



**Fraunhofer**

**IGB**

FRAUNHOFER INSTITUTE FOR INTERFACIAL ENGINEERING AND BIOTECHNOLOGY IGB

**ANNUAL REPORT**  
**2018 | 19**

70 YEARS OF  
FRAUNHOFER  
**70 YEARS  
OF FUTURE**  
*#WHATSNEXT*



**ANNUAL REPORT**  
**2018 | 19**

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## DEAR READERS,

I am delighted to be able to present the Fraunhofer IGB Annual Report to you for the first time. In March 2018 I took over the leadership of the institute. This marked the end of a longer phase of interim management. I would like to thank all those involved from the institute and headquarters for their great commitment and for keeping IGB on course during this time.

My first year as institute director was characterized by an intensive exchange with the employees of IGB, the colleagues at Fraunhofer-Gesellschaft as well as the continuous deepening of existing partnerships and the establishment of new contacts.

It was particularly important for me to sharpen the profile of IGB. To this end, we have worked across organizational units with our technological self-image and our extensive professional competencies. Proven strengths of the institute have emerged as important unique selling propositions: to combine different disciplines through process engineering competence and to be able to recognize new trends with foresight.

We are currently engaged in a comprehensive strategy process in which we are developing the conceptual, content and organizational foundations of the institute for the coming years. Our goal is to strengthen future-oriented business areas at IGB and to integrate new fields of activity with potential for disruptive changes. Our partners and customers are the focus of our attention.

The development of sustainable chemicals and processes and new technologies for medical applications will play an important role, as will environmental issues. Furthermore, we deal intensively with questions of digitization and the increasing networking of knowledge areas. In this context, our contribution is also part of the "biological transformation", which unites many disciplines from bioeconomy to production technology and is rapidly gaining in importance.

The integration and close interaction of the institute in Stuttgart and the branches in Straubing and Leuna are at the forefront of our current and future activities. By continuously strengthening this link, we want to increasingly map overarching value chains and become even more involved in large, cross-institutional initiatives of Fraunhofer-Gesellschaft as well as on a national and international level.



In several programs within Fraunhofer-Gesellschaft, we have assumed responsibility for important future topics, for example in the Life Sciences Group. At the national level, IGB is active in numerous committees, in particular within the framework of bioeconomic topics. Internationally, we are involved in various project center initiations on the topics of “Drug Discovery and Delivery” in Israel, “Water and Environment” in South Africa and “Sustainable Chemical Products from Solar Energy” in Morocco.

Parallel to our medium- and long-term initiatives for the future, we initiated and successfully implemented a whole series of positive changes at the institute last year. Some development projects were successfully completed, exciting new projects were launched. Selected examples can be found in this report.

Additionally, we have also initiated many organizational changes and restructured internal processes in recent months. Mr. von Ritter zu Groenesteyn, who brings with him many years of experience in the administration of research organizations, has been appointed to manage the administration. Mr. von Ritter will start his work at IGB in April 2019.

But most important for the sustainable development and success of IGB are its employees and their commitment to the institute. It is very important to me to further strengthening the concept of working with and for each other and to experience it in daily practice.

We are on the right path. I would therefore be delighted if this annual report could inspire you to new cooperations and the continuation of established partnerships with IGB.

Markus Wolperdinger  
Director





8

Fraunhofer Alliances

5

19 Members of Advisory Board

2 Fraunhofer Groups

2

Branches of the institute

Departments

45 %

Proportion of women

62 University employees

3888

26

Nationalities

6

BOGY high school students

Employees

37

Doctoral students

24 Apprentices

95

Students

326

Fraunhofer employees

€ 1.7 million Investments

€ 13.9 million Personnel costs

€ 26.5 million

Total budget

61.2 % Own revenues

€ 10.9 million Non-personnel costs

# PROFILE

## INNOVATIONS AT INTERFACES

The Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB develops and optimizes processes, plants, products, and technologies in the fields of health, chemistry and the process industry as well as environment and energy. With new molecular biological tools and personalized approaches, on the one hand we create options for improved medical care. Moreover, the concepts and solutions we develop aim to ensure that a growing world population is supplied with healthy food, clean water, high-quality raw materials, biobased basic chemicals and renewable energy. Resource-efficient and circular processes, bioeconomy and new insights into “biological transformation” are the strategies we rely on to contribute to sustainable development of the economy and society.

### Application-oriented and interdisciplinary

Our overriding goal is the translation of scientific and engineering research results into similarly economically efficient and sustainable processes and products for industrial application. We offer our customers research and development (R&D) along the entire material value chain and process engineering issues, complemented by a broad range of analysis and testing services. Our strength lies in offering complete solutions from laboratory to pilot plant scale. As a result, we are a strong partner for industrial companies and small or medium-sized enterprises in a wide range of industries, for municipalities and special-purpose associations and also for the EU, federal and state contract research.

More than ever, the success of new products and processes depends on the constructive interplay of different disciplines – such as natural sciences and process engineering or materials and biosciences. Experts in the fields of chemistry, physics, biology, and engineering work together effectively at Fraunhofer IGB, its branches at Leuna and Straubing and our partner institute IGVP at the University of Stuttgart. Thus, creative interaction at our institute facilitates novel approaches and innovative solutions in areas such as medical engineering, the production of “green” chemical products from biogenic waste streams or atmospheric CO<sub>2</sub>, and environmental technologies.

### Areas of expertise

#### Departments in Stuttgart

- Interfacial Engineering and Materials Science
- Molecular Biotechnology
- Physical Process Technology
- Environmental Biotechnology and Bioprocess Engineering
- Attract Group Organ-on-a-Chip

#### Branches of the institute

- Fraunhofer Center for Chemical-Biotechnological Processes CBP, Leuna branch
- Bio, Electro, and Chemocatalysis BioCat, Straubing branch

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## BOARD OF TRUSTEES

The Fraunhofer Institutes are advised by boards of trustees whose members are drawn from industry, public authorities, and the scientific community.

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### Members (as of December 31, 2018)

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**Dr. Susanne Arbogast**  
Indivumed GmbH

**Prof. Dr. Sara Brucker**  
University Hospital Tübingen

**Dr. Gerd Eßwein**

**MinR Dr. Hans-Jürgen Froese**  
Federal Ministry of Food and Agriculture  
(BMEL)

**Prof. Dr. Matthias Frosch**  
(until February 1, 2018)  
Faculty of Medicine, University of  
Würzburg

**MinDirig Dipl.-Ing. Peter Fuhrmann**  
(until May 1, 2018)  
Ministry of the Environment, Climate  
Protection and the Energy Sector of the  
State of Baden-Württemberg

**Dr. Jürgen Groß**  
Robert Bosch GmbH

**Prof. Dr. Elke Guenther**  
AIT Austrian Institute of Technology  
GmbH

**Dr.-Ing. Bernd Krause**  
(until June 30, 2018)  
Gambro Dialysatoren GmbH

**Dr. Caroline Liepert**  
Ministry of Science, Research and the  
Arts of the State of Baden-Württemberg

**Dr. Christian Naydowski**

**Prof. Dr.-Ing. Dr. h.c. Dr. h.c.**  
**Prof. E.h. Michael Resch**  
Institute of High Performance  
Computing, University of Stuttgart

**Prof. Dr. Dr. h.c. Ralf Riedel**  
Institute of Materials Science,  
TU Darmstadt

**Prof. Dr. techn. Günter Scheffknecht**  
Institute of Combustion and Power Plant  
Technology, University of Stuttgart

**Prof. Dr.-Ing. Ralf Takors**  
Institute of Biochemical Engineering,  
University of Stuttgart

**MinDirig Dr. Jörg Wagner**

Federal Ministry for the Environment,  
Nature Conservation and Nuclear Safety  
(BMU)

**MinR Dr. Joachim Wekerle**  
Ministry of Economic Affairs,  
Labour and Housing of the State of  
Baden-Württemberg

**Dr. Günter Wich**  
Wacker Chemie AG

**Prof. Dr. Karl-Heinz Wiesmüller**  
EMC microcollections GmbH

**Dr. Wieland Wolf**  
ProBioGen AG

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### Permanent guests

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**Prof. Dr. Herwig Brunner**  
(Former Director of Fraunhofer IGB)

**Prof. Dr. Dieter Jahn**  
(Chair of Advisory Board 1999–2013)



## SERVICES AND INFRASTRUCTURE

Fraunhofer IGB is a research and development partner for customers from the business and public sector. In our business areas, we develop, implement and optimize processes, products and systems as well as new technologies – from feasibility studies and initial laboratory tests to technical and pilot plant scale, including deployment. Our R&D is accompanied by a broad range of analysis and testing services.

### Quality management and assurance systems

For many years, standardized and internally as well as externally validated processes and procedures at Fraunhofer IGB have been safeguarding a reliable and consistent quality of our services and products. An efficient quality management system ensures that selected test procedures are accredited according to the international DIN EN ISO/IEC 17025 standard. Our quality assurance system ensures that the statutory guidelines of Good Laboratory Practice (GLP) are complied with.

### Accredited testing

The accreditation of reference laboratories and test procedures of our analytics according to DIN EN ISO/IEC 17025 guarantees that our proprietary, in-house test methods and procedures are validated and that the quality of our tests is assured even where no standardized methods are available.

Accredited analytical methods and test procedures:

- High-performance liquid chromatography (HPLC)
- Ion chromatography (IC)
- Gas chromatography (GC, GC/MS)
- Atomic emission spectrometry (ICP-OES)
- Electron spectroscopy for chemical analysis (ESCA/XPS)
- *In vitro* cytotoxicity testing (DIN EN ISO 10993-5)
- *In vitro* phototoxicity testing

With our in-house method for *in vitro* testing of phototoxicity, we can investigate solutions and substances with respect to their phototoxic potential on our in-house designed three-dimensional skin model. The test method is in accordance with the OECD Guideline 432 and the INVITTOX Protocol no. 121.

### Good laboratory practice (GLP) test facility

Several non-clinical tests are running at our category 9 GLP unit ("Cell-based test systems for the determination of biological parameters") to support R&D projects that investigate biological parameters of samples using cell-based assays. Examples are the testing of bioactivity, cytotoxicity and immunogenicity of compounds using immune receptor-based assays, screening of TLR agonists/antagonists, testing of antimicrobial properties of substances or surfaces, as well as detection of pyrogens and microbial residues (pathogen-associated microbial patterns, PAMPs).



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### Infrastructure and laboratory equipment

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Cutting-edge technologies and extensive, modern equipment are indispensable to our scientific work – and an added benefit for you as our customer. Our laboratories are designed for work up to biological safety level S2. A new building commissioned in 2017 has, among other things, roll-to-roll coating plants and technical centers for aseptic work (foodstuffs), for the treatment of process waste water as well as for wastewater and sludge treatment on a pilot scale.

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### Spectrum of services

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#### Process, technology and product development

- From laboratory to technical and pilot scale
- Design, construction and demonstration of pilot plants and prototypes
- Implementation of new technologies
- Licensing of technologies and processes

#### Studies and consultancy

- Feasibility studies and technology analyses
- Profitability studies and life cycle assessment

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### Analysis and testing services

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Our broad range of biological and physical/chemical examination methods makes the institute a versatile partner in the fields of medicine and pharmacy, food production and chemistry as well as environmental and water analysis.

#### Physico-chemical analysis

Quality control, food analysis, trace analysis, analysis of residues, environmental analysis, water analysis

#### High-resolution 400 MHz NMR analysis

Molecular structure elucidation, reaction monitoring, low-temperature analysis

#### Surface and particle analysis

Characterization of chemical, physical and morphological properties of surfaces, thin layers, powders, and particles

#### Microbial evaluation

Testing of antimicrobial effects and photocatalytic properties of surfaces

#### Biochemical and biomolecular analysis

Diagnostic microarrays, protein expression profiles, protein analysis using MALDI-TOF/TOF mass spectrometry (also quantitative)

#### Next-generation sequencing

*De novo* genome/transcriptome sequencing, meta-genomics and meta-transcriptomics, microbiomics, next generation diagnostics (infectious diseases, COPD, etc.)

#### Cell biology analysis

Cell characterization (also non-destructive), flow cytometry

#### Cell-material interactions

Testing of cytotoxicity/biocompatibility of R&D materials and industrial products, assessment of phototoxicity of substances and solutions

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**For detailed information on  
our analytical and testing services:**

[www.igb.fraunhofer.de/analytics](http://www.igb.fraunhofer.de/analytics)

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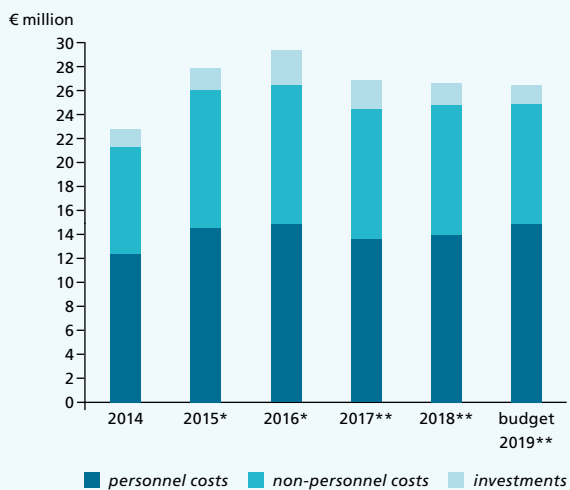
## KEY FIGURES

### Budget of Fraunhofer IGB

The total budget for 2018 amounted to €26.5 million, of which €24.8 million were allocated to the operational budget (personnel costs: €13.9 million; non-personnel costs: €10.9 million). A total of €1.7 million was spent on investments.

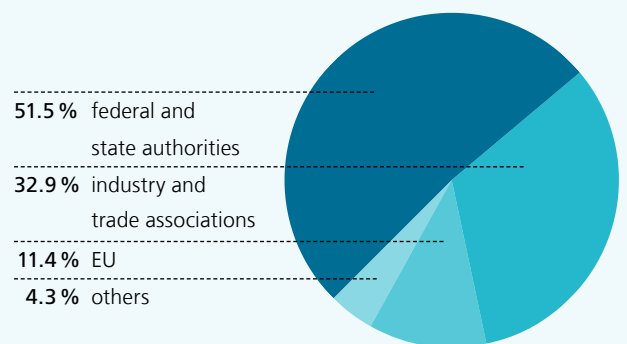
61.2 percent of the operational budget was financed from Fraunhofer IGB's own revenues generated from contract research projects. 32.9 percent of the institute's revenues came directly from industry.

#### Development of budget



\* incl. CBP (after state government initial financing completed)  
 \*\* incl. CBP; without Translational Center, Würzburg branch

#### Revenue from contract research 2018



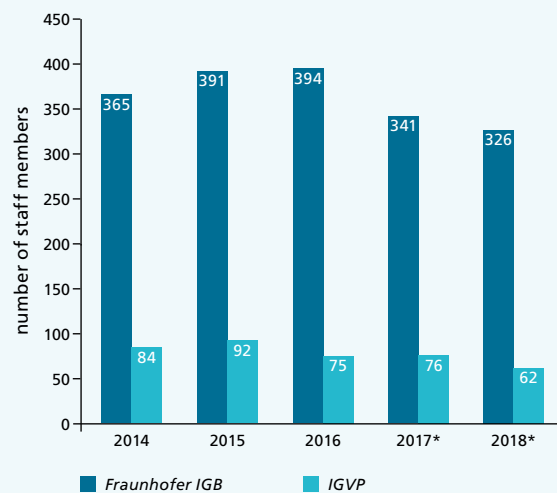
## Personal

At the end of 2018, Fraunhofer IGB (in Stuttgart and its branches in Straubing, and Leuna) had a staff of 326 of which some 80 percent were scientific or technical employees. Women made up 48 percent of the total.

The Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart counted a staff of 62 as of December 31, 2018, predominantly scientists and doctoral students as well as technical staff and student research assistants. Women constituted 29 percent of the total.

The employees of Fraunhofer IGB, of its branches, and of IGVP work together closely and have very culturally diverse backgrounds, with 31 staff members coming from 26 different countries outside Germany.

## Development of staff members



\* since 2017, without Translational Center, Würzburg branch

## Staff composition as of December 31, 2018

	Fraunhofer IGB	IGVP
Scientists	81	13
Technical staff	85	9
Doctoral students	9	20
Administrative and secretarial staff	40	4
Apprentices	17	7
Scholarship holders	5	3
Work students/Master students/student apprentices	16	–
Student research assistants	73	6
	<b>326</b>	<b>62</b>

# ORGANIZATION CHART

## Director

Head of Administration (interim)



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## Deputy Director



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## Deputy Director



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- Membranes
- Particle-based Systems and Formulations
- Plasma Technology and Thin Films
- Polymeric Interfaces and Biomaterials

- Infection Biology and Array Technologies
- Functional Genomics
- Molecular Cell Technologies
- Industrial Biotechnology



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**FRAUNHOFER CENTER FOR CHEMICAL-  
BIOTECHNOLOGICAL PROCESSES CBP,  
Leuna branch**



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- Biotechnological Processes
- Chemical Processes
- Pretreatment and Fractionation of Renewable Feedstocks

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**BIO, ELECTRO AND CHEMOCATALYSIS  
BIOCAT, Straubing branch**



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- Biocatalysis – Catalyst Design and Process Development
- Chemical Catalysis and Electrochemistry – Catalyst Design and Process Development

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- Heat and Sorption Systems
- Physico-chemical Water Technologies
- Nutrient Management
- Aseptic Technologies
- Prototype Development

---

**ENVIRONMENTAL BIOTECHNOLOGY  
AND BIOPROCESS ENGINEERING**



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- Technical Microbiology
- Bioprocess Engineering in the Water Sector and Circular Economy
- Accredited Analytics

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**ATTRACT GROUP ORGAN-ON-A-CHIP**



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## NETWORKS

Fraunhofer IGB is an active participant in numerous national and international research networks. Cooperative ventures with various universities and non-university research institutes, as well as interdisciplinary collaboration with other Fraunhofer Institutes, complement our own expertise and enable us to exploit synergies in developing new solutions for the needs of industry. We are also actively engaged in shaping research policies through championing strategic, economic, and sustainability standpoints.

### Networking with universities

Basic research is a prerequisite for the applications of tomorrow. Fraunhofer IGB therefore maintains contacts with numerous universities. There is particularly close cooperation with the neighboring universities in Stuttgart and Tübingen, both through scientific collaboration and through professorial or other teaching commitments of Fraunhofer employees. Through connections of the IGB branch in Straubing with the Technical University of Munich and the Leuna branch with the Universities of Halle and Leipzig, our scientific network extends far beyond the region.

Fraunhofer IGB is particularly closely allied to the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart through various teaching activities as well as a joint operation. In addition, we are networked with numerous other universities such as Hebrew University of Jerusalem, Berkeley University and Stanford University as well as Stellenbosch University in South Africa, non-university research institutions and clinics.

### Institute of Interfacial Process Engineering and Plasma Technology IGVP

The Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart is dedicated to interdisciplinary and cross-disciplinary research and teaching in the field of materials sciences, life sciences, process engineering and plasma technology. The IGVP is part of the Faculty 4 (Energy-, Process- and Bio-Engineering) and is structured in the research departments »Interfacial Engineering« and »Plasma and Microwave Technology«. The institute has well-equipped laboratory and technical facilities both on the university campus and at Fraunhofer IGB.

Close cooperation of the IGVP with Fraunhofer IGB makes it possible to pursue projects from basic research to application. In 2018, the research budget accounted for 2.46 million euros. At the end of that year, a staff of 62 scientific, technical and administrative employees, among them 20 doctoral students, worked at the institute. In addition, 43 students have completed their master or bachelor thesis at the IGVP.

