Activities report 2020–2021

National Center of Competence in Research Bio-Inspired Materials
Who we are

The National Center of Competence in Research (NCCR) Bio-Inspired Materials was launched in June 2014 with the vision of becoming an internationally recognized interdisciplinary hub for research, education, and innovation in the domain of “smart” bio-inspired materials.

We take inspiration from natural materials to establish design rules and strategies for the creation of macromolecular and nanomaterial-based building blocks and their assembly into complex, hierarchically ordered stimuli-responsive materials with new and interesting properties. We seek to develop a predictive understanding for the interactions of these materials with living cells and use the generated knowledge to develop innovative applications, particularly in the biomedical field.

For the second phase of our activities, our research is organized in four modules that focus on mechanically responsive materials across different length scales, biologically inspired assembly of optical materials, responsive bio-interfaces and surfaces, and dynamics of interacting cell-material systems. Each of these modules tackles major unsolved problems, provides opportunities for great scientific advances on its own, and requires an interdisciplinary research approach.

Our research activities are complemented with many programs that integrate research and education, support structured knowledge and technology transfer, and promote equal opportunities in science.
Message from the directors

The NCCR Bio-Inspired Materials prepares its third phase.

Research

Fat-based nanocarriers that change their structure in response to pH to transport anti-microbial peptides.

Initiatives

Our Center prepares for the longer term by valorizing research results, boosting internal collaborations, and fostering scientific vocations though extensive outreach activities.
Message from the directors

Dear reader

Over the past year, the NCCR Bio-inspired Materials defined its strategy for the third and last funding phase, a period that brings various challenges and opportunities to the center.

In the coming years, the NCCR seeks to achieve a long-lasting impact on its home institution, the University of Fribourg, and the Swiss academic community as a whole. This objective requires a prioritization of the center's areas of intervention and is fostered by the customary reduction in the financial support by the SNSF, which expects an increased involvement of the home institution towards the stabilization of a structure that will carry the legacy of the NCCR beyond the third phase. In the face of these challenges, and with a strong support from the University of Fribourg, our NCCR succeeded in putting together a pre-proposal that focused on maintaining the high standard of the center's activities in all areas, prioritized the stabilization of key programs, and preserved what should be one of the main legacies of the NCCR, a bio-inspired materials research community linking three Swiss research institutions. The pre-proposal was refined with the feedback from the SNSF and our center's review panel, and a full proposal was recently submitted. We now look forward to start implementing the new strategy, which will guide our center from June 2022 to the expected end of the NCCR in 2026.

The last months have inevitably been also marked by the Covid pandemic, which forced us to either adapt or cancel many of the NCCR activities. This includes round tables, workshops and scientific seminars that went online, outreach activities that were cancelled, and the annual center conference, which had to be celebrated online and with a reduced program. In this turbulent context, the NCCR researchers suffered from lock-downs and delays in the delivery of scientific consumables, which led to substantial project delays and career-related stress among the young researchers. The NCCR accompanied its researchers in these difficult times addressing their needs, offering a workshop on mental health, and coordinating with the SNSF, which we would like to thank for its flexibility towards the multiple requests received from our researchers. This support was key to minimize the impact of the pandemic on their career and to make the best out of this peculiar situation.

In a different context, the NCCR celebrates the new institutional agreements signed between the Swiss Universities and some of the most important publishers in the domain of our NCCR. These agreements are key elements to achieve the SNSF’s open science goals, relieve the pressure put on the researchers, and are helping our NCCR to increase the fraction of gold and green open access publications over 70%.

We invite you to browse the present report, which collects a selection of research highlights, news, programs and general figures of our center in the last year. We wish you a good reading and invite you to follow the activities of our NCCR in the future.

Ullrich Steiner & Esther Amstad
Directors NCCR Bio-Inspired Materials
The overarching research theme of the NCCR Bio-Inspired Materials is to use inspiration from nature for the design of artificial materials that can change their properties on command, so to speak, or, in other words, in response to an external stimulus. These materials, sometimes referred to as “smart” or “intelligent”, are of fundamental scientific interest and potentially useful in countless applications that range from climate control for buildings to drug delivery systems in the body.

In the recent past, scientists have begun to consider nature’s principles as inspiration for the design of artificial materials with intriguing stimuli-responsive properties. Previous examples of materials studied by individual research groups that belong to the Center include mechanically adaptive nanocomposites inspired by sea cucumbers, drug-delivery nanoparticles that mimic the structure and stealth behavior of viruses, and optical elements that emulate the nanoscale patterns found in butterfly wings.

With the aim of carrying out paradigm-changing scientific breakthroughs and harnessing the enormous innovation potential in this domain, the Center has developed into a large-scale interdisciplinary effort that merges competences in chemistry, physics, materials science, biology, and medicine.

At the start, our research was organized in three modules that emphasized research on mechanically responsive materials, responsive materials made by self-assembly, and the interactions of responsive materials with living cells, respectively. As hoped and expected, the boundaries between the original projects and modules have started to blur, and several new research endeavors were launched that take full advantage of the Center’s interdisciplinary environment.
Clouds, milk, bones – all have one thing in common: they’re white because their constituents are sized and arranged in ways that efficiently reflect light. Now, NCCR Bio-Inspired Materials researchers showed that a specific type of material can diffusely reflect nearly all rays of incoming light – a finding that paves the way for applications in solar energy, telecommunications and light-based computing.

The work could also help to realize a phenomenon that is known to happen for all kinds of waves, but hasn’t yet been observed experimentally for light. The phenomenon was described in the 1950s by late theoretical physicist and Nobel-prize winner Philip Anderson, who showed how an electron and its quantum wave can get arrested in place in a disordered medium. This so-called ‘Anderson localization’ was then proposed to be applicable also to light waves, and many researchers have tried to study it in disordered optical materials.

“Anderson localization is a kind of holy grail in condensed matter and optical physics,” says NCCR Principal Investigator Prof. Frank Scheffold of the University of Fribourg’s Department of Physics.

