Fraunhofer
IGB

FRAUNHOFER INSTITUTE FOR INTERFACIAL ENGINEERING AND BIOTECHNOLOGY IGB

ANNUAL REPORT 2013 | 14

The cover picture shows *giant unilamellar vesicles* of different sizes in a solution stained with trypan blue. These liposomes are microscopic lipid vesicles filled with buffer. Fraunhofer IGB researchers insert transmembrane proteins such as ATP synthase into the vesicles in order to study their catalytic functions under different environmental conditions.

ANNUAL REPORT
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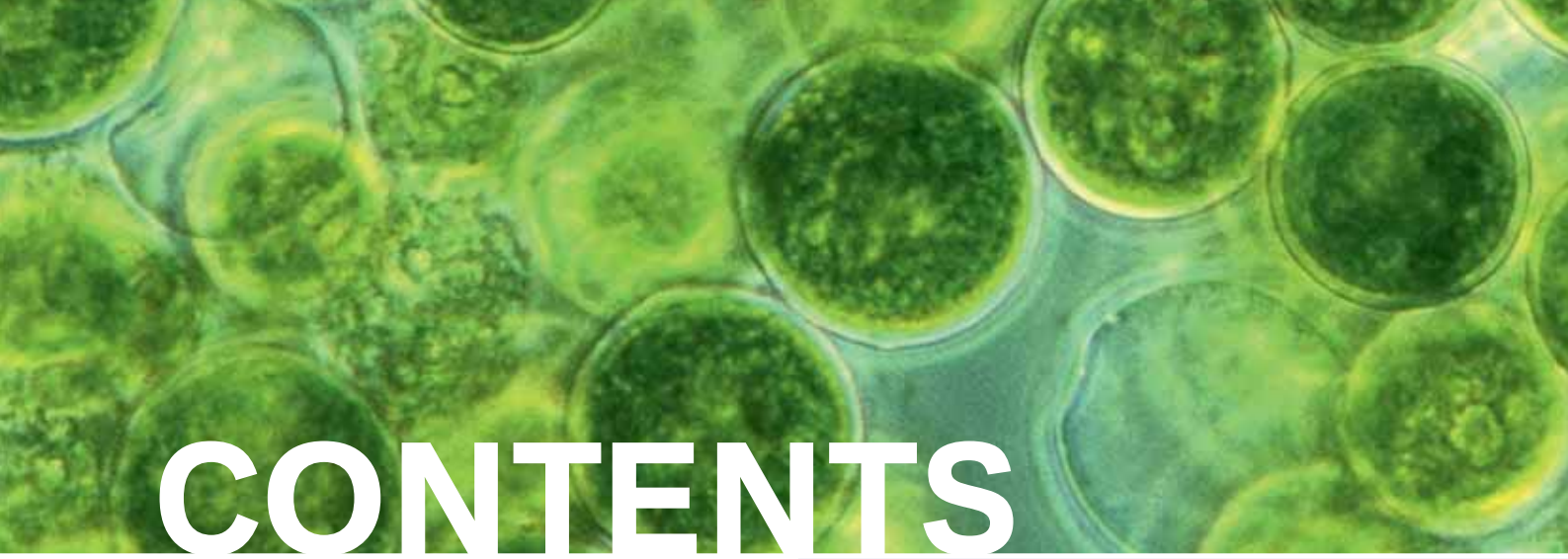

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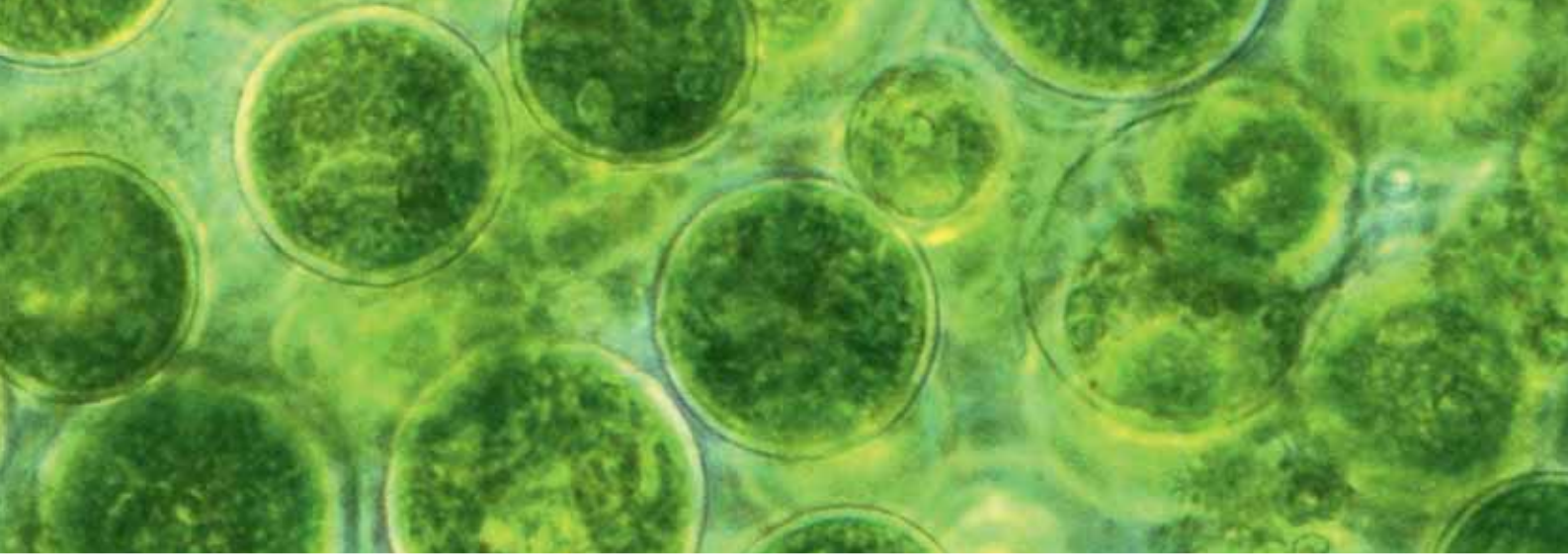


"60 YEARS OF FRAUNHOFER IGB – 60 YEARS OF RESEARCH INTO INTERFACES – 60 YEARS OF INNOVATION FOR SCIENCE, TECHNOLOGY AND SOCIETY"

Last year the Fraunhofer IGB turned 60 and – as at its inception in 1953 – still bears "interfaces" in its name. Equally, research into interfacial phenomena still accounts for a major share of the R&D activities at the institute. Interfaces separate two phases or substances from each other. At interfaces, properties change abruptly, or, in other words, they are the place where new phenomena occur – and give rise to the innovations of today, facilitated through the interplay of various disciplines.

60 years mean six decades of innovations and contributions to the sustainable development of science, economy and society. Thanks to its employees, the Fraunhofer IGB has evolved over the last 60 years into an innovative body at the forefront of interfacial R&D. The respective directors have each exercised their own particular formative influence on the subject areas and the disciplines pursued by the institute. Today, the institute serves the five business areas Medicine, Pharmacy, Chemistry, Environment and Energy with its core competences in Interfacial Engineering and Materials Science, Physical Process Technology, Environmental Biotechnology and Bioprocess Engineering, Molecular Biotechnology, and Cell and Tissue Engineering.

Through its memberships in the Fraunhofer Life Sciences and MATERIALS groups as well as eight Fraunhofer alliances, the Fraunhofer IGB is firmly rooted in the Fraunhofer-Gesellschaft. Over and above this, the institute benefits from its close association with the universities of Stuttgart, Tübingen, Hohenheim, Würzburg, Munich and Halle-Wittenberg, which provide it with inspiration and insights from basic research that filter into the translation of research results into industrial practice.

The reduction of global CO_2 emissions, combating disease and hunger, and securing a global supply of water, raw materials and energy are the major challenges facing humanity in the 21st century. Against this backdrop, developing and realizing sustainable processes and products is becoming ever more vital. The sustainable use of natural resources and developing efficient value chains, processes and products are core priorities in bioeconomy research. Through our work on the sustainable material and energetic utilization of renewable raw materials in Baden-Württemberg, Germany and Europe, we want to make a leading contribution toward realizing the bioeconomy. Last July, we joined with the universities of Baden-Württemberg in presenting the concluding report of the Bioeconomy Strategy Group to Science Minister Theresia Bauer, as the basis for Baden-Württemberg's bioeconomy research strategy.

Besides its work on organic raw materials, the IGB is working intensively on developing technologies for the extraction of rare earth elements from primary raw and residual materials. The focus here is on processes for chemical and biological leach liquors, as well as selective separation using electrochemical and membrane-based processes. The IGB is therefore also one of the partners on the Fraunhofer "Criticality of rare earth metals" lighthouse project.

Developing resource and energy-efficient processes continues to be a central focus of research at the Fraunhofer IGB. We are working together with partners from industry and academia to improve production process chains in both the Fraunhofer "E^3 production" lighthouse project and the industry-on-campus project "Raw material and energy efficiency through process innovations" funded by the Baden-Württemberg Ministry of Science, Research and the Arts. This constitutes a key contribution by the Fraunhofer IGB to the regional resource efficiency strategy.

In the interfacial area, we have significantly expanded our basic research capabilities in the past year by the integration of the IPF into the IGVT and its renaming as the Institute of Interfacial Process Engineering and Plasma Technology IGVP. Plasma physics fundamentals are now complemented by competence in plasma dynamics and diagnostics, microwave technology and plasma technology. Together with the Fraunhofer

IGB the IGVP now constitutes a center of excellence in the field of plasma technology in Stuttgart with strong international visibility.

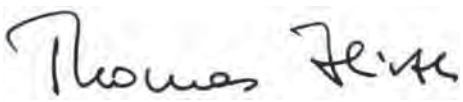
Last year we also saw great success in the development of new biocompatible materials and material surfaces. Together with University of Stuttgart institutes in the areas of biology and chemistry, we obtained funding from the Carl Zeiss Foundation for the "NanoBioMater" project house. The house will enable biologists, chemists, materials scientists and engineers to develop intelligent biocompatible functional materials for medical technology, diagnostics and environmental analysis under one roof.

The world's future energy supply depends not only on the increased use of renewable energies, but also on novel energy storage systems. We are therefore working intensively at our Stuttgart and Straubing sites on developing and testing thermal and chemical energy storage systems and their integration into the energy complex. The main highlights here in 2013 were the groundbreaking ceremony for the building extension to be used by the BioCat project group ("Catalytic Processes for a Sustainable Supply of Raw Materials and Energy on the Basis of Renewable Resources BioCat") and the handing over of the funding approval for the Center for Energy Storage, which will be developed over the coming years together with the Fraunhofer UMSICHT institute at the Straubing and Sulzbach-Rosenberg sites. The BioCat project group is carrying out intensive research into chemical energy storage, investigating the role of catalysis in the generation of chemical energy carriers and the processes involved in chemical storage.

Apart from realigning our research and development activities to maximize achievement of our goals, we also continually strive for solid and stable financing of the institute's budget and for long-term staff development that will allow us to meet future challenges. In 2013, we acquired many new customers from industry, as well as attracting additional public funding for upcoming R&D projects.

Our future work will be essentially characterized by the vision "Ever better together", developed as part of our strategy and mission-statement process, and by our mission "to contribute through innovation to the sustainable development of the economy, society and the environment" by carrying out "application-oriented research in the areas of medicine, pharmacy, chemistry, the environment and energy" in accordance "with the principles of good scientific practice and on the basis of our competences and guiding principles."

This annual report aims to give you an insight into the Fraunhofer IGB's R&D projects, and illustrate the institute's contribution to the sustainable development of science, industry and society. I would be delighted if the 2013 report arouses your interest in our R&D activities and in future collaboration. Together with our customers and partners, we aim to shape the future of the region, of Germany and of Europe through innovative, sustainable developments and to open up "markets beyond tomorrow". I hope you enjoy your read, and look forward to your ideas and working with you.



Best regards
Thomas Hirth

PROFILE

BRIEF PROFILE

The Fraunhofer IGB develops and optimizes processes and products for the business areas of medicine, pharmacy, chemistry, the environment and energy. In addition to contract R&D we offer our clients services in analytics and advise on the introduction of novel technologies. Our customers come from various industries as well as municipal, state (*Länder*) and federal authorities.

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. Our strength lies in offering complete solutions from laboratory scale to pilot plant.

More than ever, the success of new products and processes is dependent on interdisciplinary and constructive cooperation between science and engineering. Some 380 experts in the fields of chemistry, physics, biology and engineering work effectively together at Fraunhofer IGB and IGVP, our partner institute at the University of Stuttgart. Customers benefit from the synergies and multidisciplinary potential at our institute, which facilitate novel approaches and innovative solutions in areas such as medical engineering, nanotechnology, industrial biotechnology and environmental technology.

Competences

Departments

- Interfacial Engineering and Materials Science
- Molecular Biotechnology
- Physical Process Technology
- Environmental Biotechnology and Bioprocess Engineering
- Cell and Tissue Engineering

Project groups

- Fraunhofer Center for Chemical-Biotechnological Processes CBP, Leuna
- Project Group BioCat, Straubing
- Project Group Oncology, Würzburg

Guiding principles: mission statement and vision

"At the Fraunhofer IGB we carry out application-oriented research according to the principles of good scientific practice and on the basis of our competences and guiding principles in the areas of medicine, pharmacy, chemistry, the environment and energy. With our innovations we contribute to a sustainable development of the economy, society and the environment."

EVER BETTER TOGETHER.

ADVISORY BOARD OF THE FRAUNHOFER IGB

The Fraunhofer Institutes are advised by Advisory Boards whose members are drawn from industry, public authorities, and the scientific community.

Members

Dr. med. Susanne Arbogast
Roche Diagnostics GmbH

Dr. Gerd Eßwein
Freudenberg New Technologies SE & Co. KG

Ltd. Ministerialrätin Dr. Renate Fischer
Ministry of Science, Research and the Arts of the State of Baden-Württemberg

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

Prof. Dr. Matthias Frosch
Faculty of Medicine, Julius Maximilian University of Würzburg

MinDirig Dipl.-Ing. Peter Fuhrmann
Ministry of the Environment, Climate Protection and the Energy Sector of the State of Baden-Württemberg

MinDirig Dr. Fritz Holzwarth
Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB)

Prof. Dr. Dieter Jahn
(Chair until April 17, 2013)

Dr.-Ing. Bernd Krause
Gambro Dialysatoren GmbH

Dr. Henk van Liempt
Federal Ministry of Education and Research (BMBF)

Dr. Christian Naydowski
VOITH Paper

Prof. Dr. Klaus Pfizenmaier
Institute for Cell Biology and Immunology, University of Stuttgart

Prof. Dr. Prof. h. c. Dr. h. c. Ralf Riedel
Faculty of Materials- and Geo-Sciences, TU Darmstadt

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

Dipl.-Ing. Otmar Schön
HYDAC Technology GmbH

MinR Dr. Joachim Wekerle
Ministry of Finance and Economics 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

Dr. Markus Wolperdinger
(Chair since April 18, 2013)
Linde Engineering Dresden GmbH

Permanent guests

Prof. Dr. Herwig Brunner
Former Director of Fraunhofer IGB

SERVICES AND INFRASTRUCTURE

Our contract R&D services range from natural sciences and engineering basic research to the development of new applications in laboratory, technical, and pilot plant scale; including the design, construction, and testing of pilot plants. We also offer patent and market surveys, feasibility studies and comprehensive consultancy in our areas of expertise as well as analysis and testing. We provide seminars and workshops for executives and introduce young students to the fascinating world of science and technology.

Infrastructure and laboratory equipment

The Fraunhofer IGB has modern laboratories equipped with the latest technology. A new pilot plant building is scheduled for completion mid-2015. Our central storage facilities for chemicals and hazardous substances are shared with the other institutes on the Stuttgart Fraunhofer campus.

Analytics: quality management and accreditation

Our quality assurance system ensures that the requirements in our analytical reference laboratories are in accordance with legal regulations as well as with the standard DIN EN ISO/IEC 17025. The accreditation of our analytics guarantees that our proprietary, in-house test methods and procedures are sufficiently validated and that the quality of our tests is assured even where no standardized methods are available.

The following analytical methods and test procedures are accredited according to DIN EN ISO/IEC 17025:

- High-performance liquid chromatography (HPLC)
- Ion chromatography (IC)
- Gel permeation chromatography (GPC)
- Gas chromatography (GC, GC/MS)
- Atomic emission spectrometry (ICP-OES)
- Electron spectroscopy for chemical analysis (ESCA/XPS)
- In-vitro cytotoxicity testing of medical devices
- Transport assay with cell line model (2D intestinal assay with Caco-2 cell line)

Accredited cytotoxicity and bioavailability testing

We perform tests for in-vitro cytotoxicity of medical devices according to DIN EN ISO 10993-5 using cell lines or our in-house designed 3D skin equivalent. Additionally, our two-dimensional intestinal assay (Caco-2) was included in the accreditation audit report as an in-house method for the classification of substances by their transport characteristics at the intestinal barrier.

GMP unit for manufacturing of clinical materials

The manufacturing of medical devices, investigational medicinal products (IMPs) and cell-based and tissue engineering products (e.g. ATMPs) for clinical trials requires processes according to Good Manufacturing Practice (GMP). We develop GMP-compliant manufacturing processes in our 215 m^2 certified GMP unit in Stuttgart – also for collaborative development with partners from industry. Different manufacturing authorizations (collagen, cartilage) have already been granted.

Good laboratory practice (GLP) test facility

Our area of expertise 9 GLP test facility ("Cell-based test systems for the determination of biological parameters") is used in research and development projects for investigating different biological parameters of samples/substances using cell-based assays. Examples are the testing of bioactivity and immunogenicity, the screening of TLR agonists/antagonists and antimicrobial substances as well as the detection of pyrogens and microbial residues (pathogen-associated microbial patterns).

Special services

Physico-chemical analytics
quality control, food analysis, trace analysis, analysis of residues, environmental analytics, water analysis

High resolution 400 MHz NMR analytics
molecular structure elucidation, reaction monitoring, development of novel experimental NMR methods, low temperature analytics

Surface and particle analytics
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 molecular biological analytics
diagnostic microarrays, RNA and protein expression profiles, protein analysis using MALDI-TOF/TOF mass spectrometry (also quantitative)

Cell biology analysis
cell characterization, single cell preparation/microdissection, quality and sterility control of tissue engineering products

Cell-material interactions
testing of cytotoxicity/biocompatibility of medical devices and of bioavailability of drug candidates, evaluation and testing of chemicals (REACH) and nanomaterials

For detailed information regarding our services and infrastructure, please visit:
www.igb.fraunhofer.de/analytics

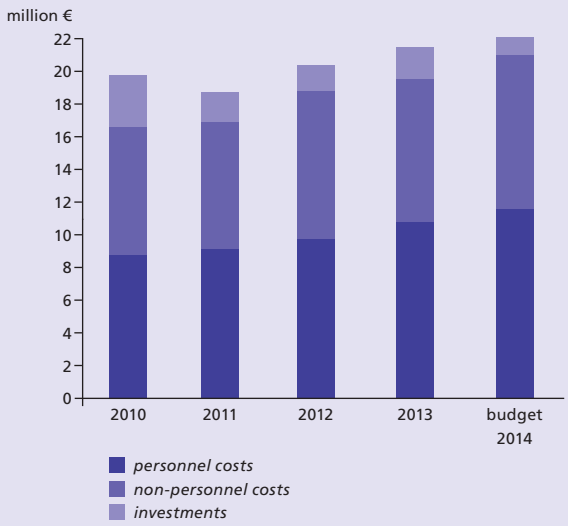
KEY FIGURES

Budget of Fraunhofer IGB

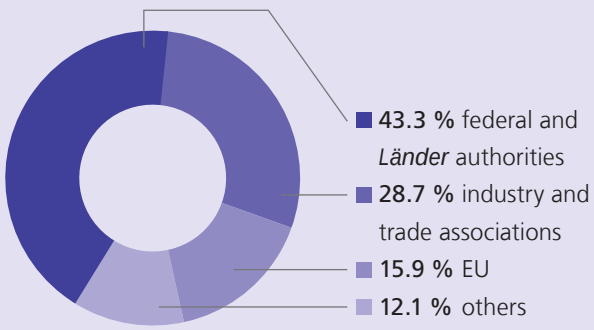
The total budget for 2013 amounted to 21.4 million euros, of which 19.5 million euros was allocated to the operational budget (personnel costs: 10.8 million euros; non-personnel costs: 8.7 million euros). A total of 1.9 million euros was spent on investments.

75 percent of the operational budget was financed from Fraunhofer IGB's own revenues generated from contract research projects. 29 percent of the Institute's revenues came directly from industry.

Development of budget



Revenue from contract research 2013



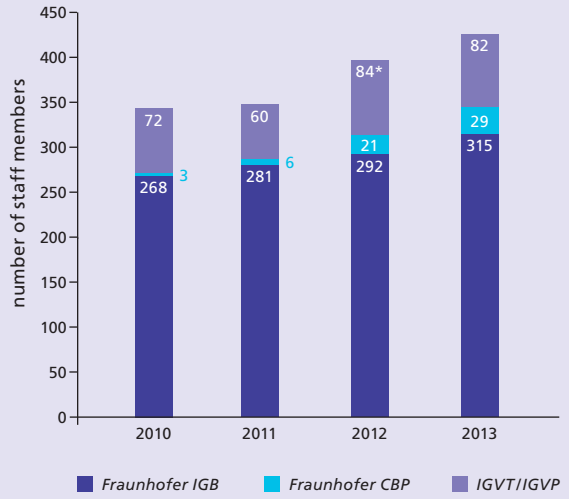
Personnel

At the end of 2013, the Fraunhofer IGB had a staff of 315 of which some 90 percent were scientific or technical employees. Women made up 56 percent of the total. The Project Group at the Fraunhofer CBP in Leuna was able to expand its staff once more, giving a year-end headcount of 29 (proportion of women: 45 percent).

The Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart counted a staff of 82 as at December 31, 2013, predominantly scientists and doctorate students as well as technical staff and student research assistants. Women constituted 35 percent of the total. Stuttgart University's Institute for Plasma Research IPF had been integrated into the Institute for Interfacial Engineering IGVT in January 2013, which was renamed IGVP.

The Fraunhofer IGB and IGVP employees work closely together and have remarkably culturally diverse backgrounds, with 49 members of staff coming from 27 different nations outside Germany.

Development of staff members



* Stuttgart University's Institute for Plasma Research IPF was integrated into the IGVT in January 2013. Numbers since 2013 refer to the merged Institute of Interfacial Process Engineering and Plasma Technology IGVP.

Staff composition as at December 31, 2013	Fraunhofer IGB	Fraunhofer CBP	IGVP
Scientists	82	8	17
Technical staff	73	13	14
Doctorate students	4	–	43
Administrative and secretarial staff	35	2	3
Apprentices	10	–	1
Scholarship holders	3	–	–
Work students/masters students/student apprentices	24	1	(19)*
Student research assistants	84	5	4
	315	**29**	**82**

* academic theses

ORGANIZATION CHART

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

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- Infection Biology and Array Technologies
- Functional Genomics
- Molecular Cell Technologies
- Enzyme, Strain and Process Development for Biotechnology
- Analytics

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- Physico-chemical Water Technologies
- Nutrients Management
- Aseptic Technologies
- Prototype Development

Business Development
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- Bioprocess Engineering
- Bioenergy
- Integrated Water Management

CELL AND TISSUE ENGINEERING

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- Biomaterials and In-vitro Test Systems
- Cardiovascular Tissue Engineering, Bioimaging and Bioreactors
- GMP Production of Cell-based Products

PROJECT GROUPS

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Project Group Oncology, Würzburg
Prof. Dr. Heike Walles
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THE FRAUNHOFER IGB'S NETWORKING ACTIVITIES

The 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 competences and enable us to exploit synergies in developing new solutions for the needs of industry. We are also actively engaged in shaping research policy through championing strategic, economic and sustainability standpoints.

Networking with universities

Basic research is a must for the applications of tomorrow. Thus the Fraunhofer IGB maintains close contacts with neighboring universities, both through scientific cooperation and through the professorial and other teaching commitments of Fraunhofer employees. Our project groups have enabled us to extend our scientific network to locations outside of Stuttgart, including the USA. The Fraunhofer IGB is particularly closely allied to the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart, which is chaired by Fraunhofer IGB director Prof. Hirth.

- Priv.-Doz. Dr. Susanne Bailer
  Private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Dr. Kirsten Borchers
  Associate lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Prof. Dr. Dieter Bryniok
  Professor of Environmental Biotechnology at Hamm-Lippstadt University of Applied Sciences
- Prof. Dr. Thomas Hirth
  Professor, Chair and Director of the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart
- Prof. Dr. Petra Kluger
  Professor of Tissue Engineering at Reutlingen University, Faculty of Applied Chemistry; Associate lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Dr. Christian Oehr
  Associate lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Priv.-Doz. Dr. Steffen Rupp
  Private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Prof. Dr. Katja Schenke-Layland
  Professor of Biomaterials in Cardiovascular Regenerative Medicine at the University Hospital for Women of the Eberhard Karls University Tübingen; Adjunct Associate Professor at the Medical Faculty/Department of Cardiology at the University of California Los Angeles (UCLA), Los Angeles, CA, USA
- Dr.-Ing. Ursula Schließmann
  Teaching activity in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart

- **Prof. Dr. Volker Sieber**
  Professor and Chair of Chemistry of Biogenic Resources at the Technische Universität München
- **Prof. Dr. Günter Tovar**
  Adjunct Professor and private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart;
  Vice Director of the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart
- **Prof. Dr. Heike Walles**
  Professor and Chair of Tissue Engineering and Regenerative Medicine at the University of Würzburg

Fraunhofer Sustainability Network

Sustainable development is arguably the key political objective of our time. What sustainability means in concrete terms for the Fraunhofer-Gesellschaft was defined early on by the society's Sustainability Network, to which over 20 institutes belong. The Fraunhofer IGB was significantly involved in this process, with Prof. Thomas Hirth acting as spokesman of the network. Projects were conducted, whose results fed into the compilation of a guide for sustainability reporting within the Fraunhofer-Gesellschaft according to the internationally recognized Global Reporting Initiative (GRI) standard. Thanks to its vanguard role in the German research landscape, since 2013 the Fraunhofer-Gesellschaft has been instrumental in coordinating a joint BMBF-funded research project designed to help provide scientific organizations with a framework for implementing internal sustainability management in the research context.

Fraunhofer International Business Development (IBD) Network

International cooperations and joint development activities with globally active partners are also of strategic importance for the Fraunhofer-Gesellschaft. The Fraunhofer IGB is an active member of the Fraunhofer-Gesellschaft's International Business Development Network, where various Fraunhofer institutes exchange views on specific issues regarding cooperation with international partners. Best-practice examples serve as the basis for an even more efficient use of resources when initiating and pursuing cooperation projects.

Fraunhofer EU Network

The EU Network is a platform accessible to all Fraunhofer employees where they can exchange information and experience both with regard to strategic aspects of funding and how to handle application and tendering procedures effectively, as well as on how to ensure the smooth implementation of EU-financed projects.

EU Working Group for Research and Technological Development Organizations (RTOs) in Baden-Württemberg

The Fraunhofer IGB is a member of the EU Working Group for Research and Technological Development Organizations (RTOs) in Baden-Württemberg, which aims to promote the regional exchange of information concerning EU funding for non-university research establishments.

THE FRAUNHOFER CBP'S NETWORKING ACTIVITIES

Leading-edge BioEconomy Cluster

The leading-edge BioEconomy Cluster integrates research and industrial activities relevant to the bioeconomy in Central Germany. The cluster's core objective is the sustainable value creation from non-food biomass such as wood as input for the production of materials, chemical products and energy. The Fraunhofer CBP assumes a pivotal role in scaling up and industrial implementation of the production processes developed.
www.bioeconomy.de

Science Campus Halle – Plant-Based Bioeconomy (WCH)

The Science Campus Halle (WCH) pursues the systematic and sustained development of a multi-disciplinary center for plant-based bioeconomy. The WCH thus provides an important base for future applications such as those implemented industrially in the neighboring regional leading-edge BioEconomy cluster, as well as interdisciplinary-trained professionals for industry. The Fraunhofer CBP is an associate member of the WCH.
www.sciencecampus-halle.de

Competence Center for Wood Composites and Wood Chemistry (Wood K plus)

The Competence Center Wood k plus is one of the leading research institutes in the fields of wood composites and wood chemistry. The Fraunhofer CBP is a partner in the COMET program (Competence Centers for Excellent Technologies), where it contributes its expertise in lignocellulose fractionation and the development of biotechnological and chemical processes.
www.wood-kplus.at

FRAUNHOFER GROUPS AND ALLIANCES

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 competences collaborate in the form of Fraunhofer "alliances" to develop business areas together and offer and market solutions along the entire value chain. In addition, Fraunhofer Institutes carry out joint activities within Fraunhofer internal research programs. Examples of IGB involvement are the Fraunhofer Beyond Tomorrow Projects "Molecular sorting" and "SKIN HEAL" as well as the Lighthouse Projects "Cell-free bioproduction", "Rare earth metals" and "E^3 production".

Fraunhofer Group for Life Sciences

The Group for Life Sciences is a key R&D partner to the pharmaceutical and medical engineering industries and to the biotech industry. By pooling complementary areas of expertise, the group is able to offer a broad spectrum of technologies and services. The group has an international outlook that reflects the globalized nature of this scientific field and the related commercial market. The Life Sciences Group is active in business areas such as medical translational research and biomedical technology, regenerative medicine, healthy foods, industrial biotechnology, and process, chemical, and herbicide safety, thus including numerous Fraunhofer IGB key competences. Professor Hirth was appointed Group Chairman at the beginning of 2012.

www.lifesciences.fraunhofer.de

Fraunhofer Group for Materials and Components – MATERIALS

Materials research covers the entire value chain, from the development of new materials and the enhancement of existing ones, to industrial-scale manufacturing technology, characterization of material properties and evaluation of service behavior. The same research scope applies to the components made from these materials and the way they function in systems. The Fraunhofer Group for Materials and Components addresses the entire range of materials and their composites, including metallic, inorganic/non-metallic, polymeric and renewable materials. The Fraunhofer IGB's strong competence in materials science qualified it to become a guest member of the Group in 2008.

www.vwb.fraunhofer.de

Fraunhofer Building Innovation Alliance

The Building Innovation Alliance offers single-source construction expertise in the form of integrated systems solutions. It has particular know-how in the systematic assessment of buildings – from construction materials to structural elements, from rooms and buildings to complete residential estates. The alliance's portfolio also includes the chronological assessment of a building in terms of its entire life cycle from drawing board to recycling. The Fraunhofer IGB participates here with its innovative infrastructure concepts for semi-decentralized energy and water management as well as with its competence in the microbiological aspects of construction.
www.bau.fraunhofer.de

Fraunhofer Energy Alliance

The Fraunhofer Energy Alliance is a gateway to R&D services in energy technology and economics. Above all small and medium-sized companies, but policy makers, too, benefit from Germany's technology leadership in energy efficiency and the development of renewables. The Fraunhofer IGB contributes its knowledge in the exploitation of energy resources contained in raw, residual and waste organic materials (e.g. for biogas production) as well as in membrane technology, particularly for gas purification/reforming and fuel-cell applications. Additionally, the Fraunhofer IGB carries out research into concepts and technologies for the storage and use of energy in the form of heat, while chemical energy storage is a new research topic of the BioCat Project Group.
www.energie.fraunhofer.de

Fraunhofer Food Chain Management Alliance

The Fraunhofer Food Chain Management Alliance is focused on new approaches in food safety, microelectronics and logistics that can be easily integrated in the entire food chain and are characterized by highest possible added value at low cost. The Fraunhofer IGB's specialization here is superheated steam for drying processes and the development of new physical methods for the hygienization and stabilization of food.
www.fcm.fraunhofer.de

Fraunhofer Nanotechnology Alliance

The Fraunhofer Nanotechnology Alliance bundles the nanotechnological expertise that is spread across nearly a third of the Fraunhofer Institutes. The alliance's activities cover all aspects of nanotechnology, such as multifunctional layers for automotive applications, the design of special nanoparticles as carrier substances for biotechnology and medical applications, and the use of carbon nanotubes in actuators. Prof. Günter Tovar is the Alliance's spokesperson.
www.nano.fraunhofer.de

Fraunhofer Photocatalysis Alliance

Nine Fraunhofer Institutes are involved in this alliance, the aim of which is the development of more effective and higher-performance photocatalysts for application to various surfaces such as glass, ceramics, plastics or metals. Vacuum plasma processes, sol-gel techniques and water-based paints are used to develop self-cleaning layers that break down organic compounds and destroy microorganisms. In order to determine the photocatalytic activity of a layer quickly and reliably, the Fraunhofer Photocatalysis Alliance is engaged in developing analytical methods for both chemical-physical and microbiological evaluation – the latter being Fraunhofer IGB's remit within the alliance.

www.photokatalyse.fraunhofer.de

Fraunhofer Polymer Surfaces Alliance POLO®

The Fraunhofer Polymer Surfaces Alliance POLO® pools the core competences of seven Fraunhofer Institutes in using functional surfaces, barrier layers or thin films to develop polymer products with new or improved properties. POLO® was one of the first Fraunhofer alliances, and products such as coatings on foils as a barrier against oxygen and humidity, as well as anti-microbial polymer surfaces, have already been successfully conjointly developed and marketed. The Fraunhofer IGB's Dr. Christian Oehr, deputy spokesman of POLO®, has been a member of the alliance's board of directors since its inception, and has contributed significantly to its success.

www.polo.fraunhofer.de

Fraunhofer Cleaning Technology Alliance

The alliance covers the entire spectrum of cleaning technology, including special cleaning technologies like laser, plasma or mechanical jets, specific-cleaning planning of plants including cleanroom technology, and the recycling of cleaning and process media, including the recovery of energy and material streams. The Fraunhofer IGB's expertise includes plasma cleaning and plasma coating, and assessment using surface analytical and microbiological methods. Further competences are the conditioning and recycling of cleaning and process media as well as cleaning and hygienic aspects in design.

www.allianz-reinigungstechnik.de

Fraunhofer Water Systems Alliance (SysWasser)

SysWasser's mission is to develop sustainable solutions for water and wastewater treatment, utilization, reuse, and management, as well as sustainable water infrastructure systems and adapt them for use in practical applications, taking into consideration relevant social, economic and environmental aspects. The participating institutes provide a wide range of expertise on water treatment technologies, water infrastructures, system control and measurement techniques, automation and resource management, which enables the alliance to develop and implement system solutions based on a variety of technologies. The alliance's managing director is Prof. Dieter Bryniok of the Fraunhofer IGB, where the SysWater office is based.

www.syswasser.de

HIGHLIGHTS 2013

ANNIVERSARY YEAR AT THE FRAUNHOFER IGB

60 years of research into interfaces – a commemorative symposium at the IGB

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The Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB celebrated its 60th anniversary on September 25, 2013 with a commemorative symposium. Founded in 1953 as a small research lab for interfacial physics and chemistry in the Palatinate region (southwest Germany), the institute still bears "interfaces" in its name to this day. At an interface, a transition layer between two phases or substances that is only a few atomic or molecular layers thick, physico-chemical properties change almost abruptly. An interface is thus a place where new phenomena occur. Today, innovations are realized through the cross-fertilization of interface research with other disciplines at the institute.

In his welcome speech at the commemorative symposium "60 years of research into interfaces" Prof. Thomas Hirth described his strategic focus at the Fraunhofer IGB: "Thanks to the tremendous support of the federal and state ministries and the Fraunhofer-Gesellschaft, we have been able to focus our research consistently on the business areas of medicine, pharmacy, chemistry, energy and the environment, and anchor key issues of the future such as sustainability and biobased economy in the institute."

Fraunhofer president Prof. Reimund Neugebauer in turn in his address expressed his pleasure that almost a year ago he and Prof. Hirth had been able to greet Chancellor Angela Merkel at the inauguration of the Fraunhofer CBP in Leuna. The Rector of the University of Stuttgart, Prof. Wolfram Ressel, gave words of thanks for the trust and mutually beneficial cooperation with the Fraunhofer IGB and its partner institute at the university, which is headed by Prof. Hirth. Representatives of the federal government and the state of Baden-Württemberg – including MinDirig Dr. Fritz Holzwarth from the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB), MD Rolf Schumacher from the Baden-Württemberg Ministry of Finance and Economics and Swantje Nilsson from the Federal Ministry of Food and Agriculture (BMEL) – paid tribute to the evolution of the Fraunhofer IGB into an innovative research facility which, shaped by the respective institute directors, has played a decisive role in research into interfacial phenomena. In their words of welcome, they underlined Prof. Hirth's contribution in paving the way toward a biobased and sustainable economy in Baden-Württemberg, Germany and Europe through embracing the themes of bioeconomy and sustainability.

Prof. Wolfgang Peukert from the University of Erlangen and Prof. Christoph Syldatk from the Karlsruhe Institute of Technology (KIT) gave commemorative lectures on interfacial engineering and biotechnology in which they showcased today's areas of competence at the Fraunhofer IGB. One of the highlights was the short presentations by five young scientists from the Fraunhofer IGB, following the concept of an "Elevator Pitch". Philipp Grimmer, Lea König, Florian Groeber, Matthias Stier and Silke Grumaz presented ideas and research approaches relevant to their research interests and thus provided a potted overview of current topics at the institute: an innovative approach for an ice-free pavement, the varietal

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separation of rare earth metals, the automated production of skin models in the "Skin Factory", the catalytic conversion of methane and carbon dioxide (biogas) to methanol and the elucidation of protein interactions with synthetic proteins. Dr. Johannes Strümpfel of Von Ardenne GmbH and Dr. Markus Wolperdinger of Linde Engineering Dresden GmbH (chairman of the Fraunhofer IGB's advisory board since early 2013) rounded off the program with presentations from the perspective of industry.

From IGf to IGB

The roots of the Fraunhofer IGB lie in Germany's Palatinate region, where, in 1953, the renowned physicist and chemist Prof. Karl Lothar Wolf established a laboratory – initially on the premises of the local high school – for investigating the physics and chemistry of interfaces. Here he could devote himself to the study of interfacial processes on powdered solids. A short time later, the institute moved to nearby Marienthal, and in 1962 it was taken over with its handful of employees by the fledgling Fraunhofer-Gesellschaft as the Fraunhofer Institute for Physics and Chemistry of Interfaces IGf. When the institute moved to Stuttgart in 1969, Prof. Karl Hamann, director of the 2nd Institute for Technical Chemistry at the University of Stuttgart and head of the thriving Stuttgart-based Research Institute for Pigments and Coatings e. V. (a member of the AiF German Federation of Industrial Research Associations network) took over as acting head.