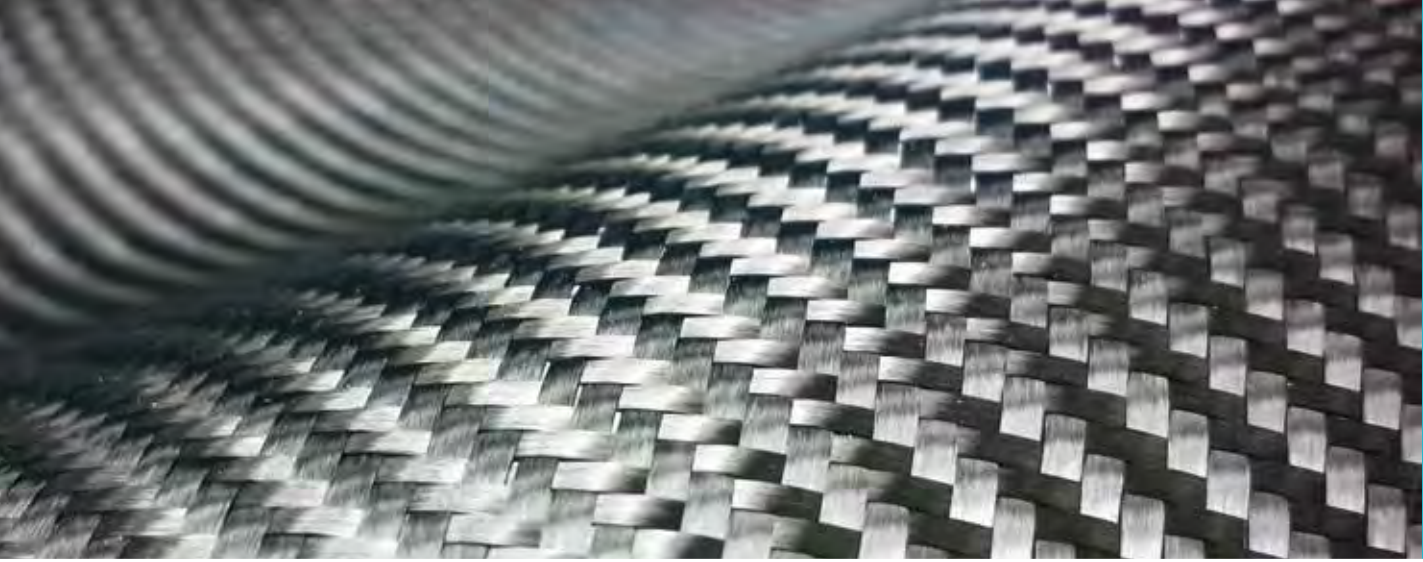
### Contact

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Pfaffenwaldring 31, 70569 Stuttgart, Germany  
Fax +49 711 685-63102 | [www.igvp.uni-stuttgart.de](http://www.igvp.uni-stuttgart.de)



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Director (acting)  
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### Fraunhofer Groups and Alliances

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Fraunhofer Institutes working in related subject areas cooperate as groups, foster a joint presence on the R&D market and help define the Fraunhofer-Gesellschaft's business policy. Institutes or departments of institutes with complementary expertises collaborate in Fraunhofer "Alliances" to develop business areas together and offer market solutions along the entire value chain.

Fraunhofer IGB is an active member of the Fraunhofer Group for Life Sciences and, due to its strong focus on materials science, an associated institute of the Fraunhofer Group for Materials and Components – MATERIALS. Furthermore, it is a member of various Fraunhofer Alliances and thus optimally integrated within the Fraunhofer network.

#### Fraunhofer Groups

- Fraunhofer Group for Life Sciences  
[www.lifesciences.fraunhofer.de](http://www.lifesciences.fraunhofer.de)
- Fraunhofer Group for Materials and Components – MATERIALS (associated institute)  
[www.materials.fraunhofer.de](http://www.materials.fraunhofer.de)

#### Fraunhofer Alliances

- Fraunhofer Energy Alliance  
[www.energie.fraunhofer.de](http://www.energie.fraunhofer.de)
- Fraunhofer Food Chain Management Alliance  
[www.fcm.fraunhofer.de](http://www.fcm.fraunhofer.de)
- Fraunhofer Additive Manufacturing Alliance  
[www.generativ.fraunhofer.de](http://www.generativ.fraunhofer.de)
- Fraunhofer Nanotechnology Alliance  
[www.nano.fraunhofer.de](http://www.nano.fraunhofer.de)
- Fraunhofer Polymer Surfaces Alliance POLO®  
[www.polo.fraunhofer.de](http://www.polo.fraunhofer.de)

- Fraunhofer Cleaning Technology Alliance  
[www.allianz-reinigungstechnik.de](http://www.allianz-reinigungstechnik.de)
- Fraunhofer Water Systems Alliance (SysWasser)  
[www.syswasser.de](http://www.syswasser.de)
- Fraunhofer Technical Textiles Alliance  
[www.textil.fraunhofer.de](http://www.textil.fraunhofer.de)

In addition, Fraunhofer Institutes carry out joint activities within Fraunhofer internal research programs. Examples of IGB's involvement are the High Performance Centers "Mass Personalization" (Stuttgart) and "Chemical and Biosystems Technology" (Halle-Leipzig region) as well as the Fraunhofer lighthouse project "Electricity as a Raw Material" and those successfully completed like "Theranostic Implants", "Critical Rare Earths" and "E<sup>3</sup>-Production".

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**For further information  
on IGB's networking activities:**

[www.igb.fraunhofer.de/network](http://www.igb.fraunhofer.de/network)

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**For further information  
on CBP's networking activities:**

[www.cbp.fraunhofer.de/network](http://www.cbp.fraunhofer.de/network)

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# HIGHLIGHTS 2018

## PROJECTS

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### **BMBF – Industrial Biotechnology Innovation Initiative Alliance Biosurfactants**

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The Innovation Alliance Biosurfactants is the first strategic alliance in Germany between renowned companies and research institutions to produce functionally optimized biotechnologically produced surfactants starting from domestic renewable raw materials and residual materials in an economical way.

By systematic investigation of the performance profile, production and purification of these biosurfactants are to be optimized in such a way that they can be used in application areas such as detergents and cleaners, cosmetics, bioremediation, crop protection and food as an alternative to chemically synthesized surfactants. The alliance initiated by IGB was approved on January 1, 2018.

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### **License agreement 1 Process for the environmentally friendly processing of liquid manure comes onto the market**

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The BioEcoSIM® process developed at Fraunhofer IGB for the processing of liquid manure is introduced to the market by SUEZ Deutschland GmbH as an operator of large-scale plants in Europe. This creates a possibility for farms to dispense excess liquid manure and fermentation residues from biogas plants. In the process, various preparation stages were combined to form an overall process and integrated into one plant. This allows the valuable nutrients to be recovered as phosphorus and ammonium fertilizer salts, which can then be applied again for fertilization in a manner that is appropriate for plants. The solid organic components are also recycled and hygienized and conditioned using an energy-efficient process.

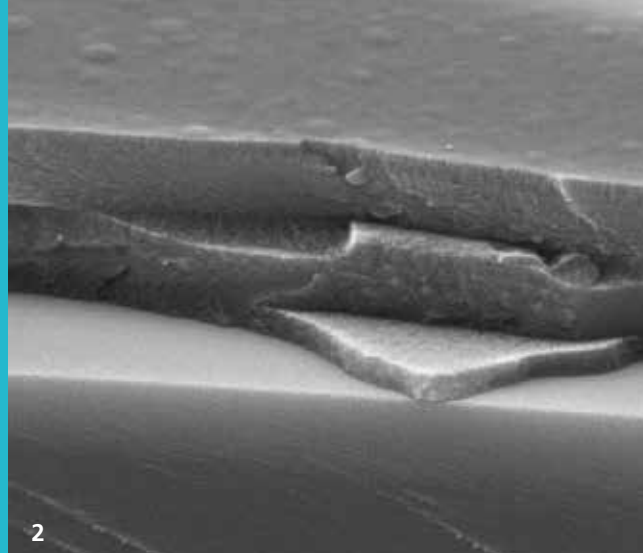
They are then available as humus-forming soil conditioners. Liquid manure is therefore recycled and the recycled components are returned to the soil as needed.

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### **Fraunhofer lighthouse project 2 “Theranostic Implants” – Cell-compatible coatings**

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In the project “Theranostic Implants”, twelve Fraunhofer Institutes have developed a toolbox for the development of intelligent implants over the past four years. Intelligent “Theranostic Implants” combine diagnostics and therapy in a medical device by recording vital parameters in a closed loop and initiating therapeutic measures on this basis. IGB participated in the project in various innovations for the optimization of the implant surface. On the one hand, barrier layers were developed for encapsulating the electronic implant components (see p. 52). On the other hand, surface modifications were developed to improve the growth of bone cells: as a coating with a biopolymer that accelerates the growth of mesenchymal stem cells and as a printable hydroxyapatite-containing bioink based on photo-curable gelatine (see Annual Report 2017/18).



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### Fraunhofer lighthouse project “Critical Rare Earths” – Substitution, efficiency, recycling

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As a component of many high-tech products, rare earths are among the strategically most important raw materials for German industry. For a more efficient use of these valuable elements, eight Fraunhofer Institutes have developed new solutions in the now completed joint project. These include optimized manufacturing processes, concepts for recycling processes and technologies, and new materials that can replace rare earths. Fraunhofer IGB focused on the processing and reuse of recycled material from used magnets produced by hydrogen embrittlement. Biochemical and chemical leaching processes were optimized for the release of rare earths from the recycle matrices and filtration membranes with selective adsorber particles were developed for concentration. We were able to show that particles coated with phosphate groups, which were incorporated into the membranes, can be selectively enriched with Dy and Nd and can also be selectively eluted again. A separation by type could then be achieved by means of the free-flow electrophoresis developed in-house.

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### Fraunhofer lighthouse project “Electricity as a Raw Material” – Ethylene from CO<sub>2</sub>

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The expansion of wind power and photovoltaics associated with the energy revolution will further increase the supply of electricity from fluctuating energy sources. In the project “Electricity as a Raw Material”, ten Fraunhofer Institutes have developed new electrochemical processes to use excess electricity for the production of chemicals. In a subproject, Fraunhofer IGB has developed a process with which ethene, one of the most important chemical starting materials, can be produced electrochemically from CO<sub>2</sub> and water in just one process step. For this purpose, novel, efficient catalysts

for CO<sub>2</sub> reduction to ethylene and the gas diffusion electrode required for this purpose were developed. On the other hand, the electrosynthesis process could be successfully validated with a fully automatic demonstrator on 130 cm<sup>2</sup> electrode area in flow-through operation (see p. 64).

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### Fraunhofer Max Planck Cooperation Program eBioCO<sub>2</sub>n – Power-driven CO<sub>2</sub> conversion through synthetic enzyme cascades for the production of specialty chemicals

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Not only chemical-catalytic processes can be considered for the current-driven synthesis of chemicals. It is also conceivable to combine CO<sub>2</sub>-fixing electron-transmitting biocatalysts with further enzymatic conversion steps in the form of an enzyme cascade for the production of fine chemicals. The “eBioCO<sub>2</sub>n” project, which was approved at the end of 2018 and is being carried out jointly by Fraunhofer and Max Planck researchers, meets this challenge. The aim of this ambitious project is to demonstrate the feasibility of such bioelectrocatalytic syntheses with a demonstrator on a 10–100 mL scale. To this end, suitable CO<sub>2</sub>-fixing enzymes are to be assembled on electrodes (cathodes) using new molecular architectures and – depending on the target product – combined with other specific enzymes to form continuous and coupled reaction cascades. Recently discovered redox enzymes, enoyl-CoA carboxylases/reductases (ECRs), are used as CO<sub>2</sub>-fixing biocatalysts. They are among the most efficient CO<sub>2</sub>-converting biocatalysts described so far.





1



2

## INTERNATIONAL

### New Horizon 2020 EU projects

Horizon 2020 is the European Union's eighth Framework Programme for Research and Innovation – providing funding amounting to almost 80 billion euros over the period from 2014 to 2020 – and is simultaneously the largest self-contained global research and innovation program.

In 2018, Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB was delighted to receive approval for participation in six further H2020 EU projects in all three focus areas, also including two projects in coordination. The outcome of a further application is pending.

### New projects in Section I "Excellent Science"

#### EUROoC

1

Since December 1, 2018, Fraunhofer IGB has been coordinating a Marie Skłodowska-Curie Innovative Training Network for the first time. This involves setting up a European research network to promote organ-on-a-chip technology. This technology allows the small-scale reproduction of human organs. It is viewed as an alternative to animal experiments in the future and as a technology with high potential, including for research into new pharmaceutical active ingredients and personalized medicine. The development of organ-on-a-chip technology requires multidisciplinary skills and the EUROoC network is therefore focusing, in particular, on the interdisciplinary training and further education of 15 scientists. The eleven primary contract partners include nine participants from the academic sector, one medium-sized company and a federal agency in the field of health-related consumer protection. In addition, the network incorporates ten partner organizations, of which three are academic institutions, five are from the industrial sector and two further

organizations are regulatory authorities in the field of human medicines.

#### iP-Osteo

In February 2019, the MSCA-RISE project iP-Osteo will commence work with the participation of Fraunhofer IGB. This involves 14 institutions from ten European countries conducting research into the development of novel cell-based scaffolds for the repair of bone and cartilage in patients with a low capacity for regeneration. The strengthening of partnerships and the promotion of knowledge transfer across national borders and across different sectors takes priority in MSCA-RISE.

### New projects in Section II "Industrial Leadership"

#### Liberate

Through its branches BioCat and Center for Chemical-Biotechnological Processes CBP, Fraunhofer IGB is involved in the project Liberate, which commenced its four-year research activity on October 1, 2018 and is coordinated by Leitatz. The project aims to create a prototype of an electrochemical plant to demonstrate the commercial options for converting low-cost raw materials containing lignin into high-value, biologically sustainable chemicals, such as vanillin, antioxidants or polyamide.

#### CO<sub>2</sub>EXIDE

2

The project CO<sub>2</sub>EXIDE – "CO<sub>2</sub>-based electrosynthesis of ethylene oxide" – that is coordinated by Fraunhofer IGB commenced on January 1, 2018, as already announced in the last annual report. The Straubing branch, BioCat, is developing combined electrochemical-chemical technology for the production of ethylene oxide from biobased CO<sub>2</sub> within the scope of this project that is funded by the public-private partnership SPIRE (Sustainable Process Industry through Resource and



Energy Efficiency). The CO<sub>2</sub>EXIDE approach unites physicists, chemists, engineers and communication experts from five research institutions, two industrial enterprises and three SMEs in this project. Through their key technologies, they will make a contribution towards the development of an unprecedented process based on CO<sub>2</sub>, renewable energies and water, thus demonstrating that the chemistry sector can be synergetically combined with the energy sector.

### New projects in Section III “Societal Challenges”

#### UNRAVEL

3

Since June 1, 2018, Fraunhofer CBP has been coordinating the project UNRAVEL (see p. 62) in the public-private partnership BBI, an abbreviation for Bio-Based Industries. Over the course of the four-year project, ten European partners will develop advanced pretreatment, separation and conversion technologies for complex biomass containing lignocellulose.

The project brings together specialists from a variety of fields who cover the entire value chain with their expertise. This includes the composition of the raw material, chemical production and pretreatment of wood pulp, enzyme production, polymer chemistry, separation and reactor technology, the techno-economic and sustainability assessment and the transfer, exploitation and communication of knowledge.

#### SUSBIND

Since May 1, 2018, the consortium SUSBIND has been developing, producing and testing biobased binding agents as an alternative to the current fossil-based binders that often contain formaldehyde, which are used for composite wood boards used in the manufacture of furniture.

The aim of the project is to replace chemicals based on fossil raw materials with those from renewable resources. Excess raw material from existing European biorefineries will be used for the production of binding agents and interim products. SUSBIND has set itself the target of producing and validating these biobased binders for two types of product at leading

composite wood manufacturers: P2 particleboard and medium-density fiberboard. Fraunhofer IGB is participating in this BBI project with four other research institutions and five industrial partners, under the coordination of the RTDS Group.

#### Completed projects

In 2018, our first two Horizon 2020 projects, ELSi and Steam-Bio, were successfully finalized.

#### Perspectives

We have now already reached the year before the end of Horizon 2020 and are also planning some new project submissions in 2019.

Furthermore, we are looking forward to the ninth Framework Programme for Research and Innovation “Horizon Europe” with great excitement and are participating in numerous preparative measures that are currently taking place.



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For further information on the  
Fraunhofer IGB EU-funded projects:

[www.igb.fraunhofer.de/eu-projects](http://www.igb.fraunhofer.de/eu-projects)






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### Global challenges – sustainable solutions

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The greatest challenges currently facing humanity are global challenges. These can only be overcome through the joint efforts of the global community that has coalesced through globalization. Research and development can make a significant contribution towards this if it orients itself according to sustainability objectives and implements these in international cooperation.

In the first wave of globalization, German companies moved parts of their production to so-called low-wage countries, however, instead of remaining a cheap “extended work-bench”, many of these countries are now developing into new self-confident partners, with their own research and economic infrastructure. In this process, they are more and more frequently acting on the same level – not as dependent service-providers or suppliers, but as equal clients and partners of the future.

Fraunhofer IGB recognized these signs of the times at a very early stage: research projects together with international partners were already being conducted strategically in the 1970’s, taking into consideration materials cycles and with the aid of newly developed interdisciplinary system approaches. These research concepts were continuously further developed through intensive collaboration with German companies, who were also active on a global basis at an early stage, as well as excellent international partners in science and research. In this process, IGB mainly placed an emphasis on a targeted build-up of joint activities aimed at the longer term.

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### Israel – active drug screening and transport

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One highlight of successful collaboration is the set-up of the Fraunhofer Project Center for Drug Discovery and Delivery. The joint center at the Hebrew University of Jerusalem emerged from the project “JRHDD – Joint Research Hub

for Drug Discovery and Delivery”, which was funded by Fraunhofer-Gesellschaft and the Hebrew University to show mutual interest. This research institution, designed as a bilateral research and development platform for companies, focuses on new methods for the screening and targeted transport of active pharmaceutical ingredients for applications in pioneering precision medicine. IGB is strengthening its health-related business area at an international level through its activities conducted within the scope of the project center (see p. 55).

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### South Africa – sustainable water supplies

1

IGB Director, Dr. Markus Wolperdinger, also signed a contract for cooperation with the University of Stellenbosch in South Africa last year, within the scope of a first meeting with delegates from this renowned university. The aim of this collaboration is to combine know-how and technologies in the field of water treatment and use of water and to work out solutions for South Africa through joint research and development. A first joint research project “Energy efficient and sustainable water supply technologies for desalination and microbial control in food production for Africa – WASTEC” is to carry out research into the options for use and tailoring of technologies developed at IGB in the field of water treatment and use of water in South Africa. The WASTEC project is being realized within the scope of the Fraunhofer line of funding “ICON – International Cooperation and Networking”. The project draws on IGB expertise in the business area of environment and energy.

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### Morocco – green ammonia synthesis

2

In North Africa, IGB is committed in the area of sustainable green chemistry. Hereby, it places the core statements of a sustainable bioeconomy at the center of developments, i.e. the transformation of the oil-based economy into a market in which fossil resources are replaced by a variety of renewable raw materials.





To this end, a joint research project was started in November 2018 on the topic "Synthesis of green hydrogen and green ammonia". Partners in this ambitious approach, which, in the future, might even replace the Haber-Bosch process that has been in common use for 100 years, are the Fraunhofer Institute for Microstructure of Materials and Systems IMWS in Halle (Saale) in Germany, the Green Energy Park and the Institut de Recherche en Energie Solaire et Energies Nouvelles, the Université Mohammed VI Politechnique and the OCP Group in Morocco. The aim is to establish technology that can be used to sustainably synthesize ammonia: using nitrogen from the air and hydrogen that is obtained through electrolysis of water using regenerative energy. The kick-off meeting took place in Morocco on November 1 and 2, 2018 with Dr. Lénárd-Istvan Csepei as representative of IGB.

Increased cooperation between African countries and researchers at IGB is taking up the Federal Ministry of Education and Research (BMBF) Africa strategy and hereby, in particular, strengthens collaborative research for the implementation of the United Nations Sustainable Development Goals, as well as for the exploitation of synergistic potential at national, European and international levels, one of the United Nations' five formulated central fields of action.