Scheffold and Dr. Luis Froufe-Pérez, a senior researcher in Scheffold’s group, teamed up with Dr. Jakub Haberko at the AGH University of Science and Technology in Krakow, Poland, to investigate Anderson localization of light in disordered hyperuniform materials. These materials, first proposed about ten years ago by a group of researchers at Princeton University, are computer-conceptualized systems with a very well-defined mathematical basis which are starting to be discovered in nature. Their structure falls between that of highly-organized crystals and that of disordered materials, Scheffold says. “It’s a designer disorder,” he adds.

Using computer simulations, Scheffold and his colleagues found that the nano-architecture of this disordered hyperuniform material can reflect
nearly all incoming light diffusely. “If you reach Anderson localization, you have perfect reflection, and if you’re close to it, you have strong reflection,” Scheffold explains. The researchers discovered that under certain conditions, the material reflects more than 99.9% of light. The findings were published in the journal Nature Communications.

“If light cannot penetrate the material, then the material acts like a perfect diffuse reflector,” Scheffold explains. This means that if researchers made a channel inside the material, light could never leave the channel — this would create an optical wire in which light could be ‘channeled’ and ‘guided’ on-demand. Because photons typically move faster than electrons, hyperuniform photonic materials could serve to develop ultrafast and energy efficient optical computers and other devices, nowadays governed by electronics.

The secret behind a perfectly reflective material lies in its complex nano-geometry. The mathematically defined distribution of points can be transformed into a disordered hyperuniform network, for example, by arranging material building blocks so that every junction has four arms that connect with other junctions. This makes every part of the structure look the same on the small scale, even though the material is disordered when zooming out.

Scheffold notes that nature has evolved very sophisticated strategies to reflect light, but to reach Anderson localization, researchers have to go one step further. Confirming and observing this effect experimentally would not only lead to applications in photonics, but it could also explain fundamental physics phenomena of how light interacts with complex structural media.

Reference
32 Research Projects

> CHF 8 Mio Funds raised by the start-ups and spin-offs

including venture capital as well as money awarded from the Swiss Climate Foundation, the W.A. de Vigier Foundation, Venturekick, and the ZKB Pionierpreis.

Partners

University of Fribourg (Home Institution), Federal Institutes of Technology Lausanne and Zürich

21 Research groups at three universities

4 international conferences supported

2 industrial associates

73% of open access publications following the Gold or Green pathways

23 undergraduate students hosted for the NCCR’s Summer Internships

Note: All figures between June 1, 2020 and May 31, 2021
Chameleons, octopuses, and cuttlefish have developed some of the animal kingdom’s most sophisticated skin, which allows them to rapidly change color to blend into the background. Inspired by the color-changing abilities of these critters, NCCR Bio-Inspired Materials researchers at the University of Fribourg have created a gel-like material that varies its hue in response to temperature and pH.

The material could be used as a drug-delivery vector or a colorimetric biosensor – among other applications. “In biology, it’s often difficult to measure alterations in pH or temperature in a very small volume, so having a material that changes in color is a big advantage,” says NCCR Principal Investigator Prof. Marco Lattuada of the University of Fribourg’s Department of Chemistry.

The ‘chameleon’ material, developed by Dr. Golnaz Isapour, a former PhD student in Lattuada’s group, is a gel-like photonic crystal. The key idea behind photonic crystals is that, depending on the exact position, size, and spacing of their components, light interacts with these materials in ways that produce different colors.

Isapour created a photonic crystal made of millions of minuscule water-swollen plastic bubbles, or hydrogel spheres, that measure several tens of micrometers in diameter. These microspheres serve as a scaffold for even smaller hydrogel nanospheres, measuring just a few hundreds of nanometers in diameter.

When temperature increases, the microspheres shrink, pushing the nanospheres closer together. This change in the spacing between nanospheres creates a shift of color that spans the entire range of the visible light spectrum — from red to green to blue. Similarly, when pH increases, the nanospheres shrink, causing the scaffolding microspheres to collapse, which ultimately results in a color change. Variations in hue happen rapidly, over several seconds or a few minutes, the researchers found.

Creating such a smart gel is no trivial task: to be able to see the different colors, the hydrogel spheres have to be packed in a precise three-dimensional arrangement, similar to that observed in opals and other crystals. “You have to make sure that these particles are able to repel each
other in such a way that they don’t clump together, so that they can arrange in an ordered manner,” Lattuada says. The researchers detailed the protocol to create the smart material as well as its color-changing properties in the journal ACS Applied Nano Materials.

“In biology, it’s often difficult to measure alterations in pH or temperature in a very small volume, so having a material that changes in color is a big advantage.” Marco Lattuada

Lattuada notes that, with some tweaks, the ‘chameleon’ gel could be employed for drug delivery. He explains that when the hydrogel spheres change their size or spacing, the material expels water, just like a sponge that is squeezed. If researchers can encapsulate a drug in the gel, they could use it to release the drug into a specific tissue after a change in temperature or pH. “You can definitely encapsulate drugs as long as they don’t interfere with the structure of the gel,” Lattuada says. Other applications of the smart gel include colorimetric biosensors — devices that change their color when blood pH or other health indicators are altered.

Reference
As a growing number of disease-causing bacteria become resistant to antibiotics, scientists are scrambling to find new ways to prevent and treat infections. NCCR Bio-Inspired Materials researchers at the University of Fribourg have developed carriers that are just a few hundred of nanometers in size and can transport and release antimicrobial peptides – naturally occurring molecules that are increasingly being considered as useful alternatives to conventional antibiotics. Because these nanocarriers can release antimicrobial peptides in response to changes in pH, they could be used to transport the bacteria-killing molecules to wounds and infected tissues, which typically have abnormal pH values. The mini-shuttles could also be employed to combat stomach infections without affecting the beneficial bacteria that reside in the gut. “Because the drug-delivery system is active at the low pH values of the stomach but is inactive at the higher pH values of the intestine, it will only kill the bacteria in the stomach,” says NCCR Principal Investigator Stefan Salentinig, Professor of experimental physical chemistry at the University of Fribourg. Salentinig and his collaborators at the Swiss Federal Laboratories for Materials Science and Technology had previously shown that, as milk is digested in a lab-grown model of the human gut, it forms highly organized nanostructures. These structures could be important for transporting poorly water-soluble milk components through the digestive tract and delivering them across the gut lining. Inspired by these findings, Salentinig and his team set out to develop a drug delivery system that could protect antimicrobial peptides against breaking down in the body and release the bacteria-killing molecules in a controlled manner.