In 1976, Dr.-Ing. Horst Chmiel, a medical technology research specialist at the Helmholtz Institute in Aachen, was appointed successor to Prof. Hamann, who retired on age grounds. Under his influence, the discipline of biotechnology was built up, and the institute focused more strongly and more application-oriented on process technology. This gave rise to the institute's current name, "Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB", or Fraunhofer IGB for short. A new focal point then emerged: the "interfacial problems of medicine", effectively the interface between the interfaces field and the new field of medical process engineering. Today's key area of environmental biotechnology dates back to 1978, when it was established to develop and optimize

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bioprocesses for applications such as the production of biogas from agricultural waste like manure and sewage sludge, for optimizing wastewater treatment, and for the production of organic acids by use of biotechnology. Membrane technology kicked off in 1979 as the research focus "Transport processes through membranes" in the area of medical technology. Within a few years the institute was able to extend the membrane technology to other applications such as product recycling and develop it into a field of research of significant importance to industry.

When the Fraunhofer IGB moved to a new building with state-of-the-art laboratories at today's Fraunhofer Campus in Stuttgart-Vaihingen in 1981, the Fraunhofer-Gesellschaft and the state of Baden-Württemberg laid the foundation for fruitful cooperation between the Fraunhofer institutes and the scientific and technical institutes of the university.

After the appointment of Prof. Chmiel to the University of Saarbrücken, Prof. Armin Fiechter from ETH Zurich initially held the post of acting director of the Fraunhofer IGB. He was followed by Dr. Herbert Bauser, head of the institute's Interfacial Process Engineering department, who served in an acting capacity until 1994 when Prof. Herwig Brunner of Boehringer Mannheim was appointed director. Brunner fetched a Fraunhofer working group from Hanover, which specialized in recombinant protein production and the design of pharmaceutical proteins. By deploying the talents of young researchers he both deepened molecular biology expertise in Stuttgart and built a bridge from biotechnology to interfacial engineering, in the shape of one junior research group working on protein screening systems and one on biomimetic interfaces. In parallel he strengthened cell biology activities at the Fraunhofer IGB and developed them systematically into cell systems research. In addition, Brunner promoted the link between natural sciences and engineering.

In late 2007, Prof. Thomas Hirth came from the Fraunhofer Institute for Chemical Technology ICT to take over as director of the Fraunhofer IGB. Hirth focused the work of the process engineering institute on the needs-oriented business areas of medicine, pharmacy, chemistry, environment and energy – and thus oriented it to the challenges of the 21st century. With his contacts in industrial biotechnology, he brought back to the institute a subject that the Fraunhofer IGB had researched in broad outline in the past, namely the manufacture of products from renewables (renewables conversion). At the same time he ensured that the topics of bioeconomy and sustainability became not only a key part of the research landscape at the Fraunhofer IGB and the Fraunhofer-Gesellschaft, but also a core aspect of national German and Baden-Württemberg research policies. Hirth also oversaw the expansion of Fraunhofer IGB activities to Würzburg, Straubing and Leuna, where project groups on oncology, on chemocatalysis and biocatalysis and the Fraunhofer Center for Chemical-Biotechnological Processes CBP were established. In the anniversary year 2013, another milestone was achieved when the Institute for Plasma Research (IPF) at the University of Stuttgart was integrated into the university's Institute for Interfacial Engineering IGVT, which is closely associated with the Fraunhofer IGB. Not only does this bring together plasma activities in Stuttgart, but it also strengthens the Fraunhofer IGB's roots in interfacial engineering.

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PROJECTS AND PROJECT GROUPS

IPF and IGVT become IGVP 1

At the beginning of 2013, our partner institute at the University of Stuttgart, the Institute for Interfacial Engineering IGVT, was expanded through integration of the Institute for Plasma Research IPF, by resolution of the Senate and the University Council of the University of Stuttgart. The merged body has been renamed the Institute of Interfacial Process Engineering and Plasma Technology IGVP.

Research activities at the IGVP are organized in two newly formed departments. The Interfacial Engineering Department comprises groups working in the five areas Medical Interfacial Engineering, Biological Interfacial Engineering, Physical Interfacial Engineering, Chemical Interfacial Engineering and Environmental Interfacial Engineering – while the Department of Plasma and Interfacial Physical Processes is subdivided in the groups Plasma Technology, Microwave Technology, Plasma Dynamics and Diagnostics, and Interfacial Physics. The integration of the IPF means that the institute has rounded off its basic research capability in the field of plasma physics and can combine this with activities in the fields of plasma chemistry and plasma process engineering.

Straubing Fraunhofer Project Group BioCat positively evaluated

Since its inception in 2009, the Fraunhofer BioCat Project Group – funded by the State of Bavaria for an initial period of three years – has firmly established itself in Straubing. At the end of this term, the group was required to submit itself to comprehensive scrutiny by independent experts from industry and academic research, in order to be allowed to continue its work. By the end of 2012, Professor Volker Sieber and his team had compiled a report of over 60 pages detailing their previous activities and submitted it to the experts. In addition to the scientific and technical aspects, the experts' remit was to evaluate the financial performance of the group and its links with regional and national partners from industry and research. The panel of experts met in Straubing in early 2013, and came to a very positive finding. In its view, the staff's performance in setting up and developing the project group has been impressive. Its ambitious goals have been achieved, and the project group is well placed for the future. Thus the group's temporary status linked to the start-up funding has been lifted and it can continue its activities as a permanent unit of the Fraunhofer-Gesellschaft.

Center for Energy Storage at the Fraunhofer BioCat Project Group in Straubing 2+3

"If we want the energy transition to succeed, we must increase investment in energy research and the development of technology. New storage technologies are a key component here – with its support for the Center for Energy Storage the Bavarian State recognizes this as the way to go". So said Ilse Aigner, Bavarian State Minister for Economic Affairs and Media, Energy and Technology and Deputy Prime Minister of Bavaria on November 15, 2013 at the handover of the funding approval to the BioCat Project Group. The Free State of Bavaria is providing financing of 4.9 million euros over a period of five years for activities in the new field of "Chemical storage – catalysis & process" at the Center for Energy Storage, plus an additional 2.5 million euros to partially finance a new

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research building. The Center for Energy Storage operates a second site at the Bavarian branch of the Fraunhofer Institute for Environmental, Safety and Energy Technology UMSICHT (Oberhausen) in Sulzbach-Rosenberg.

"Chemical storage – Catalysis & process" will focus on developing methods to compensate for diurnal and seasonal variations in electricity generation from wind and solar energy, and to store energy over a longer period of time, involving harnessing excess electrical energy to produce chemical energy carriers. First promising approaches exist, e.g. for producing methane from CO_2 with the "power to gas" technology. However, the prerequisite for developing sustainable, easily scalable and decentrally operated processes is developing and researching the necessary catalysts. The carbon dioxide substrate will come from carbon dioxide produced in power plants or biogas plants. Fixing the CO_2 instead of releasing it into the atmosphere, has the positive side effect of making a contribution to climate protection. Both chemical catalysts and biocatalysts will be investigated.

The handover of the funding approval by State Minister Aigner was celebrated by the Straubing researchers together with a second ground-breaking ceremony: just a year after the inauguration of the new laboratory building an extension is being built, which will triple the laboratory and office space for the growing team.

Global Bioenergies receives subsidy commitment for industrial pilot plant at the Fraunhofer CBP 4

Over the next three years the BioEconomy cluster company Global Bioenergies GmbH is going to construct an industrial pilot plant for the production of isobutane from biomass at the Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, also a partner in the leading-edge cluster. The German Federal Ministry of Education and Research (BMBF) is funding the project with a 5.7 million euro grant. This lighthouse project, with Fraunhofer CBP acting as a scientific advisor, is a milestone for the BioEconomy cluster on the road to a sustainable biobased economy and represents important bridge building to the chemical industry at the Leuna site. The support of the BMBF and the BioEconomy Cluster facilitates the participation of Global Bioenergies GmbH in the global transition from fossil to renewable resources, in the words of the German managing director.

Global Bioenergies GmbH, located in the BIO-CITY building in Leipzig, is the German subsidiary of Global Bioenergies, S.A. The French listed company is a pioneer in the development of one-step fermentation processes for the direct, exclusively biological conversion of renewable resources into light olefins, the key building blocks of the petrochemical industry.

The pilot plant in Leuna will combine two 5,000-liter fermenters and a complete purification system, mimicking all aspects of a commercial scale plant. The production capacity of up to 100 tons of isobutene per year will allow it to offer interested industrial companies the base material for their own testing purposes, e.g. for manufacturing plastics, elastomers or fuels. This second pilot for Global Bioenergies is the final step in its development program before full-scale exploitation of the isobutene process.

BADEN-WÜRTTEMBERG'S BIOECONOMY RESEARCH STRATEGY

Bioeconomy – a new economic system

Fossil fuels are still by far the most important basis for the chemical products we know – ranging from fuel to plastics and textiles, lubricants and construction materials to cosmetics and pharmaceuticals. However, fossil resources are finite, and climate change coupled with a growing world population present society with major challenges. A "biobased" economy – "bioeconomy" for short – promises a sustainable solution to securing food for the human race. Secondly, it uses renewable resources for the production of energy and materials, while at the same time protecting the climate and the environment.

The bioeconomy system

The bioeconomy functions on the principles of continuity – pursued consistently from basic research, followed by applied research, up to the industrial implementation of new processes and products – and of regionality, i.e. seeking wherever possible to exploit local resources and strengths. At the same time, a particularly high priority must be accorded to providing scientists with appropriately structured training, building on the holistic approach and system-oriented solutions to complex problems to which they will ideally have been introduced during their studies. The marriage of scientific expertise with a more resource-efficient, ethical and efficiency-oriented economic approach will serve as a basis for sustainable prosperity.

Bioeconomy Strategy Group

As a former member of Germany's first Bioeconomy Council Prof. Thomas Hirth headed the Baden-Württemberg Ministry of Science, Research and the Arts' bioeconomy strategy board "Bioökonomie im System" established in 2012. Under his expert direction, representatives of all universities involved in bioeconomy research and teaching drew up a comprehensive research plan with the aim of highlighting the topic bioeconomy as a fixed reference point in the Baden-Württemberg scientific landscape and establishing it as a strategy for the future. In July 2013, the group adopted a strategy paper defining concrete fields of action to promote bioeconomy research in Baden-Württemberg. These recommendations were well received by science minister Theresia Bauer, and the basis of this plan, the Council of Ministers adopted a new bioeconomy research program for Baden-Württemberg with a total funding volume of 12 million euros over the period 2014–2019.

Comprehensive research plan

The research strategy focuses on exploring the bioeconomy in terms of value creation cycles and as an overall system. To this end, the strategy circle looked at all the numerous research institutions in Baden-Württemberg, identified those all that engaged in relevant topics, and within a short time brought them together with established experts for economics, ethics and the social sciences. Thus social, economic and political parameters were taken into equal account from the outset, along with the effects on the environment and society. The expert team identified some 180 individual areas of expertise

at 24 universities, universities of applied research and non-university research institutions. From these they distilled seven scientifically suitable core research areas for Baden-Württemberg, and chose two spokespersons for each of these subgroups. The groups acted within a structure of supply and demand: thus, on the supply side, the research areas deemed most important were agricultural and plant sciences, forestry, aquatic biomass and biogenic residues. On the demand/utilization side, the key areas identified were application fields such as food production, and, subsequently, the material and energetic use of waste materials. This enabled the creation of a competence matrix, in which biodiversity, water and soil conservation, ethics, as well as economic and social sciences were named as cross-disciplinary areas.

Following in-depth data collection and its detailed analysis, the strategy group identified three areas of research that, with the help of targeted research funding, will soon be able to provide visible stimuli to research and industry in Baden-Württemberg and beyond. The plan focuses on three areas of research – biogas, lignocellulose and algae – and at the same identifies structural measures to profile and sustainably strengthen Baden-Württemberg as an innovative bioeconomy region.

Research fields for Baden-Württemberg

Biogas has been identified as a research field for which scientific know-how is already available in Baden-Württemberg along the entire value chain. It therefore lends itself as an early candidate for implementation of the bioeconomy systems approach. Lignocellulose research is characterized by a large number of individual competencies spread across a broad spectrum of knowledge. The first step must therefore be to improve the bundling and networking of existing expertise, so that implementation is realistic in the medium term. The plan ascribes the highest degree of innovation – and consequently long-term perspectives – to research into the use of microalgae. The key objective here is the economically efficient production of microalgae along the lines of a biorefinery, i.e. production by means of integrated material and energetic use and for multiple applications. The selection of the three above-named areas with their sub-themes as research priorities is expected to lead to many completely new combinations of existing scientific competences, and thus promises great potential for innovation in Baden-Württemberg.

Structural measures

To underline the systemic approach, the development of research fields will be supported through the Baden-Württemberg government's new Bioeconomy Research Program and flanked by structural measures. The strategy group proposed three measures: a competence center for modeling and simulation of bioeconomy systems, a common graduate program to integrate bioeconomy from the start in the education of doctorate students, and a concept for the joint use of infrastructure that will enable the resource-efficient use of large and technically complex equipment in future. With its manifold expertise and experience in the field of bioeconomy that is characterized by the reconciling of seemingly conflicting demands, the Fraunhofer IGB itself has been able to contribute many new impulses. It thus opens up new perspectives for innovation to its partners from science and industry both in Baden-Württemberg and further afield.

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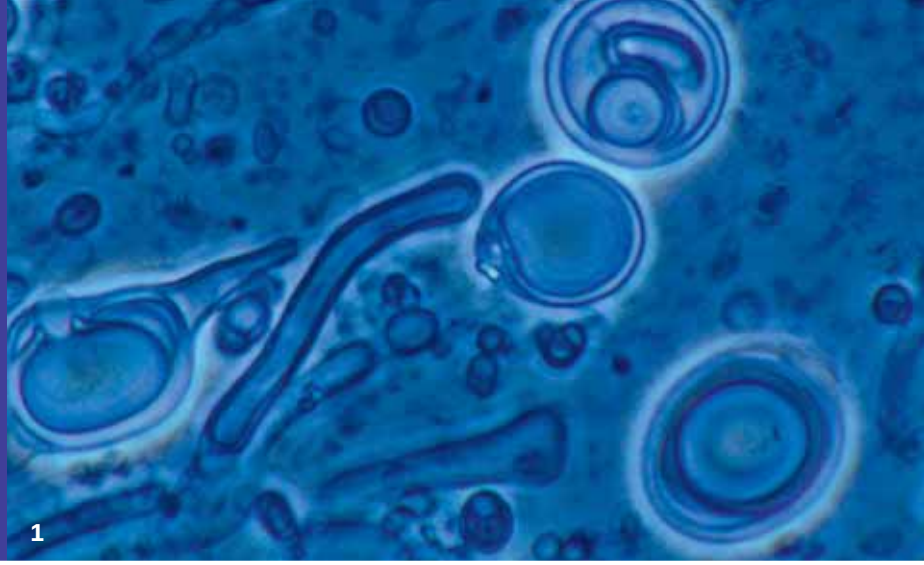

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FRAUNHOFER LIGHTHOUSE PROJECTS

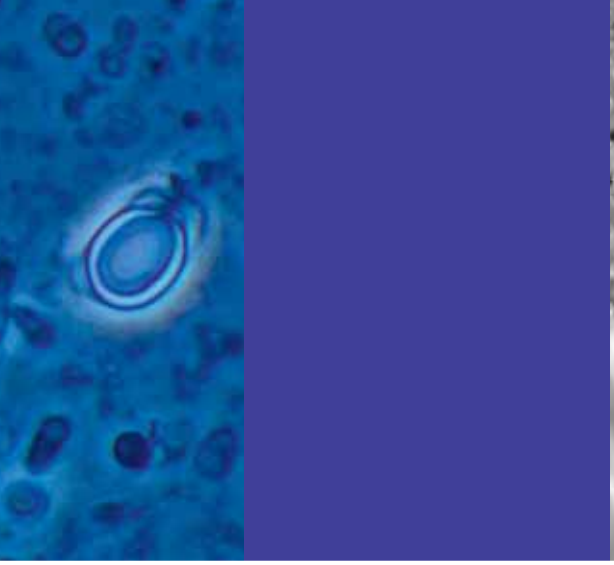
On the initiative of its president, the Fraunhofer-Gesellschaft's established portfolio management process has been used to identify new lighthouse projects that will significantly lift the profile of the six major societal areas of health and nutrition, communication and information, mobility and transportation, energy and raw materials, safety and security, production and services. The lighthouse projects – such as "Cell-free bioproduction", "Fraunhofer electromobility II system research project", "E^3 production" and "Rare earth metals" – are designed to bring together Fraunhofer expertise in a flexible, interdisciplinary approach to future-oriented areas of research and to involve industrial partners at an early stage. Due to its strategic focus on the business areas of medicine, pharmacy, chemistry, environment and energy, Fraunhofer IGB is involved as a partner in three of the four projects named above.

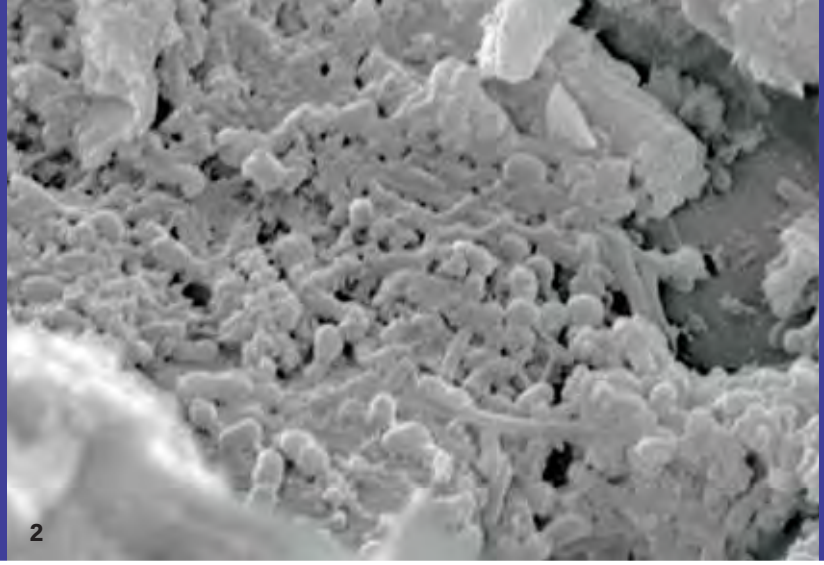
Cell-free bioproduction 1

Cell-free bioproduction is at the interface between engineering and the life sciences. In the Fraunhofer "Cell-free bioproduction" lighthouse project eight institutes (IBMT, IME, IPA, IPK, ISI, ISIT, IZM and IGB) have been working together since 2011 on developing an alternative technology platform to traditional biotechnological processes, with the goal of accelerating protein synthesis, e.g. of antibodies, by a large factor. In addition, cell-free bioproduction makes it possible to produce a far greater range of proteins by biotechnological means.

The guiding idea of this ambitious project is to find efficient ways to synthesize proteins without relying on living cells. Many proteins can only be produced to a limited extent or not at all in microbial or cell cultures – for instance, proteins toxic to cells, toxin fusion proteins of interest to the pharmaceutical industry, or membrane proteins as targets for drug development. So-called in-vitro protein synthesis overcomes these disadvantages associated with living cells: here, the biomolecules are, in contrast to conventional methods, produced in cell extracts (lysates). The extracts basically retain only the protein synthesis machinery of the cell, with the effect that, for example, there is no longer a requirement to maintain a complex cellular metabolism with a plethora of products. Instead, the synthetic potential of the lysate can be focused solely on actively synthesizing the desired product.

The project has identified, analyzed and optimized the first key parameters for the industrial realization of cell-free bioproduction, i.e. protein synthesis. The new insights acquired have already facilitated a tenfold reduction in the cost of small and medium-scale protein production. The Fraunhofer IGB is using cell-free lysates to develop specific antibodies that can modulate excessive immune reactions and which might help to moderate septic shock. One of the biggest challenges on the road to industrial scale is the supply of energy to the cell-free lysates. With its successful use of the membrane-bound protein ATP synthase as an energy regeneration system, the Fraunhofer IGB has achieved first promising results here. The





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institutes are also cooperating closely on developing the reactors for the technology platform. The three different concepts being pursued are a microfluidic platform with separate compartments, a "continuous exchange cell-free system" within hollow-fiber reactors, and upscaling in single-chamber reactors.

E^3 production 2

Against a background of competitiveness and social development (demographic change), and also of climate protection and conservation of resources, organizations have to meet the challenge not only of realizing resource- and energy-efficient processes and products, but also of producing in an overall sustainable, low-environmental-impact way under ergonomic conditions. This gives rises to three important pillars for the factory of the future: energy and resource efficiency, emission neutrality, and ergonomics (integration of people in production) – summarized as E^3.

The lighthouse project "E^3 production" addresses these three pillars and focuses, notably, on the design and implementation of ultra-short process chains, the operation of production systems that can adapt their use of energy and resources to a volatile energy supply, the establishing of closed-loop material cycles, and the use of production itself to store energy, including the integration of materials. With regard to the reduction of emissions, approaches being examined include completely closed-loop energy and material re-use cycles, and also the recovery of energy, culminating in self-regulated recycling. The Fraunhofer IGB's contribution is the demonstration of ultra-short production processes used in biotechnology and process engineering, as shown by the example of a reactor concept for the bioprecipitation of metals. The concept has the aim of facilitating integration of the bioprecipitation process into existing process chains, while at the same time taking the required product quality into account. Featuring internal recycling and loop closure, it will thus contribute to overall resource efficiency. The project involves the collaboration of the Fraunhofer institutes FIT, IBP, ICT, IFF, ILT, IML, IPA, IPK, IPT, IWU, UMSICHT and IGB.

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Rare earth metals 3

A forward-secure, affordable and predictable supply of raw materials is of utmost importance for the stability and prosperity of the economies of technologically advanced industrial nations such as Germany. Therefore the availability of metals such as the rare earths (formally: rare earth elements, REE) is of great strategic importance to make the competitiveness of producing goods in Germany, especially in the high-tech sector, less dependent on global commodity trading. In October 2010, the Federal Republic of Germany published its commodity strategy for securing its future supply of raw materials; the European Commission did so in 2008 and 2011. The respective commodity strategies are essentially based on the following three pillars: (1) trade and commodity diplomacy, (2) domestic extraction of raw materials, and (3) resource efficiency, recycling and substitution.

The Fraunhofer "Rare earths criticality" lighthouse project tackles the third pillar of commodity strategy, focusing on the use of rare earth metals in high-performance magnets. As well as the Fraunhofer IGB, the project involves the Fraunhofer institutes IWM IWM-H, IWU, IFAM, LBF and ISI, plus the ISC's IWKS project group. Its mission is to halve the specific, primary demand for heavy rare earth elements for the specific application "Dysprosium-containing Nd-Fe-B permanent magnets and systems for electric motors". To achieve this goal, the Fraunhofer-Gesellschaft is pursuing four priorities:

- Material substitution – the project involves developing novel metallic phases, which require less or no rare earth metals, from simulation to manufacture
- More efficient processes – work on refining magnet production processes, e.g. net-shape production, dysprosium-layer technology, grain-size tuning technology
- Optimized design – here the focus is on the optimization of design from miniature electrical drives to the construction of demonstrators
- "Design for recycling" – this sub-project looks at aspects of recycling and the re-use of electric motors as well as the extraction of rare earths from permanent magnets and production waste. The spotlight is on the treatment and recycling of magnets as recycled granules for magnet production, as well as material recycling for the production of the purest possible rare earth metals or metal oxides.

The Fraunhofer IGB's contribution is the sub-project "Recovery of rare earth metals from permanent magnets and production waste", which has three specific objectives. First, to develop methods for recycling sintered magnets from old electric motors in such a way that the recycled granules can make up at least 10 percent of primary production of the magnets without impacting on the magnets' properties. The second objective is to identify the extent the recycled magnetic granules can be used in the production of plastic-bonded magnets. The third objective involves granulating old magnets and combining them with production residues such as grinding swarf to make new products.. The magnetic granules and the abrasive dust are dissolved and separated into their component elements using physical-chemical or biotechnological methods, allowing recovery of rare earths as, optimally, pure metals or metal oxides.

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FRAUNHOFER IGB INTERNATIONAL

New EU-funded research projects

With its specific programmes in the categories "Cooperation", "Capacities", "People" and "Ideas", the EU's 7th Research Framework Programme (FP7) was the most important instrument of European research funding from 2007 to 2013. In 2014, the new framework programme "Horizon 2020" enters into force, which in turn promises exciting calls for the Fraunhofer IGB. At the end of the 7th Framework Programme the Fraunhofer IGB posted yet a number of major successes.

New Cooperation Programme projects

In the field of collaborative research, the Fraunhofer IGB is coordinating the **EnReMilk** project, which is being funded under the "Knowledge Based Bio-Economy – KBBE" subject area. Fifteen European partners are working together on optimizing novel water- and energy-saving technologies and integrating them into selected dairy processing lines, while maintaining the quality and safety of the corresponding products. All the process steps will be examined, and the potentials of a vast array of technologies will be analyzed using process modeling tools.

Moreover, we are partners on eight other collaborative projects under the research themes Health, Environment, NMP (Nanosciences, Nanotechnologies, Materials and new Production Technologies), as well as on the topic of "Knowledge Based Bio-Economy" under the Food, Agriculture and Fisheries, and Biotechnology research theme. The projects were invited by the European Commission (EC) to negotiations in 2013 and their respective contract periods commence at the end of 2013/start of 2014.

New Capacities Programme projects 1+2

The Fraunhofer IGB is working in close collaboration with small and medium-sized European enterprises in ten new projects on the theme "Research for the benefit of SMEs and SME associations" within the FP7 Capacities Programme. This type of project is aimed specifically at the innovation needs of European SMEs or SME associations. With the aid of financial project support from the EC, such SMEs or associations have the opportunity to outsource research and demonstration activities to Research and Technological Development (RTD) performers, for the benefit of the SMEs or the SME association members.

In the **NovEED** project, a novel energy-efficient electrodialysis cell is being developed for internal energy recovery, based on a new type of electrode. The electrodialysis cell is to be used for the recycling of acids and bases from industrial process waters.

The **OxFloc** project is also concerned with water treatment, aiming to degrade and remove hazardous substances in an integrated approach using a one-step oxidation-adsorptive process. In future, this will not only lower the operating costs of wastewater treatment, but also achieve far-reaching benefits for the environment.

Whey resulting from cheese production contains valuable proteins that still often remain unused. By refining an electromembrane process initially investigated at the University of Hohenheim, the **Whey2Food** project consortium is investigating how to selectively obtain high-quality whey proteins fractions to enrich foods and enhance their nutritional or technological-functional properties. Compared with ultrafiltration, the optimized technique fractionates and concentrates

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whey proteins and hereby increases production yields while reducing cleaning efforts.

In the **PhosFarm** project, the Fraunhofer IGB is involved in developing an enzymatic process for the sustainable recovery of phosphorus from agricultural residues. Phosphorus will be recovered as a valuable fertilizer, so that the process will provide an additional source of revenue for European farmers in the future.

The **MCure** project derives from a completely different industry. The European construction sector is facing the challenge of tackling and durably repairing damage to concrete structures that has arisen over many years. In this project, a new energy-efficient system will be developed to improve and accelerate hardening of the repaired concrete patches during renovation – and thus save costs.

The **HiPerDry** project is funded under the theme "Research for the benefit of SME associations". The principal objective of HiPerDry is to create a significant advance beyond the state-of-the-art in drying technologies currently employed in the European plastics processing sector. It involves the development of a novel microwave-enhanced superheated steam process for high performance and energy-efficient drying of hygroscopic polymers. Through the innovative combination of microwave heating and superheated steam drying, significant energy and time savings are expected. Moreover, HiPerDry aims to extensively investigate thermodynamic processes within the polymer granules during drying and respectively establish a best-practice guideline on the drying procedures for the most industrial relevant hygroscopic polymers.

Beyond these named coordinated projects, the Fraunhofer IGB is involved as a research partner in the two SME projects "MFC4Sludge" and "Nutrec". In addition, the consortia of the two successfully completed projects MicroMilk and PreserveWine were able to gain funding for a demonstration project to transfer the results into industrial scale.

New People Programme projects

As well as consortium projects, we are pleased to welcome several Marie Curie fellowship holders to the Fraunhofer IGB, including Dr. Roman Surmenev who has joined us from Russia for a two-year collaboration on the PlasmaNanoSmart project. Research scientist Dr. Michael Monaghan from Ireland is also with us for two years in Stuttgart, where he is working as a Marie Curie fellow on the "miR-Opto-FectArray" project. Furthermore, the Fraunhofer IGB is a partner in the "Bio-Inspire" and "ImResFun" Marie Curie International Training Networks, which will enable us to work concurrently with different scientists at international level in the coming years.

Further information on these and eight other new collaborative projects not presented here ("Fungitect", "AmbuLung", "Amcare", "demEAUmed", "Ensocio-La", "Carboprec", "Osyris" and "FoAM-BUILD"), as well as all other FP7 projects at the Fraunhofer IGB, can be found on our website.

Further information about the FP7 projects of Fraunhofer IGB:

www.igb.fraunhofer.de/eu-projects

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Asia – cooperation with GIZ 3 + 4

For the first time, the Fraunhofer IGB has been involved as a partner in a regional development project organized and conducted by the Deutsche Gesellschaft für Internationale Zusammenarbeit GmbH (GIZ) to provide consultancy to ten Asian cities on the integration of their respective water, energy and food security sectors. In the project "Integrated resource management in Asian cities – the urban nexus" the Fraunhofer IGB visited selected cities together with GIZ staff and identified examples of best-practice habitat-adapted solutions that are to be implemented in the course of the project.

At a workshop in Bangkok in June 2013, the Fraunhofer IGB presented potential approaches and technical solutions for an integrated water management system. Three of the carefully selected cities have already been a destination for IGB visits. Further on-site analyses are scheduled for 2014 in Mongolia, China, Vietnam and Thailand. The results of the analyses and the resulting implementation proposals will be presented at a further workshop for decision makers from all pilot cities.

China – focus on innovative biorefinery concepts

At the end of October, the Fraunhofer Center for Chemical-Biotechnological Processes CBP welcomed a delegation of high-ranking representatives of the Shanghai Advanced Research Institute, Chinese Academy of Sciences (SARI). The visit was organized and coordinated by the Fraunhofer Institute for Mechanics of Materials IWM, Halle branch of the institute. The visit focused upon the mutual exchange of knowledge and experiences in the field of biorefineries and biorefinery concepts, particularly with regard to algae biotechnology and residue recycling. Both China and Germany see great potential for future cooperation here. During the visit, a memorandum of understanding was signed with the BioEconomy e. V. Cluster of Excellence, and a return visit was agreed.

In addition, in November the Fraunhofer CBP was an important stop on the press trip of Chinese journalists. The tour, themed "Chemicals grow here in parks", allowed for in-depth interviews with the responsible researchers and decision makers. The media representatives from the renowned news agency Xinhua, from *China Radio International*, and from the newspapers *People's Daily* and *The Economic Daily* were mainly interested in infrastructure und logistics of chemical parks in Germany, but also in the collaboration between the companies on such a site in the communication and cooperation of the companies involved. Therefore, the Fraunhofer CBP presented a number of innovative joint projects and research cooperations.

The visit was scheduled and organized by the Investitions- und Marketinggesellschaft Sachsen-Anhalt (IMG) and the Central European Chemical Network CeChemNet together with the isw Gesellschaft für wissenschaftliche Beratung und Dienstleistung mbH (isw GmbH).

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Qatar – microalgae testing in the desert 5

As part of a new, scientifically based cooperation project, Fraunhofer IGB engineers set up an algae bioreactors test unit on the Qatar University campus. The Subitec photobioreactor test plant produces microalgae for the production of oil-rich algal biomass. The particular operating conditions of the desert belt allow the drawing of comparisons with previously established open-pond plants. Of specific interest are data relevant to plant design and technical process details, but also conclusions on the selection of particularly suitable microalgae strains. The first project results are eagerly awaited in 2014.

Brazil – Green Chemistry

Dr. Werner Sternad gave a talk at the annual meeting 2013 of the Brazilian Society for Chemistry (Reunião Anual da Sociedade Brasileira de Química – RASBQ), that took place May 25–28 at Aquas de Lindóia. His presentation in the scientific workshop program "Green Chemistry: Limits, Challenges and Future Perspectives" addressed possibilities of recovering raw materials from residues. Dr. Sternad followed a personal invitation from Prof. Dr. Vânia Zuin, an Alexander von Humboldt-Stiftung alumna who coordinated the agenda of the top class workshop.

Argentina bioeconomy fact-finding at the Fraunhofer IGB

In May 2013, a delegation from Argentina stopped off at the Fraunhofer IGB as part of their fact-finding mission on the topic of bioeconomy. Participants included a representative from the Argentinian Ministry of Science, Technology and Productive Innovation (MINCyT), several delegates from the government research coordination and funding agency, CONICET, as well as researchers from several universities with different research interests. The visit was scheduled and organized by the International Bureau of the German Federal Ministry of Education and Research, who provided staff to accompany the visitors, along with representatives of the German-Argentinian Chamber of Commerce. During the course of discussions, it was possible to identify the first key topics for future joint research and teaching in the field of bioeconomy, with more in-depth discussion planned for 2014.

France – 50th anniversary of the Elysée Treaty

The topic of bioeconomy is already strongly associated with the Fraunhofer IGB, both internationally and on the European stage. It was therefore the thematic focus of a tandem presentation titled "Bioeconomy, the German approach" given by Prof. Thomas Hirth together with Prof. Ulrich Schurr from Forschungszentrum Jülich during a bioeconomy seminar at the Institut national de la recherche agronomique (INRA, National Institute of Agronomic Research) on October 8 in Paris. The presentation was part of a two-day French workshop program and a series of carefully selected talks by representatives of French ministries and a number of European research institutions.

The purpose of the workshop was the presentation and discussion of national strategies on bioeconomy, the comparison of structures already in place, the identification of challenges and potentials, and – not least – the strengthening of the links between research and industry, as well as the generation of joint ideas for setting up and expanding German-French bioeconomy research projects.

In the context of other events during the anniversary year "50 years of the Elysée Treaty" between Germany and France, it was possible to further whittle down the choice of topics for new joint strategic projects. The focus is on cooperation in the areas of green and white biotechnology, as well as the development of joint research activities. At the same time, the choice of topics represents a continuation of discussions held during the 4th Franco-German Research Forum 2011, where key themes were agreed. An intensification of these discussions at the highest level is planned for February 2014. The workshop titled "Perspectives for industrial biotechnology and bioeconomy: paths toward biologization of key industries" will address important questions at the European level against the background of Horizon 2020.

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APPOINTMENTS AND AWARDS

Hugo Geiger Prize for Yannick Bantel 1

Yannick Bantel from the Department of Molecular Biotechnology was awarded one of last year's Hugo Geiger prizes at the the annual meeting of the Fraunhofer-Gesellschaft's General Assembly for his diploma thesis "A protein-protein interaction analysis of the transcription factor Tup1p using the extended genetic code". The thesis examines the opportunistic fungal pathogen *Candida albicans*, which is responsible for more than 10,000 deaths in Germany every year. The pathogenicity of the fungus is caused, in part, by certain proteins and their interaction mechanisms, and while many of the proteins are known, little has been known – to date – about their interactions.

Bantel used the method of the expanded genetic code for his research, inserting an unnatural amino acid into the genetic code of *Candida albicans*. In this way, it is possible to manufacture tailor-made proteins that do not occur in nature. Using this method, the young scientist was not only able to detect protein-protein interactions in living organisms, but also identified previously unknown interactions, and did so with high specificity and efficiency. His analyses form an important basis for the development of potential therapeutics and are evidence of the potential of the expanded genetic code for medical and industrial biotechnology.

Appointment of Petra Kluger at the University of Reutlingen

Dr. Petra Kluger, one of the two heads of the Fraunhofer IGB Cell and Tissue Engineering department and manager of the department's Biomaterials and Test Systems group, accepted a professorship at the Reutlingen University on November 1, 2013. She is to hold a so-called "shared professorship", which gives her the option of working in parallel at the university and at a research institute.

Dr. Kluger is taking over a series of lecture on tissue engineering on the Biomedical Sciences bachelor's course in the Faculty of Applied Chemistry in Reutlingen. The aim of this course is to produce chemical engineers with a biomedical specialization; the focus is on biomaterials and their characterization and interaction with the biological system. Besides her expert knowledge, Kluger can above all contribute her practical experience as a long-time associate lecturer at the universities of Stuttgart and Hohenheim. Last year she was awarded the VDI (Association of German Engineers) Ring of Honor particularly for her commitment to supporting young scientists in both practical and academic matters.

At the Fraunhofer IGB, Dr. Kluger focuses on the interaction of human cells with biomaterials, which is essential for medical and biological applications such as the optimization of implants or cell culture substrates. Both partners benefit from the enhanced cooperation – the university through increased access to the practical, applied Fraunhofer research, the Fraunhofer IGB from new impulses and research conducted by the students, who represent the next generation of scientists.

Susanne Bailer becomes a private lecturer ("Privatdozent") at the University of Stuttgart

After completing a higher doctoral degree in the Department of Biochemistry and Molecular Biology at the University of the Saarland, Homburg, in 1985, Susanne Bailer subsequently

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acquired permission to teach independently at professorial level at Ludwig-Maximilians-University of Munich. In 2013, she underwent the equivalent conversion process to obtain the title of private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart. On November 18, 2013 Dr. Bailer held her inaugural lecture at the University of Stuttgart on the topic "Herpes viruses – a mixed blessing?" In addition to teaching, she holds the post of group manager, both at Fraunhofer IGB (Infection Biology and Array Technologies Group, Department of Molecular Biotechnology), as well as of the research area Biological Interfacial Process Engineering at the University of Stuttgart's Institute of Interfacial Process Engineering and Plasma Technology IGVP.

