daniel Seiler's lab is revolutionizing how personalised orthopaedic insoles are made

Orthopaedic insoles help redistribute pressure and relieve sensitive areas of the feet, making it more comfortable for people with foot misalignments to walk and perform daily activities. Orthopaedic insoles are also a crucial tool for patients whose foot nerves have lost sensitivity, which can unknowingly lead to pressure sores or even amputation. In non-medical applications, insoles can help increase comfort and stability for adults, offer support to people who spend a lot of time working on their feet, and boost performance in running and other sports.

Even to this day, personalised insoles are primarily produced using computer numerical control (CNC) machines and are fine-tuned manually. This traditional method of milling insoles is not only energy-intensive but also generates a substantial amount of noise, dust and chip waste.

The shift toward 3D printing of personalised insoles can reduce waste by 95%. However, the key challenge is the printer's ability to manage several types of materials with different hardness levels and properties.

In an Innosuisse project performed in collaboration with the company Orthopodo Malgaroli. Daniel Seiler's lab at the Institute for Medical Engineering and Medical Informatics has developed an automated digital production process

process for 3D printing of personalised orthopaedic insoles.

"Orthopodo Malgaroli approached us with a desire to make their production process more digital, efficient and sustainable" says Seiler. "This involves not only a shift toward 3D printing processes, but also new methods in scanning patients' feet and arriving at the optimal insole design. We envision an end-to-end solution from foot scanning to insole output that can revolutionise how personalised insoles are made."

Yves Letz and Roman Santschi from Seiler's team began by designing a fused deposition modeling (FDM) 3D printer capable of managing at least four different types of soft materials that can help relieve pressure. They engineered new printheads to accommodate materials with degrees of flexibility ranging from 60 to 90 shore A. The printer can automatically switch materials and printheads based on the insole designs it receives. These innovations enable the 3D printer to produce insoles that meet diverse comfort and support requirements.

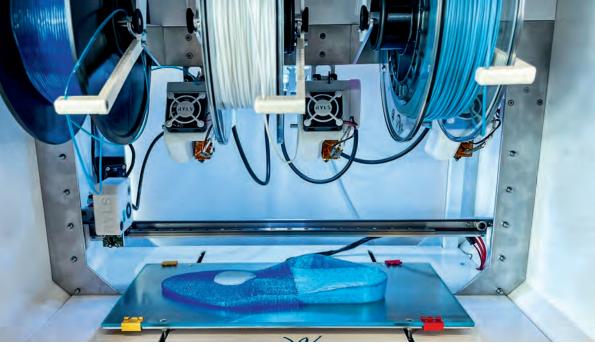
But let's take a step back: how are personalised insole designs created in the first place? A 3D scan of the foot combined with dynamic foot pressure measurements are used with clinical data such as varus/valgus legs as input for the

insole design. Based on three decades of real data and experience from Orthopodo Malgaroli, Seiler's team is developing artificial intelligence models and algorithms that can automatically design customised insoles for patients.

"Our shared vision is for patients to come into a clinic or a store, scan their feet and have the computer create a 3D insole model. The insole will then be produced by the 3D printer. Within one hour, patients can walk out wearing their new custom-made insoles" says Seiler.

Thinking ahead, the partners have conceptualised a user-friendly interface for the foot measurement and printing platform for point-of-care and point-of-sale settings. A stackable design will accommodate multiple printers vertically, for clinics that produce many insoles each day. Finally, Seiler's team is refining a secure cloud solution for patient or customer data storage and processing.

"The 3D printer developed by the FHNW now gives us the opportunity to produce orthopedic insoles quickly and sustainably" says Mario Malgaroli, owner of Orthopodo Malgaroli. "In the future, it could be used not only in our offices, but also in doctors' offices, by podiatrists and physiotherapists, and in shoe and sports stores." Seiler believes it could also be used to triage normal support requirements from medical



capable of managing up to four different soft materials required for insole printing.

conditions that require the expert advice of podiatrists, acting as a diagnostic device.

The transition to automated design and 3D printing of insoles is a paradigm shift for orthopedic firms. "The FHNW has helped Othopodo derisk the transition to Manufacturing 4.0 by making advanced knowledge accessible and workable in practical, real-world situations" says Seiler.

In the next step of the project, a trial is planned to validate the effectiveness and accuracy of the automated insole manufacturing process. This will involve testing the 3D-printed orthopaedic insoles in real-world conditions to ensure they meet patient or customer comfort requirements.