The researchers designed nanocarriers based on the assembly of a type of fatty molecule, known as DODAP, with the antimicrobial peptide LL-37, which is found in humans. At pH values of about 4.5, the fatty molecules that make up the nanocarriers form organized structures containing tiny water channels. Under these conditions, the antimicrobial peptide sits inside the nanocarriers, at the oil-water interface of the channels, the researchers found. At lower pH values, the fatty molecules form tiny sacs filled with water and...
Because the peptides sit within the nanocarriers, either inside the water-filled sacs or at the oil-water interface of the channels, they are protected from degradation.

Things start to change as the pH becomes higher. When it reaches values of about 6, the fatty molecules turn into emulsion droplets, like those that form when oil and vinegar are whisked together into a salad dressing. Now, the antimicrobial peptides can be released and perform their antimicrobial function. The findings were published in the Journal of Colloid and Interface Science.

The structures that the nanocarriers form as the pH changes are similar to those observed during milk digestion, Salentinig says. “By changing the pH, we can blueprint the whole range of structures that you would find during milk digestion, and then we can use them to deliver antimicrobial peptides and switch on and off their activity,” he says.

Besides killing bacteria, the antimicrobial peptide LL-37 can favor cell proliferation, previous research has shown, thus promoting wound healing. Salentinig and his team developed a gel-like coating that contains the LL-37 antimicrobial peptide assembled with nanocarriers made of a food-grade fatty molecule called glycerol monooleate. In a study published in ACS Applied Bio Materials, the team tested the coating on two kinds of disease-causing bacteria grown in a dish and found that it could kill both. The coating could find applications in wound pads to protect wounds and speed up healing, Salentinig says.

Reference
As night falls on certain beaches around the world, the sea can glitter like stars in the sky. This ‘sea sparkle’ arises from single-celled organisms that have evolved to emit light at night when disturbed by movements such as a wave breaking or a fish swimming by. This natural phenomenon inspired NCCR Bio-Inspired Materials researchers to create polymer-based nanoreactors that can be switched on by shear stress, allowing the activation of chemical reactions on demand. The nanoreactors could be used for drug delivery, 3D printing and scratch-and-smell items, among other applications.

In the plankton *Noctiluca scintillans*, mechanical stimulation generates an action potential that activates proton channels in the membrane of organelles called scintillons, changing their permeability. The influx of protons then triggers a chemical reaction that produces light. NCCR Principal Investigator (PI) Prof. Nico Bruns – now at the Technical University of Darmstadt in Germany – and his colleagues set out to develop mimics of scintillons made of synthetic polymers called polymersomes. “We didn’t invent polymersomes, but we asked ourselves, can we switch the permeability of polymersomes by mechanical perturbation?” Bruns says.

To create such force-responsive polymersomes, the researchers turned to a second source of inspiration: DNA. The inside of the DNA double helix repels water; but when the nucleobases that join two DNA strands together unpair, the whole molecule becomes water-soluble.

Bruns and his colleagues created vesicles in which a fluid is enclosed by an outer, double-layered membrane. The membrane consists of heads made of water-loving polymer chains and tails made of water-repellent polymer chains that are linked to nucleobases. The nucleobases cluster together when paired, but after applying shear force to the vesicles, for example by aspirating them with a syringe, the nucleobases unpair, making the membrane permeable to water-soluble molecules.

Next, the team enclosed in the vesicles an enzyme that produces light and provided the substrate on the outside. “If the membrane is non-permeable for the substrate, nothing will happen, but when the membrane becomes permeable, then substrate can get into the vesicle and...”
the enzyme can do its job,” Bruns says. Indeed, in response to shear force, the polymersomes light up - like tiny glowing *Noctiluca scintillans*, the researchers found. “It was nice to show that we could mimic the biological role model,” Bruns says.

Finally, the team used shear-responsive polymersomes to trigger a chemical reaction that transforms polymers into a gel. In this case, the force generated by mild ultrasound was enough to make the nanoreactors permeable and switch on the gellation reaction. Gel formation on demand could be used in biomedicine to create hydrogel patches that gradually release drugs. It could also be useful in 3D printing to turn liquid inks into gels only after the ink is squeezed through a nozzle.

Another possible application of polymer nanoreactors could be in scratch-and-smell items. “One could use mechanical perturbations – for example, rubbing a garment – to release a fragrance,” Bruns says.

The researchers detailed the structure and the properties of the polymer nanoreactors in the journal *Angewandte Chemie International Edition*. The work stems from a collaborative effort between the research teams of Bruns, and NCCR Bio-Inspired Materials PIs Prof. Esther Amstad (EPFL) and Prof. Marco Lattuada (University of Fribourg). Lattuada brought fluid dynamics expertise to the project, while Amstad and her team provided a sophisticated experimental setup to prove that nanoreactors are activated by shear force, Bruns says.

The work, he adds, showcases the highly collaborative nature of the NCCR Bio-Inspired Materials. “The NCCR allowed us to collaborate with Marco, Esther and their groups with a very low level of activation energy,” he says. “This merging of expertise is key for highly interdisciplinary research.”

Reference

From the soft fibrous tissue found around our joints to the gluey threads that mussels secrete to stick to rocks, many natural materials can stretch, bend and bear weights thanks to the particular way in which they are assembled. Now, NCCR Bio-Inspired Materials researchers have developed a 3D-printing approach that mimics the assembly process of natural materials to produce stronger and tougher hydrogels. These hydrogels could find applications in soft robotics, for example for making medical tools that can better navigate the tortuous architecture of blood vessels.