Fraunhofer symposium "Network Value" – rewarding Fraunhofer IGB ideas 2 + 3

The Fraunhofer symposium "Network Value", held at the beginning of December 2013 in Munich, was well attended with 360 guests. Two candidates from the Fraunhofer IGB were invited to participate in the symposium's "ideas contest", where in each of two rounds, ten scientists presented original ideas in the form of a 90-second "elevator pitch". Due to a technical problem that arose counting the votes of the spectators, all ten proposals in the first round were awarded sponsorship of 25,000 euros – including Dr. Kai Sohn with his "genetic fingerprint" project idea. In the second round, the audience voted Philipp Grimmer and his "ice-free road surfacing" into second place, securing him funding of 25,000 euros.

Genetic fingerprinting for the diagnosis of infection

Thanks to the fact that all humans have their own individual genetic fingerprint, it is possible to trace perpetrators from the marks they leave at the crime scene. Similarly, bacterial pathogens are characterized by a genetic profile. Dr. Kai Sohn wants to exploit this analogy for the diagnosis of sepsis pathogens. Every year, more than 56,000 people in Germany die of sepsis – more commonly known as "blood poisoning" – often because the pathogens, mostly bacteria, are not identified in time and hence cannot be fought in a targeted way. His idea is that the DNA of the pathogen circulating in the blood of patients should be isolated and decrypted using the latest methods of high-throughput sequencing. Within a few hours, the doctor at the treating hospital would know which pathogens the patient is infected with and which medications are to be given – on the basis of DNA fingerprinting.

Ice-free roads

Snow and ice in the winter lead to accidents and traffic chaos. A road surfacing that could thaw ice and snow of its own accord would make the roads safer in the time it takes before a snowplow arrives for gritting. The doctorate student Philipp Grimmer came up with the idea whereby a chemical de-icing agent is incorporated in the surfacing itself, encapsulated in polymer particles. If the temperature drops below the freezing point, the particles release the thawing agent into the asphalt. The de-icing agent diffuses onto the surface of the road where it causes the ice and snow to melt. Empty particles will be replenished after discharging – by means of the de-icing agent spread by the oncoming gritters.

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PROMOTING YOUNG TALENTS – EXHIBITIONS

The Fraunhofer-Gesellschaft is keen to make early contact with the researchers of tomorrow and give them exciting insights into research opportunities. Thus the Fraunhofer IGB is active in both promoting young talents and getting young people interested in research and technology. We do this through events at the Fraunhofer campus in Stuttgart, as well as exhibits at various exhibitions.

Fraunhofer Talent School

After a year's break, the Fraunhofer Stuttgart Talent School took place again in 2013. Dr. Kai Sohn, deputy head of the Molecular Biotechnology Department, led a workshop on the topic of genetic analysis for the fourth time. The aim of the workshop, titled "CSI Stuttgart – from genetic fingerprint to identification of the perpetrator" was to create a better understanding of the fundamentals of the genetic code. For this, DNA was isolated from the participants' saliva samples and characterized molecularly. Every participant got to take home his or her personal "DNA portrait". The high-school students were very enthusiastic about the opportunity to gain insights into the way a scientist works and into fascinating research topics. Kai Sohn will hold another workshop in 2014, once again contributing to the success of the Fraunhofer Stuttgart Talent School.

Girls' Day at Fraunhofer Stuttgart campus 1 + 2

In Germany we currently have the best educated cohort of young women of all times, with girls making up more than 50 percent of high-school graduates. Despite this, girls still tend to opt disproportionately in favor of typical female jobs or courses when choosing an apprenticeship or higher studies. Girls' Day – a nationwide event initiated by the German Federal Ministry of Education and Research (BMBF) – at the Fraunhofer campus in Stuttgart gives young women an insight into the Fraunhofer Institutes and the careers available in engineering, IT and the natural sciences. The researchers open the doors to laboratories and test areas, offices and workshops, where they use practical examples to demonstrate how interesting their work is. For girls, this is a good chance to find out more about what scientists do through talking to the scientists in real life, on a one-to-one basis. 2013 saw once again 89 interested participants in Stuttgart, some of whom visited the "How to manufacture emulsions and shampoos" and "Here's looking at you, kid" information stations at the Fraunhofer IGB. The next Girls' Day will take place on March 27, 2014.

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BOGY – vocational and academic career orientation at academic high schools

18 high-school students completed their "BOGY" internships at the Fraunhofer IGB in 2013. They gained insights into the work of scientists and graduate students in different disciplines (engineers, biologists, chemists and physicists) as well as finding out about typical "recognized" (i.e. requiring formal training) vocational occupations in a research institute, such as technical assistant or laboratory technician. The students were introduced to various working groups in the respective departments and their laboratories, assisted on real projects, became acquainted with methods for identifying particular substances and helped out with the planning and performing of experiments as well as the documentation of the test results. The internship gives the youngsters a detailed picture of the work that goes on in a research institute and helps them to make better-informed career choices.

Open day for university students

In November 2013, science and engineering students from various universities and universities of applied sciences visited the Fraunhofer campus in Stuttgart. Through presentations, interviews and tours they had the chance to find out about the institutes' highly varied fields of work as well as opportunities for starting their careers at the Fraunhofer-Gesellschaft – in particular at the Stuttgart institutes. Answering the question "Why not go into industry straight away?" the participants were shown the various career paths at the Fraunhofer-Gesellschaft. Extremely positive feedback and constantly high numbers of participants, reflect the success of the event, which has taken place once a year since 2007.

Training at the Fraunhofer IGB 3

The IGB is not only dedicated to the training of young people pursuing academic studies; we are also expressly committed to enabling young people of all backgrounds to train at Fraunhofer. For over ten years we have been providing youngsters with apprenticeships in the recognized (requiring formal training) vocational occupations of office administrator, chemical lab technician and biology lab technician and since 2013 also of IT specialist for system integration. When not attending vocational training college, the apprentices have the opportunity to work alongside more experienced colleagues in the many diverse fields of activity of a research institute, and so learn the handiwork for a career in research or industry. Many of our apprentices choose to go on to study or to participate in an advanced occupational training course designed for full-time employees and sponsored by the institute.

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Ideas 2020 – A Tour of Tomorrow's World 4 + 5

What will our future look like? Where will tomorrow's energy come from? How can we stay healthy into old age? To meet the need of present and future generations for sustainable solutions to society's issues, scientists are developing visions, opening up new options through research, and accompany global change with new ideas.

"Ideas 2020 – A Tour of Tomorrow's World" is an initiative of the Helmholtz Association in cooperation with the Fraunhofer-Gesellschaft, the Leibniz Association, the Max Planck Society and other scientific institutions. The exhibition is based on an innovative, interactive concept that aims to make the fascinating complexity and diversity of today's scientific research accessible to the public. "Ideas 2020" highlights some of the major scientific research projects being carried out in Germany, in line with the aims and priorities set out in the "High-Tech Strategy for Germany", the German government's concept for national research and innovation policy.

On their "Tour of Tomorrow's World", visitors encounter seven "pillars" that stand for seven great challenges facing society today. Touching and interacting with the arresting 3D installations is encouraged, and accompanying multi-touch screens give the visitors fascinating insights into the work of scientists and allow them to ask questions about our future. The exhibition also includes photographs and film footage showing details of future-oriented Fraunhofer IGB topics and projects like the "DEUS 21" infrastructure concept for semi-decentralized urban water and wastewater management and the "EtaMax – fuel from market waste" project, as well as research on various aspects of "nature as a chemical factory". "Ideas 2020 – A Tour of Tomorrow's World" was launched in March 2013 in Berlin, and can be viewed at various locations in Germany until the end of 2014.
www.ideen2020.de/en

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SUSTAINABLE DEVELOPMENT IN DIALOG

While in 2013 we could look back at five years of the Fraunhofer Sustainability Network and 300 years of "Sylvicultura oeconomica" by Hans Carl von Carlowitz, the founder of the idea of sustainability, the focus at the Fraunhofer IGB is firmly on the future and how we can make it sustainable. Last year's activities of the cross-institutional Sustainability Working Group (based at the Fraunhofer Campus in Stuttgart) were concerned with cross-linking research into sustainability; the Fraunhofer IGB also contributed ideas for responsible development of the Fraunhofer Institutes within the framework of the "Sustainability Reporting Guidelines" project, which will make a wide-ranging platform of experience and knowledge on the subject available to all Fraunhofer Institutes.

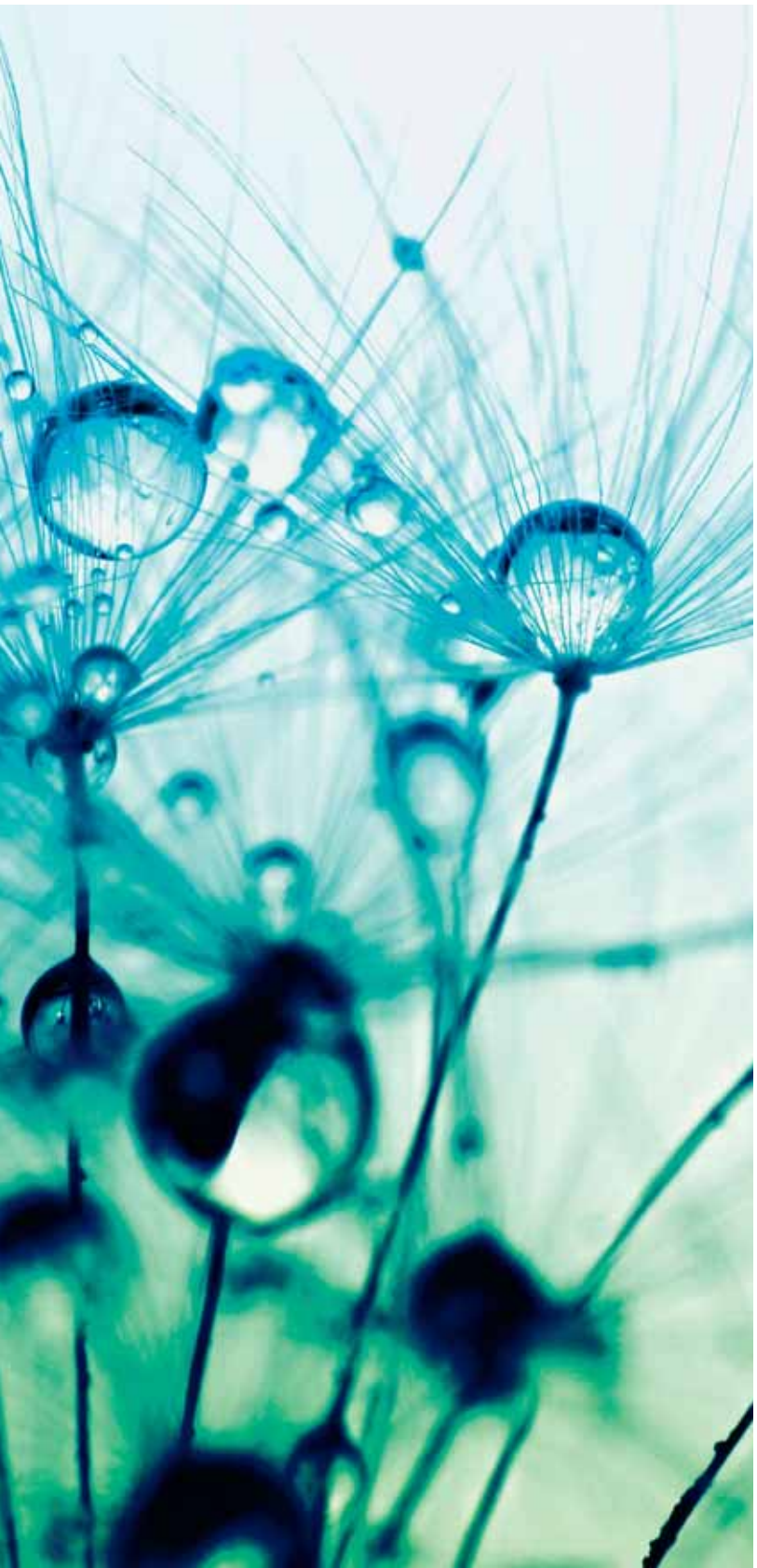
"IZS – one campus – countless ideas" 1

Following the first Sustainability Action Day in the previous year, the Sustainability Action Week in June 2013 offered the opportunity for scientific exchange as well as for information and discussion on all aspects of sustainability. All the scientific staff at the Stuttgart Institute Center (IZS) were invited to take part in a research "bourse" or "exchange", which constituted the prelude to a campus-wide project competition. The participants had the opportunity to present project ideas, discover synergies and find cooperation partners. The ideas presented ranged from a smartphone app for conservation-conscious angling to a location concept for a science and discovery center for young researchers.

Besides regional dishes in the "piccante" company cafeteria, the Action Week offered presentations on sustainability management at the Fraunhofer-Gesellschaft as well as on integrating phone- and video-conferencing into one's everyday work, which were followed with interest by the listeners. The presentations formed part of the Sustainability Working Group's ongoing information drive consisting of leaflets distributed center-wide and events intended to encourage all employees to act in a resource-conscious manner.

The research exchange workshop was followed by a competition, lasting until the fall, for funding of 30,000 euros made available by the five Stuttgart-based Fraunhofer Institutes. Project teams drawn from at least two institutes elaborated ideas for sustainable development projects and presented these at the second workshop. In the end, the jury made up of institute directors and representatives of the Sustainability Working Group selected three projects to receive initial funding, two with Fraunhofer IGB participation:

- "Software tool for building responsibles for the environmental and economically optimized renovation of built-up urban districts" (IAO, IBP),
- "Substantial recycling of carbon dioxide in algae production" (IBP, IGB),
- "Development of a concept for a center for future issues, including an academy for sustainability technologies, in the metropolitan region of Stuttgart" (all five institutes).



Learning from best practices

During the "Sustainability Reporting Guidelines" project, the second sustainability project funded by the Fraunhofer Executive Board, the Fraunhofer IGB engaged in intensive dialog with the other institutes in the Sustainability Network. The project delivered not only a printed guide, but also an intranet-based platform for sustainability reporting. "iLENA" contains interesting and pertinent information on sustainability topics at Fraunhofer, and can be accessed by all Fraunhofer employees. It makes a wealth of experience gained through the networking activities available in order to support the Fraunhofer Institutes with developing their own sustainability management systems, writing a sustainability report or initially simply implementing effective measures in their daily operations.

"iLENA" contains a description of the international Global Reporting Initiative standard for the preparation of sustainability reports as adapted to the Fraunhofer context; the platform also includes a large collection of best-practice examples of the manifold aspects of responsible corporate leadership, which are intended to inspire emulation. The Fraunhofer IGB has already contributed numerous examples, such as offering in-house German courses for foreign employees or its utilization concept for the dismantling phase of the old demonstration center building.

The project also included developing a modular training concept aimed at making the experiences of sustainability reporting actively available to other institutes. Fraunhofer IGB scientists were involved both in the development of the concept and in the test training courses. Both course content and project experiences are now being incorporated into the Institute Center's second site-wide sustainability report.

Dialog with stakeholders

How can we utilize biomass sustainably now and in the future and what contribution can research make to this? These were some of the questions asked at the first Fraunhofer Research Dialog, a series of events started in November 2013 in the spirit of getting our stakeholders involved in the development of the Fraunhofer-Gesellschaft. Representatives from science, politics, industry and society discussed this key Fraunhofer IGB research topic as well as further subjects.

A guide for research organizations

With its varied activities relating to sustainable development, the Fraunhofer-Gesellschaft has assumed a vanguard role in the German research landscape. Therefore Fraunhofer has been tasked by the Federal Ministry of Education and Research (BMBF) to initiate a joint research project with other major non-university research institutions (Helmholtz Association and the Leibniz Association), based on its own experience. The project was launched in December 2013, with the participation of the Fraunhofer IGB. The scientific objective is to develop an approach that serves all facilities, centers and institutes as a guide to research-specific sustainability management.

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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 67 institutes and research units. The majority of the more than 23,000 staff are qualified scientists and engineers, who work with an annual research budget of 2 billion euros. Of this sum, more than 1.7 billion euros is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and *Länder* 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.

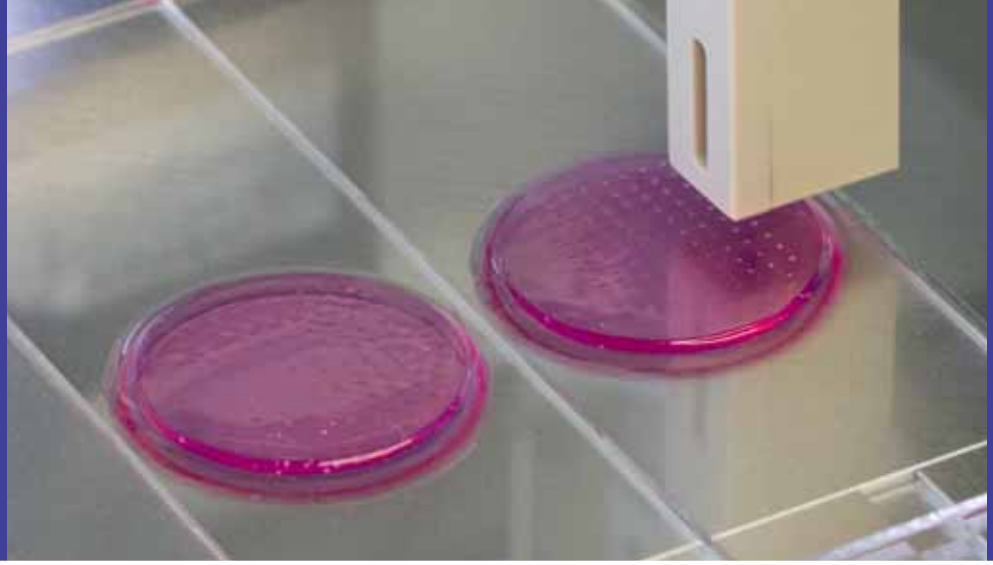
With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits 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.

www.fraunhofer.de

1 *Joseph von Fraunhofer (center) (1787 – 1826).*



INTERFACIAL ENGINEERING AND MATERIALS SCIENCE

Interfaces play a key role in many technical areas such as the automotive sector, technical textiles and in medical technology. For many surfaces, properties are required that are very different from those intrinsic to the bulk of the material concerned. Besides these material surfaces, inner interfaces in composite materials are becoming increasingly important. Examples are membranes used in separation technology as well as materials for energy conversion, such as separators in fuel cells or thin films in photovoltaics. Another instance of the growing significance of interfaces is as barriers in packaging materials.

Finally, in response to the growing complexity of demand, we combine various technical processes under the aspects of material and energy efficiency. With regard to technical realization, we have established a large variety of methods which involve either films being deposited from the gas phase or the precipitation of thin films or particles from the liquid phase.

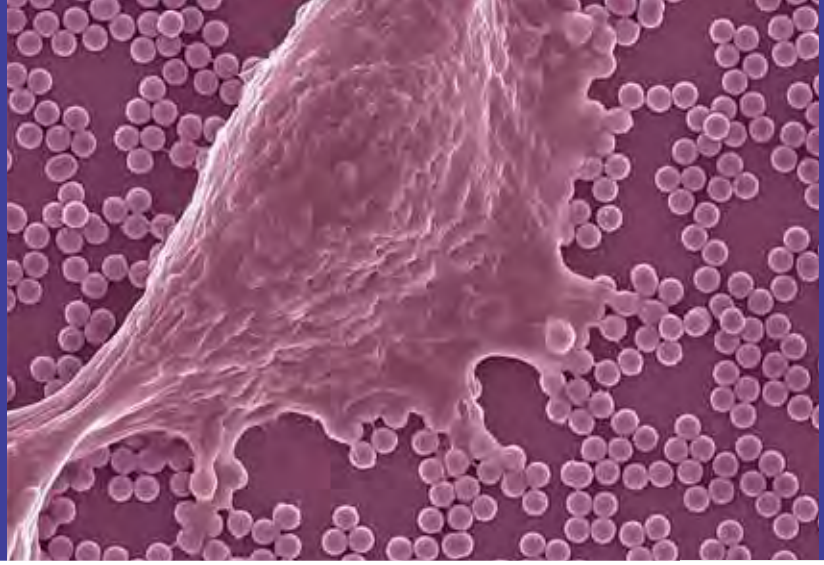
Established preparation methods

- Deposition of thin films by chemical and physical means, i.e. chemical or physical vapor deposition
- Deposition of nanoparticles using various polymerization methods
- Production of separation membranes by sol-gel processes and consecutive annealing
- Deposition of thin layers by layer-by-layer (LbL) techniques as well as by self-assembly monolayers (SAM)
- Deposition of thin films via spin-coating
- Generation of nanofibers by electrospinning

To achieve reliable processes, all steps of the process development have to be controlled. In addition, the products have to be characterized in detail. For this purpose a multitude of analytical tools is available and can partly also be used for in situ monitoring of processes (process diagnostics). Due to the fact that the majority of our products are characterized by nanometer dimensions (ultra-thin films and nanoparticles), we use several methods to deliver information which is space-resolved on the nanometer scale. Application-relevant properties such as the separation and permeation properties of films (membranes, barriers and corrosion protection) as well as the specific separation capabilities of molecularly imprinted nanoparticles or the dispersibility of modified carbon nanotubes and graphene are examined in customized experimental set-ups.

Established characterization and diagnostic processes

- Determination of interfacial energy with different types of tensiometers
- Logging of the topography and geometric patterning of surfaces on the nanometer scale using a variety of AFM probe modes as well as scanning electron microscopy
- Determination of adsorption properties either by means of microcaloric measurements at the liquid phase (measurement of adsorption enthalpy) or by means of gas adsorption with simultaneous measurements of specific surface area (BET)
- Determination of film thicknesses using ellipsometry or microscopic techniques
- Qualitative and quantitative estimation of the chemical functions at surfaces and in thin films using IR spectroscopy in ATR mode, IR microscopy, confocal Raman and fluorescence spectroscopy as well as MALDI-TOF-MS



(matrix-assisted laser desorption-ionization time-of-flight mass spectroscopy)
- Determination of elemental composition, using electron spectroscopy for chemical analysis (ESCA) and energy dispersive X-Ray analysis (EDX)
- Quantitative estimation of chemical radicals via electron spin resonance spectroscopy
- Plasma process diagnostics: probe measurements, optical and mass spectrometric methods

Apart from the quality of the products, the material and energy efficiency of processes is of foremost concern. One way of tackling this is to miniaturize entire functional units which are manufactured as a combination of several thin films. The internal structure and the chemical composition of these layers are significant for the role of the films in modulating the transport of materials (membranes), of electrons (conductors and semi-conductors) or photons (fiber optics). This also opens up applications for thin-film components in photovoltaics, in batteries and in organic electronics. The challenge and objective of our process engineering development work is to find the best ways of combining thin films using a variety of specialized techniques.

Thanks to our combination of preparation methods and analytical tools, we are well prepared to successfully handle the development challenges of our clients across the Fraunhofer IGB portfolio – whether in the medicine, pharmacy, chemistry, the environment or energy business area.

Range of services

- Development of processes for the plasma modification of surfaces
- Thin films as protective layers (scratch and corrosion protection), barriers against permeation, and for use as reservoirs for the targeted release of substances (formulations)
- Functionalization of surfaces (chemical and biochemical)
- Development and evaluation of plasma-cleaning and plasma-sterilization processes

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- Development of inks by using biomaterials to create biocompatible or bioactive printed structures
- Synthesis and preparation of nanostructured materials with tailored surfaces
- Novel formulations using core-shell particles
- Characterization of nanoparticles, measurement of the particle sizes and particle size distribution by optical methods or in an electrical field
- Development of membranes and membrane modules
- Manufacturing and testing of membranes in pilot scale
- Surface and layer characterization
- Development of methods and plants
- Scaling up of laboratory processes to produce thin films on large format surfaces and scaling of nanoparticle production for greater volumes

Infrastructure and technical equipment

- Plasma reactors for cleaning, sterilization, coating and functionalization
- Equipment for sputtering and parylene coating
- Electron (SEM) and probe (AFM) microscopes
- Equipment for the analysis of surfaces and thin films
- Chemical-nanotechnical laboratories for the synthesis and preparation of nanostructured (bio)materials and surfaces
- Pilot plants for the manufacturing and testing of membranes

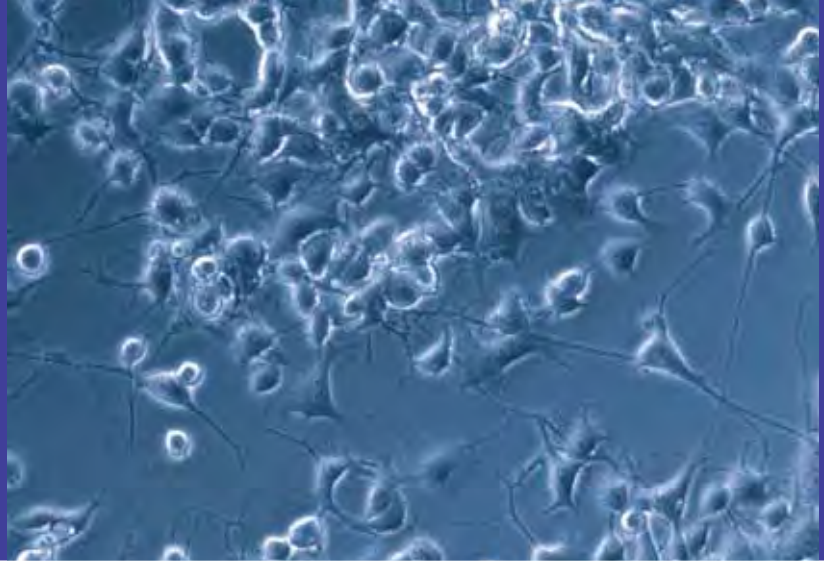
MOLECULAR BIOTECHNOLOGY

The Molecular Biotechnology Department focuses on work in the fields of pharmaceutical biotechnology, diagnostics and chemistry. Thus, for instance, we use our know-how for the functional genome analysis of pathogens (infection biology) in order to develop new approaches for the screening of anti-infectives. We develop new diagnostic methods based on nucleic acid technologies (diagnostic microarrays and next generation sequencing based diagnostics) or by means of cell-based assays, e.g. for a cell-based pyrogen assay. A further focus is the development of production strains or cell lines for industrial and pharmaceutical biotechnology. In the past, we have developed production processes for pharmaceutical proteins such as interferons and factor VII as well as for chemical products such as biosurfactants and dicarboxylic acids. Our work extends from the metabolic engineering of production strains to the development of integrated bioprocesses for effective downstream processing. In addition to microorganisms, we also focus on enzymes as a key to render sustainable raw materials available for biotechnological processes as well as for the enzymatic synthesis of chemicals (e.g. epoxides from fatty acids).

The core competences of the department lie in the application of molecular-biological and biotechnological methods for genomics, transcriptomics and proteomics. A further asset is our accredited analytics, which can also be used for metabolome analyses. Metabolic engineering for strain development, integrated in a bioprocess and focused on simplified product purification, is a central competence for both microbial production processes and for the production of pharmaceutical proteins from mammalian cell lines. In infection biology, the combination of methods of functional genome analysis with our expertise in cell culture technology and biology of pathogens gives us a unique selling point in the development of infection models and diagnostics.

Our goal is to use nature's toolbox to create biotechnological value chains and to develop new diagnostics and therapeutics. The new technologies in genome and proteome analysis, for example, allow comprehensive analysis of entire microbial communities or of the interaction between microorganisms and the human individual in the shortest of times. This enables the identification of the impact of microbiota on human health – both via host-pathogen interactions and in synergistic form (probiotics). The malignant transformation of the body's normal cells can also be investigated. Using this information, measures for specific treatments for individual groups of the population can be applied. Thus personalized medicine may become reality. In industrial biotechnology, too, the quick availability of genomes and the analysis of cellular circuits make it possible to identify and optimize new metabolic pathways, which can then be ideally exploited for the production of chemicals or proteins.

Using these competences, the Molecular Biotechnology Department in cooperation with other departments of the Fraunhofer IGB, is active in the business areas of medicine, pharmacy and chemistry. In the field of biocatalysis we work closely with the BioCat Project Group based in Straubing, while we collaborate with the project group at the Fraunhofer CBP in Leuna to develop our laboratory-scale bioprocesses up to 10 m^3 scale. We also cooperate with the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM on developing processes for manufacturing pharmaceutical proteins, up to GMP-compliant production of biologicals for clinical phases of pharmaceutical development.



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Range of services

- Screening of targets and active compounds for anti-infectives (2D and LC proteomics, DNA microarrays, parallel sequencing, infection models, screening assays)
- Gene expression analyses and genome sequencing for customers
- Next-generation sequencing of genomes and transcriptomes
- Development of DNA microarrays: design of probes, production of PCR fragments, contact printing, and hybridization
- Cell-based assays: antiviral assays (GLP), pyrogen detection, mutagenicity, toxicity
- Development of production cell lines and processes for recombinant production of proteins (biosimilars), protein purification and characterization
- Development of high-throughput enzyme assays and screening
- Strain and parameter screening in multi-fermenter systems
- Development of integrated fermentation processes for industrial biotechnology with a focus on downstream processing of raw materials and products
- Chemical-physical and biochemical analysis

Infrastructure and technical equipment

- Molecular-biological laboratories conforming to safety levels L2, S1 and S2 of the German GenTSV (genetic engineering safety regulations)
- Microarray facility, universal microarray platform
- Quantitative real time PCR (qRT-PCR LightCycler 480)
- Next generation sequencing facility (Illumina HiSeq2000, Roche GS Junior)
- Proteomics facility using high-resolution MS techniques (2D gel electrophoresis, nano-LC-MALDI-TOF/TOF, HPLC-ESI-MS/MS)
- Fermentation plant for suspension and adherent mammalian cell culture up to 10 liters (non-GMP)
- Protein purification equipment
- Pulping machines (ball mills, etc.), multi-fermentation bioreactors for bioprocess development, and small bioreactors (up to 30 liters) S2
- Picking robot for the systematic storage of DNA- and microbial libraries
- Accredited analytical lab: GC-MS/MS, LC-MS/MS, GPC, IC, ICP-AES and ICP-MS

PHYSICAL PROCESS TECHNOLOGY

The Physical Process Technology Department is involved in developing processes and process components based on physical and physical-chemical principles. Our customers are manufacturers of process components, contractors and process system suppliers, and come from sectors such as pulp and paper, metal processing, the food industry and the supply of drinking water.

Current main themes

- Heat storage using thermo-chemical processes
- Use of sorption systems to remove moisture from gases, in particular from air to provide water
- Drying in a superheated steam atmosphere with integrated recovery of volatile materials
- Recovery of inorganic nutrients
- Production of soil-improving substrates from organic residuals
- Electrolytic and photolytic water treatment
- Stabilization of foods and biogenic products using pressure change technology
- Use of electric fields for selective substance separation
- Microwave technology for defined and fast energy charge

Apart from our technical competence and specialized expertise, a hallmark of the quality of our R&D activities is our focus on sustainability. Thus, for example, we replace flows of raw materials by recycling, upgrading or overhauling processes for the efficient use of regenerative energy and find ways to improve the efficiency of energy use. This also leads to improved economic efficiency of processes, meaning that our approach satisfies both ecological and economic demands at the same time. One example of this is the development of a process to store heat from waste heat or solar heat without losses during the time of storage. The intention is to be able to provide heat energy for industrial use at any time and, thanks to the high energy density, at any location; thus the supply is not directly linked to when and where the energy has been generated. Potential applications are drying processes in production, supplying heat to buildings, or the concentration or thickening of highly contaminated process wastewater with vacuum vaporization.

Our development work on processes and process components extends from initial laboratory-scale characterization and analytics via simulation and software modeling to design and system integration in industrial applications. For developing and designing our technical solutions, we have access to the latest 3D CAD design software, which is directly linked by data interface to various numerical simulation programs. For standard modeling we use COMSOL Multiphysics® like the theoretical modeling of multi-phase processes such as the behavior of solid particles in a fluid flow; and CST Microwave Studio® for the calculation of high frequency electromagnetic fields in cavities and the design of antennas to generate them in a defined way. From the data thus gained we can proceed to realize demonstration prototypes using the many resources at our disposal – workshops, laboratories and pilot plant facilities, as well as a network of industrial partners.

The Physical Process Technology Department is staffed by scientists from various disciplines – such as process engineering, chemical engineering, food chemistry, mechanical and electrical engineering – who work together in multi-disciplinary project teams. Projects may also involve collaboration with specialists from other Fraunhofer IGB departments, such as microbiologists and bioengineers, or from other Fraunhofer Institutes, leveraging synergies in expertise to address specific issues.

Range of services

- Process development carried out by an interdisciplinary team drawn from the areas of process, mechanical and chemical engineering
- Design and operational specifications including characterization of automation algorithms, to enable industrial prototypes
- Feasibility studies and preliminary investigations in laboratory and pilot-plant scale

Infrastructure and technical equipment

- Laboratory systems for investigating the treatment options for industrial process water e.g. like floculation and oxidation properties
- Pilot plants for advanced oxidation processes (AOP) such as electro-physical precipitation, ozone, hydrogen peroxide, photolysis by UV radiation, ultrasound, anodal oxidation (direct or indirect), and cathode reactions
- Mobile pilot plants for on-site feasibility investigations and demonstrations, for example for drying with superheated steam or for water treatment
- Design and simulation software (SolidWorks, CST Microwave Studio®, COMSOL MultiPhysics®, Design-Expert Workstation)

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ENVIRONMENTAL BIOTECHNOLOGY AND BIOPROCESS ENGINEERING

The activities of the Environmental Biotechnology and Bioprocess Engineering Department are focused on the development of processes to convert organic raw materials, residuals and waste products into bulk chemicals, valuable compounds and sources of energy. These processes are often coupled with the recovery of inorganic substances for reuse as fertilizers and the treatment of the water arising from bioconversion, where it serves as a solvent. We generally use anaerobic methods to treat organic residuals such as biodegradable waste or sewage sludge, as these allow commercially viable generation of biogas as a regenerative source of energy. The use of specific anaerobic microorganisms also enables new approaches in communal and industrial wastewater purification, as well as the realization of innovative semi-decentralized prototype wastewater treatment plants. The retention or immobilization of biocatalysts plays a key role here, and we leverage our expertise in this area extensively – both in researching biological surface reactions (biocorrosion, biofilm formation, biomineralization, biofouling, biosensors, and bioleaching) and in the testing of antimicrobial technical equipment. An additional – aquatic – source of raw material we use is microalgae. Natural and sustainable, algae provide a large number of basic chemical materials and an easily digestible biomass.

The core competence of the department is developing robust biotechnological processes for the production of basic chemicals, which may either be used as raw materials or as sources of energy (methane, ethanol and methanol). In this context "robust" means processes that are resistant to contamination and thus can be operated continuously under aseptic (non-sterile) conditions. Processes are designed exclusively on the basis of microbiological parameters, such as the growth and degradation kinetics of the different organisms concerned. Our engineering activities extend from the planning, commissioning and optimization of laboratory and pilot plants to the planning, construction, commissioning and optimization of innovative demonstration plants in cooperation with our industrial partners. Intelligent combination of the unit operations of mechanical and chemical process engineering (including downstream processing) with bioprocesses using modeling and simulation methods gives us a unique selling proposition, as does our expertise in the targeted colonization and depletion of microorganisms on surfaces.

- Both classic and "continuous" high-throughput screening methods for autochthonic production strains as high potentials for robust processes or new product lines
- Fermentation processes, including those involving partial or total cell retention
- Cultivation of microalgae in photobioreactors
- Microbiological characterization of surfaces using standard processes and application-oriented processes, including development of test procedures
- Psychrophilic, mesophilic, and thermophilic bioprocesses
- Development of real-time processes for monitoring water systems for contamination
- Modeling of processes and simulation of process lines
- Scale-up of processes and scale-down of unstable process states to solve problems during technical operation
- Downstream processing technologies such as membrane-based filtration processes, liquid-liquid extraction, and extraction with supercritical media
- Integrated models for management of energy, waste and water

The use of anaerobic biocatalysts to produce bulk chemicals or energy carriers has the advantage of a 90 percent carbon-source-to-product yield. The use of rapidly growing photoautotrophic cells (microalgae) also leads to comparatively higher productivities than is achievable with terrestrial plants. Further benefits are reduced water requirements and the feasibility of water-based production of algae.

The Environmental Biotechnology and Bioprocess Engineering Department is thus in a position to take part in solving socio-political challenges such as the greenhouse effect, energy supply and freshwater shortage. By offering sustainable technology options, the department can help industry, communities and policymakers design a balanced future. Combining our competences with those of other Fraunhofer IGB departments, we serve the needs of the chemical, energy and environmental business areas.

Range of services

- Wastewater and water purification methods
- Biotechnological purification processes and hybrid processes for industrial wastewater
- Development of utilization concepts for both inorganic and organic residual materials
- Development of regional-level system concepts for energy and water management
- Digestion processes to produce biogas from a range of organic substrates
- Development of photoautotrophic processes for microalgae and cyanobacteria in flat-panel airlift (FPA) reactors
- Biotransformation of renewable raw materials and industrial waste materials into basic chemicals
- Development of processes for the isolation, separation and purification of biotechnically manufactured products
- Analysis of microbial contamination on surfaces and in processing media
- Aerobic and anaerobic degradation tests
- Fermentation tests according to the Association of German Engineers guideline VDI 4630
- Bioleaching, biosorption and bioprecipitation to obtain metals from different process waters and waste streams, using various reactor configurations

Infrastructure and technical equipment

- Pilot plant for environmental and bioprocess engineering applications
- Bioreactors of various sizes (laboratory, pilot and technical scale)
- Analytics for substrates and fermentation products, protein analytics
- Mobile membrane bioreactors for wastewater treatment
- Mobile pilot plants in m^3-scale to generate basic engineering data in situ for the planning of innovative demonstration plants
- Demonstration sites Knittlingen (DEUS 21); Stuttgart-Gaisburg (bioenergy); Reutlingen and Fraunhofer IGB (cultivation of algae); Franca, SP, Brazil (bioenergy)
- Photobioreactors of various sizes for lab, outdoor and greenhouse applications
- Test facilities for different membrane processes (e.g. rotating disk filtration)
- Official approvals for handling pathogenic organisms
- Apparatuses for testing antimicrobially finished materials
- Test facilities for cell disruption and extraction with supercritical fluids
- GIS applications using the ESRI ARC-INFO software; process simulation and automation (MATLAB, Siemens programming)

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CELL AND TISSUE ENGINEERING

The focus of the Cell and Tissue Engineering Department is the development of functional in vitro 3D tissue models from isolated primary human cells under GLP (Good Laboratory Practice) or GMP (Good Manufacturing Practice) guidelines for applications in regenerative medicine, tissue engineering, medical device development and cell-based assays for toxicology. We develop biomaterials and biofunctionalized micro- or nano-structured material surfaces for the isolation of pure cell cultures from human tissues, particularly adult stem cells. The physiological culture of 3D tissue models is achieved with specially developed PC-controlled bioreactor systems which mimic the biomechanical environment of a specific organ or tissue. The sterility and quality control for cell-based transplants is a complex process, which typically requires multiple transplants for testing. Therefore, we have established non-invasive test methods, Raman spectroscopy and multi-photon microscopy, for the pre-implantation analysis of tissue engineered constructs, which drastically reduces production and quality assurance cost, while increasing the safety of the transplanted constructs.

