Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB

Sustainable Technologies for Human Health and the Health of our Planet

Annual Report 2024/25

#precision-medicine #wastewater-solid-gaseous-waste #biopolymers

Profile

Fraunhofer IGB develops and optimizes processes, technologies and products in three business areas: Health, Sustainable Chemistry, Environment and Climate Protection. We rely on our unique combination of expertise in biology and the engineering sciences, unparalleled within the Fraunhofer-Gesellschaft. This allows us to design resource-efficient, circular processes based on the approach of bioeconomy and bioinspired, biointegrated and biointelligent solutions, in order to contribute to human welfare, a sustainable economy, and an intact environment.

Our vision: We combine biology and engineering

Now more than ever, innovative processes and products call for the convergence or constructive interplay of different disciplines in systems approaches. One such systems approach, which IGB is continuously enhancing, is bioeconomy. By combining biology and engineering – especially in biotechnology and bioprocess engineering, but also through the genetic engineering of viruses, bacteria and mammalian cells, the combination of cell culture and interfacial engineering, or DNA sequencing using bioinformatic algorithms, as well as through the interaction of biological systems with technical materials – the institute paves the way to new approaches and future-oriented solutions for industrial value creation.

Partnering industry and public authorities – from laboratory to pilot-scale applications

One of the IGB's main goals is to translate its research findings into economically viable, sustainable processes and products for industrial application. By doing so, the institute is helping to shape the society of tomorrow. Fraunhofer IGB provides its customers and partners with research and development services encompassing the entire material value chain, accompanied by a wide range of analysis and testing services. The ability to deliver end-to-end solutions, from laboratory to pilot-scale applications, and a demonstration of the developed processes, is one of the institute's unique selling points.

This all-round service makes IGB a reliable partner for industrial companies, small and medium-sized enterprises operating in many different sectors, local authorities and special-purpose associations. The institute also performs contract research for the EU as well as Germany's federal and regional governments.

▸ *www.igb.fraunhofer.de/profile*

Sustainable Technologies for Human Health and the Health of our Planet

Annual Report 2024/25

Contents

Foreword

Dear readers,

The world is experiencing radical change and we are right in the middle of it. Despite the increasing geopolitical and economic uncertainties, most people, companies and politicians remain convinced that the transformation to a circular economy is a necessity. With our innovative solutions, Fraunhofer IGB continues to contribute to advancing along this path and thus increases the resilience of the German and European economy.

Last year, various events emphasized the excellence of our institute which was also acknowledged in the public eye. I would like to highlight two awards in our Health business area: Dr. Kai Sohn, in collaboration with his partners from Essen University Hospital and Noscendo GmbH, a Fraunhofer IGB spin-off, received the 2024 Stifterverband's Science Prize for optimized pathogen identification using next-generation sequencing. Another prize was awarded to Dr. Anke Burger-Kentischer and her team for their research work. Together with partners from Beiersdorf AG, they received the Hamburg Research Award for Alternatives to Animal Testing for developing a reporter skin model as a tool for the risk assessment of cosmetics.

After obtaining funding from the state of Baden-Württemberg in October 2023 to set up a new "Virus-based Therapies" branch, I am delighted to give an update on the progress made. In the meantime, the team has moved into its new premises in Biberach and we have already welcomed 10 new colleagues who are committed to this promising field of research.

With the participation of high-ranking personalities from politics and industry, the business area Environment and Climate Protection celebrated the successful completion of the projects of the European Regional Development Fund (ERDF) funding program “Bioökonomie Bio-Ab-Cycling” which focused on developing modular biorefineries. The projects have been funded by the state of Baden-Württemberg and the EU since 2021. The example of the Erbach sewage treatment plant demonstrates a successful collaboration: innovative pilot plants have enabled nutrients from the wastewater to be recovered for fertilizer production, CO_2 from the digester gas to be used as a raw material for new products and nitrous oxide emissions, a potent greenhouse gas, to be reduced on the wastewater treatment plant.

Further positive results can be reported from the Sustainable Chemistry business area: We are involved in several projects as a partner of the model region “Digitalization of Plant Value Chains” in Saxony-Anhalt. This initiative fosters structural transformation in the Central German region and aims to establish the area as a pioneer in the bioeconomy. In Straubing, one focus is on the implementation of Green Chemistry. Based on renewable raw materials, natural or modified biopolymers are used in a completely new context due to their suitable chemistry and material properties. This knowledge is also incorporated into the Fraunhofer flagship project Sustainable Biobased and Biohybrid Materials, which is driving forward the “biotransformation” of plastics technology.

As our research results show, transformation to a sustainable and circular bioeconomy is not only possible in theory, but is already being implemented. However, there are still some obstacles to be overcome. The corresponding recommendations to policymakers are outlined in the position paper of our Bioeconomy Initiative. Here, as leading experts, we emphasize eight necessary steps that need to be implemented now so that the German economy can continue to keep up with the competition. The message is clear: strengthening the bioeconomy strengthens Germany as a business location.

I would like to thank our customers and partners for their excellent cooperation and the trust they have placed in us to drive forward the transformation of the economy together.

In particular, I would also like to thank all employees for their commitment, creativity and perseverance. With great motivation, they have contributed to the Institute’s cohesion and success.

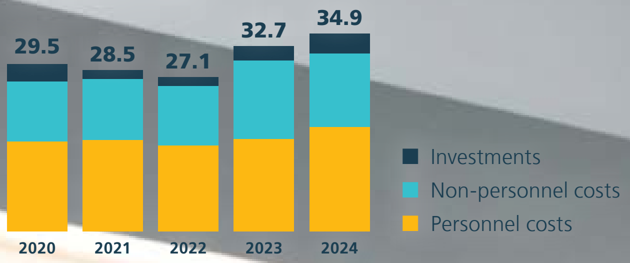
I wish you an informative read and look forward to working with you in the future.

Markus Wolperdinger
Director

Key figures

Development of total budget

Mio €



Revenue from contract research 2024

%

Dissertations

8

Academic theses

43

- **32** Master theses
- **7** Bachelor theses
- **4** Work placement reports

Teaching activities

76

Projects

261

- **4** Fraunhofer flagship projects
- **27** Fraunhofer internal projects
- **63** Projects funded by German federal ministries
- **21** Projects with universities, municipalities or funded by foundations
- **12** Projects funded by German states
- **14** EU projects
- **120** Industrial projects

Newly granted patents

6

Scientific publications

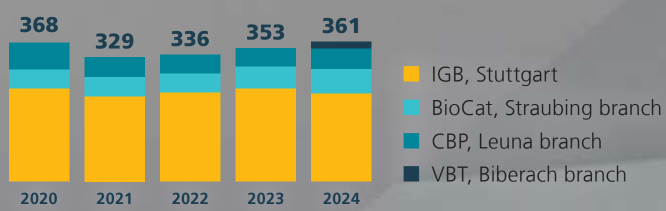
46

Proportion of women

52 %

Development of staff numbers

as of December 31, 2024

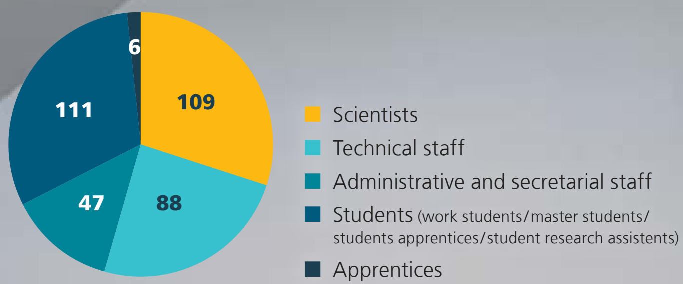


Nationalities

22

Numbers of staff members

as of December 31, 2024



Highlights 2024

Prizes, awards and scholarships

In-vitro Diagnostics at IGB receives Stifterverband Science Prize 2024

Rapid and precise detection of pathogens saves the lives of intensive care patients – for example in the case of sepsis, where every minute counts. Researchers at Fraunhofer IGB and their partners have now succeeded in establishing a new detection principle using next-generation sequencing. Using DNA traces, the novel method can reliably and accurately identify pathogens in the shortest possible time. This medical milestone was recognized by the German Stifterverband Science Prize 2024, which was handed over to Dr. Kai Sohn, head of In-vitro Diagnostics at IGB, together with the partners involved, the Fraunhofer spin-off Noscendo GmbH and Essen University Hospital.

www.igb.fraunhofer.de/ngs-prize2024

Hamburg Research Award 2024 for reporter skin model as an alternative to animal testing

In the Department of Cell and Tissue Technologies, IGB researchers have developed a new reporter epidermis model for detecting the skin-sensitizing effects of substances. This artificial skin can be used to reliably and precisely test pharmaceuticals, cosmetics, pesticides, biocides and other chemicals without animal testing. In September 2024, Dr. Anke Burger-Kentischer and her team, together with the Beiersdorf AG project partners involved, received the €30,000 Research Award for Alternatives to Animal Testing from the Hanseatic City of Hamburg.

www.igb.fraunhofer.de/reporter-skin2024

EUSAAT Congress 2024: IGB scientist Hanna Glasebach honored twice

The European Society for Alternatives to Animal Testing, EUSAAT for short, honored the research work of IGB scientist Hanna Glasebach with two awards at its annual congress in 2024. She received the "Young Scientist Travel Award" (YSTA) for her research on the 3D in-vitro skin model for psoriasis, which was developed at IGB as an alternative to animal testing. The award and the associated funding are used to support the travel activities of young scientists as part of their work. At the EUSAAT Congress, Glasebach was also able to impress the audience with a presentation that won her the "YSTA Best Talk Award".

- *s.fhg.de/eusaat-ysta (German)*

"Honoring the best" – award for IGB trainee Max Witte

After successfully completing his vocational training as a chemical laboratory technician, Max Witte was delighted to receive special recognition: At the Fraunhofer event "Honoring the best" in January 2024, he was awarded for his outstanding achievements during his vocational training. Witte had previously passed his final exams with 92 out of 100 points and thus with the grade "very good". In addition, his instructor Melanie Dettling and his colleague Tobias Götz, who accompanied and supervised him during his vocational training in the Membranes department, were also honored.

DBU doctoral scholarship for Simon Krake

Twice a year, the German Federal Environmental Foundation (Deutsche Bundesstiftung Umwelt, DBU) awards doctoral scholarships to doctoral students who are working on solutions for environmental protection and nature conservation. Simon Krake was one of the successful applicants in 2024. The biotechnology graduate is working on environmentally friendly and sustainably produced fuels as part of his doctoral thesis. Specifically, he is researching microbial processes for the production of hydrogen in the Industrial Biotechnology department at Fraunhofer IGB. The DBU is now supporting Krake's work over a period of three years with monthly base funding and a grant for material costs.

- *www.igb.fraunhofer.de/en/smartbioh2bw*

Events

Research transfer: "break2innovate" online event series launched in February 2025

In line with the motto "Our expertise is your solution!", Fraunhofer IGB has launched the monthly online series "break2innovate". Experts from the institute present their research, development and services they provide to improve processes and products of industrial customers. The online event series is aimed in particular at small and medium-sized companies. The emphasis is on presenting innovative solutions for industry-specific challenges in just 30 minutes – focused, brief and compact. The IGB experts cover the entire process chain, including innovative analysis and testing methods. The topics of break2innovate are announced for each individual session, tailored to the specific industry and target group. On February 26, 2025, the first edition started with the topic "Circulation of process water: treatment options on-site".

- *www.igb.fraunhofer.de/break2innovate (German)*

Wastewater colloquium: high-load digestion and use of digestate

In October 2024, Fraunhofer IGB hosted its 23rd Colloquium on Wastewater and Waste Treatment. This event series is aimed at municipal administrations, operators of wastewater treatment plants, politicians, employees from authorities and interested parties from industry. The thematic focus this time was on high-load digestion and the utilization of digestate. IGB experts and the institute's project partners presented solutions and process developments for sewage treatment plants on the basis of case studies and provided insights into current projects.

- *www.igb.fraunhofer.de/abwasserkolloquium (German)*

Regional workshops on the "urban BioEconomyLab" project

The "urban BioEconomyLab" is a Fraunhofer living lab that aims to demonstrate how cities can move towards a sustainable bioeconomy. To this end, the participating stakeholders and potential users exchanged ideas at regional workshops and discussed measures for the bioeconomic transformation of the respective regions. The first edition in January 2024 focused on the greater Stuttgart area, while the second in July 2024 looked at the Karlsruhe region. Relevant research results were presented, possible future scenarios were developed and concrete measures were derived from these. The aim was to develop an individual bioeconomy roadmap for each region.

▸ *www.igb.fraunhofer.de/urban-bioeconomylab*

"Once the molecular causes of a disease have been identified, this enables an exact diagnosis of the disease and creates the basis for correcting the malfunction(s) underlying the disease."

Prof. Dr. Steffen Rupp
Head of business area Health

Precision medicine

Targeted therapies based on the molecular causes of diseases

Technological advances in the identification of disease-specific molecular characteristics and in the biotechnological manipulation of cells and organisms of all kinds create the basis for understanding diseases at a molecular level. This makes it possible to develop new specific therapeutics and target treatment strategies to individual patients. At Fraunhofer IGB, we are developing the technologies for such precision medicine.

Biomarkers – the key to precision medicine

The enormous increase in scientific knowledge in the life sciences over the last two decades has significantly improved our knowledge of the molecular causes of diseases. Once the molecular causes of a disease have been identified, it is possible to look for ways to correct the underlying dysfunctions.

Diseased cells or tissues are characterized by certain molecular features, so-called biomarkers, which distinguish them from healthy cells and tissues. Precision medicine, also known as individualized or personalized medicine, makes use of the knowledge of these characteristic molecular features. In the clinic, the biomarkers, for example of a patient's tumor, are determined using various diagnostic procedures and used for therapy planning.

The aim of precision medicine is to tailor medical care for patients as specifically as possible to their disease in order to treat them more effectively and with fewer side effects. New technologies make it possible both to generate more precise diagnoses in the clinic and to design more precise therapies for diseases. Fraunhofer IGB is working on developing these technologies and putting them into practice.

Precise treatment options already exist today for a number of diseases, enabling recovery even in cases that were previously inconceivable. In many clinical centers, the systematic molecular analysis of malignant tumors for specific biomarkers using genetic profiling now determines primary diagnostics, the prediction of the reaction of malignant cells to cancer drugs as well as prognosis assessment and therapy planning.

Precision diagnostics as an essential step

Comprehensive diagnostics that can determine the biomarkers characterizing the disease are essential for precision medicine. As these diagnostics must always be carried out on individual patients, the term personalized medicine is often used, although treatment planning is based on known therapeutic agents with the best prognosis for the tumor being analyzed, for example.

The characteristic markers for tumor treatment are often identified in clinical studies, which look for conspicuous changes in different patient groups compared to healthy individuals on a genome-wide level. Methods of artificial intelligence, which are predestined to identify these changes or biomarkers, are increasingly being used here.

At Fraunhofer IGB, we develop bioinformatic and biochemical methods with which characteristic biomarkers tumor diagnostics can be clearly determined. For example, we use next-generation sequencing technology at the institute to identify new biomarkers for improved diagnosis of prostate cancer or pancreatobiliary cancers at the nucleic acid level.

Targeted therapeutic viruses

Our knowledge of tumor development and its defense mechanisms against our immune system enables the development of new immuno-oncological forms of therapy. At Fraunhofer IGB, we are developing immunomodulating oncolytic viruses to fight cancer.

Oncolytic viruses are viruses that – directly or indirectly – kill tumor cells. They can infect and lyse tumor cells and generate an immune response against specific tumor antigens through the resulting inflammatory reaction. In addition to this direct effect, they can also be used to introduce so-called tumor suppressor genes into tumor cells. These genes cause the immune system to recognize the aberrant cells and subsequently eliminate them.

In-vitro disease models for more efficient drug development

The development of ever better in-vitro disease models also enables more efficient drug development and therapy planning. Animal models used to date are often not suitable for high-precision therapeutics, as the differences between animals and humans are usually too great. The reconstitution of diseased tissue, possibly even with the patient cells themselves, enables improved therapeutic success by selecting the most suitable therapeutic agent, but also more efficient drug development for new precision therapeutics.