Hydrogels are water-loving polymers that can absorb and retain water; they’re found in everyday products such as disposable diapers as well as in several medical applications including wound dressing. Hydrogels used in biomedicine are biocompatible, but they are too weak to bear weights. On the other hand, hydrogels used in material science are stiff but also very brittle, so they can’t be printed into complex shapes.

To produce hydrogels that are soft and strong at the same time, NCCR Principal Investigator Prof. Esther Amstad and her team at Lausanne’s Federal Institute of Technology (EPFL) set out to develop a novel 3D-printing approach inspired by nature.

Nature produces many of its tough materials from tiny compartments filled with reagents that merge together. For example, the adhesive threads that allow marine mussels to firmly hold onto rocks in oceans are produced from compartments filled with the protein collagen. These vesicles are released on demand and self-assemble into threads in the foot of the mussel.

In contrast, researchers usually mix reagents in bulk to produce synthetic materials – like cooks combine ingredients in the kitchen. “This method is simple, cheap and easy to scale-up, but it doesn’t allow us to control the local composition of the material or to process it into complex 3D shapes,” says Amstad. To overcome this hurdle,
her team designed hydrogels that are composed of microgel grains that assemble together. This approach has the advantage that each grain can carry different reagents, so researchers can easily vary the material’s local composition.

First, the team converted a reagent-filled liquid drop into a hydrogel. They then exploited the sponge-like property of hydrogel particles to load a second reagent – a component of a glue – inside the particles. Next, the researchers concentrated the particles so that they started touching. As soon as the particles touched each other, they no longer behaved as a liquid. Instead, they became a paste that could be 3D-printed and solidified once it exited the nozzle.

Using this approach, the researchers printed different objects, including a hydrogel strip the size of an SD card that could bear a weight of one kilogram. Further tests showed that a hydrogel cylinder produced with the new approach could be compressed and crushed without breaking. “We even stood on it,” Amstad says. The findings were published in the journal Advanced Functional Materials.

Stronger and tougher hydrogels could be used to make soft grippers such as prosthetic hands, for example, or tools for introducing stents in narrowed vessels to restore the blood flow. To insert stents, doctors need tools that are soft enough to navigate arteries and veins, but also stiff so that stents can be placed correctly, Amstad says.

The team is now working to produce recyclable hydrogels, she adds. “A material that can be disassembled and reassembled will be more sustainable, and has the potential to contribute to the reduction of the plastic pollution our environment currently suffers from.”

References
145 Researchers
incl. PhD students, postdocs, senior researchers and professors

CHF 9 million
of funding including CHF 4.4 million from the SNSF

39 Nationalities
including Switzerland, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Costa Rica, Croatia, Estonia, France, Germany, Greece, Hungary, India, Indonesia, Italy, Lebanon, Lithuania, Luxembourg, Macedonia, Netherlands, New Zealand, Peru, Portugal, Russia, Serbia, Slovakia, Slovenia, South Africa, South Korea, Spain, Taiwan, Turkey, UK, USA and Vietnam.

3 Grants
1 ERC Starting Grant, 1 Werner Siemens Foundation Grant, 1 EPSRC’s New Horizons Grant by NCCR participants

66 Papers
including 58 original contributions and 8 reviews

1 Innosuisse project
worth CHF 0.4 million to develop a chemical reactor for nanomaterial production

Note: All figures between June 1, 2020 and May 31, 2021
In brief

Mental health workshop

To respond to the mental health challenges faced by young academics during the Covid crisis, the Center organized a special seminar in collaboration with the non-profit platform Dragonfly Mental Health to address some of these issues.

The seminar, led by Dragonfly’s Dr Olga Vvedenskaya, covered topics such as how the body and mind function during global disease outbreak and subsequent isolation; the main areas of everyday life affected by the pandemic; and provided suggestions how to regain a feeling of stability. The workshop was particularly appreciated by the participants, and NCCR management is considering organizing further sessions.

Gender equality

NCCR Bio-Inspired Materials PI and Equal Opportunities delegate Professor Barbara Rothen-Rutishauser was interviewed for Elsevier’s special report “The researcher journey through a gender lens: A global examination of research participation, career progression and perceptions”.

The interview covered notably Rothen-Rutishauser’s realization that the academic playing field was anything but level for men and women, and that concrete actions were required to correct the gender imbalance in the sciences at least.

In her role as Faculty Delegate for the Advancement of Young Researchers and Women of the National Center of Competence in Research Bio-Inspired Materials, Rothen-Rutishauser has been instrumental in organizing roundtables for female researchers to share their experiences and get feedback and advice.

External advisory board

The first president of the NCCR’s external advisory board, Prof. Marcus Textor, formerly of the Department of Materials at Zurich’s Federal Institute of Technology (ETHZ), stepped down from the board in 2020.

He was replaced by Prof. Dr. Katharina Maniura, of the Materials Meet Life Department of the Swiss Federal Laboratories for Materials Testing and Research (Empa).
Dr. Alessandro Ianiro, an NCCR postdoctoral researcher in the Adolphe Merkle Institute BioPhysics group, was selected to become a prestigious Marie Skłodowska-Curie Fellow in 2021.

His project funded by the European Commission will focus on developing a novel class of nanocomposite materials that mimic natural muscles by combining stimuli-responsive hydrogels and colloidal liquid crystals. The hydrogels are soft and shape-compliant actuating materials like muscles, but they generally exhibit poor mechanical resistance and they expand in no specific direction. These limitations will be overcome by attaching them to the colloid particles and assembling them to make them function along a single axis. Ideally, this will lead to a novel class of soft actuators that will bring significant advancement to fields like robotics and medicine.

Dr. Stephen Schrettl

NCCR postdoctoral researcher and group leader Dr. Stephen Schrettl (Adolphe Merkle Institute, Polymer Chemistry and Materials) was awarded a Spark grant by the Swiss National Science Foundation to investigate innovative composites that respond to external stimuli.