We have developed a two-layer 3D human skin equivalent that has been patented (EP 1 290 145B1) and certified for medical devices biocompatibility tests (DIN ISO 10993-5). The skin model can be extended to include cell types, such as melanocytes or tumor cells. Furthermore, the skin model is a cost-effective human-based preanimal test system for penetration and distribution tests of chemicals under EU REACH regulations. Further questions in regard to cell differentiation and death, as well as tumor development and metastasis, can be studied with our model. Recently, vascular structures have been integrated into the skin model and the automated production of the avascular skin model could be achieved.

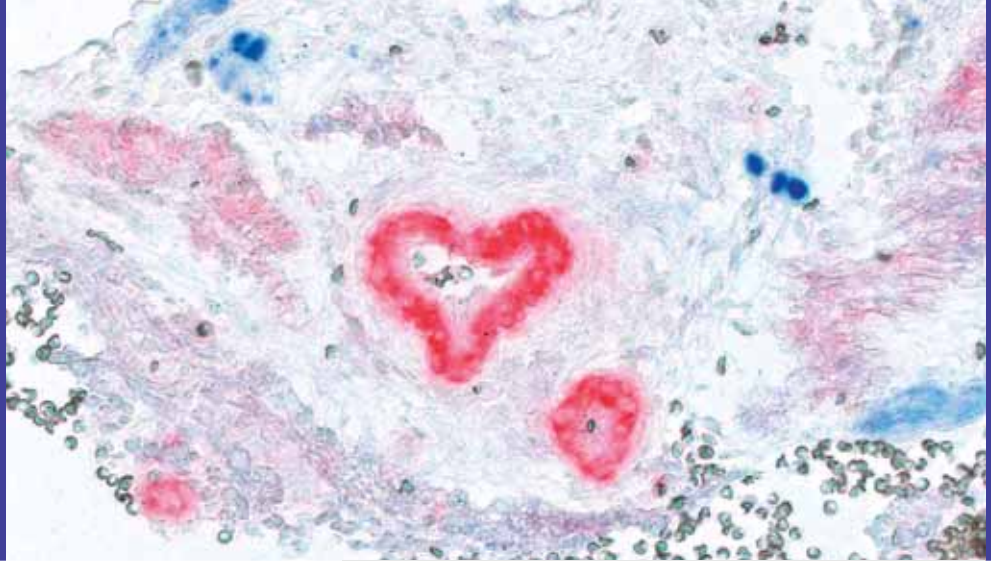
Another main focus is the further characterization of our 3D intestinal test system and the development of new intestinal disease models. Our accredited 2D intestinal test system with integrated colon carcinoma cells (Caco-2) is used for transport studies to validate the permeability of potential drug candidates and other compounds.

Additionally, we are developing methods for the creation of cardiovascular implants, regenerative therapies and 3D test systems. Due to the lack of regenerative potential in the adult cardiovascular system, we primarily work with human embryonic and induced-pluripotent stem cells, as well as complex bioreactor systems.

Competencies

- Isolation and culture of primary cells from different tissues and species in accordance with current GLP or GMP regulations
  - Biomaterial using tissue-specific extracellular matrix proteins
  - Micro- or nano-structured material surfaces
  - Skin and skin tumors, as well as intestinal and cardiovascular tissues
- Method development for constructing 3D organotypic cell cultures for in vitro test models or tissue reconstruction
  - Biological and biologic matrices
  - Tissue-specific, computer-driven bioreactors
- Establishing methods for the non-destructive characterization of cells and tissues by means of Raman spectroscopy and multiphoton microscopy

ADMET (absorption, distribution, metabolism, excretion and toxicity) are pharmacokinetic and toxicological properties that must be tested during drug development. Using our test



systems, we are able to test these properties in a more human situation than animal experiments, with the hope to eventually replace animal tests, as required by the 3R's initiative (replacement, refinement, and reduction).

Another goal is the use of our complex tissues as transplants in regenerative medicine. In our GMP manufacturing unit, we offer process development and manufacturing of autologous transplants (Advanced Therapy Medicinal Products, ATMPs) as investigational medicinal products (IMPs). The first step involves establishing and verifying the specific manufacturing process for a particular ATMP, which is then adapted to regulatory demands. The final step is applying for the manufacturing authorization for investigational medicinal products. At present, we possess manufacturing authorization for an autologous cartilage transplant.

Range of services

- Cell culture technology of primary human cells and specific cell culture media
  - In vitro testing of biocompatibility according to DIN ISO 10993-5
- Cell biology analysis
  - Molecular-biological, histological and immunohistological methods
  - Flow cytometry (FACS)
  - Modern digital image processing techniques such as microdissection
  - Raman spectroscopy and multiphoton microscopy
- Establishing of various 3D tissue models
  - Accredited for REACH testing
  - Alternatives to animal testing in cosmetics R&D
  - ADMET testing in substance and drug screening
  - Target screening for new therapeutics and infection biology
- Development of specific computer-controlled bioreactor systems for the culture of 3D tissue models
- Process development, manufacturing and testing of cell and gene therapeutics as investigational medicinal products or ATMPs (phase I/II clinical studies)

Infrastructure and technical equipment

- Cell culture laboratories conforming to safety levels S1 and S2 of the German GenTSV (genetic engineering safety regulations)
- State-of-the-art equipment such as an inverse fluorescence microscope, a multiphoton microscope system, a Raman spectroscope, FACS and PALM microdissection instrumentation
- GMP production unit (cleanrooms, separate quality control area, storage facilities)

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FRAUNHOFER CENTER FOR CHEMICAL-BIOTECHNOLOGICAL PROCESSES CBP

The Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, central Germany, closes the gap between the lab and industrial implementation. By making infrastructure and plants (pilot scale and miniplants) available, the center makes it possible for cooperation partners from research and industry to develop and scale up biotechnological and chemical processes for the utilization of renewable raw materials right up to industrial scale.

The Fraunhofer CBP building, that houses several plants, labs, offices and storage facilities on over 2000 square meters, was completed in September 2012 and inaugurated on October 2, 2012 in the presence of the German Chancellor Angela Merkel. The Center represents a hitherto unique platform for developing new processes up to commercially relevant scale, with a direct link to the chemical industry on the one hand, and to Fraunhofer research on the other.

Joint projects involve partners from industry, academia and non-university research establishments, and currently focus on the following specializations:

- Obtaining high quality extractives from biogenic raw and residual materials
- Pulping of lignocellulose, separation and use of its components to make further products
- Development of processes to obtain new technical enzymes
- Manufacturing of biobased alcohols, acids and olefins using fermentation and chemical processes
- Functionalization of vegetable oils, e.g. biotechnological epoxidation and ω-functionalization

The core focus of the Fraunhofer CBP's activities is the sustainability of processes along the entire value chain involved in generating products based on renewable raw materials. The goal is to achieve integrated, cascading material and energetic utilization of ideally the entire components of any given plant biomass, using the biorefinery concept.

Process development thus concentrates on the following aspects:

- Exploiting the carbon synthesis potential provided by nature
- The energy and resource efficiency of the processes developed
- Minimizing waste streams
- Reducing CO_2 emissions
- Utilizing plants that are not suited as either human food or animal feed
- Integration of the processes developed into existing systems, for example to obtain biogas from residual biomass

Small and medium-sized enterprises frequently do not have the resources of their own to realize the transfer of these new technologies from the laboratory to industrially relevant orders of magnitude. The center's pilot scale and miniplant facilities offer these customers an excellent platform for process development.

Range of services

The Fraunhofer CBP provides modular process capacities of up to 10 m^3 fermentation volume and continuous plants capable of high-pressure processing up to 20 kg per hour, plus a wide range of processing, treatment and reconditioning techniques and methods. This versatile "flexible biorefinery" facilitates the conversion of raw materials such as vegetable oils, cellulose, lignocellulose, starch and sugar into chemical products.

Infrastructure and technical equipment

- Pulping and component separation of lignocellulose using organic solvents, with a capacity of 1 metric ton of biomass per week
- Fermentation capacities of 10/100/1000 and 10,000 liters, equipment for downstream processing of fermentation products
- Reactors for enzymatic processes up to 1000 liters
- Various process units for chemical reactions (continuous up to 20 kg/h or batch up to 100 liters at temperatures up to 500°C and pressures up to 300 bar)
- Mechanical and thermal separation processes (including high-temperature rectification up to 350°C at reduced pressures and extraction with l-propane and sc-CO_2)

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FRAUNHOFER BIOCAT PROJECT GROUP

The BioCat Project Group develops catalytic processes and new renewables-based products to enable a sustainable future supply of raw materials and energy to industry and society. The focus is on the development of new chemical catalysts and biocatalysts and their application in technical processes. We work with the entire spectrum of catalysis – comprising heterogeneous and homogeneous chemical catalysis, enzymatic and whole cell catalysis, and the combination of these – which we use to synthesize new products from substrates such as biomass, CO_2 and waste streams. These new products include, for example, epoxides and monomers from terpenes, which are obtained from plants and residual materials in wood processing. Further examples are monomers derived from lignin for use in conductive polymers, functionalized carboxylic acids and biobased surfactants derived from sugars, plant oils and fatty acids. Additionally, the project group develops processes to convert excess electrical energy into fuel through the capture and conversion of CO_2. These products and their production processes are made available to companies for the production of bulk and fine chemicals. Alternatively, they can be used to store energy in chemical carriers such as long chain hydrocarbons, and therefore contribute to the success of the energy turnaround. The group's goal is the best possible utilization of resources along the entire value chain from raw material to biobased end product.

It is vital that society turns its efforts today – and no later – to developing the next generation of catalysts and processes that will allow the international community to replace crude oil with biomass, residues and waste material as well as CO_2 as key sources of raw materials. BioCat aims to accelerate and play a major role in shaping this trend in "sustainable chemistry". Its approach is concentrated on developing novel chemocatalytic and biocatalytic processes for the material utilization of renewable raw materials, focusing on identifying ways of combining chemical and biotechnological methods to optimally exploit the diversity of plant biomass and leverage the advantages of combined chemocatalysis and biocatalysis.

Besides wide-ranging expertise in biotechnology (enzyme technology, fermentation, screening of biocatalysts) and chemistry (organic synthesis, analytics, homogeneous and heterogeneous catalysis), the BioCat Project Group, which is composed of biotechnologists, molecular biologists and chemists specialized in catalysis and synthesis, can offer in-depth knowledge in the field of biogenic raw materials and natural materials. By pooling these interdisciplinary specializations, we are able not only to provide scientific and technical consulting services, but, in particular, to carry out developmental work hand in hand with future customers in the following areas: new catalysts, as well as the optimization of existing catalysts and processes, new materials, and new reactions. For this work we use a broad range of analytical methods, including GC-MS, LC-MS, NMR and electroanalysis.

Research combining biocatalysis and chemical catalysis is carried out in close cooperation with the TU München, the departments of the Fraunhofer IGB, with the Fraunhofer ICT in Pfinztal and the Fraunhofer UMSICHT institute's branch in Sulzbach-Rosenberg. Collaborative projects offer an opportunity to address the conversion of renewables and the use of hydrocarbons to store electrical energy.

Range of services

- Screening of biocatalysts and chemical catalysts
- Optimization of enzymes and enzyme reactions by enzyme engineering and immobilization
- Custom synthesis of fine chemicals
- Design of processes for utilizing waste material
- Design of processes for integrating renewable raw materials into existing processes
- Carrying out of studies in the field of renewable resources
- High-resolution NMR spectroscopy (400 MHz) in solution for determining molecular structure, reaction kinetics, deep temperature analytics and developing techniques
- Electroanalytics (e.g. cyclic voltammetry, chronoamperometry, electrochemical impedance spectroscopy)

Infrastructure and technical equipment

- Autoclave unit with several laboratory-scale parallel reactors (material: Hastelloy C22; volume: 100 ml/reactor; pressure: up to 300 bar; temperature: up to 400°C)
- Various bioreactors up to 40 liters
- Automation platform for high throughput applications
- Electrochemical equipment
- Analytics: GC-MS, LC-MS, HPLC and FT-IR with online probe
- 400 MHz NMR spectrometer

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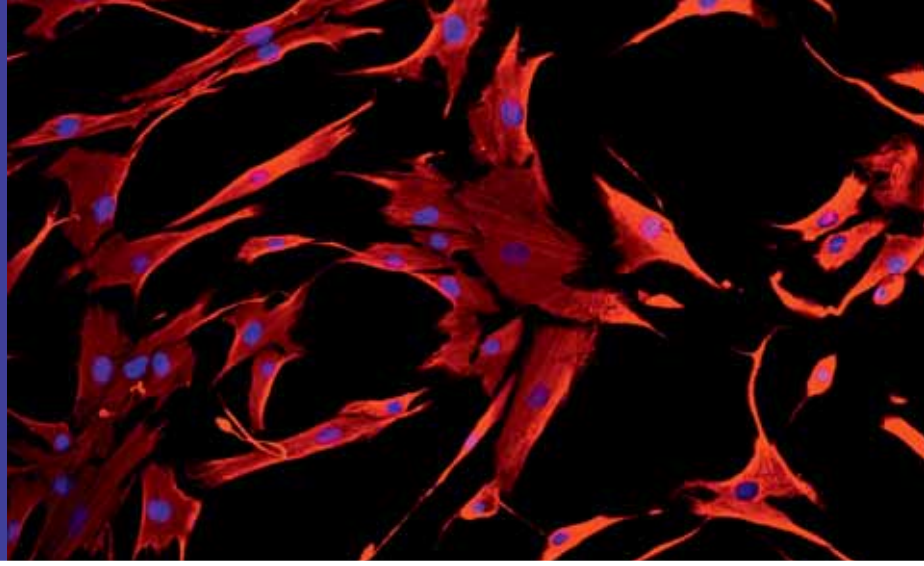


FRAUNHOFER PROJECT GROUP "REGENERATIVE TECHNOLOGIES IN ONCOLOGY"

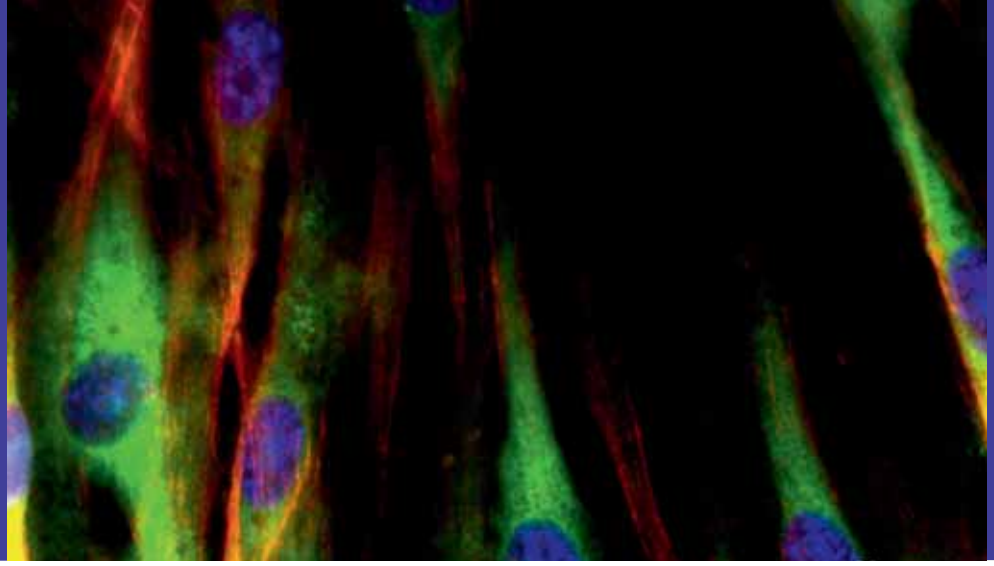
The project group "Regenerative Technologies in Oncology" performs in close collaboration with the Institute for Tissue Engineering and Regenerative Medicine at the University Hospital Würzburg methods and procedures to develop therapeutics for cancer. These therapeutics are placed along the value chain in an interdisciplinary and international team – as a Würzburg Fraunhofer interface between health research and medicine engineering – applying human vascularized 3D (tumor) tissue models in preclinical and clinical studies.

In Germany, 450,000 people suffer and 216,000 people die from cancer each year. After cardiovascular diseases, cancer is the second leading cause of death. Cancer cells grow uncontrollably and form their own nutrient-supplying blood vessels. Many tumor cells move through the blood or lymphatic system to distant organs and form metastases, which often lead to incurable cancer. An important goal of our work is to therefore discover the mechanisms of cancer growth, metastasis, and their distribution in the human body.

The scientific focus of our research is on the development of human 3D tissue equivalents on an acelluarized, vascularized intestinal scaffold: BioVaSc. By applying tissue engineering methods, we produce human 3D tumor tissue on the BioVaSc in combination with primary tumor cells and various tumor cell lines to get the mechanisms of new therapy strategies in a complex human pathological environment examined.

The project group succeeded in establishing various tumor models in different complexities such as lung tumor models or models for colorectal carcinoma, for breast cancer, leukemia and for malign peripheral nerve sheath tumors (MPNST). Beyond the standard divisional rate and apoptosis of tumor cells, various molecular activations and inhibitions of signal cascades can now be measured after a treatment with agents. Based on these data, "in silico"-models are created, refined, and validated in cooperation with the Department of Bioinformatics of the University Hospital of Würzburg. The co-culture with cells from the tumor stroma additionally allows the examination of the reciprocity of agents, among them biologicals such as anti-bodies, with stromal and with tumor cells of their surroundings, and to further examine the formation of resistance or metastases. In the future, we want to refine characteristics of metastasizing tumor stem cells.

The application of 2D monolayer cultures and cell lines is limited when clarifying certain regenerative mechanisms, the examination of physiological barrier functions, and the resorption processes in humans. Based on the BioVaSc, we developed complex tissue models of the human barriers skin, intestine, trachea, lung and the blood-brain-barrier. We adapt these tissues to diseases (disease-models) or we simulate infections of germs and, accordingly, we establish long-time cultures. Equally, we simulate reciprocal effects of medical products such as stents to optimize the surface of the implants. In the EU project IDEA, we use vascularized tissue models to develop diagnostics (nanoparticles) and to test their safety. In the EU projects Bio-Inspire and VascuBone, we are developing stem cell-based musculoskeletal therapies; the necessary preclinical studies are in progress with international partners from



Norway, Austria, and Australia. Clinical studies of these novel innovative ATMPs (Advanced Therapies Medicinal Products) are prepared in Germany, Austria, and Norway. The culture of our vascularized scaffold BioVaSc in specific bioreactors where we can also generate complex vascularized implants has now also been established under GMP conditions in cooperation with the University Hospital Würzburg. Under a BMBF-funded project, we are preparing first clinical studies for a trachea implant based on the BioVaSc.

Our research services can be used for the entire value-added chain in the development of cancer therapies.

Range of services

- Production and biochemical modification of tissue engineered electrospun 3D scaffolds
- Isolation of primary human stem and tumor cells
- Establishment of co-cultures for the generation of human solid tumors in vitro and tumor test systems
- Development of specific bioreactors for various tumor models
- Development of human vascularized tumor tissue for the establishment of individual diagnostics and personalized treatments
- Biological cell analysis of tumor tissue: molecular-biological, histological and immunohistochemical methods, flow cytometry (FACS)
- Target screening for new cancer therapeutics

Contact

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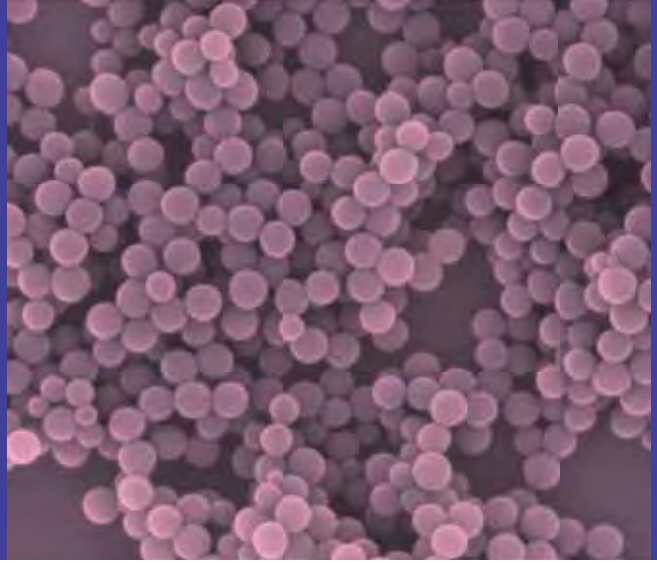
Value chain

- Investigation of the active principle and/or the side effects of new drug candidates utilizing vascularized human tumor test systems
- Use of the tumor model in the process development of optimizing drugs or diagnostics
- Implementation and validation of in vitro tests as alternatives to animal testing at the end of the preclinical development phase
- Efficacy experiments of new drugs that are currently undergoing evaluation for clinical use
- Cooperation with the Medical Faculty of the University Hospital of Würzburg for the organization of the clinical phases I–III

Infrastructure and technical equipment

- Cell culture laboratories for work on safety levels S1 and S2 GenTSV (genetic engineering safety regulations)
- Cell analysis: Fluorescence microscope, FACS, microdissection system, Raman spectroscopy



INSTITUTE OF INTERFACIAL PROCESS ENGINEERING AND PLASMA TECHNOLOGY IGVP

The Institute of Interfacial Process Engineering and Plasma Technology IGVP is headed by Prof. Dr. Thomas Hirth and is part of the University of Stuttgart's Faculty of Energy Technology, Process Engineering and Biological Engineering. At the end of 2013, the institute had a research budget of around 3.4 million euros. It had a staff of 31 scientific, technical and administrative employees along with 43 doctorate students and 23 other student researchers and student assistants investigating various research topics at the three IGVP facilities (Pfaffenwaldring 31, Allmandring 5b and Nobelstrasse 12) on the Stuttgart-Vaihingen campus (see page 13).

Close cooperation with the various Fraunhofer IGB departments makes it possible to pursue projects from basic research to application. This integrated approach is also reflected in the variety of sources of research funding received by the IGVP, including the German Federal Ministry of Education and Research (BMBF), the German Federal Foundation for the Environment (DBU), the German Research Foundation (DFG), the European Union, the Land of Baden-Württemberg, various foundations, and industry.

The institute is organized in the two departments "Interfacial Process Engineering" and "Plasma and Interfacial-physical Processes", with research carried out by nine working groups. The IGVP focuses on the design, functionalization and characterization of surfaces and materials of inorganic or organic origin and their interactions with biological systems, as well as on the simulation and development of interfacially driven processes. The institute is also active across the entire spectrum of plasma-physical basic research, combining this with plasma chemistry and plasma process engineering.

Teaching activities at the institute are centered on the subject areas biomaterials, interfacial process engineering, industrial biotechnology and nanotechnology, as well as plasma physics and plasma technology.

Biological Interfacial Engineering

- Screening for enzymes and microorganisms
- Process development for industrial biotechnology
- Microarray technologies for diagnostics and biomedical research
- Interactions between microorganisms and surfaces
- Host-pathogen interactions

Chemical Interfacial Engineering

- Composite materials, hybrid materials, ionic liquids
- Biomaterials and nanobiomaterials
- Nano- and microstructured (bio)functional surfaces
- Biomimetic functional layers for medical and biotechnological applications
- Core-shell nano- and microparticles, particularly with biomimetic shells
- Surfaces for molecular recognition

Medical Interfacial Engineering

- 3D tissue engineering
- Generation of vascularized tissue
- Cells and biomaterials
- Development of tissue-specific bioreactors
- Organoid human test systems as a substitute for animal experiments
- Toxicity studies using organoid tissue models

Physical-technical Interfacial Engineering

- Adsorption/desorption processes for heat storage and dehumidification
- Drying processes using superheated steam
- Electrochemically stimulated crystallization and recovery of inorganic nutrients
- Particle suspensions and emulsions in electric fields

Environmental Interfacial Process Engineering

- Membranes for gas separation and fuel cells
- Membrane processes for water treatment, cell retention and water hygienization
- Development of processes for the energetic and material use of biomass
- Production of valuable products from microalgae in photo-bioreactors

Plasma Technology

- Design and development of linearly extended and large area plasma sources at low and atmospheric pressure
- Plasma diagnostic and characterization of plasma
- Modeling and simulation of plasma
- Investigations of plasma physical and chemical processes
- Development of plasma processes for industrial applications

Microwave Technology

- Microwave heating and diagnostics relating to fusion experiments
- Development of heating systems, complete microwave transmission systems and specialty antennae
- Testing of components in the microwave excitation spectrum
- Mode converters for oversized waveguides
- Millimeter-wave photonic components
- Simulation of millimeter-wave propagation in fusion plasmas

Plasma Dynamics and Diagnostics

- Magnetic plasma confinement
- Fundamentals of turbulent plasma dynamics
- Probe and imaging diagnostics
- Physics of turbulent transport
- Flow/turbulence interaction
- Investigation of wave phenomena
- Heating mechanisms using microwaves
- Conversion between different wave types

Interfacial Physics

- Chemical vapor deposition (CVD)
- Plasma-enhanced chemical vapor deposition (PECVD)
- Microplasmas
- Interface characterization
- Nanoscopic surface functionalization
- Plasma diagnostics and physical-chemical modeling
- Development of plasma processes
- Processes for the dispersion of nanomaterials

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MEDICINE

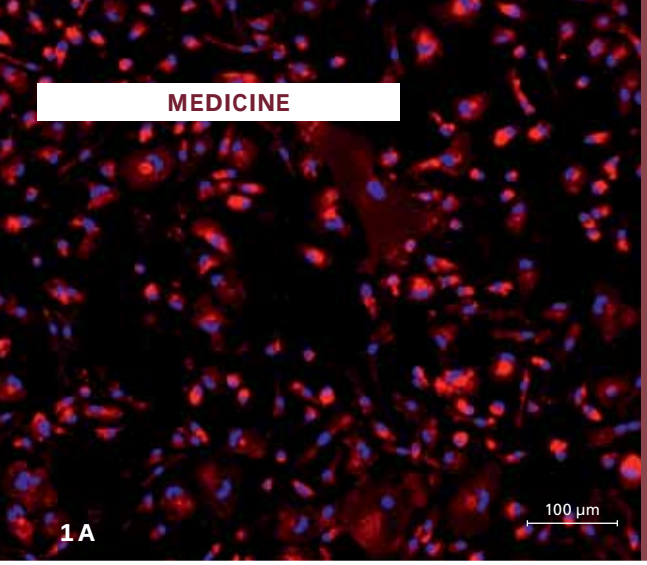
Prof. Dr. Petra Kluger, Prof. Dr. Katja Schenke-Layland

Increased survival rates offered by regenerative medicine, quicker and more accurate diagnostics using molecular-biological approaches, and coordinated interaction between medical implants and their physiological environment are scientific trends which improve healthcare provision and reduce costs. In the Medicine business area at the Fraunhofer IGB, we frequently work on interdisciplinary projects, addressing topics in the areas of tissue engineering, regenerative medicine, immunology, infection biology, diagnostics, and the "biologization" of established medical products.

The focus of regenerative therapies is on the development of human in-vitro test systems and biologized implants that can be individualized through the use of the patient's own cells. The Fraunhofer IGB covers the entire value-added chain right up to GMP-compliant manufacturing of cell-based implants (advanced therapy medicinal products or "ATMPs") and – together with a network of physicians – phase I clinical studies. The Fraunhofer IGB will expressly make the experience and competence gained through these studies available to small and medium-size enterprises. To promote the role of tissue engineering products in healthcare, we have developed a GMP-conform plant for the standardized, fully automated in-vitro manufacture of skin through a joint Fraunhofer research project financed by the Fraunhofer-Zukunftsstiftung (Fraunhofer Future Foundation).

New scientific strategies to combat infectious diseases are a high priority. Thanks to the various array technologies and a high-throughput sequencing method, as well as human tissue models it has developed on the basis of its own patents, the Fraunhofer IGB is in a position to elucidate host-pathogen interaction and make targets available for new anti-infectives. We develop new diagnostic methods based on nucleic acids (diagnostic microarrays, biomarker development using high-throughput DNA sequencing) or that utilize cellular reporter systems (cell-based pyrogen assay). This information can be used to institute measures for specific treatments or to develop personalized drugs for different population groups.

A further focal point, enabled by the interdisciplinary collaboration at the Fraunhofer IGB, is the optimization of surface properties of established medical devices such as tracheal stents and contact lenses. This is achieved primarily by using plasma processes to generate bioactive or antibacterial surfaces; we then proceed to test the effectiveness and biocompatibility of these surfaces on in-vitro tissue models. Furthermore, we make a contribution to preventive healthcare through the development of processing techniques and methods for hygienization and pasteurization that preserve the foodstuff's original properties.



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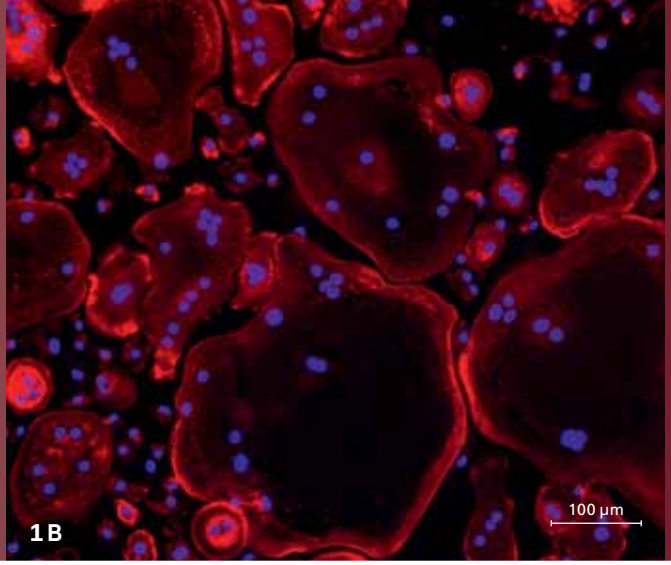


1B

IN-VITRO TEST SYSTEMS FOR THE EVALUATION OF NOVEL BONE IMPLANTS

Dipl.-Biol. Claudia Kleinhans, Prof. Dr. rer. nat. Petra J. Kluger

Overview

Treatments for the diseases and injuries of the musculoskeletal system are currently focused on the development of new composite materials. Many of these material developments are aimed at improving the biodegradability and mechanical properties of the load-bearing areas of the implants. To ensure the utility of the new material, the establishment of biological test systems for the analysis of ingrowth into the bone and the degradation behavior of implant materials are of particular relevance. Although certain animal tests of implant materials are still essential, there is a clear directive to develop new human-based in vitro test systems due to ethical considerations, a better correlation to the human system and increasing regulatory restrictions on animal experiments. However, there are no standardized systems for the appropriate analysis of material resorption and osteoinduction, which is the material's ability to stimulate the formation of new bone, analyzing both osteoblast and osteoclast function. The establishment of such systems is part of the Fraunhofer joint project "DegraLast" as an alternative or supplement to animal experiments.

Standardized in vitro test systems with bone-forming and bone-degrading cells

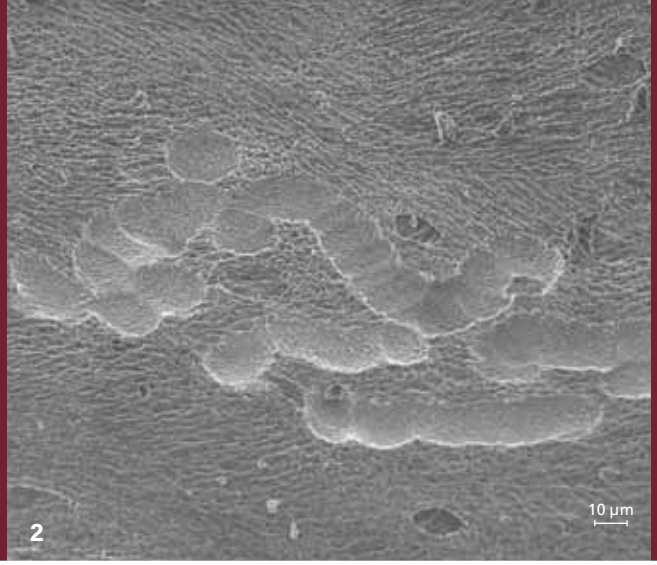
The standardization of cell-based test systems using osteoblasts and their precursor cells to simulate bone formation, as well as bone-resorbing cells, the osteoclasts, to mimic bone loss, is the goal of the subproject at the Fraunhofer IGB. To mimic the in vivo situation, a co-culture of primary osteoblast precursor cells and osteoclasts is to be established.

Ingrowth and osteoinductive properties

To assess the ingrowth and the osteoinductive properties of a material, we investigate the differentiation of human mesenchymal stem cells (hMSCs) into osteoblasts by analyzing specific differentiation markers on standard materials, as well as newly developed materials and coatings. Cell adhesion, proliferation and differentiation are characterized by the qualitative analysis of type I collagen as well as the quantitative examination of alkaline phosphatase and calcium, which showed a significant increase in differentiated cells relative to control cells.

Loss of bone substance

Osteoclasts are largely responsible for the resorption of bone. For the osteodegradation test system, monocytes were isolated from human peripheral blood and successfully differentiated into osteoclasts. The characterization of differentiated osteoclasts was demonstrated by polynuclear size, the restructuring of the cytoskeleton and the expression of specific marker proteins (Fig. 1). Furthermore, the activity of the cells was determined by the absorption of a bovine bone substitute material (Fig. 2).



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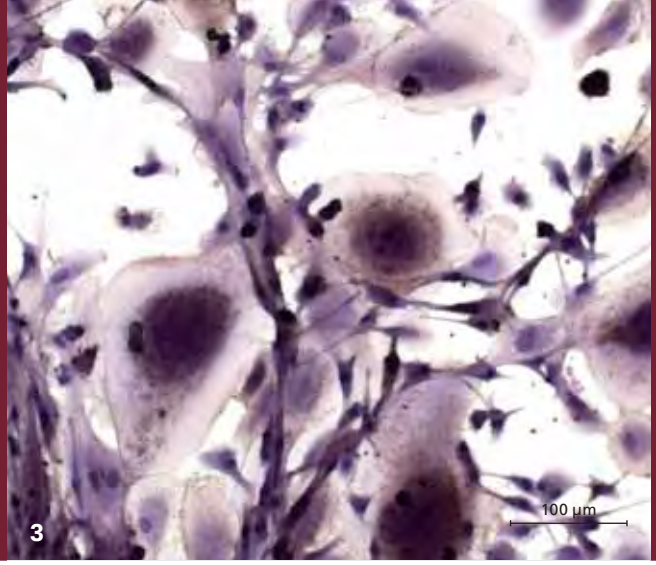

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Advanced model by the co-culture of osteoblasts and osteoclasts

The recapitulation of the physiological process of bone remodeling is an effective method to obtain the desired properties for bone replacement materials. While osteoclasts resorb the material, osteoblasts form new bone. Current in vitro studies focus only on one type of cell and investigate either bone resorption or bone formation. Therefore, we aimed to establish a co-culture of both cell types to simulate the bone remodeling process and to extend current test systems. In the development of in vitro co-culture systems, we first identified optimal culture conditions for the two cell types. Then we developed a method that leads to osteoclast differentiation without addition of differentiation factors, which allowed for the co-culture of both cell types (Fig. 3).

Outlook

A decisive advantage of our in vitro test system is the ability to work with human cells in the testing of new materials or coatings. The results generate the initial evidence on the suitability of newly developed implant material.

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Funding

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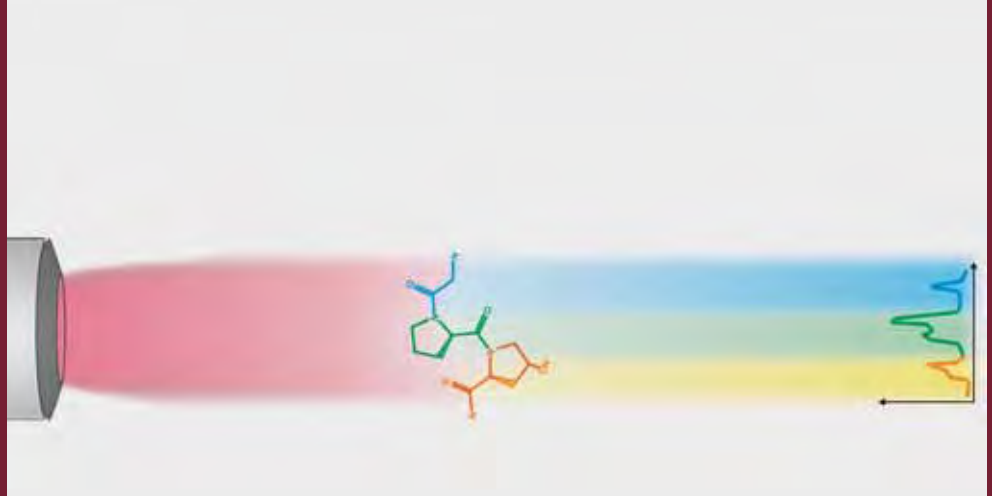
Project partners

Fraunhofer IFAM, Bremen and Dresden | Fraunhofer ILT, Aachen | Fraunhofer IBMT, St. Ingbert

1 *Actin cytoskeleton (red) and cell nuclei (blue) of undifferentiated (A) and differentiated (B) monocytes.*

2 *Scanning electron microscopic image of resorption lacunae after removal of osteoclasts cultured on bovine bone substitute material.*

3 *Histological staining of the vitronectin receptor and the cell nuclei of human mesenchymal stem cells and monocytes. In co-culture, the cells develop an osteoclast phenotype.*



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RAMAN-SPECTROSCOPY IN BIOMEDICAL ENGINEERING AND REGENERATIVE MEDICINE

Eva Brauchle M.Sc., Prof. Dr. rer. nat. Katja Schenke-Layland M.Sc.

