An undeserved reputation

Plastics offer great potential

Plastics have something of an image problem at the moment. Vast amounts of artificial packaging litter the world's oceans, and there is no question that we need to reduce the amount of marine rubbish we create. But packaging our food is by no means all that plastics are good for. They offer innovative solutions for applications in medicine and in everyday life that would be impossible with other materials. Various research groups in the SNI network are devoted to the intelligent use of plastics.

Plastics are materials that consist primarily of long molecule chains known as polymers, which in turn are made up of anywhere from a few thousand to over a million repeating basic units (monomers). Some occur naturally, while others are created by altering natural polymers, and yet others are entirely synthetic, obtained for the most part from crude oil.

The spatial arrangement of the individual components determines the properties of a given plastic. Moreover, there are different ways in which the long molecule chains are linked together and interact. Accordingly, the resulting materials can be rigid, flexible or elastic, and are suited to a wide range of applications.

Telephones used to be made of Bakelite, the first plastic to be produced on a large scale (image: Shutterstock).

First created long ago

Deliberate creation of a natural plastic dates back to the 16th century. Wolfgang Seidel, a Benedictine monk from Augsburg, found out how to make casein from low-fat cheese by repeatedly heating and reducing the curds. The resulting material was used to make cups or items of jewellery. In the 18th and 19th centuries, other natural plastics arrived on the scene. Rubber and linoleum were discovered, as were nitrocellulose and celluloid, made from nitrocellulose and camphor. The first fully synthetic plastic to be industrially produced on a larger scale was Bakelite, which is made from phenol and formaldehyde and is still in use today.

Although numerous researchers in Europe and the US were involved in these initial achievements, the composition of early plastics was not well understood to begin with. It was not until the early 20th century that the chemist Hermann Staudinger published his theory that plastics were macromolecular compounds consisting of long chain molecules, laying the foundations for the field of polymer chemistry.

Since then, countless plastics have been invented to cater to a huge variety of applications, and it has become impossible to imagine our everyday life without them. Various research groups in the

SNI network are working to expand the range of intelligent applications and exploit the unique properties of different plastics.

Inspired by natural membranes

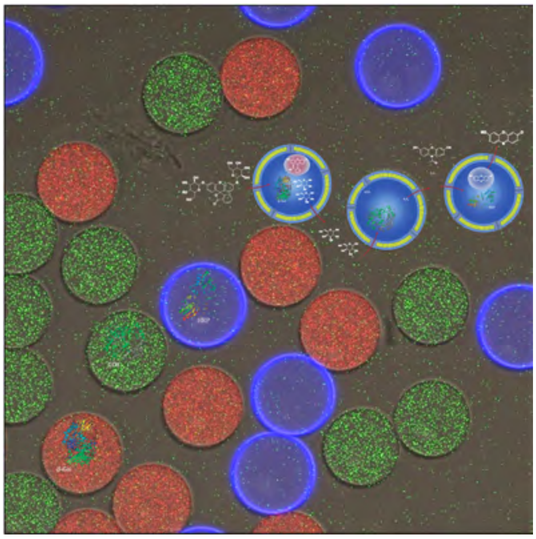
The teams led by Professor Cornelia Palivan and Professor Wolfgang Meier from the University of Basel's Department of Chemistry, for instance, use artificial polymers to create tiny capsules that can be used to treat various diseases. The capsules can be loaded with active substances or enzymes that are protected by the flexible polymer membrane until they are released at the point of delivery.

To produce these capsules – or nanocontainers – the researchers use a class of materials known as block copolymers, which are constructed from at least two different monomers.

Like the building blocks of natural membranes, block copolymers have a hydrophilic and a lipophilic component. In an aqueous environment, they independently arrange themselves in such a way that the hydrophilic components shield the lipophilic components from the surrounding water, resulting in the creation of tiny capsules enveloped by a double membrane. The structure of this membrane resembles that of the phospholipid bilayer in natural cells, although the polymer membrane is significantly more robust and stable than its natural counterpart.