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### **New Zealand – bark as a raw material**

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The global relevance of IGB topics was also revealed at a workshop in New Zealand: in June, a joint workshop took place there at the SCION Research Institute in Rotorua on the topic Bark Biorefinery, with scientists from IGB and CBP. The objective of this workshop was to develop a concept for the sustainable use of bark waste, as well as to establish connections between stakeholders as actors in a potential value-added chain relating to the products of bark.

The following aspects, in particular, were discussed during the meeting:

- First approaches to up-scaling of bark processing in New Zealand and consideration of their profitability.
- Development of products and identification of markets to build up a complete value-added chain through to end-use applications.
- Production of a SWOT analysis on the topic for the joint exploitation of opportunities.

In a next step, a concrete project is to be worked out that will be driven forward in a joint effort when the SCION scientists come to IGB on their planned return visit in spring 2019.

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### **Japan and Hong Kong – bioeconomy in the Far East**

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Representatives of IGB and the CBP branch traveled to Japan and Hong Kong in October 2018 on behalf of the Fraunhofer Group for Life Sciences to discuss acquisitions in the fields of bioeconomy and industrial biotechnology. The IGB delegation was supported in Japan by Fraunhofer Representative Office Japan, such that the Institute was given the opportunity of introducing itself to well-known companies and laying the foundations for future cooperation. Successful collaboration between CBP and a Japanese biotechnology company serves as a model for this. In Hong Kong, initiated by the Fraunhofer Group for Life Sciences, IGB representatives held discussions with representatives of the Hong Kong PolyU on the creation of a joint project center. Collaboration in the fields of biocompatible materials, industrial biotechnology and environmental process engineering is to take place at this center.



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## PEOPLE

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### **Jun.-Prof. Dr. Peter Loskill: Junior Professor in Tübingen and Vice-Chair of the Organ-on-Chip Society**

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At the beginning of 2018, IGB scientist Dr. Peter Loskill was appointed junior professor at the Eberhard Karls University of Tübingen. The physicist heads the research group "Organ-on-a-Chip" at Fraunhofer IGB, which develops microphysiological systems so-called organs-on-a-chips. With their help, the development of medical active substances, which has been very tedious so far, is to be accelerated considerably. Now Loskill is also researching and teaching in the field of experimental regenerative medicine at the Medical Faculty of the University of Tübingen. One focus of his work is in the field of women's health.

Furthermore, in November 2018, Loskill took over a position on the board of the newly founded European Organ-on-Chip Society (EUROoCS). This international network of scientists has set itself the goal of promoting the development of organ-on-a-chip systems throughout Europe and enabling new innovations in this field. Loskill was significantly involved in the foundation of EUROoCS and is now represented on the board of the company as Vice-Chair.

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### **Christina Funk is doing her "summa cum laude" doctorate**

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In her doctoral thesis at the University of Stuttgart, biologist Christina Funk investigated the function of the herpes simplex virus type 1. In spring 2018, the young scientist completed her doctorate at the Institute of Interfacial Engineering and Plasma Technology (IGVP) and received the distinction "summa cum laude" for her doctoral thesis. During her doctorate at IGB partner institute of the University of Stuttgart, Funk worked in the research group Biological-Medical Interfaces, whose leader Prof. Dr. Susanne Bailer also supervised her doctoral thesis. The graduation was promoted by a scholarship of the Peter and Traudl Engelhorn Foundation.

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### **Fabian Haitz was accepted into the Young Research Class 2018 / 2019**

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The Young Research Class is an annual Fraunhofer promotion program for young research talents. IGB doctoral student Fabian Haitz had successfully applied for this career promotion and will now be supported financially and with further training measures in his professional further development over a period of two years. As a first step, Haitz took part in the Young Research Camp, a workshop lasting several days at the Waischenfeld research campus of the Fraunhofer Institute for Integrated Circuits IIS, from 18 to 22 June 2018. The focus of the current Young Research Class is on the current Fraunhofer theme "Biological Transformation", which is also the subject of intensive research at IGB.



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### **Dr.-Ing. Christopher Probst successful with Retina-on-a-Chip at Science2Start Competition**

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Researchers at IGB and at the University of Tübingen have jointly succeeded in simulating the complex human retina in a microphysiological system. The retina model created in this way will help to research new treatment options for eye diseases. IGB scientist Dr.-Ing. Christopher Probst, who works at the Institute in the research group “Organ-on-a-Chip”, was in charge of this ambitious project. With their “Retina-on-a-Chip” innovation, Probst and his team from across different departments of the institute finished third in the Science2Start competition in summer 2018. This is hosted by BioRegio STERN Management GmbH, which is dedicated to promoting biotechnology and life sciences in Baden-Württemberg.

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### **Dr. Markus Wolperdinger speaks at the Global Climate Action Summit 2018**

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At the Global Climate Action Summit in San Francisco in September 2018, international decision-makers from politics, research and industry met to discuss solutions to the problem of climate change. In addition to numerous celebrities from all over the world, Dr. Markus Wolperdinger also took part in the summit meeting and spoke as a guest speaker on the contribution of applied research to climate protection. The IGB institute director visited the summit as a member of a delegation from the state of Baden-Württemberg, which under the aegis of Prime Minister Winfried Kretschmann travelled to California and the Canadian region of Ontario to explore possible economic and scientific cooperation.

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### **Student Teresa Krumm receives the Boehringer Ingelheim Award for her Bachelor Thesis**

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In November 2018, the student Teresa Krumm received a study award from the pharmaceutical company Boehringer Ingelheim for her bachelor thesis on “CRISPR/Cas9-induced knockout of thymidine kinase 1”. Krumm successfully completed her bachelor’s degree in pharmaceutical biotechnology at the University of Biberach with this thesis. For her thesis she worked at IGB in the research group Molecular Cell Technology and was supervised by group leader Dr. Anke Burger-Kentischer.



## TRADE FAIRS AND EVENTS

Last year, Fraunhofer IGB presented itself at various trade fairs and events. 2018 was a particularly eventful trade fair year, as AICHEM and IFAT simultaneously represented two major trade fairs that take place every several years and were of considerable relevance to the institute. Furthermore, IGB has repeatedly hosted various congresses, symposia and training sessions at the institute.

### Energy Storage Europe

1

Energy Storage Europe, the leading international trade fair for energy storage, took place in Düsseldorf in March 2018. IGB presented its work in the field of sorptive heat storage. Furthermore, the development of catalysts and catalytic processes for the conversion of electrical energy and CO<sub>2</sub> into liquid energy carriers is one of the institute's areas of expertise. In this field of research, IGB is currently working on several projects, which were presented by the scientists at the fair.

### Leuna-Dialog

Leuna is a chemical location rich in tradition and home to numerous industrial, commercial and service companies in the chemical industry. InfraLeuna GmbH, the operator of the Leuna Industrial and Chemical Park, organizes the annual Leuna Dialog trade fair to give local companies the opportunity to present themselves and their range of services to potential customers and partners. At the 13<sup>th</sup> event in April 2018, as in previous years, Fraunhofer CBP, the Leuna-based part of IGB, which deals in particular with the scale-up of biotechnological-chemical processes, presented itself there.

### EUROoC conference

2

The newly founded research network EUROoC has set itself the goal of promoting research on organ-on-a-chip systems in Europe. These innovative systems make it possible to reproduce human organs on a very small scale and can be used as test systems in medical drug development and in personalized medicine. At the end of May, the network invited to the first EUROoC conference to discuss current challenges. IGB was involved in the organization in a leading capacity and also provided the institute with the premises for the conference.

### Biowaste forum

A biowaste forum was held in Stuttgart in June 2018 under the auspices of the Baden-Württemberg Ministry for the Environment, Climate Protection and the Energy Sector. Experts from industry and research met here to exchange information on current topics relating to biological recycling economy. IGB made an excursion possible for the participants. This initially took them to the institute's pilot plant on the Fraunhofer Campus in Stuttgart and provided insights into the topics of bioenergy, nutrients recovery from residues, use of biogas and wastewater treatment.





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### **Biointelligence – A new perspective for sustainable value creation?**

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As part of the Fraunhofer BIOTRAIN project (see p. 61), IGB and other Fraunhofer Institutes jointly investigated the possibilities of sustainable value creation through the application of materials, structures and principles of living nature in technology. The aim of this project was to analyze what contribution the biological transformation of industrial value creation can make to Germany as a business location. The results of this study were presented at the Fraunhofer Forum in Berlin at the end of June 2018.

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### **Medical technology day**

**3**

On medical technology day 2018 at the Fraunhofer Forum in Berlin, the Fraunhofer-Group for Life Sciences brought together Fraunhofer scientists and experts from politics and industry to provide information on current developments and challenges in biomedical technology. Hon.-Prof. Dr. Christian Oehr, Deputy Director of IGB, represented the institute on the medical technology day and gave a lecture on the research focus of IGB: biofunctional materials, next-generation diagnostics and organ-on-a-chip systems.



3

### **Current exhibitions**

#### **Energy Storage**

March 12 – 14, 2019, Düsseldorf

#### **ICE Europe**

March 12 – 14, 2019, Munich

#### **Hanover Trade Fair**

April 1 – 5, 2019, Hanover

#### **3<sup>rd</sup> Joint Symposium on Nanotechnology**

April 9 – 10, 2019, Stuttgart

#### **Chemspec Europe**

June 26 – 27, 2019, Basel, Switzerland

#### **Biosurfactants International Conference**

September 25 – 27, 2019, Stuttgart

#### **22<sup>nd</sup> Colloquium on Wastewater and Waste Treatment**

October 8, 2019, Stuttgart

#### **K 2019**

October 16 – 23, 2019, Düsseldorf

#### **parts2clean**

October 22 – 24, 2019, Düsseldorf

#### **SEPAWA Congress**

October 23 – 25, 2019, Berlin

#### **Bio-Europe**

November 11 – 13, 2019, Hamburg

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### **21<sup>st</sup> Colloquium on wastewater and waste treatment “Technology with a future”**

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As part of IGB’s annual wastewater colloquium, the institute invites experts from the water industry to discuss the latest developments and trends in wastewater technology. The event is aimed in particular at representatives of municipalities and politics, as IGB has many years of expertise in the development of processes for wastewater treatment and for biowaste and sewage sludge recycling and on this basis can set trends in the implementation of municipal solutions. The focus of the 21<sup>st</sup> edition of the colloquium in September 2018 was on the recovery of substances from water and wastewater, for example nutrients such as nitrogen and phosphorus, which can be used as resources.

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### **36<sup>th</sup> Annual World Methanol Conference**

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At the beginning of October, international experts for the production and use of methanol met in Vienna for the 36<sup>th</sup> edition of the World Methanol Conference. The focus this year was on “Methanol-to-Olefins” (MTO), a process for the production of special hydrocarbons for the chemical industry. This process was also the subject of the accompanying training workshop “Introduction to methanol: featuring MTO and small-scale technical plants”. IGB scientist participated as speaker in the panel discussion on “Are there limits to the size of methanol units? How can small-scale plants be profitable?”.

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### **Congress BW – 7<sup>th</sup> Resource Efficiency and Recycling Congress Baden-Württemberg**

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How can economic interests and environmental objectives be reconciled? The participants of the annual Baden-Württemberg Resource Efficiency and Recycling Congress, to which decision-makers and experts from industry, research and politics have been invited, will deal with this question. In addition to keynote speeches, the program offered plenary discussions and forums on various specialist areas as well as an accompanying trade show. The forum “Bioeconomics” was moderated by Dr.-Ing. Ursula Schließmann on behalf of the head of IGB.

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### **Algae technology training**

**1**

IGB is researching the use of microalgae as a sustainable raw material for the food industry. In order to share their expertise with potential users of algae technology, the institute’s experts invited interested parties from research and industry to a two-day advanced training course on “Algae biotechnology and its potential for a sustainable bioeconomy”. The aim of this training, which was funded by the EIT Food Network, was to provide a practical introduction to the topic and to teach the basics of the cultivation, analysis and utilization of microalgae.

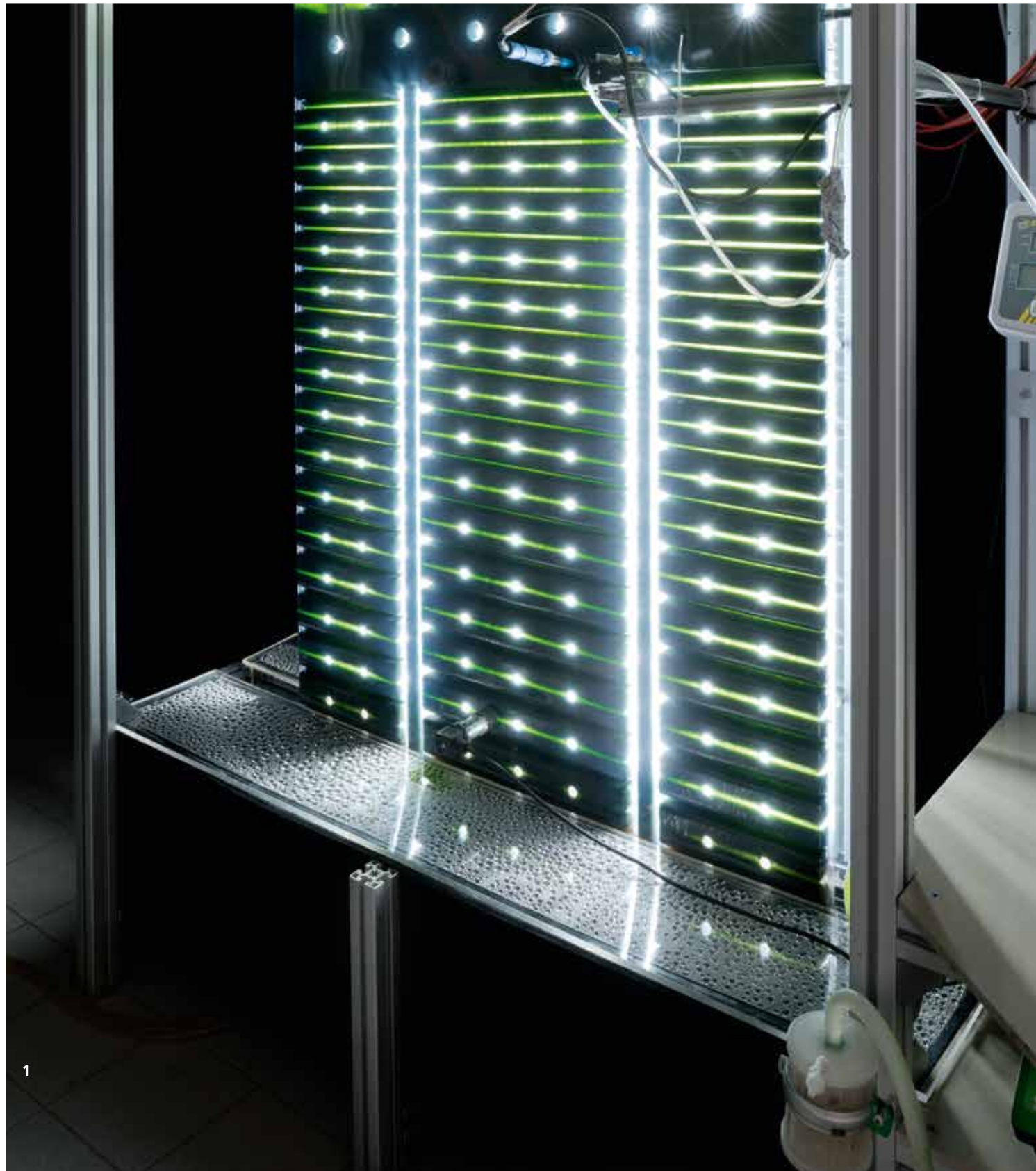
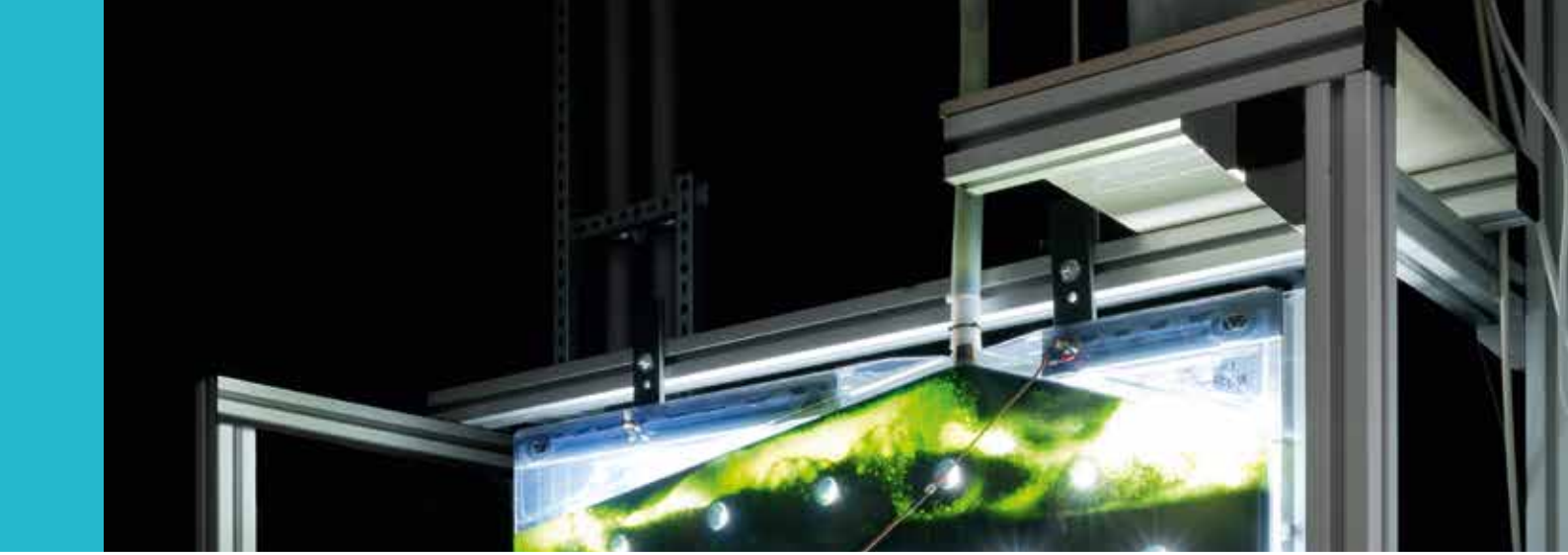
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**For further information and  
current events see:**

[www.igb.fraunhofer.de/events](http://www.igb.fraunhofer.de/events)

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## PROMOTION OF YOUNG TALENTS

In order to be successful in the long term, it is crucial for research institutions to recruit qualified young talent. For this reason, Fraunhofer IGB is strongly committed to promoting young talent – with the aim of getting young people interested in applied research. IGB therefore participates in a number of inter-institute recruiting events organized by the Fraunhofer Institute Center in Stuttgart. Within this framework, pupils can find out about MINT subjects (mathematics, computer science, natural sciences and technology) and students can learn more about career entry and career opportunities at Fraunhofer.

### Fraunhofer Talent School

1

Once a year, the Fraunhofer Institute Center in Stuttgart invites students interested in science and technology to its Talent School. During this three-day event, they gain an intensive insight into the world of applied research and can already become active as young researchers themselves. Within this framework, the participating institutes offer practice-oriented workshops to participate in. At the IGB Workshop “CSI Stuttgart”, the participants solve a fictitious criminal case under the expert guidance of the staff of the Research Group Functional Genomics by convicting the perpetrator with the help of DNA characterization carried out by themselves.

[www.stuttgart.fraunhofer.deltalents](http://www.stuttgart.fraunhofer.deltalents)

### Girls' Day

Girls' Day is a nationwide action day to promote girls and young women in scientific and technical professions. It is intended to help overcome outdated gender and role clichés and inspire girls to take up MINT occupations at an early age. Even today, the proportion of women in supposedly typical “male professions” is still too low. The Fraunhofer Institutes in Stuttgart have been participating in Girls' Day since 2003 and are opening their laboratories and workspaces to female students interested in applied science. Last year, IGB offered two guided tours of the institute on the topics of plasma technology and microalgae technology.