Analysis of cell and tissue samples

In biomedical engineering and regenerative medicine, the analysis of rare tissues and cells is often limited to a few biological properties. Complicated processes make the analysis error-prone and time-consuming, typically altering sample characteristics and rendering the sample unusable for further studies. At the Fraunhofer IGB, we are investigating non-invasive technologies such as Raman spectroscopy for the global analysis of cell and tissue samples. Raman spectroscopy is an optical technology based on the effects of light scattering on a sample. Here, photons of incident monochromatic light interact with sample molecules, thereby shifting their frequency. The Raman spectrum represents the frequency shift of the inelastic light scattering. The spectral bands create a "fingerprint", which are specific to molecular bonds that can be identified in complex samples, such as biological tissues [1, 2]. Due to its simple sample preparation, as well as the ability to gain biochemically relevant information under physiological conditions without the use of dyes, the method can be applied to a wide range of medical applications [2].

Non-contact cell culture quality control

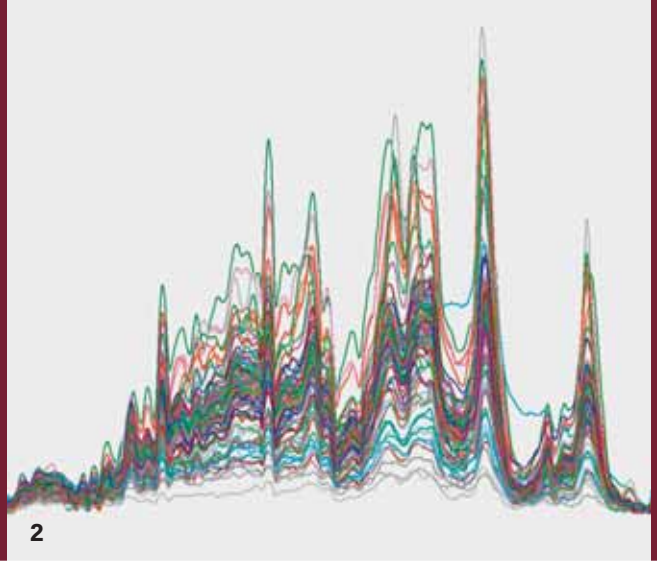
The proper characterization of primary cells from patients' tissues is a critical step in regenerative medicine. Using Raman spectroscopy, the current state of an individual cell can be detected without contact. Apoptotic and necrotic cells have an altered Raman spectrum, which allows their identification within a population of viable cells. The molecular vibrational bands in the spectrum allow the identification of the early and late phases of apoptosis. Our studies show that the Raman spectroscopy is not only a valid method for the continuous monitoring of primary cell cultures, but is also suitable for cytotoxic studies where the accurate detection of the cell death plays an important role.

Analysis of in vitro differentiated stem cells

Stem cells have great therapeutic potential because they can differentiate into diverse types of tissue-specific cells. Although immunohistological methods can identify the differentiation state of cells via marker proteins, they require the manipulation of the cell culture. Stem cells and their derivatives have a molecular profile, which corresponds to their current cell phenotype. Raman spectroscopy can non-invasively monitor the differentiation process at the molecular level, providing a unique profile of different cell types that can arise from a stem cell. In molecular patterns of fibroblasts, keratinocytes and melanocytes, which all originate from skin, Raman bands were related to the biological functions of the respective cell type, exhibiting characteristic Raman signals [3]. In other studies, Raman spectroscopy was able to identify the pathological loss of tissue-specific cell phenotypes in degenerating cartilage [4].

Pathological changes in tissues

In natural tissues, cells are in close contact with a complex network of fibrous and soluble components known as the extracellular matrix. The extracellular matrix is specific for each tissue, often consisting of collagen, elastin and proteoglycans,



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which can be identified by specific signals in the Raman spectrum [4, 5]. The remodeling of matrix components is often associated with pathological conditions. Using Raman spectroscopy, we examine the extracellular matrix in healthy and diseased tissues. Together with our expertise in immune and histochemical methods, we can correlate these results with our Raman spectra to identify new diagnostic markers.

Outlook

We are currently developing the Raman technology for intraoperative tumor diagnostic methods. We are also using Raman spectroscopy in the field of women's health in order to analyze different pathologies at the molecular level.

1 *Principle of Raman spectroscopy.*
2 *Raman spectra of stem cells.*
3 *Raman microscope at the Fraunhofer IGB.*

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Funding

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Project partners

University Hospital for Women of the Eberhard Karls University of Tübingen | IGVP, University of Stuttgart | Queensland University of Technology, Australia | University of California Los Angeles, USA | Beiersdorf AG, Hamburg | ERBE Elektromedizintechnik GmbH, Tübingen | Karl Storz GmbH & Co. KG, Tuttlingen

Further Information

www.schenke-layland-lab.com

1

FUNCTIONAL GENOMICS VIA NEXT-GENERATION SEQUENCING

Dipl.-Biol. Christian Grumaz, Dr. rer. nat. Kai Sohn

Sequencing technologies – the next generation

The human genome was first decoded in 2001 after 10 years of work by over 100 scientists and a cost of 3 billion US dollars [1, 2]. Today, the enormous advancements in sequencing technologies over the most recent years enable a single researcher to decode a human genome within days and for under 10,000 US dollars. The special feature of the technology referred to as next-generation sequencing (NGS) [3] is the possibility to sequence hundreds of millions of fragments at the same time, as opposed to just individual fragments. These high-throughput or parallel sequencing technologies have opened up entirely new dimensions in nucleic acid analysis and revolutionized countless areas of research in Life Sciences – from de novo genome sequencing up to the early diagnosis of tumor tissue [4]. And the discovery of novel, innovative areas of application has only just begun.

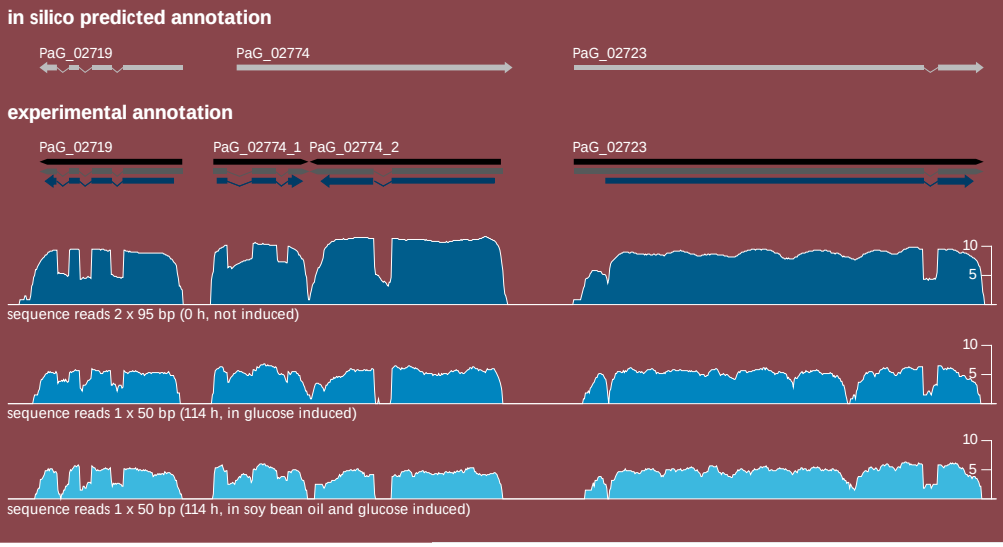
The technology at a glance

In order to be able to use next-generation sequencing the samples must be processed differently depending on the starting material and purpose of the research. For example, genomic DNA from unknown organisms is used for de novo genome sequencing while a variety of RNA populations (mRNA, small RNA, ncRNA) can be examined in transcriptome analyses. Several sample preparation protocols can also be fully automated using the Biomek FX laboratory automation workstation (Beckman Coulter) at the Fraunhofer IGB. Once a (c)DNA library has been completed it is sequenced either on the Illumina HiSeq2500, with very high read depth and shorter fragments (up to 2 x 100 bases) or by using the Roche GSjunior, which has far lower read depth but can process longer sequences (up to 400 bases). The raw sequencing data can finally be subjected to bioinformatics analysis for the most varied questions, with the aid of the IT infrastructure optimized for NGS at the IGB.

We have hereby established a three-step process that encompasses the various steps in sample preparation and sequencing in the laboratory, as well as subsequent bioinformatic analysis. The now extremely comprehensive selection of sample preparation protocols and analysis strategies then opens up areas of application, extending from sequencing human genomes with a focus on early detection of cancer, to de novo transcriptome sequencing of biotechnologically relevant production strains or human pathogens, through to the detailed identification of complex biocenotic bacterial populations (metagenomes). Examples of these are briefly presented below.

Non-coding RNA as biomarkers

The aim of the Fraunhofer project RIBOLUTION is the identification of novel diagnostic indicators for diseases such as COPD and prostate cancer. This involves sequencing of the whole non-coding RNA (ncRNA) population present in blood, a still largely uncharacterized class of molecules. We suspect that they play a decisive role in disease development and therefore have especially great potential as diagnostic biomarkers.



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Sequencing the biosurfactant-producing strain *Pseudozyma aphidis*

The majority of surfactants required by the cleaning and food industry are chemically produced from petroleum or plant oils. However, despite currently being comparatively costly, the production of biosurfactants from microorganisms offers great potential. Within the BioSurf project, we were able to use NGS in genome-wide investigations of a particularly efficient producer of the biosurfactant MEL to identify genes required for MEL biosynthesis. These now serve as a blueprint for the metabolic engineering of the strain, with the aim of gaining MEL variants with customized properties.

Characterization of microbial populations in biogas production

Knowledge of the spatial and temporal composition of microbial populations in ensiling and biogas processes and their targeted manipulation provides innovative possibilities for the optimization of the processes to yield more biogas. To this end, NGS technology enables the comprehensive characterization of complex microbial communities in the GOBi project. This also includes the capture of organisms previously impossible to identify using classical microbiology methods as they show poor or no growth in vitro.

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Funding

We would like to thank the Fraunhofer-Zukunftsstiftung (Fraunhofer Future Foundation) for funding the project "RIBOLUTION" and the German Federal Ministry of Education and Research (BMBF) for funding the projects "BioSurf" and "GOBi".

1 *NGS at the Fraunhofer IGB: from sample preparation, to sequencing, through to the complete biocomputational solution.*

2 *Visualizing the sequencing data from P. aphidis using the GeneScapes Viewer, which was developed at the Fraunhofer IGB.*

1

STRATEGIES FOR HEART VALVE TISSUE ENGINEERING AND CARDIOVASCULAR REGENERATIVE MEDICINE

Svenja Hinderer M.Sc., Shannon Layland B.A., Prof. Dr. rer. nat. Katja Schenke-Layland M.Sc.

Lack of regeneration of damaged heart valves and heart muscle tissue

Despite significant advances in cardiology and cardiac surgery, diseases of the cardiovascular system are still the number one causes of death worldwide. Heart valves and heart muscles are often affected causing a significant reduction of heart function and quality of life for the patient. There is very little to no regeneration of the adult heart in cases of acute or chronic damage. As with a large number of research groups, the Fraunhofer IGB is working on the important goal of restoring the normal function and performance of the heart.

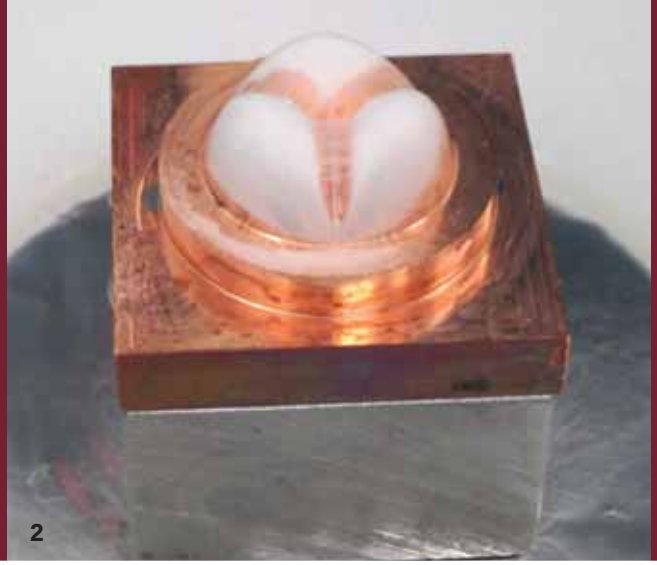
Producing a synthetic heart valve mimicking nature's blueprint

There are currently a number of different transplants available to replace a defective heart valve. However, the currently available prostheses are limited to a maximum use of 25 years. For pediatric patients, prostheses must be exchanged after a number of years because they do not grow with the child. To overcome this limitation, we are developing a heart valve designed to grow with the body by mimicking the valves natural architecture. The adhering, proliferating and differentiation of cells is influenced by their environment. Synthetic substrates with varying mechanical and biochemical properties can greatly affect the behavior of cells. After a detailed analysis of the native heart valve for architecture, mechanical and biochemical properties, we have developed a synthetic, biocompatible hybrid material by electrospinning, whose properties resemble those of the native heart valve. We were further able to biofunctionalize the synthetic materials with extracellular matrix proteins that we discovered were essential for human heart valve development. Using a specially designed bioreactor system, we were able to demonstrate the in vitro function of the heart valve, showing that it could perform under the intense pressure of the heart [1].

Due to the lengthy and complicated process of medicinal product authorization, we are working on an "off the shelf" cell-free heart valve replacement that can be adapted to the size of the patient. The material is currently being modified to attract circulating endothelial progenitor cells in the blood.

Protein production for heart valves tissue engineering and heart muscle regeneration

We have identified extracellular matrix proteins that are important in the development of human heart valves and myocardial regeneration. At the Fraunhofer IGB, we are producing these proteins which we have applied to a carrier substrate in the development of a cardiac valve replacement. In collaboration with our partner, Dr. Ali Nsair of the University of California (UCLA), the proteins have been injected into the infarct region of mouse hearts, which led to a significant improvement in cardiac output that is similar to current adult stem cell therapies. Based on this data, patents have been filed for the use of our proteins in cardiac regeneration therapies.



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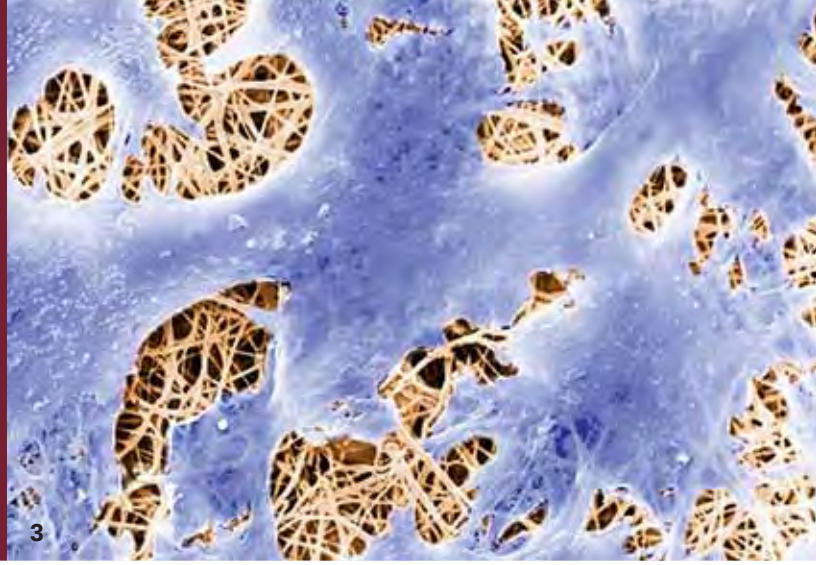

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Outlook

Mimicking the structure and mechanical properties of the native heart valve, as well as using proteins to "attract" cells in vivo, enables the production of a cell-free off-the-shelf product. The previous limitations of cardiac valve replacement systems, such as the thickening and shortening of valve leaflets or the lack of growth for pediatric patients, may be resolved.

Current approaches to cardiac regeneration, such as injecting stem cells into the heart muscle, have shown modest clinical improvement in function, but at increasing production costs. Injecting the matrix proteins produced in our lab provides a way to stimulate the regeneration potential of the heart muscle at lower costs and risks to the patient. It is planned to produce the proteins under GMP conditions for use in clinical applications.

1 *An electrospun-based substrate is stitched into a porcine heart valve.*

2 *Electrospun polymer on a heart valve shaped copper collector.*

3 *Scanning electron microscopy image of valve cells (purple) seeded on an electrospun scaffold.*

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Funding

We would like to thank the Fraunhofer-Gesellschaft for support of the Attract Group to develop cardiovascular regeneration technologies and the California Institute for Regenerative Medicine (CIRM) and the German Federal Ministry of Education and Research (BMBF) for funding the project "Characterization and Bioengineering of the cardiac stem cell niche".

Project partners

University Hospital for Women of the Eberhard Karls University of Tübingen | IGVP, University of Stuttgart | University of California Los Angeles (UCLA), Los Angeles, CA, USA

Further information

www.schenke-layland-lab.com

1

ELECTRON SPIN RESONANCE (ESR) FOR MEASURING RADICALS IN IRRADIATED FOODS AND MEDICAL DEVICES

Dr. rer. nat. Michael Haupt

Sterilization with gamma rays

Gamma sterilization is increasingly being used to preserve foods or to sterilize heat-sensitive pharmaceutical products. For drugs and medical devices, the World Health Organization (WHO) explicitly recommends this sterilization, which involves products being irradiated with high-energy gamma rays from a cobalt-60 radiation source (Fig. 1). As a result of the irradiation, the genomes of germs and pathogenic microorganisms are destroyed and the organisms killed, which has the effect of considerably extending the shelf life of the product. Compared with sterilization with ethylene oxide or steam sterilization, the treatment is very gentle. A further advantage of the treatment with gamma rays is, that products can be sterilized in their packaging – without any appreciable temperature increase or the use of chemicals.

Disadvantage: radicals are formed

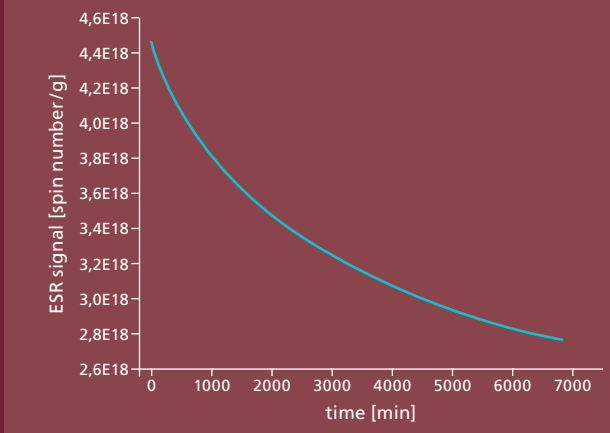
Through the irradiation, however, chemical bonds in the products themselves are also broken which results in the generation of free radicals. Radicals are atoms with an unpaired electron and are highly reactive, which means that they can react in an uncontrolled manner with their environment. As a consequence, it is possible for new, in some cases toxic, compounds to be formed, which may later cause adverse effects when the product, e.g. a drug, is used.

The latest research results at the Fraunhofer IGB show, that the radicals created through gamma sterilization can be extremely stable. Fig. 2 shows how the quantity of radicals in a gamma-irradiated antibiotic decays over time. Even several hours after exposing the product to gamma rays, most of the radicals can still be detected. In addition, continuous measurements show that even after weeks, the quantity of radicals no longer decays significantly. The knowledge as to whether and how many radicals have been created through the sterilization processes has made it possible to come below the threshold values for toxic compounds.

Measurement principle of Electron Spin Resonance spectroscopy

At the Fraunhofer IGB we have been using ESR spectroscopy for a long time for the detection of radicals, for example in order to detect the decay curves for radical density on the surfaces of materials following plasma treatment.

Because of unpaired electrons, radicals demonstrate quantum mechanical spin which in turn is linked to a magnetic moment. Electron Spin Resonance spectroscopy (ESR spectroscopy) benefits from this: By applying a directed magnetic field to a sample that contains radicals, the energy levels of unpaired electrons are split (Zeeman effect). If the sample is exposed to microwave radiation whose quantum energy corresponds to the Zeeman splitting, resonant absorption takes place. Using sensitive microwave absorption measurements, the spin number, number of radicals and also the type of radical can be determined.



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Detection of free radicals and Reactive Oxygen Species (ROS)

In order to determine the quantities of radicals, only a few milligrams of solids or powders or a few milliliters of liquids are required. The measurement is performed as a function of time, radiation dose and/or temperature after the irradiation. Besides free radicals, we can also quantify reactive oxygen species (ROS) and nitrogen monoxide (NO) in biological systems e.g. cells or blood by means of ESR spectroscopy.

Analysis of the antioxidative potential

Over and above this, we use ESR spectroscopy to determine the antioxidative effect of antioxidants. Ascorbic acid (Vitamin C), for example, is a radical scavenger. Thanks to its antioxidative effect it protects cells from damage. We can detect ascorbic acid radicals generated through the scavenging of undesired radicals by means of ESR spectroscopy.

Areas of application

Using ESR spectroscopy, we can examine quickly and safely how high the maximum gamma radiation dose has to be so as on the one hand, to kill germs and pathogens and, on the other, to keep the radical load in the product as low as possible.

In the following products we quantify the amount of radicals and also detect, as the case may be, the type of radicals:

- Foods (coffee, malt, cereals, fruit, vegetables, herbs and spices etc.) and food packaging
- Cosmetics and toiletries
- Disposable medical products
- Implants and drugs
- Pharmaceutical precursors and packaging

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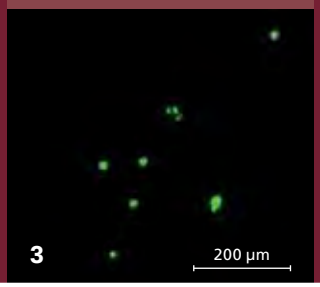
1 *Sterilization with gamma rays is explicitly recommended for drugs and medical devices.*

2 *Over time, the quantity of radicals in a gamma-irradiated antibiotic decays, but radicals can still be detected weeks after irradiation.*

3 *In foods such as cereals gamma rays can kill germs and pathogens.*



PRINTABLE 3D MATRICES FOR THE ENGINEERING OF BIOARTIFICIAL CARTILAGE

Dr. rer. nat. Eva Hoch, Dr. rer. nat. Kirsten Borchers

The challenge of regenerating articular cartilage

Because of the lack of circulation articular cartilage has no access to regenerative cell populations. Cartilage damage is therefore close to irreversible and frequently results in progressive destruction of the joint affected. One promising therapy is matrix-associated autologous chondrocyte transplantation (MACT), in which a suitable material (matrix) is seeded with the patient's cartilage cells (chondrocytes) and then implanted into the damaged cartilage. However, the cultivation of the chondrocytes of the generally used collagen-based matrices can lead to dedifferentiation, i.e. a loss of cellular function.

Reproduction of tissues by modifying natural tissue components

In order to preserve the function of chondrocytes it seems highly significant to create a reproduction of the native extracellular matrix (ECM) that is as natural as possible. Articular cartilage has outstanding properties in regard to strength and water content. These are due to the composition of its ECM, of collagen fibers and hydrophilic polysaccharide units (glucosaminoglycans). In order to represent cartilage-like hydrogel systems, researchers at the IGB modified biological molecules of the natural ECM by means of a chemical reaction with methacrylic acid, thereby making crosslinking possible. A two-component system made of gelatin (denatured collagen) and chondroitin sulphate (glucosaminoglycan) can thereby be chemically crosslinked into ECM-mimicking hydrogels in a controlled way.

By varying the degree of crosslinking and solid content we were able to produce gelatin hydrogels with strengths of about 5 kPa to 370 kPa. This approximately corresponds to the strength of soft fatty tissue and nasal cartilage, respectively [1]. The integration of chondroitin sulphate enables the swelling ability of the matrices to continue being increased, while retaining their strength. Thus we could improve the hydrogel properties and increase the similarity to native articular cartilage.

Stabilization of chondrocytes: the right matrix composition provides biofunctionality

A distinct effect of the composition of the hydrogel on the morphology and proliferative behavior of the cells was found during the encapsulation of chondrocytes in three-dimensional hybrid hydrogels. By contrast with hydrogels containing collagen or pure gelatin, chondrocytes in hydrogels containing chondroitin sulphate showed a cell type-specific spherical morphology and low cell division activity. Our biomimetic hydrogels, which imitate the natural cartilage environment, therefore represent a promising 3D system for the construction of replacement cartilage tissue.

Cell matrix systems as bio-inks to print tissues

Like many other native tissues, hyaline cartilage has a characteristic micro- and macro-structure. For example, the content of proteoglycans continually increases from the joint line to the bone. Also, there are zones with high cell density as well as cell-free zones. Precise dosing techniques are necessary to be able to reconstruct the internal structures of tissues; inkjet printing is one such technique. In order to make the material systems presented here suitable for inkjet printing, the gelling

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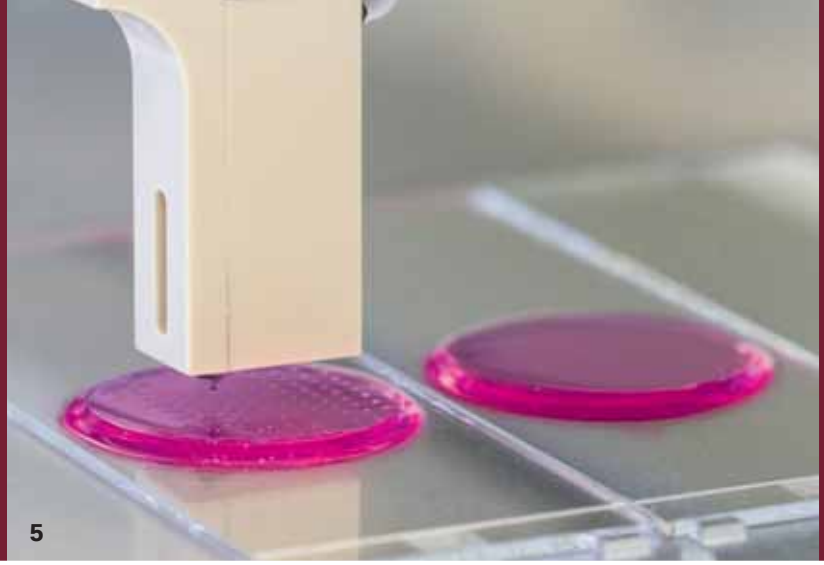
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characteristics of the biomolecule solution must be well-controlled prior to crosslinking and the viscosity must be kept low.

The twofold modification of the biomolecules, with crosslinking groups on one hand and with additional non-crosslinking units on the other, enables the properties of the non-crosslinked solutions and those of the crosslinked hydrogels to be adjusted independently. It is thereby possible to print chondrocytes in the gelatin-based "bio-inks" onto suitable substrates using inkjet printing [2].

Biomimetic biomaterials: a model for the future

The material systems shown here therefore have three properties that especially qualify them for constructing functional tissue models:
(1) They are based on natural extracellular matrix biomolecules.
(2) They can be adjusted to the mechanical properties of various tissues.
(3) They can be made into the desired structures using additive digital process such as 3D printing [3].
This means they have great future potential to contribute to the construction of functional tissue-replacement materials.

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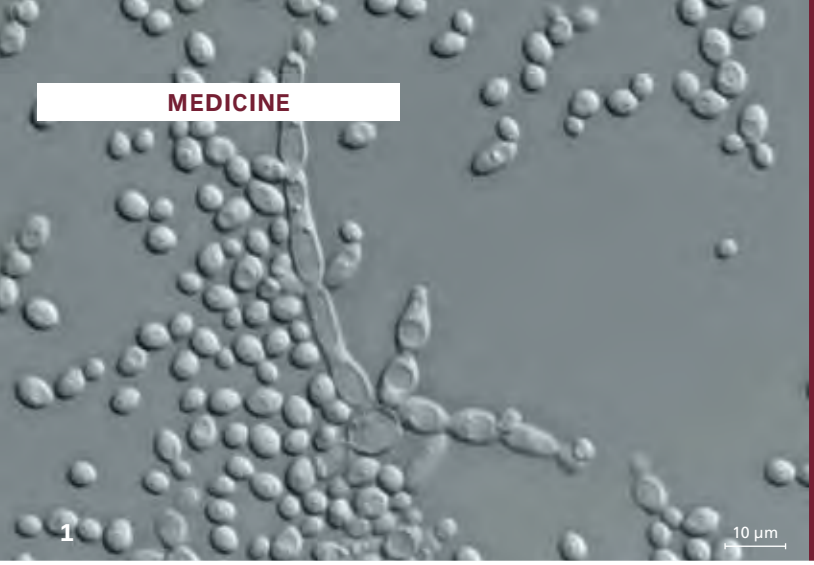
Funding

We would like to thank the Max Buchner Research Foundation for funding this research.

1 *Chemical derivatization of gelatin with crosslinkable functions and functions to control viscosity and gel strength.*
2 *Covalently crosslinked gelatin hydrogels with varying mass proportions. Left: 10 wt%, middle: 20 wt%, right: 30 wt%.*
3 *Chondrocytes with typical spherical morphology in hybrid hydrogels made of gelatin and chondroitin sulphate (below) and chondrocytes with atypical elongated morphology in pure gelatin hydrogels (top).*
4 *Unmodified gelatin gel (left) at room temperature. The non-gelling bio-ink based on modified gelatin (right) is ready for inkjet-printing.*
5 *Inkjet-printing of gelatin-based bio-ink containing chondrocytes.*



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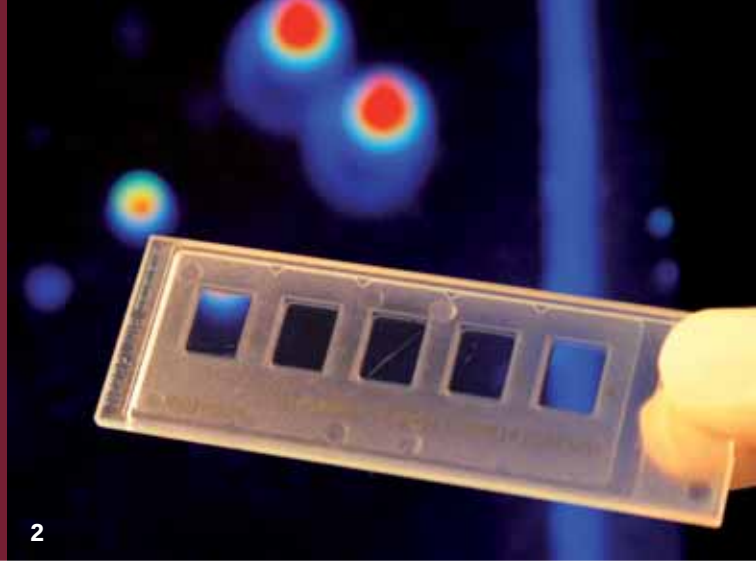
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FYI-CHIP – DETECTION OF HUMAN YEAST AND FUNGAL PATHOGENS USING A LAB-ON-A-CHIP DEVICE

Dipl.-Biol. Linda Mayer, Priv.-Doz. Dr. sc. nat. Susanne Bailer, Priv.-Doz. Dr. rer. nat. Steffen Rupp

Requirement: Rapid detection of pathogenic agents

Infections by yeasts and mold fungi lead to severe illnesses, especially in immunocompromized and patients in intensive care. With a mortality rate of between 30 and more than 80 percent, the rapid detection of a pathogen and its resistance spectrum plays a particularly decisive role in the success of treatment. The classical detection of pathogens using culture-based methods (Microdilution, Etest®) can take up to 14 days for yeasts and mold fungi. Furthermore, it is known from clinical studies that phenotypical resistance testing contains an error of up to 15 percent. Culturing often fails completely, even when the patient displays clear clinical symptoms. In these cases, a therapy on suspicion, which cannot be specifically adapted to the relevant pathogen, has to be initiated.

For this reason, molecular biology methods such as sequencing or PCR are increasingly being used for the identification of pathogens. However, these methods have a limited multiplex capability. This means that only a small number of the multitude of commonly occurring pathogens or resistances can be tested concurrently (≤ 10 parameters). As a result, numerous tests become necessary, which reduces the time advantage of the method.

Microarrays as the diagnostic tool of choice

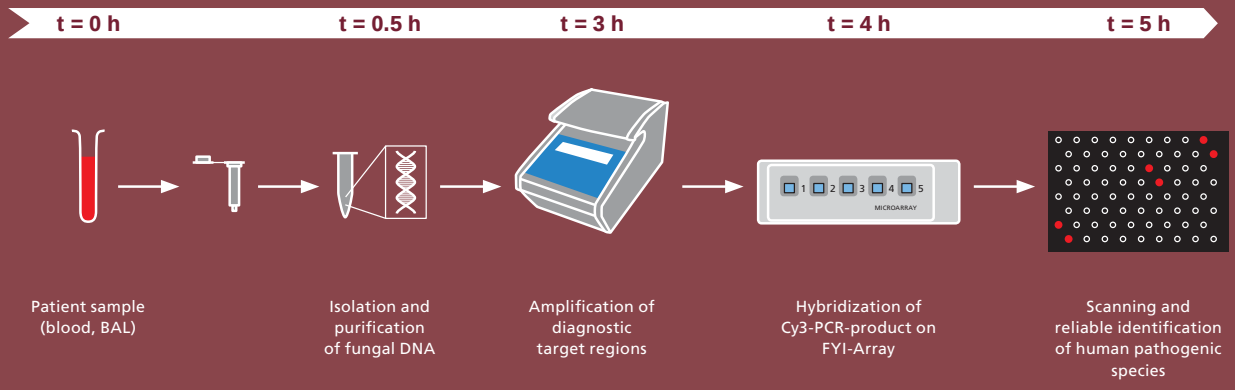
It is possible to compensate for this diagnostic gap by using microarrays, which enable the simultaneous examination of up to several thousand parameters. To date, such tests have been rarely used in routine diagnostics due, among other things, to the high experimental and instrumental efforts involved in the processing of microarrays. These problems can be minimized by the application of automated sample preparation steps that combine the entire testing process into a so-called lab-on-a-chip (LOC).

Aim: A fully integrated lab-on-a-chip system

The Fraunhofer IGB and the Institute of Interfacial Process Engineering and Plasma Technology (IGVP) of the University of Stuttgart, in cooperation with partners from medicine, science and industry and in the context of the BMBF-funded research project "FYI-Chip – Fungi Yeast Identification", are therefore developing a fully integrated lab-on-a-chip system (LOC) for the rapid identification of fungal infections in respiratory secretions and primarily sterile body fluids of immunocompromized patients. To this end, the scientists at the Fraunhofer IGB and IGVP are working closely with the company Euroimmun, based in Lübeck, Germany, with doctors at the Heart and Diabetes Centre North Rhine-Westphalia, as well as with developers at the Reutlinger Multi Channel Systems MCS GmbH and Robert Bosch GmbH, Gerlingen. Their aim is to combine the individual functional components such as sample preparation, microfluidics and the detection of pathogenic DNA into a single fully integrated LOC.

Results

To date, it is possible to detect 45 relevant yeast and fungal pathogens (including *Candida* spp. or *Aspergillus* spp.) definitively and with high sensitivity using newly developed PCR systems and DNA probes on microarrays at the IGVP. In order to identify this many pathogens, PCR systems have been



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developed for a number of genes that show highly conserved areas, but are also variable enough to enable discrimination between the species with DNA probes. The time required is currently 3 to 4 hours from the isolation of the DNA to detection on the array. Parallel to this, LOC systems, in which the DNA microarrays that we developed are currently being integrated, have been developed by our project partners. LOC-compatible cell disruption techniques are being worked out here in cooperation with our partners for different patient probes, such as respiratory secretions for the diagnosis of patients with cystic fibrosis. In this context, the use of disposable cartridges makes the system flexible and economical.

Outlook

As a miniature laboratory, the LOC combines sample preparation with highly sensitive and rapid molecular biological diagnostics of yeasts and mold fungi directly on the chip – with high specificity and sensitivity. This enables them to support clinicians in their diagnoses and facilitates the rapid and adequate initiation or adjustment of therapy. The LOC system is designed such that it can be adapted for further sample materials, such as biopsy tissues or bacterial pathogens. Upon completion, the LOC will be introduced to the market by the partners.

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Project partners

Euroimmun Medizinische Labordiagnostika AG, Lübeck (coordinator) | Heart and Diabetes Centre NRW, Bad Oeynhausen | IGVP, University of Stuttgart | Multi Channel Systems MCS GmbH, Reutlingen | Robert Bosch GmbH, Gerlingen

1 *Candida spp., dangerous pathogen for immunocompromized patients.*
2 *DNA microarray.*
3 *Time and process diagram for pathogen detection.*

PHARMACY

Priv.-Doz. Dr. Steffen Rupp

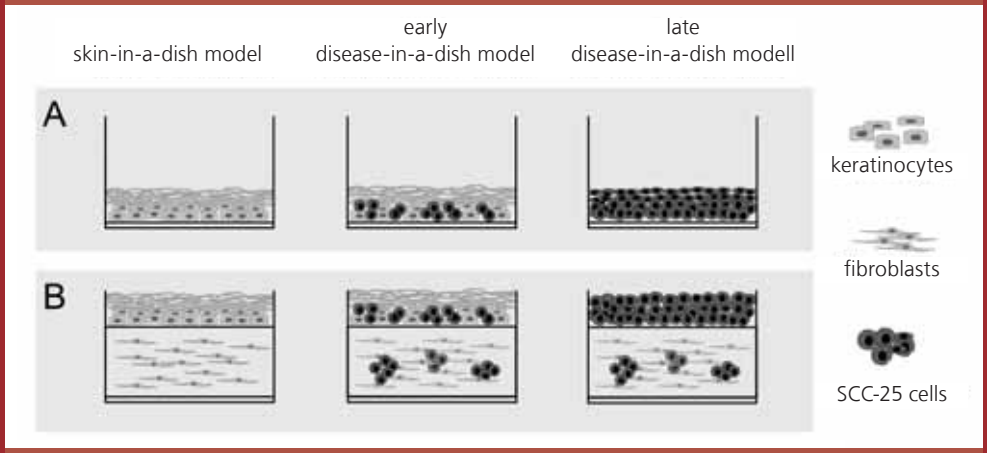
The current challenges faced by the pharmaceutical industry include improving personalized therapy, the development of new active agents, and enhancing the effectiveness of drugs through improved formulations. The Pharmacy business area at the Fraunhofer IGB works on developing solutions for drug screening, on questions in the fields of pharmaceutical biotechnology and chemistry, as well as on drug formulation and targeted release.