"Besides their greater stability, another benefit of the artificial membranes is that they can be customized as needed," explains Wolfgang Meier. "For instance, we can fine-tune their thickness and size with a high degree of precision," he adds. What is more, the researchers can incorporate natural membrane proteins into the structure that serve as gateways, allowing selective transport of certain substances into and out of the nanocontainers.

"We produce nanocontainers into which various enzymes are packed," says Cornelia Palivan, adding that "by equipping these minute containers with the right membrane proteins, we can use them to trigger a cascade of biochemical reactions." The end product of a reaction from one type of container serves as the input for a second type. In turn, the product of the second reaction acts as the substrate for a third reaction. This enables complex syntheses that are physically isolated from each other, as in a natural cell.



These tiny nanocontainers are loaded with different enzymes and equipped with corresponding membrane proteins. Various biochemical reactions can then take place separately from one another inside the containers (image: Department of Chemistry, University of Basel).

Controlled production with microfluidics

To control the production of these nanocontainers, the researchers in Basel recently developed a microfluidic platform employing a special silicon-glass chip in collaboration with IBM.

The chip features six channels that converge at a junction where the components of the polymer membrane, buffer solutions and the enzyme cargo come together. Under the right conditions, the tiny capsules join at this junction of their own accord. They are uniform in size, but envelop different enzymes as they form. During the production process, membrane proteins allowing

Sources and additional information:

Seilnacht — Didaktik der Naturwissenschaft

https://www.seilnacht.com/Lexikon/k_gesch.html

Kunststoff Deutschland:

https://www.kunststoff-deutschland.com/html/geschichte_des_kunststoffs.html

Deutsches Kunststoff-Museum

http://www.deutsches-kunststoff-museum.de/rund-um-kunststoff/zeittafel-zur-geschichte/

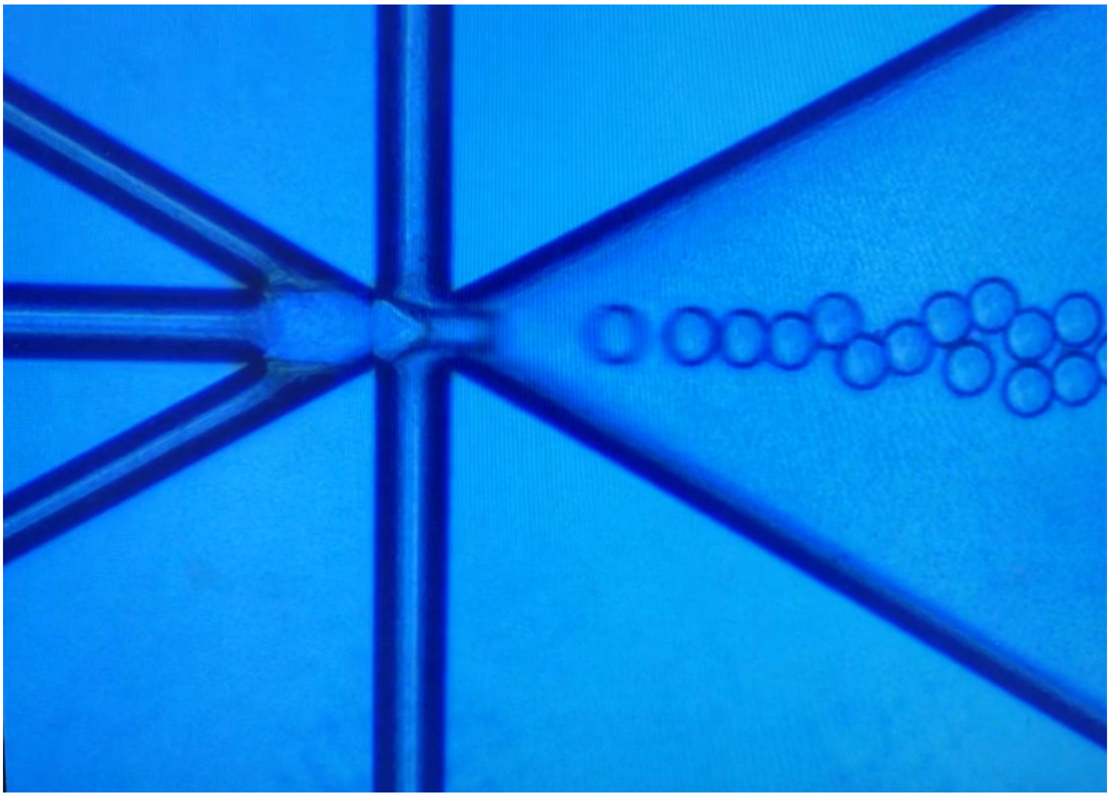
Information about block copolymers:

Advanced Materials:

https://onlinelibrary.wiley.com/doi/10.1002/adma.202004804

Video:

https://youtu.be/lftbbVRce4k



The constituents of the polymer membrane meet at the junction of the microfluidic platform. All of the capsules are formed with a uniform size but can be loaded with different cargoes (image: Swiss Nanoscience Institute, University of Basel).

transport into and out of the capsules are also incorporated into the membrane by self-assembly.

This microfluidic system was recently described by its creators in the journal Advanced Materials. For the paper, they loaded the nanocontainers with β-galactosidase, glucose oxidase or horseradish peroxidase. In a succession of steps, these three enzymes were used to transform a starting product into the end product Resorufin, which is easy to detect as a result of its distinctive color. As in a natural cell, the biochemical reactions in this artificial system occurred in spatially separate compartments.

The Palivan team has also published in the journal Small that it is possible to combine the synthetic nanocontainers with natural biomolecules for a simultaneous detection and therapeutic response. The researchers showed that natural enzymes and imaging compounds function *in vitro*, allowing the therapeutic enzyme to remain effective while simultaneously enabling controlled imaging.

Active in living cells too

Further work by Palivan's team has demonstrated that nanocontainers of this sort can be introduced into living cells, where they have the ability to amplify natural signaling pathways. In a paper published in the journal ACS Nano, the researchers describe how nanocontainers working in tandem can remain functional in mammal cells for several days.

The block copolymers used protect the enzymes against degradation. As well as being robust and very simple to manufacture, they have so far shown no toxic effects in animal models, as shown by a team led by Professor Jörg Huwyler in collaboration with Palivan and Meyer's group.

"The nanocontainers are operational as soon as they have been absorbed into the cells, where they begin their synthesizing activity. In the future, they could be used to treat diseases involving malfunctions in biological signaling pathways," say Palivan and Meier, summarizing the

Information about block copolymers:

ACS Nano

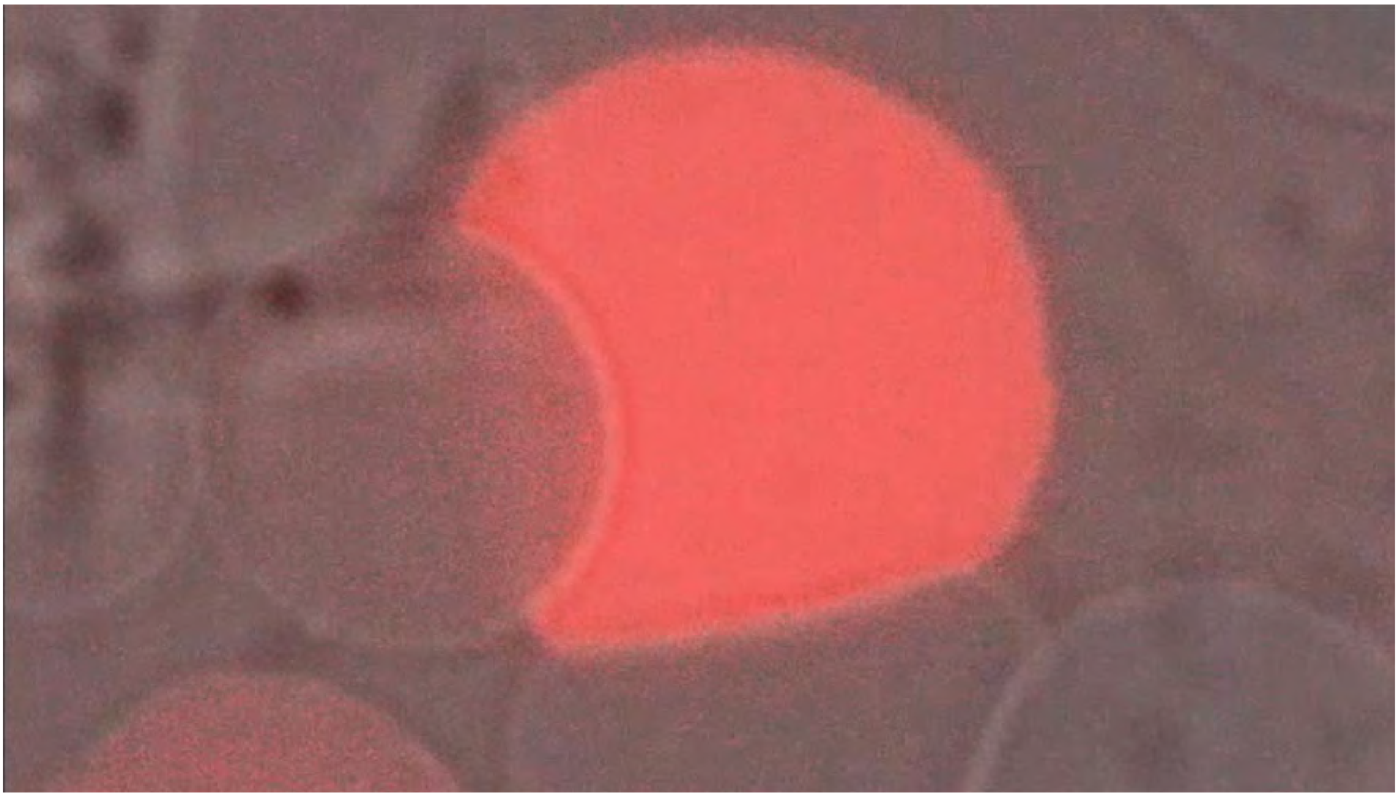
https://pubs.acs.org/doi/10.1021/acsnano.0c05574

Advanced Science

https://onlinelibrary.wiley.com/doi/full/10.1002/advs.201901923

Small

https://onlinelibrary.wiley.com/doi/pdf/10.1002/smll.201906492



In molecular factories injected into zebrafish embryos, a color reaction occurs when the trapped enzyme (peroxidase) is working. The researchers thus prove that the combination of synthetic organelles and natural vesicles also works in the living organism. (Image: Department of Pharmaceutical Sciences, University of Basel)

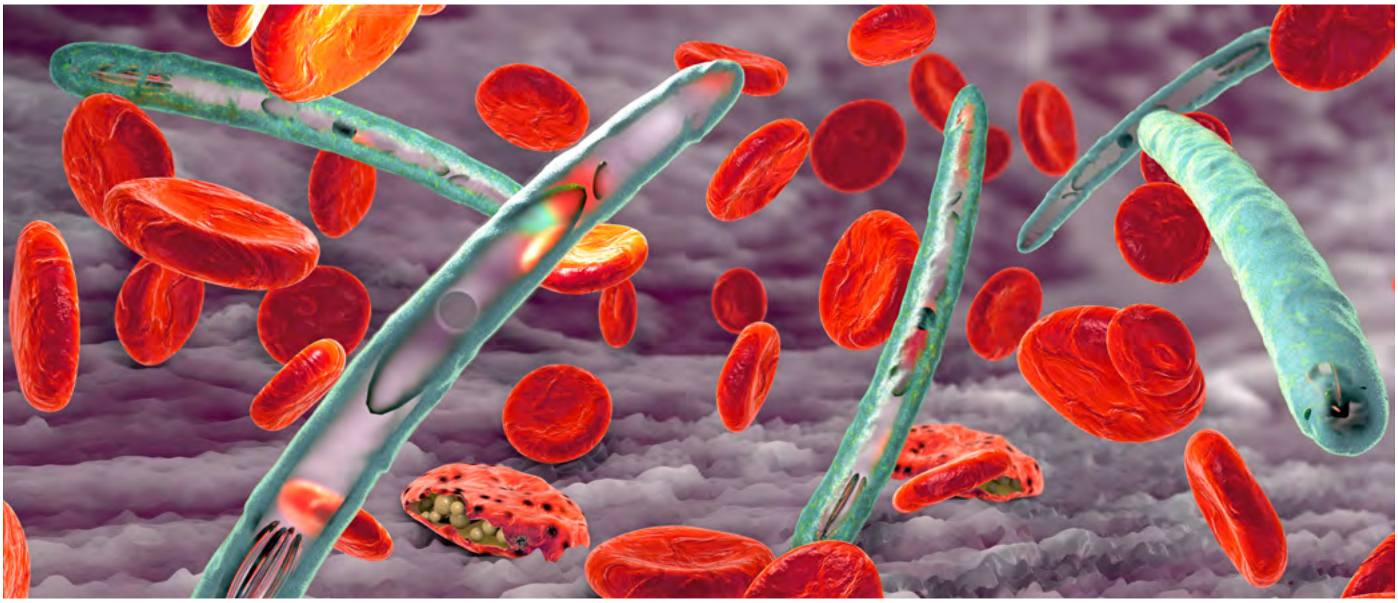
approach, which they are also pursuing at the NCCR Molecular Systems Engineering.