3D tissue models can also be used to better identify potential side effects, and even to test to the safety of chemicals of all kinds. Some of these so-called NAMs (new approach methods) are already available at Fraunhofer IGB and are being continuously developed further.

Further information

www.igb.fraunhofer.de/precision-medicine

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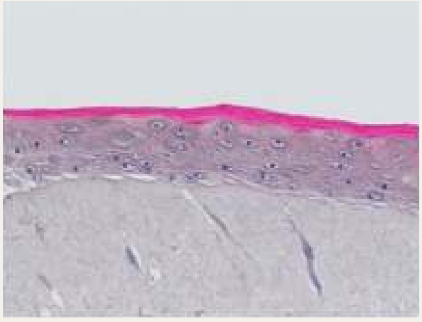
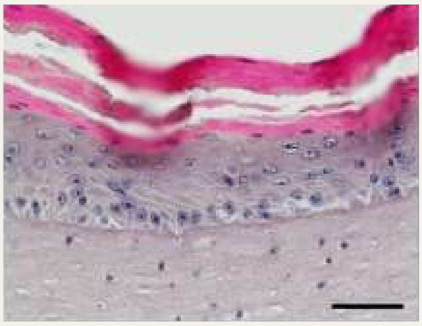
Disease models

In-vitro skin model for modeling psoriasis with reconstituted skin

Skin model



Psoriasis skin model



Psoriatic skin (in vivo)

At Fraunhofer IGB, we develop disease models using reconstituted in-vitro models. For example, we model psoriasis from genetically modified, immortalized primary skin cells. Psoriasis is a chronic autoimmune disease that affects around two percent of the world's population, causing inflammation and scaling of the skin. Our psoriasis models are reconstructed epidermis and full-thickness skin models whose keratinocytes overexpress the psoriasis-associated transcription factor STAT3.

Proinflammatory stimuli such as the addition of cytokines or the integration of T cells trigger typical psoriasis features in these skin models. The psoriasis models express characteristic protein markers (e.g. S100A7, CK16, IL-8) and exhibit morphological features such as thickening of the epidermis (acanthosis), impaired final differentiation of keratinocytes (parakeratosis) and thickening of the stratum corneum (hyperkeratosis).

Further information

www.igb.fraunhofer.de/disease-models

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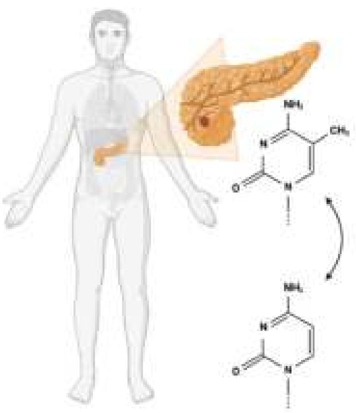
Innovative tumor diagnostics for precision medicine



Diagnosis of pancreatic diseases using differential DNA methylation analysis

Although great progress has recently been made in the personalized treatment of certain tumors due to cell-based therapeutics, cancer still represents one of the main causes of death in medicine just like cardiovascular diseases.

The challenge of early detection

It is becoming increasingly clear that (in addition to the most specific and effective treatment option possible) the earliest possible diagnosis is becoming more and more important. For some of the most common tumor diseases, including breast, prostate and colorectal carcinomas, early detection screenings are therefore routinely offered to help reduce the severity of the disease.

Despite promising possibilities for detecting and removing certain tumors at an early stage, the corresponding examinations require partially invasive procedures that are not only unpleasant but also involve additional risks. This also reduces the acceptance of such diagnostic procedures. In addition, for some of the most severe tumor diseases with an exceptionally poor prognosis, such as pancreatic cancer, there are no corresponding early detection screenings available. There is therefore a considerable need for diagnostic procedures that can reliably detect tumors non-invasively with high precision and at an early stage.

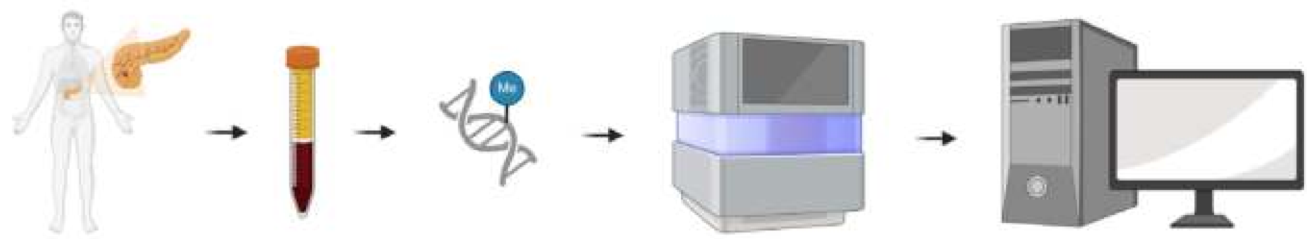
Novel method for diagnosing pancreatic cancer

Building on many years of expertise in the development of non-invasive diagnostics for complex diseases, the In-vitro Diagnostics department at Fraunhofer IGB, in cooperation with clinical partners from the University Hospital Erlangen under the direction of Prof. Dr. Georg Weber and GeneData, a company in the field of bioinformatics, has established an innovative method for the early detection of pancreatic cancer.

This method is based on the analysis of so-called cell-free tumor DNA from the blood of patients. This cell-free DNA is first isolated from the corresponding blood plasma and then examined for certain pathological changes. Tumor DNA often differs from healthy DNA in chemical modifications – known as methylations – at certain positions in the DNA, which we can be identified using high-throughput sequencing.

However, this method can not only be used to differentiate between healthy and tumor patients, but also between different gastrointestinal tumors. Another special feature of this method is the ability to differentiate between malignant pancreatic tumors and inflammatory, non-malignant pancreatitis, which has to be treated completely differently according to clinical guidelines.

Method for differential DNA methylation analysis



After a blood sample has been taken, the plasma is separated from cellular blood components by centrifugation. Cell-free DNA is then isolated from the plasma and analyzed by means of high-throughput sequencing in combination with bioinformatic methods screened for relevant methylation patterns.

Successful technical and clinical validation

As part of a clinical study in collaboration with the gastroenterology department of the University Hospital Erlangen, a technical validation was carried out on blood samples from patients who either had pancreatic cancer at various stages or who were suffering from pancreatitis. Clinical validation was demonstrated in a proof-of-concept study. Using AI-based methods, we were also able to show that the diagnostic procedure can even be used to classify non-malignant preliminary stages in several cases.

The results of the study have now been published in the renowned journal Molecular Cancer: Discrimination of pancreato-biliary cancer and pancreatitis patients by non-invasive liquid biopsy. Hartwig C, Müller J, Klett H, Kouhestani D, Mittelstädt A, Anthuber A, David P, Brunner M, Jacobsen A, Glanz K, Swierzy I, Roßdeutsch L, Klösch B, Grützmann R, Wittenberger T, Sohn K, Weber GF. Mol Cancer. 2024 Feb 2;23(1):28. PMID: 38308296.

Based on this approach, Fraunhofer IGB is now aiming for translation into clinical routine. In addition, the technologies developed will also be used for other tumor diseases and other clinical indications with clinical collaborators.

Further information

www.igb.fraunhofer.de/tumor-diagnostics

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Virus-based Therapies VBT

Establishment of the VBT branch of Fraunhofer IGB in Biberach

The laboratories of the new branch for virus-based therapies in Biberach were inaugurated and put into operation at the beginning of 2024. This laid the foundation for the development of biotechnological processes for the optimized production of therapeutic viruses.

Viruses and viral vectors represent a new and promising class of therapy that demonstrates high effectiveness and durability with few side effects. Experts see enormous potential in these innovative therapeutics, particularly in the fight against cancer and genetic defects.

In order to exploit this potential sustainably, however, profound biotechnological developments are necessary for their production, purification and analytics. Only by increasing productivity and quality, the high costs can be reduced.

State of Baden-Württemberg supports novel branch

First and foremost, we would like to thank the state government, for the generous support of the novel branch. We see this as a great deal of trust and a mandate to make our branch for virus-based therapies successful in the long term and visible regionally and internationally. With the handover of the funding notice in September 2023, we were able to immediately start with the project work at the Stuttgart site based on Fraunhofer's own oncolytic virus platform TheraVision.

Start in Biberach an der Riß

At the same time, we rented laboratory space in Biberach and equipped it with the necessary infrastructure. Thanks to intensive preparatory work, we were able to equip the branch in accordance with the complex legal framework for handling therapeutic viruses. At the beginning of April 2024, we were able to inaugurate our new laboratories and start concrete project work on site.

To this end, we have succeeded in recruiting young and motivated staff with high levels of expertise in virology, cell and immunobiology, and process technology. Almost 25 employees are now working in the field of virus-based therapies. Five of our new colleagues are researching the development of technologies for optimizing therapeutic viruses as part of their doctoral theses. Their supervisors are professors at both the University of Ulm and the University of Stuttgart, which shows the close networking of the VBT branch with academic institutions in Baden-Württemberg.

Successful networking in the cluster

We are already very successful acquiring new industrial orders: After we signed a framework agreement in summer 2024 between Fraunhofer and Boehringer Ingelheim, we initiated our first scientific cooperation with Boehringer Ingelheim in September 2024. The aim is to better understand the production process of viruses, especially at the cellular level, and thus gain insights for the efficient production of these new therapeutics. We are in continuous exchange with companies in the BioPharmaCluster South Germany as well as other regional and national potential partners.

Further information

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Therapeutic viruses to enhance precision medicine

Viruses are evolutionary masterpieces as they are able to selectively infect and successfully replicate in their hosts despite their small genome with limited coding capacity. Based on those capabilities, viruses have emerged as a promising class of therapeutics for diverse diseases such as cancer and genetic disorders or even to treat antibiotic-resistant bacterial infections.

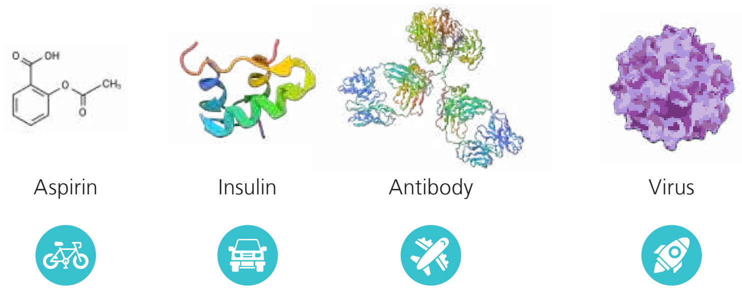
Therapeutic viruses to treat cancer and gene defects

Oncolytic virotherapy is based on the ability of viruses to selectively infect and replicate in cancer cells, while sparing healthy tissue. Productive virus replication induces lytic cell death, the release of cancer-specific antigens and an inflammatory response in the immune-suppressed tumor microenvironment which is then potentiated into a multi-faceted activation of the immune system and a systemic tumor vaccination. It is also worth noting that oncolytic virotherapy does not only provide high levels of therapeutic efficiency, but also results in significantly fewer side effects compared to conventional anti-tumor therapeutics.

While oncolytic virotherapy is based on the tumor-selective infection and replication of certain viruses, virus-based gene therapy relies on the ability of viruses to deliver or even permanently integrate genetic information into their target cells. This virus-mediated gene expression then results in reduced disease burden or even complete remission in patients suffering from genetic disorders.

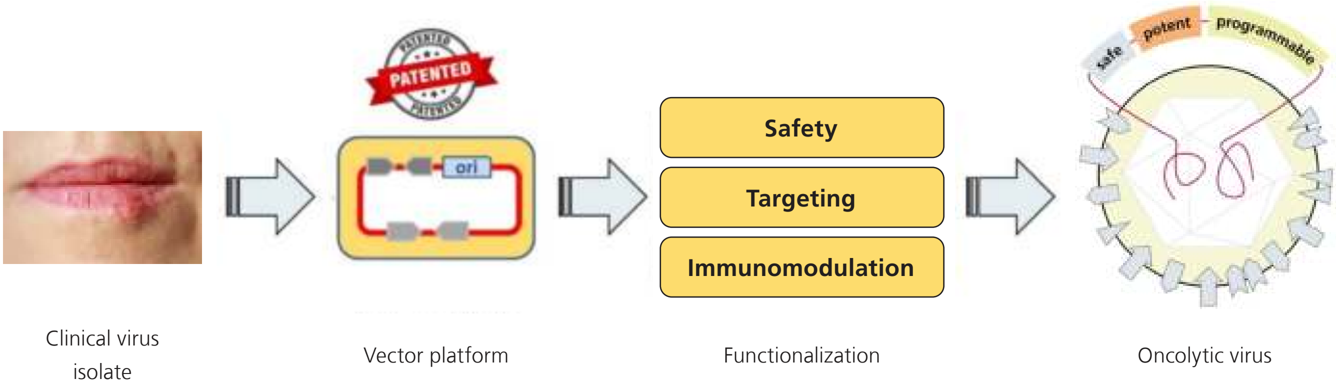
Strategies to personalize oncolytic virotherapy as part of precision medicine approaches strongly depend on genetic engineering of viral genomes resulting in therapeutic viruses especially tailored to an individual's tumor phenotype. Such therapeutic viruses for instance express surface proteins that only bind to receptors selectively present on an individual's tumor cells or which deliver a specific therapeutic payload leading to the targeted destruction of already therapy-resistant malignancies. By combining those engineered oncolytic viruses with other treatment options such as therapeutic antibodies, cell- or radiotherapy, individually tailored treatment regimens with higher efficiency are generated.

Viral therapeutics as a new class of active ingredients



As a result of their complex structure and mode of action, virus-based therapeutics require novel, alternative approaches for early development, manufacturing, and clinical testing compared to more established therapeutic modalities such as aspirin or antibodies.

Schematic representation of the patented TheraVision platform



Schematic representation of the proprietary TheraVision vector platform. The in-house developed patented TheraVision platform is based on a clinical HSV-1 isolate. While two recombination sides allow to introduce two different DNA sequences into the virus genome to facilitate cancer cell-specific retargeting or the delivery of immunomodulators into tumors, the mutagenesis of three viral genes results in an attenuated virus phenotype to guarantee a safe and well-tolerated virus therapeutic. Based on those features, the TheraVision virus acts as modular platform technology for future developments.

Production of virus therapeutics – a major challenge

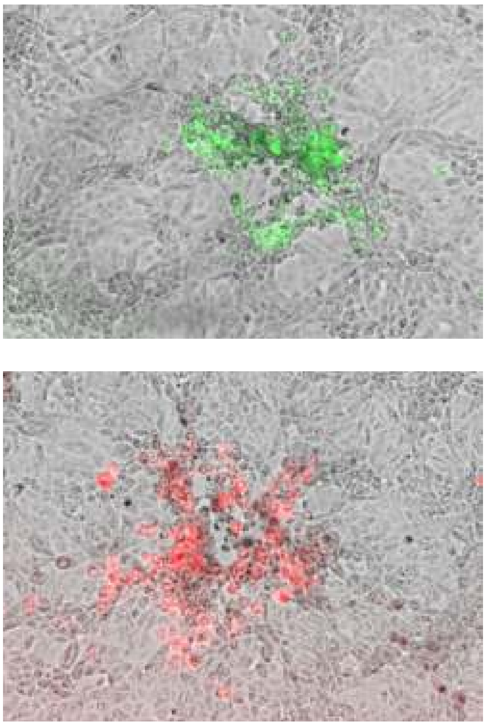
Despite their obvious potential as efficient therapeutic modality, currently only eight virus-based therapies have been approved by the responsible regulatory agency in America, the FDA, and its European counterpart, the EMA. Among those eight approved virus therapies, only one is an oncolytic virus, whereas 94 registered clinical trials were on-going in February 2024 to obtain approval for virus-based cancer therapy, making it clear that compared to other anti-cancer treatments such as small molecules or therapeutic antibodies, the successful clinical translation of virus-based cancer therapies is still in its infancy.

While this lack in clinically approved oncolytic viruses partly originates from their more complex structure and mode of action compared to conventional cancer therapeutics (Figure page 22 bottom) it also illustrates that further biotechnological research spanning the entire pharmaceutical value chain from early to late stage development is required to path the successful transition of (oncolytic) viro-science into the clinic.