Examples of such innovative stimuli-responsive materials include those that adapt their mechanical properties as needed, some that signal wear and tear before a failure, or micro-capsules that release an active ingredient on demand. However, currently available capsules are incompatible with standard polymer processing methods, which constitutes a significant barrier for their use. The goal of Schrettl’s project is to develop capsules that are stable enough to withstand the rigors of processing, while also performing the designated task of rupturing and releasing a cargo after integration into a polymer. The aim of the Spark program is to fund the rapid testing or development of new scientific approaches, methods, theories, standards, and ideas for applications for example.

Marie Skłodowska-Curie Fellowship

Dr. Alessandro Ianiro

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PhDs

Johannes Bergmann (Steiner group, AMI) Production of bio-based surface wrinkled colloids

Aristotelis Kamtsikakis (Weder group, AMI) Leaf cuticle-inspired membranes

Subhajit Pal (Kilbinger group, UniFR) Development of Synthetic methodology for Phase Display

Sarah Raffiee (Rüegg group, UniFR) Targeting individual cancer cells by sensoreponsive nanoelements

Mirela Malekovic (Steiner group, AMI) Optics of disordered materials

Arnivan Guha (Mayer group, AMI) Energy generation using ion gradients across bio-inspired membranes

Samuel Raccio (Bruns group, AMI) Detection of malaria by atom transfer radical polymerization.

Mathias Steinacher (Amstad group, EPFL) Surface Acoustic Wave Based Spray-Dryer
**Promotions**

Bodo Wilts, a senior NCCR researcher and group leader at the Adolphe Merkle Institute was appointed to a professorship at the University of Salzburg, where he took up his position in October 2021. Wilts was a member of the NCCR from 2015 onwards until his appointment in Austria. He will pursue his collaboration with the Center as an Associate PI.

Two other NCCR and Adolphe Merkle Institute alumni were appointed to new positions at universities abroad. Yoshimitsu Sagara, who was an NCCR postdoctoral fellow from 2013 to 2015, was appointed as Associate Professor in the Department of Materials Science and Engineering at the Tokyo Institute of Technology, after serving for several years as an Assistant Professor at the University of Hokkaido.

Céline Calvino, who completed her PhD in 2018, was appointed Junior Research Group leader at the University of Freiburg’s Cluster of Excellence livMatS in Germany. LivMatS develops life-like materials systems inspired by nature that adapt autonomously to their environment, harvest clean energy from it, and are damage resistant. After her graduation, Calvino first joined the University of Chicago as a postdoctoral fellow.

**Special issues**

Two special issues of journals were edited by members of the Center. A first one for Macromolecular Rapid Communications, was guest edited by NCCR Principal Investigator Prof. Christoph Weder (AMI), and focused on mechanochromic polymers.

These are macromolecular materials that change their color in response to deformation, either on account of altered absorption or reflection, as well as polymers in which other optical characteristics change upon application of mechanical force. The special issue includes several contributions from Center members. The second special issue for the open-access journal Materials was guest edited by NCCR PIs Profs. Alke Fink and Barbara Rothen-Rutishauser, as well as postdoctoral researchers Dr. Barbara Drasler and Dr. Dedy Septiadi. The issue emphasized the entire range of bio-inspired materials used in medical applications, including synthetic approaches of formulating functional systems that can be used in drug and molecule (gene) delivery, bioimaging, and biosensing, regenerative medicine, and cancer treatment.
Annual Center Conference

Due to the Covid pandemic, the Annual Center Conference was held in a reduced format in 2020.

The now traditional two-day meeting was cancelled in Charmey and replaced with a hybrid format, with online sessions on the first day for all NCCR members with research and management presentations, as well as two invited talks. The first one focused on ethics in publishing, given by Prof. Gianfranco Pacchioni (University of Milano Bicocca, Italy).

The second was given by Prof. Magali Lingenfelder (EPFL) on bio-inspired nanointerfaces across time and spatial scales. On the second day for the Principal Investigators met in Fribourg at the Adolphe Merkle Institute to discuss the future direction of the Center’s research modules.

Publication highlights


Malekovic, M.; Bermudez-Urena, E.; Steiner, B.; Wilts, B. D. Distributed Bragg reflectors from colloidal flake solutions, APL Photonics, 2021, 6, 026104.


Celebrating female researchers

A national campaign was launched to promote academic careers for women.

To celebrate Women’s Day 2021 and the 50th anniversary of women’s right to vote in Switzerland, all 22 National Centers of Competence in Research across Switzerland joined forces to publish a series of videos showcasing their women researchers. As part of the #NCCRWomen campaign, the videos, aimed at women and girls of school and undergraduate age, attempted to show what daily life as a female scientist is like and make it more accessible. Each NCCR hosted a week’s worth of short films on Youtube and other social media, covering a variety of research fields.

The Center featured in September, with five videos of Principal Investigators Prof. Katharina Fromm (University of Fribourg, Department of Chemistry), Prof. Barbara Rothen-Rutishauser (Adolphe Merkle Institute, NCCR Equal Opportunities Delegate), postdoctoral researcher Dr. Maria Taskova (Adolphe Merkle Institute, BioPhysics), as well as PhD students Ivana Domljanovic (University of Fribourg, Department of Oncology, Microbiology, and Immunology) and Hanna Traeger (Adolphe Merkle Institute, Polymer Chemistry & Materials).

The complete series of videos can be seen on the special #NCCRWomen Youtube channel. Further actions are now being discussed as part of the campaign.

Winning startups

Two NCCR supported startups were among the five winners of the 2020 W.A. de Vigier Foundation awards, each worth CHF 100,000.

FenX and Microcaps, companies which are both based on technologies developed in the Complex Materials laboratory of NCCR Principal Investigator André Studart, where chosen from 192 submitted projects. FenX has developed technology to turn industrial waste into high-performance insulation panels that are safe, non-flammable and have a minimal carbon footprint. Microcaps has created a system that enables precise size control of microcapsules that can be used for pharmaceuticals, fragrances, flavors and probiotics.

New specialist

The Center hired in 2020 a new specialist to complete its instrument platform team.

