Fraunhofer IME

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Annual Report 2021

Preface

The year 2021 was once more overshadowed by the ongoing global COVID-19 pandemic. Not only were the economy and healthcare systems faced with enormous challenges, a great deal of resilience was required from the population as well. Despite the difficult situation, Fraunhofer IME was able to continue its research activities and projects, under the consistent adherence to all protective measures, and set important milestones.

The highlight for Fraunhofer IME was the nomination of the team dandelion in Münster for the Federal President's Award for Technology and Innovation 2021. Along with Carla Recker from Continental, the colleagues Dirk Prüfer and Christian Schulze Gronover were nominated for the project "Sustainable tires from dandelions - innovations from biology, technology and agriculture". Even though the team did not win the award, they are very proud to have been nominated for it and to have been accepted in the "Circle of the Best". Congratulations went to the BioNTech team for their development of the COVID-19 mRNA vaccine.

The Aachen location could enforce the bioeconomy sector with its two research fields "Biohybrid Technology" and "New Agricultural Systems". Both topics are also the focus of the Fraunhofer lighthouse projects "ShaPID" and "FutureProteins", which the other three Fraunhofer IME locations Münster, Gießen and Schmallenberg are involved in as well. The lighthouse project "ShaPID" is concerned with the de-fossilization of chemical production processes as well as the establishment of sustainbale and resilient material and energy cycles. The lighthouse project "FutureProteins" is coordinated from the Aachen location and combines the production of alternative protein sources, such as wheatgrass, insects, filamentous fungi and micoalgae, in closed agriculatural systems with the integrated utilization of all bypass to provide protein resources for the food industry.

At the Branch for Bioresources in Giessen, we're developing a unique center for the exploitation of bioresources that can be applied in medicine, plant protection and the food industry. Due to funding from the LOEWE program, which will continue until the end of 2022, we were able to establish into the leading institution for insect biotechnology.

In Schmallenberg, construction activities - one year before the planned occupation of the 6,000 sqm new laboratory building and due to the renovation work of the administration building - reached their peak. Associated organizational constraints, exacerbated by the second pandemic year, could not stop the steady increase in operating and overall budgets since 2010. The second highest industrial and total revenues after 2020 were achieved.

Important topics such as resource technologies and bioeconomy will remain a focus of our various research activities. Our aim is to put the results of these acitivites to the most efficient use in industry.

Frank Treppe

Prof. Dr. Christoph Schäfers

Prof. Dr. Stefan Schillberg

Content

The institute

Fraunhofer IME profile

As of 2021, the Fraunhofer Institute for Molecular Biology and Applied Ecology comprises the "Molecular Biotechnology" Division and its Branch for "Bioresources" as well as the "Applied Ecology" Division. In 2021, Frank Treppe was the executive, acting institute manager. Prof. Dr. Stefan Schillberg and Prof. Dr. Christoph Schäfers were acting members of the institute management.

The Fraunhofer IME is a strong partner for contract research in the areas of pharmaceuticals, medicine, chemicals, bioeconomy and agriculture as well as environmental and consumer protection. Our research and development portfolio focuses on industry, small and medium enterprises and on the public sector. In 2021, Fraunhofer IME collaborated with more than 110 national and international industrial clients and several international industrial associations, for whom confidential projects were conducted. Our interdisciplinary organization allows us to process complex projects across departments and where appropriate, also focuses on cooperation with external institutes and partners. We work closely with basic research and are internationally networked. Our laboratories with state-of-the-art equipment and complex environmental simulation facilities allow us to offer a wide range of research and services as well as studies according to good laboratory practice (GLP).

At the end of 2021, the institute employed about 430 people at the locations in Aachen, Münster, Schmallenberg and Gießen. We have close ties with the Department of Biology and Biotechnology of Plants at the University of Münster, the Department of Applied Entomology at the Justus-Liebig University Giessen, and the world's first Institute for Insect Biotechnology, founded in Giessen in 2016. We cooperate with many international research partners and remain in close contact with universities and other research organizations. Our aim is to recognize trends and developments as they emerge, and to develop and implement novel research strategies and technologies.

Molecular Biotechnology

Molecular Biotechnology is the basis of a modern bioeconomy and contributes sustainably to the knowledge-based production and industrial use of renewable raw materials. On behalf of our customers, the Molecular Biotechnology Division develops tailored plants, animal cells and microbes for applications such as the production of food and feed as well as renewable raw materials, the manufacture of technical and pharmaceutical proteins, and the handling of anthropogenic pollutants including greenhouse gases, which we can exploit to produce valuable substances. In recent years, we have established ourselves successfully in the research landscape and on the market due to our synergistic activities in the fields of green and white biotechnology. We offer our partners in academia, industry and the regulatory authorities a comprehensive research and service portfolio.

Symbol used in the annual report MB

Bioresources

We exploit groups of organisms with a large biodiversity such as insects, bacteria and fungi as bioresources by using innovative technologies and established platforms to isolate and characterize naturally occuring substances. We evaluate them with regard to their application potential in medicine, plant protection and industrial biotechnology. Thus, new molecules will be identified in order to develop antibiotics or substances for the food and feed industry, like aromatics, preservatives and enzymes, as well as to open up new applications and to form a basis for the creation of value-added chains. Moreover, we develop insect models for toxicological studies and deploy biotechnological methods to control pest and vector insects, for example RNA inference in plant protection or sterile insect technology.

Symbol used in the annual report BR

Applied Ecology

Our objective is the risk assessment of synthetic and biogenetic substances for the environment and consumers. We develop experimental and model-based methods for the analysis and prediction of the environmental concentration and the hazaroudness of substances with regards to the environment as well as for the analysis of consumer exposition to substances in th environment. We often act as scientific mediators between commercial producers and the regulatory authorities and are involved in the new and further development of international test guidelines. We conduct contract research for industry and the public and use our analytical expertise to increase food safety and quality.

Symbol used in the annual report AE

Fraunhofer IME within the Fraunhofer-Gesellschaft

The Fraunhofer-Gesellschaft is the world's leading applied research organization. With its focus on developing key technologies that are vital for the future and enabling the commercial exploitation of this work by business and industry, Fraunhofer plays a central role in the innovation process. As a pioneer and catalyst for groundbreaking developments and scientific excellence, Fraunhofer helps shape society now and in the future. The Fraunhofer-Gesellschaft currently operates 76 institutes and research institutions throughout Germany. More than 30,000 employees are qualified scientists and engineers, who work with an annual research budget of 2.9 billion euros. Of this sum, 2.5 billion euros is generated through contract research.

The Fraunhofer Institutes are organized in nine thematically oriented alliances. Their goals are the technical coordination within the Fraunhofer-Gesellschaft, the bundling of core competencies and a joint appearance on the market. Fraunhofer IME is a member of the Life Sciences Network, a scientific-technological community of highly qualified experts from key areas of modern life sciences from six Fraunhofer institutes and one Fraunhofer Research Institution.
www.fraunhofer.de/en/institutes/institutes-and-research-establishments-in-germany/fraunhofer-groups/resource-technologies-and-bioeconomy

Institutes or departments of institutes with different competencies cooperate in Fraunhofer alliances to jointly develop and market a business segment. The Fraunhofer Alliances make it easier for customers to access the results and services of the Fraunhofer-Gesellschaft. Fraunhofer IME is involved in two alliances:
Chemimal Industry: **www.chemie.fraunhofer.de/en**
Agriculture and Food Industry: **www.fcm.fraunhofer.de/en**

High Performance Centers organize the collaboration between university and non-university research with industry. Universities, higher education institutions, Fraunhofer Institutes and further non-university research institutions work together at one location on specific topics in order to quickly transfer innovations to application. Fraunhofer IME in Aachen is involved in the "Networked, adaptive production" High Performance Center.
www.vernetzte-adaptive-produktion.de/en

Fraunhofer lighthouse projects put the focus on strategic objectives with a view to developing practical solutions from which economies such as Germany's can benefit. The projects aim to turn original scientific ideas into marketable products as quickly as possible. Fraunhofer IME coordinates the lighthouse project "FutureProteins" and is involved in the project "ShaPID".
www.ime.fraunhofer.de/en/trends/futureproteins
www.shapid.fraunhofer.de/en

The Fraunhofer Sustainability Network is an initiative of 20 Fraunhofer Institutes aiming to raise awareness within the Fraunhofer Gesellschaft for the integration of sustainability issues.
www.fraunhofer.de/en/about-fraunhofer/corporate-responsibility/governance/sustainability/fraunhofer-sustainability-network

Advisory board

Advisory Board members advise the Fraunhofer-Gesellschaft as well as the individual institutes and promote their connection to partners from industry, science and the public sector. Members of the Fraunhofer IME Advisory Board:

Dr. Harald Seulberger (Chairman)
BASF SE, Limburgerhof

Dr. Friedrich Dechet
Industrial Association Agrar, Frankfurt am Main

Prof. Dr. Adolf Eisenträger
German Federal Environment Agency, Dessau-Roßlau

Stefan Lütke Entrup
Gemeinschaft zur Förderung von Pflanzeninnovation e.V., Bonn

Prof. Dr. Annika Jahnke (guest)
Hemholtz Centre for Environmental Research, Leipzig

Prof. Dr. Joybrato Mukherjee
President of the University of Giessen, Giessen

Ministerialrätin Andrea Noske
Federal Ministry of Education and Research, Berlin

Dr. Dr. h.c. Christian Patermann
Formerly director Directorate-General for Research and Innovation, Bonn

Prof. Dr. Dr. h.c. mult. Ulrich Rüdiger (guest)
Rector of RWTH Aachen University, Aachen

Dr. Karin Schlesier
Federal Institute for Risk Assessment, Berlin

Prof. Dr. Johannes Wessels
Rector of the University of Münster, Münster

Dr. Hans-Ulrich Wiese (permanent guest)
Formerly member of the Executive Board of the Fraunhofer-Gesellschaft

Business fields

Molecular Biotechnology

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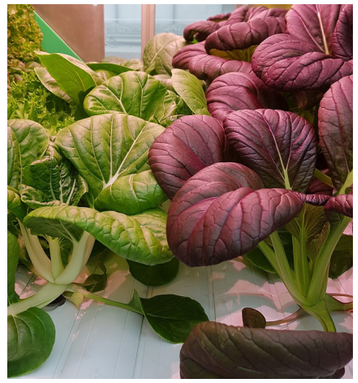
Bioproduction and Industrial Biotechnology

The business field Bioproduction and Industrial Biotechnology focuses on the identification, sustainable production, processing and optimization of high-value natural compounds, including chemical building blocks, bio based fuels, fine chemicals, biomaterials and proteins for industrial applications and consumer products. This can be produced using a diverse array of organisms, from microorganisms and plant cells through to animal cells. Here the value chain is covered: From target discovery and screening, the development and optimization of production strains and the transfer of laboratory-scale processes to scale up and pilot-scale manufacturing for future industrial production and downstream processes, including the evaluation of economic feasibility.
Fraunhofer IME provides comprehensive expertise in the development of innovative biotechnology platforms and optimized processes. The departments and project groups involved cover a range of different product types, from bulk chemicals and fuels such as isopropanol, isoprene and hexanol, through to plant-based metabolites and polymers such as rubber, inulin, cellulose and industrial starches, and high-value fine chemicals, proteins and industrial enzymes.



Agroscience for Food and Feed

The business field Agroscience for Food and Feed covers the agricultural value chain “from farm to fork” and focuses on the development and improvement of plant traits, crops and enabling technologies to increase the biomass of crops, the quality and yield of agricultural products, the ability of plants to grow in diverse environments, and to withstand pests and diseases. These traits are developed using both genetic modification (GM) and non-GM approaches, and key technologies such as genome editing and TILLING.

The departments and project groups involved in this business field focus on precision breeding techniques and the development and testing of GM crops. Based on this wide-ranging expertise, Fraunhofer IME acts as a preferred partner for academic laboratories, SMEs and major agribusiness companies.

Production of Recombinant Proteins

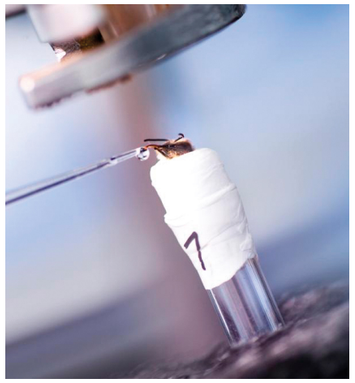
The Fraunhofer IME offers expertise in all aspects of the design, production, purification and characterization of recombinant proteins, including process development and scale-up from a laboratory process to the manufacture in kilograms. Different systems are available for the production of specific protein products, involving microorganisms, plant cells, animal cells and whole plants as well as cell-free expression systems. There has been a recent increase in the demand for recombinant proteins produced at the kilogram scale for the pharmaceutical, agriculture and cosmetic sectors, and for technological applications. In addition, the institute has its own new protein candidates in the pipeline, particularly technical enzymes, foodstuff proteins, diagnostic reagents and therapeutic proteins.

Business fields

Bioresources

Bioresources for the Bioeconomy

We use groups of organisms with great biodiversity as bioresources, including insects, bacteria and fungi. We combine innovative technologies and established platforms to isolate and characterize natural substances, and to evaluate their potential for use in medicine, plant protection and industrial biotechnology. In this way, novel molecules are identified to develop as antibiotics or ingredients for the food and feed industry, such as flavoring agents, preservatives and enzymes, leading to novel applications and value chains. With the world's largest industrial strain collection of microorgasnisms, taken over from Stanofi, we are also open to projects with other industrial partners from non-competing fields of application.



Insect Biotechnology

The development and application of insect biotechnology allows us to use insects, insect-derived molecules, cells or organs, and insect-associated microbes as products or systems for diverse applications in medicine, industrial biotechnology, and the food and feed industry. We also exploit insect cells as protein expression systems and insect antennae as biosensors for drugs and explosives. Furthermore, we develop insect models for toxicology studies and use biotechnology to control pest and vector insects, for example RNA interference and the sterile insect technique. We also use insects for the conversion of organic waste into proteins and fats for the food and feed industry.

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Business fields

Applied Ecology

Environmental Risk Assessment of Substances

We use our expertise in environmental analysis, experimental environmental chemistry and ecotoxicology, and modeling the bioaccumulation and effects of substances, to assess the risks such substances pose to the environment. We liaise with the regulatory authorities to formulate critical questions and draw up test guidelines to address these risks. On behalf of our partners in industry, we perform and evaluate complex experimental and model-based studies to the highest scientific standards. We use the analysis and classification of molecular mechanisms as screening tools to assess the environmental impact of candidate products. We manage the national Environmental Specimen Bank and perform environmental monitoring projects to identify potential environmental pollutants and check prospective assessments.

Food Safety and Quality

The safety and quality of food depend on the production method and on the primary and further processing of agricultural raw materials. We focus on the qualitative properties of raw materials and foods, and the damage caused by harmful substances. For example, we take existing methods used to analyze the metabolism of plant protection products in crops and farm animals and adapt them to study the metabolism of veterinary pharmaceuticals and feed supplements, and we develop cell-based alternatives to animal testing. We track breakdown and conversion products by radioactive labeling throughout the food production cycle Within the Fraunhofer Food Industry Alliance, the focus is on issues along the entire food chain, with emphasis on food analysis/processing, microsystems technology and logistics. The research is being expanded to include R&D activities on the upstream and downstream areas such as agriculture or utilization networks.

Sustainable Agricultural Production of Substances

We develop across divisions concepts for the sustainable agricultural production of substances for a diversified bioeconomy: To achieve this, amongst other things, we use Fraunhofer technologies of the lead project „Cognitive Agriculture“ to meet socio-economic and ecological requirements (Community claims) with new crops, improved seeds and exposure models adapted to the new technologies. We take into account differentiated soil and microclimate properties, the use and optimization of plants for the production of valuable and active substances (Aachen and Münster), and waste and insects for obtaining protein (Gießen). Regulatory requirements arising from digital agriculture in the application of plant protection products, veterinary medicines and fertilizers, and other agricultural adjuvants, are also taken into account (Schmallenberg).