Seiler's group is also starting a new project financed by the Forschungsfonds Aargau to refine the soft material filaments used to produce the insoles and give them antimicrobial properties. This work is being conducted in collaboration with the Institute for Chemistry and Bioanalytics and

Research associates Yves Letz and Roman Santschi designed a fused deposition modelling 3D printer



3D printing of personalized insoles can reduce waste by up to 95%.

the Institute of Polymer Engineering. Lastly, the team is aiming to reduce the amount of glue needed between layers of different materials by integrating the glue into the printing process. They are also designing new soft materials that will be recyclable, two further steps toward increased sustainability of customised insoles.

Patients / Target Groups: Foot misalignment patients, Adults with reduced balance, Standing occupations, Sports Partners: Orthopodo Malgaroli Financing / Support: Innosuisse Project 107.955 IP-LS Forschungsfonds Aargau Project 20220930\_17 Forschungsfonds Aargau Project 20240331\_03



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## Improving wound healing after C-sections

Reto Wildhaber's team has developed a visualisation technology to better illuminate corrective surgery after caesarian sections



A pulsing red LED light in the tip of the instrument is used in digital enhancement equations to generate a 2D augmented reality during surgery.

In Switzerland, 32% of babies are delivered by caesarean section. While hospitals are working to reduce the number of procedures that are not medically necessary, Switzerland's rate remains one of the highest in Europe.

Caesarean sections pose several risks to the mother, one of which is poor healing of the uterine scar. Unknown tissue factors can lead to hampered wound healing and gaps in the anterior uterine wall. These gaps, also called niches, weaken the uterus in a subsequent pregnancy. It can take 1-2 years for women to observe pain and other complications from improper wound healing, which might require follow-up corrective surgery. Chronic pain and multiple surgical interventions can prevent women from performing childcare duties and returning to the workforce, and can considerably reduce their guality of life. If the niche breaks during a subsequent pregnancy, there are significant risks for both mother and baby.

Surgeons at the University Hospital Zürich approached Prof. Dr. Reto Wildhaber with the idea of integrating a light source into a uterine manipulator, a tool used during gynaecological surgery. Current laparoscopic tools and camera systems for imaging the uterus during corrective surgery emit light only outside the uterus, and provide an unclear view of different layers of tissue inside the uterus.

Wildhaber, who specialises in signal analysis and digital biomarkers, came up with the idea to use a pulsing light that is inserted into the uterus through the vagina and cervix. He supported the development of the first prototype while working at the Berner Fachhochschule (BFH). In 2021 he joined the Institute for Medical Engineering and Medical Informatics and continued to work on the project in collaboration with BFH, with whom a joint patent has now been filed.

First, Wildhaber's team tackled the physical challenges of refining the prototype. They selected the material and process to produce the instrument tip where the pulsing red LED light source is housed: 3D printed biocompatible polymethyl methacrylate. The tips were subjected to mechani cal force testing to ensure they can bend during surgery without snapping.

To facilitate sterilisation, the instrument can be disassembled into components and laid flat in an autoclave. The conical design of one component acts as a 'plug' for the cervix, stabilizing the instrument and preventing gas injected into the abdomen during surgery from escaping the uterus.

To keep the tip of the instrument cool and prevent damage to uterine cell tissue, fibre optic cables are used to transmit light from the pulsing red LEDs into the uterus.

The team then put mathematics into action, developing a digital enhancement equation that exploits the difference between the pulsing interior light emitted by the prototype, and the exterior light emitted by laparoscopic tools, to create an image overlay on the surgical monitoring screen.

The 2D augmented reality will help quide surgeons by displaying the boundary of different tissues in the uterus and the location of the surgical tool. It will enable them to see the niche and precisely remove scar tissue.

Overall, the instrument provides an intrauterine light source that allows direct localisation of the niche while stabilizing the uterus, and is compatible with the DaVinci robot that assists the corrective surgery. The small computer required to perform the digital enhancement equations and the screen that displays the 2D visualisation can be easily integrated into existing laparoscopic set-ups.

The visualisation technology underwent a proof-of-concept pilot study in Wildhaber's lab in the summer of 2024, which will be followed by clinical studies at the Department of Gynecology at the University Hospital Zürich after approval by Swissmedic and the local ethics authorities.

"We believe that women with lower abdominal symptoms and women with a niche that wish to conceive a second child will profit from the new

device" says Prof. Dr. med. Cornelia Betschart Meier. "We are looking forward to applying the so-called scar light device in a first clinical trial. It will enhance the surgical technique and we expect it will yield a good outcome for mothers and children."