Dr. Jozef Adamcik worked previously at ETHZ. His expertise in atomic force microscopy has been particularly welcome as it helps compensate for the retirement of former NCCR Principal Investigator Prof. Michal Borkovec (University of Geneva) and his group’s technical knowhow.
Valorization

Moving from the benchtop to application

Knowledge and Technology Transfer (KTT) has been one of the NCCR Bio-Inspired Materials’ core activities since its launch in 2014. With the Center nearing the end of its second phase, and preparing for its final four years, translation of research will be a benchmark when determining the NCCR’s ultimate success writes the Knowledge Transfer and Innovation Manager, Dr. Eliav Haskal.

The goals for Knowledge and Technology Transfer (KTT) of the NCCR Bio-Inspired Materials are to advance scientific research while promoting and assisting the social and/or economic valorization of research results as well as training, supporting and mentoring innovation and entrepreneurship among the NCCR collaborators.

In the past eight years, a series of activities were established to develop interdisciplinary interactions on an international level, which have led to many scientific collaborations and publications. Ranging from national and international scientific conferences to workshops, seminars and an annual NCCR event, the development of a sense of community, shared curiosity and interdisciplinary skills have contributed to successful knowledge transfer and excellent journal publications.

In terms of technology transfer, where the focus lies on valorization of the NCCR’s scientific research, there has been tremendous progress in many aspects, led by concrete results that are currently being realized as to their economic value, multiple company creations, and a growing spirit of entrepreneurial curiosity and willingness to learn innovation skills. Several NCCR spinoff companies have been created, already employing tens of people, and in second-round capital funding, including FenX AG, Microcaps AG and Spectroplast AG, with more still in incubation at the NCCR partner universities. Industrial research agreements with companies (which are often confidential) have been finalized and are typically always running.

Developing an ecosystem

To create an environment propitious for more innovation activities, the first challenge was to address the common academic perception that applied research, entrepreneurial and innovation activities, and collaboration with industry were “uninteresting”. This could be done by introducing excellent speaker seminars from industry, showing...
the results of successful industrial collaborations and explaining their win-win situations, and sensitizing personnel to the challenges and benefits of entrepreneurship.

In addition, effort was invested in improving the Fribourg innovation ecosystem and align the many academic, political and industrial stakeholders. Ecosystem development had already begun at the University of Fribourg before the start of the NCCR, but the NCCR contributed with new workshops on innovation skills, sensitization to the potential of entrepreneurship as a career goal, assistance in matching research results to companies, mentoring and coaching of projects and personnel in innovation, and teaching and training.

The goal of improving KTT in Fribourg has always been to leverage the close physical location of the five Fribourg universities (University of Fribourg, School of Management, School of Engineering, School of Health, School of Social Work) and create an interdisciplinary skill ecosystem which could assist students at any university to develop their ideas into a transferable activity. The Innovation Club Fribourg was thus created to be open to all students, and to guide them to where they could find help.

During the pandemic, many activities were curtailed – speakers moved online, workshops were abandoned and Zoom fatigue set in – yet most speaker activities continued with varying success. Contacts with companies, still usually managed face-to-face, dwindled before recovering with the introduction of new communication channels.

Translation

As Phase 3 approaches, and NCCR technology translation becomes vital to the Center’s success, the KTT manager will take on a role for the Translation PhDs, in addition to the many training, coaching, teaching, and networking roles developed in the last eight years. The Translation PhDs are students whose pre-defined research projects were selected competitively as having a high potential for successful valorization, either with companies already interested in the scientific results, or as having a good chance to be spun off. The challenge to find enthusiastic researchers, and training them with innovation skills throughout their PhDs, is a long-term, prototypical experiment as to how to embed these skills into a (natural) science doctorate, which could be rolled out at the University of Fribourg beyond the NCCR’s lifespan.

Finally, the many research projects in the NCCR will also be supported for technology translation. To target projects efficiently, the first step was to interview the principal investigators, to identify any potential market interest in the results, with the purpose of contacting specific companies and developing partnerships. It became clear that approximately half of the current projects could indeed result in valorizable results in the NCCR’s Phase 3. These projects will be focused upon for translation, while the remaining projects will be tracked for their progress and potential. In summary, a clear path forward for ecosystem enhancement, training activities and innovation support is in place, with a focus on projects likely to succeed.
These activities are designed for example to spark children’s interest in science, encourage teenagers to pursue a scientific career, or help teachers develop teaching concepts.

The most high-profile outreach program is KidsUni, founded in 2014 by two of the NCCR’s Principal Investigators, Prof. Alke Fink and Prof. Andreas Kilbinger, both affiliated with the University of Fribourg’s Department of Chemistry. Since then, the popular program has expanded to include other participants from the Faculty of Science and Medicine. Organized in two sessions per year, it allows children between the ages of 10 and 13 to spend 12 afternoons discovering a variety of scientific disciplines, including geosciences, mathematics, physics, biology, computer science,
as well as chemistry and nanoscience, under the
guidance of the NCCR Outreach Coordinator, Dr.
Sofia Martin Caba.

“The aim is to show youngsters how cool sci-
cence can be, and motivate them to study it more,”
she explains. “The participants are usually already
interested in science, so the idea is to boost that
motivation. These activities also have an addition-
al benefit for the Center postdocs and PhD stu-
dents who take part, as they get to practice their
supervision and communication skills, as well as
be role models for the children.”

“Activities involving primary schoolchildren also
backed by the NCCR include the Goûters scienti-
ﬁques/Wissenschaft zum Zvieri, which are orga-
nized by the University of Fribourg, the NCCR’s
home institution, and cover both scientiﬁc and
non-scientiﬁc disciplines. Others are the National
Futures Day, workshops run for the Passport
Vacances (holiday passport) program in Fribourg
and Payerne, another within the Environnement
& Jeunesse program, and for Fritime Schmitten.
The NCCR is also more directly involved with
school classes, either hosting groups to perform
lab experiments, or going on the road to class-
rooms across Switzerland, both in primary schools
and with teenagers in high schools and colleges
to demonstrate and talk about science. The NCCR
has been notably involved in the TecDays orga-
nized by the Swiss Academy of Engineering Sci-
ces (SATW) through the participation of its
Principal Investigators. The days are aimed at en-
couraging teenagers to take up STEM careers.
Students attend three module classes from a se-
lection of between 30 and 80 possibilities de-
pending on the school’s size. So far, more than
60,000 teenagers have attended one of the Tec-
Days events since their launch in 2007.