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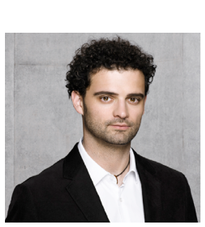

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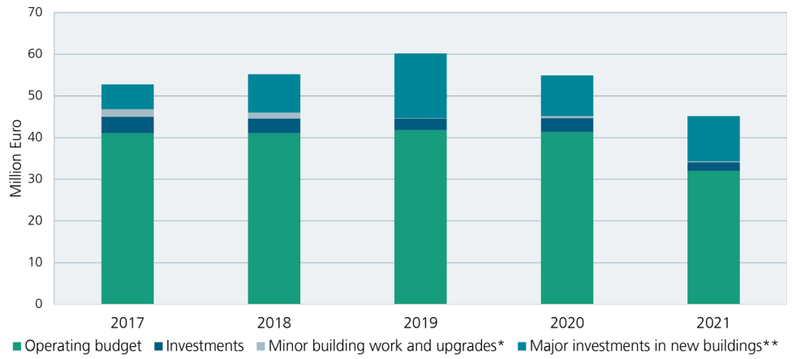
Institute data

As of January 1, 2021, Fraunhofer IME comprises the four locations Aachen, Münster, Giessen and Schmallenberg. At the turn of the year, the former Fraunhofer IME locations Frankufrt a.M., Hamburg and Göttingen became the the newly established Fraunhofer Institute for Translational Medicine and Pharmacology ITMP. Consequently, the budget and financial numbers of 2021 are lower in comparison with previous years.

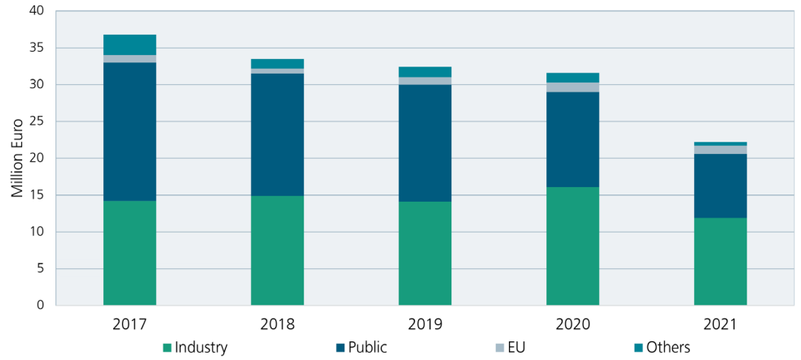
Total budget of Fraunhofer IME



* Small construction measures incl. own contribution
** Major Investments

In 2021, Fraunhofer IME had an operating budget of 32.1 million euros. In addition, about 2 million euros were invested in equipment. Fraunhofer IME recorded an expense of 11 million euros for construction activities, primarily the new institute buildings in Giessen and Schmallenberg.

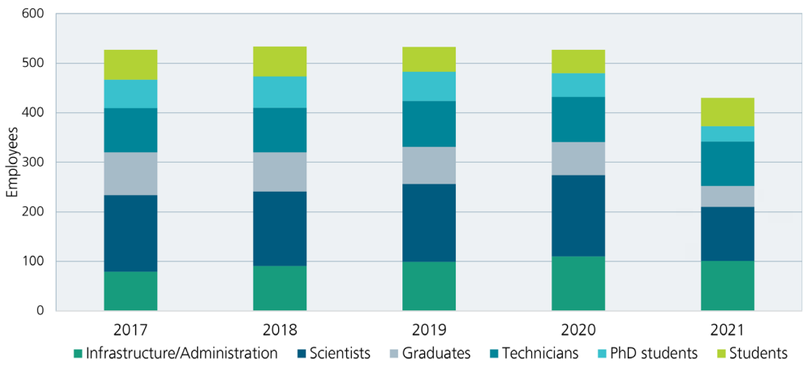
External financing of Fraunhofer IME



69.3 percent of the budget was financed by external income. Economic earnings of 11.9 million euros remain at a constantly high level. This corresponds to an economic revenue share (Rho Wi) of 37.1 percent.

In 2021, Fraunhofer IME once again achieved excellent results in the key figures of the Fraunhofer-Gesellschaft.

Employees of Fraunhofer IME



At the end of 2021, 430 people were employed at Fraunhofer IME locations in Aachen, Münster, Schmallenberg and Giessen. 53.5 percent of Fraunhofer IME employees were female.

Highlight 2021

Nominated for the Federal President’s Award for Technology and Innovation – Team dandelion in the "Circle of the Best"

Team Dandelion Dirk Prüfer, Christian Schulze Gronover and Carla Recker with Federal President Frank-Walter Steinmeier (f.l.t.r.) on November 17, 2021.

For 25 years, the Federal President has been awarding the German Future Prize for Technology and Innovation to individuals or teams for outstanding technical, engineering or scientific innovations. On September 15, the team Dr. Carla Recker (Continental), Dr. Christian Schulze Gronover (Fraunhofer IME) and Prof. Dr. Dirk Prüfer (WWU Münster, Fraunhofer IME) was nominated for the Federal President’s Award for Technology and Innovation 2021 with the project "Sustainable tires from dandelions - innovations from biology, technology and agriculture". The team is developing the Russian dandelion as a crop for the future along the entire value chain. Providing a regional alternative to counteract further deforestation of the tropical forests in the producing countries is a primary goal.

Natural rubber - a raw material in demand

Without natural rubber, no tire rolls. The greater the load on the tires, the higher the proportion of natural rubber. Car tires contain up to 20 percent natural rubber, truck tires up to 30 percent and aircraft tires up to 100 percent. Although synthetic rubber has been produced and continuously optimized since the beginning of the 20th century, its mechanical properties cannot compete with the unique characteristics of its natural counterpart - we continue to rely on natural rubber. It is used not only in tires, but also in around 50,000 other products such as seals, mattresses, shoe soles and condoms.
Up to now, almost exclusively one plant species is cultivated for the production of natural rubber - the rubber tree *Hevea brasiliensis*. The tree grows in tropical regions which are designated as rubber belt. The main producing countries are located in Southeast Asia: Indonesia, Malaysia and Thailand. Since Europe is completely dependent on imports, in 2017 the European Commission included natural rubber as the only biogenic substance in the list of critical raw materials for the EU. The main purpose of this list of 30 materials is to identify raw materials with a high supply-risk and significant economic importance for key sectors in the European economy.

At the same time, it is also intended to create an incentive for the production of critical raw materials in Europe.

While global production of natural rubber was just two million tons per year in the 1960s, it already exceeded six million tons in the early 1990s and reached almost 14 million tons in 2020. In 2000, a total of around 9.6 million hectares were under cultivation for natural rubber worldwide, rising to 14.8 million hectares by 2020. To provide the space for the Hevea plantations, large areas of valuable tropical forest have been cleared in producing countries such as Thailand and Indonesia. Global demand for natural rubber continues to rise, and by 2030 it is estimated that there will even be a shortage of around 400,000 metric tons on the market. The tropical forests are threatened by additional clearing for the cultivation of the rubber tree with further fatal effects on biodiversity and climate change.
The researchers aim to counteract these developments. In order to be successful, a sustainable, alternative source of raw material must be developed. However, only very few plants produce the raw material in demand in equivalent quality to the rubber tree.

Flower and separated root of Taraxacum koksaghyz*, with the whitish milky juice emerging from the root.*

"The protection of our tropical forest is a top priority in the fight against climate change. For this reason, the natural rubber processing industry also needs to rethink. Our approach to sustainably gaining natural rubber from dandelions can counteract many socio-economic and ecological challenges in these regions."

Dirk Prüfer

Dandelion - the rubber source of the future

At Fraunhofer IME in Münster, researchers have been focusing on a dandelion species (*Taraxacum koksaghyz*) as an alternative for many years. Russian dandelion originates from Kazakhstan, it grows on undemanding soils and is particularly suitable for the extraction of natural rubber due to its quality. The rubber is produced and stored mainly in the root, which, if damaged, releases the whitish milky sap.

In the beginning, the team was often ridiculed. Many thought growing dandelions to produce rubber was a crazy idea. And indeed, when the team started, they faced major challenges. Russian dandelion was still a wild plant which contained only low amounts of natural rubber, too low for industrial use. First, they wanted to understand natural rubber biosynthesis in the Russian dandelion: How do the individual small building blocks – activated isoprene – become the polymer with more than 10,000 such units? Which proteins and genes are involved and which key regulators significantly influence the metabolic pathway?

Plant growth and yield of wild plants were anything but stable. However, the basic prerequisite for the economic and sustainable cultivation of bio-commodities is high-yielding and resistant documented by a large number of publications in peer-review journals.

Based on the knowledge of biosynthesis and its key regulators, it was possible to develop vigorous and robust plants together with the plant breeding expert ESKUSA. Through targeted breeding, the researchers doubled the rubber content in the roots within a short time. The scientists analyzed dandelion DNA and defined DNA markers that indicate the presence of a desired trait. In this way, they can already determine in seedlings whether they possess such traits that have a positive impact on rubber production. In terms of yield, the optimized Russian dandelion, with a rubber content in its roots of around 10-15 percent, can now almost compete with the rubber tree. Breeding is a never-ending process; even modern high-performance varieties of our crops are constantly being developed. Breeding goals are therefore also geared to the long term: For example, to global challenges such as climate change. Breeding of the Russian dandelion is also progressing steadily, focusing not only on further yield increases but also on important agronomic traits such as resistance to diseases and herbivores, efficient nutrient uptake and thus rapid growth of the plant in the juvenile stage.

Extracting natural rubber from the plant was another challenge. For this purpose, the scientists developed an environmentally friendly process, which has since been patented, in which the harvested roots are crushed since the leaves contain very little rubber. To extract the natural rubber, the roots are first precooked. Subsequently, they are transferred into a specially developed ball mill. By adding water, the balls crush the roots and the solid rubber particles are subsequently washed out with water and processed further.

In the process of establishing an entirely new value chain for the Russian dandelion from breeding to product, a large number of technical innovations for good agricultural practice for cultivation were also required. Together with the extended network, the scientists developed, for example, a special sowing and harvesting technique as well as the first digitized weed control system, which quickly and sustainably, removes the unwanted herbs in and between the dandelion rows. Each year, the experience and observations from field cultivation are incorporated into the further development of good agricultural practice.

Without the help of courageous, motivated, and forward-looking people in all areas of the project, we would never have come this far. I see us as pioneers in how we can increasingly generate innovations with and from plants for a sustainable, biobased economy and life in Germany in the future."

Christian Schulze Gronover

The desired resource is produced and stored inside the root.

The commercial product - the tire

The rubber extracted from dandelion is of equivalent quality to that from the rubber tree. Continental was able to prove this early on in the collaboration in extensive material tests: chemically and physically, there are no significant differences between natural rubber from Hevea and dandelion. In 2014, things got exciting when the first tests on the driving properties of the tire made from dandelion rubber were due. Continental decided to test it with passenger car winter tires, which - like commercial vehicle tires - have a particularly high natural rubber content and are exposed to extreme loads. The extensive driving tests under various conditions showed: The tires with treads made of pure dandelion rubber were equivalent to those made of Hevea rubber. In 2016, a first truck tire with dandelion technology was presented at the IAA.

The suitability tests with these truck tires also showed that the dandelion alternative is ideally suited for the commercial vehicle sector and meets the most stringent requirements in demanding freight traffic.

At the end of 2018, Continental opened the "Taraxagum Lab Anklam" research and testing laboratory for the further development of the innovation, an important milestone on the road to industrialization of dandelion rubber. In 2019, Continental presented the Urban Taraxagum, the first mass-produced bicycle tire made of dandelion rubber. The dandelion for these tires is grown in Mecklenburg-Vorpommern. The tires are manufactured in Korbach, Hessen. The much shorter distances between the cultivation fields and the tire plant drastically reduce logistics and transport costs, and resources can be used more sustainably. Provided the innovative establishment of dandelion as an industrial crop continues to develop successfully, car and truck tires made of dandelion rubber will also roll off the production line in the future. Continental presented the Conti GreenConcept tire concept at the IAA Mobility 2021.

Although Carla Recker, Christian Schulze Gronover and Dirk Prüfer did not receive the German Future Prize for the Taraxagum project, they are very proud to have been nominated for this award and to be included in the "Circle of the Best", an honor that only few researchers experience. Federal President Frank-Walter Steinmeier emphasizes in the foreword: "The nominees of the 2021 Deutscher Zukunftspreis are also making our world a better place with their ideas. They are whetting our appetites for the future. Thank you very much for this." Congratulations to the winners: the team from BioNTech for the development of the COVID-19 mRNA vaccine.

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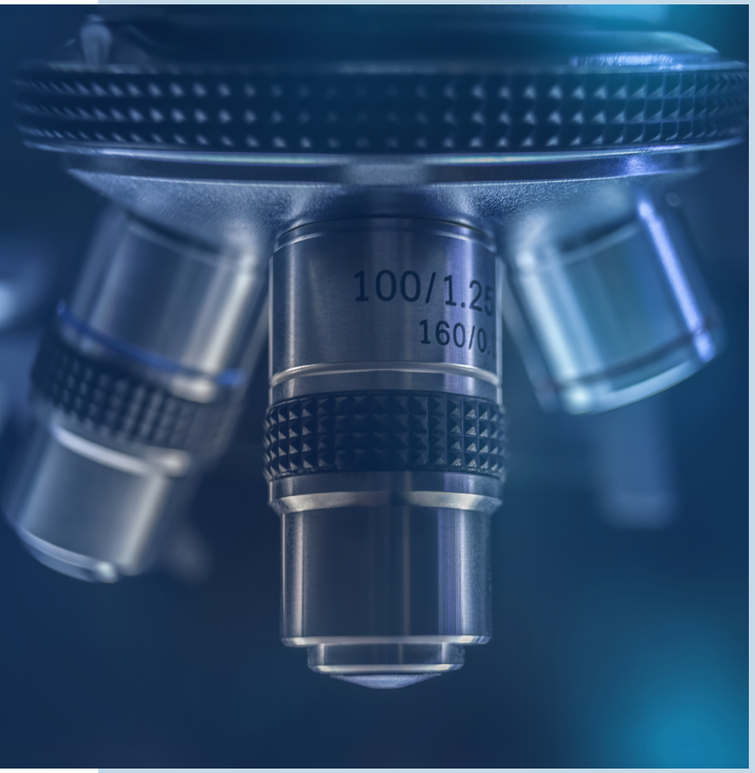
Continental's Urban Taraxagum is the first series-produced bicycle tire made from dandelion rubber.



Insights into our research

LEDitSHake: An innovative lighting system for plant cell cultures

Production of flavor-optimized foods based on insect protein

Targeted biosynthesis of pharmaceutically relevant terpenoids

Molecular markers of neurotoxic mechanisms of action in aquatic model organisms

Emerging viruses are a threat to managed pollinators and wild insects

Insect Farming 4.0 – Insect protein as competitive and sustainable animal feed

Biotechnological crop protection using RNA active ingredients

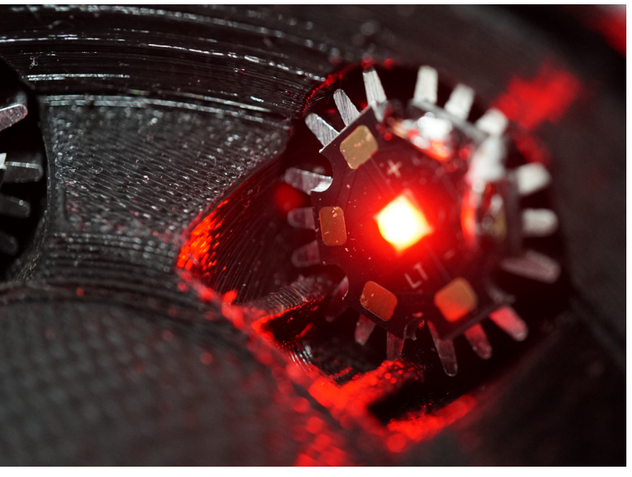
Reduction of pesticide concentrations in surface water caused by surface run-off

LEDitSHAKE: An innovative lighting system for plant cell cultures

By Ann-Katrin Beuel

Plants produce valuable ingredients that people have been using for thousands of years. However, obtaining those ingredients is a major challenge. For this purpose, the Molecular Biology division of Fraunhofer IME in Aachen relies on plant cell cultures grown under standardized conditions. With a newly developed lighting system, the optimal conditions for sustainable production of the ingredients can be found - without using genetic engineering.

Ecological sustainability and a healthy diet despite a growing population are among the greatest challenges we face as a society. Here, the conflict between the cultivation of food crops and crops for the production of technical raw materials or active ingredients also plays a significant role, so that the supply of these substances is also at risk in the near future. The UN has therefore formulated 17 specific Sustainable Development Goals (SDGs), such as Goal 12: Ensure sustainable consumption and production patterns. Valuable ingredients from plants are used in pharmaceutical development, e.g. for the treatment of various diseases such as diabetes, but often cannot be chemically synthesized at all or only at economically unjustifiable costs. The production of these ingredients using traditionally grown plants is limited by various environmental factors and requires a lot of arable land. Alternative microbial production systems are based on genetic engineering and therefore are "struggling" with acceptance and approval.