"This device has the potential to simplify a medically necessary procedure, and make it safer and more reliable, thanks to today's technology" says Wildhaber.

If clinical tests are successful, a spin-off company at USZ could be formed, or the technology could be licenced to a surgical or imaging instruments firm in order to bring it to the market.

Patients / Target Groups : Gynaecological health Partners: University Hospital Zürich, Fachhochschule Bern Financing / Support: Innosuisse (101.964 IP-LS)



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Prof. Dr. med. Reto Wildhaber



Reto Wildhaber developed a prototype that will help surgeons see different types of tissues inside the uterus during surgery.

## **Intelligent drug formulation**

Two teams at the Institute for Pharma Technology and Biotechnology are advancing research on intelligent formulation of oral drugs

#### **Predicting solubility and formulation** composition to reduce animal testing

About 80% of existing and new oral drugs are poorly soluble in the gastrointestinal tract. Assessing the performance of oral formulations has largely relied on animal testing, which is increasing despite the EU's commitment to reducing animals in research.

To offer new solutions and reduce animal testing, researchers at the Institute for Pharma Technology and Biotechnology are participating in the EU project InPharma. The project aims to develop an end-to-end modelling approach to the formulation of drugs for oral administration.

Prof. Dr. Martin Kuentz, Team Leader in Oral Formulation of Chemical Drugs, is leading the project's work package 1, Computational tools to develop optimal oral drug formulations. The goal of the work package is to find suitable excipients and formulations, for example using quantum chemical methods and molecular simulation.

"Artificial intelligence and mechanistic modelling are increasingly shaping the development of drug products" says Kuentz.

InPharma actively contributes to training 13 early-stage researchers, who are completing their European Industrial Doctorates as part of the project. Kuentz is supervising the work performed by two of these early-stage researchers.

One of them is Shaida Panbachi, who is collaborating with the firm Zentiva on testing the industrial feasibility of novel deep eutectic solvent formulations. For the first part of the project, Panbachi used computational tools such as molecular dynamics simulations to predict physical and chemical properties of deep eutectic mixtures, which she completed at the FHNW School of Life Sciences in Muttenz.

Then Panbachi travelled to Prague to work on capsule compatibility and prototype development with Zentiva, a leading manufacturer of generic medicines. Under the supervision of Dr. Josef Beranek, Panbachi is studying the in vitro release properties of innovative deep eutectic formulations, which bridges over to Work package 2 led by the University of Athens.

Shaida Panbachi has already published a first scientific paper, which contributes to the overarching project objective, to promote formulation innovation using computational tools and in vitro tests to reduce preclinical animal studies.



Martin Kuentz and his team analyse new liquid formulations chemically.

Financing / Support: EU Horizon 2020 InPharma 955756 Partners and Beneficiaries: 18 organisations, including Zentiva



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#### **Precision pharmaceuticals**

Living longer is a benefit of modern society, yet our lifestyle and age increase our disease burden. A guarter of people who are 65 and older take five or more medicines every day, cocktails that sometimes have unexpected adverse effects or little efficacy.

Understanding how we metabolise drugs individually (drug-gene interaction), and how the drugs interact with each other (drug-drug interaction), becomes increasingly complex the more medicines we take.

A cross-disciplinary team from three institutes is collaborating to develop precision pharmaceuticals that predict the right doses of the right drugs at the right times.

Real-world drug combinations from proton-pump inhibitors, blood thinners, anti-hypertensives, statins, pain killers and more are tested in organ-on-chip human in vitro models to study their interactions when absorbed and metabolised.



A guarter of people who are 65 and older take five or more medicines per day. In the future, personalised formulations made using micropellets will help ease the pill burden and make treatment more effective.

Those models comprise patient-derived cells with different metaboliser profiles to reflect the heterogeneity of our population.

Feeding this data into in silico models allows prediction of dosage adjustments to achieve the best treatments with the fewest side effects.

In the next phase of the project, the team will join forces with drug manufacturers to work on the next generation of medicines that can be individually dosed. Instead of fixed-dose tablets, drugs will be formulated in so-called micropellets, which are easy to swallow and perfect for personalised dosages.