This is precisely where the state of Baden-Württemberg's funding to establish a novel Fraunhofer IGB branch in Biberach an der Riß comes in, as this newly founded research unit focuses on the biotechnological development of virus-based therapeutics with a focus on virus, cell, and process technologies. The set-up and launch of the novel facility in Biberach was significantly supported by the expertise and existing infrastructures at the Fraunhofer IGB headquarter in Stuttgart.

Virus technologies: development of customized virus therapeutics

The virus technology group focuses mainly on molecular virus engineering. By introducing targeted modifications into viral genomes, efficiency and activity of therapeutic viruses and viral vectors will be increased. An essential starting point of our current activities here was the previously developed proprietary



TheraVision vector platform as foundation for future virus engineering. Reporter viruses expressing GFP (top) and Katushka (bottom) can be used to monitor the viral amplification cycle and replication efficiency in infected cells.

herpes simplex virus 1 (HSV-1)-based TheraVision platform. While TheraVision was designed as a modular vector technology for the production and testing of viruses for tumor therapy, its particular benefit arises from its modularity, which allows the rapid genetic manipulation of the underlying complex herpes virus. Based on those features, we recently developed so-called reporter viruses which express fluorescent proteins. Once their target cells become infected expression of those fluorescent proteins then allows to monitor viral replication kinetics in real-time (Figure left).

Next to HSV-1-based oncolytic viruses, other therapeutically relevant vector systems, such as vesicular stomatitis virus and adenovirus, are also established in our laboratories. By using those various viral vector systems, we are planning to comprehensively assess structure-function relationships of the underlying virus species to gain insights into their therapeutic safety, specificity, efficacy, and stability.

Cell technologies: cell engineering to increase yield and activity of therapeutic viruses

Research activities in the virus technology group such as fluorescent reporter viruses will also be utilized within the cell technology group as part of cell line engineering, a particular focus of our work. Targeted cell line engineering aims to modify common production cells to increase the yield of functional viruses for therapeutic use, as in contrast to conventional vaccinations to prevent infectious diseases, treatment doses for immuno-oncology are much higher which limits their broader therapeutic roll out. Innovative methods such as CRISPR-CAS technology which enable the modification of cell metabolism, apoptosis, cell division or the antiviral innate immune response will be used to make production cell lines more resistant to virus-induced stress responses. Bespoke fluorescent viruses will allow here a direct at-line monitoring of the improved production capacity of CRISPR-CAS modified cell lines. Last, our reporter viruses can also be used for preclinical efficiency testing to analyze replication kinetics and tissue penetration in complex tumor models. Such patient-derived models can also be utilized to dissect the differential or synergistic anti-tumor and immune-activating effects of the TheraVision virus compared to other viral systems such as vesicular stomatitis viruses and adenoviruses. This makes it possible to identify factors that influence the individual efficacy of oncolytic virotherapy.

Process technologies: optimization of production, purification and analysis of virus therapeutics

The process technology group complements the scientific research conducted within the virus and cell technology divisions by providing expertise in process development, analysis and scaling. In downstream processing, chromatographic bio-separation processes to minimize infectious titre losses throughout virus purification or cryopreservation and formulation studies in order to achieve maximum product stability are developed.

Further information

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Bacteriophages for efficient and targeted destruction of bacteria

While viruses that target human cells are used in oncology and gene therapy, bacteriophages (viruses that exclusively infect bacteria) are gaining increased attention of scientific research. Their ability to precisely and efficiently target bacteria makes them a promising alternative or complement to conventional antibiotics, particularly in the fight against antimicrobial resistance (AMR).

Beyond their role in precision medicine, bacteriophages hold great potential across various fields where control of bacteria is mandatory. In addition to treating bacterial infections in humans and animals, they can be applied in plant protection as well as food preservation, exemplifying the One Health approach. Their versatility underscores their value as a sustainable and innovative solution for bacterial management.

In the future, we will further expand our expertise in bacteriophage research and focus on translating scientific insights into practical applications. This includes developing efficient production processes and reliable detection methods to enhance safety and efficacy of those natural antimicrobial agents and unlock the full potential of bacteriophages across various fields.

Bacteriophage infection leads to plaque formation, indicating bacterial lysis.

From virus engineering to analyzing the formulated virus: Fraunhofer IGB provides expertise along the entire drug development process

Our competencies established at both the Stuttgart and Biberach VBT branch span the entire pharmaceutical development process starting with molecular virus engineering to increase activity and efficiency and ranging to process developments to improve virus production and novel methods to analyze the formulated virus. Consequentially, we will contribute to establish oncolytic viruses and bacteriophages as accepted and broader-used therapeutic modalities.

Further information

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"The higher the concentration of recyclable materials, the better they can be recovered. We adopt this principle in our research."

Dr.-Ing. Marius Mohr
Head of Department Water Technologies, Resource Recovery and Scale-up

Circular economy: use of wastewater, solid and gaseous waste

Development, piloting and market launch of sustainable processes for the use and recovery of residual materials

The transformation to a sustainable circular economy requires new processes for the utilization of residual materials. Fraunhofer IGB develops processes for recovering valuable substances from wastewater, solid waste and waste gas – from laboratory to pilot and demonstration scale. With its expertise in the digitization, scaling of processes and own pilot plants, the institute supports start-ups, SMEs, municipalities, public utilities and special-purpose associations in the implementation of new technologies.

Until now, by-products and waste from industry and local authorities have often been disposed of. In a sustainable circular economy, however, residual and waste materials represent an essential resource for new products. For a sustainable transition it is imperative that …

- carbon from fossil deposits is no longer released into the atmosphere. It should be recycled and, where possible, bound in valuable materials.
- nutrients, such as nitrogen and phosphorus are equally recirculated, with minimal energy consumption and without any negative impact on the environment (thus avoiding over-fertilization and eutrophication).
- intelligent management (e.g. avoiding impurities or dilution) and good process engineering (material separation, purification, conversion, etc.) enable economical and efficient resource recovery and recycling.
- companies, municipalities and countries use the finite natural and fossil resources more efficiently and intelligently and to recover ingredients for material or energy use in line with the circular economy approach.

Wastewater treatment plant in Erbach

Fraunhofer IGB – pioneer in the use of residual and waste materials as secondary raw materials

Pilot plant for recovering nitrogen from wastewater

Although residual materials, solid waste, wastewater and exhaust air from incineration can be used and reconditioned into so-called secondary raw materials, they are usually heavily contaminated or the usable recyclable materials are mixed or diluted. For a long time, this has meant that it was preferable to send them to a landfill or incinerate them – and thus dispense with purification. However, it is becoming increasingly clear that our society can no longer afford this type of disposal.

Selective separation as the key to recycling

Innovative processes are therefore needed to enable the recycling of more complex mixtures. Specific processing is required so that ingredients can be extracted and recovered from an extremely complex matrix.

The most selective separation possible is another decisive step for the use of secondary raw materials. The steps involved in separating materials have so far been costly and therefore have a significant impact on operating costs, but also on the sustainability of the processes. To solve this problem, Fraunhofer IGB develops processes that significantly increase energy and cost efficiency compared to established processes or enable the selective separation of certain waste materials in the first place.

Scaling and piloting build a bridge to the market

Scale-up plays a key role in the development of secondary material flows for the transformation to a sustainable bioeconomy. New processes must not only work on a small scale, but also on an industrial level. Pilot plants support the scaling of recycling processes and thus the market launch of new secondary products.

Fraunhofer IGB is a partner for municipalities and industrial manufacturers to utilize residual materials and minimize waste at the same time. For over 40 years, the institute has been developing processes for the treatment of waste and wastewater – from basic process engineering to pilot plant scale through to industrial-scale plants. With our know-how and expertise, we also provide support in the digitization of processes, the technical implementation and commissioning of the plants as well as in questions of process safety, sustainability and economic efficiency.

In addition, we provide state-of-the-art infrastructure and apparatus technology with our own pilot plants. This not only saves you costs, but also reduces development risks.

Further information

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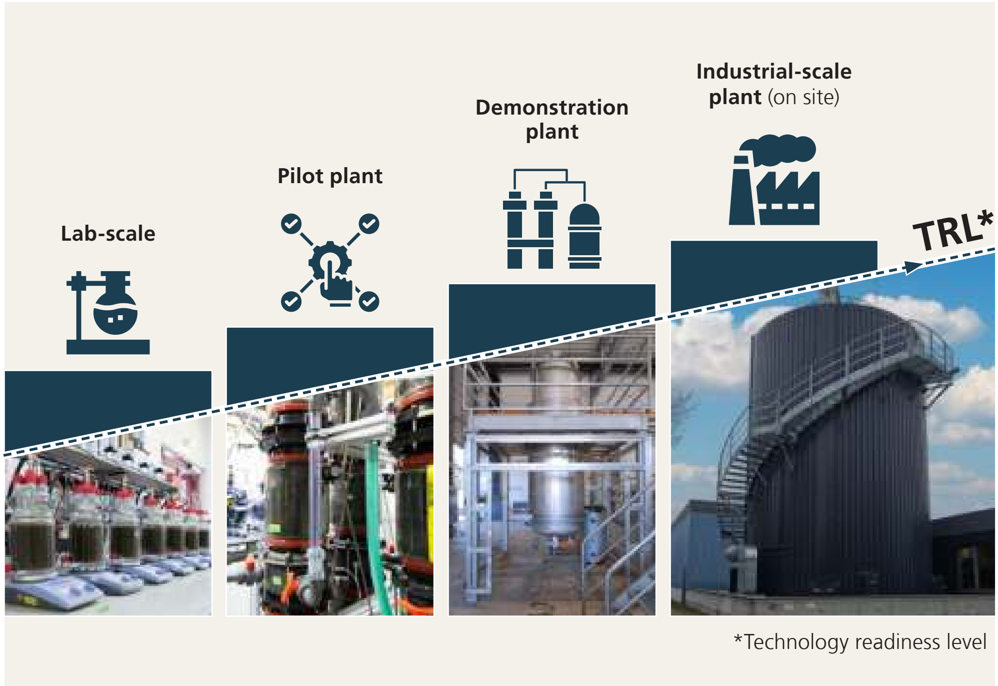
Development and scaling from pilot plant to industrial scale

Benefit from know-how and infrastructure

In our laboratories and technical centers, we investigate basic principles such as the torrefaction or fermentability of various biogenic residues and possibilities for recovering nutrients, and develop concepts for large-scale implementation.

Pilot and demonstration plants are available for some processes so that they can be used and tested either in our technical centers or directly on site at locations where waste is produced.

Our range of services also includes the planning, design and construction of pilot and demonstration plants for specific applications. For large-scale plants, the basic and detailed engineering is carried out by plant engineers from our industrial partners.



From laboratory to industrial scale: Newly developed processes are gradually transferred to a larger scale. Scaling up results in differently dimensioned plants, each with larger processing capacities.

How to work with us

Development and piloting on behalf of customers

We transfer processes to pilot scale.

- Selection of the most suitable equipment
- Process design for optimal integration of all process steps
- Optimization in terms of product yield and quality, material and energy efficiency
- Support up to implementation in the company/handover to a contract manufacturer or plant design

Examples

Cométha: Innovation partnership between SIAAP and Syctom for the treatment of organic waste and sewage sludge in the greater Paris area
The Cométha research partnership was set up to make the best possible use of the large quantities of waste generated in the greater Paris area. One of the consortia entrusted with researching and piloting the treatment of organic waste materials is a French-German consortium with the support of Fraunhofer IGB. The pilot plant uses an innovative combination of processes which achieves a significantly higher biomethane yield compared to conventional processes. In addition to biomethane production, the plant contributes to the recovery of important nutrients such as nitrogen and phosphorus. The pilot plant in Paris, which was realized with the significant contributions of Fraunhofer IGB, was officially put into operation in December 2024.

www.igb.fraunhofer.de/en/cometha

The Cométha pilot plant at Triel-sur-Seine near Paris

Funded research and development projects

We demonstrate new processes in a funded (joint) project.

- Identification of suitable grant initiatives and necessary partners
- Elaboration of project structures
- Coordination of joint projects as required
- Scaling in existing plants or conceptual design and new construction of dedicated plants
- Joint marketing and licensing with shared intellectual property

Selected current examples of cooperation in joint research projects (RoKKa, InBiRa, SmartBioH$_2$-BW, KoalAplan, BW2Pro, H$_2$Wood – Black-Forest) can be found on the following pages of this report.

Fraunhofer pilot plants as a bridge to implementation

You use our know-how and our pilot plants to optimize your processes.

We provide our pilot plants, some of which are mobile, for testing processes in our technical centers or on your premises.

- By working with us, you save on investments in your own pilot plants.
- The use of existing pilot systems saves you time, so that the market launch is significantly accelerated.
- You do not need to assign staff to operate the plants.
- We support you in identifying grant initiatives, for example as part of the "Industrial Bioeconomy" call for proposals from the German Federal Ministry for Economic Affairs and Climate Action (BMWK).

Torrefaction of lignocellulosic residues
A pilot plant for torrefaction with superheated steam (SHS) is available at Fraunhofer IGB for investigations into the energetic and material use of lignocellulosic biomass. The material to be dried or torrefied is introduced into the SHS atmosphere, where it is convectively supplied with heat. The volatile compounds released during torrefaction are recovered as a condensate fraction for further processing and use.

www.igb.fraunhofer.de/torrefaction

Fermentation of organic residues and pilot plant for high-load digestion at wastewater treatment plants
A reasonable way to utilize complex waste streams such as sewage sludge, liquid manure, biowaste or other organic residues is to digest the organic matter using high-load digestion. The process developed at IGB to increase the efficiency of sewage sludge digestion is characterized by a significantly improved efficiency, short retention times and a high degree of degradation compared to conventional digestion processes, combined with a significantly increased yield of biogas as a regenerative source of carbon and energy.

High-load digestion systems are individually dimensioned and designed with regard to their integration into the overall sludge treatment process of a wastewater treatment plant. For the successful implementation of a high-load digestion system, we investigate the digestibility, e.g. of the raw sludge, in high-load operation on a lab scale beforehand. If required, we can also implement the high-load digestion process on a pilot/demonstration scale at the wastewater treatment plant and operate it on site.

www.igb.fraunhofer.de/high-load-digestion

High-load digestion at the wastewater treatment plant Erbach

Recovery of nutrients
As the main components of fertilizers, nutrients are indispensable for global food production. Until now, they have been removed from the agricultural ecosystem with the harvest of crops. Not only liquid manure and fermentation residues, but also municipal wastewater and residues from the food industry are rich in nitrogen, phosphorus, potassium or calcium. Fraunhofer IGB has developed various technologies and processes to recover valuable nutrients from agricultural and municipal waste fractions and process them into plant-available fertilizers. We would be happy to investigate how nutrients can also be recovered from your waste materials.

- *www.igb.fraunhofer.de/nutrient-recovery*

Left:
ePhos®: encased magnesium ingot as sacrificial anode

Right:
The pilot plant for nitrogen recovery consists of four hollow fiber membrane modules arranged in parallel, which currently produce around 300 liters of process water per hour.

ePhos® – electrochemical process for the recovery of phosphorus
With ePhos®, the nutrients are precipitated in an electrochemical process as plant-available magnesium ammonium phosphate (MAP, struvite). Struvite is a high-quality slow-release fertilizer and can be used directly as a fertilizer in agriculture.

- *www.igb.fraunhofer.de/en/ephos*

Recovery of ammonium from wastewater
At Fraunhofer IGB, we are investigating the process of chemical transmembrane absorption as a new method for recovering ammonia from concentrated material flows for use as a fertilizer.

- *www.igb.fraunhofer.de/ammonium-waste*

Insect biorefinery pilot plant complex
For insect farming, IGB holds a permit from the regional council to use animal by-products (fish, meat) as a substrate for the insect larvae. We are happy to test waste and residual materials on behalf of customers or in groups with partners and investigate their usability by the larvae, analyze the primary fractions of fat, protein and chitin and convert them into fatty acid esters, biosurfactants, soaps, protein hydrolysates and chitosan.