Fighting malaria

Another potential application of the polymer capsules is secure packaging of drugs or their precursors. A few years ago, Dr. Adrian Najer, a member of Meier and Palivan's team, developed a concept based on this idea to treat malaria infections.

Malaria is caused by a parasite of the genus *Plasmodium*, which is transmitted by mosquito bites. The parasite infects red blood cells in the human body and multiplies inside them. When these infected blood cells burst, the parasites released go on to infect new blood cells.

Najer developed a polymer capsule that contains a malaria drug and is absorbed by infected blood



In malaria, red blood cells are infected by a parasite of the genus Plasmodium that is transmitted via mosquito bites. Polymer capsules could potentially prevent the multiplication of the Plasmodium species (image: Shutterstock).

cells. The protective polymers gradually break down in response to changes in the intracellular environment caused by the Plasmodium infection, so the drug is released in the infected cells, where it can kill the parasites.

A second application of the treatment consists in using tiny polymer bubbles equipped with specific sugar molecules on their surface to make them 'look like' red blood cells. The parasites bind to these 'nanomimics', which prevents them from infecting new blood cells.

Adrian Najer is currently refining the approach in the course of his postdoc fellowship at Imperial College London.

These examples show that the block copolymers are able to perform the researchers' intended functions. Before they can be deployed in practice, further research and detailed analysis are needed to ascertain how they behave inside the body, and what happens to their degradation products.

Optical effects produced by minute structures

A key benefit of plastics is the diverse range of ways in which their surface can be structured and functionalized, yielding entirely new properties. The Institute of Polymer Nanotechnology (INKA) of the FNHW School of Engineering and the Paul Scherrer Institute specializes in modifications of this kind.

A research team led by INKA director Professor Per Magnus Kristiansen works on countless different applications, mostly in collaboration with an industry partner. Some of their projects are supported by the SNI.

Micro and nano structures on material surfaces can be used as security features on identity documents, for example: the intricate structures reflect light in different ways and minute plastic lenses can create optical effects.

In the Nano Argovia project LASTRUPOL, the team has devised a novel surface

Additional information:

Institute of Polymer Nanotechnology (INKA):

https://www.fhnw.ch/en/die-fhnw/hochschulen/ht/institute/institut-fuer-nanotechnische-kunststoffanwendungen

Institute of Product and Production Engineering (IPPE):

https://www.fhnw.ch/en/die-fhnw/hochschulen/ht/institute/institut-fuer-produkt-und-produktionsengineering

Plastic surfaces can be structured or treated in different ways. Here, the team from the FHNW Institute of Polymer Nanotechnology (INKA) selectively treated a film with plasma so that it shows the FHNW logo (image: INKA, FHNW).

structuring fabrication process in collaboration with the company Gemalto/THALES designed to produce optical structures of this kind with a high degree of precision and surface quality as cost-effectively as possible. Also involved in the project are researchers from the Institute of Product and Production Engineering (IPPE), which the INKA has collaborated with on numerous projects in the past.