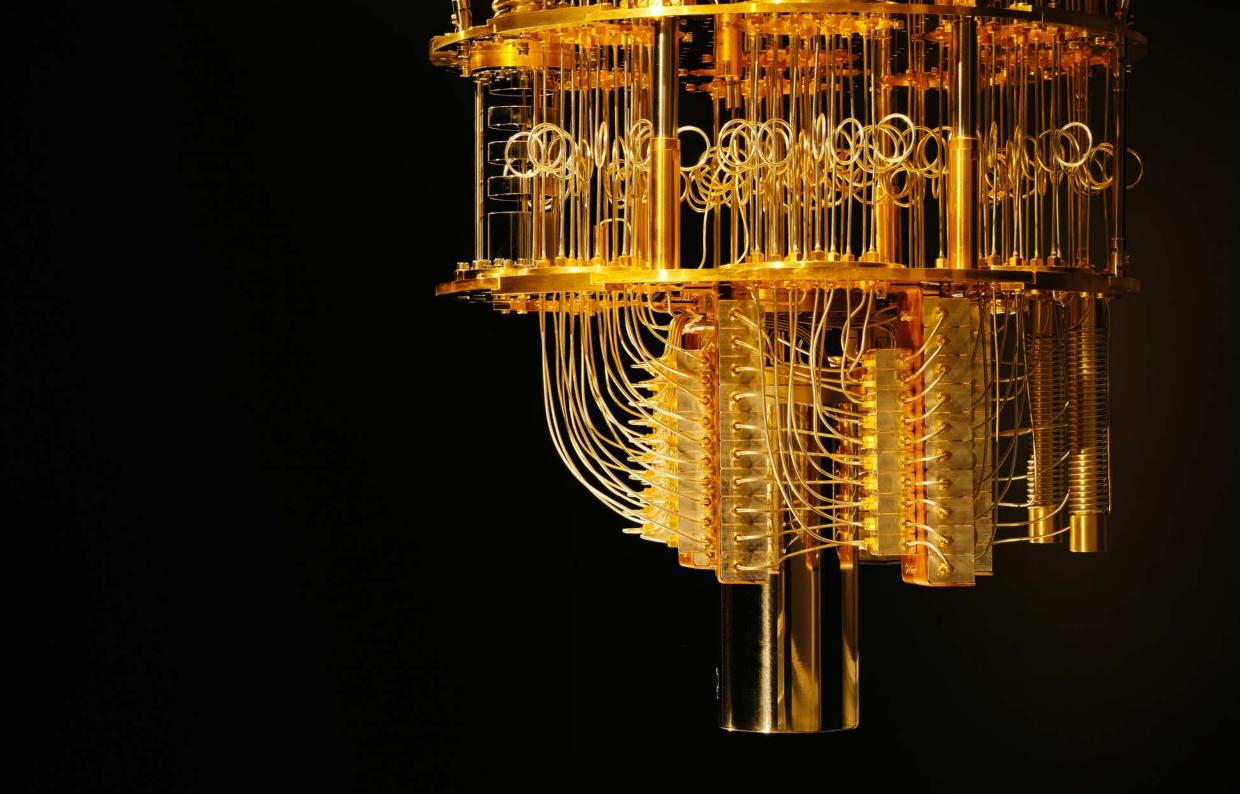
"Imagine! In the future, patients can go to their pharmacy, and based on their pharmaco-genetic profile and prescriptions, receive precision pharmaceuticals that have been custom-made for them" envisions Prof. Dr. Johannes Mosbacher. who is leading the project. As it once was in the past, pharmacists would be those who prepare

the medicines for patients, this time with help of 3D printers or micropellet sorting machines.

Patients / Target Groups : Older adults, people taking multiple medicines Partners: DOPPL SA, Glatt GmbH Financing / Support: Stiftung FHNW, Innosuisse 44386.1



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# Technology in focus

Artificial intelligence, data science and quantum computing are developing at an exponential pace. This rapid evolution is generating opportunities to harness, as well as responsibilities to shoulder. At the forefront of these changes, the FHNW School of Life Sciences provides scientific vision and ethical leadership to develop the digital technologies of the future and apply them to research questions in life sciences.

## **Qubits and bits** with Clément Javerzac

In 2022, the FHNW School of Life Sciences made the bold move to establish a research group focused on applied quantum computing, becoming the first University of Applied Sciences in Switzerland to enter the quantum space. Led by Clément Javerzac, the group is on a mission to apply quantum computing to life sciences.



Javerzac's team develops quantum sensors for new medical devices.

#### **Quantum for everyone?**

Classical computers used to take up entire rooms and be used by specialists. Now they fit in our pocket. Do you see a similar trajectory for quantum computers?

I don't think quantum computers will replace current computers, because different types of processing units have different functions.