A red LED in the LEDitSHAKE system.

Securing the future of active ingredient and food supply through plant cell cultures

Plant cell cultures (PCCs) can make a significant contribution to securing the supply of active ingredients for the pharmaceutical, cosmetics and crop protection industries, as well as food supply, in a sustainable way. PCCs already represent an important alternative to conventionally grown plants for the production of secondary plant ingredients used primarily in cosmetics and personal care products, but also as food additives and active ingredients. In contrast to whole plants, PCCs can be cultivated in bioreactors regardless of seasonal conditions, available acreage and without using pesticides, which enables high quality, security of supply and local production of the required substances.

Using light instead of genetic engineering

Currently, improvements in the cultivation of PCCs are mainly addressed by the type of cultivation process or media composition. However, light of specific wavelengths is able to stimulate receptors in PCCs, thereby influencing the growth behavior and metabolism of the cells. Thus, the production of biomass as well as desired ingredients can be positively influenced. This is a non-invasive, non-chemical influence without using genetic engineering, which is an important factor for the acceptance of the products by the end consumers, especially in the case of cosmetics and food.

Therefore, a lighting system for PCCs has been developed at Fraunhofer IME in Aachen to investigate the effect of light with specific wavelengths on the cultures in order to find optimal light recipes for the production of secondary plant ingredients. LEDitSHAKE allows the use of 12 lighting conditions in parallel within a single shaking incubator, while only white light is possible in commercially available shaking incubators. With LEDitSHAKE, the intensity, photoperiod and spectrum of the light (red, green, blue, white, farred, UV) can be controlled and the respective effect can be investigated.

The LEDitSHAKE system: 12 individually lit conical flasks in a shaking incubator.

The patent-pending lighting system thus allows the factor light on the cultivation of PCCs to be investigated using statistical design of experiments (DoE) methods. DoE is used to investigate the interaction of light and media formulations with general process parameters such as temperature, shaking speed and oxygen supply - this approach can then be used to uncover both synergistic and antagonistic interactions between different influencing factors and to optimize the process.

The method established at IME (combination of DoE and LEDitSHAKE) is unique and represents the current state of the art. This allows a systematic identification and optimization of lighting conditions for PCCs. The LEDitSHAKE system is modular and can be installed in any standard shaker incubator for the cultivation of plant cell cultures, making it universally applicable.

Light optimized plant cell cultures

By using LEDitSHAKE, we have not only positively influenced the anthocyanin content in grape cell cultures, but also shown that the production of an active ingredient against diabetes is 10 times faster in plant cell cultures than in conventional field cultivation.

The year-round availability of the active ingredient, as well as compatibility with the SDGs - since there is no competition with the cultivation area of food crops - are further advantages. In addition, production can be local and independent of seasonal influences. This leads to short supply chains and security of supply for the companies that use the active ingredients.

In order to further exploit the potential of using plant cell cultures for the sustainable production of active ingredients for various application areas (cosmetics, pharmaceuticals and crop protection industries) and, in the medium term, also for food, LEDitSHAKE participates in the 2022 Fraunhofer AHEAD program to be further developed towards spin-off or licensing. Intensive market research and systematic surveys of potential customers conducted as part of the program will help to place the lighting system ideally on the market. The LEDitSHAKE technology will also be used in regular research projects, for example in investigating the effect of light on various plant cells, but also cyanobacteria.

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Production of flavor-optimized foods based on insect protein

By Dr. Daniel Bakonyi

The world population is growing steadily and with it the global demand for food. At the same time, climate change in connection with a severely limited availability of agricultural land threatens the stable supply of food. Therefore, the food industry is confronted with the challenge to utilize the available resources for food production as comprehensively as possible. At the same time, novel innovative ideas such as meat-like products are necessary, since many consumers want to eat less meat or no traditional meat at all for ethical reasons, undignified animal husbandry conditions or because of meat scandals.

Benefits of insects

With more than one million described species, insects are the most diverse group of animals in the world. In many parts of the world, various insects have traditionally been part of the human diet for a long time. About 2,000 edible insects are known; these include mainly beetles, ants, wasps and bees. Apart from that, insects are also on the menu of animals. As insects are found ubiquitously, they represent an excellent alternative source of protein for humans and animals. Compared to livestock, such as cattle, pigs or poultry, insects have a much better ecological balance, require fewer resources such as feed or water and significantly less land. Pigs or chickens are often reared in laying batteries or fattening facilities, whereas edible insects are reared in species-appropriate and food-safe containers that correspond to the natural swarm behavior of insects. Meat production also causes land and water pollution, which leads to climate and other environmental problems. 70 percent of the area used for agriculture, including the area for growing feed for livestock, is used for breeding conventional livestock. Another advantage of insects is the feed conversion efficiency, which is very low in conventional livestock with conventional feed. Insects are cold-blooded animals, so none of the energy provided by the feed is needed to maintain body temperature. For consumption, the usable proportion of farm animals in relation to their total weight is significantly lower than that of edible insects. More than 80 percent of grasshoppers and 100 percent of mealworms may be consumed. A currently (still) underused resource is the feces of insects, also known as *frass*. Due to its high nitrogen content, the frass may be used as a biofertilizer. In contrast to mineral fertilizers, the phosphate contained in *frass* is less soluble in water and thus remains longer in the soil. Studies have shown that the phosphate is nevertheless absorbed by plants without phosphate leaching.

Necessity for an alternative protein source based on insects

Due to the increasing demand for food proteins caused by the growth of the world population and the increasing consumption of animal-based foods, new protein sources are urgently required. First plant-based alternatives, such as products based on pea or soy protein, have been commercially available for some time. A disadvantage of a supply with vegetable proteins is their lower biological value compared to that of animal-derived proteins. In addition, a one-sided diet with vegetable proteins may lead to vitamin deficiencies due to the low concentration of essential vitamins. By breeding insects, essential vitamins and fatty acids are introduced into the innovative food in addition to the high-quality proteins.

Insect sausage from mealworm larvae.

As a result, the alternative products are rich in essential nutritional components and thus, typical deficiency symptoms that may occur when nourishing exclusively or predominantly on plant-based meat-like foods currently available on the market, are avoided.

Insects are largely omnivorous, allowing them to consume a wide variety of organic feeds. The use of industrial side streams of the food and agricultural industry as feed enables a resource-efficient insect breeding. This makes it relatively easy to generate high-quality protein from worthless or low-value side streams. The sustainable development of insect rearing in the project »InWu - Establishment of a novel protein source based on insects for the production of taste-optimized food« was carried out with both, solid and liquid side streams of the food industry. The larvae of the mealworm beetle (*Tenebrio molitor*) and the lesser mealworm beetle (*Alphitobius diaperinus*) were selected as suitable candidates. For product development, priority was given to the mealworm, as the European Food Safety Authority (EFSA) has approved it as a novel food since June 2021. For the InWu project, regional side streams were used for the cultivation of mealworm larvae. In direct comparison to a reference diet based on chicken feed, it was shown that the mealworms developed on a mixture of certain side streams at comparable rates to those on the reference diet. Furthermore, it was shown for the first time that liquid side streams may be successfully employed as wet feed, which serves as a source of moisture, after simple processing. This additional feeding can compensate for any limitations of the dry food.

Insect sausage made from mealworm larvae

Studies showed that the willingness of Western consumers to eat insects increases when they are included in familiar products such as burger patties or protein bars on the one hand,and when the insects were added as flour (not recognizable as insect) in the product on the other hand. By adapting to the European/Western taste with spices and creating a familiar consistency and texture of the product, the willingness to eat insects should be increased and thus the »disgust factor« is reduced. Consumers can thus be slowly habituated to insects as food. In the project, a spreadable sausage was created that consists of 60 percent mealworm larvae. Tastings showed that the vast majority of consumers would eat this product regularly. Meat substitute products made from insects can thus be an attractive alternative for consumers who take care of sustainably produced food.

Mealworm larvae (Tenebrio molitor).

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Targeted biosynthesis of pharmaceutically relevant terpenoids

By Dr. Christian Schulze Gronover, Dr. Boje Müller and Jos David Cox

Plant secondary metabolites are more and more used in green, red and white biotechnology. A scientifically and especially economically interesting group of natural products are terpenoids. In order to meet the increasing demand for these valuable substances, as well as to increase product diversity, microorganisms can be used as sustainable "factories" for the production of tailor-made molecular variants of high quality

From medicinal plant to bioreactor

With over 40,000 compounds, terpenoids represent the largest class of natural substances and are synthesized by all known organisms. The number of different terpenoids in flowering plants is particularly impressive. In nature, they fulfill a variety of functions: For example, as pigments they give color to flowers and fruits, as fragrances they attract pollinators, and as components of resins or waxes they serve as defense against herbivores and microbes. The economic importance of terpenoids is enormous. However, their extraction from plants poses major challenges: Depending on environmental conditions, composition and quantities can vary. In addition, extraction from plant biomass is associated with high consumption of energy and resources and is therefore often not economically viable.

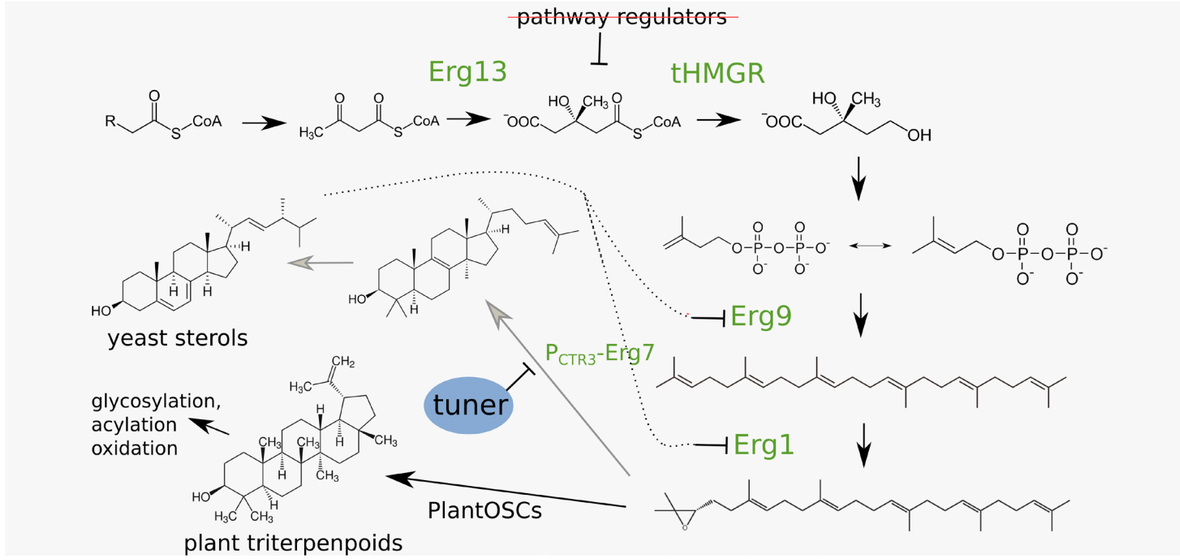
The seeds of the horse chestnut are a rich source of triterpenoids and its extracts are used in phytomedicine.

Chemical synthesis from petrochemical feedstocks, in turn, struggles with the enormous complexity of natural products. Alternative, sustainable systems for production and purification are needed to achieve the United Nations Sustainable Development Goals (SDGs).

Therefore, the use of microbial organisms such as the baker's yeast *Saccharomyces cerevisiae* came into focus. Yeasts are unicellular fungi that generally grow quickly and are very adaptable in terms of feedstock and environmental conditions. As eukaryotic microorganisms, yeasts, unlike *Escherichia coli*, also possess the mevalonic acid (MVA) biosynthetic pathway, which leads to the production of the terpenoid precursor isopentenyl pyrophosphate (IPP). To produce small amounts of terpenoids, only the final steps of biosynthesis need to be transferred to yeast. In contrast to extraction from plants, the products are of high purity and consistent quality. Nevertheless, the yeast strains require optimization to overcome bottlenecks in biosynthesis and to enable an efficient, cost-effective and sustainable production method.

Huge variety and broad applications of terpenoids

The structure of terpenoids is derived from their basic building block isoprene, a branched hydrocarbon chain with five carbon atoms (C_5). The linkage, modification by functional groups and cyclization of these units leads to the high diversity of these molecules. The terpenoids described so far include low to high molecular weight structures. The industrial use of low molecular weight structures such as mono, di-, sesqui- and triterpenoids ranges from aroma and fragrance compounds to vitamins as well as components of cosmetic products or food products to pharmaceuticals. Two pharmaceutically relevant examples are the diterpenoid paclitaxel (C_{20+27}), known as the anticancer drug Taxol®, and the sesquiterpenoid artemisinin (C_{15}), used as an antimalarial agent. High molecular weight compounds ($C_{>25000}$), such as natural rubber,



Modification of the biosynthetic pathway of plant-based triterpenoids in yeast.

are also widely used for the industrial production of various consumer products.

Of particular interest are cyclic triterpenoids (C_{30}). For numerous plant species, some of these constituents have been described to have very versatile bioactive functions. The potential includes antimicrobial, antioxidant, anticarcinogenic, and antiallergic activities, making them attractive for agricultural and pharmaceutical applications.

Interdisciplinary research project on the production of tailor-made triterpenoids in yeast

In the framework program "National Research Strategy Bioeconomy 2030", a consortium of SMEs and research institutions has joined forces for the project "ASPIRANT" with the aim of the targeted biosynthesis of pharmaceutically relevant triterpenoids in yeasts. The consortium, coordinated by the Fraunhofer IME, combines expertise from the fields of chemistry, biology, process engineering and pharmacy and pursues the entire value chain in a system-oriented manner. The focus lies, among other things, on the production and pharmaceutical evaluation of new substances.

Following a knowledge-based selection of suitable triterpenoids, the enzymes required for their biosynthesis were identified and introduced into yeasts. Plant oxidosqualene cyclases (OSCs) form the desired triterpenoid from 2,3-oxidosqualene, which occurs naturally in yeast. Further enzymatic modification such as oxidation or incorporation of sugar residues change its chemical properties and bioactivity. A yeast strain with an MVA pathway optimized at Fraunhofer IME in Münster is used for this purpose. In this strain, a key regulator is switched off. In its active form, the regulator inhibits the transcription of the MVA synthesis genes and thus prevents the formation of the necessary enzymes. In a further step, the researchers overexpressed genes that are essential for the production of the precursor molecules to increase their quantity. Furthermore, they modified a side branch that also converts 2,3-oxidosqualene in yeast allowing it to be turned on and off in a controlled manner.

The implementation of this yeast platform increased the overall productivity and redirected the metabolic flux toward the desired triterpenoid. The success is reflected in a drastically increased yield. The purified triterpenoids exhibit high purity and consistent quality. In vitro, these substances showed positive effects on inflammatory parameters. The iterative optimization of the modification of competitive metabolic pathways enables production in economically relevant quantities. The yeast platform is being further expanded and is now available for the synthesis of additional terpenoids.

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Molecular markers of neurotoxic mechanisms of action in aquatic model organisms

By Dr. Sebastian Eilebrecht, Julia Pfaff and Hannes Reinwald

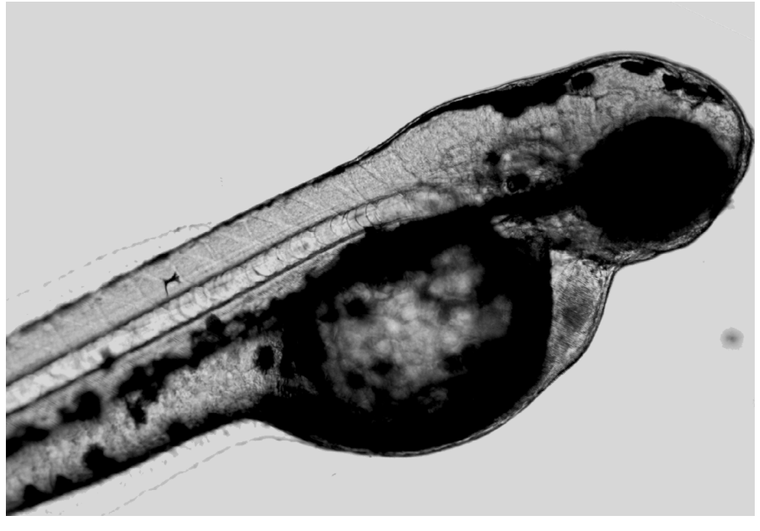
Toxic effects of environmental chemicals on the nervous system can have far-reaching effects on the living environment, with possible lethal consequences. The Fraunhofer Attract group Eco'n'OMICs at the Schmallenberg site of the Fraunhofer IME has investigated the modes-of-action of various neurotoxic insecticides on vertebrates and invertebrate model organisms and identified biomarker candidates that can be used to predict specific neurotoxic modes-of-action.