- *www.igb.fraunhofer.de/insect-biorefinery*

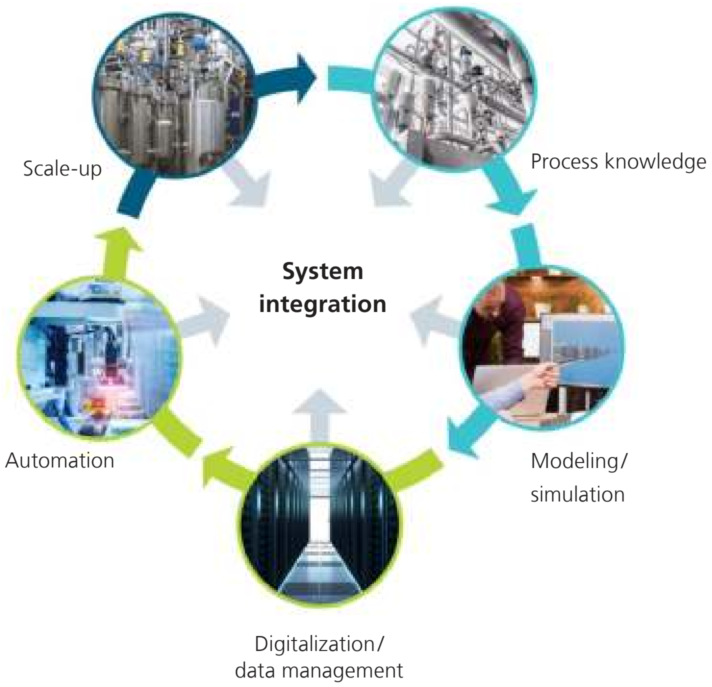
Optimization of the biological treatment of poorly degradable substances in industrial wastewater
Through targeted investigations, simulations and biotechnological approaches, we optimize biological treatment processes for the elimination of pollutants that are difficult to break down biologically under normal conditions. To this end, we initially investigate biodegradability according to OECD standards on a laboratory scale in order to identify initial measures for an adapted treatment strategy. We verify these on a larger scale (20 L, 200 L) in our sequencing batch reactors (SBR) and simulate the effects of the optimization measures on biodegradability.

- *www.igb.fraunhofer.de/persistant-substances-wastewater*

Digitalization of (bio-)process engineering plants

We optimize your processes through digitalization

We combine process knowledge with digitalization. We understand your processes and digitize your data for the cost-efficient optimization of your process management. We achieve this with initial data analysis, efficient data communication and simulation-based control using digital twins.



Digitalization in process engineering is creating the basis for far-reaching progress and new opportunities: Processes can be optimized through the intelligent networking of plants and systems via communicating sensor networks and the combined use of data analysis and digital twins. But that's not all: different process steps can also be seamlessly merged, integrated and automated.

However, in reality – from a digitalization perspective – many processes are still in the pilot phase. There are many reasons for this: the existing measurement technology and database are often separate data and isolated software solutions that cannot be integrated. In addition, communication between individual system modules is frequently still inadequate and important process data only displayed as a snapshot. Also, the introduction of digital and AI-based tools is time-consuming and requires process engineering expertise along the entire process chain in addition to IT skills for the implementation of system integration measures.

A large number of companies, especially SMEs, can hardly perform time-consuming and cost-intensive digitalization tasks due to limited capacities, a lack of skills and the simultaneity of various other challenges, meaning that the benefits that would result from process digitalization are still used far too rarely.

Example of a digitized plant

We transfer your processes to the digital world

At Fraunhofer IGB, we have been working for several years on projects to develop digital applications and integrate them into process engineering practice – also as a service provider for companies. We have extensive expertise in process technology and our know-how in modeling, simulation and data management. This enables us to provide companies with the best possible advice and support on the path to process digitalization and automation. You benefit from our many years of experience and expertise in automation technology, scaling, design and construction of process plants.

This enables us to support you along the entire development chain of a process – from research and development on a pilot plant scale to implementation in the technical, automated process with remote monitoring in real time.

Digitalization of your processes

Data structuring: We create the prerequisites for the application of AI in process technology
In order for analyzed process data to be used for the digital optimization and control of processes, it must first be made accessible to the respective users (process operators, planners, scientists).

To this end, we are creating an organized and process-oriented data structure at Fraunhofer IGB. This is a prerequisite for the use of any AI tools for data evaluation and modeling or simulation. Structuring the available data is therefore a fundamental milestone on the path to the digitalization of processes.

Data management: We ensure that your data communicate with each other and make it AI-enabled
Our main focus at Fraunhofer IGB is on integrated and process-oriented data management. To this end, we analyze your measurement data and ensure that all data is collected, integrated into the structure and can communicate with each other: The networking of a wide variety of data and protocol formats, automated transfer and backup of plant data (including offline data such as analytics data) create the prerequisites for smart process control and automation as well as efficient data processing (operational analysis, modeling etc.).

Our data management is cost-efficient, as it requires only a small amount of hardware and dispenses with expensive commercial solutions.

Optimization and automation of your processes

We optimize operational management through remote monitoring in real time

Thanks to the efficient data structure, the process data can be used simultaneously for visualization, automation and modeling tasks. We use it to visualize the process, for process optimization through operational analysis and for the development of innovative automation concepts. We use this knowledge to implement system monitoring and system control for your process as remote monitoring in real time.

We select the necessary sensors and actuators in such a way that the right data is collected to control the system. We also develop soft sensors to save costs for complex measurement technology, such as flow sensors. With the right programming, these can calculate the required data from measuring points that have already been collected.

> **"We understand your processes and use your digital data to optimize your operations cost-effectively. We combine process knowledge with digitalization."**
>
> **Dr.-Ing. Antoine Dalibard,**
> Group Manager Physical and Chemical Separation Processes

We also develop models, so-called digital twins, which we can use to program a simulation-supported control system in order to optimize your process. This makes it possible to vary process parameters dynamically, for example to minimize energy input or maximize product yield.

Plant planning: design and scenario evaluation through process simulation

We design your system with the required system components. To do this, we balance and model your processes using mass and energy balances. We rely on physical modeling methods, but also use AI tools or hybrid models if required. Using process simulations, we can predict the efficiency of your planned plant and thus increase the profitability of your project. Unpredictable parameters are often also crucial for the optimal operation of plants: different locations, seasons or weather conditions make it necessary to adjust the process control. This dynamic data can be incorporated into our calculations (MatLab/Simulink), enabling us to forecast models for various scenarios with our simulations.

Further information

www.igb.fraunhofer.de/process-digitalization

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Pilot plants for the demonstration of waste and wastewater biorefineries

Biorefineries can be used to recycle organic residues in a variety of ways. Apart from the raw materials used, the principle of a biorefinery is similar to that of an oil refinery, in which a complex raw material is separated into individual fractions or components.

Through the biotechnological, chemical, electrochemical or thermal conversion of residual materials according to the principle of a biorefinery, various value-creating products can be produced: Basic chemicals and biohydrogen, algae biomass and biochar, high-quality organic fertilizers and many more.

For the demonstration on a larger scale, various processes were combined for the first time in pilot plants and tested under real conditions. These pilot plants are available for use at Fraunhofer IGB so that the technologies and processes developed can be put into practice and wastewater and waste can be used as a source of raw materials.

European Regional Development Fund (ERDF) program "Bioeconomy Bio-Ab-Cycling" promotes the establishment of biorefineries

From October 2021, the Baden-Württemberg Ministry for the Environment, Climate Protection and the Energy Sector enabled five biorefinery projects with funding from the European Regional Development Fund (ERDF). The funding was provided as part of the initiative "Bioeconomy – Biorefineries for the recovery of raw materials from waste and wastewater – Bio-Ab-Cycling".
The IGB played a leading role in three of these five bioeconomy projects: In the InBiRa project, an insect biorefinery for the production of proteins, fats and chitosan was set up at the institute for the first time; the RoKKa wastewater biorefinery focused on using sewage sludge as a source of raw materials and improving the carbon footprint of wastewater treatment plants; and Smart-BioH$_2$-BW linked two biotechnological processes to produce biohydrogen and other products from industrial wastewater and residual waste streams.
Fraunhofer IGB was also involved in the BW2Pro project led by the University of Stuttgart to process biowaste into high-quality products and raw materials. In the other wastewater biorefinery KoalAplan, IGB researchers contributed their expertise to use municipal wastewater as a source of bioplastics.
All five projects were successfully completed in October 2024. In order to bring the developed technologies and processes into application, the infrastructure for upscaling is also available at IGB – up to industrial scale.

Project RoKKa converts sewage treatment plants into biorefineries

With the sewage treatment plant of the future to a circular economy

The RoKKa joint project coordinated by Fraunhofer IGB and Umwelttechnik BW has shown that sewage treatment plants can contribute to a municipal circular economy and climate protection. Seven pilot plants were operated at the sewage treatment plant of the city of Erbach (Danube) to recover phosphorus and nitrogen compounds for fertilizer production, to use CO_2 from the digester gas as a raw material for new products, and to reduce nitrous oxide emissions at the sewage treatment plant.

Sewage treatment plants clean our wastewater – in Germany, over 9 billion cubic meters per year. They not only remove organic impurities, but also large amounts of nutrients such as nitrogen and phosphorus. However, with conventional wastewater treatment, the important plant nutrients are lost: nitrogen compounds are converted into molecular nitrogen, which escapes into the atmosphere as a gas, using a lot of energy. Phosphorus is usually precipitated in the form of water-insoluble iron or aluminum phosphates, which are not available to plants, and disposed of with the sewage sludge – even though natural phosphate deposits for the production of fertilizers are becoming increasingly scarce.

After three years of research, development and operation, the project "RoKKa – Raw Material Source Sewage Sludge and Climate Protection at Sewage Treatment Plants" shows that sewage treatment plants not only treat wastewater, but can also contribute to a climate-friendly circular economy. At the Erbach (Danube) sewage treatment plant, ten project partners have piloted and tested forward-looking processes for recovering raw materials from wastewater over several months. A total of seven innovative demonstration plants were operated for this purpose, each of which can also be integrated as a stand-alone module into existing sewage treatment plants.

The results are also relevant in view of the entry into force of the revised Urban Waste Water Treatment Directive on January 1, 2025. According to this, stricter limit values for phosphorus and nitrogen elimination will apply in the EU in the future in order to further reduce nutrient discharges into water bodies.

In RoKKa, new processes for the recovery of raw materials from wastewater were piloted and tested over several months at the Erbach wastewater treatment plant.

Top:
Large-scale measurement of nitrous oxide emissions in the biological nitrogen elimination at the Erbach wastewater treatment plant

Bottom:
In the ePhos® pilot plant, phosphorus and nitrogen are recovered from the sludge liquor as magnesium ammonium phosphate (MAP).

Sewage sludge as a source of raw materials

RoKKa makes use of the established process of sewage sludge digestion, in which organic solids in the wastewater are fermented to produce biogas as a renewable energy source. Since 2016, a high-load digestion plant at the Erbach sewage treatment plant has been converting the sludge into biogas faster and more efficiently than conventional digestion plants. After digestion, the sludge is dewatered using a chamber filter press to reduce its volume. The filtrate from the dewatering process contains high concentrations of the plant nutrients phosphorus and nitrogen.

Increased energy consumption and nitrous oxide emissions due to nitrogen back-loading

Usually, the nutrient-rich filtrate from the sludge dewatering is fed back into the aeration tanks of the wastewater treatment plant; this back-loading accounts for 20 to 30 percent of the nitrogen inflow load of a wastewater treatment plant. Accordingly, it increases the energy consumption for the aeration of the biological treatment stages. In the aeration tanks, microorganisms consume oxygen as they convert not only organic substances into carbon dioxide (CO_2) and biomass, but also nitrogen compounds. The risk of back-loading is that the concentration of ammonium or nitrate in the effluent from the treatment plant increases, which in turn increases environmental pollution.

In addition, biological nitrogen removal leads to emissions of nitrous oxide (N_2O), which has an impact on the climate that is around 265 times stronger than that of CO_2. Using large-scale measurements, the University of Kassel has now been able to demonstrate in RoKKa that the recovery of nitrogen from sludge water and the resulting reduction in nitrogen back-loading into the main stream of the wastewater treatment plant can achieve a reduction in nitrous oxide emissions during biological nitrogen elimination.

The sewage treatment plant as a biorefinery

Since the higher the concentration of a substance, the better it can be recovered, RoKKa starts with the nutrient-rich sludge water. Instead of being returned to the aeration tank, the filtrate passes through various modules that can be used to turn sewage treatment plants into biorefineries.

Electrochemical phosphorus recovery with ePhos®

The first module is the ePhos® plant, a process module developed at Fraunhofer IGB for the recovery of phosphorus and nitrogen. With ePhos®, phosphorus is electrochemically precipitated as magnesium ammonium phosphate, also known as struvit. The magnesium required for this is added in an electrolytic cell via a magnesium sacrificial anode, which is gradually consumed in the ongoing process. The product struvite can be used as a regionally produced long-term phosphorus fertilizer in agriculture.

The pilot plant installed at the collective sewage treatment plant in Erbach was designed to treat approx. 600 L/h. This corresponds to half of the full flow of filtrate water that occurs at the treatment plant. For the first time, a new process was used to separate the crystallized struvite, in which the precipitated phosphate salts were scraped off a belt filter. However, due to the low phosphate concentrations in the influent, the precipitation efficiencies in RoKKa were lower than in previous pilot tests, where 80 to 90 percent recovery was achieved.

The experience gained from the RoKKa project shows that the prerequisite for the efficient use of the ePhos® process is the highest possible concentrations of dissolved phosphate in the sludge liquor. This is ensured by the operation of a biological phosphorus elimination (Bio-P) at the wastewater treatment plant.

Nitrogen recovery to ammonium sulphate fertilizer

In contrast to phosphorus, the filtrate water from the sludge dewatering in Erbach contained high concentrations of nitrogen. The approach investigated by Fraunhofer IGB in RoKKa involves recovering nitrogen as a fertilizer for use in agriculture by a process of chemical transmembrane absorption (Trans-Membrane ChemiSorption, TMCS).

The recovery process works on the principle of gas absorption with membrane contactors and is highly selective for nitrogen. For this, it is necessary that nitrogen in the water is converted to gaseous ammonia (NH_3). The higher the pH and temperature of the wastewater, the higher the proportion of gaseous ammonia. A hydrophobic membrane in the membrane contactor retains the liquid flow but allows gaseous ammonia to diffuse through its pores to the other side of the membrane. Here, ammonia is absorbed by sulfuric acid, producing an ammonium sulfate solution.

Ammonium sulfate can be used directly as a regional fertilizer. In the RoKKa pilot plant, the ammonium concentrations achieved in the product solution were initially still relatively low. However, it was shown that the ammonium sulfate solution can be further concentrated to obtain an economically viable product.

Electrochemical formate synthesis from CO_2

The digestion tank of a sewage treatment plant produces a gas mixture consisting of approximately 65 percent methane (CH_4), which is rich in energy, and about 35 percent carbon dioxide (CO_2). Using a new process from Deukum GmbH, CO_2 was separated using an amino acid solution and recovered using an electrodialysis device. What remains is highly pure biomethane that can be fed directly into the natural gas grid.

The carbon dioxide (CO_2) separated from the digester gas is a potential resource for carbon-based platform chemicals. One way to convert CO_2 into a valuable material using renewable electrical energy is the electrocatalytic conversion to formate, the salt of formic acid.

Microalgae in a novel photobioreactor system bind CO_2 and produce a plant-strengthening biomass.

In RoKKa, this process, which had previously been developed on a laboratory and pilot plant scale and with technical CO_2, was carried out for the first time with CO_2 obtained directly from the digester gas, and the target product formate was successfully produced in an aqueous solution. At around 45 g/L, the formate concentration was comparable to that obtained in previous pilot plant trials with CO_2 from the Fraunhofer IGB gas supply.

During the electrocatalytic CO_2 conversion, oxygen (O_2) is produced at the anode, similar to the case of electrolysis for hydrogen production. This oxygen often remains unused, but it can be used at the wastewater treatment plant to aerate the aeration tanks.

Microalgae cultivation: beta-glucan for plant strengthening

Microalgae are multitalented: through photosynthesis, they convert nutrient-rich process streams from the wastewater treatment plant and CO_2 from the digester gas into biomass

Top:
Since 2016, high-load digestion at the Erbach wastewater treatment plant has been supplying biogas and nutrient-rich sludge water – highly concentrated material flows from which recyclable materials can be recovered.