- Central processing units (CPUs) make up the core of today's laptops and mobile devices.
- Graphic processing units (GPUs) first appeared for graphic design and video game applications and are now used to train deep learning models.
- Tensor processing units (TPUs) and data processing units (DPUs) are the next generation of processors designed specifically for big data applications and centres.
- Quantum processing units (QPUs) are best for solving hard, combinatorial problems without replacing classical computing.

Before quantum computers can make it to prime time, we need to increase their size: not only the number and quality of qubits, but the number of operations they can do, which is called circuit depth. The National Center of Competence in Research: Spin Qubits in Silicon (NCCR-SPIN) is working on alternative waferscale quantum circuits that can be fabricated by the semiconductor

#### It starts with education

#### Prof. Dr. Javerzac, tell me what's happening at the FHNW School of Life Sciences in quantum computing?

We're starting with education: making students and faculty quantum aware. We held a first course in the Master's in Medical Informatics in 2023. which gave students the courage to tackle what can seem like a complex technology. In 2024, a guantum computing module was included in both BSc and MSc programmes, and we held a summer school at the FHNW on this topic.

You don't need to be a mathematician or a physicist to try quantum computing. There are user-friendly tools and packages like the IBM Quantum Composer that can help you get started What you do need is an understanding of which types of problems quantum computing is good at solving.

#### Bring your problems

#### How do you identify the right research questions to apply quantum to?

Working alongside life science researchers provides an excellent opportunity for interdisciplinary exchange. I ask people to bring me their problems! But I don't guarantee that guantum can solve them all.

One application we are working on is simulating nuclear magnetic resonance (NMR) spectra that are too complex for classical supercomputers Quantum algorithms can be used to decode the composition of matter for new materials, for example to identify the best structure for a material that can capture  $CO_2$ .

Quantum sensing is more mature and promising for medical applications, for example, diagnosing functionally relevant coronary artery disease (fCAD). The heart's tiny magnetic field can be measured with quantum sensors. Together with Joris Pascal from the Institute for Medical Engineering and Medical Informatics, we are developing a magneto-cardiograph (MCG) as a point-ofcare device powered by quantum sensors, in collaboration with CSEM and the University Hospital Basel.

#### The quantum-AI handshake

#### What types of problems should quantum computing stay out of?

In contrast to AI, quantum computing is not good at solving problems that involve big data. because it is slow to load it. Quantum is ideal for solving combinatorial problems where there are few variables in the input, and many possibilities in the output. Think supply chain and logistics,

scheduling shift work or DNA sequencing. With hybrid algorithms, you can get the best of both worlds: you can ask AI to solve a part of the problem (very fast), and quantum the other (very hard).

#### Quantum communities

Which quantum computers is the FHNW School of Life Sciences currently accessing? We book computation time on the best infrastructures in the world, including IBM's quantum computers in the United States. This privileged access is made possible through our partnership with QuantumBasel.

We're also excited about building European capacity in quantum computing. lonQ is establishing a European guantum data centre in collaboration with QuantumBasel, consisting of two systems with 35 and 64 algorithmic gubits respectively. This will position the Basel region as one of the most powerful quantum computing centres in the world.

Atomic vapor cells can be used to measure tiny magnetic fields such as the one emitted by the human heart.

industry. Scaling up from gubits in the double digits to the millions will bring us into a new era of quantum computing.

#### Quantum utility

#### What does the future of quantum computing look like?

We're moving away from guantum supremacy toward quantum utility - understanding where quantum can make a practical difference. At our HackLife events, companies bring us their problems and we look at a variety of approaches, including AI and guantum, to see how we can solve them.

As the next generation of applied guantum experts graduate from the FHNW and other organisations, they will move to industry and become ambassadors of the technology. I'm excited to see where we stand in five years, with this new cohort applying the technology to drug discovery, materials science and medical devices.

Partners: uptownBasel, QuantumBasel, CSEM, University Hospital Basel, Creative Destruction Lab (CDL), NCCR Spin, Swiss Quantum Initiative Financing: SNSF 51NF40-180604, Innosuisse, NCCR-Spin, SCNAT.



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## **Splice it up!**

Abdullah Kahraman is harnessing long-read sequencing to identify new biomarkers and drug targets

#### **Sequential improvements**

Prof. Dr. Kahraman, your team at the FHNW School of Life Sciences are analysing patterns in gene sequences to understand and predict disease. Tell us how gene sequencing has evolved. The first generation of DNA sequencing began in 1977 when Fred Sanger published his method of sequencing fragmented DNA molecules. Later, in 1987, it became possible to automate Sanger's sequencing method, speeding up the process to a scale where the sequencing of the entire human genome could be initiated. Before the first draft of the human genome was announced in 2000, a second generation of DNA sequencers was developed that could sequence millions of tiny DNA fragments in a massively parallel fashion. Now, the third-generation of DNA sequencing machines can sequence single long DNA fragments that, in combination with single-cell and location information, can give us an unprecedented view of how DNA and RNA molecules underline human biology and diseases.