Teachers have also been targeted by the Cen-
ter’s outreach program. High school teachers
were for example invited to take part in a one-day
training event, organized by the outreach coor-
dinator and the scientiﬁc coordinator, Dr. Lucas
Montero. They showed the 20 attendees how to
use currently relevant topics such as plastics pol-
lution and fake news to teach concepts such as
the scientiﬁc method, and how to set up attractive
lab experiments for students. The goal here was
to create a multiplier effect once the teachers
returned to their classrooms. Primary school
teachers from canton Fribourg have also received
coaching from the NCCR to help prepare for a
new science curriculum.

The NCCR has also regularly participated in the
biannual Swiss Science in Youth Chemistry and
Materials Science Study Week, which offers high
school students from the entire country the op-
portunity to spend a week in a laboratory to work
on a short research project. The Center was the
sponsor and host of the last two Study Week na-
tional closing ceremonies at the Adolphe Merkle
Institute.

The NCCR’s outreach and equal opportunities
activities intersect at times when it comes to en-
couraging young women to join the ranks of sci-
ence. The Center has notably helped coordinate
the University of Fribourg’s Women in Science
(WINS) program, which hosts second year female
college students over two days at the university’s
Faculty of Science and Medicine. The aim is to
encourage these students to consider a scientiﬁc
career. The program is now being expanded more
than 20 years after its launch to include male stu-
dents as well, while maintaining a strong focus on
gender-related issues in science.

The NCCR has also taken part in more general
outreach activities for the wider public. These
include an exhibition co-curated by the Center at
the Fribourg Natural History Museum, which was
open to the public for 6 months, and included
parallel group activities for visitors around the
topic of bio-inspiration.

Other events including NCCR participation
were the Museum Night in Fribourg where the
Center presented its research activities and or-
ganizing experiments for children at the Adolphe
Merkle Institute, the University of Fribourg’s Ex-
plora open days, the “Going Wild” exhibitions at
Zurich Zoo, or the European Heritage Days events
in Zurich, in collaboration with the ETHZ Insect
Collection, on the theme of colors.

“These events are important,” says Martin
Caba. “People are open to what we have to show,
and it allows us to reach families, and get parents involved.”

Finally, a collaboration with the Migros Magazine, edited by Switzerland’s biggest retailer, led to the Center preparing science experiments aimed at children for publication in the weekly. After this collaboration ended, the Center brought together the other participants from the project (Espace des inventions, Lausanne; Scienscope, University of Geneva; and EPFL) to compile the best experiments and release them as a book. “Pschitt!” was published late in 2021 and is distributed for free in hard-copy format to primary schools. Its 150 pages can also be downloaded for free.
Strengthening ties

Internal collaborative projects to foster integration

The NCCR Bio-Inspired Materials has always encouraged collaborations between its different research groups. To further exchanges within the Center, a special funding mechanism was introduced for specific projects shared by different teams.

The new scheme is designed to foster collaborations within the NCCR and across its modules. These research grants support interdisciplinary projects led by at least two NCCR researchers, of which at least one must be a Principal Investigator, from different NCCR groups. The grants, worth a total of CHF 750,000, include funds to cover the salary of a postdoc, consumables, and travel expenses for a period of two years. Three initial projects were selected from seven proposals by members of the NCCR’s External Advisory Board, after an international panel examined them.

The projects cover very different fields of research, stretching from the detection of circulating tumor cells, to optically manipulating objects on the colloidal scale nanoparticles via membranes for power conversion from salinity.

Detecting circulating tumor cells

Detecting circulating tumor cells (CTCs) in the blood of cancer patients is particularly significant for the early diagnosis and prognosis of disease, but also challenging due to the low numbers of CTCs in the bloodstream. NCCR Bio-Inspired Materials researchers had previously developed a DNA-based hybridization chain reaction (HCR) system as signal amplifier for CTCs. It was possible to detect a single CTC among 200 blood leukocytes, but that figure remained far below what was needed for clinical application. To overcome this shortcoming, NCCR researchers Dr. Samet Kocabey (Department of Medicine, University of Fribourg) and Prof. Guillermo Acuna (Department of Physics, University of Fribourg) teamed up to increase the sensitivity of the CTC detection system. Their solution consisted in combining the HCR method with surface-enhanced Raman scattering (SERS). Raman spectroscopy is typically used to identify molecules. In this case, it is achieved by conjugating DNA with gold nanoparticles. After initial testing on breast cancer cells, the goal is to adapt this approach to other types of cancer cells using a variety of cell surface markers.

A platform for optical micromanipulation

Optical tweezers, provide the unique capability to remotely manipulate small objects on the colloidal scale. Biology, physical chemistry, and
soft condensed matter physics have all benefited from this development. This collaborative project between the groups of Prof. Frank Scheffold (Department of Physics, University of Fribourg), Prof. Alke Fink (Adolphe Merkle Institute), and Prof. Stefan Salentinig (Department of Chemistry, University of Fribourg) aims to design an optical micromanipulation platform building on the Scheffold group’s existing know-how and integrating it into the research agendas of the other two groups. This platform, which integrates different optical microscopy techniques (bright-field, dark-field and polarized microscopy), will allow the study of colloidal phenomena on a single-particle level and particle-cell interactions. This should provide additional insights for their research on cell-nanoparticle interactions, and the design and operation of colloidal nutrient and drug delivery systems. The new platform has been used already for preliminary studies in the context of milk-inspired colloids for drug delivery, helping ‘immobilize’ a soft particle in solution for online imaging, as well as structural and compositional analysis.