Bottom:
Nitrogen is recovered in the form of an ammonium sulphate solution.

and valuable storage materials. In this way, the CO_2 cycle was closed in RoKKa in addition to the nutrient cycle.

The project demonstrated microalgae cultivation in a novel flat-panel airlift photobioreactor system of Fraunhofer IGB with a volume of 125 liters. To do this, a process developed on a 6-liter laboratory scale was transferred to the new photobioreactor system with LED lighting. The photobioreactor system is equipped with a comprehensive sensor system for process control, which allows for partial automation. In addition to the filtrate water, which is rich in ammoniacal nitrogen, magnesium ammonium phosphate produced in the ePhos® module was added to supply the microalgae with nutrients. This was done to compensate for the low concentration of phosphate in the filtrate water and to achieve an optimal nitrogen to phosphorus ratio.

The microalgae strain used, *Phaeodactylum tricornutum*, produces plant-stimulating polysaccharides, known as beta-glucans, under defined process conditions. These can help plants to defend themselves against fungal infections such as downy mildew and, in the future, will partially replace chemical pesticides, for example in viticulture. Alternatively, the harvested algal biomass can be used to improve soil quality.

The carbon from approximately two kilograms of CO_2 is bound per kilogram of microalgal biomass produced. The electricity demand for microalgal production is the biggest cost driver of the process. In the RoKKa project, an energy requirement of less than 150 kWh/kg of produced biomass was achieved for the two-stage process investigated. In order to further increase the economic efficiency of the process, the aim is to achieve an energy requirement of less than 100 kWh/kg for the two-stage process used by further developing the reactor and lighting concept and adapting the process control.

RoKKa: successful update for the wastewater treatment plant

RoKKa impressively demonstrates how existing wastewater treatment plants can be modernized and made more sustainable in order to improve their carbon footprint and recover valuable raw materials. New approaches such as nutrient recycling not only reduce the use of fossil raw materials, but also energy consumption. At the same time, the implementation of nitrogen recovery processes avoids the climate-damaging nitrous oxide emissions caused by the back-contamination of ammonium in the aeration tank. Expanded into biorefineries, wastewater treatment plants make a valuable contribution to raw material security and climate protection, thus contributing to resilience and to achieving national climate and sustainability goals.

The aim now is to implement the project results on an industrial scale. For this reason, the Ulm-Steinhäule wastewater treatment plant was involved in the project from the outset. With a design capacity of 440,000 population equivalents, it is ideally suited for transfer to a larger scale. The construction of a high-load digestion plant is currently being planned. As a direct result of the RoKKa project, nitrogen recovery is also being considered in order to minimize the negative impact on the sewage treatment plant. Meanwhile, the individual process modules such as ultrafiltration, ePhos® and nitrogen recovery are available to interested sewage treatment plants for testing with real wastewater at Fraunhofer IGB or on site.

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InBiRa – the insect biorefinery

From the utilization of residual and waste materials to the production of chemical products

In the InBiRa project, an insect biorefinery was set up for the first time as a pilot plant in which organic residues and waste can be converted into new, technically usable products. The insect biorefinery approach is made possible by the larvae of the black soldier fly. These are fed on overstocked food, organic waste from gastronomy and organic waste bin and convert these into biomass during their development. The insect biomass is rich in fats, proteins and chitin, from which new secondary products can be produced.

Insect biorefinery pilot plant for utilization of all fractions

In the project, an insect biorefinery plant complex was planned, built and commissioned on the premises of Fraunhofer IGB, which includes all the necessary process steps. In the plant, the respective process steps, starting with the production of feed for masting the larvae (farming), through the separation of the fat and protein fractions (primary refining) and their conversion to the respective chemical intermediate product (secondary refining), were carried out and evaluated on a pilot scale.

To this end, the project team defined around 20 process units and designed the process engineering for the existing material flows. The process units include technical processes as grinding, sieving, pressing, drying, microfiltration, extraction, centrifugation and evaporation as well as several chemical reactors and a bioreactor for the conversion of the fats, proteins and chitin obtained.

Larvae of the black soldier fly

Waste processing, insect mast and primary refining

Initially, the waste and residual streams were processed in such a way that they could be efficiently utilized by the insect larvae. Challenges here included the seasonal variability of the organic waste bin, the unpacking of any packaged food returns, pesticide residues in fruit and vegetables from non-organic farming and discards (e.g. cutlery) from canteen waste. When preparing the feed, attention must also be paid to a balanced ratio of nutrients and water content. If there is too much water, the larvae can drown. Too much fat in the feed leads to phase formation and thus to poor and non-reproducible larval growth, and the separation of the larvae from the remaining substrate is also impaired later on.

Top:
Residual material streams can be utilized in the insect biorefinery.

Bottom:
Insect larvae on substrate

In a specialized mast container designed for the insect biorefinery, young insect larvae were then cultivated with the processed waste and residual materials, converting them into biomass. Here it was crucial to ensure good ventilation and climate control so that the larvae had the same growth conditions throughout the mast container and that the substrate had a suitable residual moisture content for further processing at the end of the mast.

The insect larvae that have grown on the waste and residual materials were first separated from the residual substrate by sieving during primary refining. The larvae were then inactivated and dried. The subsequent pressing of the larvae initially enables coarse separation into a fat and a protein fraction. The raw fat could then be purified in further process steps and refined for further use. The protein fraction, the so-called press cake, was chemically degreased further in order to contain the purest possible protein.

In addition to the refined fat and protein fractions, several residual fractions remain from the insect biorefinery: unutilized substrate and excrement of the larvae (frass), chitin-containing larval skins and adult flies. These residual fractions can also be converted into valuable raw materials in the course of secondary refining.

Secondary refining into intermediate products for fuels, cosmetics, cleaning agents, plastics and plant fertilizers

The project partners have each developed specific process steps for converting the three fractions from primary refining (fat, protein, residual fraction) into higher-value products, i.e. secondary refining.

The fat fraction could be converted by chemical or microbial conversion into precursor molecules for lubricants or fuels as well as biosurfactants or soaps for cleaning and personal care products. The particular advantage here is that the fat of the black soldier fly has a similar fatty acid composition to coconut or palm kernel oil due to its high lauric acid content and therefore offers a local alternative to tropical oils.

The protein fraction could be cross-linked in the future to produce composite materials for agronomy (e.g. degradable plant pots) or used as wood adhesives or coatings. Hydrolyzed protein is also used in cosmetics and personal care products.

The residual materials produced during the rearing, mast and processing of insect larvae were also utilized. The residual substrate mainly contains cellulose, insect excrement or larval exoskeleton products. While the larval exoskeleton products were investigated for isolating chitin or chitosan, the residual substrate, the so-called frass, was examined with regard digestion into biogas and the recovery of nutrients for fertilizer production.

Visit to the insect mast on the roof of Fraunhofer IGB in Stuttgart as part of the closing conference

"With our insect biorefinery, we can use biowaste from canteens and retail as raw materials for high-quality technical products. For the first time, we are tapping into a domestic source of medium-chain fatty acids, replacing fossil raw materials and contributing to climate protection."

Dr.-Ing. Susanne Zibek,
Group Manager Process Development

Insect fat and crushed dried insect larvae

Marketability and holistic assessment

The InBiRa project investigated the feasibility of manufacturing various products from the refined insect larvae of the black soldier fly. Discussions on the marketability of the new technologies with various user groups revealed great interest in a large-scale insect biorefinery for the utilization of biogenic waste streams. In addition, the entire production process was subjected to a comprehensive sustainability assessment and life cycle assessment.

Closing conference and outlook

At the end of the three-year project, the project consortium led by Fraunhofer IGB presented the project results and the technical modules of the established biorefinery at a closing conference on October 21, 2024. Finally, the participants from research, politics and potential users from the waste sector discussed the potential of the new technology as well as the challenges with regard to regulatory framework conditions and possible solutions in a panel discussion.

Even after the official conclusion of the project, which was funded by the Baden-Württemberg Ministry of the Environment, Climate Protection and the Energy Sector with state and EU funds, research on the insect biorefinery continues in order to be able to implement the developed process steps on a large scale in waste management.

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BW2Pro – Biowaste to Products

In the biorefinery of the BW2Pro project, one ton of biowaste was processed daily into high-quality products and raw materials.

The BW2Pro project supported the construction of a biorefinery demonstration plant on the site of the municipal biowaste fermentation plant of Abfallwirtschaft Rems-Murr AöR (AWRM) in Backnang, Germany. The aim was to optimize the recycling of municipal biowaste. To this end, processes were optimized and demonstrated on different scales in order to obtain products from renewable materials as well as secondary raw materials such as fibers, flower pots, fertilizer and biogas.

The focus of the working group led by Christiane Chaumette in the Fraunhofer IGB's "Water Technologies, Resource Recovery and Scale-up" department was the recovery of nutrients from the liquid digestate of the biogas reactor. Over several processing steps, phosphorus salts and ammonia were recovered from the digestate in order to produce components for a transportable complex fertilizer. The remaining nutrient-poor process water can be reused or used for irrigation.

The hydrolysate, rich in dissolved organic compounds like carboxylic acids, was obtained by treating biowaste under high temperature and pressure through a process developed by the project partner. This hydrolysate was then microbially converted into polyhydroxyalkanoate (PHA) biopolymers by Dr. Susanne Zibek's research group. The team successfully established and optimized a fermentation process that enabled microorganisms to produce PHA with a high valerate content, scaling up production to reactor volumes of up to 1 m^3.

Further information

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The polyhydroxyalkanoate biopolymer

Film made of polyhydroxyalkanoate

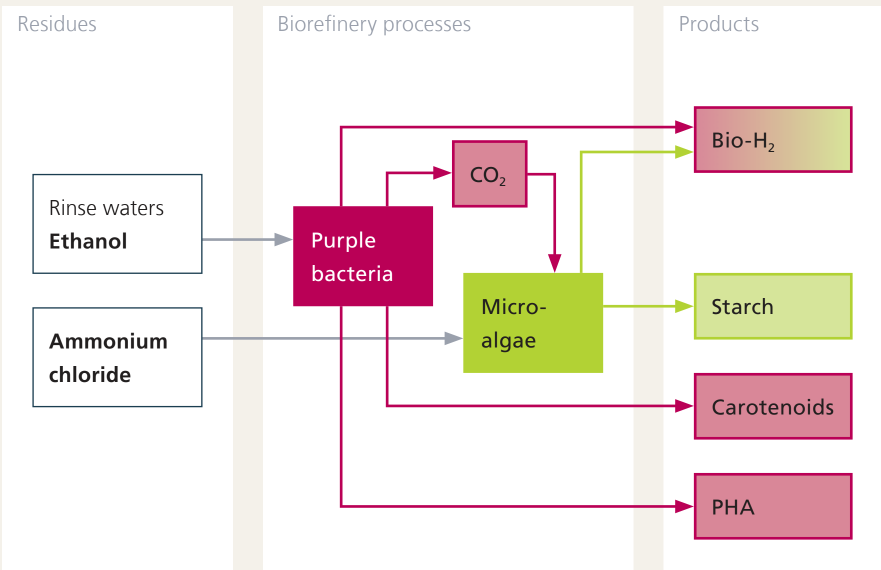
SmartBioH$_2$-BW

Integrated biorefinery and biohydrogen from industrial wastewater and residual material streams

The goal of the biorefinery project SmartBioH$_2$-BW was to integrate a biorefinery into an existing industrial environment. Using two interconnected biotechnological processes (purple bacteria and microalgae), biohydrogen and other bio-based products were to be produced from industrial rinsing water and residual material streams. In particular, the chemical industry generates by-product streams in many manufacturing processes, which are usually burned or disposed of in sewage treatment plants. Therefore, Evonik Operations GmbH in Rheinfelden was an associated partner in the project.

Green hydrogen and co-products from residual material streams

Hydrogen (H_2) is considered a key element in the energy transition. Processes using photosynthetically growing purple bacteria or microalgae to produce hydrogen have been studied for a long time. However, these have not yet been implemented on a larger scale. This is where the SmartBioH$_2$-BW project comes in. As part of the initiative, a biorefinery was developed based on two processes of biotechnological hydrogen production, which were interconnected in a demonstration plant at the Evonik Operations GmbH site in Rheinfelden.



In the SmartBioH$_2$-BW project, two interlinked biotechnological processes (purple bacteria and microalgae) are used to produce biohydrogen and other products such as carotenoids and biopolymers (PHA) from industrial wastewater and residual material streams.

Initially, purple bacteria are cultivated in a bioreactor under controlled microaerobic conditions. This process generates not only hydrogen from ethanol-containing rinsing waters but also usable carotenoids, the biopolymer polyhydroxyalkanoate (PHA), and CO_2 as a by-product. The second step is the so-called "Direct Photolysis": here, microalgae produce both hydrogen and oxygen from water using light energy. To maintain this reaction, IGB utilizes a new type of photobioreactor that can remove the oxygen produced during hydrogen production. To minimize CO_2 emissions from hydrogen production with purple bacteria, the CO_2 is fed into a coupled microalgae system, which produces usable products such as starch from CO_2, light, and the residual material stream ammonium chloride. The microalgae system is a compact photobioreactor illuminated by LEDs. Its special feature is its modular design, a high degree of automation, and a significant volume on a small footprint.

Bacterial hydrogen production: from laboratory to demonstration scale

With the help of the first process step, hydrogen production using bacteria, a previously unutilized ethanol-containing material stream could be tapped. To accomplish this, a fermentation was carried out in a 75-liter bioreactor in which the purple bacterium Rhodospirillum rubrum metabolized ethanol – with the help of sugars such as fructose – and produced hydrogen under so-called microaerobic conditions. Microaerobic conditions mean that by controlling the aeration and stirring within a bioreactor, the production of oxygen is limited so that the bacteria "work" exactly at the threshold between respiration and anaerobic fermentation.

To achieve the project goals, the first step in the actual implementation was to analyze the material stream generated at Evonik and evaluate it using growth trials and toxicity tests. This was to clarify in which concentrations the substrate could be used, as ethanol at high concentrations has a growth-inhibiting effect even for these bacteria. An optimal compromise between the maximum consumption of ethanol and still high growth rates turned out to be a substrate combination of ethanol and fructose, each at 15 g/L. Subsequently, the composition of the nutrient solution was optimized to further increase growth.

Building on this basis, the bacterial cultivation could then be transferred from the flask to a small laboratory-scale bioreactor. The laboratory reactor offered the advantage that growth and hydrogen production could be controlled by regulating various cultivation parameters, thus already showing parallels to scaling up to the demonstration scale.

In the bioreactor, the project team divided the process into two phases. Initially, the bioreactor was aerated with air, i.e., operated aerobically, because respiration in bacteria is more efficient in this case, achieving higher growth rates and cell densities. This, in turn, resulted in a more efficient process with higher hydrogen production rates. Subsequently, the air supply was limited, creating conditions under which the bacteria could produce hydrogen through microaerobic dark fermentation.

Since more bacteria also produce a larger amount of hydrogen, a feeding process was developed. During fermentation, new nutrients are gradually supplied to maintain a constant growth of the bacteria. It is important for the feeding solution that carbon sources like ethanol and fructose, nitrogen sources, trace elements, and vitamins are in the right ratio to prevent nutrient deficiencies, which could inhibit further growth. After comparing various concepts, the IGB researchers established a pO_2-dependent feeding profile. This involves measuring the partial pressure of oxygen (pO_2) in the fermentation medium. When the cells respire, oxygen is consumed and the partial pressure decreases. When ethanol and fructose are completely consumed, metabolism slows down, and less oxygen is consumed by the bacteria – recognizable by an increase in partial pressure, the so-called "hunger peak". Based on this hunger signal, researchers can recognize that substrate is lacking and can supply fresh nutrient solution so that the bacteria continue to grow. In the laboratory scale, a cell density of up to 34 g/L of bacterial dry mass was achieved.



Left:
The purple bacterium Rhodospirillum rubrum is facultatively phototrophic and can grow with light as well as with simple organic substrates as an energy source.