#### Alternative splices reveal biomarkers of disease

What types of information can be found using long-read sequencing?

When RNA is transcribed from DNA, non-coding regions in the RNA sequence are cleaved off

(spliced out). The remaining coding regions are combined into different messenger RNAs. This cellular process called alternative splicing is the reason why the small number of genes in our DNA can generate all the different proteins that cells in our body need.

In cancer cells, alternative splicing is often broken. As a result, proteins are produced that promote the survival and growth of tomour cells. With second-generation sequencing, accurately identifying the complete sequence of long transcripts has always been challenging. However, long-read sequencing now enables the determination of the entire sequence of individual transcripts, providing us with an unprecedented opportunity to explore the full diversity of RNA molecules in normal and cancer cells.

In collaboration with the Functional Genomics Center in Zurich, my team uses the newest sequencing technologies to study tumour development and therapy resistance in cancer patients. We develop software, machine learning and databases, and integrate the novel datasets with mutational, structural and protein expression data. Our goal is to identify patterns that can predict disease progression and drug response, aiming to detect cancers early enough that patients can be treated without their tumours spreading into metastases.

#### Form and function

What are some challenges in analysing RNA sequences?

Figuring out if a transcript isoform is a driver of cancer is not easy. Although long-read sequencing allows us to examine the diversity of all cell transcripts, it also tends to reveal many novel transcripts for which no biological function is known. Our first studies suggest that most of these transcripts are technical artifacts or the result of unfinished splicing. Understanding which transcripts are biologically relevant and which are only artifacts is an important scientific question that we address in my research group using our broad expertise in machine learning and omics data analysis.

#### **Targeting transcripts**

What types of drugs or therapies can be developed to target disrupted alternative splicing?

There are currently two types of therapies for disrupted splicing. One class of drugs targets the protein-RNA complex called splicesome, while the other binds to pathogenic RNA molecules to modify their splicing. Splicesome inhibitors are approved therapies for cancer patients who have mutated splicesome genes. Splicing modifiers, in contrast, are antisense RNA and small molecule



Abdullah Kahraman uses machine learning and AI, aiming to detect cancer before tumours spread into metastases.

drugs that target splicing events in rare diseases, for example, the drug Risdiplam by Roche. It's a small molecule that can activate the gene SMA2 by inducing the inclusion of an exon in its RNA, thereby restoring muscle motor function in Spinal Muscular Atrophy patients.

#### The next frontier: Whole protein sequencing

Which technologies will shape the future of our genetic understanding of cancer? We currently lack a thorough understanding of proteins and protein complexes in cancer. The problem with current proteomics methods is that they can only detect single short peptides from long protein sequences. I believe, therefore, that the next frontier will be whole protein sequencing A promising technology in this field is nanopore sequencing. Uncovering entire protein sequences will be a game changer for target discovery, not only as a tool to validate alternative splicing

identifications but also to assess protein expression and regulatory modifications of proteins. At the same time, machine learning and

artificial intelligence will become fundamental technologies for future cancer treatment in hospitals. Clinicians are already using large language models to write structured diagnostics reports or automatically detect tomour cells in biopsy images. Artificial intelligence agents in hospitals are enabling the collection and integration of heterogeneous data from patients and will help clinicians identify the best therapy path for their patients. My team is involved in developing both machine learning and AI agents through collaborations and contributions to flagship grant proposals. We hope our work will improve the treatment journey of cancer patients in hospitals and contribute to fighting this devastating disease. Partners: University of Zürich and University Hospital Zürich, Functional Genomics Center Zürich, University Hospital Basel

Financing: Krebsliga Zürich, EMDO Grant, SNF Practice to Science



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## **Artificial intelligence in the** age of adisciplinarity

Enkelejda Miho puts different fields to work to develop new medicines, diagnostics, and a better understanding of the health-disease continuum

#### Developing new medicines for unmet medical needs

Prof. Dr. Miho, there are many ways to apply AI to research in life sciences. What is your team at the FHNW School of Life Sciences focusing on? One of our applied projects for therapeutics is the design of broadly neutralizing antibodies against the Dengue virus. Currently, there is no medicine to treat the virus – existing therapies focus on alleviating symptoms, while current vaccines only protect against some serotypes.