[www.stuttgart.fraunhofer.de/girlsday](http://www.stuttgart.fraunhofer.de/girlsday)





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## **BOGY – Career and study orientation at the High School**

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Choosing the right profession is one of the most important decisions in young people's lives. For this reason, high school students in Baden-Württemberg complete one-week BOGY short internships (vocational and study orientation at the high school) between grade 9 and 11, which are intended to provide them with orientation at an early stage. The Fraunhofer Institute Center in Stuttgart supports this initiative. Pupils with an interest in science and technology will gain an insight into the world of applied research and learn about study, career entry and career opportunities. For this reason, the Institute Center arranges several BOGY internships at the Stuttgart institutes every year. In 2018, IGB accepted a total of six pupils on two dates in April and October.

[www.stuttgart.fraunhofer.de/bogy](http://www.stuttgart.fraunhofer.de/bogy)

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## **Career day "The future lies in Sciences" 2**

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The Career Day of the Fraunhofer Institute Center in Stuttgart is aimed at students and university graduates. The event will focus on the various career entry opportunities for young academics. At the Career Day, participants learn that they can already enter applied research at Fraunhofer during their studies, after graduation or later as experienced professionals. Fraunhofer employees at various career levels – research student, doctoral students and executives – report on their personal experiences as part of the "Insider Insights" and give valuable tips for starting a career. Furthermore, the guests receive an insight into the daily work of Fraunhofer researchers during guided tours of the institute.

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## **Dual training at Fraunhofer IGB**

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In addition to young academics, trainees also enter the world of work at IGB, as non-university education is also a top priority at Fraunhofer. At the end of 2018, a total of 18 young women and men completed vocational training at IGB and IGVP, IGB's partner institute at the University of Stuttgart, seven of whom were newly hired at IGB in 2018. The range of training occupations on offer is broad. Office management clerks learn their profession in the administration and IT specialists are trained in the IT department. In the scientific field, the institute trains biology and chemistry laboratory assistants. The administrative trainees go through several stations at the institute within three years. In this way, they get to know the different fields of work of a research institute and acquire all the necessary qualifications that are important for a later career in research or industry. In addition, IGB supports its trainees when they are aiming for a degree after completing their training.

[www.igb.fraunhofer.de/ausbildung](http://www.igb.fraunhofer.de/ausbildung)

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**For further information on promotion  
of young scientists and training:**

[www.igb.fraunhofer.de/career](http://www.igb.fraunhofer.de/career)

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# COMPETENCES

## FRAUNHOFER-GESELLSCHAFT

Research of practical utility lies at the heart of all activities pursued by the Fraunhofer-Gesellschaft. Founded in 1949, the research organization undertakes applied research that drives economic development and serves the wider benefit of society. Its services are solicited by customers and contractual partners in industry, the service sector and public administration.

At present, the Fraunhofer-Gesellschaft maintains 72 institutes and research units. The majority of the more than 26,600 staff are qualified scientists and engineers, who work with an annual research budget of more than 2.5 billion euros. Of this sum, more than 2.1 billion euros is generated through contract research. Around 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Around 30 percent is contributed by the German federal and state governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions of the greatest importance to present and future scientific progress and economic development.

With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits perceived by the customer: Through their research and development work, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their local region, and throughout Germany and Europe. They do so by promoting innovation, strengthening the technological base, improving the acceptance of new technologies, and helping to train the urgently needed future generation of scientists and engineers.

As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills that will allow them to take up positions of responsibility within their institute, at universities, in industry and in society. Students who choose to work on projects at the Fraunhofer Institutes have excellent prospects of starting and developing a career in industry by virtue of the practical training and experience they have acquired.

The Fraunhofer-Gesellschaft is a recognized non-profit organization that takes its name from Joseph von Fraunhofer (1787–1826), the illustrious Munich researcher, inventor and entrepreneur.

Figures are for January 2019.

[www.fraunhofer.de](http://www.fraunhofer.de)





### Interfacial Engineering and Materials Science

Material surface requirements are often very different from the properties intrinsic to the bulk of the material concerned. The department offers a variety of processes for film deposition from either the gas or liquid phase. We also develop polymeric and inorganic material systems with large surface areas such as particles, porous membranes, non-woven materials and foams as well as biomaterials, especially hydrogels. A multitude of analytical tools are available for the monitoring of processes (process diagnostics) and the characterization of the generated material surfaces. Apart from the quality of the products, the material and energy efficiency of processes is of foremost concern.

#### Technology and expertise

- Deposition of thin monolayers or multiple films from the gas phase (e.g. plasma)
- Chemical modification of surfaces (dip coating, doctor-blading, printing etc.)
- Generation and loading of functional nanoparticles using polymerization methods or spray drying
- Production of polymeric and ceramic separation membranes by phase inversion processes
- Synthesis of biocompatible polymers, chemical modification of biomolecules, development of biomaterials
- Determination of interfacial energy, topography, adsorption, and chemical composition of surfaces
- Plasma process diagnostics: probe measurements, optical and mass spectrometric methods



#### Contact

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### Molecular Biotechnology

The biological transformation of industrial society is one of the most important issues of the 21<sup>st</sup> century. New sequencing technologies and proteome analyses, the targeted modification of organisms of all species and the development of enzymatic or fermentative production processes provide new ways for the production of fine and bulk chemicals as well as for the development of diagnostics and therapeutics. We apply these new technologies for the development of diagnostics in infection research and in personalized medicine as well as in the development of antimicrobial drugs and for the production of therapeutic proteins. In the field of industrial biotechnology, we convert renewable raw materials to new products for the chemical industry using biotechnological processes.

#### Technology and expertise

- Molecular-biological workflows for clinical samples
- Diagnostic microarrays
- Next-generation sequencing (NGS)
- Bioinformatic workflows for NGS data
- Development of stable cell lines and production strains
- Cell-based assays, e.g. antiviral and pyrogen detection assays (GLP), and complex 3D infection models
- Virus-like particles and therapeutic viruses
- Protein purification and characterization
- Strain and enzyme screening
- Development and scale-up of bioprocesses



#### Contact

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## Physical Process Technology

The department is involved in developing technologies, processes and process components based on physical and physico-chemical principles. A hallmark of our R&D activities is improving economic efficiency and sustainability of production processes at the same time – by minimizing material consumption, recovery of high-value substances in a quality equal to primary raw materials, and saving and reuse of energy. Our customers are either manufacturers of process components, contractors, and process system suppliers, or industrial companies from sectors such as metal processing, the food industry, biotechnology and the water sector with a specific problem to be solved.

### Technology and expertise

- Thermo-chemical heat-storage (adsorptive and absorptive)
- Evaporation and drying with superheated steam combined with winning of volatile fractions
- Stabilization of liquid food and biogenic products
- Cell-desintegration and extraction with high-pressure technique
- Chemo-physical water treatment (mechanical, electrolytic, photolytic)
- Primary/secondary winning of materials
- Processes and techniques to recycle organic and inorganic products for agricultural applications
- Electrolytic and photolytic synthesis
- Electrophoretic separation of substances
- Integration of the technologies into customized processes
- Design, construction and operation of demonstrators

## Environmental Biotechnology and Bioprocess Engineering

The core areas of the department are the development of (bio)engineering processes along the value chains in the fields of water management, wastewater treatment, bioenergy, environmental technology, algal technology, product recovery from organic raw/waste materials and interfacial biology. Based on these processes, we are following new approaches to the development of system concepts for energy, waste and water management in industry and for municipalities. The aspects of resource and energy efficiency as well as integrative biorefinery concepts as defined by the bioeconomy approach are of particular importance to us when designing industrial processes.

### Technology and expertise

- Process development in bioreactors from laboratory to pilot and technical scale
- Development and operation of demonstration plants for aerobic and anaerobic wastewater treatment, high-load digestion, bioenergy, algal technology
- Analysis of substrates and fermentation products, protein analysis
- Real-time mass spectrometry
- Isolation and downstream processing of bioproducts (membrane-based filtration processes, process chromatography, liquid-liquid extraction, extraction with supercritical CO<sub>2</sub>)
- Development and operation of apparatuses for testing antimicrobially finished materials
- Evaluation of microbial contaminations
- Process simulation and automation (Mat-Lab, Siemens)



### Contact

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### Attract Group Organ-on-a-Chip

The integration of physiologically relevant human tissue in artificial, microfluidic systems, known as organ-on-a-chip systems, is a novel technology for testing chemicals and drug compounds under conditions replicating the human physiology. *In vitro* organ-on-a-chip systems combine the unique features of classic cell assays (human genetic background, standardizability) and animal models (3D tissues, blood circulation). Thus, they offer the possibility to reduce the need for animal testing according to the 3R principle (replace, reduce, refine) and to increase the transferability of preclinical results to clinical phases; as such, they make the entire development of drugs and cosmetics less expensive, faster and safer.

#### Technology and expertise

- Development of microfluidic approaches for biomedical questions
  - Microfabrication
  - Prototype development
  - Embedding of biomaterials
  - Scaling and automation concepts
- Microphysiological organ-on-a-chip systems
  - Development of tailor-made systems
  - Studies and screening using heart-on-a-chip, adipose-tissue-on-a-chip, retina-on-a-chip, choroid-on-a-chip, pancreas-on-a-chip and heart-valve-on-a-chip systems
- Application of organ-on-a-chip systems for non-clinical studies and personalized medicine
  - Integration of patient-specific cells (induced pluripotent stem (iPS) cells, primary cells)



#### Contact

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### Bio, Electro and Chemocatalysis BioCat, Straubing branch

The focus of BioCat, the Straubing branch of the institute, is on the development of new chemical catalysts and biocatalysts and their application in technically relevant synthetic and electrochemical processes. Based on substrates such as biomass, CO<sub>2</sub>, organic and inorganic waste streams, the entire spectrum of catalysis is used to develop new sustainable and resource-efficient chemical products. BioCat is also developing new catalytic methods of managing electrical energy by binding and converting CO<sub>2</sub> to produce long-chain hydrocarbons, making it possible to store electricity from regenerative power generation in the form of chemical energy for later use.

#### Technology and expertise

- Chemical (homogenous and heterogeneous) catalysis, biocatalysis (enzymes, whole cells), electrocatalysis, screening for catalysts, organic synthesis
- Molecular-biological and technical optimization of enzymes and enzyme reactions
- Analyses of natural materials and chemical reactions (e.g. high-resolution NMR analytics, high-throughput LC-MS and GC-MS)

#### Contact

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## Fraunhofer Center for Chemical-Biotechnological Processes CBP

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Fraunhofer CBP in Leuna develops and scales up chemical and biotechnological processes for the utilization of renewable raw materials – from upstream processing of raw materials and several conversion processes to separation and downstream processing of transformation products. By making infrastructure and plants (pilot scale and miniplants) available and by providing high-qualified personnel, Fraunhofer CBP closes the gap between the lab and industrial implementation and makes it possible for partners from research and industry to scale up processes right up to production-relevant dimensions and thus to accelerate process developments.

### Technology and expertise

- Processing of raw materials – integrated pilot plant for pulping and fractionation of lignocellulose
- Biotechnological processes – modular process units up to 10 m<sup>3</sup> reactor volume for fermentations
- Cultivation of microalgae in automated greenhouse and outdoor pilot plants, with a total volume of photobioreactors of 11.7 m<sup>3</sup>
- Chemical processes – various process units for chemical reactions under ATEX conditions (continuous up to 20 kg/h or batch up to 100 liters)
- Downstream processing for separation, purification and reconditioning of products

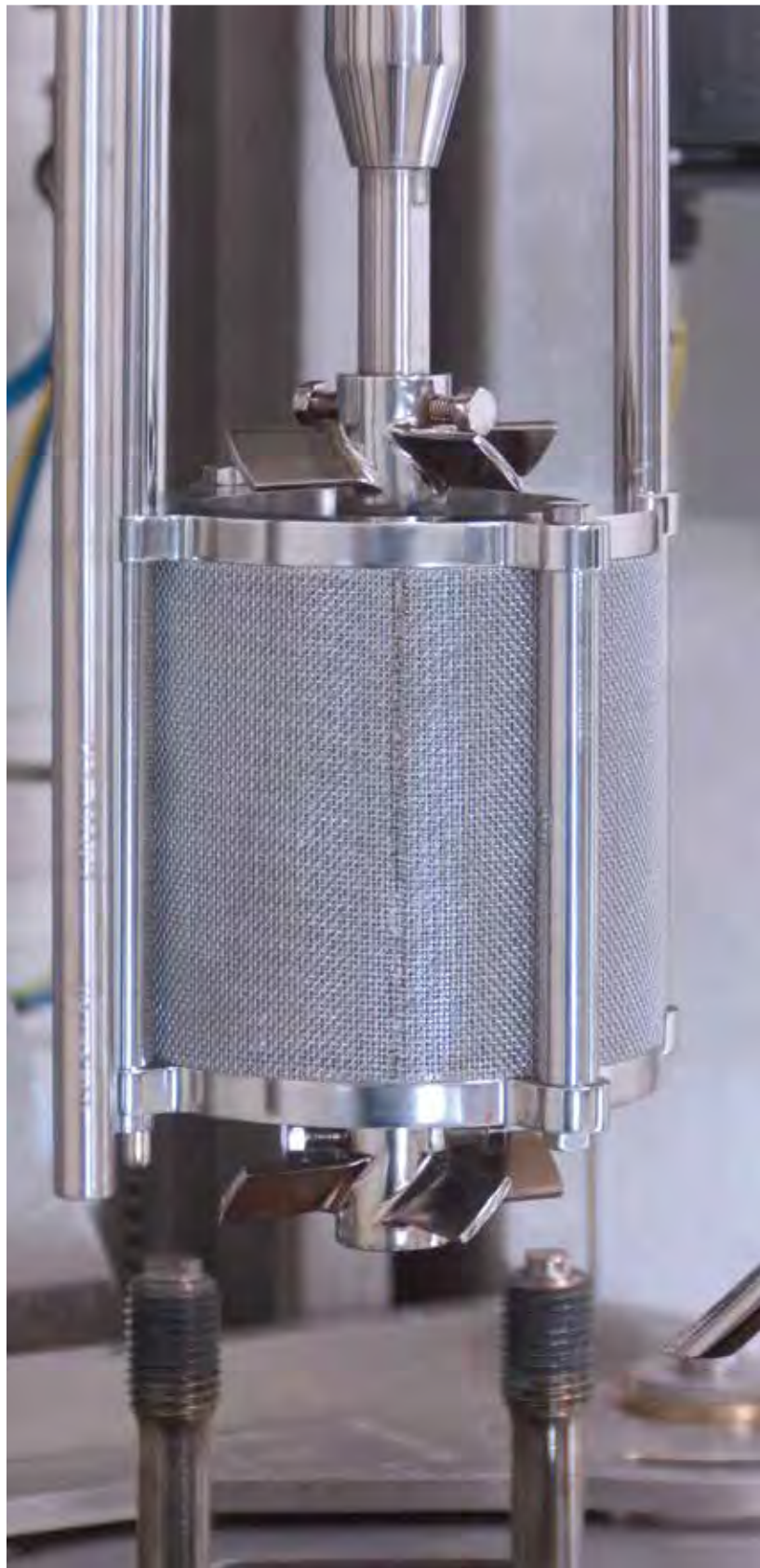
### Contact

#### Fraunhofer CBP

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16

Projects with universities, municipalities or funded by foundations

61

Industrial projects

32

Fraunhofer internal projects

2

Fraunhofer lighthouse projects

49

Projects funded by German federal ministries

14

Projects funded by German states

20

EU projects

194

Projects

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# BIOLOGICAL TRANSFORMATION

## Sustainable industrial value creation through the use of biological principles, systems and biotechnological processes

Starting with chemistry and physics at interfaces, the technology spectrum of Fraunhofer IGB was expanded in the mid-1970s already to include bioprocess engineering. With the development of molecular biotechnology, the Institute today is able to handle an extensive range of different biotechnological methods and biological systems – from bioinspired materials and the use of nucleic acids, enzymes and viruses, to microorganisms and human cell lines, to tissue and organ models. The convergence of biotechnological processes with physical-chemical methods of interfacial engineering is unique at Fraunhofer. It enables the Institute to use interdisciplinary approaches to convert principles from biology into technical applications, to develop biotechnological processes and biobased materials, and to establish bioinspired and biointelligent value chains for different industries.

Humans have always been inspired to apply biological processes, long before the highly complex biological systems such as the organisms used today to produce protein active ingredients, vitamins and enzymes were even identified as “production systems”. The spectrum ranges from the use of fermentation processes to preserve food to the imitation and application of plant interaction using fungi and algae as examples in the “production system” of lichens to complex biotechnological processes for the production of pharmaceutical products, food additives and chemical base materials based on biogenic raw materials.

The aim of biology as a core discipline of the life sciences is to grasp, investigate and understand the principles, structures and systems of living nature and its functions. The understanding of biological processes, especially at the molecular biological level, as well as the discovery and application of new molecular biological tools allow, in addition to classical bioprocess engineering, the direct transfer of knowledge to industrial applications – in medicine, environmental protection, agriculture, the food industry and chemistry. They therefore make an essential contribution to the protection of our livelihoods and to the further development of society.

The growing world population, climate change, islands of plastic waste in the sea, micropollutants in drinking water and many other global challenges are raising awareness of the basic principles and ecological relationships of our planet and the need to develop ecological and sustainable production processes, if possible without limiting the basis of our prosperity. This results, among other things, in the demand for materials that are not only produced from CO<sub>2</sub>-neutral raw materials, but are also degraded through natural material cycles or made available again for new production cycles through innovative recycling processes. For raw material- and energy-efficient production processes in recovered materials cycles (Smart Cities), natural food from an environmentally friendly agriculture, clean drinking water for all or novel therapy methods, the different facets of biotechnology enable solutions and allow the change to a “biologized” economy. Fraunhofer IGB is helping to shape this change.



## **SUSTAINABLE VALUE CREATION THROUGH “BIOLOGICAL TRANSFORMATION”**

The “biological transformation” has long since begun. Like the “digital transformation”, which has become an indispensable part of people’s everyday lives due to the Internet and the use of smart phones, it has also changed production processes with new biological active substances in medicine and with the systems approach of bioeconomy, which we will consider separately because of its great importance for the Institute’s research strategy. In particular, the interaction between digital technologies and artificial intelligence on the one hand and the interconnection of life, materials and production sciences on the other will make far-reaching innovations possible in the future. As an example, self-learning systems are conceivable whose learning processes are controlled by simulating processes of real cells in combination with digital algorithms and are used in the manufacture of completely new products.

According to the definition given by Fraunhofer-Gesellschaft, biological transformation makes use of the principles, materials and structures of living nature. These are not necessarily synonymous with the use of biological systems (cells, tissues) – as the highest level of integration. Rather, the production systems of the future will also be able to imitate and adapt the principles of biology or its materials and structures. This means that the production process of the future has learned from nature and its principles and processes and applies them to biotechnologically produced pharmaceuticals and “biologized medicine” or – in the case of other sectors – in the sense of natural material cycles.

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### **IGB: Pioneer and key player in biological transformation**

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For more than 40 years, IGB has focused its work on the development of biotechnological processes and biobased products, which are used in the medical, pharmaceutical and diagnostic, food processing, chemical and renewable energy sectors, among others, based on the added social value of new and sustainable products while maintaining functionality and quality. At IGB, industrial value creation and environmental aspects were linked at an early stage as a solution for sustainable economic activity.

With its commitment to the innovation process of biological transformation, the Institute is actively addressing the challenges of biologized medical care for people and bringing together individual value chains – “from raw material to product”, “nature’s own chemical plant”, “Nexus water, nutrition and energy” – to create holistic value creation cycles for the production systems of the future. The abundance to which the Institute draws on in this respect is illustrated by the examples selected below for the various biological “system levels”.