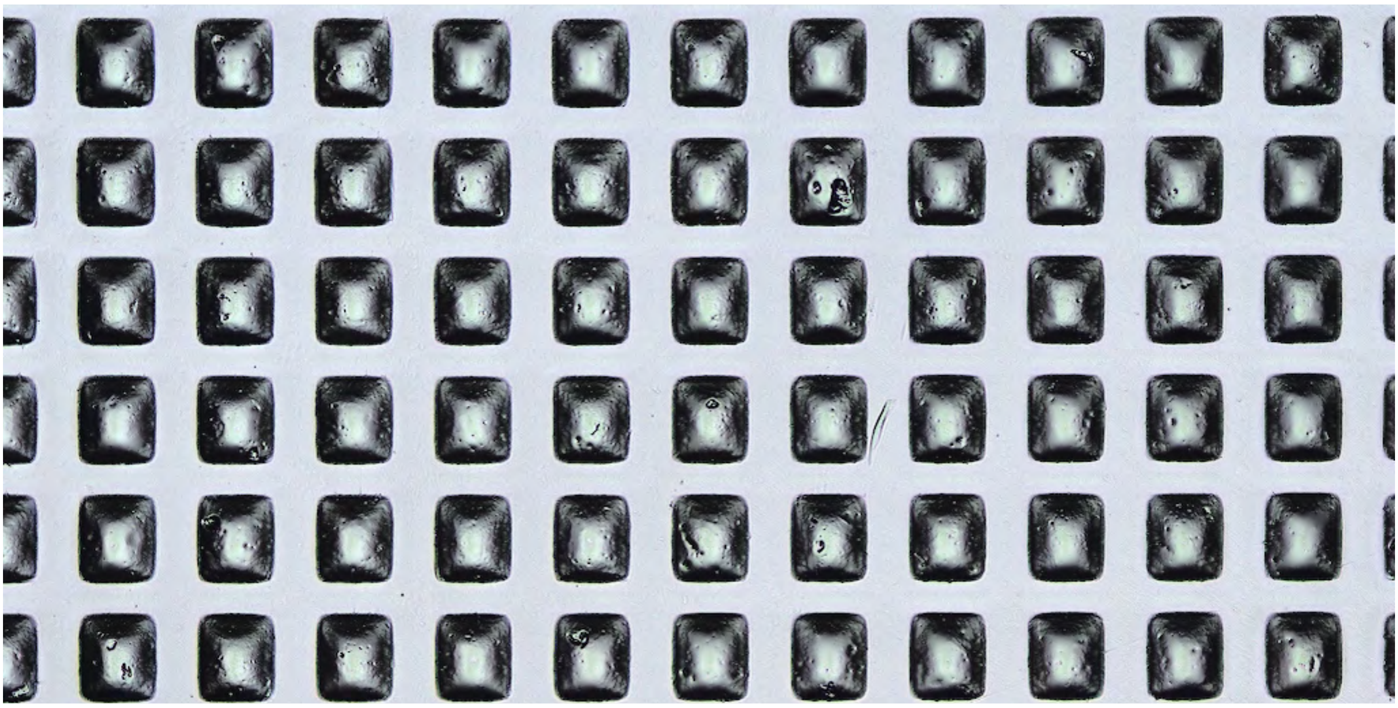
To begin with, the researchers use ultrashort laser pulses to selectively remove material from the plastic surface – a speciality of the IPPE's laser group. As the resulting microscale structured surface is too rough, however, it has to be smoothed in a subsequent production step – without altering the laser-engraved structures. This is achieved with the help of a method developed in the Nano Argovia project SurfFlow that selectively changes the material properties of part of a given sample.

Using UVC radiation, the surface is selectively modified so as to lower the temperature required for the polymers to change from a solid state into a thick molten mass, known as the glass transition temperature. When the sample is subsequently gently heated, the treated uppermost layers reach their glass transition temperature and become smooth. Deeper layers remain virtually unaffected, and the microstructure on the surface is retained.

"The technology allows us to create precise templates with which we can reproduce different security features," explains project leader Per Magnus Kristiansen. However, further work is required before this goal can be achieved: toward the end of the project, it became apparent that successful smoothing of laser-engraved structures requires a different approach. Efforts to this end will continue in a follow-on project backed by the Aargau Research Fund – once again in collaboration with the IPPE and Gemalto/THALES.