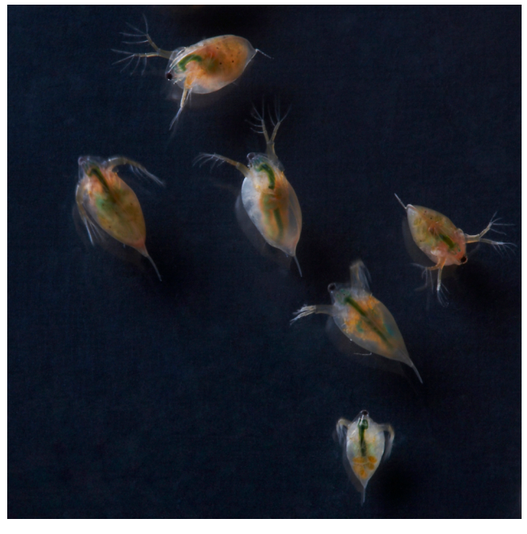
Distinguishing harmful modes-of-action to predict environmental safety of substances

Chemicals that enter the environment unintentionally or through their use can have adverse effects on all trophic levels of the ecosystem. Especially, adverse effects that impact populations and are caused by very low concentrations of substances are of great concern in the mandatory environmental hazard and risk assessment of substances. Particularly potent effects are induced by substances that specifically bind to cellular receptors and inhibit, modulate, or activate them. Hormone-active substances are a prominent example, as they activate signalling cascades in a highly potent manner through their specific interaction at the molecular level, which can impair the reproductive capacity of the organism and thus the population. Such endocrine disruptors, as they are called, which upset the hormonal balance of the organism, are subject to separate regulation precisely because very low concentrations may affect specific life stages and performances with lasting damaging effects on the ecosystem: if a substance is identified as an undesirable endocrine disruptor, no marketing authorization is granted for this substance.

Neurotoxic substances also frequently cause effects in organisms of an ecosystem even at very low concentrations. This high potency often stems - similar to endocrine disruptors - from a specific interaction with cellular receptors of the nervous system. Binding to these receptors can result in a restricted mobility of the organism and therefore impair escape behavior from predators, for instance, or the organism's own search for food. Thus, even very low concentrations of neurotoxic substances can have indirect lethal consequences and endanger populations. For this reason, the EU Commission is striving to extend the generic approach, which applies to endocrine disruptors, for example, to other harmful modes-of-action, such as neurotoxicity, immunotoxicity or respiratory toxicity in the future.

To date, standardized tests for the detection, evaluation and differentiation of these modes-of-action have not yet been established or involve time-consuming and costly studies with sometimes considerable numbers of test animals. In the Fraunhofer Attract group Eco'n'OMICs, we use a combination of ecotoxicological, molecular and systems biological methods to investigate specific environmentally harmful mechanisms of action, such as neurotoxicity, in a range of model organisms. The aim is to identify biomarkers for these modes-of-action, which can then be used as indicators in screening procedures to rapidly and in high throughput distinguish particularly harmful environmental effects from harmless effects.





Right: The large water flea (Daphnia magna) is a model organism for aquatic invertebrates.

Left: The zebrafish embryo (Danio rerio) as a model organism for aquatic vertebrates.

Molecular markers of neurotoxicity in the zebrafish embryo and water flea

Neurotoxic effects can be triggered by a variety of molecular key events like impairment of neurotransmitter production, activation or blockage of nerve cell receptors. Among the particularly well-characterized substances with neurotoxic effects are insecticides targeting nerves and muscles. The classification of the specific effects of these insecticides by the *Insecticide Resistance Action Committee* actually serves to prevent the development of resistance, but also forms a comprehensive overview of mechanisms of action and the associated model substances.

As part of a doctoral and a Master's thesis, we investigated molecular fingerprints of the modes-of-action of a selection of neurotoxic insecticides in the zebrafish embryo (*Danio rerio*) and the large water flea (*Daphnia magna*). The zebrafish embryo is a commonly used aquatic vertebrate model organism in ecotoxicology, which is not subject to animal testing regulation until the time of independent feeding.

Because it also plays a major role in basic research in developmental biology and medicine, its genome is accordingly well-characterized and particularly well-suited for research questions in systems biology. The large water flea is used as a model organism for assessing toxicity in aquatic invertebrates. Its genome is far less studied than that of the zebrafish, which poses challenges for biomarker identification.

By applying high-content molecular biology methods to ecotoxicological guideline tests, we identified biomarkers for a number of neurotoxic mechanisms of action in the zebrafish embryo and the large water flea, including acetylcholinesterase inhibition, GABA-gated chloride channel antagonism, sodium channel modulation, nicotinic acetylcholine receptor modulation, or glutamate-gated chloride channel modulation. In the future, the investigation of these markers in short term test approaches will allow the identification and differentiation of neurotoxic modes-of-action of chemicals in high throughput, contributing to the development of environmentally safe compounds.

Further literature

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Emerging viruses are a threat to managed pollinators and wild insects

By Kateřina Vočadlová

The growing evidence of inter-species pathogen transmission implies that emerging diseases could be one of the potential drivers of the pollinator declines. Species-poor communities of managed bees kept at high density serve as an effective reservoir of pathogens, including viruses, whose spillover can have fatal consequences on wild insect abundance and biodiversity. A dedicated strategy to control the pathogen spillover events is necessary for the protection of both the managed bee colonies and the wild insects.

Global insect declines

The first reports on global insect declines were published at the beginning of the new millennium. However, significant attention has been drawn to this topic when scientists brought forward the actual numbers. According to entomologists, more than 75 percent of insect mass has been lost over the last decades and more than 40 percent of insect species are threatened with extinction. The declines have been attributed to a multitude of factors, such as parasites and pathogens, chemical pesticides, habitat degradation, including agricultural expansion and urbanization, and climate change. Insects play a key role in many environmental processes, e.g., they contribute to nutrient cycling, biological control of weeds and pests and enable the reproduction of entomophilous plants. Pollination significantly increases both the yield and quality of agricultural crops. With the growing human population and the demand for agricultural crops for food consumption, shortage of pollination raises concern. Loss of these services would have a detrimental impact on plant and animal biodiversity and the global food supply.

Emerging viruses associated with the introduction of Varroa destructor

Among pollinators, honey bees are the most intensively studied group of insects. The large honey bee colony losses in the last decades have particularly been associated with the introduction of the ectoparasitic mite *Varroa destructor* and with the application of some groups of pesticides. *Varroa* mites feed on bee's fat body and can significantly impair the physiological condition of the bees. More importantly, *V. destructor* is an effective replication-competent vector of viruses. The *Varroa* mites-mediated transmission has considerably increased the prevalence and virulence of some viruses, such as DWV (Deformed wing virus), ABPV (Acute bee paralysis virus) and KBV (Kashmir bee virus), and viral infections became a serious threat to bee colonies.

The possibilities to control honey bee viruses are limited, since there is no antiviral treatment, and include rather prevention of their spread, for instance by controlling the *Varroa* mite infestation. Nevertheless, some natural substances have a potential as antiviral agents, e.g., thymol, propolis or some fungal extracts.

Antiviral effect against honey bee viruses DWV and LSV has been demonstrated for the fungal extracts of genera *Fomes* and *Ganoderma* (*Basidiomycota*). The addition of the extracts to the diet reduced the levels of both viruses in honey bee body in both the lab and the field conditions.

In our study, we tested the effect of dietary addition of organic extracts of *Talaromyces sp.* (*Ascomycetes*) isolated from bee bread on the experimental infection of honey bees with Chronic bee paralysis virus (CBPV). Even though a steep decline of survival was observed within the 3-4 days post injection in each group infected with the virus, some extracts significantly prolonged the lifespan of infected bees. We suppose the extracts might stimulate the innate immunity response of the bees. Nevertheless, based on the further test, some of the extracts can also inactivate the viral particles. The discovery and characterization of fungal compounds exhibiting antiviral activities has become an emerging field of research during the past decade. The current findings can provide a basis for studying their potential use in beekeeping.

Top: Forager bees of Apis mellifera *at the hive entrance.*

Bottom: Preparation of the CBPV inoculum from an infected bee pupa.

The managed bee colonies as a reservoir of pathogens for wild pollinators

The protection of honey bees as producers of valuable bee products and effective pollinators of about 96 percent of animal pollinated plants remains a topic of high interest. However, managed honey bees can supplement, rather than substitute, the wild pollinator services of both agricultural crops and wild plants. An increasing number of publications has pointed out that commercial beekeeping poses a threat to wild pollinators. The international trade of honey bees and their products is a major factor contributing to the introduction of invasive parasites and pathogens, including new viruses. The detection and diagnosis of viral infections are difficult, due to common covert infections and unknown symptoms and pathogenicity of many viruses. Moreover, the managed bee colonies are usually kept on site at high densities, therefore, can be a hot spot for pathogen reproduction, in particular the underdiagnosed viral infectious agents that can be effectively transferred to other pollinators within the shared floral resources. With the addition of other environmental stressors, such as pesticides, even less virulent viruses might have a fatal impact on insect populations. To protect both the apiculture and the wild insects, a dedicated strategy is necessary to control the pathogen incidence in the managed bee colonies and the bee material for the international trade.

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Insect Farming 4.0 – Insect protein as competitive and sustainable animal feed

By Marius Wenning

Feed production is destroying ecosystems worldwide. Insects represent a high-quality alternative to classic feed. By recycling industrial side streams, insects enable a circular economy and mitigate an emerging protein gap. Fraunhofer IME develops automated production systems to scale competitive production volumes.

Soy demands for livestock farming are a major driver for the ongoing deforestation of the Amazon rainforest. Similarly, fishmeal fed in aquaculture contributes to overfishing of the oceans. With the world's population on the rise and an increasing global demand for meat and fish, new feeds are required to produce more proteins while reducing its environmental impact.

Insects as feed

Insects are highly resource efficient. Compared to mammals, they require a fraction of water and land. As they can even thrive on food waste, insects do not require additional feed. For example, the larvae of the black soldier fly could be used to upcycle the EU's 88 million metric tons of food waste into high-quality animal protein. This resilient insect could even recover nutrients from manure and sewage sludge.

The protein meal extracted from black soldier fly larvae has a balanced amino acid profile, making it an attractive substitute, particularly for fishmeal. Moreover, the replacement of fishmeal by insect proteins reduces the risk of marine pathogen contamination in aquaculture.

Profitability crucial for market penetration

Worldwide, about half of the consumed fish is produced in aquaculture. Feeds may make up about 50 percent of the aquaculture costs and are therefore crucial for its profitability. Consequently, the price of insects must compete with a fishmeal price of about 1,500 euros per ton.

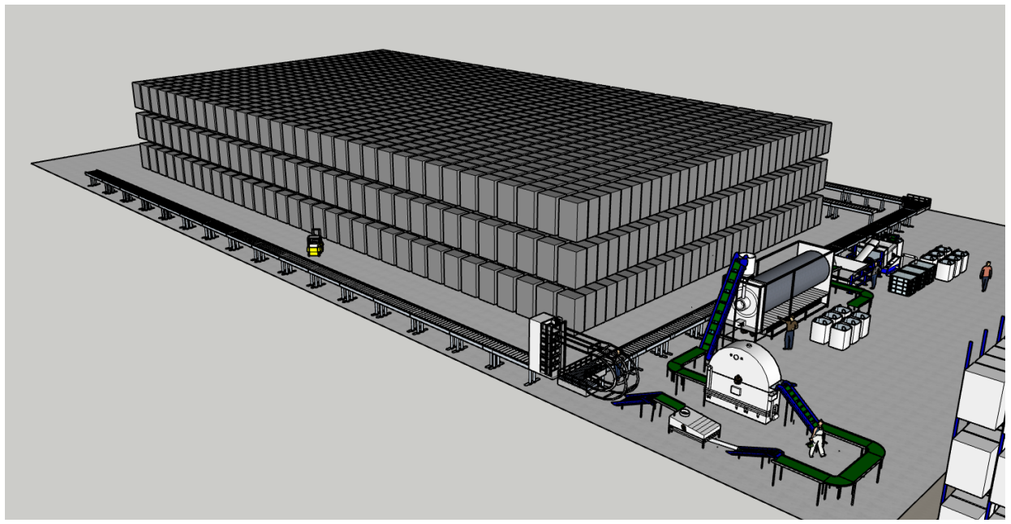
Small-scale insect production is governed by the feed substrate and labor costs. The feed substrate costs can be minimized by using side streams. According to the law of mass production, increases in production volume can lower the specific production costs. However, economies of scale in large-scale insect production go along with highly priced automated production technology. The required capital expenditures have made investors shy away so far. In addition, organic side streams such as municipal waste occurs in a distributed manner. Their transport to a few centralized factories increases costs and is not sustainable.

Production technology to reduce costs

At the Branch for Bioresources of Fraunhofer IME, the development of new production technology for insect farming largely aims at medium-sized enterprises. These include farms, companies in the food industry and regional waste management companies, which typically require low-investment facilities with low personnel expenses in order to be able to utilize side streams locally. To engage successfully in the novel insect farming sector, expert knowledge on insect biology and farming must be available in a simplified and cost-effective manner.

To reduce complexity, insect production can be divided into the reproduction and the fattening of larvae. Reproduction can be outsourced so that the facility focuses on the utilization of side streams in the fattening process. A production control system regulates environmental parameters such as temperature, humidity and oxygen to ensure ideal conditions. Observation of larval weight gain using computer vision algorithms enables fully automated monitoring. Merging sensor data in cloud software and its evaluation employing machine learning guarantees optimized process control for each substrate and situation dependent instructions. A digital twin – a virtual model of the insect life cycle – can predict the protein and fat content, as well as the amino acid profile. Thereby controlling the composition of the insect larvae, the feed can be utilized to support animal growth and health. Thus, the antibiotics application is reduced, in addition to conserving bioresources.

Top: The production of fishmeal as aquaculture feed contributes to overfishing of the oceans.



Bottom: Production system for larvae fattening with a daily capacity of 60 tons of side streams and an investment of 5.8 million euros.

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Biotechnological crop protection using RNA active ingredients

By Dr. Christoph Hellmann

Ribonucleic acid (RNA) as an essential building block of all life represents bioactive molecules with enormous potential to design sustainable and highly species-dependent plant protectants. Such RNA-based plant protection approaches rely on the natural process of RNA interference (RNAi), wherein double-stranded RNA (dsRNA) molecules as the highly selective and active substances lead to a knockdown of target genes to trigger e.g. lethal effects in target organisms. As a consequence, undesirable side effects to non-target species and in particular to numerous beneficial organisms such as bees, can be minimized or even completely avoided.

Formulation chemistry as key for RNA-based plant protection products

Annually, pest insects cause billions of dollars agricultural damage. The agricultural processes of the future need to adapt to the associated challenges of combining security of food supply for the growing global population and preserving the biodiversity of our global ecosystem. For next generations it is crucial to develop sustainable, tailored crop protection systems that specifically target pest insects and protect non-species organisms. One key milestone for the success of such RNA-based plant protecting technology is an optimal chemical formulation of the active RNA molecules. A well-designed formulation will protect the active dsRNA against undesirable degradation on plants and in the digestive tract of the target pest during feeding. At the target location within the organism, the formulation must enable the cellular uptake and release of the active ingredient. Current development approaches uses various micro- and nanoparticles in colloidal dispersions. The formation process of such particulates is controlled by ionic interactions of cationically charged substances and anionically charged RNA. Cationic, amphiphilic substances such as fatty amines or phosphocholines provide lipophilic and hydrophilic characteristics within its molecular structure. By self-assembly such molecules form complex structures consisting a lipid bilayer in water, i.e. liposomes, which are able to act as carriers for various pharmaceuticals. Such liposomes pharmaceuticals were introduced in the 1990s and gain currently much attention due to excellent structure-property-correlations as carriers for mRNA vaccines.

Our research focus on the development of RNA plant protection formulations using liposome building blocks. We are validating the capability and efficacy of innovative formulation technology for regulating various pest insects in laboratory, greenhouse and field trial.

Aphids in sugar beet cultivation

Agricultural damage caused by insects often results not only from direct feeding, but can also result from insect-transmitted pathogens. In this context, aphids play a distinctive role, as they transmit up to 25% of all known plant viruses to numerous plants and crops during phloem feeding.