We identify new drugs e.g. for immunomodulatory substances or anti-infectives by means of the targeted use of cell-based assays and structure-activity correlations. Using complex organotypic 3D primary cell models (skin, intestine, lungs), potential active compounds are characterized in vitro for effectiveness, absorption, distribution in organ models and toxicity. These investigations – corresponding to phase I clinical studies – are complemented by molecular methods such as gene expression and proteome analysis, as well as by histology and confocal Raman spectroscopy. The aim is to identify toxic side effects of potential active agents and their metabolites at a pre-clinical stage.

In the field of pharmaceutical biotechnology we work on developing processes to manufacture pharmaceutical proteins. These range from the development of expression vectors and strain development in microorganisms and mammalian cells to the optimization of fermentation processes and the purification of the pharmaceuticals. Cooperation within the Fraunhofer network enables us to supply customers with proteins produced in compliance with GMP (Good Manufacturing Practice) for clinical testing. With regard to the formulation of active agents, we are developing nanoparticle-based structures that deliver drugs directly to the target location and then release them in a controlled manner. We are increasingly also making use of cell-free biotechnological methods, which allow fast optimization of pharmaceutical proteins, production of milligram amounts and characterization using the cell-based systems cited above. Other highly efficient “cell-free” applications are the introduction of non-canonical amino acids and the coupling of drug and targeting molecules.

In addition, our activities include developing cell-based therapeutics and the production of GMP-compliant sample amounts. Our quality control systems identify potential contaminants (microorganisms, viruses) by non-destructive means, using spectroscopic, cell-based or molecular methods based on GLP (Good Laboratory Practice) and GMP guidelines.

We contribute our expertise to the Fraunhofer Group for Life Sciences, facilitating a scope of activity covering the development of medicines from screening for active agents to the production of test samples.



1

IN-VITRO MODEL FOR HUMAN SQUAMOUS CELL CARCINOMA

Dipl.-Biol. (t.o.) Sibylle Thude

White skin cancer caused by UV radiation

With 400,000–600,000 new cases per year worldwide, human squamous cell carcinoma (SCC) in addition to basal cell carcinoma are the most common types of skin cancer [1]. SCC has its origin in the development of atypical epidermal keratinocytes and may result from so-called precancerous tissue changes associated with an increased risk of cancer, such as actinic keratosis or Bowen's disease [1]. Caused by chronic photo damage, white skin cancer occurs mainly in fair-skinned people with light-sensitive skin after years of exposure to UV. It primarily affects the skin areas on the head, forehead, nose, lips, forearms or hands, the human body's most frequently exposed "sun terraces". Despite high cure rates, the early treatment of superficial skin cancer is recommended because the formation of cancer metastases is still a potential threat [2].

New therapies require new test models

In addition to the surgical removal of cancerous cells, other methods such as freezing (cryotherapy), X-ray surface irradiation, local chemotherapy and local immunotherapy are available. A promising new therapeutic approach is photodynamic therapy (PDT), in which a chemical compound accumulates selectively in the tumor cells and makes them more sensitive to light. Subsequently, the tumor and the healthy tissue surrounding it are irradiated with light of a suitable wavelength. This photochemical process generates toxic substances, leading to cell death. A minor side effect of this therapy is only a temporary light sensitivity of the irradiated skin. However, only a few photosensitizing agents are known and the effect of the radiation on normal cells have not been sufficiently studied.

In the development of new drugs, new test methods that generate human relevant and translatable results are essential. New therapies are typically tested in animal trials and later on patients in clinical trials. Animal studies do not always reflect how a drug will work in the human body and clinical trials are very risky, causing great physical and psychological stress for the patient. However, the use of a three-dimensional skin cancer model could fill this gap in the development of new topical treatments.

In vitro model depicts early and late tumor stage

At the Fraunhofer IGB, we are developing a white skin cancer model for the testing of new photosensitizers that allow for the optimization of novel therapy approaches. We introduced white skin cancer cells (cell line SCC-25) into our well-established three-dimensional skin model creating the first in vitro model for squamous cell carcinoma.

Various strategies have been used to integrate the SCC cell line into the skin model. When the SCC cells are simultaneously introduced with healthy keratinocytes in defined ratios, both cell types can be co-cultured in the skin model producing a test system that is morphologically comparable to the early stage of squamous cell carcinoma in humans. For late stages of the disease, full-thickness skin models were developed where the epidermis is composed solely of SCC cells. In addition, SCC cells were integrated into the dermal part of the model to allow the development of tumor nests, which is similar to nests found in the very late stage of squamous cell carcinoma. Using Raman spectroscopy, we were able to non-destructively distinguish healthy keratinocytes from tumor cells in non-fixed model without the use of cell-specific markers.

2

New model for optimization of photodynamic therapy

There is now an in vitro model of squamous cell carcinoma that can be mapped to the different tumor stages, which are comparable to the in vivo situation in humans. Because we can clearly distinguish healthy and diseased cells, it is possible to investigate new photosensitizing substances and their effects on healthy and sick cells. We can further use the model to test different irradiation protocols for photodynamic therapy and develop comparative studies of various radiation sources to apply to the tumor cells more effectively. Furthermore, the model can be used for the development of new photosensitizer formulations that reach tumor cells located in the deep layers of the skin.

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Funding

We would like to thank the Fraunhofer-Gesellschaft for funding the project "SkinCancer" within the scope of its internal SME-oriented research program (MEF).

1 *The in vitro construction of healthy skin models and the different stages of squamous cell carcinoma. A: epidermis models, B: full thickness skin models.*

2 *Comparison of the in vivo situation with the in vitro model of squamous cell carcinoma. Early stage: bugle beads-like structures as they occur in vivo. Late stage: tumor nests.*

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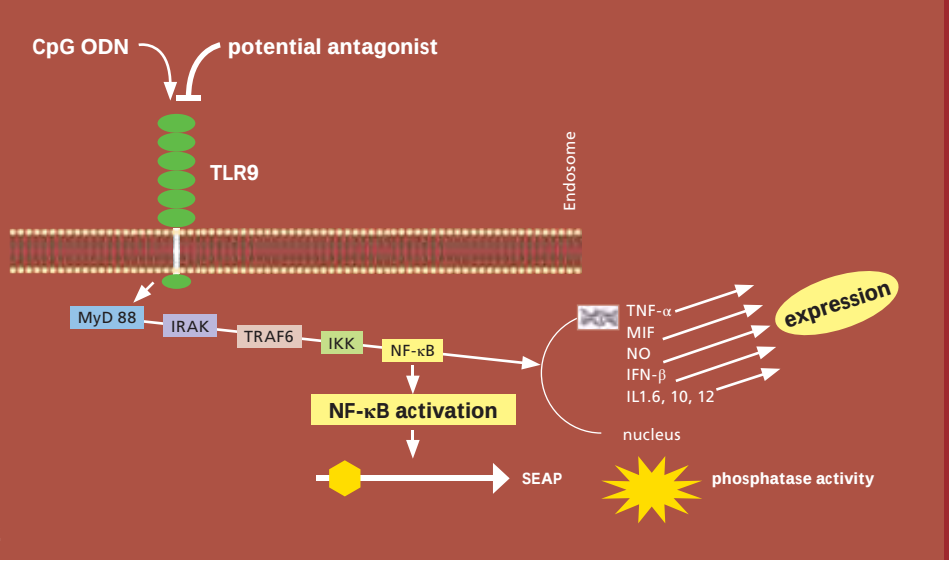


2

SCREENING FOR NEW IMMUNMODULATORS

Angela Mattes B.Sc., Dr. rer. nat. Anke Burger-Kentischer

Initial situation

The receptors of the innate immune system recognize not only conserved molecular patterns of infectious pathogens, but also isolated chemical structures (PAMPs, pathogen-associated molecular patterns), and are referred to as pattern recognition receptors (PRRs) [1]. Among the PRRs, the toll-like receptors represent the largest and most well-known family. Stimulation of the TLRs leads, via the activation of various signal cascades and transcription factors, to the production of pro-inflammatory cytokines and thereby plays a significant role in the development of pathological processes in acute and chronic diseases in humans [2].

Agonists and antagonists of TLRs are therefore a new therapeutic approach for immunotherapy by using them as immunomodulators. Agonists stimulate the innate immune system and are frequently used as adjuvant drugs, while antagonists inhibit inflammatory processes [3]. The possible spectrum of indications ranges from allergies, infections and tumors, up to autoimmune diseases. It is the aim of an international project at the IGB to seek out new TLR antagonists/agonists, in order to be able to treat inflammatory reactions and allergies.

Molecular simulation of screening for drug candidates

The search for TLR antagonists/agonists is conventionally carried out using high-throughput screening (HTS). However, this procedure is very time-consuming and expensive. Our project partner, the Institute for Drug Research at the Hebrew University of Jerusalem, is able to use computer-assisted simulations to vastly reduce the time and cost of the screening process. The process is greatly simplified through 3D binding models for the relevant receptors. The software used contains a broad range of functions, such as the integration of molecular properties, statistical evaluation and research algorithms.

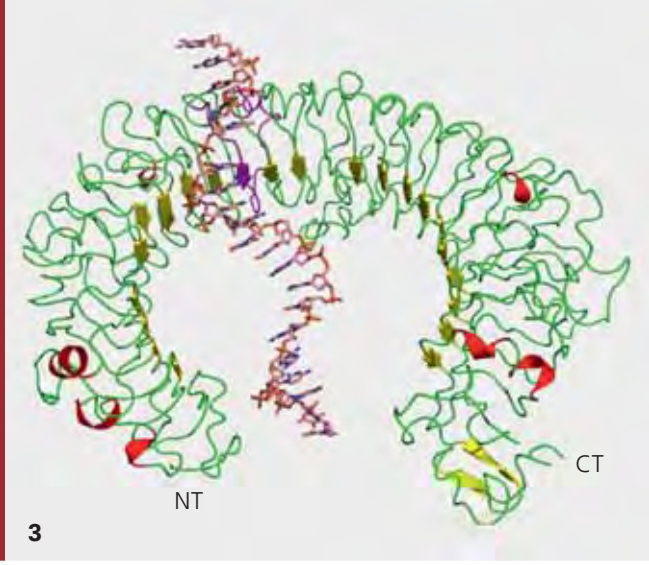
Verifying the TLR-modulating effect in a reporter gene assay

The compound library predicted by the simulation of specific TLR agonists/antagonists is synthesized and validated in a cell-based test system established and patented at the Fraunhofer IGB [4, 5]. This test system enables the detection and differentiation of PRR-modulating substances via a simple reporter gene assay and can also be carried out in accordance with GLP (Good Laboratory Practice). In establishing the assay, the relevant human PRR receptor was stably introduced into the NIH3T3 fibroblast cell line, which naturally expresses very low endogenous levels of TLRs. Additionally, a reporter gene, which is induced by PRR activity, was stably integrated into these cells. The induction of the receptor by a specific ligand leads to the activation of the transcription factor NF-κB. This, in turn, induces the expression of the reporter gene, e.g. a secreted alkaline phosphatase (SEAP) (Fig. 2) [4, 5].

There is direct and quantitative evidence of the effect of substances, antagonists as well as agonists, on the expression of the reporter gene. The PRR-specific cell-based assay is therefore a quick and flexible tool to identify lead compounds for drug development.

First hits identified

Initially, antagonists for TLR9, based on the algorithms of our cooperators The Hebrew University were identified. The initially predicted compound libraries for specific TLR9 binding molecules were synthesized and examined in the cell-based reporter assay established at the IGB (Figs. 3 and 4). In doing this we discovered, among other things, the relevant average inhibitory concentration (IC50) of an antagonistic substance. The level at which half the maximum inhibition is seen is referred to as IC50. These promising hits will be optimized by



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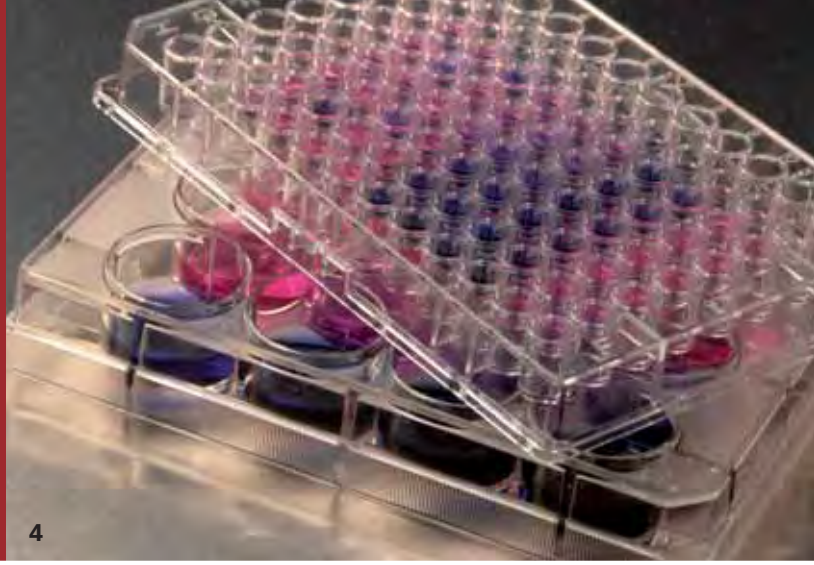
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the experts at the Hebrew University, using the data gained by the IGB, and finally tested again at the IGB.

Outlook

The molecules identified with the aid of the cell-based assay at the IGB represent potential drug candidates for the prevention and therapy of immunological diseases. The complementing expertise of the partners, the unique, patented procedure for molecular simulation by the Hebrew University and the cell-based TLR screening assay developed at the IGB, have provided significant added value regarding the chances of this challenging aim: to find new TLR-based immunomodulators for the therapy and prevention of various medical indications.

1 *Cell-culture flasks.*
2 *Schematic representation of the cell-based reporter gene assay.*
3 *Structure of the human TLR9 when bound to the antagonist ODN (receptor-antagonist-complex) [6].*
4 *Cell-based reporter gene assay in cell-culture plates.*

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Project partner

Hebrew University of Jerusalem, Institute for Drug Research (IDR), Jerusalem, Israel

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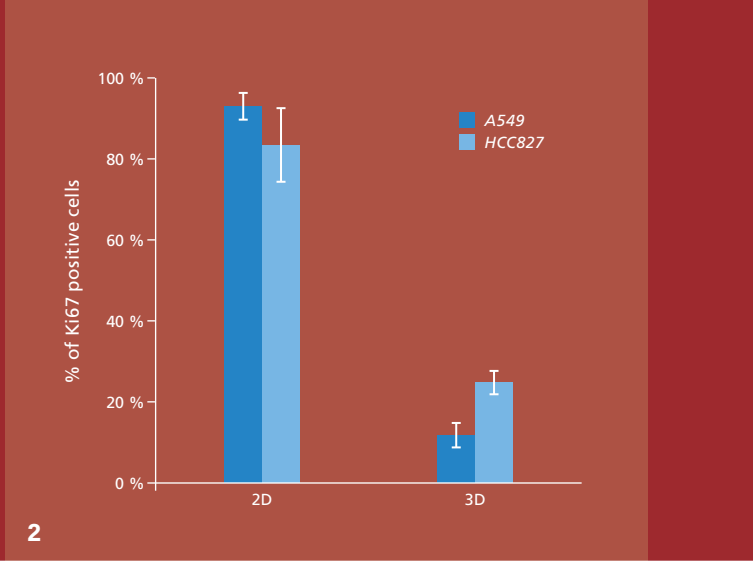


2

DEVELOPMENT OF A COMBINED IN-VITRO / IN-SILICO LUNG TUMOR MODEL FOR PERSONALIZED THERAPY

Claudia Göttlich M.Sc.

Lung cancer is the most common cancer-associated cause of death worldwide [1]. One reason for this is that chemotherapy treatment is limited to inoperable tumors. It has been shown in clinical studies that patients with activating mutations of the EGF receptor (EGFR, epidermal growth factor receptor) benefit from tyrosine kinase inhibitors (TKI) treatment, which act on the EGFR [2]. For example, the clinically available gefitinib treatment inhibits signal transduction through the EGF receptor, leading to slower growth or even tumor regression. For the development of personalized treatment strategies, biomarker profiles must be identified for patients groups that can be selected for targeted therapy. A promising new approach to this is the study of cellular signaling networks and their changes through targeted agents in tumor models that have specific mutations. Through this network analysis, modes of drug action can be understood and new therapeutic targets can be found. Tumor models should reflect the clinical situation as accurately as possible in the laboratory (in vitro) and their correlation with bioinformatics (in silico) models should be developed and used to evaluate complex signaling networks.

Three-dimensional in-vitro lung tumor models

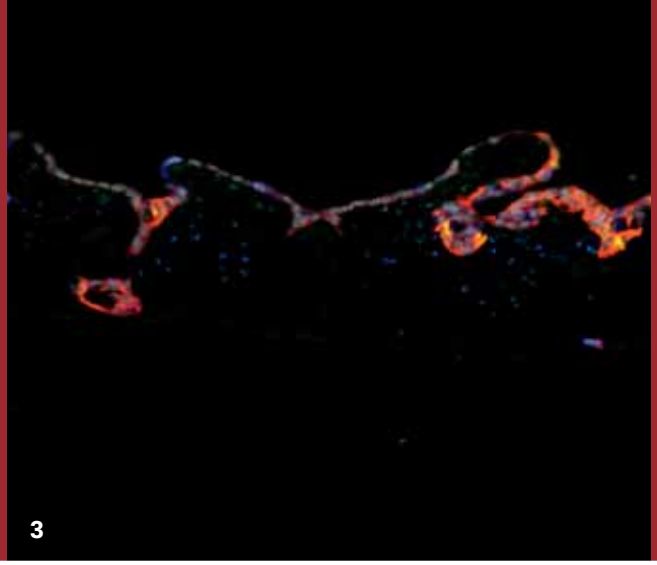
The production of human three-dimensional (3D) tumor models in the Project Group Regenerative Technologies for Oncology is made on the SISmuc (small intestinal submucosa with preserved mucosa). This decellularized intestinal segment is derived from the complex structure of the BioVaSc (Biological Vascularized Scaffold [3]), which is composed primarily of collagen. We currently culture cell lines with (HCC827) and without (A549, H441) the EGFR activating mutation on the matrix (static culture) in order to map the genetic heterogeneity of lung cancer.

In-vitro tumor models reflect the clinical situation

After 14 days of static culture, the cell lines form a largely homogeneous epithelial layer on the SISmuc and grow along the typical crypt structures. When compared to conventional two-dimensional (2D) culture plastic dishes, the cells have a lower division rate and altered expression of tumor markers in the 3D culture, which is much closer to the situation of patient tumors. The treatment of the cell line HCC827 carrying activating EGFR mutation with the TKI gefitinib leads to a reduced rate of division as well as increased tumor cell death. In contrast, the cell lines A549 and H441, which do not carry this mutation, have no change in these parameters with the treatment of gefitinib. We only observed significant effects of the drug gefitinib in the 3D tumor model. Thus, we achieve the same positive results that are described in the clinic in patients with activating EGFR mutation in our in vitro 3D tumor model [4].

In silico modeling of the EGFR signaling networks

In parallel with the in-vitro tumor model, a bioinformatics-based in-silico tumor model was developed in collaboration with the Department of Bioinformatics at the University of Würzburg (Prof. Dr. Thomas Dandekar), which was based on research and clinical data on the activation and network



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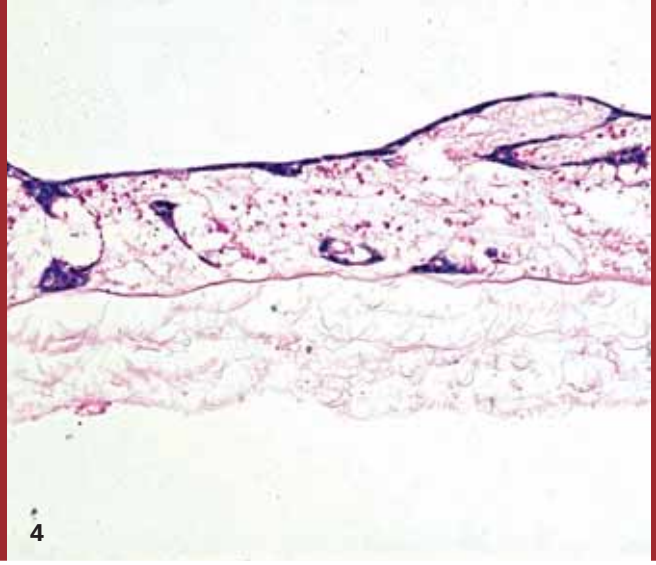

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complexes of the EGFR signaling pathways. First, a map (topology) of the EGFR signaling network with connections to other important tumor development pathways, such as TGF-β (transforming growth factor), was established. The pathway of the signal cascades over various nodes where signals cross were programmed to specific cell responses, such as division or death. There already exists a sound groundwork on other cell types using these semi-quantitative Boolean models [5]. The in-silico model can thus provide predictions of the changing division, death and invasion of tumor cells when certain nodes of the network are stimulated or blocked by drugs or other factors.

As in the clinic, two different lung tumor types were tested in the network – with and without the EGFR-mutation – in response to changes of the blocking the EGFR on cells (simulation: gefitinib therapy). The optimized in-silico model predictions were consistent with the in-vitro model as well as with observations from the clinic. The data obtained from the in-vitro experiments were used to further refine the in-silico model, adding new nodes in the network topology. Thus, we want to find other therapeutic targets and validate their clinical relevance in the in-vitro lung tumor model.

Outlook

With the combined in-vitro/in-silico lung tumor model, we were able to simulate a clinically successful therapy [6]. This shows the high potential of our models to produce clinically relevant results. The goal is now to find other therapeutic approaches and to test the models in order to establish effective treatment methods. We are currently investigating KRAS-mutated cell lines (A549, H441) to identify biomarkers for personalized medicine. In addition, we want to create models with primary cells from patient samples in static and dynamic cultures on the SISmuc with bioreactors in order to better reflect the in-vivo situation.

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Development of other 3D tumor in-vitro models

Other than the lung tumor model, we are working on the development of further 3D tumor models. These include models for colorectal cancer, breast cancer, leukemia and malignant peripheral nerve sheath tumors (MPNST).

1 *E-cadherin/β-catenin staining of lung carcinoma.*
2 *Reduced rate of division in 3D in comparison to the conventional 2D culture.*
3 *Activation of EGFR by HCC827 cells cultured on the SISmuc.*
4 *HCC827 cells form a layer of epithelium on the SISmuc (H&E staining).*


1


2


3

CORNEA ORGAN MODEL-TEST SYSTEM

Angela Rossi, Pharmacist

Draize test

Chemicals, cosmetics and pharmaceutical products must be tested and classified. Currently, the tolerability and irritation potential of substances that come in contact with the eyes are performed with the "Draize test" where the test substance is added to the lid sack of a rabbit eye and the chemical injury is observed for several days or weeks. Partly due to the high pain sensitivity of the cornea, this test is highly controversial. To date, there are no full replacement tests for these animal studies.

Culturing corneas

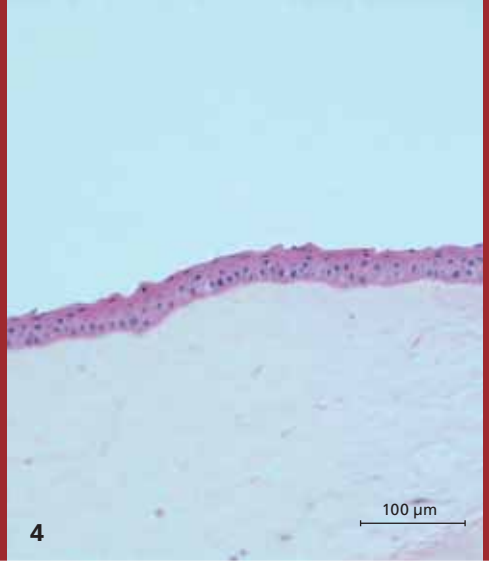
The ex-vivo culture of pig corneas' is a method that may make experiments on living animals unnecessary. The eyes are removed after the slaughter of the animal, prepared so the corneas retain their natural curvature and then kept in a suitable medium in culture. The condition of the corneas is tested before and after preparation and at regular intervals during the culture time for possible changes such as swelling, turbidity, injury, and the condition of the epithelium and endothelium. The corneas are only used in the cornea model after all criteria are met.

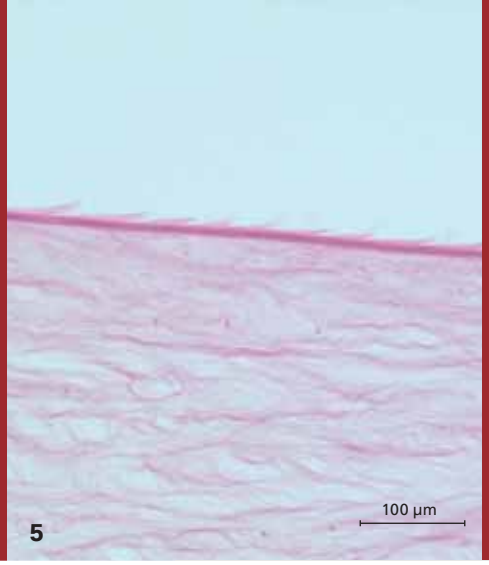
Testing of substances on the corneal model

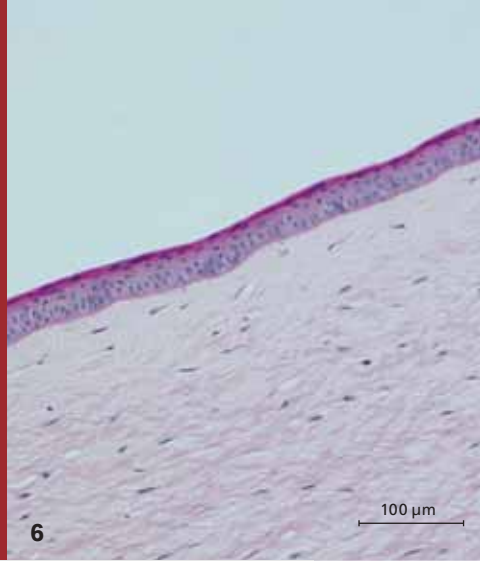
We test substances on cultured corneas by adapting the OECD guideline 405. With our model, acute changes from poisons, corrosive substances, and mechanical and physical action can be detected, as well as long-term changes and potential tissue regeneration. The corneal model allows substances to be applied several times, as it is the case with eye drops, to examine the consequences of multiple applications in sequence over a defined period of time while observing the resulting reaction from each sequence. We distinguish between substances that cause irreversible damage – either after single or repeated administration – and substances that cause a reversible or no damage. Since corneas can be cultured past the required time for substance testing, we can also model the typical healing process of the cornea in the laboratory as well as the regression or healing of the damage to the eye.

Evaluation

Changes in the surface and the deep cornea can be investigated by specific methods. Treatment with sodium fluorescein, which is also used in ophthalmology for diagnostic purposes, shows damages of the epithelium. Histological studies can make the status of the various layers of the cornea clearly visible. For example, damage to the epithelial and endothelial layers or swelling of the stromal region can be identified. Cornea cell viability is examined by means of a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. More complex measurements, such as impedance and OCT measurement (optical coherence tomography, imaging of tissue density with lasers) are appropriate procedures to visualize corneal damage.







Outlook

Culturing the cornea near in vivo conditions with a specialized bioreactor has been accomplished. Using the bioreactor, we can mimic the natural moistening blink of the eye and the natural supply of nutrients on the endothelial side of the eye, as well as the intraocular pressure on the epithelial side of the cornea.

Our cornea organ model-test system allows the testing of substances making experiments on living animals unneeded while performing with an equivalent or even significantly stronger power. Because the metabolism of the corneas remains active during long-term culture, the healing of the damaged tissue can take place, making it possible to test the damage caused by different concentrations of certain substances. Moreover, drug counter-measures can be monitored simultaneously.

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Funding

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Project partner

University Hospital of Würzburg

1 *Cornea EtOH: Treated with ethanol and then stained with fluorescein cornea.*
2 *Cornea NaOH: Treated with sodium hydroxide solution and then with fluorescein stained cornea.*
3 *Cornea PBS: Negative control. Treated with isotonic saline and then with fluorescein stained cornea.*
4 *Histology EtOH: Histological cross-section of an ethanol-treated cornea.*
5 *Histology NaOH: Histological cross-section of a cornea treated with caustic soda.*
6 *Histology PBS: Histological cross-section of a cornea treated with isotonic saline.*

CHEMISTRY

Dr. Christian Oehr

The chemical industry is one of the most important and research-intensive economic sectors in Germany. Many innovations in other sectors such as the automotive, electrical and electronic, construction and packaging industries would not be possible without the contribution of chemistry. The chemical industry is characterized by its resource- and energy-intensive processes. Dependence on imports of raw materials, the limited availability of fossil resources worldwide – including competition for their energetic utilization – and the necessity of considering the effects on both climate and the environment mean that our work, too, is concentrated on approaches focusing on more efficient utilization of fossil resources, or their substitution:

Use of renewable raw materials

Our activities are aimed at developing biotechnological processes to manufacture chemicals and energy carriers from renewable raw materials and coupling these with chemical processes.

Process intensification for a more efficient utilization of energy and resources

The focus here is on developments in the field of upstream and downstream processing, with effective separation of material flows by means of membranes or through the recirculation of material flows (recycling, sustainable waste management).

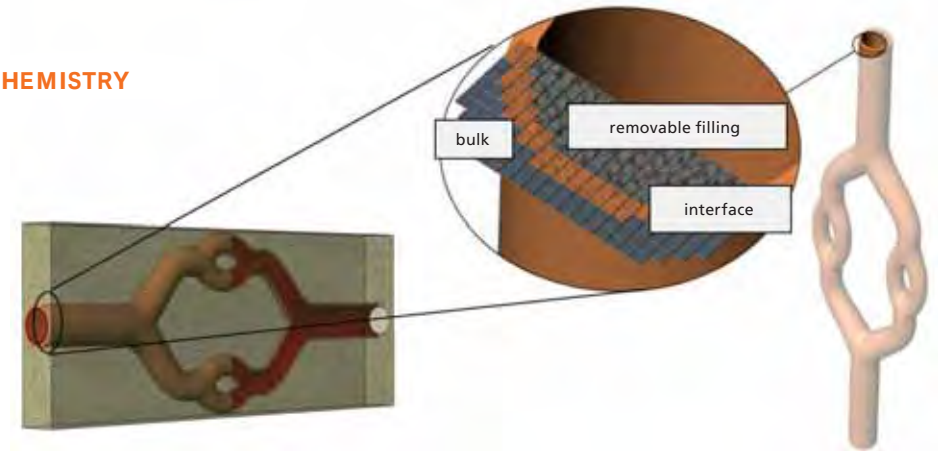
Decoupling of volume and surface properties by means of interfacial process engineering

Tailored coatings which are themselves geared towards resource-efficient process engineering create new possibilities as to the choice of base materials for workpieces and thus for new products based on a selection of sustainable resources.

Evaluation and substitution of critical substances

Chemical substances, insofar as they are represented in the market on a large scale, are systematically investigated with regard to their risk potential, in accordance with EU regulations.

The diversity of our research and development work shows how we are tackling the challenges of these new approaches. This may involve cooperation with other institutes of the Fraunhofer Group for Materials and Components – MATERIALS, or with the Fraunhofer Nanotechnology, Photocatalysis, Polymer Surfaces POLO®, and Cleaning Technology Alliances. New impulses for transferring the material utilization of renewable raw materials to industrial scale will also be given by the Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, which is being jointly operated by the Fraunhofer IGB and ICT institutes.



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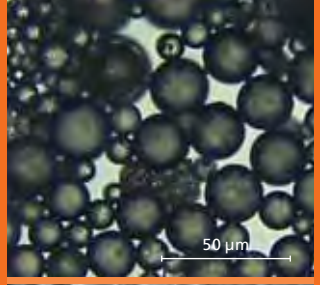
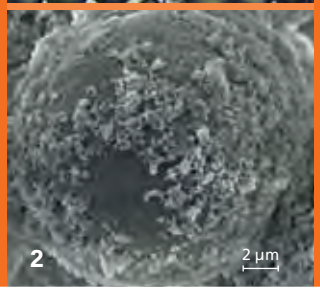




2

LASER PRINTING POLYMER PARTICLES FOR BIOMATERIAL APPLICATIONS

Dr. rer. nat. Achim Weber

The challenge of manufacturing cell-compatible 3D objects

Electrophotography has developed into one of the leading digital technologies in graphic printing. The process, which is also known as xerography and laser printing, offers the possibility of arranging a variety of differently colored toner particles with high resolution and thereby individually designing a paper substrate. However, the printing process is currently largely limited to two-dimensional (2D) applications, although the large solid content of toner particles provides a good prerequisite for the fast construction of three-dimensional (3D) objects. The first commercial 3D laser printing applications are aimed at the construction of simple molded parts. The layered laser printing of cytocompatible objects like artificial arteries or other tubular structures represents a special challenge.

Fixation by a chemical reaction of the toner particles

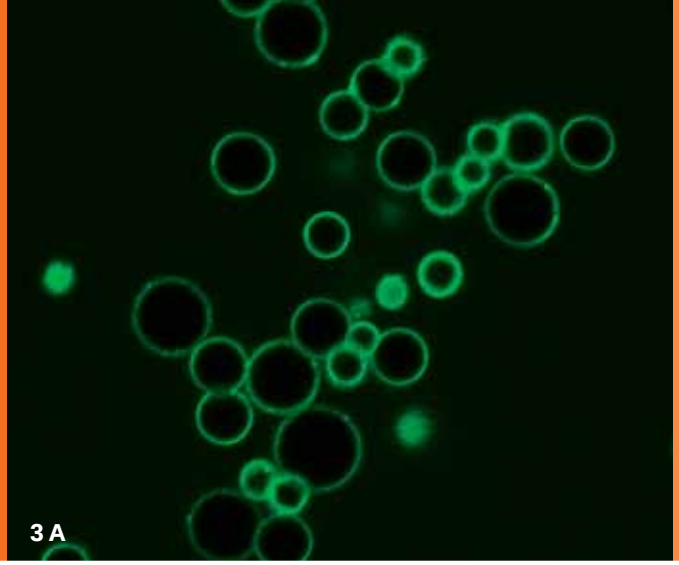
At the Fraunhofer IGB and the Institute of Interfacial Engineering and Plasma Technology at the University of Stuttgart a new method is being investigated, in which the use of different toner components ensures that the spatial arrangement of complex structures is maintained. To do this, the structure was first printed in layers as a three-dimensional block. After each application of particles, instead of the conventional melting fixation, a chemical reaction between the particle surfaces to be fixed occurs. The stability of the 3D objects rests on the formation of covalent bonds and does not require complete melting of the individual particles. The complex geometry of the object is created by support materials, which consist of non-crosslinking toner components and can selectively be removed after printing (Fig. 1). Subsequently the stability of porous or tubular structures, that are required as support materials in applications such as tissue engineering, is assured by the presence of a stable matrix material.

Optimized glass transition temperature and particle size

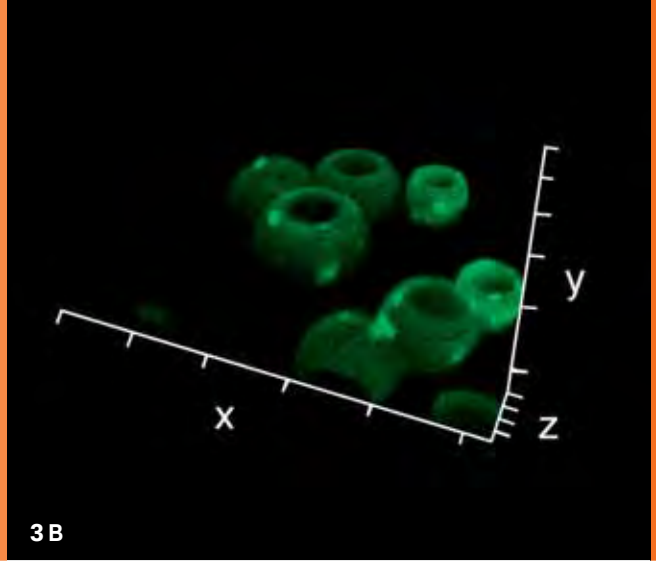
Because of their construction, laser printers function very well with particles in the size range of 3 µm to 30 µm, as well as with polymers with softening temperatures below 110°C. We produce toner particles that are suitable for use as biomaterials out of poly (methyl methacrylates) (PMMA). The selection of the comonomer composition enables the glass transition temperature of the amorphous poly (methyl methacrylate) to be varied over a large temperature range of between –48°C and 110°C. Low reaction temperatures of 20°C lead, within 24 h to spherical poly (methyl methacrylate) (Fig. 2), which show a similarly low glass transition temperature of approx. 40°C. The controllable glass transition point enables the sintering temperature to be optimized so as to achieve a high number of covalent bonds during the three-dimensional fixation of the polymer particles. The covalent bonds between the polymer chains prevent the formation of a solvate sheath, while the non-bonded polymer particles can be selectively dissolved. These are therefore suitable as removable support material for porous and tubular structures in 3D printing. The desired particle size can be very accurately set to between 3 µm and 30 µm by UV-initiated suspension polymerization.

Modification of the particle surface via click chemistry

The poly (methyl acrylate) surfaces are modified with the aid of polymeric analogous conversions. The main chains of the polymer surface remain unchanged during this, while the side chains are chemically modified. The activated surface enables the progressive functionalization of the toner particles with



3 A



3 B

click functions like thiol, azide and alkyne groups, which are available for a chemical 2D fixation via the thiol-ene reaction or the 1,3 dipolar cycloaddition. Fig. 3 shows the successful functionalization of the toner particles via specific binding of a fluorescent dye. Viewing under a laser microscope can show that the dye is only located on the hydrolyzed particle surface, while no emission is detected in the interior of the particles (Fig. 3A). Overlaying different two-dimensional image planes enables a three-dimensional representation of the fluorescent particle surfaces to be realized (Fig. 3B).