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### **The tools of the trade – Molecular biology and bioprocess engineering as the basis of value creation**

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Biological systems consist of individual or a large number of cells that multiply through metabolisms and processes organized in control loops and interact in complex structured networks. The understanding of these intracellular (metabolism) as well as extracellular (cell differentiation in the organism) control and regulation mechanisms is an essential tool for the development of effective microorganisms, not only for the production of enzymes or biopolymers, but also for the development of drugs that balance disturbed cellular control and regulation mechanisms. Examples of this are the administration of insulin for diabetes or highly individualized therapies such as CAR-T cell therapy for tumor diseases.

#### **From recognition at molecular level...**

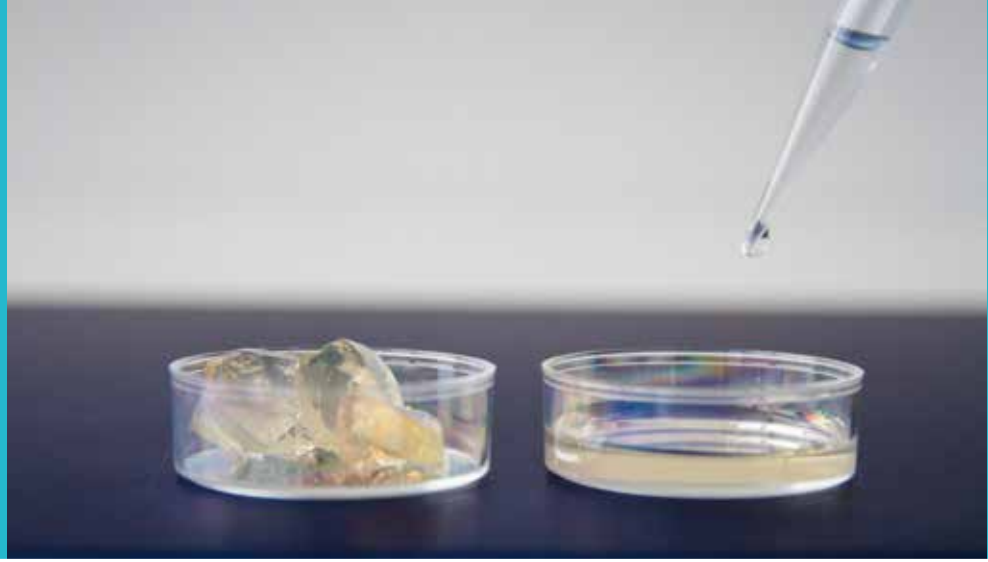
Among other things, IGB contributes to the decoding of these networks and control mechanisms by developing and applying innovative methods in the field of high-throughput sequencing (Next-generation sequencing). IGB is therefore laying the foundation for the identification of biomarkers for the personalized diagnosis of various diseases, for the molecular analysis of infection processes or for the characterization of microorganisms for industrial biotechnology. Furthermore, the Institute uses this technology to capture complex microbial metagenomes and transcriptomes for diagnostics as well as for environmental biotechnology. Based on these findings, new production organisms for biobased chemicals or pollutant-degrading microorganisms are identified and subsequently optimized using molecular biological methods.

#### **...to material conversion with bioprocess engineering**

As a further core element of biological transformation, bioprocess engineering deals with the development, modelling, operation and scaling of biotechnological processes in order to implement them in industrial practice. On the one hand, the optimal cultivation conditions for the targeted build-up of products or degradation of pollutants by the organisms must be set. In addition to material conversion, IGB also integrates the appropriate digestion, extraction or purification procedures into the process. In this context, our aim is to achieve maximum material and energy efficiency as well as product quality throughout the entire process chain.

We therefore also develop specific reactor systems for the various tasks, for example membrane reactors for immobilizing enzymes or bioreactor systems, with which the hydraulic residence time can be decoupled from the biomass residence time and thus the space-time yield can be increased.

The complex control mechanisms inside and outside the cells also require comprehensive measurement and control technology for the entire system. The integration of artificial intelligence into these systems will enable both process intensification and accelerated adaptation to rapidly changing conditions.



## SYSTEM LEVELS OF BIOLOGICAL TRANSFORMATION AT IGB

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### Bioinspired materials and biologized surfaces

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Wherever materials come into contact with biological systems, the properties of the materials and their interaction with the physiological environment play a decisive role. In the case of medical devices, our focus is on the interaction at the interface between the technical and the biological system. Depending on the objective, we modify the surface of the material used in such a way that the function of the biological component is not only not impaired (biocompatible), but in many cases even supported (bioactive). Depending on whether the interfaces are to adhere to each other (implants) or be moved against each other (joints), adequate mechanical properties are required in addition to the chemical properties to stabilize the bond.

To optimize the mechanical properties, the third dimension comes into play. The two-dimensional boundary surface becomes a three-dimensional boundary phase. For this case nature has developed and combined special materials with unusual mechanical properties. One example is joints. With its special viscoelastic properties, joint cartilage, together with synovial fluid or its defined viscosity, ensures that joints can fulfill their function even under greater mechanical and intermittent stress. The implementation of such systems in technology still requires a great deal of fundamental research. Cartilage, for example, is anisotropic in its mechanical properties. We tackle this challenge with special printing techniques using “bioinks” developed at IGB.

In future, new materials from the matrix of tissues, bioinspired structures and biofunctional or biologized surfaces will ensure that medical devices, prostheses and implants are better tolerated. Materials that replicate the biochemical and mechanical properties of natural tissues can minimize irritation in the organism and prolong the shelf life of medical devices: In the future, materials will be available that can be fully integrated by the body, making them both patient-friendly and cost-effective.

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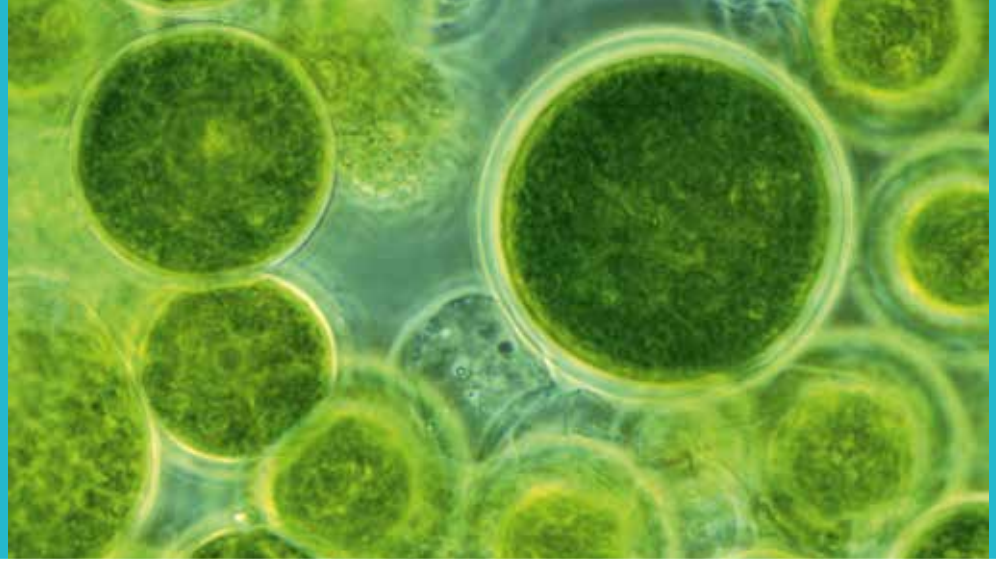
### Enzymes – Specific conversion under mild conditions

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The catalysts of biological cells are enzymes, proteins that bring about all chemical reactions in the metabolism. Enzymes have conquered numerous areas of everyday human life, from detergents to shampoo and toothpaste. As sensors, they reliably measure pollutants and help determine the blood sugar content of diabetics. Biocatalysts are highly specific to the substrate being converted and can also be used to produce compounds that are chemically difficult to access. Due to this specificity, the biocatalytically prepared products are of high purity – no by-products are formed.

IGB uses enzyme reactions for its own developments, but also produces new enzymes on behalf of customers. Development begins with the screening of suitable enzymes, e.g. in soil samples or in sequence databases. Once candidates have been found, bacteria or yeasts are used for the efficient production of the enzymes and the cultivation is optimized from laboratory to pilot scale.





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### **Big data of biology – Mass data through DNA sequencing**

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While the decoding of the human genome in the Human Genome Project still took more than 10 years, today entire organisms are sequenced within days or hours thanks to new and considerably faster sequencing methods for DNA, the so-called high-throughput or next-generation sequencing methods. This rapid development makes a lot of data accessible that allows the analysis of complex biological systems in unprecedented ways. This ranges from the understanding of cellular communication in complex organisms to the analysis of biological networks in microbial communities, so-called microbiomes. In the future, platforms of machine learning (artificial intelligence) and artificial neural networks can be used for the analysis and evaluation of these complex data sets in order to further accelerate the understanding of complex biochemical processes in cells and organisms and the identification of biomarkers for diagnostics and therapy.

Metagenome-wide data analysis has also created completely new possibilities in the diagnosis of diseases. IGB uses these possibilities to develop new methods for NGS-based diagnostics. Procedures for the preparation of patient samples and new bioinformatic methods have been developed in order to determine, for example, genetic identification traits from the sequence data of a blood sample, with which microorganisms can be unambiguously diagnosed as pathogens of infectious diseases. Since resistances are also determined by genes, high-throughput sequencing even makes it possible to identify not only the biological type of the pathogen in the same analysis, but also its resistance genes – and thus a further starting point for the respective optimal therapy. Patient benefit and cost reduction go hand in hand here.

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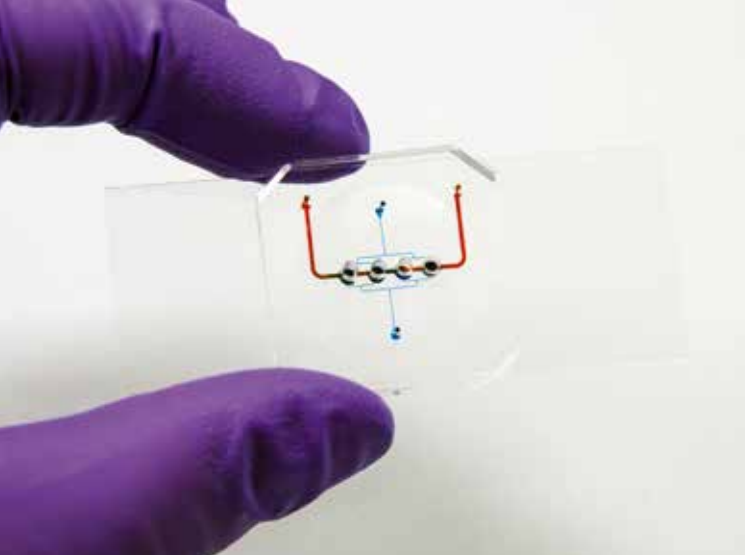
### **The cell as a production system**

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Microorganisms are particularly well suited for the production of biobased chemicals or for food production, as they can multiply very quickly using biogenic nutrients and are therefore highly productive in the long term. In particular, higher microorganisms such as fungi or algae have a large number of metabolic networks that generate metabolic products that can be used by us. Penicillin is one of the most important products derived from fungi, but basic molecules for polymers (succinic acid, malic acid, itaconic acid) or biosurfactants for use as detergents, emulsifiers or as active ingredients in cosmetics and crop protection can also be obtained as biobased chemicals from fungi and other microorganisms, as we demonstrated at IGB.

It is often possible to achieve increased production by microorganisms of the desired substance through selection procedures without genetic modification. However, the metabolic networks often have to be modified in such a way that molecules that are normally used differently by the organism are converted into the desired substance (metabolic engineering).

In many cases, completely new metabolic pathways are implanted into the organism. This is the case, for example, in the production of enzymes, but also for pharmaceutical proteins in mammalian cell lines. Although mammalian cell lines are much more sensitive than microorganisms, due to their similarity to human cells, they form, in contrast to microorganisms, most of the desired proteins with comparable modifications to humans. This dramatically increases their effectiveness. With our molecular biological expertise in the modification of microorganisms and the recombinant production of proteins in mammalian cells, we contribute to the biotechnological production of biobased chemicals as well as to the production of therapeutic proteins through the recognition and modification of metabolic networks.



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### Human tissue and organ models for game-changing preclinical tests

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Tissues and organs consist of different differentiated cells which in each case take over specific functions for a common task via cellular communication and regulatory mechanisms. In order to understand these mechanisms and be able to reproduce them in a manageable system, we reproduce models of human tissues and organs in the laboratory, with which human physiology and its diseases can be reproduced much better than in animal models.

Complex models made up of human cells also contain components of the immune system and we use them as test systems for the development and evaluation of new pharmaceuticals. 3D tissue models can also be used to set up test systems with disturbed control and regulation mechanisms (e.g. from patient biopsies or via specifically modified human cells), on which active substances that compensate for this disturbance can be validated.

The cultivation of the smallest functional unit of an organ into artificial microfluidic systems, so-called organ-on-a-chip systems, is another new technology for providing meaningful test systems for drug development. IGB constructs such organ-on-chips from human induced pluripotent stem cells. These hiPS cells can be specifically differentiated so that tissue can also be obtained that cannot be isolated from primary biopsies. Since the cells of the organ-on-chip in the micro-physiological system react to drug candidates in the same way as would be the case in the human organism, they are used to investigate active substances that cannot be evaluated in animal experiments – and animal experiments can be increasingly replaced.

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### Recovery and reuse – material cycles based on nature

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Waste does not arise in living nature. In the biological cycle, plants and microalgae from carbon dioxide and inorganic nutrients such as nitrogen, phosphorus and sulphur form organic matter by means of photosynthesis, which is used by other organisms via the food chains to build up their biomass. Through respiration and microbial degradation of dead organic matter, CO<sub>2</sub> and nutrients are finally available again for new biosynthesis cycles.

IGB research at the “environment” system level is oriented towards natural material cycles that are not influenced or disturbed by humans. The aim of our concepts for the treatment of wastewater, for example, is to recover ingredients in a recyclable form. In our system approach “semi-decentralized integrated water management” we use anaerobic microorganisms to convert the organic matter present in the wastewater into biogas. The remaining nutrients can be precipitated in a plant-available form or, with the purified water, used for fertilizing irrigation.

In addition to the wastewater treatment plants common in Western civilization today, in which nutrients are disposed of in non-recyclable form instead of being processed for return to the biological cycle, it is above all industrial agriculture that withdraws nutrients from the natural cycles. When the plants are harvested, the nutrients are removed from the agroecosystem and hardly any return takes place. This makes the supply of synthetic fertilizers necessary. With our newly patented technologies, we focus on the recovery of nutrients from wastewater and liquid manure, fermentation residues and residual materials from the food industry and on agriculture that is oriented towards natural material cycles.



**HEALTH**

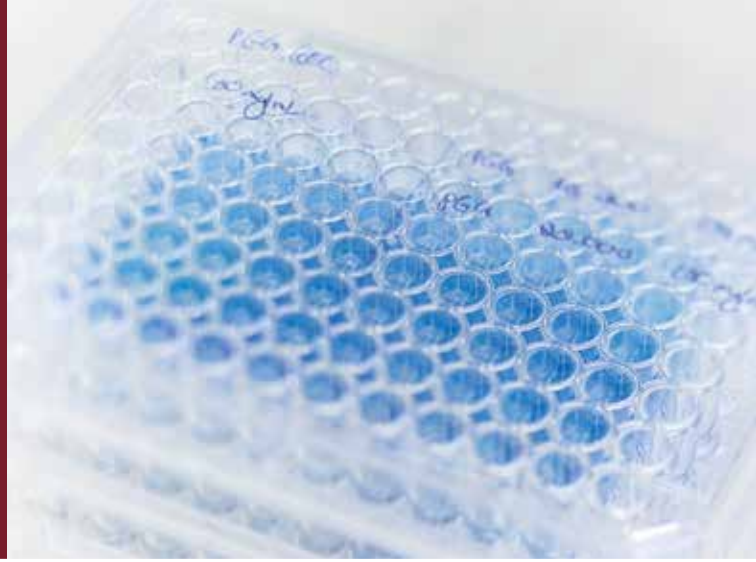


Faster and more precise diagnoses using molecular biological approaches or new opportunities for recovery through individualized therapy approaches – one example is the coordinated interplay between a (“biologized”) implant and its physiological environment – are scientific trends that are becoming more important because of the increase in life expectancy. Hence, drug efficacy has to be improved, for example by optimizing formulations and targeted release of active ingredients at the sites where they are needed.

Fraunhofer IGB is developing solutions in these research areas. The aim is to improve medical care for patients and simultaneously reduce healthcare costs. One focus here is on the development of three-dimensional *in vitro* models from human tissues up to organ-on-a-chip systems, as human test systems allow conclusions about effects and side effects of potential drug candidates already in preclinical research and thus can replace animal experiments. Personalized medicine is another promising field of application for organ-on-chips.

#### **Networking and cooperation**

With our expertise, we contribute to the Fraunhofer Group for Life Sciences' offer of covering R&D for drug development from initial screenings to the production of test samples. In addition, we are networked in the Fraunhofer Generative Manufacturing Alliance. With the Fraunhofer Project Center for Drug Discovery and Delivery @ Hebrew University of Jerusalem, Israel, we have an important partner for the identification of new immune modulators and their formulation for the fight against infectious diseases and immune-mediated diseases.



### Coatings and biomaterials for medical technology

Properties of the materials and interactions between the material and the biological system are key factors in the manufacture of implants and medical devices. Fraunhofer IGB is developing bioactive, biocompatible or bioinert materials for use in medicine and medical technology, e.g. for stents, catheters and implants. We are testing biocompatibility of the materials using an accredited testing method according to DIN EN ISO 10993-5.

For implants, we are investigating cell-material interactions and developing materials such as biodegradable fibers or hydrogels that are developed further to bioinks for additive manufacturing of tissue models. In addition to biological carriers, Fraunhofer IGB is also developing miniaturized tubes as supply systems for larger tissue models.

### Molecular diagnostics

Precise diagnosis of a disease is a fundamental prerequisite for any therapy and the basis for personalized medicine. Fraunhofer IGB is developing novel molecular biology technologies based on nucleic acids (microarrays, high-throughput DNA sequencing) or using cellular reporter systems (pyrogen assay system) that can be used for clear and unambiguous diagnoses. This information helps to initiate measures for specific treatments or develop personalized medicines for different population groups.