The Green peach aphid (*Myzus persicae*) plays a major economic role in German sugar beet cultivation because of a transmitted virus that leads to yellowing of the sugar beet plant and thus a strong reduction in fruiting body formation. Plant protection products based on neonicotinoid currently provide the only effective protection against these insect pests or their pathogens. If these pests are not treated, the annual damage in German sugar beet cultivation can exceed several hundred million euros. The peach aphid also attacks numerous other crops and is therefore one of the most devastating pest insect worldwide.

The "ViVe_Beet" project is dedicated to the research and development of an RNA-based pest control against aphids and thus to reduce damage associated with plant viruses in sugar beet cultivation. The implementation of this project, which is funded by the German Federal Ministry of Food and Agriculture (BMEL), requires the identification of suitable RNA sequences and the appropriate formulation for final field-testing and application. Various approaches will be investigated throughout the end of 2024 in partnership with Julius Kühn Institute (JKI) and the Institute for Sugar Beet Research (IfZ).

Top left: Scanning electron micrograph of a liposome-based RNA crop protection formulation (dried on silicon surface).

Green peach aphid feeding on leaf surface.

Top right: Schematic representation of a liposome particle enclosing dsRNA by a double lipid layer

Comparison of conventional insecticides and RNA-based crop protection technology

The global use of conventional crop protection products has increased significantly in recent years. The "Pesticide Atlas 2022" reveals that pesticide residues can be nowadays found in all areas of daily life, especially in soil, water and ultimately food. The intensive use and bioaccumulation of these compounds is probably directly related to the globally observed decline in insect diversity, and numerous insect feeding birds.

In natural life cycles, RNA as a component of all plants and animals, is ingested and utilized by all living organisms. In the environment, unprotected RNA biodegrades within a few hours or days. Accumulation of RNA molecules used as active ingredients in RNAi-based crop protection is therefore highly unlikely. Our research activities in this area explicitly aims for developing species-dependent plant protection agents and to the same extent, demonstrating the biosafety to non-target organisms. Our efforts include biological stability studies of the developed crop protection formulations in order to demonstrate the rate of biodegradation and biocompatibility of all ingredients.

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Investigation of the biomagnification of chemicals in a lake food web

By Verna Kosfeld and Dr. Heinz Rüdel

The aquatic bioaccumulation potential of chemicals is a crucial property for their regulatory assessment. Currently, parameters are mainly predicted by their physicochemical properties or determined in laboratory tests. A relatively new approach is the determination of trophic magnification factors (TMFs), which integrate enrichment processes in a food web. Fraunhofer IME scientists conducted the “Food web on ice” study at Lake Templin near Potsdam, which was the first TMF investigation in a German inland water body.

Size measurement of a perch.

Towards a realistic assessment of the biomagnification of chemicals in food webs

Various parameters such as bioconcentration factors, bioaccumulation factors and biomagnification factors are determined experimentally to characterize the bioaccumulation potential of chemicals for the assessment under different regulations. In recent years, the use of trophic magnification factors (TMFs) has been discussed as an alternative for the assessment of chemicals in use. TMFs describe the average trophic magnification of a chemical in the analyzed food web under realistic environmental conditions. So far TMFs, which were determined in a variety of different aquatic ecosystems worldwide, are mainly available for legacy chemicals. However, TMFs already have been derived for a few current-use compounds only, although they bear some potential. They are not only interesting for questions related to the chemicals’ assessment, - for example, assessments with regard to substances that are potentially persistent, bioaccumulative and toxic (PBT) or very persistent as well as very bioaccumulative (vPvB). They may also be applied for the evaluation of data from the biota monitoring implemented under the European Water Framework Directive (WFD).

To this end, the German Environment Agency initiated a field study to collect, freeze and store food web samples at ultra-low temperature to form a "food web on ice". The collected food web samples were to be used for the investigation of bioaccumulation and biomagnification of chemicals in the covered freshwater ecosystem. Since there is also a lack of sufficient practical experience in protocol standardization and the use of derived TMFs for regulatory substance evaluations, these aspects were to be addressed appropriately. The project was contracted to Fraunhofer IME and ran from 2017 to 2021.

The "Food web on ice" study at Lake Templin

After assessing several water bodies, we decided to conduct the "Food web on ice" study at Lake Templin near Potsdam. First, we gathered as much information as possible on the lake, its ecosystem and potential chemical burdens. The sampling of biota samples was performed by a local partner. As intended, our sampling campaign yielded large amounts of 15 types of samples covering plankton, mussel and seven fish species. We characterized the food web items for parameters such as lipid and protein content as well as carbon and nitrogen stable isotope ratio. The sampled biota comprise three trophic levels. Wherever possible, we used methods already applied for the German Environmental Specimen Bank (ESB), an environmental monitoring program involving long-term storage of homogenized biota samples at ultra-low temperature. The collected large-scale food web samples from Lake Templin are ready-to-use for a broad variety of analyses.

The food web magnification of appropriate benchmark chemicals was investigated. The procedure followed existing guidance and allowed to derive reliable TMFs. We analyzed the food web samples for polychlorinated biphenyls (PCBs), polybrominated diphenylethers (PBDEs), mercury and methylmercury. The evaluation of the trophic transfer was possible for 35 substances and we could show that 32 of the compounds analyzed had TMFs significantly above 1 expressing their bioaccumulation along the food chain. In the case of PCBs, for example, TMFs ranging from 1.7 to 2.5 were determined for the Lake Templin food web. In the remaining three cases, correlations were not statistically significant. Comparisons to TMFs from literature determined in other freshwater ecosystems confirmed that those determined in the Lake Templin food web are plausible.

The potential of the "Food web on ice" sample set

In the next project phase, we used the samples for characterizing the trophic transfer of a set of less well-characterized chemicals such as cyclic volatile methyl siloxanes and per- and polyfluoroalkyl substances (PFAS). While for some of these chemicals trophic magnification could be confirmed, in one case also a significant biodilution was observed with lower concentrations in fish of higher trophic levels. This finding is probable due to the higher metabolic capacity of these species.

Overall, the project data allow an assessment of the tested TMF study approach. Since not only lipophilic legacy chemicals but also substances with non-lipophilic accumulation properties were included in the list of analyzed compounds, we conclude that the ‘Food web on ice’ provides samples that could be used to characterize the trophic magnification potential of substances with unknown bioaccumulation properties in the future. Moreover, results could be compiled to form a database of TMF data for a multitude of chemicals, which can be evaluated to predict biomagnification of additional compounds.

The "Food web on ice" project was introduced comprehensively to the scientific community by researchers from Fraunhofer IME, the German Environment Agency and project partners during a two-day online workshop in March 2021. An invited keynote presentation on TMF research provided the basis for the scientific exchange. Examples from other studies on trophic magnification presented by scientists from Italy and France provided a broader picture. About 75 scientists from regulatory agencies, research institutes and industry participated in the workshop. Participants came from 12 countries including Canada and the USA.

Aliquots of all "Food web on ice" samples remain available for future analyses. They are ready-to-use and allow the on-demand analysis of numerous additional parameters. Aliquots of the food web samples have been provided to research partners to investigate the possible trophic enrichment of further chemicals (e.g., chlorinated paraffins) and to apply new analytical methods (suspect and non-target analysis of polar compounds).

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Reduction of pesticide concentrations in surface water caused by surface run-off

By Dr. Michael Klein

Surface run-off from agricultural fields is a major input pathway for pesticides into surface waters. In order to reduce this pollution several mitigation measures are available. In this project, we first evaluated the effectiveness of these measures followed by analysing whether their reductions are also quantifiable. Two options were recommended as principally suitable in the risk assessment: vegetative filter strips and micro-dams

Heavy rainfall often leads to a pollution of surface water with pesticides in the neighbourhood

In order to reduce pesticide concentrations in German surface water bodies to an acceptable range, registration for these substances is often only possible if additional risk mitigation is included. Especially after heavy rainfall events, a high load of pesticides is observed. Consequently, the extent to which the entry to surface water is reduced by the mitigation measure is a key factor in environmental risk assessment. Misestimation or incorrect use of the mitigation measure can cause unwanted negative effects on the environment might occur when the product is applied.

The best measures were evaluated by various experts

During literature research at the beginning of the project, 42 different reduction measures were found. These mitigation measures were subsequently prioritized and narrowed down to a list of three groups of measures considering their effectiveness and acceptability:

- Several variations of vegetated filter strips (in the field and at the edge of field),
- Soil conservation measures in the field (no-till, strip-till, reduced tillage, contour-cropping, contour tillage, deep rooting cover-crops, cover crops, mulch-tillage, strip-cropping, intercropping)
- Micro-dams

The creation of micro-dams for corn cultivation is exemplarily shown in the photo. For the practical evaluation of the measures, five recognized experts with a scientific and agricultural background and different perspectives on the topic (pesticide exposure assessment, erosion protection, run-off reduction, conservation tillage, water protection, plant protection) were consulted.

Vegetated filter strips and micro-dams were found to be particularly suitable mitigation options

The mitigation effectiveness, regarding pesticide exposure of the selected measures, was then analysed based on heterogeneous data from reviews, compilations of test data and individual studies. The evaluation showed that there is an evident correlation. However, the applicability of this type of analysis is limited because quantitative results are hardly achievable without process-oriented computer simulation. There is an evident correlation, however, the applicability of this type of analysis is limited because quantitative results are hardly achievable without process-oriented computer simulation.

Nevertheless, it was obvious that the traditional vegetated filter strips are very effective. Yet, it was not possible to base the measured reduction factors only based on statistical techniques. This is caused by the complexity and non-linearity of the involved processes. Consequently, unique reduction factors for surface run-off, soil and pesticide loss don't make sense. Instead, mechanistic modelling should be conducted, which calculates the reduction depending on field characteristics, rainfall events and the quality of the filter strip with infiltration and sedimentation as key processes.

Based on the available studies, it could be deduced that the installation of micro-dams—a second, more recently developed measure—could also be very effective. However, their reduction factors very much depend on the soil's moisture state at the beginning of the rain event. Therefore, similar to filter strips, a standard reduction factor in the exposure assessment does not guarantee sufficient reduction. Instead, the reduction factors should be calculated based on computer models considering different scenarios. Furthermore, it is important that the micro-dams are installed correctly in order to achieve the desired effect. The correct installation should be randomly checked during on-site inspections because it is not possible to control the micro-dams by remote sensing.

Finally, the evaluation of the remaining measures in the field (for example mulch-tillage) showed that it is very difficult to quantify their reduction. Yet, in general, a synergetic effect can be assumed if measures in the field are combined with a vegetated filter strip. In this respect, it is recommended to always use combinations of in-field measures with edge of field filter strips. Having said this, the effectiveness of combinations should be checked based on a mechanistic computer simulation instead using constant reduction factors for individual measures in the risk assessment.

Creating micro-dams for corn cultivation.

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Honored doctoral thesis

Dr. Tim Lüddecke
Biochemist and zoologist at
Fraunhofer IME in Giessen

Spiders are the most successful group of venomous animals. Their toxins promise to cure some dreadful diseases, but still we know little about them."

Unknown poisoners: Exploring spider venom for novel biomolecules

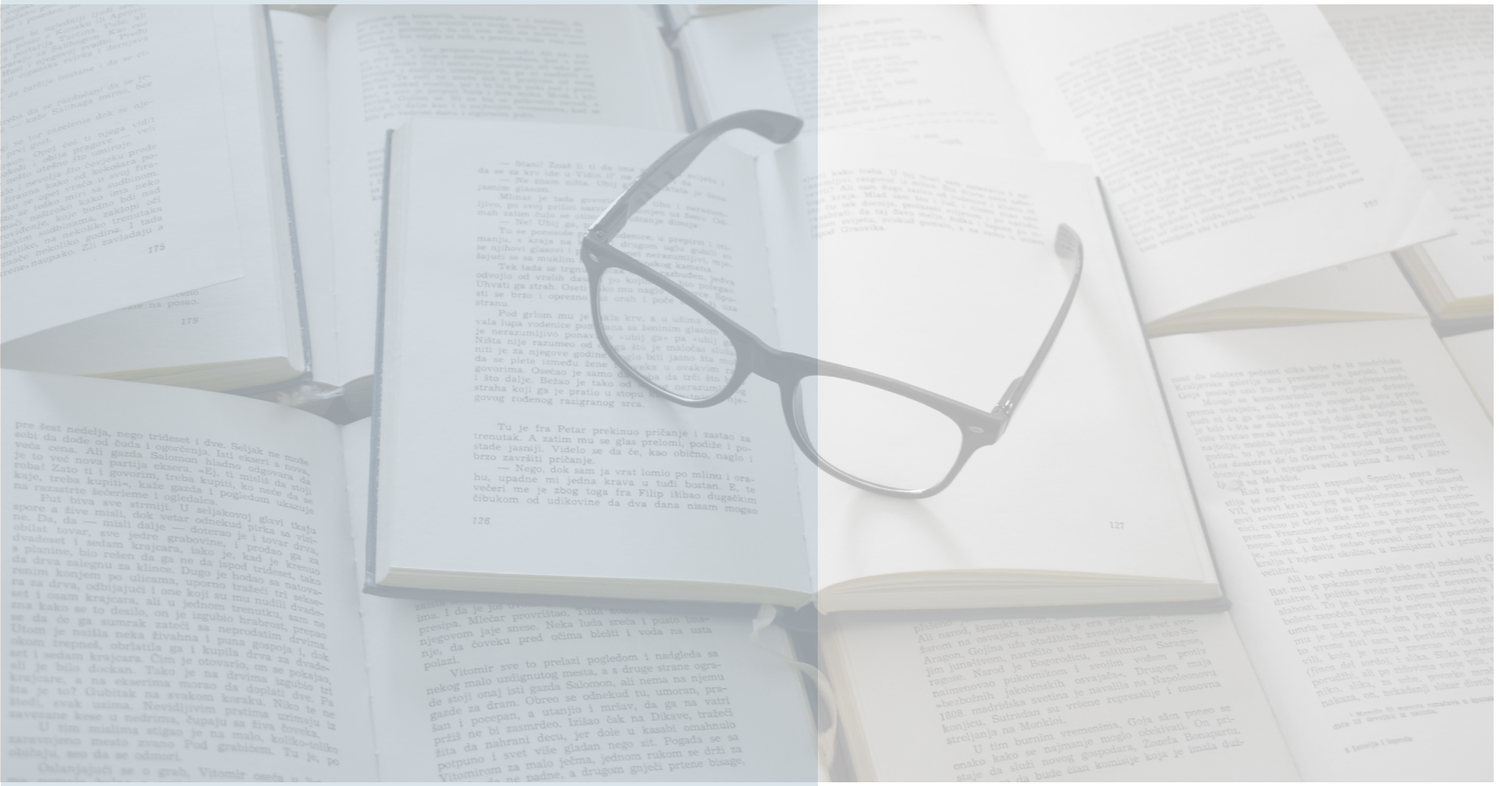
Spiders evoke fear in many people. However, not in Dr. Tim Lüddecke from the department of bio-resources of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME in Giessen. He devoted his doctoral thesis to spiders and their weapon arsenal.

Spiders use venom to overpower their prey. However, the evolutionary optimized toxins that constitute spider venom also carry great potential for humanity. Because they target the central nervous system, spider venom toxins represent powerful key components for the development of future drugs against neuronal diseases. "Spiders are the most successful group of venomous animals. Their toxins promise to cure some dreadful diseases, but still we know little about them", says Lüddecke. "Previously, the selection of species for venom studies was performed rather uncoordinated. Scientists focused almost exclusively on the few larger and dangerous species and thereby neglected the vast majority of spider species". In his doctoral research, Lüddecke developed a strategy that optimizes the species selection for venom biodiscovery. "Rather than relying on size or toxicity as a basis for decision-making, I derived an approach that uses evolution as the main criterion. I focus on lineages within the spider phylogeny that remain venom-wise untouched so far".
By applying his strategy to the native arachnofauna, he encountered the wasp spider and investigated its venom by most modern methods of systems biology. Thereby he recovered that also from native species new insights can be gained. The wasp spider venom yielded several new toxin classes, previously unknown to science. "The venom of wasp spiders is also special because it taught us, that not all spider venoms follow the commonly made assumptions on their general composition. Usually, these venoms are highly complex and dominated by smaller peptides. In contrast, the venom from wasp spiders is relatively simple and contains more high molecular components. Throughout its evolution, this species developed a hunting strategy that favors the silk apparatus over the venom system, and we think, that this transition led to this remarkable venom profile".

This work has been conducted as a part of the LOEWE-Centre for Translational Biodiversity genomics and supervised by Prof. Dr. Andreas Vilcinskas. For his thesis, Dr. Lüddecke received the best possible grade »summa cum laude« and was awarded the dissertation prize for the best doctoral thesis of the Justus Liebig University Giessen.