Application as biomaterial and outlook

In order to test the suitability of the manufactured polymer toner particles as support materials for tissue engineering, we examined the cytocompatibility compared to human fibroblasts and keratinocytes. These cells indicated high viability on all polymers with a glass transition point above room temperature, which is comparable with growth on commercial cell-culture plates. The functionalization of the surfaces leads to increased cell proliferation that is up to 178 percent above that of the reference material. Printing tests with the functionalized surface toner material have been successfully carried out by our project partner Fraunhofer IPA using an electrophotographic printer. The particle systems developed to date allow us to print reactive structures on level surfaces and thereby bind materials that do not otherwise readily adhere.

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Project partners

Fraunhofer IPA, Stuttgart | IGVP, University of Stuttgart

1 *Tubular structures are created by removing the non-fixed supporting structure after printing. The matrix structure provides stability for the 3D object even after this.*

2 *Spherical poly(methyl methacrylate) toner particles created by suspension polymerization.*

3 *Confocal laser microscope image of the fluoresceinamine-functionalized particle surfaces. Overlaying the two-dimensional image planes (A) provides a three-dimensional image of the functionalized particles (B). Scale: x-axis = 27.5 µm, y-axis = 27.5 µm and z-axis = 3.5 µm.*

1

NEW CHEMICAL BUILDING BLOCKS FROM TERPENOID WASTE STREAMS

Dr. rer. nat. Michael Hofer

Terpenes as raw materials

Biomass is gaining more and more importance as a feedstock for the production of bulk and fine chemicals, thus replacing the limited supply of fossil resources such as oil or gas. Terpenes, for example, have been used for centuries as essential oils in medicine and for flavors and fragrances. They are abundant and inexpensive as they accumulate as waste streams in industrial processes such as cellulose production from conifers, making them an ideal starting point for the development of new chemicals and materials. The Fraunhofer Project Group BioCat focuses on the development of new catalytic processes for the targeted functionalization of terpenes in order to produce novel bulk and fine chemicals.

Chemo-enzymatic catalysis

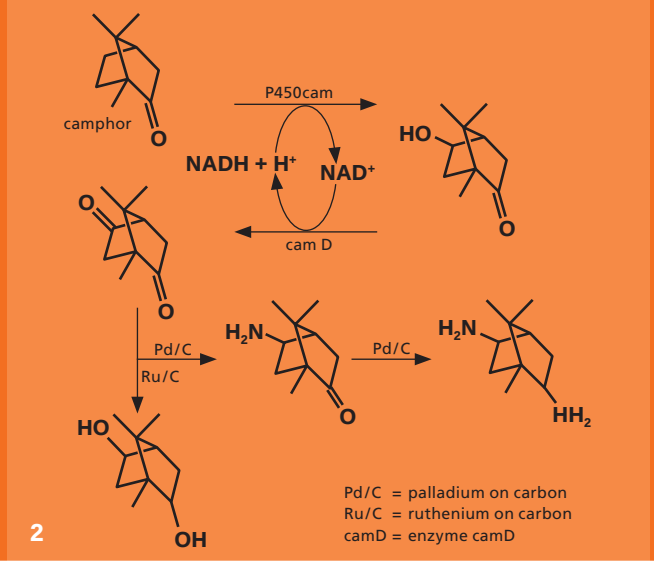
The selective functionalization of terpenes is a major challenge which can be addressed by combining biotechnological and chemical catalysts. To achieve this, the Fraunhofer Project Group BioCat uses P450 monooxygenases from natural and engineered enzyme libraries for the stereo- and regioselective oxyfunctionalization of terpenes. The targeted introduction of hydroxyl groups can already lead to a new product although the further modification of these hydroxyl groups by chemical synthesis results in a much broader product portfolio. Through oxidation and amination bio-derived mono-, di- and polyamines can be synthesized to create interesting building blocks for the chemical industry.

New catalytic processes for the production of novel molecules

The combination of P450 monooxygenase with an alcohol dehydrogenase resulted in an enzymatic cofactor neutral and a very efficient production process for diketocamphene. The further reduction of this molecule to a diol was successfully performed with a ruthenium-based catalyst. Besides, the amination of the diketone to the corresponding diamine was performed using a palladium catalyst. Therefore the combination of a natural enzymatic system from *Pseudomonas putida* with heterogeneous catalysts led to the production of new camphor-based bifunctional molecules.

Purification and analysis

GC as well as HPLC specific protocols for the selective detection of the synthesized functional groups were established and validated for the analysis of these new compounds. We also used NMR analysis to determine the configuration of the products. For this task and for future application tests by our customers, the molecules have to be purified from the synthesis broth. A quick and easy extraction process was developed for this purpose.



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Outlook

New polyfunctional bio-derived molecules from waste streams are interesting as a replacement for existing products obtained from fossil resources but also for the development of new materials. Our aim is therefore to develop more chemo-enzymatic processes for the production of new molecules. The first processes are already upscaled for the production of larger quantities of these molecules, which are then used for application tests by our customers. At the same time we are working on solutions for the simultaneous application of chemo- and biocatalysts in a one-pot reaction.

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Reference

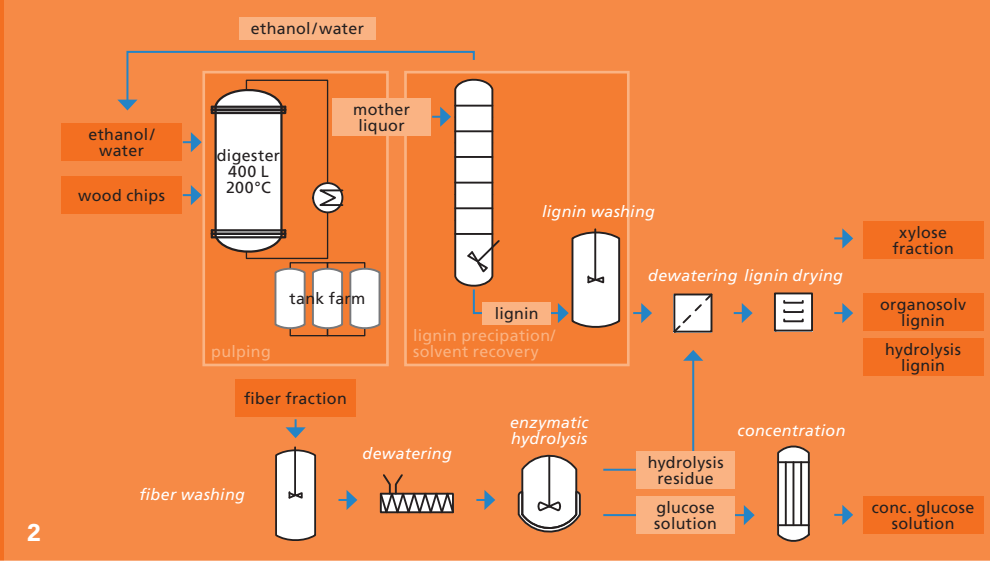
[1] Hofer, M. et al. (2013) ChemCatChem 5(11): 3351 – 3357

Funding

We would like to thank the Bavarian Ministry of Economic Affairs and Media, Energy and Technology for funding the project "Catalytic processes for a sustainable supply of raw materials and energy on the basis of renewable resources".

1 *Cellulose production.*
2 *Combined chemo-enzymatic catalysis based on the example of camphor.*
3 *Batch reactor for the conversion of diketocamphene.*

1



2

LIGNOCELLULOSE BIOREFINERY – SUCCESSFUL IMPLEMENTATION ON THE PILOT SCALE

Dr. rer. nat. Moritz Leschinsky, Dipl.-Chem. (FH) Gerd Unkelbach

Sustainable use of renewable resources

Rising prices for raw materials and the increasing scarcity of mineral oil resources are boosting the interest in renewable resources and in strategies for the sustainable production of special materials, fine chemicals or platform chemicals. Emulating the concept from the petrochemical industry these biobased materials will in future be made available by biorefineries. Native hardwoods offer themselves as a chemical feedstock that is available sustainably and without competing with foodstuff production. For the conversion of wood or lignocellulose into platform chemicals for the chemical industry of the future, the wood first of all has to be broken down and separated into its basic chemical components.

Organosolv lignin for a wide range of applications

In the second phase of the collaborative project "Lignocellulose Biorefinery" the concept of a wood-based biorefinery was successfully implemented on the pilot scale at the Fraunhofer CBP in Leuna. The necessary preliminary work for this was carried out together with the Fraunhofer Institutes IGB and ICT as well as twelve other industrial and research project partners. The "organosolv process" developed in the first phase of the project uses mixtures of alcohol and water to fractionate wood under pressure and at high temperature into its basic components cellulose, hemicelluloses and lignin. Cellulose and hemicelluloses can then be converted to sugars with the help of enzymes. Unlike with other fractionation processes, the resulting lignin is very pure and neither contaminated with sulfur nor with inorganic salts. This permits applications for a wide range of materials.

Scaling of the fractionation process to the pilot plant

The work at the Fraunhofer CBP focused on the scaling of the fractionation process to the pilot scale. The basic questions concerning the process specifications were worked on in joint preliminary work with the project partners. The plant was designed and planned in detail on the basis of these results.

The pilot plant comprises a large number of individual process steps for the production of concentrated sugar solutions and lignin powder obtained from wood chips. Up to 70 kg of wood (oven dry weight) can be processed in one batch. The plant was designed in such a way that the material and energy cycles are closed. The simplified diagram of the plant in Fig. 2 shows that the wood is first of all digested in a 400-liter reactor at up to 200°C; here lignin and hemicelluloses are solubilized in an ethanol-water mixture. The additional tanks and heat exchangers of the "tank farm" permit a fractional washing of the material under reaction conditions and the recovery of energy during the pulping process. From the pulping liquor enriched with lignin and hemicelluloses lignin is precipitated by adding water or distilling the ethanol; it is then filtered off and, after washing, dried. The ethanol used is entirely recovered by distillation from the filtrate and the hemicellulose sugars remain as an aqueous solution. The solid fibrous residue of the pulping process is disintegrated and washed, dewatered, enzymes are added and then, in stirred reactors specially designed at the Fraunhofer IGB, it is saccharified with a high concentration of the pulp. After a filtration step a glucose solution is obtained which is concentrated into a sirup to stabilize it.

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The pilot plant was built at the same time as the CBP was constructed. The pilot plant was successfully put into operation in spring 2013. Since then we have been further optimizing the individual processes as well as the overall process. Additionally, complete mass balances were recorded and product samples on the kilogram scale were distributed to the project partners so that they could carry out technical application tests.

Basic feedstocks for chemical and material utilization

The intermediate products obtained in the pilot plant – lignin and sugar – serve as feedstocks for utilization as chemical substances and other materials. The sugars achieved from the wood were used by the project partners as a feedstock for industrial biotechnology processes, in order to produce for example basic chemicals such as lactic acid, acetic acid, succinic acid or ethanol. The advantage of the sugars extracted from wood is that they do not compete with food production.

Because of its good thermoplastic properties the lignin obtained was used directly by the project partners in compounds for the extrusion of molded parts or as an alternative for the mineral oil-based phenol in resins and polyurethane compounds. The project partners also examined various chemical and biotechnological possibilities for lignin cleavage to create basic aromatic constituents. Altogether a large number of processes and products were developed with the sugar and lignin samples from the pilot plant.

Outlook

With the successful transfer of the organosolv fractionation process to the pilot scale we were able to demonstrate that the chemical utilization of wood using a biorefinery concept works on the technical scale. The pilot plant is being used within various international and national research projects to further optimize the process, to integrate the intermediate products obtained in various value chains and finally to pave the way for the industrial implementation of lignocellulose biorefineries.

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Funding

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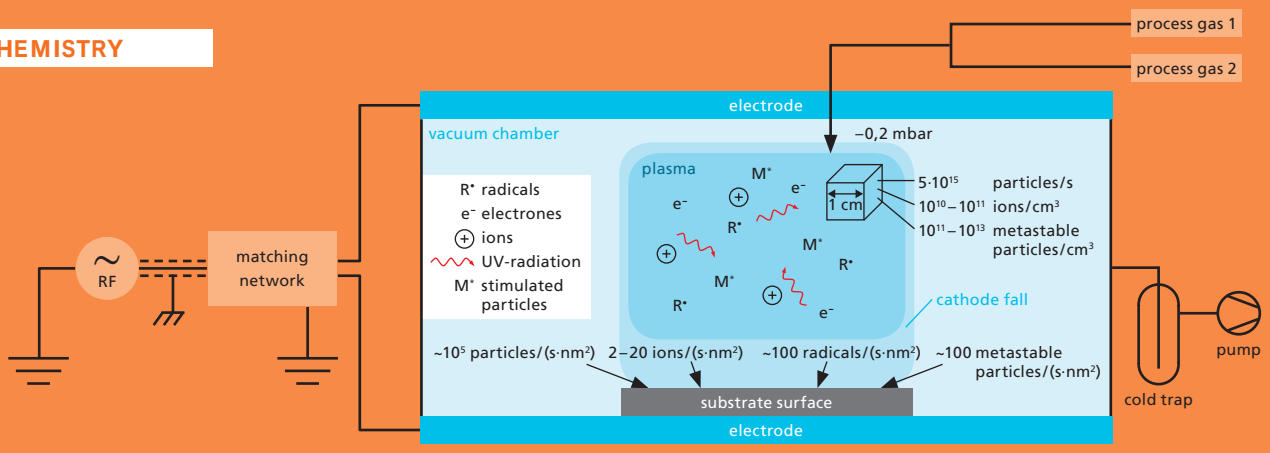
Project partners

DECHEMA (Coordinator) | Bayer Technology Services GmbH | Evonik-Degussa GmbH | Dynea Erkner GmbH, Tecnaro GmbH | InfraLeuna GmbH | Wacker AG | University of Hamburg | Fraunhofer ICT | Fraunhofer IGB | TU Kaiserslautern | Karlsruhe Institute of Technology (KIT) | Justus-Liebig-Universität Gießen

Further information

www.lignocellulose-bioraffinerie.de

1 *Pulp washing tank.*
2 *Simplified flow chart of the lignocellulose biorefinery pilot plant in Leuna.*
3 *Beech wood stem with pattern for sawing – the sawmill residues are used as a feedstock for the lignocellulose biorefinery.*
4 *Dewatering of the pulp.*



1

RAPID TESTING METHODS FOR MATERIAL CHARACTERIZATION – PLASMA WEATHERING OF SURFACES

Dr. rer. nat. Jakob Barz

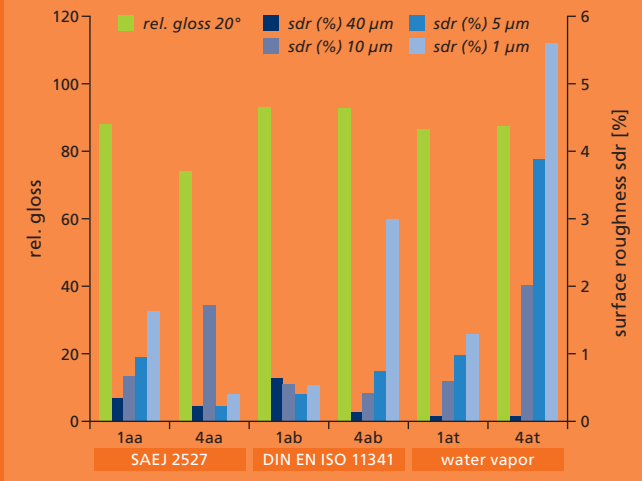
Costly time-consuming outdoor weathering for new materials

The product development cycles for new paints, coatings and other polymeric materials are complex, expensive and time-consuming, above all because of the testing methods used. The material surfaces, especially those for outdoor applications, have to be tested at outdoor weathering locations to determine their resistance to weathering. These tests may take several months or even years; the alternative is several thousand hours in weathering chambers with beam sources. If the facilities are certified outdoor weathering locations, the necessary testing equipment is, as it were, constantly in use and it is difficult for the developers to obtain test stands for new developments at short notice. Alternatively there is weathering equipment on the market that accelerates these tests. Even so, the test cycles take several thousand hours with this equipment too. At the same time, considerable running costs are incurred for electricity and beam sources. In both cases, there are major delays in the material development.

In order to develop and market product innovations more quickly, new testing methods need to be developed that permit developers to analyze the degradation characteristics of polymer surfaces, within a very short time and with a low consumption of energy. These evaluations should be comparable to those obtained with the conventional certified methods.

Imitation of natural weathering using plasma processes

Plasma-based processes are especially promising for weathering purposes. Here, the plasma serves as a source of radiation and particles. The effects of radiation, temperature, erosion and moisture, as well as the changes induced by them on the surfaces of polymers, can be obtained in a single process step with plasma processes. For the treatment the surfaces to be tested are placed in a specially adjusted atmosphere. By igniting a plasma, atoms and molecules are stimulated in the gas phase and partially ionized; existing molecules are fragmented and thus chemically activated. Many particles are stimulated in the plasma and relax under light emission, resulting in a broad electromagnetic spectrum. Radical chemical as well as photochemical reactions take place in the plasma phase and on the surface of the samples exposed to the plasma. If required, plasma ions can also be used to erode the surface. The composition of the plasmas can be controlled via the process parameters (pressure, plasma power, gas flow and gas type, duration of treatment). Fig. 1 shows the numerical ratios of the particles generated in a low-pressure plasma plasma.



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Verification of the degradation characteristics just hours later

In studies carried out by the Fraunhofer IGB for Bayer Material Science, polyurethane paint samples were weathered in various plasma atmospheres. Fig. 2 shows the results obtained using water vapor plasmas, compared with two standard weathering processes. Weathering with the addition of gaseous water produces degradation to the surface after only 60 minutes, whereas with classical artificial weathering according to SAE J2527 degradation characteristics become evident only after more than 1000 hours. This shows that artificial and plasma weathering result in a comparable degradation pattern, here reflected in the measurements for surface roughness and gloss.

Outlook

The results to date show, that plasma weathering has the potential to substantially shorten production development cycles. We are therefore currently investigating the specific effects of individual process parameters on the aging behavior of polyurethane and other polymers, to further optimize the plasma weathering process and to verify equivalence with recognized artificial and natural outdoor weathering procedures. Patents have already been filed for various technical solutions.

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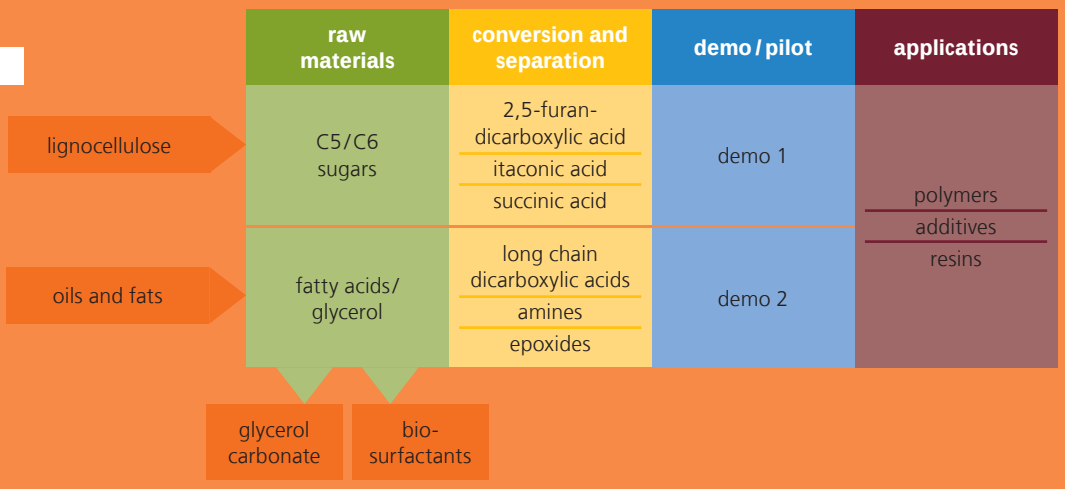
Project partner

Bayer Material Science, Leverkusen

1 *Particles in a plasma. The particle streams shown always refer to 1 nm² of the surface.*

2 *Comparison of various plasma and standard weathering processes for polyurethane paint. The bars show the results from the standard testing methods according to SAE J 2527 and DIN EN ISO 11341 as well as with a water vapor plasma. The measurements shown are the relative gloss and the surface roughness (sdr).*

3 *Paint surface before and after plasma weathering.*



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BIOCONSEPT – FROM PLANTS TO PLASTIC

Dr. rer. nat. Nicole Helber, Fabian Haitz M.Sc., Priv.-Doz. Dr. Steffen Rupp, Dr.-Ing. Susanne Zibek

Biobased polymers from second generation raw materials

The raw materials for industrial biotechnology come mainly from agricultural products – glucose from sugar-containing plants such as sugar beets, starch-containing plants such as cereals or plant oils from seeds. These "first generation" biobased raw materials are, however, in competition with food production and their use for the production of biofuels or biobased chemicals is controversial. A concept already being implemented in a biorefinery is the complete utilization of "second generation" raw materials. This includes lignocellulose from woodchips or agricultural waste streams and plant oils that are not used in the food industry.

The EU-funded project BioConSepT, in which 30 European partners from research and industry are participating with the Fraunhofer IGB, will demonstrate the exploitation of second-generation raw materials for the production of biobased polymers. The aim of the project is to provide processes which convert second-generation raw materials into valuable chemicals; it is intended that these processes will be up to 30 percent cheaper and more sustainable than corresponding chemical or biotechnological processes working with first-generation raw materials. The partners have developed methods for the production of chemicals from second-generation raw materials in which enzymatic, microbial and chemical reactions are used and combined with one another. The following have been identified as target molecules in an initial selection process: 2,5-furandicarboxylic acid, itaconic acid, succinic acid, long-chain dicarboxylic acids, diamines, diamides and epoxides. In addition, the production of biosurfactants and glycerol carbonate is being considered. The intention is to achieve breakthroughs in cost reduction and sustainability of the selected processes by introducing continuous processes, new reactors and selective separation technologies. An additional aim of the project is the provision of sample quantities for market testing of biobased polymers, resins, plasticizers, biosurfactants and solvents.

Dicarboxylic acids from plant oils

Long-chain dicarboxylic acids are chemically complex and expensive to produce, but are of interest as an intermediate for the synthesis of plastics such as polyesters. Yeasts of the species *Candida* or *Pichia* are capable of oxidizing fatty acids to form the corresponding dicarboxylic acids. The Fraunhofer IGB has already been able to establish a method for the production of dicarboxylic acids with the yeast *Candida cenakerosene*. It was possible to produce up to 100 g/l 1,18-octadecenedioic acid through fermentation in an optimized process from oleic acid [1]. As a part of the BioConSepT project, the formation of dicarboxylic acids from additional fatty acids from plant oils is being investigated at the Fraunhofer IGB. Alongside process development, new yeast strains for dicarboxylic acid production are currently being studied and robust production strains are created which permit high dicarboxylic acid yields.

Epoxides from plant oils

The epoxidation of unsaturated fatty acids and triglycerides generates products with increased polarity and reactivity. These epoxides can be used as PVC stabilizers, plasticizers or in biobased polymers. In terms of the stabilizers or plasticizers used in different plastics such as polyvinylchloride (PVC) or polylactic acid (PLA), epoxidized soybean oil (ESBO) is mostly used [2, 3]. In addition, the use of plant oil epoxides for photo-initiated cationic polymerization in thin-layer applications has been described in the plastics industry [4]. Within BioConSepT, a process is being developed at the Fraunhofer

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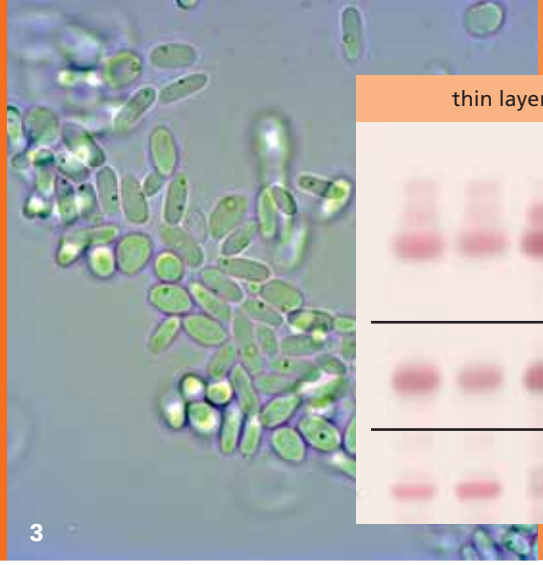

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IGB for the enzymatic production of epoxides using an immobilized enzyme to convert second-generation plant oils, including plant oils from waste flows.

Closing the gap between the laboratory and industrial practice

In 2014, BioConSepT will select the two most promising production processes for scale-up in order to generate product quantities of the order of 100 kg to 1000 kg. Conversion of the selected processes from laboratory to industrial scale will take place in the multifunctional facility of the Fraunhofer CBP in Leuna. In this way, BioConSepT should help to further reduce the gap between laboratory and industrial practice for the production of chemicals from biomass.

1 *Second-generation raw materials are to be converted into valuable chemicals.*
2 *Fermentation of Candida in a 42-liter bioreactor.*
3 *Candida cells and formation of dicarboxylic acid (DCA) from oleic acid methyl ester (OME).*

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Funding

We would like to thank the European Union for funding the project "BioConSepT" within the scope of the Seventh Framework Programme (FP7/2007–2013), grant agreement no. 289194.

Project partners and further information

www.bioconsept.eu

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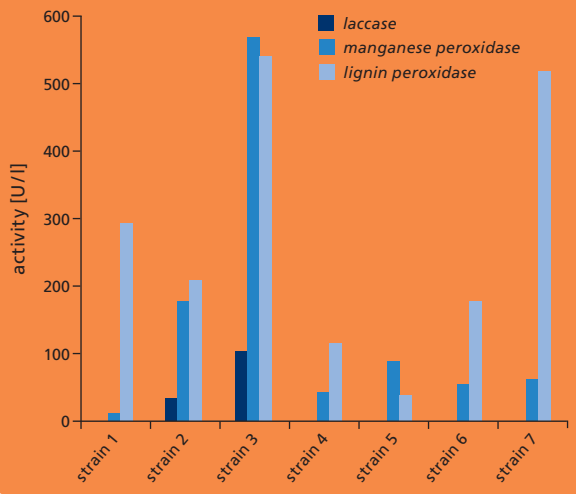


2

NEW ENZYMES FOR THE MODIFICATION OF LIGNIN

Dipl.-Biol. (t. o.) Dominik Rais, Priv.-Doz. Dr. Steffen Rupp, Dr.-Ing. Susanne Zibek

Lignin – a natural source of aromatic compounds

The cell walls of woody plant material consist of the composite material lignocellulose which is made up of the components cellulose, hemicellulose and lignin. Being a primary constituent of straw and wood, lignocellulose accumulates in large quantities as a waste material from agriculture and forestry and therefore is not in direct competition with food production. All components of this renewable raw material are used within the concept of a lignocellulose biorefinery.

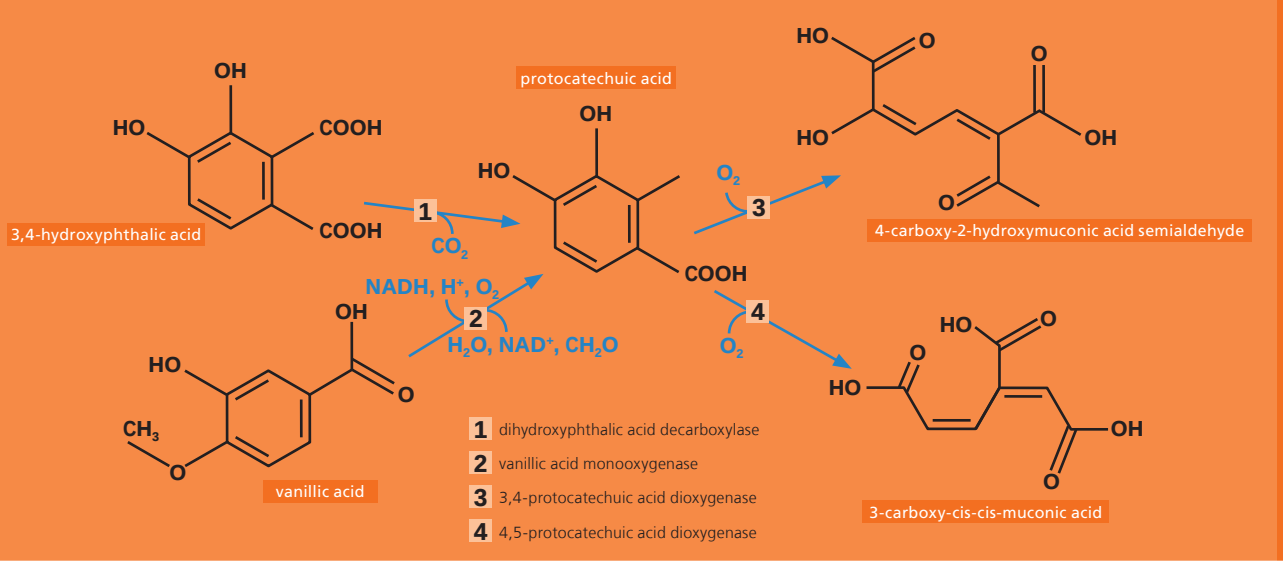
Cellulose and hemicellulose can be isolated from lignocellulose, hydrolyzed and the sugar monomers obtained can be converted chemically or by fermentation into many different chemicals. Lignin has until now primarily been used to generate energy, but it offers major potential for utilization as a building block in polymers. Lignin is formed from a combination of coniferyl alcohol, sinapyl alcohol and coumaryl alcohol and is the biggest natural source of aromatic compounds. Lignin can be used in the form of aromatic oligomers or monomers for the substitution of lots of petrochemically-based plastics and chemicals such as polyurethanes, synthetic resins or phenol. To do this, the lignin polymer must first be broken down at least partially and the pieces functionalized to become synthesis buildings blocks. Here, enzymatic methods promise ecologically efficient and selective conversion of lignin.

Lignin-modifying enzymes from fungi

White-rot fungi are the most well-known examples of lignin-degrading organisms. In the enzymatic degradation process of these fungi, predominantly the enzyme categories lignin, manganese and versatile peroxidases and laccases play an important role. The lignin peroxidases have a high redox potential and are capable of attacking non-phenolic structures in lignin directly. Manganese peroxidases oxidize Mn(II) to Mn(III), which in turn diffuses into the lignin molecule and oxidizes phenolic structures. The versatile peroxidases are hybrids of lignin and manganese peroxidases. Laccases have a low redox potential and can only attack non-phenolic structures by means of mediators [1]. Apart from the laccases, these lignin-modifying enzymes are only available at very high prices. An optimization of the production process for lignin, manganese and versatile peroxidases therefore continues to represent a challenge. At the IGB it has been possible, through the co-cultivation of different strains of fungi in submerged culture, to achieve an increase in the production of lignin-modifying enzymes [2] (Fig. 1). In collaboration with the Fraunhofer CBP, the yield of ligninolytic enzymes in submerged fungal cultures has been further optimized and transferred to a larger scale of up to 10 liters.

Bacterial lignin degradation

In addition to the production of ligninolytic enzymes from fungi, bacterial lignin degradation is also being researched. Some bacterial strains within the group of actinomycetes and among the α- and γ-proteobacteria capable of breaking down lignin are described in the relevant literature [3]. The bacterial mechanism of lignin degradation and its enzymatic background have, however, hardly been researched yet. In the culture supernatants of ligninolytic bacterial strains cultivated with lignin we have been able to detect peroxidase and laccase enzyme activity (Fig. 2). In order to exploit new bacterial enzymes, we are also studying the genomes of ligninolytic bacteria. Here, both DyP-type peroxidases, which may be



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involved in the degradation of lignin via similar mechanisms to those of the lignin or manganese peroxidases, and intracellular enzymes which metabolize lignin fragments, are of interest [3]. In the genome of a strain of *Pseudonocardia* sp., which was sequenced at the Fraunhofer IGB, we were able to find a number of putative enzymes for the metabolism of aromatic compounds. An interesting reaction here is the demethylation of vanillic acid by a monooxygenase, which generates a new functional hydroxyl group (Fig. 3).

DyP-type peroxidases from a variety of ligninolytic bacteria are being expressed and their catalytic properties investigated. The results should provide information as to what extent DyP-type peroxidases in bacteria assume the role of lignin-peroxidases.

Outlook

Enzymes that are very promising with respect to the modification and the degradation of lignin shall be produced on a larger scale and made available for industrial applications.

1 *Co-culture of Pleurotus ostreatus and Phlebia radiata in a shaking flask after 168 h incubation at 25°C. In the submerged culture it was possible to increase the enzyme production.*

2 *Ligninolytic enzyme activity in the culture supernatant of various bacterial strains.*

3 *Enzymes of protocatechuic acid metabolism from Pseudonocardia sp. may be of interest for the material utilization of lignin.*

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Funding

We would like to thank the German Federal Ministry of Food and Agriculture (BMEL) and the Agency for Renewable Resources (FNR) for funding the project "Lignocellulose Bioraffinerie Phase II", promotional reference 22019309.

Project partners and further information

www.lignocellulose-bioraffinerie.de

1


2

MANUFACTURE OF ORGANICALLY CERTIFIED COSMETICS FROM RENEWABLE RAW MATERIALS

Dr. rer. nat. Ana Lucía Vásquez Caicedo, Dr.-Ing. Susanne Zibek, Priv.-Doz. Dr. Steffen Rupp, Dipl.-Ing. Siegfried Egner

Increased demand for organic cosmetics

More and more, consumers are viewing the use of petrochemicals-based ingredients in cosmetic products critically and are increasingly asking for natural or organic cosmetics. However, the range and variety of the natural products are limited owing to the restricted availability of organically certified ingredients. Furthermore, the production of these cosmetic ingredients involves some technological challenges and is still very expensive. The cosmetics industry is therefore endeavoring to meet the rising demands of consumers as regards safety – for the environment and for health – of the raw materials used, and to replace fossil-based with renewable resources.

Certifiable manufacturing production process from the cultivation of the raw materials through to the biobased product

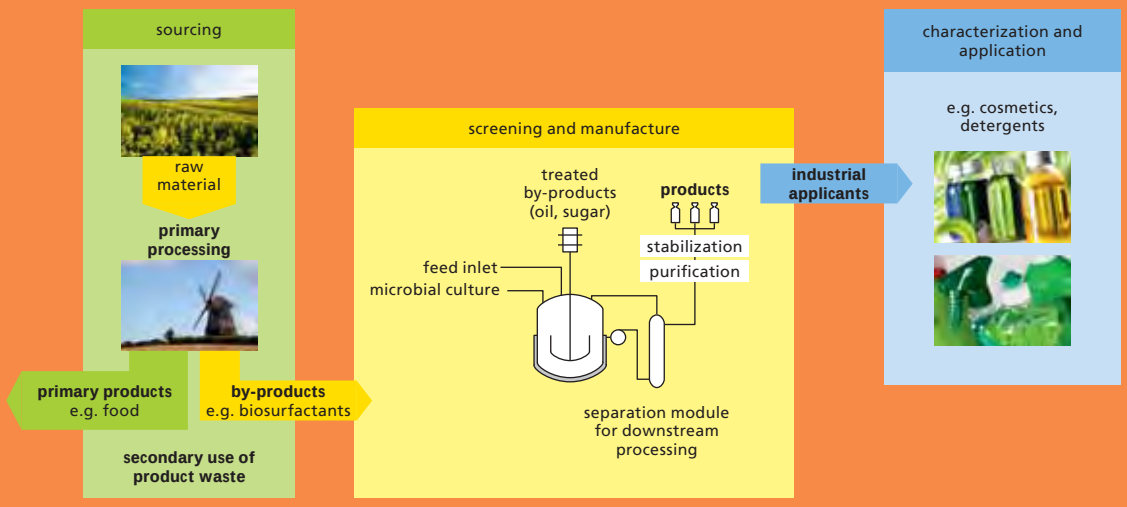
This challenge is being tackled by the consortium of the EU-funded project "O4S – Sustainable surfactant production from renewable resources through natural fermentation for applications in natural, organically-certified products". The O4S project is developing a fully certifiable process chain by means of which renewable resources can be obtained from certified organic crops using environmentally-friendly methods to produce biobased emulsifiers and biosurfactants, in order to use them in organically certified cosmetics. Accordingly, the aims of the project are the identification of organically certified, affordable substrates such as sugars and oils and the development of a certifiable manufacturing process for biosurfactants. The substrates should be obtained from waste materials from organic agriculture and by-products from food production.

Biosurfactants – alternatives to chemically synthesized biosurfactants

Surfactants and emulsifiers can be found not only in cleaning agents and detergents, but also in cosmetics. Shampoos, shower gels and bath additives consist of up to 40 percent surfactants, which lower the surface tension of water. A large proportion of the surfactants currently used are chemically derived. Although oils from renewable raw materials are increasingly being used as raw materials in addition to petroleum, the coconut or palm kernel oils generally used are classified as ecologically critical. Biosurfactants are an alternative to this. These are washing-active substances produced by microorganisms. Currently, only a few of these biosurfactants are produced industrially, since their production is still relatively expensive. In order to make biosurfactants profitable for natural cosmetics, the Fraunhofer IGB is developing, in the O4S project, a sustainable, cost-reducing and certifiable manufacturing process, which includes the biotechnological fermentation and the purification of biosurfactant products.

Manufacture of organically certified biosurfactants

In order to be able to classify biosurfactants as 100 percent certified "organic", the whole process chain must be evaluated and certified. This starts with the selection of the feedstocks: their suitability as a source for a certifiable fermentation process is examined on the basis of the standardized



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specifications of the International Natural and Organic Cosmetics Association Natrue. For example, we initially investigated the availability of waste materials such as husks and olive oil residues and the particular conditioning and/or conversion steps required and assessed the relevant ensuing costs. In a subsequent step we tested biosurfactant formation in a variety of selected microorganisms on these substrates along with the separation and purification of the surfactants. Furthermore, we determined their chemical and physical properties (solubility, pH stability), sensory properties (color, smell) and application-related properties (foaming, emulsifying and antimicrobial properties) in collaboration with research and industry partners.