To design an antibody-based treatment, we investigated the B-cell immune response to Dengue virus antigens in mice and humans. Specifically, we looked at B-cells in murine bone marrow, which is where long-term immune memory is headquartered. Using high-throughput single-cell sequencing, we obtained 47.8 million raw reads of B-cells and the antibody sequences they produced after exposure to Dengue antigens of various complexity.

Then we had to make sense of this large-scale data. We applied machine learning to detect patterns in the antibody repertoires and sequences against Dengue. But do these findings apply to humans? To determine this, we looked at memory B-cells (MBC) from human patients affected by acute Dengue Virus 2.

We concluded that, in both mice and humans, exposure to Dengue generates long CDR3s and Y-rich motifs in the antibody repertoire. Our hypothesis is that these features could be respon sible for guickly activating memory B-cells and generating broadly neutralizing antibodies that bind to the E protein on the surface of Dengue viruses.

Not only did we identify promising antibody sequences for neutralisation of infections but we also gained new knowledge about the antigens. Dengue whole E-2 complex antigen generates the most diverse antibody response and could therefore be suitable for the development of new vaccines against the virus.

The next step of this project will involve humanizing antibody sequences we isolated in mice so that they can be used as potential therapeutics for Dengue infection and to prevent severe disease.

#### Software as a diagnostic device

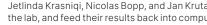
What about Dr. Al? Do you see a big role for Al-assisted diagnosis?

I see an increasing potential in using AI to support precise diagnosis in diseases that can be difficult to identify because of their overlapping and unspecific symptoms, for example autoimmune

and rare diseases. This involves unravelling which data is most useful for diagnosing which diseases, and finding ways of combining and standardizing that data. My team is integrating clinical data from electronic health records, laboratory values and multi-omics data. We have developed new integration methods that can do this.

The second element involves benchmarking machine learning models to determine how well a given model can identify disease and which model is the most accurate. We have enhanced our findings from real patients with virtual patients like a digital twin of a patient. We have worked with European hospitals and medical experts from Germany and France, and we hope to apply the findings to implement digital clinical trials to improve not only diagnoses but also therapy regimen outcomes.

To bring software as a diagnostic device to hospitals and the market, we maintain close ties with Swissmedic and the Swiss Network for Digital Medical Regulation.



#### Listening to the secrets of the immune system

In both examples you've given, it seems that understanding the immune system's response to disease is key. Which research directions will vou take in the future?

Often, the immune system reveals what is going on before disease strikes. We'd like to map out the immune imprint of diseases – a colossal task. I'm interested in exploring and revealing the relationships between infection, cancer and immune diseases.

To do this, my team is studying molecular dynamics. These are giant networks that feature large input data, which AI is well suited to handle but also complex combinatorial intermediate scenarios, for which quantum concepts and quantum computing could help. I expect we will use a hybrid approach to uncover the secrets of how infection, cancer and immune diseases are related.

#### Al in the age of adisciplinarity

Al and life sciences are coming together. Do you consider yourself an interdisciplinary researcher?



Jetlinda Krasnigi, Nicolas Bopp, and Jan Kruta use machine learning to extrapolate immune responses, validate their work in the lab, and feed their results back into computational models, to better understand disease and the body's response.

I think it's useful to use the concept of adjsciplinary instead of interdisciplinary. Multiple disciplines are evolving in parallel. Some fields are merging, while others are splitting apart (e.g. the emerging biochemistry between biology and chemistry). My team and my students use concepts from life sciences, computer science and business to solve a problem at hand by applying principles from various and emerging disciplines. So we are agnostic to disciplines in a sense.

This applies not only to research projects but also to teaching, for example in the Digital Transformation in Healthcare course and even in the HackLife hackathon we've been organizing with Prof. Javerzac at the FHNW School of Life Sciences since 2022. We ask organisations to present their industry-relevant challenges, and we use a variety of approaches including AI, ML and quantum computing to develop solutions that should be practical to implement in a business context.

And a final word about 'hacking' - it used to mean learning to code, now it means learning

to prompt. Large language models have changed the rules of the game. The most famous is ChatGPT and there are many others. Using language to formulate prompts is the latest development that might revolutionise not only complex scientific disciplines but everyday work and life.