Middle:
Rhodospirillum rubrum in a 1-liter bioreactor

Right:
First experiments with Rhodospirillum rubrum under laboratory conditions in 1-liter bioreactors

In the microaerobic phase, the so-called microaerobic dark fermentation takes place, producing hydrogen. In respiration, oxygen is transferred as a so-called terminal electron acceptor. This allows the bacterium to regenerate central molecules for the respiratory chain and maintain respiration. However, if this oxygen is limited at that point, respiration is at risk of stopping. As a survival mechanism, purple bacteria then produce hydrogen. In this case, electrons can be transferred to protons and excreted as gas from the bacteria. To implement this functional principle in the bioreactor, the project first established reliable hydrogen analytics. Subsequently, it was assessed how different oxygen concentrations in the fermentation medium affect hydrogen yield. The hydrogen yield was maximized by adding additional nitrogen to the aeration air.

After establishing and optimizing both phases of fermentation at the laboratory scale, the next step was to implement the process into a biorefinery concept. During the transfer to the demonstration scale at Evonik in Rheinfelden, it was demonstrated that the construction of a biorefinery for climate-neutral hydrogen production is technically feasible through the successful coupling to the algae reactor and the hydrogen production from ethanol-containing material streams.

Through the establishment of the feeding process and the scale-up, hydrogen production could be increased by approximately five times compared to the laboratory scale. The result: Extrapolated over a month, up to 3400 L of hydrogen gas could be produced with fermentation at this scale. Particularly exciting was the finding that during hydrogen production, polyhydroxyalkanoates (PHA) were also formed, which made up to 54 percent of the bacterial mass. PHA are biopolymers and can be purified and used as biodegradable bioplastics for packaging and films. This opens an exciting perspective for obtaining even more valuable products within this biorefinery and making the process more profitable in the future.

Closed 50-liter stainless steel bioreactor for cultivating purple bacteria on a larger scale

Microalgae bind by-product CO_2

The goal was to establish a biorefinery that utilizes residual streams and CO_2 from the chemical industry, thereby connecting circular economy and hydrogen production. For this purpose, the project team selected the following microalgae strains: *Chlorella sorokiniana* and *Chlamydomonas reinhardtii*. Both can produce hydrogen under suitable conditions and accumulate starch as a storage product, thus serving as a potential fermentation substrate. Additionally, *Chlorella sorokiniana* is characterized by a high lutein content. However, due to current legal regulations, lutein obtained from residual streams of chemical production cannot be used in food or animal feed.

The project also investigated the toxicity of contaminants from chemical production in residual streams of ethanol-containing rinsing waters and ammonium chloride, which could affect the growth of the microalgae strains. It was found that both algae strains can utilize the residual streams. However, ethanol provides only a small additional biomass increase. Ammonium chloride can replace previous nitrogen sources, but additional pH control is required.

Another residual stream – CO_2 produced during the fermentative hydrogen production with *Rhodospirillum rubrum* – can be efficiently converted into starch-rich algal biomass by *Chlorella sorokiniana*. At the same time, ammonium chloride can be used for growth. The utilization of CO_2 and ammonium chloride was initially transferred to 6-L laboratory photobioreactors. In this scale, researchers investigated the key parameters of algal production: light input and biomass concentration. Depending on these two factors, biomass productivity in the reactor increases. The light yield, or the efficiency of converting light into biomass, remains high only up to a specific strain-dependent biomass concentration and light input and then decreases.

After establishing and optimizing this residual stream utilization at the laboratory scale, the next step was to transfer the process to the demonstration scale. The SmartBioH_2 demonstration plant that was set up for this purpose is a compact and modular photobioreactor system, illuminated with LEDs and characterized by a high degree of automation.

The conclusion: For the establishment of the biorefinery concept at the demonstration scale at Evonik Industries in Rheinfelden, it was demonstrated through the successful coupling of the algae reactor to the *R. rubrum* fermentation that residual streams and fermentation offgas streams can be utilized, and that the construction of a biorefinery for climate-neutral hydrogen production is technically feasible.

Hydrogen production via direct photolysis with microalgae

For hydrogen production using microalgae in the second process, a novel concept based on direct photolysis was chosen. By immobilizing the algae and using a special reactor setup, the oxygen produced as a by-product along with hydrogen by the algae is to be efficiently separated to a partial pressure of less than 100 ppm in the reactor gas volume. The continuous removal of oxygen to a very low oxygen partial pressure in the reactor is crucial for the functioning of the process. If the oxygen content in the system is too high, the extremely sensitive enzymes needed for hydrogen production are being oxidized.

After setting up the experiment in the laboratory, hydrogen was successfully measured in short-term experiments. However, the system has not yet been optimized. In particular, the method for immobilizing the microalgae still needs to be further developed. The chosen concept for hydrogen production with microalgae can be easily scaled up and is planned to be applied on a pilot scale.

In a second laboratory setup, the separation of oxygen from the gas phase was also successfully tested, using a known oxygen separation method. With this setup, it was possible to reduce the oxygen partial pressure to below the critical threshold for hydrogen production within a short time.

Opening the demonstration plant of the SmartBioH$_2$ biorefinery at Evonik in Rheinfelden on August 3, 2024 (from left): Marion Dammann (District Administrator of Lörrach), State Secretary Dr. Andre Baumann, Hermann Becker (Site Manager Evonik), Dr.-Ing. Ursula Schließmann (Fraunhofer IGB, Deputy Director, and Project Coordinator)

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KoalAplan

Valorization of municipal wastewater into bioplastics

The biodegradable plastic polyhydroxyalkanoate (PHA), produced from organic acids

Valorization of wastewater as a resource into new valuable and sustainable products was the main goal of the KoalAplan project. At the University of Stuttgart's wastewater treatment Research plant in Stuttgart-Büsnau, the particulate organic carbon in municipal wastewater, which is obtained by sedimentation in the pre-treatment stage, was to be separated and converted into a high-quality product. At the same time, ammonium is recovered from the particle-free wastewater, which can be used as a nitrogen fertilizer for agriculture.

From the particulate organic carbon or the primary sludge, a hydrolysate rich in organic acids was produced by the project partners via anaerobic decomposition.

The main objective of Fraunhofer IGB was the fermentative conversion of this acid rich hydrolysate into polyhydroxyalkanoate (PHA), a biodegradable bacterial polymer.

New process control strategy: perfusion with cell retention

The hydrolysate, which contains many volatile fatty acids (VFAs), could be used by the microorganisms as a carbon source to produce PHA, but they are toxic in higher concentrations. Therefore, it was not possible to carry out a simple batch process. Instead, the VFAs had to be added continuously and the volume in the reactor removed again in parallel. Our established perfusion method with cross-flow filtration made it possible to retain the cells in the reactor and continuously feed with fresh hydrolysate.

Microbial production of PHA from acid hydrolysate

PHAs are thermoplastic biopolymers that can be produced by various microorganisms from a wide range of substrates. Many microorganisms exhibit increased toxicity towards organic acids. The aim of our work in KoalAplan was initially to identify suitable PHA producer strains that can utilize the organic acids in the hydrolysate for their growth and the production of PHA and to establish PHA production on a pilot scale.

Cupriavidus necator proved to be the more tolerant bacterium for organic acids compared to the other tested bacteria and is a suitable bacterium for the production of PHA from organic acids in the hydrolysate. A new process control strategy was developed to prevent the growth inhibition of organic acids on the microorganisms: a perfusion process with cell retention. With the process we developed, 97 percent of the carbon was removed and approximately 20 percent of that was fixed as PHA. This new process serves as a basis for utilizing various substrates with low concentrations for the production of PHA.

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H_2Wood – BlackForest

Production of biohydrogen from wood waste

The Black Forest region wants to use wood waste as a local resource for the decentralized production of biohydrogen as a renewable energy source. To this end, the H_2Wood – BlackForest project, funded by the German Federal Ministry of Education and Research (BMBF) and coordinated by Fraunhofer IGB, is investigating the potential of wood waste for the biotechnological production of hydrogen and its use as an energy source. The production of biohydrogen is to be demonstrated in an integrated pilot plant at Campus Schwarzwald.

A plant concept for the process engineering of producing biohydrogen from wood waste using biotechnological processes is being analyzed and evaluated as an alternative to thermochemical processes. The first step consists of shredding the waste wood (scrap from house demolition or pallets and window shutters etc.) and separating impurities (e.g. iron nails from pallets) by means of sieving. The coarse cuttings of the waste/scrap wood are then boiled in a pressure reactor with solvent, which allows components such as lignin, adhesives and varnishes to be dissolved. The remaining cellulose-rich fiber can be fractionated and hydrolyzed enzymatically, yielding sugars that can be concentrated and used in our fermentation process.

To convert the sugars extracted from the wood into biohydrogen, two bioprocess modules are being investigated and combined at Fraunhofer IGB. One relies on hydrogen-producing bacteria, e.g. anaerobes such as *Clostridium* sp., which metabolize the sugars into hydrogen. In addition, the metabolic products CO_2 and organic acids are generated, which are used as substrates for microalgae. These convert them into starch and carotenoids as co-products. In a second step, the microalgae release additional hydrogen via direct photolysis in a completely new type of reactor.

The modules of the pilot plant complex were already set up and tested at Fraunhofer IGB in 2024. Planning for the installation at the Campus Schwarzwald is progressing well. The plant is scheduled to go into operation in summer/autumn 2025. This will pave the way for demonstrating the biotechnological production of hydrogen on a larger scale for the first time.

Waste wood treated with wood preservatives currently has to be incinerated in approved large-scale power plants. In H_2Wood, hydrogen, carotenoids and starch are produced from it.

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"

Bio-based building blocks not only help in the defossilization of chemistry. They are also easily accessible and highly functional, enabling innovative leaps towards green materials with new functional properties."

Dr. Michael Richter
Head of Department Bioinspired Chemistry

Biopolymers – material building blocks of the future

New raw materials and technologies for bio-based plastics

Whenever we touch something around us in our everyday and working lives, it is likely to be a synthetically produced material that contains polymers. In order to maintain and improve our standard of living and at the same time make the production and availability of high-performance materials more resource-efficient and climate-friendly, there is no alternative to the constant development of new materials based on the principles of sustainable chemistry.

For the wider use of bio-based polymers in various applications, innovations along the entire value creation cycle are essential, from raw material extraction to processing and recycling. This is the only way to catch up with the economic and technical lead of conventional fossil-based plastics and to accumulate and establish bioplastics on the market and create acceptance for their unique advantages.

We combine biology and engineering, inspired by nature

One approach being pursued at Fraunhofer IGB is to draw on solutions from nature and use them for technological applications. This refers to the world of natural polymeric material building blocks from nature, so-called biopolymers. The key here is that such natural or modified biopolymers can not only replace fossil raw materials, but can also be used in a context other than the biological one due to their matching chemistry and material properties and thus offer functional advantages over fossil-based solutions.

The synthesis of bio-based polymers is, so to speak, the embodiment of the principles of Green Chemistry. The approach is also in line with an acatech position paper *Impulsgeber Natur – Innovationspotenzial biologisch inspirierter Materialen und Werkstoffe* and the core objectives of a circular bioeconomy. The strategy also serves to biologize materials chemistry and drive forward the defossilization of the chemical industry.

Based on the innovation chain for the production of biopolymers and bio-based plastics as well as selected examples from our institute, the following will show how we support companies in the necessary change in the raw material base and what potential is hidden in biopolymers.

Biopolymers, bio-based polymers, bioplastics

Biopolymers
Biopolymers are, in the original sense, polymers that occur in living nature, i.e. are produced by organisms. These include proteins, nucleic acids, polysaccharides and the lignin contained in wood, one of the most common organic compounds on earth. Besides this, microorganisms synthesize polymers from organic acids (e.g. polyhydroxyalkanoates, PHA) as storage materials.

Bio-based polymers
The production of monomers (including non-natural bio-based monomers) and their polymerization can also take place chemically or biotechnologically, outside the cell. To distinguish them from the above-mentioned biogenic polymers (or native biopolymers), they are referred to as bio-based polymers. An example of this is polylactide (PLA). It is produced from lactide, which is obtained from lactic acid (lactate) synthesized by bacteria.

Bioplastics
Bio-based plastics, or bioplastics for short, consist largely or entirely of renewable raw materials.

Political framework conditions will increase demand for bio-based polymers

The need for alternative solutions for fossil-based materials and chemicals is likely to become even more important in the coming years as new legislation comes into force. First and foremost, this concerns the European Union's new Packaging Waste Regulation (PPWR), which will take effect from 2028. In this regulation, the EU requires producers to drastically reduce the volume of packaging waste. The regulation also sets specific recycling targets and, for the first time, includes an obligation for certain forms of packaging and materials to be compostable.

The next EU Fertilizer Regulation (FPR), which will gradually come into force from 2024 to 2028, also aims to increase the demand for biodegradable products and materials. Specifically, this concerns biodegradable mulch foils, coatings and water-retaining polymers. The amendment to the German Wastewater Ordinance from 2024 also needs to be considered, which will have an impact on the textile sector – for example, the washing out of textile coatings – and the use of flocculants in wastewater treatment.

Principles of green chemistry

- **Prevent waste**
- **Maximize atom economy**
- **Design less hazardous chemical syntheses**
- **Design safer chemicals and products**
- **Use safer solvents and reaction conditions**
- **Increase energy efficiency**
- **Use renewable feedstocks**
- **Avoid chemical derivatives**
- **Use catalysts, not stoichiometric reagents**
- **Design chemicals and products to degrade after use**
- **Analyze in real time to prevent pollution**
- **Minimize the potential for accidents**

Our solutions for sustainable bioplastics

At Fraunhofer IGB we are researching developments with different biopolymers. These include polysaccharides such as cellulose and chitin/chitosan, polyesters such as polyhydroxyalkanoates (PHA), polyamides such as proteins and complex polymer networks such as lignin. For the technical production of biopolymers, we finally use the synthesis capabilities of nature. The resulting biopolymers are then isolated from biomass, purified and, if necessary, modified for applications (e.g. PHA, chitin/chitosan, lignin, proteins).

We also obtain monomers biotechnologically, which can be converted into the target biopolymer (e.g. polymalate) by means of further steps.

Furthermore, we are researching bio-based polymers such as caramides (terpene-based polyamides) or polyethylene furanoate (PEF) as a potential PET substitute, which contains the promising polyester building block furandicarboxylic acid (FDCA). Such polymers all contain bio-based monomer building blocks.

The raw material base for biopolymers and bio-based polymers

Nature offers a broad repertoire for the biosynthesis of polymers. Depending on the organism, different raw material sources can be used. Plants and microalgae use carbon dioxide to build cellulose or starch by means of photosynthesis. Bacteria that store PHA prefer to use organic substances.

At Fraunhofer IGB, we utilize the entire spectrum of nature's synthesis potential for the production of biopolymers and bio-based polymers. This enables us to use a wide variety of raw materials such as CO_2, biogenic raw and residual materials and, as recently demonstrated, even biogenic waste materials (see pages 44 and 50).

One main focus is on the renewable raw material wood, including all its components, as well as lignin-containing biomass from agricultural side streams, such as wheat straw. To pulp lignocellulose, the component of the cell wall of woody plants, we use new processes such as organosolv fractionation, in which the lignin is solubilized using organic solvents, e,g. on our pilot plant at Fraunhofer CBP in Leuna. Expanding the raw material base for plastics to CO_2 is another goal that we are actively pursuing.

By using renewable, sustainably produced raw materials as well as biogenic residual and waste materials to produce polymers, we are contributing to the transition to a sustainable economy without fossil raw materials.

Laboratory for Technical Biopolymers – LTBP

In this project, which is funded by the Bavarian State Ministry, we cover the entire value chain of bio-based materials: from the identification of suitable starting materials to functionalization, polymerization and additivation through to recyclability and biodegradability. This makes us a competent partner for regional and national industry and research on the subject of biogenic plastics.

- *www.igb.fraunhofer.de/en/ltbp*

Our technologies for the production and modification of biopolymers

In order to be able to replace fossil-based polymers with biopolymers in the future, existing processes must be optimized, new efficient processes must be established and these must be combined into holistic value creation cycles.

By researching different raw material utilization paths and various synthesis strategies, we at Fraunhofer IGB are able to produce various chemical intermediates for polymer synthesis based on biomass. This takes place, for example, via innovative biotechnological or chemical conversions of biomass components such as carbohydrates or lignin. The spectrum ranges from so-called drop-in compounds, i.e. molecularly identical products, to bioplastics with partially new property profiles, e.g. polylactic acid and other bio-based polyesters. We are also contributing to the development of novel bio-based plastics at Fraunhofer IGB by designing and optimizing processes for the purification of the various bio-based monomers and biopolymers.