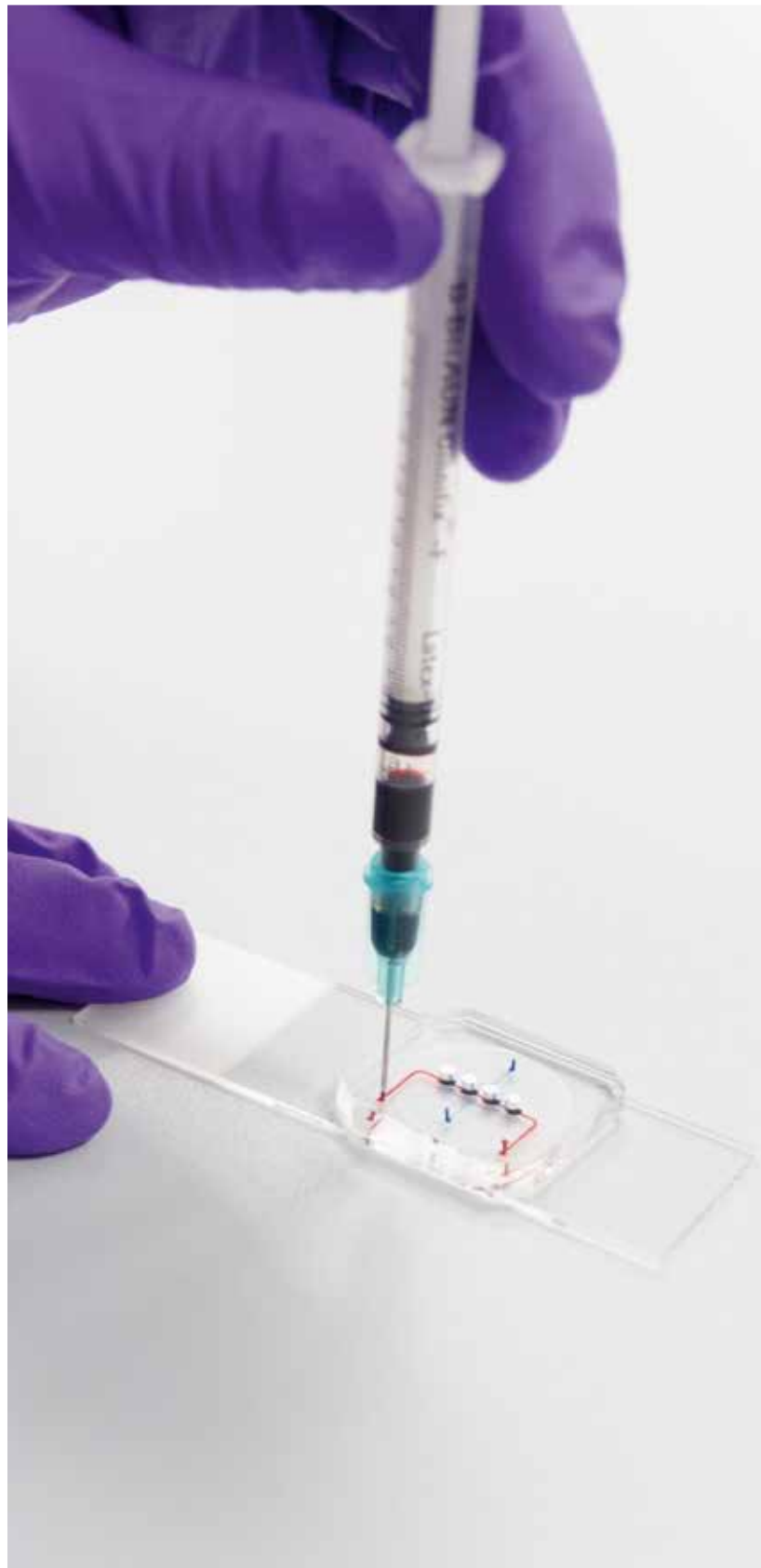
In particular for combating infectious diseases, the combination of methods of functional genome analysis with our expertise in cell culture technology and infection biology results in a unique position for developing infection models and diagnostics. In addition, based on Raman microscopy, we have established a versatile, non-invasive and marker-free diagnostic method for real-time cell and tissue analysis.

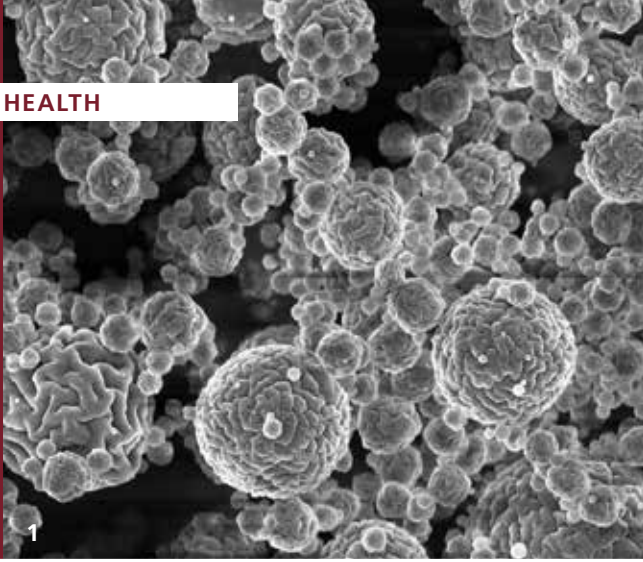
## Drug development and test systems

Diseases are often caused by faulty interactions among endogenous molecules – for example, due to modified receptors or enzymes playing a decisive role in cellular signal chains and metabolic pathways. Fraunhofer IGB has developed various screening systems – from simple cell-based assays to complex human tissue models with immune system components. These systems support the analysis of the interactions of different cell types associated with autoimmune diseases such as psoriasis or dermatitis, for example, or host-pathogen interactions on the molecular level. As a result, we are able to identify new target structures for the development of antibiotics or for the modulation of a patient's own immune system.

To analyze the effects and side effects of potential active compounds, we are developing three-dimensional *in vitro* tissue models and organ-on-a-chip systems based on human primary or iPS cells. These systems help to replace animal tests and to increase the information value of preclinical results. In addition, we are developing processes to produce pharmaceutical proteins: from the establishment of new expression vectors to strain development and purification of the pharmaceuticals.

We are pursuing a new approach with the development of "therapeutic" viruses. In this field, we use the ability of viruses to kill cancer cells. At IGB, Virus Engineering is tailoring a modular oncolytic viral vector based on HSV1 for cancer therapy.





### N2B-patch – Development of an intranasal form of therapy for the treatment of multiple sclerosis

Acting as project coordinator as part of the EU-funded joint project “N2B-patch”, Fraunhofer IGB is involved in the development of a medicine-based treatment form for drug delivery over the regio olfactoria. At this position, the brain and the fluids surrounding it are separated from the nasal cavity by only the ethmoid bone and a few layers of cells. For many diseases – for example, of the central nervous system – it is crucial to transport the active substance to the desired target site in the most efficient way possible. One example of this is the treatment of multiple sclerosis, where the active substances must exert their effects predominantly on the central nervous system (CNS).

The goal is to develop an intranasal application platform for CNS-active biopharmaceuticals. Within the project, Fraunhofer IGB concentrates on the formulation of particles containing the active substance (fig. 1), and the embedding of these into hydrogels.

The development of a new form of therapy usually requires several years of intensive research and validation. The N2B-patch team starts its work in the laboratory and ends in proof of concept and pre-clinical validation. A total of eleven project partners from research and industry are participating in the project, which started at the beginning of 2017 and has financial backing for four years. The project partners are primarily focusing their research on the treatment of multiple sclerosis but they also hope to open up further fields of application of the N2B-platform.

[www.igb.fraunhofer.de/en/n2b-patch](http://www.igb.fraunhofer.de/en/n2b-patch)



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### Barrier coatings for the biocompatible encapsulation of electronic implants

In order to ensure that implanted electronic devices can reliably fulfil their function in the longer term, they must be protected from the corrosive effects of the environment in the body. Conversely, the surrounding tissue must not be harmed by compounds released by the electronic device or react with the development of fibrous tissue. Metal or glass housing is currently used which, however, is limited in relation to its potential for miniaturization and cost reduction.

To demonstrate its feasibility, Fraunhofer IGB has produced a barrier coating, which constitutes an effective barrier against metal ions and water, on a circular electronic implant component that contains copper and nickel (fig. 2). The demonstrator remained functional after six months storage in a physiological medium and no copper or nickel ions were released.

The new approach to this problem involves multiple layers of inorganic and organic coatings that jointly produce a barrier coating that is mechanically more stable and more effective. The required biocompatibility was considered in the choice of materials. The barrier coatings were produced using PECVD and CVD methods and are composed of  $\text{SiO}_x$ , silicone-like and parylene-C coating, with a total thickness of around 20 micrometers. Factors that are to decisive for good barrier efficacy are high levels of cohesion in the bonding between the layers and a form-fit coating. The coatings that have been developed can be applied to a variety of geometric shapes and will thus facilitate the development of new miniaturized implants.

[www.igb.fraunhofer.de/biocompatible-encapsulation](http://www.igb.fraunhofer.de/biocompatible-encapsulation)



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### More reliable next-generation diagnostics for sepsis pathogens

In sepsis management, fast treatment using the correct antibiotic is crucial for patient survival. This, however, is not always possible in a targeted manner, since using the current standard (blood culture) pathogen detection is successful in only approximately 30 percent of cases. Therefore, a novel, molecular diagnostic and bioinformatic method has been developed at Fraunhofer IGB to detect DNA fragments of pathogens in patient blood using parallel sequencing (next-generation sequencing, NGS) and bioinformatic algorithms, allowing for highly-specific and sensitive identification of pathogens (fig. 3).

As part of a recent clinical study in collaboration with the University Hospital Heidelberg, we were successful in achieving significantly more positive results on pathogen identification with this technology compared to using blood culture (71 percent compared to 11 percent) in 50 patients with septic shock. A jury of independent intensive care specialists considered 96 percent of the positive NGS results to be plausible. According to the jury, treatment of 53 percent of the patients would have been adapted subsequently on the basis of these results, since they were often over- or undertreated due to the empirical antibiotic use. In this group of patients not receiving adequate treatment, the mortality rate was increased by 13 percent. These concrete effects on patient treatment success convincingly demonstrate the enormous potential of more reliable and sensitive pathogen diagnostics. The retrospective observations will now be validated in a multicenter study with approximately 15 hospitals, expected to start in January 2019.

[www.igb.fraunhofer.de/sepsis-study](http://www.igb.fraunhofer.de/sepsis-study)



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### Organ-on-a-chip platforms for the examination of beige adipose tissue

The activation of brown and beige adipose tissue (BAT) and “browning”, (generation of BAT in white fat tissue depots) has aroused great interest in biomedical research in the last few years. This is mainly due to the decoupling of the mitochondrial respiratory chain in BAT, a biochemical process that is showing considerable potential for new therapeutic approaches, in particular to obesity and diabetes. However, studies with human tissue are still rare and difficult to carry out at present. Concepts and technologies to examine browning for pharmacological studies and personalized medicine currently exist only to a limited extent.

As part of a collaborative project supported by the German Academic Exchange Service (Deutscher Akademischer Austauschdienst, DAAD), Julia Rogal, a Talenta-funded IGB junior scientist, has conducted research at the University of California at Berkeley, USA, for two months and has developed an innovative microfluidic system (fig. 4) for the integration of (beige) adipose tissue. This BAT-on-a-chip makes a variety of different assays possible, e.g. to examine activation/blocking of the functionality of BAT, the induction of browning in white adipose tissue, and characterization of endocrine and metabolic function of BAT. The BAT-on-the chip system opens up diverse possibilities as an *in vitro* model for general screens to identify substances that induce browning, as well as for approaches to examine patient-specific effects of therapy approaches.

[www.igb.fraunhofer.de/en/bat-on-a-chip](http://www.igb.fraunhofer.de/en/bat-on-a-chip)



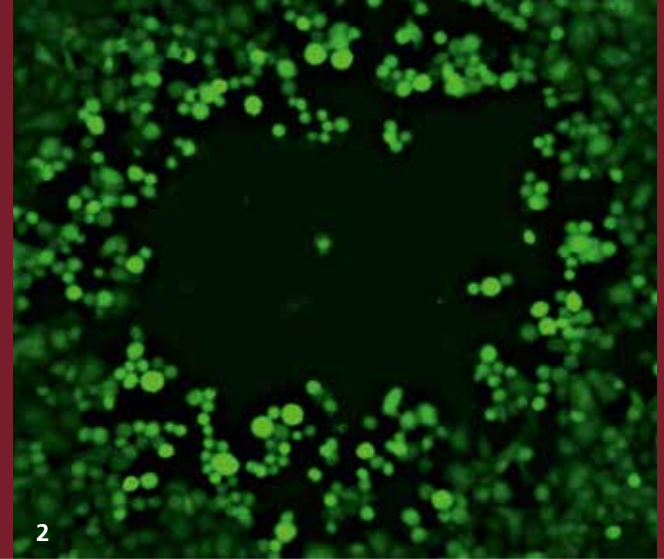
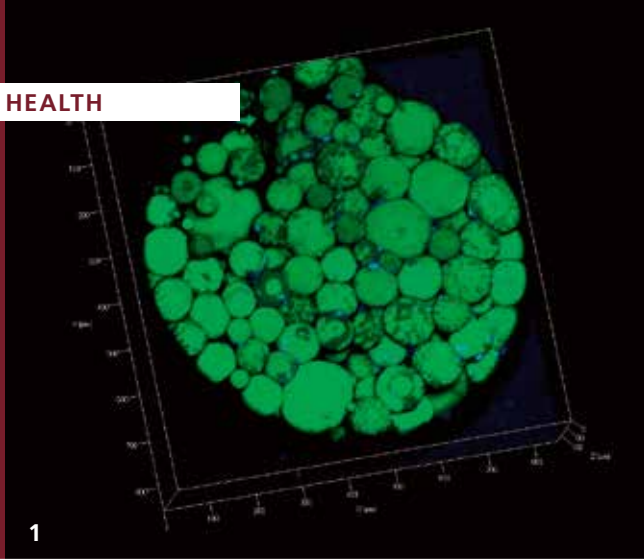
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### Micro-physiological *in vitro* model of white fat tissue for obesity and diabetes research

White adipose tissue (WAT) is an organ that is still often overlooked although it can represent approximately 20 – 25 percent of the body weight in healthy men and women and even more than 50 percent in the case of illness (obesity). WAT is a highly specialized connective tissue which has only been perceived as a storage and energy supply organ for a long time. Nowadays, it is recognized as an important endocrine organ secreting a wide array of cytokines and thus playing an important role in a wide range of diseases of the liver, heart and kidneys.

Due to the rapidly increasing prevalence of obesity and associated diseases such as type-2 diabetes, it is becoming more and more important for pharmaceutical and biomedical research to understand (patho-)mechanisms and dysfunction in fat tissues. However, at present, a limiting factor is that human adult fat tissue can only be cultivated *in vitro* to a limited extent. The Attract Group Organ-on-a-chip has now succeeded in generating a human adult WAT in a micro-physiological 3D environment (fig. 1) and keeping it functional for more than one month using blood-vessel-like perfusion. The WAT-on-a-chip system opens up a variety of possibilities for studies on mechanistic processes in obesity and diabetes research as well as for the examination of effect, toxicity and storage of pharmaceutical preparations.

[www.igb.fraunhofer.de/en/wat-on-a-chip](http://www.igb.fraunhofer.de/en/wat-on-a-chip)



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### TheraVision – Platform technology for the development, production and testing of oncolytic viruses

Viruses are able to penetrate cells, produce both foreign and viral proteins, multiply, and ultimately kill infected cells, raising new hope in cancer therapy. Clinical trials involving first oncolytic (cancer-killing) viruses are very promising, although there is still a significant need for their optimization. In the TheraVision project, the Fraunhofer Institutes ITEM, ISC, IZI, and ITWM, coordinated by IGB, the aim is to establish a broadly applicable platform technology based on Herpes simplex virus type 1 (HSV1) (fig. 2) for combinatorial oncolytic virus immunotherapy. As proof of concept, an oncolytic virus is being developed for the therapy of Non-Small Cell Lung Cancer (NSCLC).

Through genetic modification, the HSV1 platform vector has been established and is being functionalized as an oncolytic virus with not only high specificity by means of viral targeting to cancer cells but also high efficacy by encoding immune modulators. For the production of such a virus, a robust and scalable process is being developed simultaneously, optimized by bioinformatic modeling. This process addresses the regulatory stipulations of Good Manufacturing Practice (GMP) to allow for a seamless transfer to GMP production. Human 3D *in vitro* tumor models as well as complex humanized *in vivo* mouse models are established to evaluate the effect of the therapeutic viruses on primary tumors and metastases in the presence of human immune cells. The institutes collaborating in TheraVision bring together core competencies to complete the entire production process of this oncolytic virus technology.

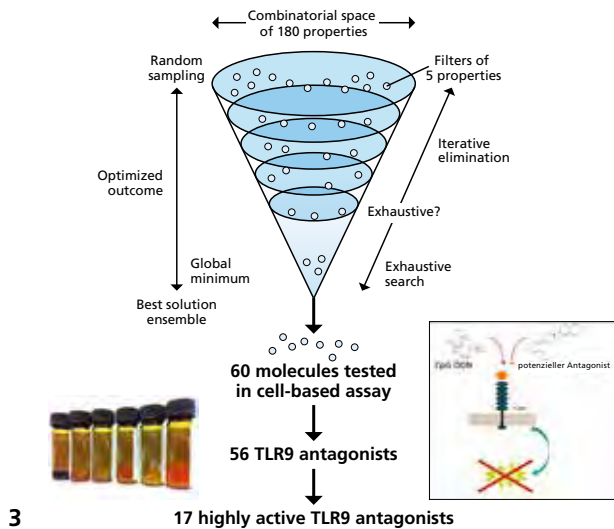
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### FPC\_DD@HUJI: Drug discovery and formulation for infections and autoimmune diseases

The “Fraunhofer Project Center for Drug Discovery and Delivery” at the Hebrew University in Jerusalem, Israel (FPC\_DD@HUJI), which was approved in 2018, focuses on discovering of new and validation of identified substances and nanoparticle delivery systems for virus infections and autoimmune diseases.

A combination of computational chemistry (on the part of HU) and a patented reporter gene assay (from IGB) is used with the aim of finding new Pattern recognition receptor antagonists (PRR) and/or agonists for modulation of the innate immune response. During the preceding project “JRHDD – Joint Research Hub for Drug Discovery and Delivery”, 17 potential antagonists with high IC<sub>50</sub> value were identified from the 1.8 million commercially available molecules, and these were registered for patent.

Another focal point is the development of new therapeutic strategies against herpes simplex viruses (HSV). Herpes viruses cause lifelong latent infections in neuronal cells and cannot be eliminated at present. Substances such as antimicrobial peptides kill the virus but are also highly toxic to eukaryotic cells. For that reason, we develop liposomal formulations with optimal physico-chemical properties. These targeted liposomal transport systems (HU) are used for encapsulation of specific substances and siRNAs which block virus replication, and are investigated and analyzed using 2D and 3D cell-based test systems (IGB). Initial navigator peptide phospholipid formulations have shown an improved delivery of the active substances to neuronal cells.

[www.igb.fraunhofer.de/en/fpc-dd](http://www.igb.fraunhofer.de/en/fpc-dd)

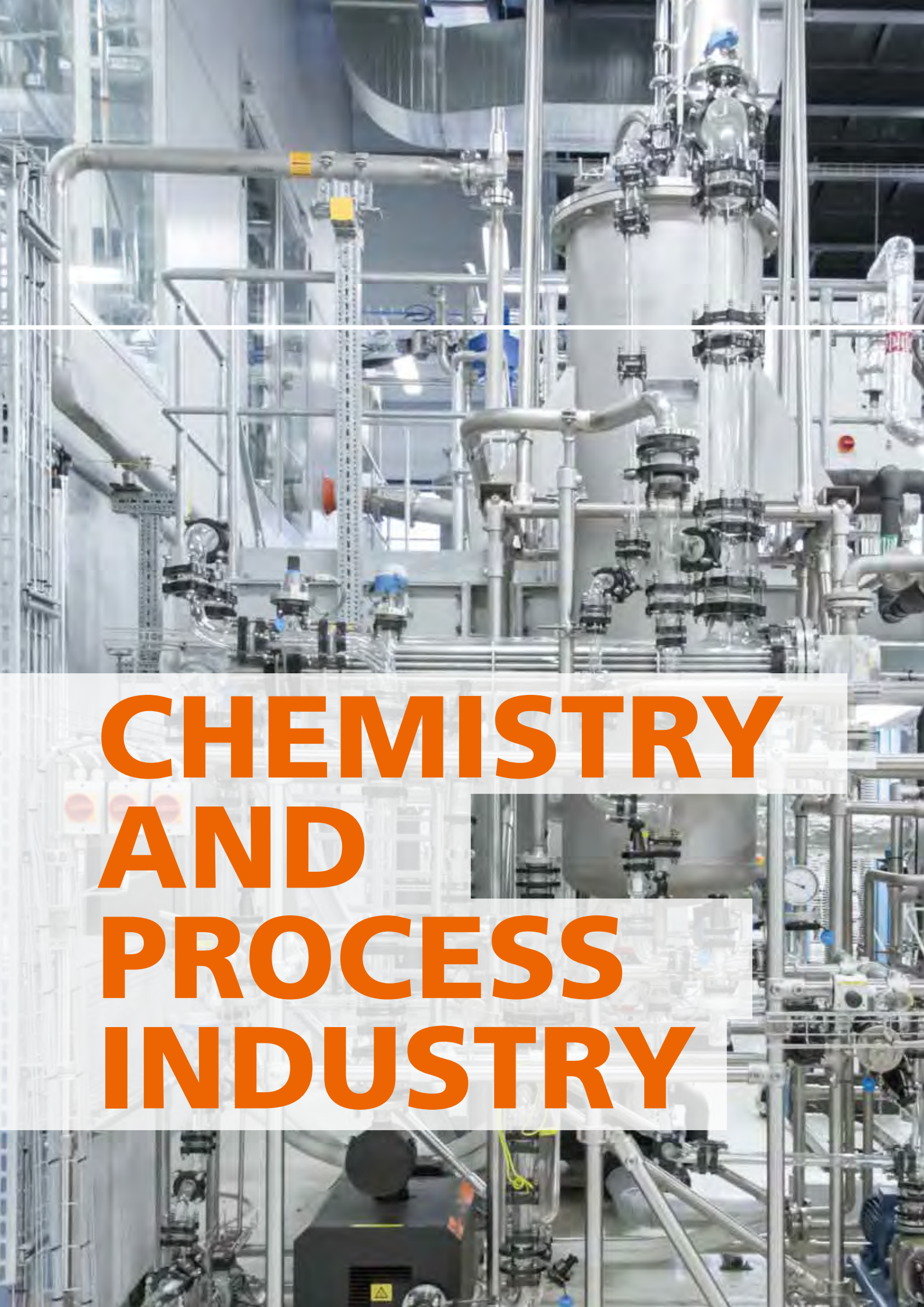


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# CHEMISTRY AND PROCESS INDUSTRY

The chemical industry is one of the most important and research-intensive economic sectors in Germany. Many innovations in the automotive, electrical and electronic, construction and packaging industries would not be possible without the contributions of chemistry.