**Ion-selective membranes for power conversion from salinity gradients**

The conversion of energy stored in gradients of salt concentration between sea and river water to electrical energy by reverse electrodialysis (RED) provides sustainable energy without carbon dioxide emissions. However, the charge-selective membranes used in this process have limited efficiency, due to their fragility, thickness, their incapacity to self-heal, and fouling due to the formation of biofilms. Inspired by the lipid membranes in electric eels, the groups of Prof. Michael Mayer, Prof. Christoph Weder, and Prof. Ullrich Steiner (Adolphe Merkle Institute) are now investigating ultra-thin, bilayer membranes that can be formed through the self-assembly of two different block copolymers at the interface of an aqueous two-phase system. By adding ion-selective carriers, the membrane could be either cation-selective or anion selective, opening a pathway towards bio-inspired salinity gradient batteries.
The National Centers of Competence in Research (NCCR) are a research instrument of the Swiss National Science Foundation.
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Abbreviations:
AMI: Adolphe Merkle Institute;  
UniFR: University of Fribourg;  
EPFL: Federal Institute of Technology Lausanne;  
ETHZ: Federal Institute of Technology Zurich
Projects

Module 1: Mechanically responsive materials across different length scales
1. Mechanically responsive and mechanically adapting polymers
2. Mechanically responsive block copolymer nanoreactors inspired by the marine bioluminescence of dinoflagellates
3. Auxetic polymer networks
4. Mechanoresponsive materials enabled by 3D Printing and high-throughput microfluidics
5. Adaptive functional polymers and nanocontainers
6. Mechano-responsive CaCO3-based coatings
7. Biomechanically-responsive nanoparticles

Module 2: Biologically inspired assembly of optical materials
8. Design of novel optical materials through self-assembly of patchy particles
9. Interplay of order and disorder in biophotonic materials
10. Structurally colored micron scale pigments for inkjet printing
11. Physical mechanisms underlying the self-assembly of living optical materials
12. Disguising the core: Photonic core-shell particles
13. Bioinspired DNA self-assembly of nano-photonic devices

Module 3: Responsive bio-interfaces and surfaces
14. Novel antiviral supramolecular materials
15. NanoRoomba®: Cellular uptake and durotaxis on "soft and rigid" nanoparticles carpet
16. Stimulation of cellular endocytosis for sensing and enhancing nanoparticle uptake
17. Self-assembly of DNA- or RNA-triggered ion channels for targeted cell killing and nanopore sensing
18. Trapping cancer cells with self-assembling biomolecules (DNA)
19. Fluorescent nanodiamonds as quantum bio-molecular probes for live cell imaging and sensing
20. Characterizing nanoparticle-membrane interactions via molecular dynamics simulations
21. Steering tissue morphogenesis via programmable microgel assemblies
22. Design of digestion-inspired functional food nano-biointerfaces

Module 4: Dynamics of interacting cell-material systems
23. Development of a microfluidic platform
24. Development of controlled delivery systems for organ-on-chip devices
25. Development of cargo carriers
26. Development of Tumor/Immune Cell Organoid Model
NCCR Collaborative Projects

27. Detection of circulating tumor cells by SERS using DNA based systems as signal amplifier
28. Development of a cross-departmental platform for optical micromanipulation
29. Ion-selective membranes for power conversion from salinity gradients with unprecedented efficiency

WINS Fellowships projects

30. Responsive pigments for Pointillist mechano-sensing
31. Unified approach for intracellular delivery of multi-modified oligonucleotide sequences
32. Swelling-driven mechanical activation of polymers at interfaces and in the networks
Publications

Module 1


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### Module 2


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Malekovic, M.; Bermudez-Urena, E.; Steiner, B.; Wilts, B. D. Distributed Bragg reflectors from colloidal flake solutions, APL Photonics, 2021, 6, 026104.

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Xu, Y.; Scheffold, F.; Mason, T. G. Diffusing wave microrheology of strongly attractive dense emulsions, Phys. Rev. E, 2020, 102, 062610.

Module 3


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Susnik, E.; Taladriz-Blanco, P.; Drasler, B.; Balog, S.; Petri-Fink, A.; Rothen-Rutishauser, B. Increased uptake of silica nanoparticles in inflamed macrophages but not upon co-exposure to micron-sized particles, Cells, 2020, 9, 2099.


Module 4


Gender balance

41% of the NCCR Ph.D. students were women

28% of the postdocs and senior researchers were women

Headquarters
Adolphe Merkle Institute, University of Fribourg

5 round tables
and workshops on topics related to equal opportunities and personal and professional development

4 start-up companies
incorporated (Nanolockin GmbH, Spectroplast AG, Microcaps AG and FenX AG) and one additional spin-off technology (Nanofertilizer)

34 oral presentations at conferences
including 27 keynote and plenary lectures at international conferences

Over
100 children
and high school students participated in NCCR outreach activities despite the covid pandemic

8 cooperations
with external partners (6 with research institutions, 2 other)

Note: All figures between June 1, 2020 and May 31, 2021
Seminars

The NCCR organizes seminars on a regular basis throughout the academic year. These seminars are both an excellent opportunity to learn about recent scientific advances from prominent researchers as well as a meeting point for NCCR participants to network and exchange ideas.

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<th>Speaker</th>
<th>Talk</th>
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<tr>
<td>Prof. Wanda Kukulski</td>
<td>The molecular landscape of growing human axons</td>
<td>University of Bern</td>
<td>October 29, 2020</td>
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<tr>
<td>Dr. Olga Vvedenskaya</td>
<td>Mental health in pandemic</td>
<td>DragonFly Mental Health</td>
<td>December 04, 2020</td>
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<tr>
<td>Prof. Albert Schenning</td>
<td>Bio-inspired polymer sensors and actuators</td>
<td>Eindhoven University of Technology, NL</td>
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<td>Prof. Maria Helena Godinho</td>
<td>Hierarchical cellulose-based chiral structures</td>
<td>New University of Lisbon, PT</td>
<td>February 11, 2021</td>
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