BR

Lüddecke, Tim
How the integration of phylogenetics and venomics resolves persistent challenges in evolutionary systemics and toxinology (2021)
Justus Liebig University Giessen



Selected publications

Bioaccumulation assessment of nanomaterials using freshwater invertebrate species

Please do not branch – straightness pays off

Insect-based bioconversion mediated by adaptations of the gut microbiome

Effects of synthetic steroid hormones on the biological lifetime performance of fish

High-throughput platform for natural product discovery

Biotechnological production of fragrant fatty aldehydes

"It has been shown that when exposed to manufactured nanomaterials bivalves can transfer these particles to other benthic species."

Dr. Sebastian Kühr wrote his dissertation at Fraunhofer IME in Schmallenberg in the working group of Prof. Dr. Christian Schlechtriem. He is currently doing research as a postdoc at NIVA in Oslo, Norway. His dissertation was honored with the "Research Prize of the District of Olpe 2022" for the best doctoral thesis.

Freshwater bivalves (Corbicula fluminea).

Bioaccumulation assessment of nanomaterials using freshwater invertebrate species

The high production volume of engineered nanomaterials (ENMs) may lead to high pressure on the environment, making a scientific assessment of ENMs, which bioaccumulate in organisms and biomagnify in the food web, necessary. Within the regulation of chemicals in several jurisdictions, such as the European regulation REACH, the bioconcentration factor is the standard endpoint and ismostly determined by flow-through fish tests. Several risk assessment regulations allow the usage of data gained during tests using invertebrates and may allow a waiver of further tests using vertebrates. As a first step of our studies, the existing literature related to the testing of nanomaterial bioaccumulation with freshwater invertebrates was screened and reviewed to find suitable test species with regard to their ecology and physiology, as well as laboratory test systems allowing to investigate the bioavailability and bioaccumulation of nanomaterials with the respective species. It was concluded that amphipods and bivalves show clear advantages to be used as test organisms.

Several laboratory studies with the freshwater amphipod *Hyalella azteca* and the freshwater bivalve *Corbicula fluminea* have then been carried out with different nanomaterials (e.g. silver and gold nanoparticles) showing the bioavailability and bioaccumulation of these test items. In a further laboratory approach, both test systems were then interconnected to investigate whether the ingestion of bivalve droppings by benthic invertebrates may lead to the transfer of nanomaterials in the aquatic food chain. We exposed bivalves (*Corbicula* sp.) to silver (Ag) and gold (Au) nanoparticles. The metal content of the bivalves' feces was analysed by inductively coupled plasma mass spectrometry (ICP-MS) and showed a high accumulation of the exposed ENMs in the feces or pseudofeces. The examination of fecal matter, using transmission electron microscopy confirmed the nanoparticulate character of the metals in it. Juvenile amphipods (*H. azteca*) were exposed to feces enriched with Ag and Au ENMs for over 21 days. The transfer of both metals (Ag and Au) from the fecal matter to the amphipods was confirmed after total metal measurements. In view of the environment, the high concentrations of ENMs in the bivalve fecal matter raises concerns about the potential accumulation and transfer of the materials and associated ecotoxicological effects in invertebrates such as benthic amphipods.

AE

Kuehr, S., Diehle, N., Kaegi, R., Schlechtriem, C.
Ingestion of bivalve droppings by benthic invertebrates may lead to the transfer of nanomaterials in the aquatic food chain (2021) Environmental Sciences Europe 33 (9). DOI: 10.1186/s12302-021-00473-3

Kuehr, S., Kosfeld, V., Schlechtriem, C.
Bioaccumulation assessment of nanomaterials using freshwater invertebrate species. Environmental Sciences Europe, 33 (9). DOI: 10.1186/s12302-020-00442-2

"The new method can provide both, qualitative as well as semi-quantitative results regarding the level of COVID-19-specific antibodies in the blood within 20 minutes."

Jan Pietschmann und Nadja Voepel, research associates at Fraunhofer IME in Aachen.

Blood sera enriched with COVID-19 antibodies in an immunofiltration column.

Detection of COVID-19 antibodies using magnetic immunoassays

Since its first appearance in the Chinese city of Wuhan in December 2019, the coronavirus (SARS-CoV-2) has become the cause of an ongoing global pandemic, with many fatalities. Particularly at the onset of the pandemic, little was known about the virus and the severity of the disease varied among patients of different age and risk groups, from very mild to even asymptomatic. The primary measure to contain the COVID-19 pandemic is the development of vaccines that stimulate the immune system to produce protective antibodies. In this context, the availability of methods for a qualitative as well as quantitative analysis of virus-specific antibody levels is of great importance.

Up until now, only complex laboratory tests can provide information about the quality and strength of antibody responses in the blood of patients. To enable decentralized tests at larger scale, a new point-of-care (PoC) assay based on magnetic immunodetection (MID) was developed at Fraunhofer IME. Here, antibodies from patient blood serum are enriched within an immunofiltration column by binding to a coronavirus surface molecule and then labeled with magnetic nanoparticles. Afterwards, these particles can be quantified by means of a special reading device

The new method can provide both, qualitative as well as semi-quantitative results regarding the level of COVID-19-specific antibodies in the blood within 20 minutes. In a study using the blood of 170 patients, a sensitivity of 97 percent and a specificity of 92 percent could be demonstrated for the method.

MB

Pietschmann, J., **Voepel, N.**, Voß, L., Rasche, S., Schubert, M., Kleines, M., Krause, H.-J., Shaw, T.M., Spiegel, H., Schroeper, F. Development of fast and portable frequency magnetic mixing-based serological SARS-CoV-2-specific antibody detection assay (2021) Frontiers in Micobiology. DOI: 10.3389/fmicb.2021.643275

"The precise regulation of plant growth allows us to optimize useful plants with regard to their economical cultivation and harvest."

Dr. Lena Grundmann, research associate at Fraunhofer IME in Münster.

Growth of axillary shoot in the control plant.

Absence of growth in the modified plant.

Please do not branch – straightness pays off

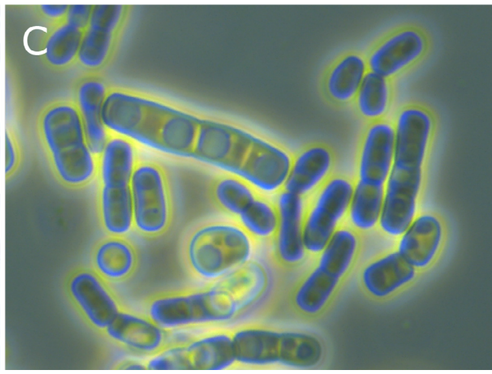
In tobacco field cultivation, so-called topping – the removal of the shoot apical meristem – is common agronomical practice. However, this stimulates the undesirable growth of new shoots (suckers) from the axillary buds at the leaf base. When such suckers grow, valuable plant resources are reallocated to axillary buds thereby reducing yield and quality of the main leaves. Therefore, after topping, axillary buds are chemically treated to inhibit their outgrowth. This chemical control is done by hand, making it time-consuming and expensive. The harmful chemicals may persist after leaf processing and can reduce product quality. Plants with inhibited or delayed growth of axillary buds would therefore significantly improve cultivation, harvesting and product quality.

In our work, we identified a regulatory axillary-specific element using modern molecular biological methods, and the targeted modification increased its activity after topping. For proof-of-concept, we expressed a growth inhibitory gene - a bacterial RNAse - in a tissue-specific manner in the axillary meristems of tobacco plants.

This significantly delayed the formation of axillary shoots before as well as their outgrowth after topping. In this way, the number of axillary shoots after topping could be significantly reduced not only in the greenhouse but also under natural conditions in the field. Our results add an important element to the body of knowledge on the control of axillary branching in plants and will contribute in the future to reduce the labor input as well as the use of chemicals for the removal of axillary shoots in field cultivation.

MB

Grundmann, L., Känel, A., Muth, J., Beinecke, F., Jekat, M., Shen, Y., Kudithipudi, C., Xu, D., Yang, J., Warek, U., Strickland, J., Prüfer, D., Noll, G.A.
Tissue-specific expression of barnase in tobacco delays axillary shoot development after topping (2021), Plant Biotechnology Journal.DOI: 10.1111/pbi.13759



Photographs of the black soldier fly (adult fly (A) and larvae (B)) and microorganisms from the larvae's intestines (C).

"Cottonseed press cake as potential diet for industrially farmed black soldier fly larvae triggers adaptations of their bacterial and fungal gut microbiome."

Dr. Dorothee Tegtmeier, research associate at the Fraunhofer IME in Giessen.

Insect-based bioconversion mediated by adaptations of the gut microbiome

Insects play an increasingly important role as an alternative source of protein for the sustainable production of food and feed. However, the economic competitiveness of farmed insects depends on the availability of large quantities of inexpensive insect feed. Cottonseed press cake (CPC) is a side-stream of cotton production that is rich in proteins and lipids but unsuitable as feed for several farmed animals, due to the presence of the anti-nutritional and insecticidal substance gossypol.

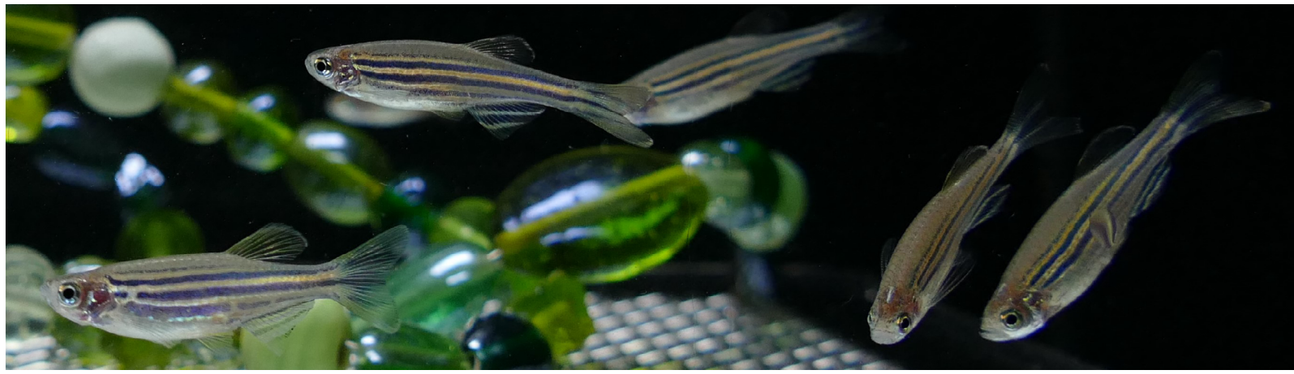
Our results showed that the larvae of the black soldier fly (*Hermetia illucens*) metabolize CPC well and that they can be reared on this side-stream at high yields over several generations. The shortened development cycle compared to control larvae that received chicken feed is particularly advantageous for industrial insect farming.

Microorganisms in the digestive tract of the larvae play a key role in the bioconversion of organic waste products and side streams into valuable insect protein. This gut microbiome is very diverse and adaptable and helps with the digestion and detoxification of various substances. We analyzed the microbiome of larvae from both diet groups (CPC and chicken feed) using amplicon sequencing to identify bacteria and fungi.

In the guts of the CPC diet group, *Actinomycetaceae* and *Aspergillaceae* were significantly enriched, which can help in breaking down compounds such as gossypol. Furthermore, we found potentially probiotic yeasts and *Enterobacteriaceae*, which belong to the core microbiome, in high relative abundance. Due to the rapid development of the larvae and the adaptation of the gut microbiome, CPC may be suitable as an inexpensive and sustainable feed for the industrial rearing of black soldier flies.

BR

Tegtmeier, D., Hurka, S., Klüber, P., Brinkrolf, K., Heise, P., Vilcinskas, A.
Cottonseed press cake as a potential diet for industrially farmed black soldier fly larvae triggers adaptations of their bacterial and fungal gut microbiota (2021) Frontiers in Micobiology. DOI: 10.3389/fmicb.2021.634503



Study of the reproductive performance of zebrafish using spawning trays.

"The investigation of the hormone-like effect of pharmaceuticals in the regulatory context is an upcoming future challenge of ecotoxicology."

Dr. Matthias Teigeler, head of the Ecotoxicology division at the Fraunhofer IME in Schmallenberg.

Effects of synthetic steroid hormones on the biological lifetime performance of fish

The amount of human pharmaceuticals that enter the aquatic environment via municipal and hospital wastewater is steadily increasing. Advances in medical research have led to the production of active ingredients with increased stability, specificity and efficacy that can cause undesirable side effects in aquatic organisms. In addition, technically advanced analytical methods enable the detection of drugs in the various environmental media in very low concentrations, which in total increases the number of substances to be evaluated by authority regulation.

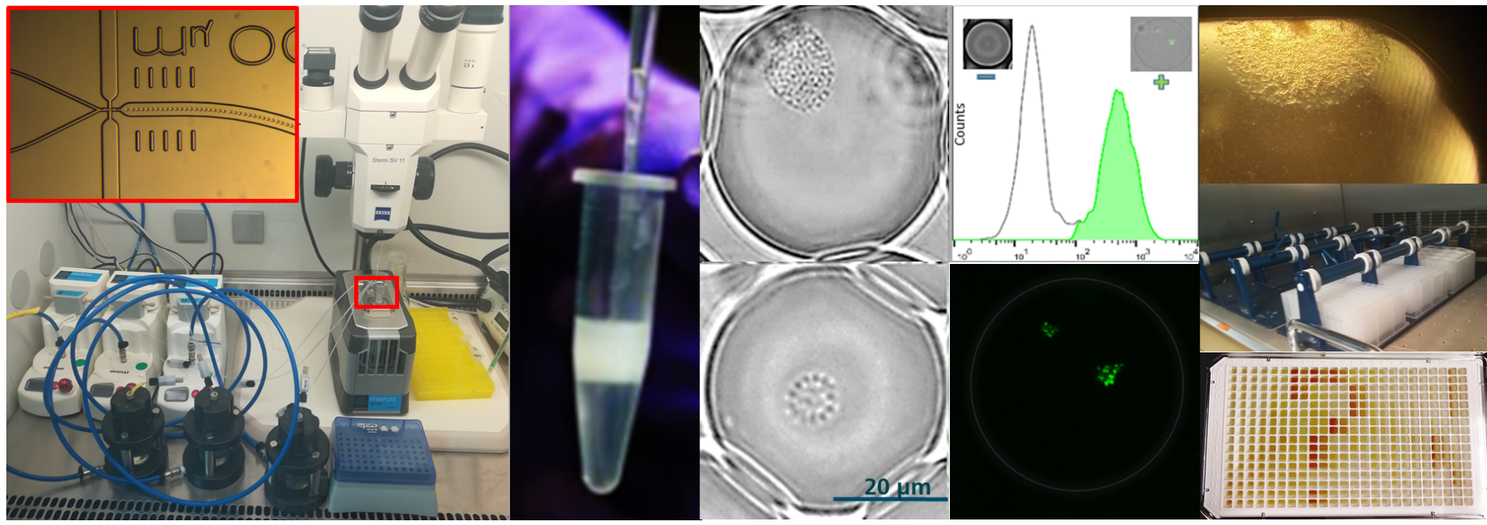
Levonorgestrel is a synthetic progestin commonly used in contraceptive medicines. Representatives of this class of substances are suspected of negatively affecting sexual maturation and the reproductive capacity of fish. In this case, life cycle tests are carried out to record the corresponding lifetime performance under exposed conditions.

The challenge in our study was to keep the very low concentrations of levonorgestrel of 0.05 to 5.0 ng/L in the water constant and to verify them analytically. In addition to the recording of lifetime performance and a biomarker analysis, the study was enriched by the histopathological examination conducted by the Fraunhofer ITEM. The results finally met the high expectations.

First indications that the substance works in this low concentration range were confirmed: The exposed fish groups showed a shift of the sex ratios towards the males. In the groups that were still capable of reproduction, the fertilization capacity of the male animals was significantly reduced. The blood concentration of the specifically male sex hormone 11-keto testosterone has been lowered. The test design allows the reliable recording of the characteristic assessment endpoints and complements the tailored environmental risk assessment of medicinal products for human use.

AE

Teigeler, M., Schaudien, D., Böhmer, W., Länge, R., Schäfers, C. Effects of the gestagen levonorgestrel in a life cycle test with zebrafish (***Danio rerio)*** (2021) Environmental Toxicology and Chemistry, 1-12. DOI: 10.1002/etc.5008



Microfluidics/FACS & extract screening platform to bioprospect new natural products from environmental bacteria.