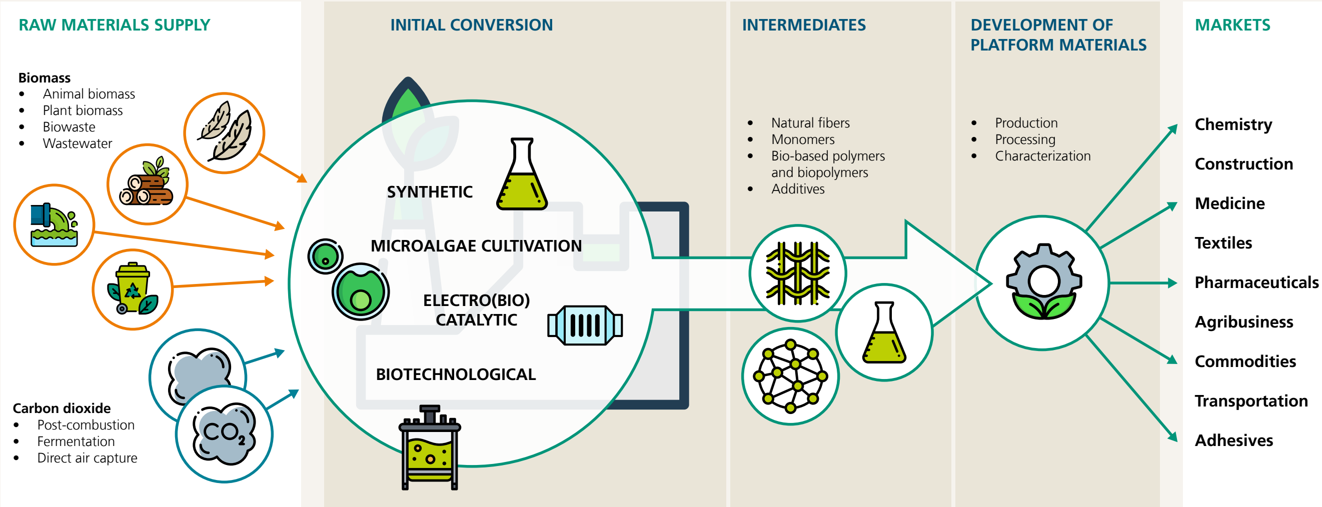
In the course of the further value creation cycle, the chemically or biotechnologically produced polymer can then also be combined with other polymers or additives in order to tailor the material properties for the subsequent plastic components. Examples include plasticizers, flame retardants, stabilizers, but also (natural) fibers or bio-based carbon fibers. After compounding – i.e. mixing – the bio-based plastics can then be processed into films, molded parts or components. In principle, all conventional processing technologies for traditional fossil-based plastics can be used, although the material properties of bio-based plastics usually require specific adaptation of the process parameters.

Biopolymers such as gelatine or chitosan can also be easily functionalized in order to adapt their properties to the respective applications. We use chemical cross-linking technologies to create tissue-like hydrogels. Through controlled cross-linking, we obtain hydrogels with adjustable mechanical and biological properties. Hydrogels play a role in a considerable number of biotechnological developments or applications in medicine, e.g. for membranes, implants, biosensors or tissue engineering.

At IGB we are working on improving technologies for the production and modification of biopolymers and testing, evaluating and optimizing new polymer building blocks with regard to their material properties and economic production.

Processing

Alongside the development of new bio-based materials, the question of compatibility with traditional material processing techniques arises for industrial and technical applications. Initial fundamental investigations into the processing of new bio-based plastics and materials, for example by means of extrusion and injection molding, are an integral part of our development work. Processing on a very small and small scale is primarily used to advance the development of new bio-based materials not only in terms of application and properties, but also in terms of processability.



The use of biopolymers follows the classic bioeconomy innovation chain of i) raw material supply, ii) conversion and iii) development of platform materials for product development or for functional integration into products.

Material characterization and testing

In addition to evaluating the processing parameters, a broad downstream method platform is available for standardized testing and analysis of the newly developed materials. This includes rheological, dynamic-mechanical and various thermal analyses.

Besides material characterization, it is important to analyze the materials with regard to desired or known effects, e.g. antimicrobial properties, but also to unexpected adverse effects on humans, which concern both toxicological and immunological aspects. Various cell-based test systems are available at IGB for this purpose, which are suitable for a variety of test procedures such as bioactivity, cytotoxicity and immunogenicity tests or the testing of antimicrobial properties.

Compared to ethically questionable and only partially transferable animal experiments and limited biochemical test methods, such cell-based test systems known as New Approach Methods (NAM) realistically simulate the in-vivo situation and enable the direct analysis of a cell reaction. The Department of Cell and Tissue Technologies at IGB offers a broad portfolio of specific in-vitro model systems, ranging from simple high-throughput cell assays to complex organoid systems and macroscopic, complex 3D tissue models. The core technology is the targeted development of cell-based reporter test systems for the simple and rapid determination of specific endpoints, such as toxicity or sensitization.

Three-dimensional in-vitro model of human skin as a NAM test system

Large-scale technical facilities at Fraunhofer CBP for scale-up

Scaling and production of sample quantities

An essential step on the way from the laboratory to industrial-scale implementation is the production of sample quantities on a pilot scale. With our know-how, experience and technical equipment, we at Fraunhofer IGB are able to optimize developed processes on our pilot plants in terms of economy and efficiency and to provide product samples on a gram to kilogram scale for polymerization and application tests. The pilot plants at the Fraunhofer Center for Chemical-Biotechnological Processes CBP, our institute branch in Leuna, are also used for this purpose.

One example is polyhydroxyalkanoates (PHA), which are produced by some bacteria as natural storage substances and can be produced from a variety of waste materials. Large-scale purification is currently still very cost-intensive. By selecting suitable production strains and establishing a new process management strategy, we have currently succeeded in obtaining a high-quality PHA copolymer with a 3-hydroxyvalerate content of approx. 10 percent from waste streams (see page 50).

End-of-life scenarios: recycling and biodegradability

In order to achieve maximum carbon recycling and minimize the need for fossil carbon, our aim is to integrate new value creation processes into existing and future material cycles. This also includes life cycle analysis (LCA).

After a component has been used, at the end of its product life cycle, the material should be returned to the value creation cycle through a recycling step. Depending on the bioplastic, there are different ways of doing this: in the case of mechanical recycling, the polymer is recovered directly; in chemical recycling, it is first broken down into small building blocks, which can then be used again for polymerization, thus closing the cycle.

Many bio-based plastics such as starch, PHA and PLA are also biodegradable. Through biodegradation, they return to the carbon cycle in the form of CO_2 without contributing to littering the biosphere. However, the directly and consciously controlled biodegradation pathway as an end-of-life scenario should only be envisaged for those product categories where emissions into the environment cannot be avoided (e.g. various products such as mulch films in agriculture or "liquid" plastic, e.g. in cosmetics) or where reuse and recycling are not practicable.

Further information

www.igb.fraunhofer.de/biopolymers-building-blocks

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Biopolymers and bio-based polymers

Our monomers, polymer products and potential applications

Plastics are often still produced synthetically on the basis of crude oil. If they are disposed of by incineration at the end of their use, this is associated with high CO_2 emissions. Due to the climate crisis, there is an urgent need to use climate-friendly resources. Bio-based plastics represent a sustainable alternative in this context: They help to achieve climate and resource protection goals, but also to reduce dependence on foreign production sources and increase the resilience of value chains.

In addition, environmental aspects such as the pollution of the world's oceans by plastic are an urgent problem of our time. The biodegradability of plastics is an important factor, especially when plastics are required for direct use in the environment (e.g. agricultural foils). The biocompatibility of plastics plays an important role in medical and cosmetic applications.

Fraunhofer IGB is making a decisive contribution to the development of new plastics derived from biological sources. Our range can be categorized into three types of polymer: polymers from bio-based monomers, microbially produced biopolymers and other native biopolymers. In the following sections, some examples from our institute will be shown and the specific end products and possible applications will be presented.

Biopolymers and bio-based polymers

Polymers from bio-based monomers (bioplastics)

- Lactic acid (**PLA**)
- Malic acid (**PMA**)
- Long-chain dicarboxylic acid (**lc-DCA**)
- Furan dicarboxylic acid FDCA (**PEF**)
- **Caramides** (terpene-based polyamides)

Microbial polymers

- Polyhydroxyalkanoate (**PHA**)
  - **PHB** (Polyhydroxybutyrate)
  - **PHA copolymers**
  - **mcl-PHA**

Native polymers

- Lignocellulose (cellulose, lignin)
- Alginate
- Chitin/chitosan
- Plant and animal proteins from technical processes

Polymers made from bio-based monomers

The production of bio-based polymers first requires the next smallest components, the monomers. Fraunhofer IGB can produce these biotechnologically by means of fermentation – also from residual and waste streams, in line with the sustainable circular economy that IGB is striving for. In the next step, the monomers are polymerized chemically or biologically, depending on the process used.

PHA and biomass containing PHA

Bio-based hydroxy and dicarboxylic acids as monomeric building blocks for bioplastics

At Fraunhofer IGB, we use various fermentative processes to produce hydroxycarboxylic acids and dicarboxylic acids from biogenic waste streams. Our portfolio includes malic acid, itaconic acid, xylonic acid, long-chain dicarboxylic acids (lcDCA) and lactic acid, which can be polymerized in downstream processes.

When using bio-based carboxylic acids, the desired polymer properties can be achieved not only via the monomer itself, but also via the polymerization conditions. Although the process development, taking into account the substrate, its feed or the microorganism, has no influence on the properties of the target molecule, it is decisive for product concentration and conversion efficiency. In the case of xylonic acid, we were able to achieve titers of over 300 g/L.

Together with project partners, we are also working on the fermentative production of enantiomerically pure malic acid, its further purification and the subsequent production of polymers. Homopolymers of racemic malic acid are water-soluble, biocompatible and biodegradable, but at the same time hard and brittle. In the Malum project, novel biopolymers with higher elasticity and toughness were produced by functionalizing or copolymerizing malic acid with other monomers. Initial application tests have shown that these polymers can be used as laminating adhesives.

▸ *www.igb.fraunhofer.de/biopolymers*

Polymers made from bio-based furanoates as a substitute for PET

One very widely used plastic is PET: polyethylene terephthalate. This fossil-based or partially bio-based plastic is used in large quantities for the production of packaging materials, among other things. The term "PET bottle", for example, is familiar to the public at large. This is why PET is also the focus of the IGB's scientists. At the institute, they are researching the development of a bio-based PET substitute: polyethylene furanoate (PEF), made from bio-based ethylene glycol and furan dicarboxylic acid (FDCA). PEF can be used as packaging material, but also as bio-based fibers. FDCA production is particularly sustainable, as it is carried out using agricultural and forestry waste. In the projects "PFIFF/PFIFFIG – polymer fibers from bio-based furanoates for industrial applications", IGB was able to further develop this production process for use on a large scale in industry.

▸ *www.igb.fraunhofer.de/en/pfiff-pfiffig*

Monomer building block long-chain dicarboxylic acids (lcDCA) and plant oil-based epoxides

Another natural starting material for plastics production that is being investigated at IGB is plant oils. These contain bi- and polyfunctional synthesis building blocks. The oils and plant oil derivatives can be converted into interesting monomer building blocks such as long-chain dicarboxylic acids (lcDCA) or plant oil-based epoxides through appropriate functionalization.

The long-chain dicarboxylic acids serve as a bio-based alternative for the production of plastics, which are usually produced on the basis of starch, cellulose and polylactic acid (PLA). They are used, for example, in the production of polyamides and polyesters. Plant oil-based epoxides, on the other hand, can be used as PVC stabilizers, plasticizers, for the synthesis of bio-based resins and coatings or, after further conversion, as components of lubricant formulations.

www.igb.fraunhofer.de/en/lcdca

Caramid-R® and Caramid-S® – novel polyamides from terpenoid waste streams

Another research focus is on monoterpenes – biomolecules that are produced by a wide variety of plants, microorganisms and fungi with a high degree of structural diversity. They can also be obtained primarily from industrial waste streams, for example from the paper and juice industry. These are potentially suitable as a starting material for bio-based plastics because they can be modified using common chemical processes, have a low heteroatom content, a molecular size that is comparable to petrochemically produced monomers and a molecular structure that endows them and the corresponding polymer with special properties.

Two specific polymers made from terpenes developed by Fraunhofer IGB are the polyamides Caramid-R® and Caramid-S®. Here too, Fraunhofer IGB is using a sustainable resource, as the terpenes are a by-product of cellulose production. The IGB scientists first synthesize lactams from the monoterpene (+)-3-carene using a patented process. These are then polymerized to Caramid-R® and Caramid-S®.

Due to their special chemical structure, these polyamides have exceptional thermal properties that make them interesting for numerous areas of application, ranging from mechanical engineering – such as for gear wheels – to safety glass, polyamide foams and safety textiles through to use as surgical suture material. Caramid-R® and Caramid-S® are now being further developed as part of the SuBi²Ma flagship project at the Fraunhofer institutes IGB, IAP, ICT, LBF, IWM and ITWM (see page 66).

www.igb.fraunhofer.de/terpenes

Top:
Plant oils as a basis for plastics production

Bottom:
Industrial waste streams, such as from the paper industry shown here, are suitable as a starting material for bio-based plastics.

Microbial biopolymers

Researchers at IGB utilize microorganisms for biotechnological polymer production, primarily focusing on polyhydroxyalkanoates (PHA). Microorganisms produce this polymer as a carbon storage under certain stress conditions – specifically: nutrient deficiency and excess carbon.

Due to their biodegradability, PHAs are particularly suitable use in agriculture, e.g. as foils.

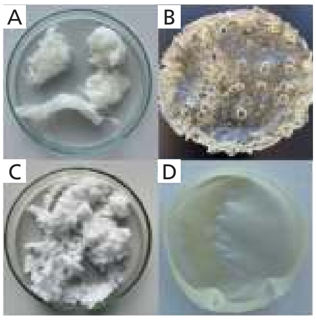
Polyhydroxyalkanoates – various PHA variations available

The microbial synthesis of PHA offers significant advantages due to the numerous adjustable parameters in the production process, allowing for the production of biopolymers with specific thermal and mechanical properties. There is a vast array of microorganisms and substrates that can be combined, along with various optimization options available within the bioprocess itself. This flexibility enables the precise variation of PHA composition.

Despite these variations, all PHAs share a common trait: they exhibit high biocompatibility and biodegradability, making them ideal candidates for applications such as packaging (e.g. disposable plastic bottles for non-food items), medical implants, and agricultural films.

Fraunhofer IGB possesses extensive expertise and years of experience in PHA production, enabling the institute to produce different PHA variants, especially PHBVV copolymer (poly-3-hydroxybutyrate-co-3-hydroxyvalerate-co-4-hydroxyvalerate) with varying valerate contents, tailored to specific application requirements. The IGB researchers also focus on sustainable substrates sourced from residual and waste streams, including waste cooking oil, volatile fatty acids from wastewater treatment, and crude glycerin. Additionally, larger sample quantities are produced at the institute's scale-up facility in Leuna, Fraunhofer CBP.