More than all other sectors, the chemical and further processing industries are characterized by resource- and energy-intensive processes. The dependence on the import of raw materials, the limited availability of fossil resources worldwide – even in competition with energy use – and the need to consider the impacts on both climate and the environment mean that our research also emphasizes initiatives to make the use of fossil resources more efficient or to create substitutes for them.

With new and optimized conversion processes, energy-efficient processing technologies, product-friendly stabilization processes and new products based on biogenic residues and microalgae, IGB addresses both the traditional chemical industries and also the food, feed and cosmetics industries.

#### **Networking and cooperation**

Our distinctive networking collaborations with other institutes of the Fraunhofer Groups for Life Sciences and for Materials and Components – MATERIALS, or the Fraunhofer Food Chain Management, Nanotechnology, Technical Textiles, Polymer Surfaces POLO® and Cleaning Technology Alliances, as well as with universities and other research institutions, guarantee competent approaches even to interdisciplinary tasks.





### Food and cosmetics

Intermediate products or residual materials in agricultural and food production may contain valuable ingredients that often remain unused. In order to separate functional ingredients economically and gently, IGB develops processes for extraction and fractionation as well as separation processes for the purification of the ingredients. Ingredients from microalgae with antioxidant or anti-inflammatory properties – for example omega-3 fatty acids (EPA) and carotenoids such as fucoxanthin, lutein or astaxanthin – are valuable natural substances for food supplements in human and animal nutrition.

In addition, we develop new physical processes such as pressure change technology to stabilize and preserve food, cosmetics, pharmaceutical substances and plant extracts without impairing the biological function of valuable ingredients. In order to dry food and feed with reduced energy requirements, we develop application-specific drying processes with superheated steam in our demonstration plants.

### Biobased chemicals and materials

The majority of basic chemicals and the products made from them are still synthesized from fossil raw materials. Biomass is an alternative, CO<sub>2</sub>-neutral and renewable raw material base for the production of chemical products. With many years of experience, Fraunhofer IGB develops and optimizes fermentative, biocatalytic and chemical as well as combined or coupled processes for the production of biobased chemical products. Already during the development of the conversion processes and optimization of the catalysts, the focus is on the scalability and cost efficiency of the processes as well as the downstream processing of the products. At the Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, the institute provides pilot plants that can be used to realize production-relevant dimensions.

For example, we have already successfully made use of different agricultural and forestry residuals (straw, wood waste), organic residues from a variety of industries (whey, crab shells and insect carapaces, terpenes) as well as renewable raw materials and – in accordance with the principle of a biorefinery – converted them into drop-in and basic chemicals as intermediates or fine chemicals and specialties using biotechnical and/or chemical processes.



Fraunhofer IGB has successfully developed fermentation and purification processes, for example, for C2 compounds (ethylene, acetic acid, ethanol) and C3 compounds (propylene, propanol, propanediol, propionic acid, lactic acid) as well as for dicarboxylic acids (malic acid, itaconic acid, furan dicarboxylic acid), amino acids and proteins. Based on renewable resources, algal lipids or biogenic residuals, we have successfully demonstrated new ways to produce basic materials (long-chain dicarboxylic acids, fatty acid epoxides, lactams) for polymer production. Further examples are aromatics, lignins, phenols and furans as well as extractives and their derivatives (terpenes, phytosterols, camphor), and gaseous and liquid hydrocarbons such as methane, olefins and long-chain alkanes. We have acknowledged expertise in the microbial production of biosurfactants for use as detergents or emulsifiers.

### Electrochemical synthesis of chemicals

With the expansion of regenerative power generation, low-cost excess electricity is generated, which – as an alternative to storage – can also be used flexibly for the electrochemical synthesis of basic chemicals. For this purpose, we are developing catalysts and suitable electrodes, electrolysis processes and equipment. In the Fraunhofer lighthouse project “Electricity as a Raw Material”, for example, Fraunhofer IGB has developed an electrochemical procedure to produce ethylene in a single process step. An electrochemical cell in which hydrogen peroxide can be produced from just water and air is already available as a prototype at the institute. In various other projects, we use renewable electricity to bind atmospheric CO<sub>2</sub> and convert it into chemicals. We are increasingly combining these electrochemical with biotechnical conversion processes.

### Functional surfaces and materials

For the surfaces of many materials, e.g. industrial components or technical textiles, the desired properties are often different from those that are intrinsic for the bulk material. Fraunhofer IGB is decoupling volume and surface properties by interfacial process engineering. We give surfaces of polymers, ceramics or metals new properties by applying thin layers or creating defined functions on surfaces. For this purpose, we use gas phase processes (CVD, PVD, PECVD), wet-chemical processes or combined processes. For open-pored polymeric foams with functional groups, we have developed a single-stage synthesis strategy.



1



2

### Application of laminarin from microalgae in plant production and human and animal nutrition

Diatoms (rock algae) use (chryso-)laminarin as energy and carbon reservoirs. The polysaccharide is a 1,3/1,6- $\beta$ -d-glucan that can be used in the food, animal feed and agricultural sectors. Laminarin can also be found in the cell wall of many fungi, including pathogenic species. Since contact with laminarin induces the immune system of vascular plants, the polysaccharide is suitable as plant strengthener. According to the literature, the application of laminarin can reduce infections with *Botrytis cinerea* or *Plasmopara viticola* in grapevines by 55 or 75 percent. Laminarin also has an immunomodulatory effect in vertebrates. The immune system in the digestive tract in particular reacts to the contact with laminarin.

The MIATEST project is examining the use of laminarin (fig. 1) as a biostimulant in viticulture in collaboration with the Landesversuchsanstalt für Wein- und Obstbau Baden-Württemberg and its application in nutrition at the Hohenheim University. To this end, Fraunhofer IGB is examining laminarin production strains, developing a two-step production process and producing laminarin-rich algae biomasses for test purposes.

In addition, laminarin is the subject of the EU-funded MAGNIFICENT BBI project, which is examining the provision of ingredients from microalgae for food, feed and cosmetics. The use of laminarin in juvenile fish rearing is currently being investigated.

[www.igb.fraunhofer.de/en/laminarin](http://www.igb.fraunhofer.de/en/laminarin)



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### Superheated steam drying of food products at atmospheric pressure

The use of superheated steam drying (SHSD) at atmospheric pressure has many advantages over conventional methods with hot air. The oxygen content in the process atmosphere is low, thus preventing oxidation processes affecting the product and thereby contributing towards maintaining product quality. The thermodynamic properties of the drying medium (water vapor) allow more intensive heat and mass transfer during the drying process. This means that shorter residence times are achieved than with conventional drying methods, resulting in less damage to the products (fig. 2) through thermal degradation during the drying process. The product quality is thereby enhanced.

Furthermore, food products contain components in their material matrix that become volatile at significantly lower temperatures than the drying temperature of approx. 120–150°C. Thanks to the partially open reactor concept in SHSD, these compounds are collected together with the excess vapor and can be separated selectively and recovered as recyclable material. This means that these highly valuable compounds are not lost, but can make a significant contribution towards covering the costs of the drying process step. The semi-open plant concept allows all conveyor techniques to be used, thus permitting the most suitable technique to be used for the food product. The plants can be designed compact and energy-efficient due to the more rapid drying process. Furthermore, the absence of atmospheric oxygen reduces the risk of explosion, resulting in a significantly simpler construction and operation.

[www.igb.fraunhofer.de/en/SHSD](http://www.igb.fraunhofer.de/en/SHSD)



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### BIOTRAIN – A new perspective for sustainable industrial value creation

Our current production systems, even when augmented by far-reaching digitalization, do not provide sufficient enablers to cater for the fair satisfaction of the material needs of finite resources of future generations. A transformation to sustainable production methods with new materials, closed cycles and the use of sustainable technologies seems more urgent than ever.

At the same time, the growing knowledge about biological processes and the new possibilities of digitalization offer new potentials to integrate the biological, technical and informational spheres. The “biological transformation of industrial value creation” is therefore understood as the systematic application of knowledge about biological processes for the purpose of holistic optimization of production systems.

With the participation of six Fraunhofer Institutes, the BIOTRAIN project identifies the strengths, weaknesses, opportunities and risks of a biological transformation of industrial value creation for Germany as a business location. The comprehensive analysis is based on extensive literature research, over 120 interviews with national and international experts from research and industry as well as numerous workshops with a total of over 200 participants. On the basis of this analysis, base technologies and their potential are also examined, and development paths as well as recommendations for action and design are developed for the public sector.

[www.igb.fraunhofer.de/en/biotrain](http://www.igb.fraunhofer.de/en/biotrain)



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### Cellobiose lipids – Microbial biosurfactants from sugars

Microbial biosurfactants such as cellobiose lipids (CL) can be produced by microorganisms on the basis of sugars. Due to their surface-active and antimicrobial properties, CLs may be used in cosmetics or cleaning agents. Based on these properties, they have great potential as a sustainable alternative to petrochemically produced surfactants. In order to exploit this potential, the Industrial Biotechnology Group at Fraunhofer IGB is developing fermentation and purification processes that allow the highest possible space-time yields and are therefore economical.

Using an *Ustilago maydis* strain, we were able to produce CL concentrations of more than 20 g·L<sup>-1</sup>. These were transferred from the shaking flask to the reactor scale (1 L, 10 L) (fig. 4). A fraction with a high cellobiose lipid concentration was collected by continuously separating the foam produced during fermentation. If this foam fraction is purified directly, only seven percent of the solvent quantity is required for the extraction of the cellobiose lipids, compared to conventional purification of the entire reactor content.

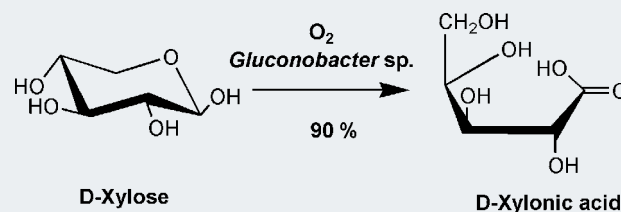
The individual process steps are evaluated by means of a life cycle analysis and a techno-economic assessment during the course of development. With the aid of these assessments, process bottlenecks are identified and validated experimentally. The findings obtained serve to continuously improve the economy and ecology of the overall process.

[www.igb.fraunhofer.de/biosurfactants](http://www.igb.fraunhofer.de/biosurfactants)



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2

### Driving on bark, building with nutshells

In order to support the European transition towards a post-petroleum society, the European UNRAVEL project will over the next four years demonstrate a sustainable and economically feasible biorefinery. A key task is the conversion of so called “second generation biomass” into fuels, chemicals and sustainable building materials. One promising solution lies in using biomass residues (fig. 1) that originate from forestry and/or agriculture such as bark, wheat straw or nutshells and that do not compete with land-use for food production or that could pose the risk of natural habitat loss.

To be able to use all valuable components that are present in a certain feedstock an efficient integrated biorefinery process is required. UNRAVEL will apply the mild biomass fractionation process FABIOLA™, which has been patented by the consortium partner ECN (part of TNO) and bring it to industrial maturity. The Fraunhofer Center for Chemical-Biotechnological Processes CBP, which coordinates the project, contributes with its expertise on the scale-up of biomass fractionation processes and its unique “lignocellulose biorefinery” pilot plant.

The new process that uses acetone as solvent has a large potential for improving the cost-effective pre-treatment of biomass and can thereby increase the industrial competitiveness of the targeted biobased products like advanced liquid biofuels for transport and biobased materials, such as biopolymers, insulation foams (polyurethane) and bitumen.

[www.igb.fraunhofer.de/en/unravel](http://www.igb.fraunhofer.de/en/unravel)



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### High concentrations of xyloic acid through process optimization

Gluconic acid is an important constituent of foodstuffs, construction materials and dyes. The acid is produced from glucose, which is obtained from plants rich in starch and thus competes with the production of foodstuffs. An alternative to gluconic acid is xyloic acid: on the one hand, this has similar properties and, on the other hand, it can be obtained from plant components containing lignocellulose or from agricultural waste material. The aim was therefore to develop an efficient process for obtaining xyloic acid from xylose.

The fermentation-based conversion of xylose is conducted using whole cell catalysis (*Gluconobacter* sp.), with addition of oxygen as a second reactant (fig. 2). In contrast to competing solutions, fermentation with *Gluconobacter* sp. has the advantage of being a specific, sustainable and efficient conversion. To date, the team of Industrial Biotechnology Group has achieved a xyloic acid concentration of over 250 g/L through optimization – with a yield of over 90 percent. In the subsequent rudimentary purification process, xyloic acid was obtained at a purity of over 80 percent, which is adequate for technical applications. The scalability of the process has already been demonstrated at the Fraunhofer Center for Chemical-Biotechnological Processes CBP by the team in the Biotechnological Processes Group with the 100-liter fermentation, a scale-up to 300 liters is planned. We are already making smaller quantities available for investigations for specific applications. For example, xyloic acid can be tested as a substitute for gluconic acid as a curing retardant for concrete or chelating agent.

[www.igb.fraunhofer.de/en/kombichempro](http://www.igb.fraunhofer.de/en/kombichempro)



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### Separation and purification of furan derivatives from coupling streams containing lignocellulose

Biobased furan derivatives, such as 2,5-furandicarboxylic acid (FDCA), are increasingly gaining in importance, in particular as biogenic building blocks for polymer applications. The Fraunhofer Center for Chemical-Biotechnological Processes CBP is conducting intensive research into the separation and purification of furan derivatives from process water of the hydrothermal conversion of raw materials containing lignocellulose, using a variety of thermal, mechanical and physico-chemical separation methods. Intensive research and development has been carried out in projects including those funded by the German Federal Ministry of Education and Research (BMBF), "KomBiChemPro" and "BBCChem", and the project "SteamBio", funded by the EU.

We use cross-flow membrane systems (fig. 3) to separate the dissolved and undissolved constituents. The aim is to separate polymers from monomers and to reduce the water content to optimize the purification process energetically. Cross-flow membrane filtration also plays a central role in the separation of temperature-sensitive substances, such as 5-hydroxymethylfurfural (5-HMF) and formic acid. Furfural derivatives can also be successfully separated from the process water using rectification, which we have demonstrated at the pilot scale with a throughput of 2.5 kg/h. Investigations into liquid-liquid extraction and adsorption/desorption revealed targeted separation of the carboxylic acids from furan derivatives. In this case, we were able to successfully demonstrate the essential feasibility of separating furan derivatives in process waters from hydrothermal conversion up to the 100-liter scale.

[www.cbp.fraunhofer.de/en/furan-derivatives](http://www.cbp.fraunhofer.de/en/furan-derivatives)



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### Malic acid made of xylose – Fermentation at 1 m<sup>3</sup> scale for the first time

To date, malic acid has been used primarily in the food and beverage industry. It improves the shelf-life of baked products and provides the sour taste of jams and juices. But it also boasts considerable potential as a building block in the chemical industry. Together with succinic and fumaric acid, it belongs to the group of C4 dicarboxylic acids. C4 acids can be converted into 1,4-butanediol (BDO) – an important precursor for further conversion into a wide variety of chemicals, including plastics, polymers and resins; the possible applications for these chemicals range from golf balls to printing inks and cleaning agents.

Fermentative production of malic acid was developed through the collaboration of the Industrial Biotechnology working group at Fraunhofer IGB and the Biotechnological Processes Group at Fraunhofer CBP. Fermentation was carried out with the fungus *Aspergillus oryzae* (fig. 4), which is designated as a harmless food additive according to the GRAS (generally recognized as safe) status of the US Food and Drug Administration (FDA). In addition to glucose, the strain can also utilize the C5 sugar xylose, which is the main component of hemicellulose and thus can be sourced from wood residues. Initially, the process was optimized at the laboratory scale; it was then established in stirred reactors and finally successfully scaled up to the 1 m<sup>3</sup> scale using the substrate xylose for the first time. Downstream processing could be demonstrated using crystallization. In doing so, several kilograms of malic acid were produced that are now available as a sample for application tests.

[www.igb.fraunhofer.de/en/kombichempro](http://www.igb.fraunhofer.de/en/kombichempro)



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### CELBICON – Cost-effective carbon dioxide conversion into chemicals

Motivated by multiple national and international climate protection agreements, Fraunhofer IGB Biocat focuses on the development of new combined chemical-biotechnological technologies for the conversion of CO<sub>2</sub> and energy into fuels and chemicals. Because of the geographical distribution of available regenerative energy and CO<sub>2</sub>, the development of small-scale, decentralized processes is of particular interest.

A prominent example of an integrated technology is the recently patented process for combined electrochemical and biotechnical CO<sub>2</sub> conversion. The process comprises CO<sub>2</sub>-based methanol synthesis, which was adapted for the combination with C1 fermentation using *Methylobacterium* ssp in an integrated reactor plant. In this way, methanol synthesis is carried out using a CO<sub>2</sub> and H<sub>2</sub> mixture over a conventional Cu-based catalyst in a plug-flow heterogeneous catalytic reactor. Subsequently, methanol and water formed in the reactor are condensed from the gas phase in a specially designed liquid/gas separator and dosed into a fermenter containing a suitable medium and preculture at given time intervals. The microorganisms use methanol as the sole carbon source for their own growth and to form the product.

This new combined chemical-biotechnological process enables the production of value-added chemicals (lactic acid, isoprene, polyhydroxybutyric acid and long-chain terpenes) in just two steps, methanol being the only intermediate. This process therefore has the potential to turn small-scale CO<sub>2</sub> valorization into a profitable business.

[www.igb.fraunhofer.de/en/celbicon](http://www.igb.fraunhofer.de/en/celbicon)



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### Single-stage electrosynthesis of ethylene from CO<sub>2</sub>

The use of carbon dioxide (CO<sub>2</sub>) to produce carbon-based basic chemicals using regenerative energy is a promising approach to reduce net CO<sub>2</sub> emissions, conserve fossil resources and therefore reduce economic dependence on oil imports from outside Europe.

As part of the Fraunhofer lighthouse project “Electricity as a Raw Material”, the electrochemical synthesis of ethylene, one of the most important raw materials in the petrochemical industry, from CO<sub>2</sub> and water was demonstrated. At Fraunhofer IGB, a fully automatic demonstrator with electrolytic cell was designed and built (fig. 2). With this demonstrator, the electrosynthesis process with an electrode area of 130 cm<sup>2</sup> and in-house catalysts was investigated and demonstrated in flow-through operation. In recent studies we were able to achieve ethylene concentrations in the product gas of 1700 ppm, corresponding to a Faraday efficiency of 8.5 percent. According to the state of the art in science and technology, comparable values have so far only been achieved on a laboratory scale, with electrode surfaces of a few square centimeters. In current and future work, the production rate of ethylene and therefore the efficiency of the process is to be further increased and long-term stability validated.