"By using combined Microfluidics/FACS high-throughput methods & analytical chemistry we deduce the »microbial dark matter« for natural product discovery."

Markus Oberpaul, research associate at the Fraunhofer IME in Giessen.

High-throughput platform for natural product discovery

Microorganisms represent a valuable source for the discovery of novel antibiotics. However, many talented natural product producers are still covered – the organisms have not yet been cultivated and their great biosynthetic potential remains untapped.

The low-hanging fruits have already been harvested, thus natural product research is increasingly becoming a numbers game. One solution is the miniaturization of processes, which enables an enormous high throughput by massive parallelization on a micrometer scale. Advanced droplet microfluidic technology makes it possible to flexibly adapt both, biotic and abiotic factors. This enables adaptation to the specific environmental and metabolic needs of the microorganisms.

We used this technology to encapsulate ~500 000 single cells per hour in agarose-solidified droplets (d = 40 µM) in all different conditions. Colony growth in droplets was detected by flow cytometry, then sorted and arrayed into microtiter plates. Outgrown cultures were subsequently scaled on a milliliter scale to obtain 1071 axenic cultures in total (therein 57 genera, 5 phyla).

The entire obtained microbial diversity was used for an arrayed bioprospecting campaign in our new natural product discovery platform. Interesting candidates - in terms of chemical innovations - were prioritized based on a comparison with our reference database using a combination of automated evaluation and UHPLC-QTOF-MS/MS-guided fractionation. This enabled us to quickly identify new natural product derivatives with bioactivities against *Mycobacterium tuberculosis* and *Zymoseptoria tritici*.

Our microfluidics/FACS platform facilitates the rapid isolation, cultivation and analysis of axenic cultures, as well as quick identification of novel biosynthesized active natural products.

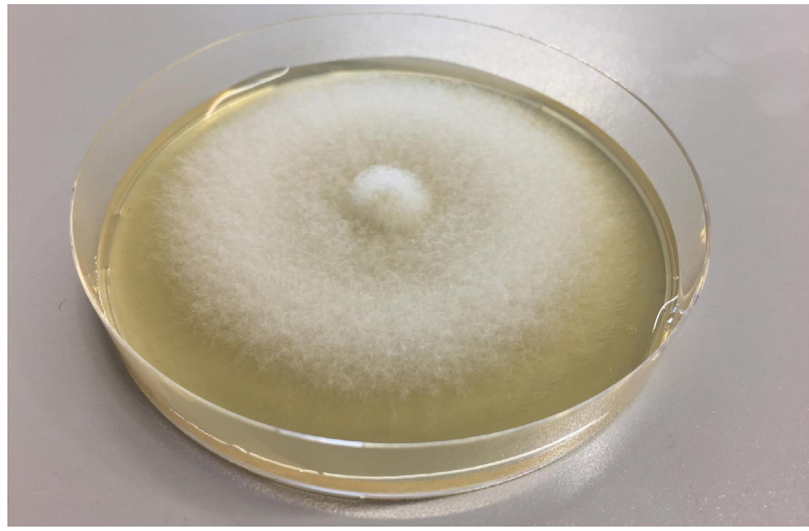
BR

Oberpaul, M., Brinkmann, S., Marner, M., Mihajlovic, S., Leis, B., Patras, M. A., Hartwig, C., Vilcinskas, A., Hammann, P. E., Schäberle, T. F., Spohn, M., Glaeser, J.
Combination of high-throughput microfluidics and FACS technologies to leverage the numbers game in natural product discovery (2021) Microbial Biotechnology, 15(2), 415–430. DOI: 10.1111/1751-7915.13872

"Some fungal lipids contain extremely scarce fatty acids, which can be converted enzymatically into aldehydes. By deploying this approach, we were able to characterize so far unknown flavor compounds."

Andreas Hammer, research associate at Fraunhofer IME in Giessen.

The "enokitake" mushroom forms dodec-11-enoic acid, possible to be converted into the fragrant dodec-11-enal.



Biotechnological production of fragrant fatty aldehydes

A great number of aldehydes play an important role as flavor and fragrance compounds, but are not easily accessible via classical chemical approaches. Their industrial production is expensive and elaborate. Modern biotechnological approaches may overcome these obstacles while meeting consumers' expectations regarding naturalness of flavorings.

In our work, we deal with various enzymes, which enable the production of natural flavorings. Carboxylic acid reductases (CARs) are particularly popular for the generation of aldehydes. They selectively reduce carboxylic acids to their corresponding aldehydes. Hence, we developed a biotechnological approach by using a CAR of *M. marinum*, heterologously expressed in *E. coli*, to transform hydrolyzed fungal lipids. Since some fungi produce extremely scarce fatty acids while being a renewable resource, this raw material is of special interest. In the current study, we applied lipid extracts of the "enokitake" mushroom *Flammulina velutipes*, which was found to generate notable amounts of terminally unsaturated dodecenoic acid. Reaction products were analyzed by means of gas chromatography-olfactometry (GC-MS-O) and dodec-11-enal was identified.

Interestingly, there is nearly no information on the sensory properties of terminally unsaturated aldehydes available in the literature. Therefore, we investigated these compounds regarding their odor qualities and thresholds in air and water. All aldehydes exhibited green odor qualities. Short-chained substances were additionally associated with grassy, melon-, and cucumber-like notes. Non-8-enal with a metallic-medicinal smell was identified as the most potent compound with an impressive low odor threshold of 0.039 ng/L air. Longer-chained homologs smelled soapy and coriander leaf-like with partly herbaceous nuances.

BR

Hammer A.K., Emrich N.O., Ott J., Birk F., Fraatz M.A., Ley J.P., Geissler T., Bornscheuer U.T., Zorn H.
Biotechnological production and sensory evaluation of ω1-unsaturated aldehydes (2021) J Agric Food Chem 69,345–353. DOI: 10.1021/acs.jafc.0c06872

Doctoral and final theses

Doctoral theses

Daniel Amsel
Elucidating the potential of microRNAs - towards a functional landscape of microRNAs in the model organisms *Tribolium castaneum* and *Galleria mellonella*.
Justus Liebig University Giessen

Catherine Rose Bernau
Rational and model-based design of purification processes for recombinant proteins.
RWTH Aachen University

Mona-Katharina Bill
Isolation and characterization of new antibacterial active secondary metabolites from microorganisms as potential starting points for drug discovery.
Justus Liebig University Giessen

Michael Czieborowski
Bacterial biofilm formation on plastic surfaces: molecular ecophysiology and antimicrobial strategies.
University of Münster

Tessa Carrau Garreta
Characterization and in vivo-studies of entomopathogenic viruses for biocontrol of the invasive pest *Drosophila suzukii*.
Justus Liebig University Giessen

Benjamin Gengenbach
Rational and model-based characterization of heterologous gene expression in biological systems.
RWTH Aachen University

Andreas Klaus Hammer
Biotechnologische Darstellung und analytische Charakterisierung aromaaktiver Fettaldehyde.
Justus Liebig University Giessen

Nils Hiebert
Entwicklung neuer biologischer Bakterien-basierter Insektizide gegen den invasiven Schädling *Drosophila suzukii*.
Justus Liebig University Giessen

Lukas Käßer
Entwicklung und Intensivierung eines Bioprozesses für die Produktion eines antimikrobiellen Peptides in einer stabilen Sf - 9 Zelllinie.
Justus Liebig University Giessen

Phillipp Peter Kirfel
From epigenetics to bacterial symbionts – towards sustainable targets of aphid pest management.
Justus Liebig University Giessen

Yolanda Kleiner
Chemische und biologische Evaluierung neuartiger Epoxychinon-Naturstoffe und -Naturstoffhybride.
Justus Liebig University Giessen

Sven Kroesen
Dependency of toxicity on time and dose in fish life-cycle tests – effects and effect thresholds of tamoxifen citrate to different life-stages of zebrafish in variable exposure scenarios.
University of Münster

Julia Kronenberg
Deciphering the role of phosphatidylethanolamine-binding proteins from *Nicotiana tabacum* and *Drosophila melanogaster* in human tumor cell survival and proliferation.
University of Münster

Sebastian Kühr
Regulatory bioaccumulation assessment of nanomaterials. Development of new concepts and testing procedures.
University of Siegen

Tim Lüddecke
How the integration of phylogenetics and venomics resolves persistent challenges in evolutionary systemics and toxinology.
Justus Liebig University Giessen

Christopher McElroy
Metabolic engineering of isoprenoids.
RWTH Aachen University

Franziska Maria Müller
Biochemical, genetic and ecological investigations on the bacterial degradation of steroid compounds.
University of Münster

Rabia Özbek
Proteo-transcriptomic analysis of the venom of the endoparasitoid wasp *Pimpla turionellae* and ist impact on host epigenetic mechanisms.
Justus Liebig University Giessen

Judith Rose
Identification and molecular characterisation of protein motifs involved in forisome assembly and function.
University of Münster

Matthias Teigeler
Wirkmuster hormonaktiver Substanzen im Zebrabärbling (*Danio rerio*) – Neue methodische Bewertungsansätze unter Berücksichtigung unterschiedlicher Belastungsszenarien.
RWTH Aachen University

Anton Georg Windfelder
High-throughput screening of insect larvae as a replacement for mammalian models of gut inflammation.
Justus Liebig University Giessen

Tassilo Erik Wollenweber
Synergistic approaches to elucidate potential factors involved in the reproductive system of *Taraxacum koksaghyz*.
University of Münster

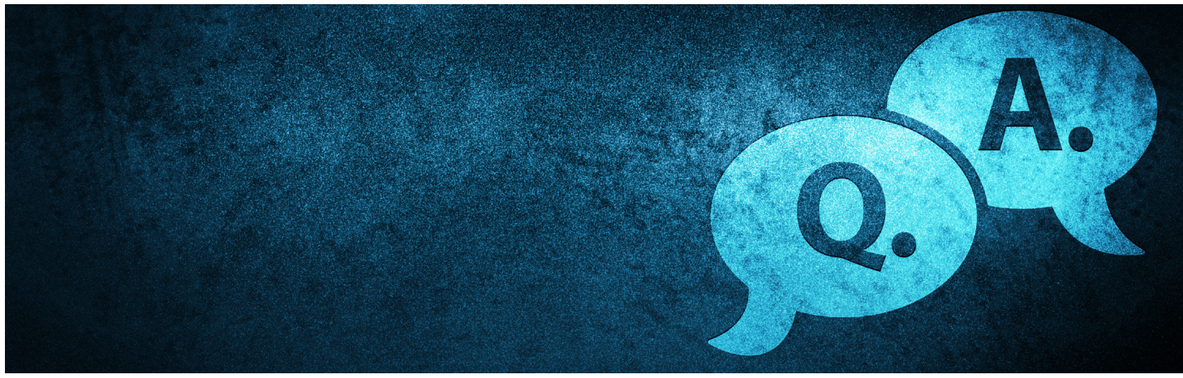
Marius Max Zimmermann
Molecular analysis of flowering time control in *Nicotiana tabacum* with special emphasis on the role of NtFT5.
University of Münster

Theses with the experimental part carried out at the Fraunhofer IME:

- 35 Bachelor's theses
- 36 Master's theses
- 1 diploma thesis
- 1 state examination thesis

In conversation

with Dr. Kerstin Hund-Rinke



"To be faced with a new professional challenge, I never had to change employers."

Kerstin Hund-Rinke studied biology at the University of Munich (LMU), specializing in microbiology, and earned her doctorate on soil microbiological issues in ecotoxicology at the Technical University of Munich and at the Society for Radiation and Environmental Research, now Helmholtz Zentrum München. After joining the Fraunhofer IME in Schmallenberg in 1988 as a laboratory manager for microbiology and soil organisms, Dr. Hund-Rinke took on various management positions in ecotoxicology, ranging from group manager to acting head of department. During the phase of development of the Federal German soil protection ordinance, she held the leadership of the temporarily independent department of Terrestrial Ecotoxicology. From a scientific point of view, Kerstin Hund-Rinke made a name for herself internationally in the environmental risk assessment of nanomaterials.

Dr. Kerstin Hund-Rinke: "Always new challenges – my professional life at Fraunhofer"

"For 34 years I have been at the Fraunhofer IME in Schmallenberg and it never got boring. To be faced with a new challenge professionally, I never had to change employers. In my case, it was the main topic that changed several times. Applied Fraunhofer research means that you have to deal with current problems, which change by their very nature. However, there was a common thread. All the topics and the answers I came up with built on each other. With my doctorate at the Society for Radiation and Environmental Research in Neuherberg on methods for recording microbial activity in soils, I already started on the topic that has accompanied me throughout my professional life: the influence of chemicals on the habitat function of soils and the (bio-) availability of pollutants."

Dr. Hund-Rinke, what was the major topic you started out with at Fraunhofer?

In the 1990s, the remediation of contaminated soils was a major topic. It became clear that substances such as mineral oil hydrocarbons, polyaromatic hydrocarbons and old armaments can massively impair soil functions. The development of remediation techniques and the assessment of remediation success were challenging. We played a leading and formative role in the development of ecotoxicological analytics to determine the bioavailable contaminant content. The results were incorporated into DECHEMA guidances and ISO guidelines, which were widely disseminated nationally and internationally. The bioavailable pollutant fractions rather than the total contents are the decisive factor in the assessment of soil functions. The gained experience flowed seamlessly into a new environmental topic: it all revolved around the idea of a circular economy.

This resulted in the Closed Substance Cycle Waste Management Act. What did Fraunhofer contribute to this?

The Circular Economy Act raised among others the question of what happens to the pollutants that get back into the soil via composting and the use of compost. For example, can treated orange peels pose a hazard through composting? Will the pesticides degrade or are we creating a chemical time bomb for ourselves? For this purpose, we developed a simulation system, which was also patented. In six incubation reactors, each with a volume of two cubic meters, in which radioactive-labeled substances could also be used, we were able to cover important areas of the waste sector. The size was necessary to minimize the risk of erroneous conclusions due to small, optimally performed laboratory experiments. At the very least, pilot scale was required. The special feature of the composting experiments was that the reactor, controlled by the microbial activity in the center, automatically heated the walls so that self-heating could be simulated with natural microbial fluctuation on a large scale. This should lead to realistic conclusions regarding pollutant degradation and fixation. In addition to composting, landfilling of residual materials was a current issue. In order to reduce gas formation in the residual waste landfills, only stable waste should be deposited. An important parameter was the C-content. However, the easily degradable carbon of organic residues or paper cannot be compared with the stable fraction of other wastes. Here we wanted to support the development of alternative waste pretreatments. Burning all waste before landfilling to meet the threshold value should be avoided. Carbon had to be considered in a differentiated way. We were able to use the reactor to simulate the processes in a residual waste landfill at a depth of ten meters using appropriate pressure plates, assess leachate forming by chemical and ecotoxicological analysis, and analyze gases produced. The simulation of relevant biological soil remediation approaches in cooperation with the proprietary companies represented a further issue. Subsequent investigations in outdoor lysimeters and time-lapse investigations in the reactors with summer and winter periods were to provide longer-term statements on the fixation of pollutants.

In recent years, nanomaterials have been a major topic at the institute. How was this development started?

In the early 2000s, the phase of the waste sector and contaminated site sector was replaced by the new topic of nanomaterials. When I started this, even some colleagues smiled at me. This seemed nonsensical, since there are many natural nanoparticles. What danger should the artificially produced ones pose? It turned out that investigations are better than assumptions. The initial investigations resulted in the world's first publication with results on the ecotoxicological effects of TiO_2 nanoparticles in standardized test systems used for regulatory approval studies. This publication is still cited today. Again, we were formative in adapting test systems used in regulation to characterize and evaluate the ecotoxicological effects of chemical substances. The expertise gained supports the authorities, but also the industry, and flows into the adaptation of test guidelines. In addition, we used the OECD Guideline 303A model sewage treatment plants to investigate the fate and effect of Ag nanomaterials released with wastewater from washing clothes, for example. Environmentally relevant loaded sewage sludge could be used in the laboratory and in field lysimeters to record the effect on soil (micro) organisms when it is used as a fertilizer, and to investigate the displacement of the particles. In cooperation with EAWAG (Dübendorf, Switzerland), we were able to show that the expected sulfidation does not lead to detoxification of the Ag nanomaterials. Since the possibility of laboratory sewage treatment plants is not widespread, sewage sludge and effluent from the plants were sent to

Release of Ag nanoparticles from sewage sludge in simulated agricultural use.

Selected committee activities throughout Kerstin Hund-Rinke's career

- Collaboration on various guidance documents and OECD guidelines
- Committee activities at BMU NanoDialog, BMEL, DECHEMA, OECD WPMN
- Expert for ecotoxicology at DAKKs
- Member of the advisory board for the course of studies "Soil, Water, Contaminated Sites" at the University of Applied Sciences / University of Osnabrück
- Member of various editorial boards (e.g. "Environmental Sciences Europe")

partners for their studies in international cooperation projects.