- *www.igb.fraunhofer.de/en/pha*



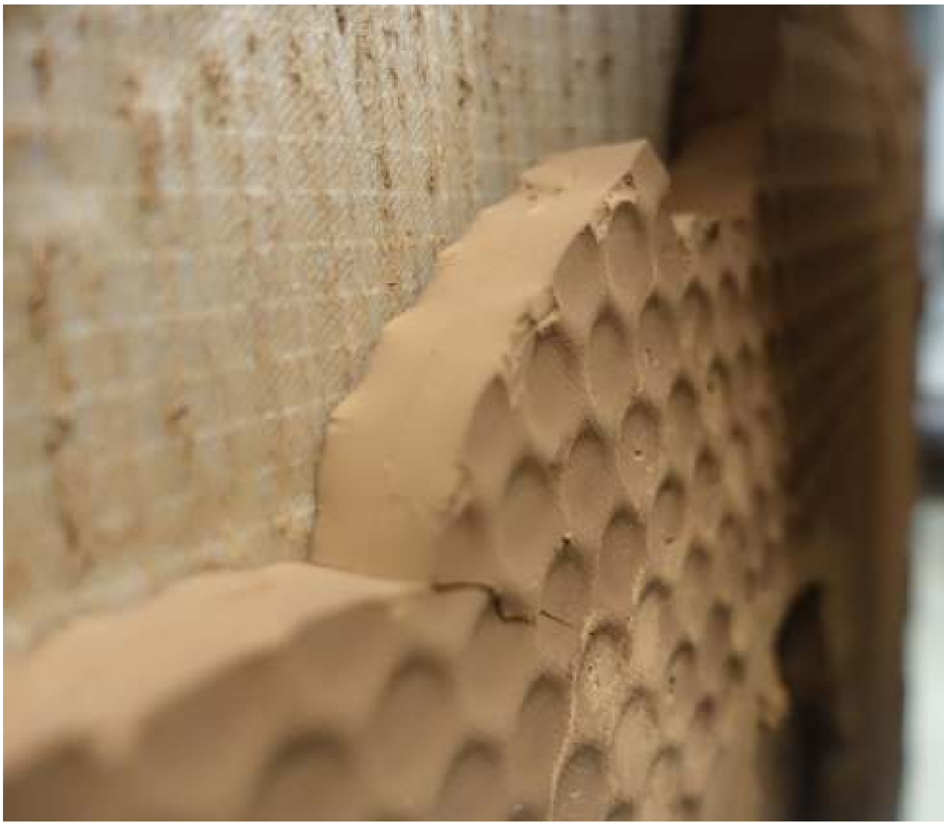
Various PHA: A and B: medium-chain PHA, C: PHBVV copolymer, D: PHBVV film

European Regional Development Fund (ERDF) program: Baden-Württemberg and the EU support the development of biorefineries

IGB's biorefinery projects are also of central importance here. Biomass is converted in biorefineries and thus developed as a raw material. The Baden-Württemberg Ministry for the Environment, Climate Protection and the Energy Sector has funded five such projects with EU funding from the European Regional Development Fund (ERDF) program "Bioeconomy – Biorefineries for the Recovery of Raw Materials from Waste and Wastewater – Bio-Ab-Cycling" (from page 36 onwards). PHA was also one of the valorization products in two of these projects. In the "KoalAplan" project, municipal wastewater in sewage treatment plants was converted into PHA, while in the "BW2Pro – Biowaste to Products" project, IGB valorized the biowaste into biodegradable bioplastics.

Native biopolymers

Polymers also occur naturally in the environment. Examples here are plant components such as lignocellulose, from which lignin and cellulose can be obtained, but also substances of animal or fungal origin, such as chitin or its derivative chitosan, which we obtain from crab shells, insect exuviae or residual material streams from industrial fermentation. We at Fraunhofer IGB are also working on the development of proteins as a raw material for technical products, for example the use of animal protein residues (feathers, wool) or insect protein, which is obtained from biowaste using our insect biorefinery (see page 41).



Lignin separation by filter press at Fraunhofer CBP

Lignocellulose – residue from woody plants

Lignocellulose is the structural material in the cell wall of all woody plants and the main component of residual materials such as straw or wood – and is therefore available on a large scale, for example from agriculture and forestry. At IGB, it is broken down via fractionation into its components cellulose (C6 sugar), hemicellulose (C5 sugar) and lignin (aromatic compounds) – an essential prerequisite for complete and high-quality material utilization as a renewable chemical raw material. At Fraunhofer CBP in Leuna, a pilot plant is available for this purpose, which can process up to 70 kilograms of wood per day.

Cellulose is used for example to produce glucose through enzymatic hydrolysis. This can be utilized as a substrate for a variety of fermentations and thus replace the higher-value raw material sources currently being used, such as sugar cane or starch. During fermentation, microorganisms such as bacteria or fungi metabolize these carbon compounds and convert them into biomass, but also into a variety of chemicals such as ethanol, succinic acid, butanediol or lactic acid, which can then be further processed into polymers such as bio-polyethylene (bio-PE), polybutylene succinate (PBS) or polylactic acid (PLA). Polymers such as polyhydroxybutyric acid (PHB) can also be obtained directly from sugar by fermentation (see above: Microbial biopolymers).

The basic building blocks of **lignin** are substituted phenols, especially guaiacol, syringol and p-hydroxyphenol, the proportion of which varies depending on the type of wood. At Fraunhofer CBP, we investigate and scale up various processes for the modification and depolymerization of lignin, which maintain or increase the structure and functionality of lignin. In this way, new, previously inaccessible aromatic structures with new functionalities and thus a new performance spectrum are identified, which can be used in a variety of industrial applications: from the production of fibers and fiber-reinforced plastics, to the use as epoxy/phenolic resins or wood preservative glaze to polyurethane rigid foams.

- *www.cbp.fraunhofer.de/lignocellulose-biorefinery*
- *www.cbp.fraunhofer.de/en/lignin*

Chitin: raw material for the production of chitosan

Chitin is the second most abundant biopolymer in the world after lignocellulose and is formed as a structural component by fungi, insects and crabs, for example. In order to convert chitin into chitosan, it must first be isolated and purified using various processes. Here too, the high bioavailability of the resource gives it enormous potential as a renewable raw material. One promising vegan source is fungal biomass from large-scale fermentation processes. The utilization of insect chitin was investigated in more detail at IGB as part of the European Regional Development Fund (ERDF) project "InBiRa – the insect biorefinery" (see page 41). Chitosan is not only used in the textile industry, for example as sizing agent to protect yarns during weaving, but can also be used as a bio-based flocculant for the treatment of complex wastewater.

- *www.igb.fraunhofer.de/processing-of-chitin*

Additional properties can be created by chemically modifying chitosan, e.g. water-repellent properties for textile coatings. The applications are very diverse and range from the encapsulation of active ingredients, coatings for medical products, biosensors and diagnostics to cosmetics.

- *www.igb.fraunhofer.de/modified-biopolymers*

Insect skins, known as exuviae, contain valuable chitin

Valuable protein: keratin from poultry feathers

Another natural resource is feathers, which are a by-product of poultry meat production. The majority of these feathers have so far been processed into meat and bone meal or disposed of as waste. However, this material can also be used sustainably: The keratin contained in the feathers, a water-insoluble structural protein, was researched at IGB in the project "KERAbond – specialty chemicals from tailor-made functional keratin proteins" as a starting material for the isolation of polythiol-containing peptides. Possible applications are seen in the production of adhesives and specialty chemicals for surface treatment.

By using proteins such as feathers, enzyme-responsive fragments can be introduced into materials, which in principle also allow new recycling strategies. This allows the intrinsic properties of natural polyamides to be utilized, which would not be easily possible using fossil-based approaches.

- *www.igb.fraunhofer.de/en/kerabond*

Starting materials for hydrogels

Modified biopolymers and hydrogels for the life sciences

All in all, the focus of polymer research at IGB is on the production of bio-based plastics, but there are also potential applications for native polymers in the health sector, for example in the form of hydrogels that can be used as tissue matrices or for drug delivery systems. Hydrogels are water-retaining and at the same time water-insoluble polymers. Suitable natural starting materials for such gels include gelatine, alginates or chitosan.

- *www.igb.fraunhofer.de/en/hydrogel*

Through chemical modification, we adapt biopolymers such as gelatine, chitosan, inulin or hyaluronic acid specifically to the different requirements depending on the area of application. By adding various chemical functions (e.g. methacrylic groups, thiol groups and benzophenones), we can change properties such as the viscosity, solubility or even the charge of the biopolymer in a targeted manner. With cross-linkable or hydrophobic groups, for example, we can create more stable and insoluble systems such as for the encapsulation of active ingredients or for functional water-repellent coatings. The modification of biopolymers is also interesting for 3D printing processes, as the viscosity can be adjusted independently of temperature.

- *www.igb.fraunhofer.de/modified-biopolymers*

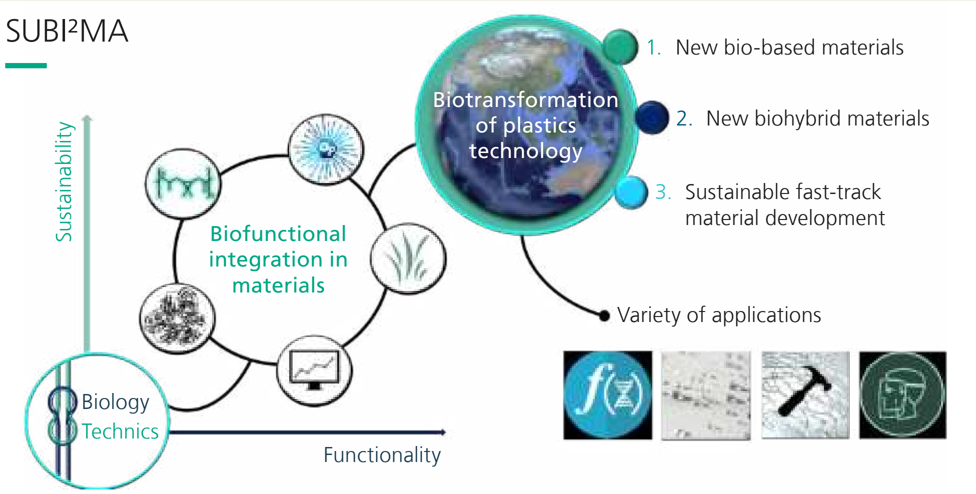
Fraunhofer flagship project SUBI²MA – sustainable bio-based and biohybrid materials

Biotransformation of plastics technology

With the flagship project SUBI²MA (Sustainable Biobased and Biohybrid Materials), we present a unique approach to biotransformation of plastics technology. The focus is on the benefits of bio-based material building blocks due to their exclusive molecular functionalities. SUBI²MA takes these criteria in the biotransformation of plastics a decisive step further: by integrating such biological components, entirely new materials can be developed, manufactured and made available to the market in the future.

Our modular approach offers a wide range of material solutions:

- New bio-based high-performance polymers
- Bio-based flame retardancy
- Hydrophilization/hydrophobization
- Fiber-matrix interaction
- Increasing the scope of application of established polymers



Approaches and the three main objectives in SUBI²MA

SUBI²MA materials provide the plastics and chemical industries or downstream markets such as construction chemicals, automotive, textile chemicals and health with an answer to the challenges of national and global sustainability strategies. Digital twins of the innovation principles created also enable the company to respond quickly and flexibly to future challenges in the transformation of plastics technology and other markets in the context of sustainability.

Three key topics/objectives are addressed in the project:

1. Provision and demonstration of **new bio-based materials** through development of synthesis routes, processing technologies, characterization and evaluation
2. Provision and demonstration of **new bio-hybrid materials** through optimization of properties, functionalization, characterization and evaluation
3. Development and establishment of **sustainable fast-track developments** through digitalization, simulation and holistic ecological assessment

Objective 1 "**New bio-based materials**" is to be achieved by developing a new bio-based high-performance polyamide, our caramide, to market maturity. This new bio-based polyamide was synthesized for the first time by the Straubing branch of Fraunhofer IGB. As part of the project, it will be further developed and its application demonstrated, both in terms of synthesis and processing methods, so that it can be used as a competitive alternative to fossil polyamides.

Objective 2 "**New biohybrid materials**" is fulfilled by integrating biological building blocks into plastics, which give them additional functions and thus expand the range of applications. The pre- and post-moulding of PET and cellulose, as mass-produced polymers, plays a decisive role here. The desired functionalities are the control of hydrophilicity, bio-based additives for flame retardancy, accelerated degradation and antimicrobial effectiveness.

Objective 3 "**Fast-track developments**" comprises the conceptualization of a digital value chain in order to significantly accelerate material substitutions in the future, as well as sustainability considerations in material development. The digital value chain includes digitalization and simulation from the molecular level of synthesis to the modelling of processes such as fiber spinning, as well as the development of digital demonstrators.

Research activities at the Straubing branch of Fraunhofer IGB focused on objectives 1 and 2.

The main task of objective 1 is to further develop caramide by optimizing its synthesis and processing. Caramide is obtained from the natural substance 3-carene after chemical modification. 3-carene, a monoterpene, is produced in large quantities during the production of cellulose in the Kraft process as a sidestream that has hardly been utilized to date. Two different monomer building blocks can be obtained from 3-carene: 3S-caranlactam and 3R-caranlactam. In objective 1, Fraunhofer IGB is focusing on optimizing the reaction conditions for the synthesis of the two monomers 3S- and 3R-caranlactam, as well as their provision in sufficient quantities. By commissioning a contract manufacturer, it was possible to provide pilot plant quantities of 3R-caranlactam. Purification took place at Fraunhofer CBP.

Monomer from the synthesis at the contract manufacturer after delivery (top) and after purification (bottom)

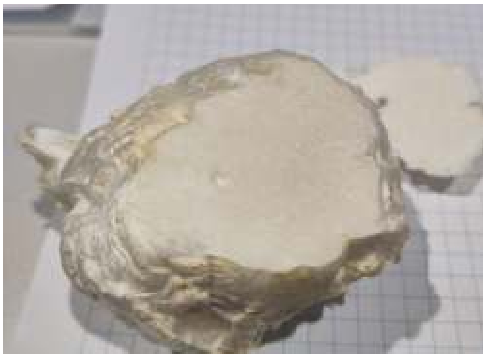
The purified 3R-caranlactam monomer and smaller quantities of the 3S-caranlactam synthesized in smaller batches at Fraunhofer IGB were handed over to Fraunhofer IAP.

Polymerization into cast polyamide was carried out at Fraunhofer IGB, hydrolytic polymerization was developed at Fraunhofer IAP, as was processing into sustainable monofilaments for textiles. At Fraunhofer ICT, caramide is foamed into bio-based polyamide foams, e.g. for lightweight construction.

Within the framework of objective 2, the focus at Fraunhofer IGB is on the hydrophobization of cellulose fibers for textile applications and on the exemplary finishing of cellulose-based membranes using the example of receptors of the innate immune system, the toll-like receptors (TLR) as a simple analysis tool for microbial contamination.

The hydrophobization of cellulose was carried out using fusion proteins consisting of a cellulose binding domain and a hydrophobin on a gram-scale. By varying both domains, different fusion proteins were produced recombinantly and analyzed. Depending on the type and concentration of the construct, successful hydrophobization of the cellulose was demonstrated in drop tests.

Polymerization of the caranlactam monomers to caramide



Further processing of the caramides into cast polyamide sheets (left), fibers (monofilaments, center) or foams (right) to demonstrate various applications

Current work is investigating the influence of hydrophobized cellulose on the production of cellulose fiber-reinforced PLA. To this end, PLA compounds with hydrophobized and untreated cellulose are being produced and compared in terms of their material properties (including tensile testing).

TLRs recognize microbial residues, isolated chemical structures, cell wall components or complete microorganisms. In contrast to antibodies, which are limited to the detection of very specific antigens, TLRs can detect broad classes of microorganisms such as Gram-negative or Gram-positive bacteria. This makes TLR particularly suitable for narrowing down unknown analytes in the sense of a sum analysis or for selecting class-specific samples. This is the strength of TLRs as analytical tools, as the individual TLRs or TLR complexes can be used to very quickly narrow down the sources of contamination (Gram-positive or Gram-negative bacteria, viruses, yeast, fungi). This knowledge significantly reduces the analysis effort, offers a time advantage and thus saves costs. The fermentative production of TLRs in mammalian expression systems and the directed functionalization of selected materials with TLRs have already been carried out. The aim is to produce exemplary structured functionalized cellulose membranes with immobilized TLR and to use them to create the first test strips for the detection of Gram-positive bacteria and their residues as a demonstrator.

Hydrophobic cellulose in the drop test (top left), comminuted cellulose fibers (cutting mill, top right) and fracture pattern of test rods 1BA (fiber content ten percent, left)

Partner institutes

Fraunhofer IAP (coordination), Fraunhofer IGB, Fraunhofer LBF, Fraunhofer ICT, Fraunhofer ITWM, Fraunhofer IWM

Further information

www.igb.fraunhofer.de/en/subi2ma

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Improving optical measurements, online monitoring, growth modelling, and automated control in microalgae production of *Phaeodactylum tricornutum*,
University of Stuttgart

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