Surfaces with novel properties

Alongside surface structuring, functionalization of surfaces is another tool with great potential for a broad range of applications. For example, polymers and molecules with functional groups can be anchored to a surface using electron beams (a process known as grafting), altering its properties. In some plastics, electron beams also alter the bonds between polymers in the outer layer (cross-linking), thereby enhancing their stability. Meanwhile, coatings of different kinds can also confer new properties on surfaces. Activating plastic surfaces by means of plasma treatment, for instance, can prepare them for subsequent processing steps such as bonding, printing or back injection.



In the Nano Argovia project ReLaFunAF, coatings are applied to surfaces so that fingerprints are repelled. This image shows a coating structured using the ReLaFun process (image: INKA, FHNW).

The team led by Dr. Sonja Neuhaus of the INKA has been working on surface functionalization processes of this sort for a number of years, and has been involved in a number of Nano Argovia projects.

Smudge-free surfaces

For example, in the project ReLaFunAF the group is currently working on coatings that repel fingerprints. The process involves applying a layer to the plastic that is cured under UV light. However, the UV LED lights do not fully cure the surface: a 'sticky' layer containing reactive groups is left behind. In a second coating step, functional molecules can be applied to this layer by covalent binding and then fixed in place with further UV curing.

"As the functional layer does not come into contact with the original substrate, functionalizations that would otherwise adhere to the sample poorly or not at all become possible. This is a decisive advantage," explains Sonja Neuhaus.

If the method is successful, a variety of different objects could benefit from this coating – who among us would not welcome a fingerprint-free screen for our mobile phone?

Rapid detection of bacteria

In a project funded by the Swiss National Science Foundation, the group led by Neuhaus is currently working on the possibility of anchoring enzymes to a plastic surface. Eventually, the researchers hope to achieve this with the enzyme luciferase. This protein, which occurs in fireflies, for example, catalyzes the transformation of luciferin into oxyluciferin in the presence of oxygen. This reaction also requires ATP (adenosine triphosphate), often referred to as the 'unit of currency' of energy in living creatures. Accordingly, the luciferin/luciferase system provides quantitative evidence of ATP, and can therefore be used to detect bacterial contamination

Biomolecules like luciferase require a favorable environment on the plastic surface, ideally an absorbent hydrophilic layer. To create this layer, electron beams are used to graft functional polymers onto the substrate. A previous plasma treatment ensures optimal moistening of the surface with the polymer solution during the electron grafting process.

Before investigating luciferase anchoring, the researchers are testing a model enzyme that catalyzes a simple color reaction. This will yield quick and relatively simple confirmation that the anchored enzymes are able to function properly on the surface.

The blue color results from the activity of a model enzyme anchored on the surface (Image: INKA, FHNW).

Custom-built for each patient

Numerous other research groups in the SNI network are also working in intelligent applications for plastics.

One such group, a team of researchers from the FHNW School of Life Sciences, the Hightech Research Center of Cranio-Maxillofacial Surgery at University Hospital Basel and the company CIS Pharma AG, has developed innovative nanostructured implants that support the regeneration of bones and soft tissue in the jaw and mouth area, and can be custom-built for each patient using 3D printing technology.

The key to these implants is a multi-layered polymer membrane based on the Cellophil technology developed by CIS Pharma. Cellophil is a combination of several natural amino acids linked by an acrylic backbone, offering a very high degree of biocompatibility. The polymers are mixed with cross-linking substances. Upon exposure to UV light, this results in membranes with different degrees of porosity depending on the amount added.

As a result, researchers can equip the various layers of the implant with different properties – according to the type of cells they will come into contact with inside the patient's body. In spite of the differences in composition among the layers, the implant can by printed in a single step and individually tailored to each patient.

A broad field with numerous challenges

These examples illustrate just a few of the numerous possible applications of modern plastics currently being researched at the SNI. Plastics have become an inextricable part of our lives, and will continue to deliver valuable benefits in a wide range of fields. Still, a great deal of work is also needed on ways to recycle and reuse plastics so as to ensure intelligent utilization of valuable resources and protect our environment.