The subject area is currently expanding from classical mineral nanomaterials towards innovative materials. I started the studies as a lone researcher, now almost all departments of the institute are involved. This makes it possible to work on increasingly complex issues.

Were there other thematic challenges?

In addition to these major topics, individual questions were always an issue and required new solutions. One example from recent years is the development of a screening assay on a microtiter scale for rapid detection of the potential degradability of chemical substances. This was done not only based on pure microbial cultures or microbial communities artificially assembled from them, but also using sewage sludge. This increases the proximity to the standardized tests that are required in the context of regulatory investigations. One challenge here was to develop ways of standardizing the sewage sludge used so that studies can be compared with each other over a period of years. Approaches to solving this problem were also found.

Parallel to these issues, microbial biodiversity has always been important to me. Here, we began to record it by means of a wide variety of tests, including miniaturized tests, to characterize microbial functions, and finally expanded the range of investigations by molecular biological studies of structural diversity. The goal should be to enable information on diversity and resilience in a regulatory relevant framework. I can no longer conclude this last point. However, the many years of preliminary work have paid off. Publicly funded projects are now initiated and I can hand over this prepared topic area to my successors.

How can such complex issues be successfully addressed?

Not all these successes would be possible without cooperation across departmental boundaries, an imaginative workshop and a great team in the laboratory. Sometimes old treasures have been taken out of the equipment cabinets to be used for a new application, sometimes for purposes other than intended. Creativity was often required to solve the task at all levels. Numerous students also participated in the context of their doctorates or final theses (diploma, later bachelors or master's degree). Furthermore, networking with other scientists and with representatives of authorities in the national and international context was indispensable. This automatically led me to various committee activities, through which I was able to move many things in the regulatory framework.

The keyword successor came up: what is meant by this?

My career at Fraunhofer is ending. With Dr. Karsten Schlich and Dr. Cecilia Diaz, a powerful team is ready to take over, one that enjoys breaking new ground just as much as I do. Karsten Schlich takes over the topics "Ecotoxicological Investigations of Particulate Materials" as well as "Functional Microbial Biodiversity" and Cecilia Diaz is competent for the molecular biological questions. In the future, the work will be supported and complemented by the cooperation with the University of Münster: the new department "Environmental Microbiology" is established under the direction of Prof. Dr. Bodo Philipp. The possibility to work with human pathogenic microorganisms under L2 conditions will also continue. Franziska Wege has built up the corresponding qualification. Through the cooperation with the University of Frankfurt and the newly established working group "Ecotoxicological Media Assessment" headed by Prof. Dr. Henner Hollert, the subject area of soil protection and soil quality assessment will also be continued and further developed.

Behavior of Ag nanoparticles in the sewage plant and adsorption to sewage sludge.

What characterizes research work in the regulatory context at Fraunhofer?

In all investigations, the aim is to pair scientific standards with pragmatism. Detailed investigations help to understand interrelationships. In the next step, however, a pragmatic approach often has to be found to answer specific questions in the regulatory context. The cost-benefit trade-off must always be considered. This pragmatism sometimes makes it difficult to publish results and conclusions. Particularly, some academic reviewers find it difficult to comprehend and accept such complex approaches and the linked interrelated thinking. The scientific fragmentation into sub-questions often results in demands of specific additional investigations This is hard to accomplish for an institute that has to acquire full costs by public or industry projects. Not everything that would be desirable for scientific knowledge is necessary, helpful and reasonable under comparative cost-benefit considerations for regulatory implementation.

AE

People and events

PD Dr. Dr. Johannes Buyel receives the “DECHEMA Award” 2021

PD Dr. Dr.-Ing. Johannes Buyel has received the “DECHEMA Award” 2021 for his outstanding achievements in biotechnology and bioprocess engineering. The DECHEMA society is Germany’s leading, not-for-profit expert organisation for chemical technology and biotechnology and represents these disciplines in science, economy, politics and society. Since 1951, the DECHEMA Award is given annually to outstanding young scientists and their research activities within these areas.

Johannes Buyel is a researcher at the Fraunhofer IME in Aachen since 2014, starting out as a group leader. As of 2015, he is head of the department Bioprocess Engineering. After two doctorates from two separate universities in different disciplines, he concluded his habilitation at RWTH Aachen University.

The primary focus of his scientific work is the research of plant-based expression platforms for transient protein production to be used as biopharmaceuticals. His versatile research activities in the areas of protein production, protein purification, bioprocess modelling and optimization as well as process integration show most promising development perspectives, particularly in the context of a sustainable bioeconomy.

MB

Funding certificate from Federal Minister Klöckner for crop protection

On April 20, 2021, the Federal Minister of Food and Agriculture, Julia Klöckner, handed over the first grant notifications for the joint project HOPE - "Development of holistic formulation methods for the biological crop protection of soft fruit" with a total funding of around 843,000 euros.

The object of the research project is the development of formulations for the biological plant protection of blueberries with the aim of developing an effective spray application based on a novel virus formulation against the spotted wing drosophila. In addition, beetle larvae that damage plant roots will be targeted by an attractive formulation based on a granule or capsule. Those contain a specific insect pathogenic fungus that kills off the larvae.

Dr. Kwang-Zin Lee, department head of pest and vector insect control at the institute's Bioresources Division, received the funding certificate of about 250,000 euros for Fraunhofer IME during a virtual meeting. "Insect pests are responsible for up to 30 percent of global crop loss," explained Dr. Lee "Our mission is to develop innovative and sustainable strategies to become independent of chemical pesticides in the long term."

BR

Louisa Brachmann - Honoring the best trainees in 2021

Louisa Brachmann from Fraunhofer IME in Schmallenberg has passed her training as an office management assistant with the grade "very good" in a shortened training period of two and a half years.

She thus belongs to one of the best trainees of 2021 of the IHK Arnsberg, Hellweg - Sauerland and was honored during a festive event of the IHK in Arnsberg. With this outstanding performance, Ms. Brachmann is also one of the 21 best Fraunhofer trainees of the year 2021. The honoring of the best Fraunhofer trainees took place during a virtual event on November 3 and 4, 2021. Ms. Brachmann received an award from the Fraunhofer-Gesellschaft for this special success, and Ms. Katharina Schaff for her performance as her trainer.

Training its own junior staff has become a very important component for the institute. For this reason the IME-AE now offers training in two other professions in addition to office management assistants. In the IT sector, training is offered as an IT Specialist for System Integration. In the institute's own workshop, we train to become a Mechatronics Technician.

The Fraunhofer IME congratulates Louisa Brachmann for her great performance and is pleased that she will continue to support the administrative team in the area of human resources after her training.

AE

Fraunhofer IME trainee honored at "Honoring the Best 2021"

Every year, the Fraunhofer-Gesellschaft honors its best trainees with an honorary certificate in a festive ceremony. Our former trainee Kristina Werner from Fraunhofer IME in Giessen was also among this year's award winners. She passed the final exam of her three-year apprenticeship as an IT specialist in June 2021 with an A grade and was invited to the "Honoring of the Best" together with her trainer Heiko Herrmann.

The event was held digitally on November 3 and 4, 2021, by HR Director Elisabeth Ewen. Afterwards, Institute Director Prof. Andreas Vilcinskas personally awarded the honorary certificates.

The Fraunhofer IME congratulates Kristina Werner on this outstanding achievement and wishes her a successful start into her professional future.

BR

Fraunhofer IME at the international symposium "SphERe"

The "International Symposium on Pharmaceutical Engineering Research - SphERe" is an interdisciplinary forum to discuss current and future trends for the cost-effective production of effective and customized drugs with experts from science and industry.

On the opening day, Boje Müller reported as an invited speaker on the innovative research of the terpenoids group at the Fraunhofer IME in Münster. The focus was on the heterologous production of plant metabolites for the pharmaceutical industry. Obtaining the substances directly from the producing plants poses challenges: For example, composition and yield vary depending on environmental conditions. Chemical synthesis, in turn, struggles with the enormous complexity of the natural products.

Therefore, the researchers developed a yeast platform that was specifically optimized for the biosynthesis of selected natural products: Competing metabolic pathways were modified and the metabolic flux was redirected toward the desired product. In this way, production of economically relevant quantities in high purity and constant quality can be achieved.

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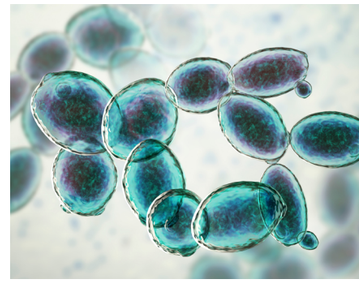

Fraunhofer Agriculture and Food Industry Alliance – Central Office at the Fraunhofer IME in Schmallenberg

The Fraunhofer lead markets were defined as strategic customer segments in order to offer industrial customers a sector-oriented range of services along the entire value chain. The industry sector around nutrition, which is very valuable in Germany, is served by the Alliance Agriculture and Food Industry. In 2021, the Food Chain Management Alliance, which was founded 13 years ago, was renamed the Food Agriculture and Industry Alliance to reflect the increased requirements.

These include new challenges arising from climate change, digitalization processes in agriculture, new marketing models or the demand for sustainable food production. This means that the focus needs to be supplemented with focal points for food analytics/processing, microsystems technology and logistics, in addition to solutions to issues throughout the food chain. The participating Fraunhofer institutes are expanding their research around R&D activities on the upstream and downstream areas such as agriculture or utilization networks.

The spokesperson for the Fraunhofer Food Industry Alliance is Prof. Dr. Andrea Büttner, Executive Director of the Fraunhofer Institute for Process Engineering and Packaging IVV. The Fraunhofer IME is represented by deputy spokesperson Prof. Dr. Stefan Schillberg, Institute Director in Aachen, and Prof. Dr. Mark Bücking, who heads the Alliance's central office in Schmallenberg.

www.fcm.fraunhofer.de/en and from mid-2022: www.food.fraunhofer.de

AE

Conclusion of the project "BioCOnversion"

After 3.5 years of intensive research by the various partners, the BioCOnversion project was successfully completed in October 2021. The aim of the project was to produce a plastic precursor for Covestro from steel mill gases from thyssenkrupp Steel Europe using biocatalytic and process engineering steps. The task of the Fraunhofer IME's Industrial Biotechnology department in the project network was to utilize the CO-containing synthesis gas with acetogenic clostridia. These bacteria are able to use gas as a growth substrate and produce industrially relevant chemicals, such as the flexibly usable intermediate hexanol. For this purpose, the bacteria were characterized and the cultivation was optimized in close cooperation with the project partners of AVT.BioVT Aachen and Fraunhofer UMSICHT. As a result, hexanol production was tripled compared to the state of research before the start of the project. The data obtained in the context of a doctoral thesis were presented at international conferences and published in a scientific journal (DOI: 10.1016/j.heliyon.2021.e07732).

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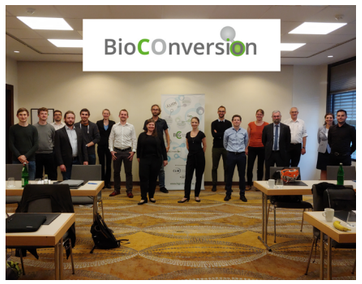

BioeconomyREVIER Rhineland: "Innovation Labs" prolonged

The German Federal Ministry of Education and Research (BMBF) is promoting the structural change in the Rhineland region away from lignite toward a sustainable bioeconomy.

An important element of the model region BioeconomyREVIER Rhineland are the innovation laboratories. Their research topics offer excellent potential for commercial implementation and should thus facilitate the rapid transfer of new processes from science to industry. A team led by Prof. Dirk Prüfer and Dr. Lena Grundmann from Fraunhofer IME already successfully contributed to the "AZUR" innovation lab. Just in time for the end of the two-year start-up phase, six laboratories in the "Innovative Agriculture" cluster receive further funding for up to five years starting in January 2022.

In "Circular PhytoRevier", Fraunhofer IME scientists in the proven consortium with Fraunhofer UMSICHT and Forschungszentrum Jülich IGB-2 are dedicated to the sustainable production of high-quality medicinal plants. Building on the successes of "AZUR", they are focusing on the development and stabilization of an economically viable process chain that ranges from breeding of yield-optimized plants to the development of new, effective cultivation and harvesting technologies to the efficient extraction and provision of the active ingredients from the raw material.

MB

Animal venom researcher from Giessen receives Justus Liebig dissertation award

As part of the Academic Ceremony at Justus Liebig University Giessen (JLU), prizes and awards are presented annually to excellent young scientists. One of this year's award winners is Dr. Tim Lüddecke, animal toxin researcher at the Bioresources branch of Fraunhofer IME in Gießen. He received the JLU Dissertation Award for his doctoral thesis on the evolution of spiders and the biochemistry of spider venom.

In September 2018, Dr. Lüddecke started his PhD on spider venoms under the supervision of institute division head Prof. Andreas Vilcinskas and completed it in less than three years. During this time, he was part of the LOEWE Center for Translational Biodiversity Genomics, where he was assigned to the project "Animal Venomics". The PhD thesis he prepared makes an important contribution to the evolution of spiders and the composition of their venoms. Among other things, Dr. Tim Lüddecke succeeded in decoding the venom cocktail of the wasp spider for the first time during this approximately three-year research phase.

BR

"Monitoring Chancengleichheit" on the agenda of the Fraunhofer IME

Already since 2013, the Fraunhofer-Gesellschaft (FhG) has had the topic of equal opportunities on its agenda. The focus is on the four topics of equal opportunities, work-life balance, inclusion and international human resources, because "No person shall be favoured or disfavoured because of sex, parentage, race, language, homeland and origin, faith or religious or political opinions. No person shall be disfavoured because of disability." (Basic Law of the Federal Republic of Germany, Section 3)

In 2020, the FhG did not reach the set targets. For this reason in 2021 the topic of "Monitoring Chancengleichheit" was declared to be a matter of top priority, as diversity leads to diverse perspectives, more innovative strength and higher team intelligence. The Fraunhofer IME commonly is participating in this process at all locations in order to generate added value for the institute through more equal opportunities. The focus is on adapting the recruiting process to attract highly qualified scientists. A team consisting of the works committee, HR managers, BfCs and institute management, led by the mandate holder Dr. Elke Eilebrecht, is driving this project forward in order to achieve the new target figures for 2025 at Fraunhofer IME.

AE

Cooperation project "BISYKA" honored

On March 29, 2021, State Secretary Dr. Jürgen Ude, on behalf of the Minister of Science of the State of Sachsen-Anhalt Prof. Dr. Armin Willingmann, announced the first place winners of the Hugo Junkers Prize 2020 live in a virtual award ceremony. For the development of a biomimetic synthetic rubber, Prof. Dr. Mario Beiner received the first prize in the category "Most Innovative Projects in Applied Research" representing a team of scientists from Fraunhofer IWMS, PAZ and IME.

The research project "Biomimetic Synthetic Rubber - BISYKA" was designed to unlock the secrets of natural rubber. Although synthetic rubber has been produced since the beginning of the 20th century, its mechanical properties cannot yet compete with the unique characteristics of natural rubber. "BISYKA" set itself the goals of elucidating these, transferring them to synthetic rubber and producing tires from the newly developed biomimetic synthetic rubber.

One of the core competencies of Fraunhofer IME in Münster is research into the biosynthesis of natural rubber in Russian dandelion. Based on this findings, it has now been possible for the first time to characterize natural rubber in detail in terms of its synthesis and composition and to break down the relationships between the individual components and the unique mechanical properties. In addition, the scientists successfully transferred the property-determining biological components to synthetic rubber in a targeted manner. Together with the partners, it has been possible to produce the first test tires with the new biomimetic synthetic rubber, which showed around 30 percent less abrasion in validated performance tests. In the future, the use of "BISYKA" rubber in series production could make a valuable contribution to minimizing microplastic input into the environment.

MB

Facts 2021

Scientific publications

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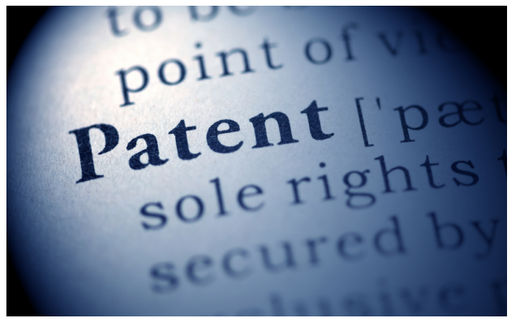

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