Besides, the design of the demonstrator can also be transferred to other electrosynthesis processes and enables screening of catalyst and electrode materials as well as projections for the scale-up of the processes.

[www.igb.fraunhofer.de/ethylene](http://www.igb.fraunhofer.de/ethylene)



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### Screening of heterogeneous catalysts for energy conversion applications

Due to the daily and seasonal differences between the availability and consumption of regenerative energy, new energy storage scenarios are under intensive R&D. Methanol is a versatile platform chemical and as an energy carrier it plays an increasingly important role in energy transition scenarios. For the synthesis of methanol from carbon dioxide and electrolytically produced hydrogen, two processes for catalyst synthesis were optimized at the BioCat branch of IGB. Various reactor systems are available for the subsequent screening of the catalysts regarding their performance.

The state-of-the-art coprecipitation of Cu-based catalyst precursors was tuned for continuous operation, enabling very significant energy, time and resource savings on the industrial scale synthesis (patent pending). Another innovative method is based on dissolution of metal compounds in deep eutectic solvents, followed by carbonization (WO2016/180973A1).

Two reactor systems are available for the screening of heterogeneous catalysts in gas phase reactions (fig. 3 + 4). A multi-purpose screening system with four parallel reactor tubes and online GC-MS analytics has been acquired. The gas dosing enables the use of technically relevant syngas mixtures with various CO/CO<sub>2</sub>/H<sub>2</sub>/H<sub>2</sub>O ratios. The system makes possible high throughput screening over catalysts and reaction conditions. It also allows evaluating the long-term stability of the catalysts under optimal operation conditions and to quantitatively collect and analyze the liquid products. The design also makes it possible to carry out various other reactions including methanization, Fischer Tropsch synthesis, and chemical conversion of methanol to olefins or liquid fuels as well as ammonia synthesis.

A single-tube system was designed and built for catalytic testing at atmospheric pressure. Two operating sizes are available, with maximum 1 g and 50 g catalyst loading respectively. The system enables the investigation of reaction cascades such as methanol synthesis coupled to the methanol-to-olefin process.

[www.igb.fraunhofer.de/screening-of-catalysts](http://www.igb.fraunhofer.de/screening-of-catalysts)



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A close-up photograph of a metal drill bit positioned vertically on a heavily rusted metal surface. The rust is a mix of orange, red, and brown tones, with some white patches where the metal is more exposed. The drill bit is dark and shows some wear at the tip. The background is blurred, focusing attention on the drill bit and the rusted surface.

# **ENVIRON- MENT AND ENERGY**

Against the backdrop of the global debate on water shortage and pollution, resource scarcity and climate change, resource and environmentally friendly economies are becoming more and more important. The transition to sustainable, environmentally friendly yet reliable supplies of clean water, food, raw materials, and energy is therefore one of the major challenges of society today – also in view of the global climate protection targets.

In national and international projects with partners from research, industry and municipalities, Fraunhofer IGB is developing innovative processes, reactors and new technologies for a sustainable water supply and disposal system, especially for the treatment of industrial process water and municipal wastewater, for the reuse of residual and waste materials, and to improve energy efficiency by making use of waste heat and regenerative energy.

The business area Environment and Energy thus stands for a variety of advanced technological developments that help to prevent emissions being released into the environment, to recycle raw materials and to develop regenerative energy, thereby combining cost effectiveness with sustainability. Potential solutions are, in some cases, linked with major topics in the business area Chemistry and Process Industry.

#### **Networking and cooperation**

At Fraunhofer IGB we are developing integrated material flow and energy concepts for industry, municipalities and entire regions with the aim of replacing historically evolved infrastructures by system solutions using the latest technologies. We are therefore actively involved in the Fraunhofer Alliances Energy, Water Systems (SysWasser), and the Morgenstadt Initiative. Also, Fraunhofer IGB is outstandingly networked nationally through the German Water Partnership, and very well connected throughout Europe. In addition, we work together with the University of Stellenbosch, South Africa, in the field of water treatment and use, and also in India the relationships that have developed through various projects (see p. 70) are being intensified.



### **Water and wastewater technologies**

Water is our most important food resource. To achieve a secure supply of water and efficient water purification, we develop innovative solutions for water extraction as well as water management concepts that are adapted to the geographical, demographic and regional conditions in each case. To ensure, as far as possible, the multiple use of industrial process water, we are working on technologies with which contaminations can be selectively removed and valuable substances can be recovered. We develop, optimize and combine aerobic and anaerobic biological processes with membrane and chemico-physical processes as required.

We employ various technologies, among them membrane adsorbers and electrooxidative processes, to prevent emissions of persistent substances into the environment. To purify water with persistent organic components, we develop technologies where treatment with electric current (electrolysis) or high-energy UV radiation (photolysis) result in reactive hydroxyl radicals that oxidize the organic molecules to recoverable compounds or completely to carbon dioxide, but without the addition of chemicals.

### **(Re)processing of raw and residual materials**

Our primary raw materials are finite resources, yet in politically unstable regions they are frequently not exploited in a sustainable or socially acceptable way. To supply a growing world population with raw materials and to reduce the dependence on importing raw materials, we develop processes for recovering and recycling secondary raw materials from production and waste streams – in a quality equivalent to that of the primary raw materials and with comparable processing complexity and costs.

New techniques, for example, enable us to selectively separate mixtures of inorganic raw materials (metals, rare earths) on a molecular or atomic level. Using new processes, important nutrients such as phosphorus and ammonium can be recovered from wastewater, sewage sludge, fermentation residues or liquid manure to be used as fertilizers. We process the residual low-nutrient organic fractions to obtain humus-forming soil conditioners.





### Conversion and storage of renewable energy

To tap new regenerative energy sources, we develop innovative membrane technologies, for example for efficient ethanol fuel cells or economically viable osmotic power plants. For the energy system turnaround to succeed, storing excess power must be practicable. For this purpose, we develop catalytic processes to convert electrical energy – especially by binding and reducing  $\text{CO}_2$  – to chemical energy reservoirs, for example longer-chained hydrocarbons. The flexible electrochemical synthesis of basic chemicals is also an option that we are exploring in various approaches (see Chemistry and Process Industry business area).

In this context, biogas occupies a special position among renewable energy sources. The mixture of methane and carbon dioxide is not just used to generate electricity and heat in combined heat and power (CHP) plants, but also – after separation of high-purity methane – as a fuel or raw material for basic chemicals. Biogas can thus not only serve as a temporary energy store, but also link the energy sector with the mobility and chemicals sectors. For the separation of high-purity methane from biogas, we are therefore investigating absorption and membrane processes that bind  $\text{CO}_2$  with high capacity, as well as new material recycling paths.

The efficient generation of biogas from sewage sludge using anaerobic technologies is a key issue at IGB. We have already converted several sewage treatment plants of different sizes to our high-load digestion process, thus enabling them to generate their own electricity. We also use our know-how about the fermentation of organic substances for the reutilization of residual matter from the food industry and agriculture. Small mass flows are becoming increasingly interesting as the energy sector is decentralized.

In many cases, waste heat that results from power generation and many industrial processes remains unused. To make excess waste heat available for temporally and spatially decoupled heat requirements, Fraunhofer IGB is working on thermo-chemical sorption systems for the long-term storage of heat.



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**Case studies on water reuse in hydroponic greenhouses**

The “HypoWave” research project is investigating a concept in which nutrient-rich treated wastewater is used for hydroponic plant production. Hydroponics is plant production without soil, the seedlings grow in closed plant containers. Case studies at four different locations in Germany, Belgium and Portugal are used to determine how the concept can be implemented. These case studies are being developed by transdisciplinary teams in cooperation with local stakeholders. The aim is to identify beneficial and limiting factors for the use of treated wastewater in the hydroponic system and possible site-specific applications of the concept. This should create the basis for the next steps of a possible realization at the sites being investigated.

Two case studies were completed in 2018 and the results are now available in the form of a brochure. In the district of Gifhorn (Lower Saxony), the effluent of a sewage pond for the cultivation of lettuce (fig. 1) was investigated. This allows the concentration of nutrients in the effluent to be reduced to such an extent that connection to a larger sewage treatment plant becomes unnecessary. In Raeren in the Euregio (the border region of Belgium, the Netherlands and Germany), a wastewater treatment plant including a greenhouse for the cultivation of cut flowers was designed for an area whose wastewater flows untreated into a body of water. A short rotation plantation will also use the remaining nutrients for biomass production.

[www.igb.fraunhofer.de/en/hypowave](http://www.igb.fraunhofer.de/en/hypowave)



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**Cooperation with India through the Water Innovation Hub**

Polluted rivers and lakes (fig. 2), a lack of sewers and sewage treatment plants – India’s rapidly growing cities are barely able to keep pace with the expansion of municipal infrastructure. As part of the “Smart Water Future India” project, a team from Germany led by Fraunhofer IGB is analyzing the demand for the water infrastructure of the city of Coimbatore in South India as an example. The methodology is based on the Morgenstadt City Lab.

German companies in the water industry have many good solutions, but so far they have had problems establishing them on the Indian market. If these solutions can be better adapted to demand and sustainable networks can be established in India, both sides can benefit. The project will therefore develop a concept for a “Water Innovation Hub” to serve as a basis for long-term cooperation. German companies are welcome to participate in this Indo-German platform.

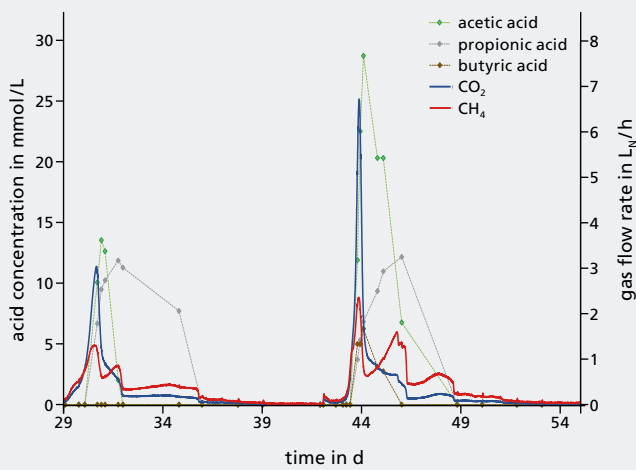
At the same time, Fraunhofer IGB is conducting a study on behalf of Umwelttechnik BW in which the need for a pilot plant for wastewater treatment in Solapur (Western India) is being investigated. Several companies in the water sector in Baden-Württemberg have already expressed great interest in testing their technologies in India with the help of a pilot plant – and adapting them to local conditions if necessary.

[www.igb.fraunhofer.de/en/swfi](http://www.igb.fraunhofer.de/en/swfi)

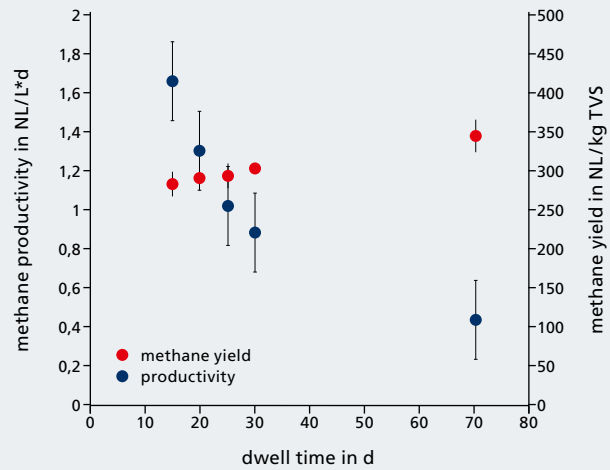


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### MOST – Model-based process control of biogas plants: Practical tests

The development goal of the subproject “Practical Tests” was to evaluate the possibility of increased operational safety in biogas plants through early detection of process disturbance, allowing a timely reaction and thus increasing the profitability of biogas plants.

Various operational conditions were experimentally simulated on a laboratory and pilot plant scale. Relevant operational changes were carried out and the effects on the process documented. The experiments focused on extreme situations in the biogas process, aimed at registering the individual reactions through measurable parameters and, if possible, incorporate the findings into the simulation program developed by the project partner Helmut Schmidt University Hamburg.

The results have clearly demonstrated the stepwise reaction that leads to biogas production (fig. 3), which characterizes the direct correlation between the concentration of acids and the production of biogas. The data density of the online measurements allowed the identification with minute-by-minute precision of the shift from one preferred metabolic pathway to another. In addition, further correlations were presented, which are currently not shown in the standard models such as ADM1. The stoichiometric distribution of metabolic products is approximately correct, a thermodynamic consideration is also relevant in the more extreme cases of the anaerobic digestion process.

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### HoLaFlor – Increasing the efficiency of biogas plants

Biogas plants that use renewable raw materials as substrates are usually operated with hydraulic retention times of 40 days. Significantly longer hydraulic retention times of up to 90 days are also not uncommon. The aim of the HoLaFlor research project was therefore to operate a biogas plant with shorter retention times at constant biogas rates and at the same time to increase methane productivity.

For a pilot-scale biogas plant with maize silage as monosubstrate, short retention times of between 15 and 30 days and corresponding organic loading rates of between 2.9 and 5.8 g/L\*d were achieved at Fraunhofer IGB. At the same time, the conventional process with a retention time of 70 days was investigated in a reference plant. It was shown that the methane productivity could be increased from 0.9 NL/L\*d to 1.7 NL/L\*d with increasing throughput for retention times of 15 to 30 days, without significant losses in the methane yield. The corresponding methane yield was between 284 NL/kg TVS and 303 NL/kg TVS. In comparison, a productivity of only 0.4 NL/L\*d was achieved in the reference plant with a retention time of 70 days. The methane yield amounted 341 NL/kg TVS (fig. 4).

The results impressively prove that biogas plants using suitable plant technology can be operated with significantly shorter retention times and thus methane productivities can be achieved which are two to four times higher than with conventional process and long retention times.

[www.igb.fraunhofer.de/en/holafloer](http://www.igb.fraunhofer.de/en/holafloer)



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### High-load digestion at the Leipheim sewage treatment plant

The city of Leipheim has decided to replace its 40-year-old digester with a modern high-load digester (HLD). The HLD process was developed by Fraunhofer IGB for anaerobic decomposition and sludge stabilization. Following preliminary investigations into the digestion of the raw sludge produced by the sewage treatment plant under high-load conditions and a thorough concept, design and planning phase for the realization of the HLD, the construction work began at the groundbreaking ceremony on September 28, 2017 (fig. 1). IGB scientifically supported the partners involved in the realization of the plant. This ranged from assistance with the tender documents, support during the construction phase, function testing and inoculation with digested sludge from the existing old digestion to trial operation. In December 2018, the HLD was turned over to the client.

Compared to the original digester, the HLD requires only one third of the active volume and was successfully integrated into the existing sewage treatment plant. It is designed as a loop reactor with gas injection. The integrated heat recovery helps to generate heat, which is also delivered to the neighboring building yard. The biogas is cleaned and freed of impurities. By mid-January 2019, more than 17,500 m<sup>3</sup> of biogas had already been produced in very good quality. The old digestion is now being converted to a biogas storage tank and is thus still useful. The next high-load digestion is already in the planning phase.

[www.igb.fraunhofer.de/hld-leipheim](http://www.igb.fraunhofer.de/hld-leipheim)



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### Innovative cascade processes for CO<sub>2</sub> conversion into fuels and chemicals

Motivated by multiple national and international climate protection agreements, Fraunhofer IGB Biocat focuses on the development of new combined chemical-biotechnological technologies for the conversion of CO<sub>2</sub> and energy into fuels and chemicals. Because of the geographical distribution of available regenerative energy and CO<sub>2</sub>, the development of small-scale, decentralized processes is of particular interest.

A prominent example of an integrated technology is the recently patented process for combined electrochemical and biotechnical CO<sub>2</sub> conversion. The process comprises CO<sub>2</sub>-based methanol synthesis, which was adapted for the combination with C1 fermentation using *Methylobacterium* ssp in an integrated reactor plant (fig. 2). In this way, methanol synthesis is carried out using a CO<sub>2</sub> and H<sub>2</sub> mixture over a conventional Cu-based catalyst in a plug-flow heterogeneous catalytic reactor. Subsequently, methanol and water formed in the reactor are condensed from the gas phase in a specially designed liquid/gas separator and dosed into a fermenter containing a suitable medium and preculture at given time intervals. The microorganisms use methanol as the sole carbon source for their own growth and to form the product.

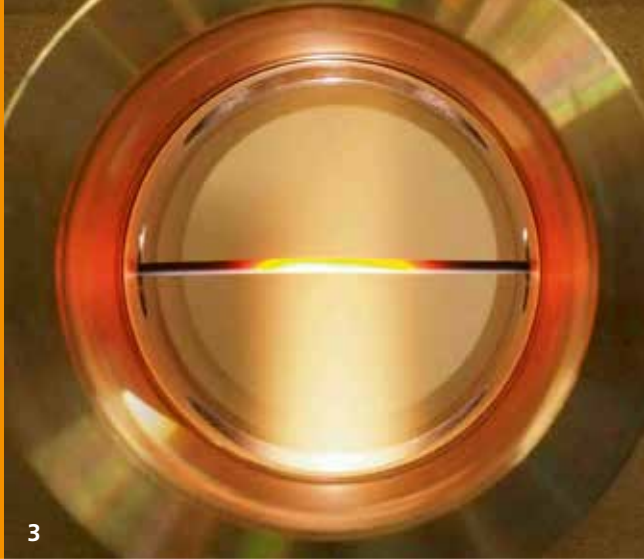
This new combined chemical-biotechnological process enables the production of value-added chemicals (lactic acid, isoprene, polyhydroxybutyric acid and long-chain terpenes) in just two steps, methanol being the only intermediate. This process therefore has the potential to turn small-scale CO<sub>2</sub> valorization into a profitable business.

[www.igb.fraunhofer.de/combined-catalysis](http://www.igb.fraunhofer.de/combined-catalysis)



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### PiCK – Plasma-induced CO<sub>2</sub> conversion

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The aim of this development is to make CO<sub>2</sub> usable as a chemical raw material and for the chemical storage of energy, thus contributing to the climate targets aimed at. Using a cost-efficient and resource-saving combination of plasma and membrane processes, CO<sub>2</sub> is split into O<sub>2</sub> and CO, which can serve as a starting product for the synthesis of platform chemicals such as methanol. The membrane process is needed to prevent the recombination of CO and O<sub>2</sub> to CO<sub>2</sub>.

The focus of the work at IGB is on the development of a suitable membrane (fig. 3), which on the one hand efficiently separates oxygen and on the other can be used in the plasma. A mixed conductive ceramic material (La<sub>w</sub>Ca<sub>x</sub>Co<sub>y</sub>Fe<sub>z</sub>O<sub>3-6</sub>; LCCF), which has already been described in the literature as CO<sub>2</sub>-tolerant, was selected for the manufacturing of the membranes. Using an established wet-spinning process and subsequent sintering, for the first time gas-tight LCCF capillaries were produced in a reproducible manner that are both CO<sub>2</sub>-stable (>200 h) and suitable for the separation of oxygen (O<sub>2</sub> permeance of 1.0 ml min<sup>-1</sup> cm<sup>-2</sup> at 900°C).

The capillaries produced by Fraunhofer IGB were investigated at IGVP in a CO<sub>2</sub> plasma. They show very good thermal stability and good oxygen permeability in the plasma (2.3 ml min<sup>-1</sup> cm<sup>-2</sup> at 1 kW). Such capillaries have not yet been described in the literature. The next step is to optimize the separation efficiency by increasing the membrane area in the plasma. This is done by increasing the number of hollow fiber membranes built into the plasma.

[www.igb.fraunhofer.de/en/pick](http://www.igb.fraunhofer.de/en/pick)



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