Partners: University Hospitals Strasburg, Mainz, Freiburg; Universities of Pavia, Pamplona, Utrecht, Heidelberg; Institute Pasteur, University of Oslo Financing: SNSF EUREKA 32ER30-213721, Wellcome Trust Innovator's Award



Prof. Dr. Enkelejda Miho

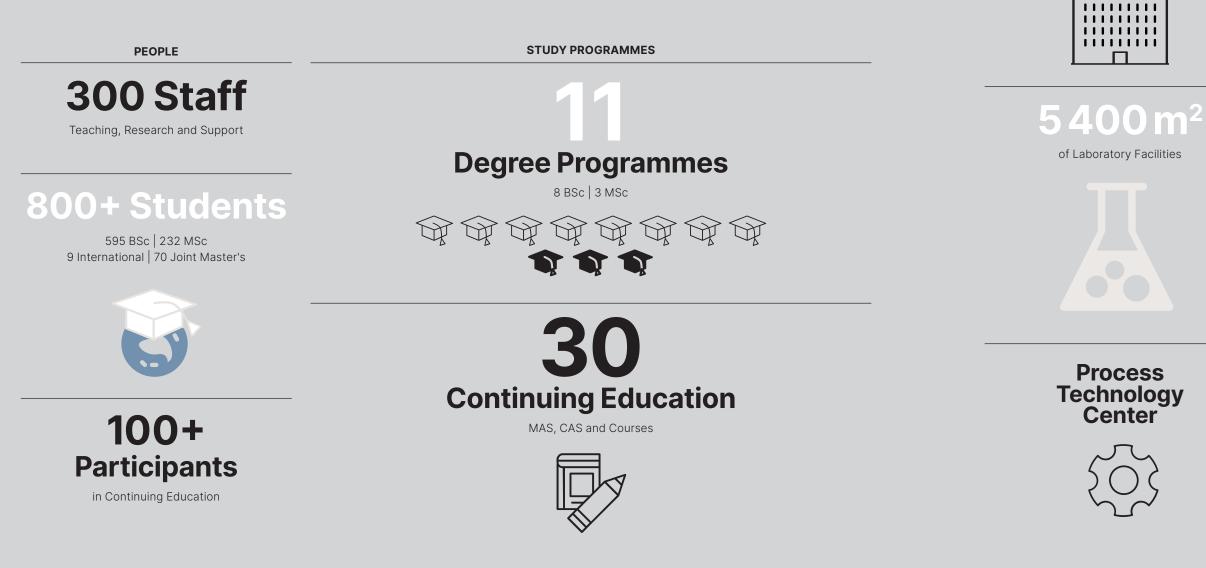
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## At a glance

Based in Muttenz near Basel, the FHNW School of Life Sciences is part of Europe's largest life sciences cluster. It is here that we train skilled specialists and come up with solutions to the social and economic challenges of tomorrow.

## At a glance: **FHNW School of Life Sciences**



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## **A leading University of Applied Sciences at** the heart of Europe's largest life science region

At the new Campus Muttenz in the heart of Europe's largest life sciences region, the FHNW School of Life Sciences does cutting-edge research for a better future. State-of-the-art infrastructure and equipment, including a new Process Technology Center, enable our researchers and industry partners to work together to develop new technologies and products from concept to market. The campus has an ideal location close to public transport and with a view over Basel.

When you collaborate with the FHNW School of Life Sciences, many advantages await you.

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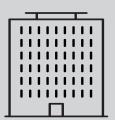
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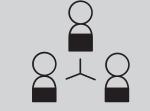
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Established relationships with the Basel Area Life Sciences cluster

## **Our applied** research expertise



### **Medical Engineering and** Informatics

- Biofabrication
- Additive manufacturing of implants and orthopaedics
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- Computer aided surgery and medical decision support
- Medical image and signal analysis
  - Al and quantum computing



### Pharma Technology and **Biotechnology**

- Bioprocessing
- Gene and cell therapy
- Drug formulation, delivery and PK/PD



### **Chemistry and Bioanalytics**

- Molecular diagnostics
- Proteins, enzymes and cell biology
- Nanotechnology, polymers and surfaces
- Chemistry, processes, and reactions
- Analytics
- Data science



### Ecopreneurship

- Water technologies
- Ecotoxicology
- Circular economy



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- FHNW School of Architecture, Construction and Geomatics
- FHNW Basel Academy of Art and Design
- FHNW School of Computer Science
- FHNW School of Life Sciences
- FHNW Basel Academy of Music
- FHNW School of Education
- FHNW School of Social Work
- FHNW School of Engineering and Environment
- FHNW School of Business

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