Integrated system approach and outlook

Of fundamental importance for the project is the integrated system approach encompassing all stages of the process chain. For example, it must be ensured that both the waste materials from organic agriculture and the methods for feedstock conditioning into substrates that can be utilized by microorganisms are suitable for the manufacture of certifiable biosurfactants. Likewise, environmentally sustainable methods must be developed and implemented for the separation and purification of the surfactants produced using biotechnological methods as well as for their subsequent stabilization and formulation.

Depending on the choice of substrates and purification strategy, products with a variety of chemical and physical properties are obtained. Using precise characterization, the surfactants obtained can be used for a suitable application. In order to be able to use the biosurfactants available in an optimum way, a formulation platform is being developed on the basis of the characterization. From this, specific product requirements in relation to the formulation can be derived, for example whether the biosurfactant should be stabilized as a powder or in liquid form, in order to ensure stability of the biosurfactant over the logistics chain. In this context, the hygiene-related and regulatory requirements play a major role in relation to product safety and consumer acceptance.

Finally, the integrated system approach takes into account the total mass and energy balance and provides an industrial design concept, which enables this manufacturing process to be transferred to industrial application.

1 *Agricultural waste from certified growers is to supply biosurfactants for cosmetic products.*
2 *Production of biosurfactants in a 42-liter bioreactor.*
3 *The whole process chain should be designed in such a way that the methods used meet the criteria of the organic associations to gain an end product that is 100 percent organically certified.*

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Project partners and further information

www.organic4surfactants.eu

ENVIRONMENT

Dipl.-Ing. Siegfried Egner

In the context of worldwide discussion on the greenhouse effect, the switch to renewable energy and the scarcity of resources, resource-efficient industrial processing and environmental protection are more important then ever. Interdisciplinary by nature, these tasks require extensive R&D – which is where we come in. The Fraunhofer IGB's Environment business area stands for a variety of technological developments that contribute toward technological progress and economic success on the one hand but which simultaneously help to prevent negative environmental impacts – thus reconciling economic and ecological sustainability.

Typically, tasks and approaches in the Environment business area are strongly linked with topics in the Energy and Chemistry business areas. In the framework of joint European and national projects with partners from research and industry, the Fraunhofer IGB is developing processes and system components which help to protect the environment as well as to recover materials and substances for recycling efficiently to prevent drawing from natural resources. Examples are the innovative DEUS 21 infrastructure concept for semi-decentralized energy and water management and research into how to avoid the emission of particulate or dissolved persistent micro-pollutants. In order to improve the quality of secondary raw materials and make them competitive with virgin materials, we are developing new treatment processes by which dissolved mixtures can be selectively separated on a molecular or atomic level. The capability to recover substances from agro-industrial residuals or from municipal wastewater treatment plants in the direct form of high-quality fertilizer and soil conditioner spells an opportunity to reduce the consumption of both material and energy resources. Another example is the regenerative production of algae biomass for material and energetic utilization. The fixation of carbon dioxide not only spares the climate, but also yields high quality raw materials, such as for cosmetics or organic crop protection.

To prove the sustainability of the products and processes developed by the Fraunhofer IGB, we carry out systematic analysis of all environmental impacts of a product during its life cycle – from production via use to its disposal. We perform this "ecobalance" known as life cycle assessment in conjunction with various specialized partners.

More complex projects in the Environment business area are carried out by interdisciplinary teams drawn from the natural sciences and engineering. Participation in the Fraunhofer Building Innovation Alliance, Cleaning Technology Alliance, and Water Systems (SysWater) Alliance, as well as in the national technology platform SusChem Deutschland, gives the Fraunhofer IGB access to further expertise, as do its excellent networking activities at an international level, particularly within Europe.

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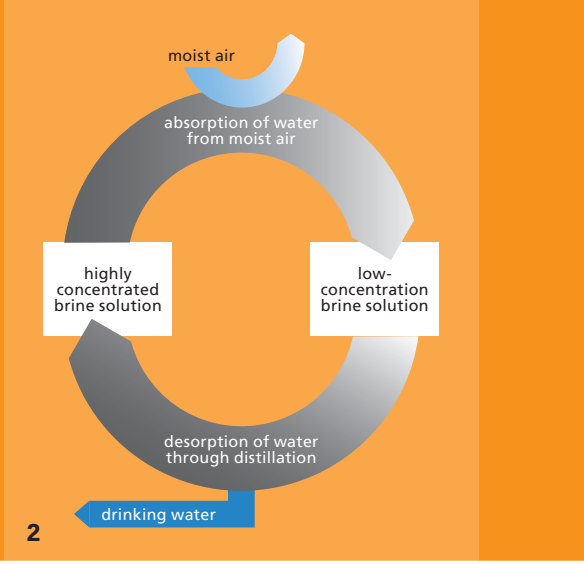

2

WATER EXTRACTION FROM AIR MOISTURE USING AN INNOVATIVE SORPTION METHOD

Dipl.-Ing. Mike Blicker

Exploiting new drinking water resources

Safeguarding a drinking water supply for a growing world population is one of the most important tasks facing the generations of today and tomorrow. Already, in several regions of the world, there is no reliable supply of drinking water and increasingly climate change is making the situation worse, particularly in arid and semi-arid areas. Above all in regions where there is no access to surface water or groundwater that is sustainably usable, the water contained in the ambient air as moisture can, essentially, provide a virtually inexhaustible source of water. The latest technology, however, has so far provided only a few systems available on the market, for example by condensation of humidity by cooling of air down to the dew point. Their disadvantage is a very high specific energy consumption and high operating and plant costs. In addition, cooling condensation only works under certain climatic conditions.

Innovative sorptive method for the extraction of water from air moisture

The approach taken by a new method developed at the Fraunhofer IGB is the extraction of water from air moisture using a combined absorption/desorption process. To achieve this, the absorption of air moisture by a liquid absorbent material, a highly concentrated brine, is combined with desorption by means of vacuum evaporator technology (Fig. 2). The aim of a project funded by the state of Baden-Württemberg and the EU was to demonstrate, together with development partners from industry, the feasibility of an energy-self-sufficient, mobile facility for the decentralized extraction of water from air.

From the laboratory to field trials

The first step was the elaboration of the technical and scientific principles, the parameterization of the system and a series of preliminary trials. On the basis of these, the subcomponents were designed and built. After manufacture of the components, the individual systems were comprehensively tested. Following amalgamation and integration of the whole facility into containers, a series of practical trials was carried out for the purposes of evaluation of performance and demonstration of the technology as a whole.

With the demonstration plant we were able, together with our development partners, to implement the technology for water extraction from air moisture on an application-oriented scale and in a quality that meets the requirements of industry. The plant consists of three containers which, alongside the absorption and desorption modules, contain all the required auxiliary units, a brine reservoir and an energy store (Figs. 1, 3 to 5).

Successful start-up and test phase

In a test phase lasting several weeks in autumn 2013 we were able to show that the subprocesses and the facility overall work well and that water can also be extracted from air moisture under real conditions. It was possible, even under what in some cases were very unfavorable environmental conditions regarding moisture content and temperature, to absorb water from the air and to separate it from the sorbent as usable drinking water.

Thus the method represents an alternative to the established facilities that use cooling condensation. An advantage of the new technology is the use of thermal energy as a main source of energy for the most energy-intensive subprocess of desorption; this can be obtained from waste heat or through solar thermal energy. Even the electric energy required for the smaller loads such as the pumps and controls can be obtained from renewable sources, via photovoltaics or wind, allowing the plant to be used in an energy-self-sufficient way. The overall design is sustainable and CO_2-neutral thanks to the use of renewable energies. In addition, no waste products are produced and all working materials are fed back into the cycle.

Outlook

It is intended that the successfully implemented demonstration plant be tried out at different locations in the future and the technology be optimized. It is planned to realize additional pilot plants together with partners, and to further develop the technology so that it is ready for the market. The method for water extraction from air moisture could in many regions make a contribution towards supplying drinking water, in particular in the Middle East, parts of South-East Asia, the extended Mediterranean region and Africa where a safe supply of drinking water is of vital significance to the population living there. Also conceivable is a transfer of the technology to applications in overcrowded areas, for example for decentralized drinking water production in megacities.

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Funding

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Project partners

Maschinenbau Lohse GmbH, Heidenheim | Michelberger Energietechnik GmbH, Bodnegg | Melotec Kunststoffverarbeitungs GmbH, Ulm | IGVP, University of Stuttgart

1 *Demonstration plant.*
2 *Principle of sorptive water extraction from air moisture.*
3 *Photovoltaic unit and tower of the demonstration plant.*
4 *Row of valves.*
5 *Plant controls.*

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CLOSING MATERIAL CYCLES TO ACHIEVE SUSTAINABLE PRODUCTION OF FERTILIZERS AND SOIL CONDITIONERS

Jennifer Bilbao M.Sc., Dipl.-Ing. (FH) Daniel Frank

Initial situation

The expansion of the bioeconomy simultaneously accompanied by a worldwide growing need for food has resulted in an ever-greater demand for fertilizers. However, the supply of fertilizers is increasingly limited, due to the high primary energy consumption for the production of synthetic nitrogen fertilizers, for example. In addition, now that the available phosphorus resources no longer have a high degree of purity, the exploitation and processing costs are rising as well. A way out of this situation in terms of sustainability is offered by the recycling of the basic nutritional elements phosphorus (P), nitrogen (N) and potassium (K). To achieve this, the nutrients have to be recovered from the material cycles of industrial production, food production, municipal wastewater and also from the bioenergetic recycling or the processing of renewable resources.

Nutrients management by closing material cycles

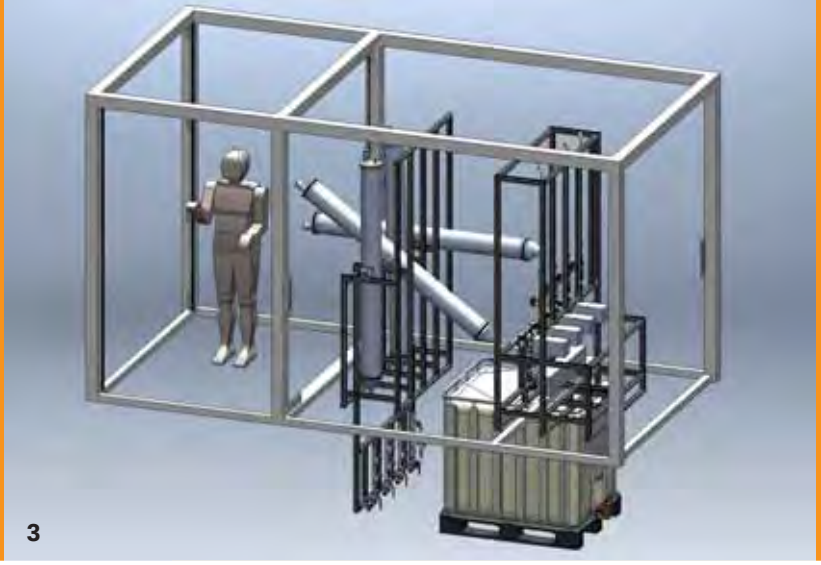
The recovery of nutrients is of vital importance for a sustainable nutrients management that will continue to be viable in the future. The Fraunhofer IGB is working on the development and implementation of sustainable cost-efficient technologies and strategies for integrated resource management. The main emphasis is on the development of new technologies for the recovery of nutrients from wastewater and organic residual matter such as liquid manure, fermentation residues and industrial residues, for example, from the food industry.

Our methodology includes the standardized characterization and evaluation of various solid and liquid residues with the prospect of recovering nutrients. Depending on the material characteristics of the initial substrate, we develop new, specific processing technologies to achieve the highest possible recovery rates. In our subsequent downstream production processes, the nutrients are precipitated or pelletized in such a way that they can be marketed as a fully fledged, specific product to be utilized in various agricultural sectors. Fertilizers can be manufactured and offered for sale both in solid and liquid form. We offer the possibility of developing customized product formulations, manufacturing sample amounts and characterizing them accordingly.

Electrochemical process for the recovery of magnesium-ammonium-phosphate

The Fraunhofer IGB has developed and patented a new electrochemical process for the recovery of ammonium (NH_4^+) and phosphate (PO_4^{3-}) from wastewater. Here NH_4^+ and PO_4^{3-} are precipitated as struvite (magnesium-ammonium-phosphate, MAP, $MgNH_4PO_4*6\ H_2O$) using a magnesium electrode. Our process has the advantages that no chemicals such as $MgCl_2$ or NaOH have to be added, and that only a low consumption of energy is required (70 Wh/m³ wastewater).

The electrochemical process was successfully demonstrated with an electrolytic cell using various approaches to testing, such as batch and continuous processes in addition to varying ion concentrations (20–500 mg/l PO_4-P and 100–1500 mg/l NH_4-N). A pilot plant is available with a throughput volume of 1 m³/h wastewater for trials at various locations with different feed streams, for example, to wastewater treatment plants.



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Soil conditioners from organic residues

The direct application of untreated fermentation residues or liquid manure to fields generally results in losses of nitrogen through emission of ammonia, by nitrate leaching as well as release of nitrous oxide, leading to concerns of climate change. The recovery of N, P and K salts as well as the conditioning and stabilization of an organic matrix can reduce these nitrogen losses from the soil and increase the efficiency of the nutrient utilization. Additionally, by using organic solid residues alone, a soil-specific substrate can be created, with which the quality of the planted areas can be improved, e.g. regarding their moisture and nutrient absorption capacity.

In various national and EU-funded research and industrial projects, we are working on the processing of such residues and nutrients recovery, from both the liquid phase (precipitation of P salts, production of an ammonium sulfate solution) and the solid phase (drying with a new type of low-energy process to produce carbonaceous soil conditioners).

Fertilizer products combined with plant protection

In EU-funded projects, we are also focusing on the development of environmentally-friendly plant protection products that can be combined with nutrients in a quantity that is optimal for the plant. For instance, a preparation suitable for the treatment of downy mildew and enriched with micronutrients is being developed in a project for organic viticulture. We utilize microalgae for the production of this natural plant protection product in order to reduce the use of copper-based fungicides in agriculture.

Outlook

Our technologies are constantly being further developed and implemented by a team of scientists and technicians to meet specific customer requirements. Our portfolio ranges from the initial idea to realization on a pilot scale and includes field trials to test the effectiveness of these special-purpose fertilizers. Together with our partners and customers, we can therefore recover nutrients from a very wide range of material cycles and process them to create designer fertilizers in order to close nutrient cycles.

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Funding

We would like to thank the European Union, the German Federal Ministry for Economic Affairs and Energy (BMWi) and the German Federal Ministry of Education and Research (BMBF) for funding various projects.

1 *Phosphate salt crystals obtained by precipitation.*
2 *Dried and pelletized organic soil conditioners from fermentation residues.*
3 *Pilot plant for the electrochemical extraction of magnesium-ammonium-phosphate from wastewater.*

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MORGENSTADT – WATER IN THE CITY OF THE FUTURE

Dr.-Ing. Marius Mohr

The Fraunhofer Morgenstadt – City of the future

Worldwide, the number of people living in cities is growing by leaps and bounds. Cities use large quantities of resources and, as a result of the high population density, place particular strain on the environment. On the other hand, cities are extremely dynamic systems in which innovations can spread rapidly. To achieve sustainable development for cities, technical and organizational innovations are required as is their rapid implementation. These innovations can only be developed and implemented through interdisciplinary cooperation. To this end, ten Fraunhofer Institutes have teamed up with local authorities and businesses to form the innovation network "Morgenstadt: City Insights".

Innovations for the city of the future

In an initial phase, from June 2012 to October 2013, researchers from the participating institutes observed six selected cities worldwide and analyzed examples of successful developments in eight key sectors. The aim was to identify action fields and impact factors for sustainable city development and from this, to develop an action-oriented model for sustainable city development. The Fraunhofer IGB made its contribution in the water infrastructure sector and adopted the management of the interdisciplinary team during a two-week research assignment in Copenhagen in March 2013, in which a total of 13 practical examples were studied. In the water infrastructure sector three practical examples were analyzed.

Reduction of water consumption

Supplying a city's population with drinking water is essential across the globe. Denmark's groundwater resources are limited. Consequently, in the 1980s it was decided in Copenhagen to reduce the per capita drinking water consumption through a series of measures. In this way it was possible to reduce the average consumption of 170 liters per inhabitant per day to 104 liters (2013). Unlike in Germany, where a reduction in the specific water consumption is now frequently viewed critically, Copenhagen is aiming to reduce its consumption to 90 liters per inhabitant per day by 2025, so that, in spite of population growth, the available water resources are also sufficient in the future.

Adaptation to climate change

The appearance of increasingly severe, heavy rainfall in the summer months is currently the most important water-related issue in Copenhagen. In 2010 and 2011, three instances of unusually severe rainfall resulted in considerable damage to the infrastructure and in insurance claims of almost a billion euros. Since as far back as 2008, the city administration has been working systematically on the development of plans to adapt the infrastructure to this trend. Since 2013, initial measures have been put in place. As with almost all strategies in Copenhagen, there is a focus here on increasing quality of life as well as on hazard prevention: through additional green spaces and bodies of water in the city, rainwater is to be stored and drained away, while at the same time spaces are created for recreation.

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Engineered ground filter for rainwater treatment

Connected with this, there is also the development of an engineered ground filter (dual porosity filter), which has been developed at the University of Copenhagen in collaboration with companies and the city administration. Requiring little maintenance, the filter takes dirty rainwater from the roads and produces high-quality water that can be fed into municipal watercourses.

Impact factors

The most important impact factors as far as the city of Copenhagen is concerned, are the pursuit of a high life quality at all levels of planning, the local scientific expertise (universities) and a highly motivated and competent city administration with numerous employees. In addition, the awareness of being an international pioneer in the field of sustainability and to be able to export successfully implemented solutions worldwide, contributes to the town's success. After all, Copenhagen is aiming to be the first climate-neutral capital city in the world by 2025.

Outlook – partner for Morgenstadt

Since January 2014, the second phase of the Morgenstadt innovation network has been under way; here the implementation of innovations in towns is being prepared on the basis of the data collected and the derived action model. Parallel to this, the Morgenstadt network is supporting the National Platform for the City of the Future, in which – coordinated by three federal ministries – a comprehensive strategic research agenda involving players from industry, science and local authorities is being developed. It is intended that in response to the calls already published from the EU research program Horizon 2020, the network will create applications for joint projects. Currently the network is still open for new partners from industry and local authorities.

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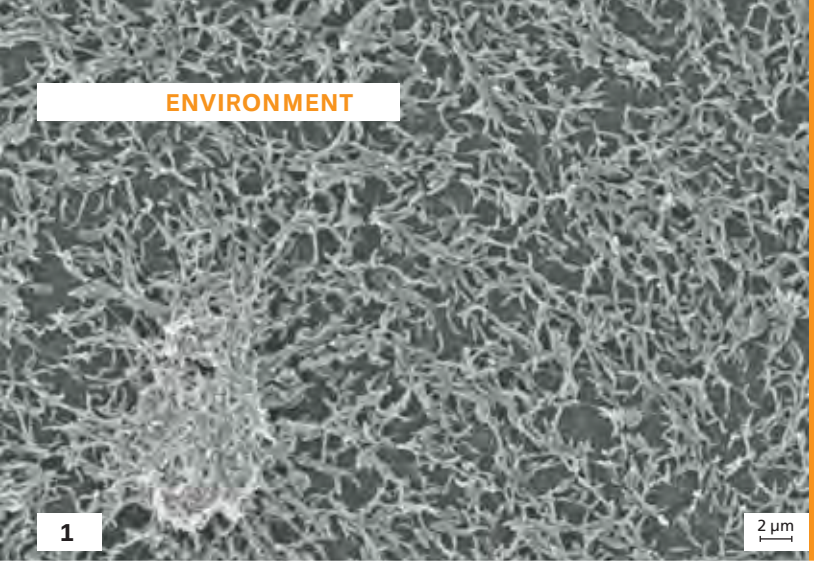
Project partners and further information

www.morgenstadt.de

Within the context of the regional project "Integrated resource management in Asian cities: the urban nexus" being carried out by the Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) [German Society for International Cooperation], the Fraunhofer IGB is already actively involved in advising Asian cities on the interconnection of the water, energy and food security sectors.

1 – 4 *Views of the city of Copenhagen.*



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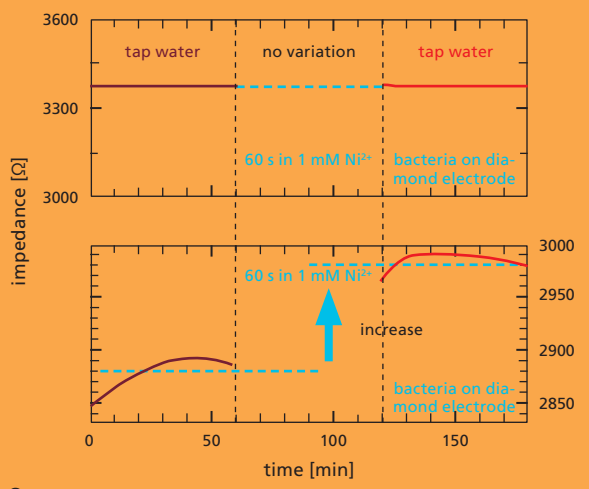

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DETECTION OF HAZARDOUS SUBSTANCES USING A COMBINATION OF PHYSICAL AND BIOLOGICAL SENSOR TECHNOLOGY

Dr. rer. nat. Iris Trick

Threat to drinking water networks from toxic substances

Contamination from industrial accidents, targeted poison attacks and pollution through the leaching of pesticides from farmland are unforeseeable events. For the population they constitute risks that should be taken seriously, as toxic substances may enter the drinking water supply systems via the groundwater or watercourses. Motivated by the need to improve the treatment and distribution of drinking water compared to the status quo by using suitable inline measurement technology, employees of the Fraunhofer IAF and Fraunhofer IGB have teamed up to pool their expertises. Physical and biological methods come together in the "TOXIKOMB" project in order to offer an innovative solution with improved, but – above all – rapid detection of hazardous substances in the field of drinking water.

Approach

The aim of the project is to detect toxic substances certainly and rapidly by combining electrochemical methods and infrared spectroscopy with biological systems. The priority is not to detect the presence of specific substances but detecting their toxic impact. Whilst chemical methods of analysis are capable of identifying specific substances, live cell sensors can show toxic influences with the aid of their reaction patterns. The first intended model application for the detection system developed in the project is monitoring of drinking water.

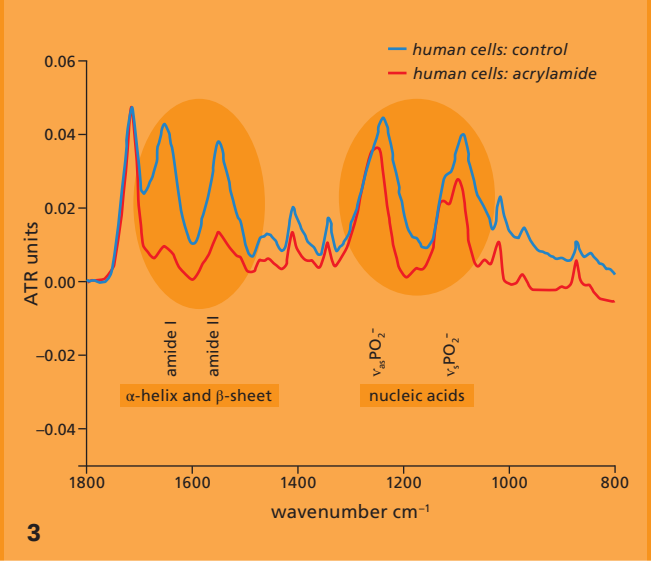
Biological sensors reveal toxic effects

In order to determine the toxic effects of substances, we use mammalian cells and microorganisms as biological sensors. The two cell types differ in respect of their sensitivity to a variety of substances. *Caulobacter crescentus* was selected as a bacterial sensor while human embryonic kidney cells were established as a mammalian cell system for the studies.

Impedance measurement of biological signals

The response of the biosensors to different substances is recorded using impedance measurement and evaluated. Here, the alternating current resistance of a cell-coated electrode is measured as a function of time. The basis for this method is the fact that the way biological systems respond to different molecules depends on their molecular structure. The associated interactions can influence both structural components of the cell and metabolic reactions. The activity of the cell is thus impaired, depending on the species-specific properties, by cytotoxic substances. This either affects the interactions at interfaces (neighboring cells, material surfaces), or results in a measurable change to cellular components. These responses can be tracked by means of impedance measurement, since they have an influence both on the charges at the surfaces and on the spectrum of cell wall components and reaction products.

The first aim was to check which electrodes are suitable for carrying out impedance measurements on immobilized microbial and mammalian cells. Fig. 1 shows *Caulobacter crescentus* grown onto diamond electrodes developed at the Fraunhofer



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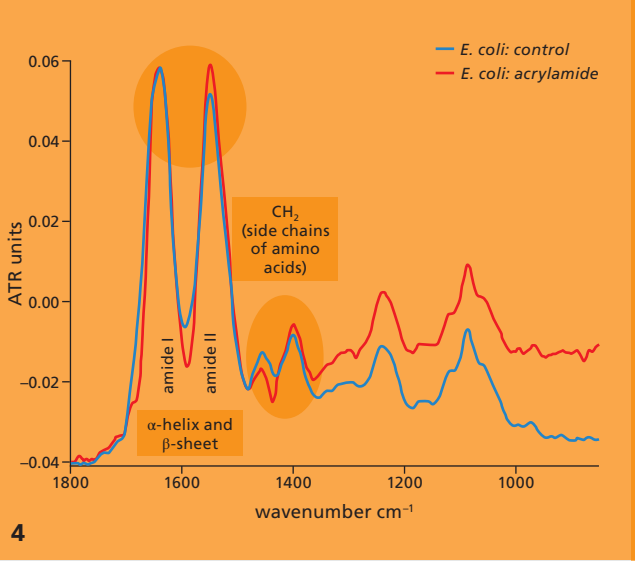

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IAF. Fig. 2 illustrates the change in the impedance as a response by the cells to nickel acetate which was used as one of the test substances.

Supplementary IR measurement technology and integration in a measuring cell

The method is supplemented by measurements using infrared spectroscopy (IR) which on the one hand permits the detection of chemical substances. On the other hand IR highlights chemical effects on proteins, amino acids and nucleic acids. The IR source used in the process is a quantum cascade laser (QCL) developed at the IAF. Measurements using infrared spectroscopy provide the proof of concept that cell components such as the protein structure of mammalian and bacterial cell systems change in a substance-specific way (Figs. 3 and 4).

It is intended that both measuring methods ultimately be integrated into a measuring cell suitable for inline monitoring.

Outlook

This subject matter is primarily relevant for drinking water suppliers but also for large residential complexes or industrial enterprises who wish to continuously monitor their facilities. In this way consumers will be offered a greater level of safety.

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Funding

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Project partners

We would like to thank our colleagues at the Fraunhofer Institute for Applied Solid State Physics IAF in Freiburg for such good co-operation.

1 *Microbial growth on a diamond electrode.*

2 *Electrochemical measurements on tap water with Caulobacter crescentus as a biosensor on diamond. When nickel acetate is added, a clear increase in the test signal is shown (below). Above: Control, no change in impedance.*

3 *Acrylamide reacts with nucleic acids and proteins of human cells, detectable from a change in infrared bands.*

4 *Response of Escherichia coli to acrylamide, reaction with amino acids detectable.*

ENERGY

Dr.-Ing. Ursula Schließmann

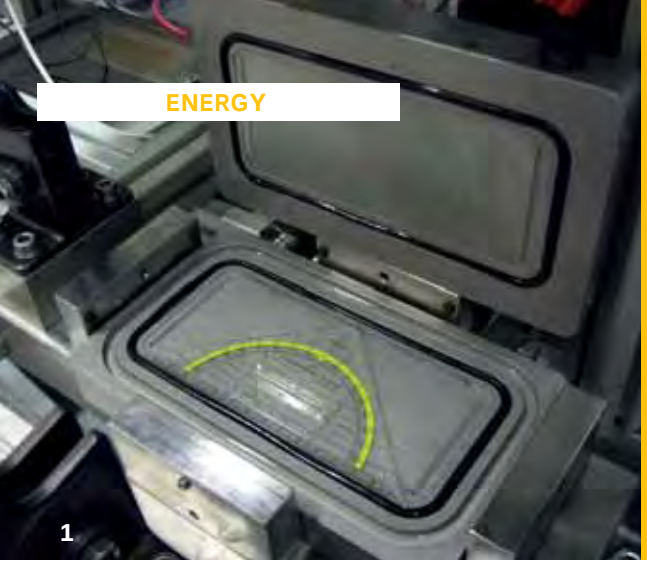
Ensuring an adequate future supply and efficient use of energy is of the highest economic priority, since the primary energy sources that we currently use to meet the greatest part of our energy needs are finite. The use of crude oil, natural gas and coal also leads to a rapidly rising concentration of CO_2 in the atmosphere – and consequently incalculable climate change. As a result of the use of these fossil energy carriers and the reduction of the overall capacity for photosynthesis, the Earth's net energy content is continually decreasing.

Making the transition to a sustainable energy supply is thus one of the 21st century's major challenges. Energy efficiency, the use of regenerative energies and energy storage are fundamental components here. At the Fraunhofer IGB we take on this challenge: key fields of action are sustainable energy conversion, the optimization of the energy efficiency of processes, e.g. through coupling processes, and developing suitable energy storage systems.

We contribute, for instance, to expanding photosynthesis capacity by developing methods for cultivating microalgae; we also advance the exploitation of regenerative energy sources by means of highly innovative membrane technology (gas separation, fuel cells, osmosis power plants). A specific example is the development of membranes for oxygen enrichment to facilitate more efficient combustion reactions in energy-intensive sectors such as the cement or steel industries. A further focal point is the development of absorption and membrane processes or ionic liquids that have a high capacity to bind CO_2 and separate it efficiently from biogas.

Further developmental work to improve energy efficiency includes the production of biogas from organic waste, by-products of the food industry and primary agricultural production, as well as energy savings achieved through process optimization at municipal and industrial sewage plants and anaerobic wastewater treatment. Noteworthy in this context are also industrial processes such as the drying of biomass and porous materials with super-heated steam at ambient pressure, and methods for rapid energy input, e.g. microwave pyrolysis. Additionally, the Fraunhofer IGB is developing systems for stable long-term storage of thermal energy in order to make waste heat available for temporally and spatially decoupled heat requirements. A further project is refining biogas for CNG-powered vehicles.

We are also active in designing integrated material flow and energy concepts for municipalities and regions, replacing the current, historically grown solutions with systematic approaches using state-of-the-art technologies. For this purpose, the Fraunhofer IGB is an active partner in the Fraunhofer Energy, Building Innovation and Water Systems (SysWasser) Alliances, as well as the Fraunhofer Morgenstadt (city of the future) initiative.



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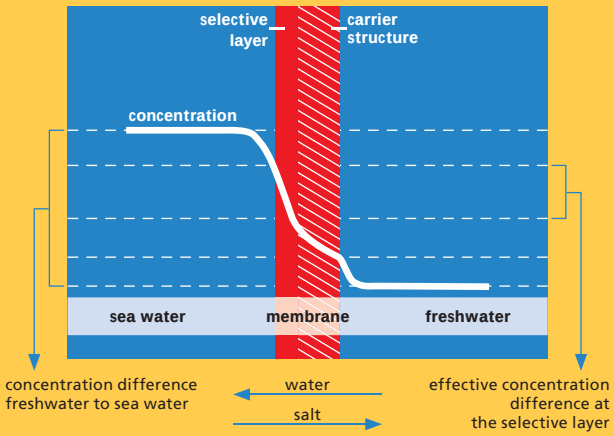


2

ENERGY CONVERSION BY OSMOSIS

Dipl.-Ing. (FH) Christopher Hänel, Dr. rer. nat. Thomas Schiestel

Emission-free energy conversion by osmosis

In energy conversion by means of osmosis two water flows with different salt contents are brought into contact via a semipermeable membrane. The membrane is permeable to water but rejects salt. Water is therefore continuously transferred to the water flow with the high salt content. As a result, a hydrostatic pressure builds up there, which is relaxed via a turbine, thus enabling the generation of electrical energy. Overall, chemical energy is therefore converted into electrical energy.

The principle of this Pressure Retarded Osmosis (PRO) has been known since the 1970s. However, because of the high price of membranes, the low water transfer and a high salt leakage rate of the available membranes, the principle has not so far been implemented on a technical scale. Though there is an immense potential at river estuaries for osmotic power plants producing emission-free electrical energy [1] and in times of climate change and increasing energy prices the interest in implementing this potential has grown.

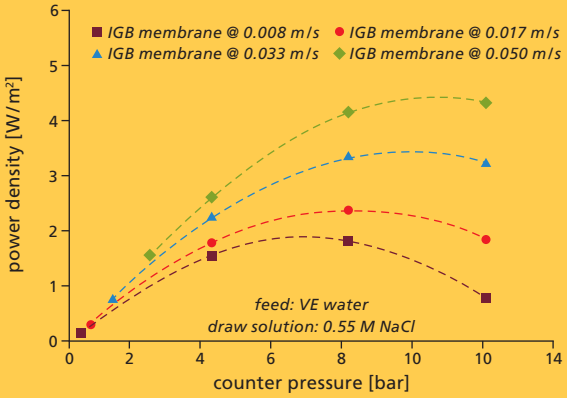
In addition, Pressure Retarded Osmosis also offers the possibility of using osmotic power in technical processes that result in water flows with a high salt content. An example is desalination of seawater, in which a highly concentrated retentate remains after the reverse osmosis or the thermal desalination. Using this retentate, a PRO process could be carried out with seawater as a low-concentration process stream. Energy could be recovered in this way and the overall process could be made more energy-efficient.

The challenge of concentration polarization

It is well known that the concentration polarization (CP, Fig. 2) in particular is decisive for the performance of a membrane. Here, a distinction can be made between the internal and the external CP. In the case of the internal CP, there is an increase in the salt concentration in the carrier structure of the membrane because of the low salt transport via the separating layer, and thus, there is a reduction of the driving force for the osmotic process. In the case of the external CP, the water and/or salt transport results in a reduction of the concentration difference in the surface layers on both sides of the membrane. The structure of the membrane in particular plays a role in the internal CP; in the case of the external CP the process parameters are especially important.

The objective – optimized membrane structure and process parameters

The objective of the Fraunhofer IGB is to develop new types of osmosis membranes by optimizing the inner structure. We measure the performance of the optimized membranes with an automated test facility (Fig. 1). We also determine the influence of important process parameters such as the flow velocity, the saltwater concentration and the temperature.



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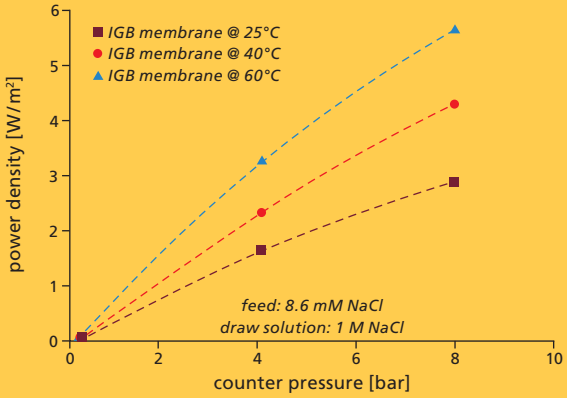

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Increased power density

The membranes developed at the IGB have a special open-porous carrier structure with a thin separating layer. The power densities are therefore substantially higher. Besides the membrane structure, process parameters also play a decisive role in the overall performance of the process. Increased flow velocities (Fig. 3) reduce the external concentration polarization at the membrane boundary and result in higher power densities. With realistic flow velocities for technical PRO processes, we currently achieve power densities of 3 W/m^2. Tests also show the strong influence of the temperature. With a rise in temperature, the power density increases significantly (Fig. 4). The reason for this is the temperature dependence of the diffusion coefficient, which rises with the increase in temperature. As a result, more water can be transported through the membrane at higher temperatures.

Outlook

An economically viable implementation of osmotic power stations assumes a power density of approx. 5 W/m^2. We can achieve this objective in the near future by further developing the material and structure of the membrane as well as optimizing the process parameters.

The principle is also ideally suited for energy recovery from the retentate of seawater desalination plants or using (warm) saline process wastewater from the chemical industry.

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References

[1] Loeb, S. J. (1998) Energy production at the Dead Sea by pressure-retarded osmosis: challenge or chimera?, Desalination 120: 247–262

[2] Touati, K.; Schiestel, T. (2013) Evaluation of the potential of osmotic energy as renewable energy source in realistic conditions, Energy Procedia 42: 261–269

Funding

We would like to thank the European Union for funding the project H2OCEAN within the scope of the Seventh Framework Research Programme (FP7/2007–2013), grant agreement no. 288145.

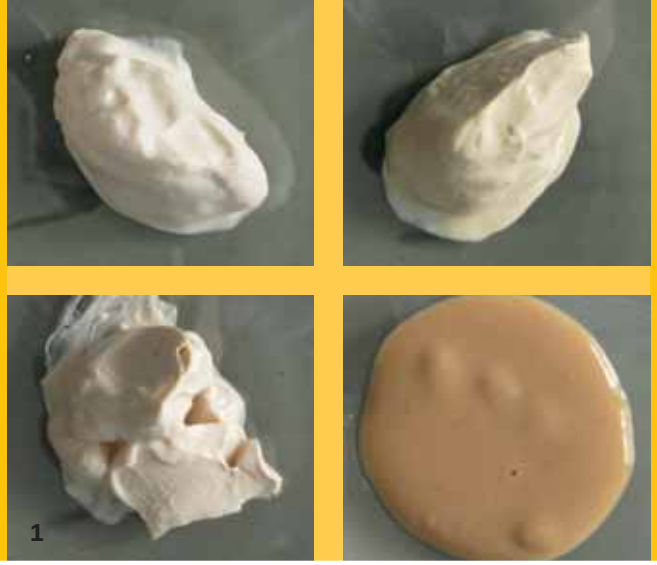
Project partner

Prof. Fernando Tadeo, University of Valladolid, Valladolid, Spain

Further information

www.h2ocean-project.eu

1 *Measuring cell to determine the performance of the membranes.*
2 *During the filtration process a boundary layer forms on the membrane which results in a concentration difference, the concentration polarization.*
3 *Comparison of the power density at different flow velocities and ambient temperatures.*
4 *Comparison of the power density at different temperatures and a flow velocity of 0.017 m/s.*



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2

BIOGAS PRODUCTION USING BY-PRODUCTS FROM CRAB SHELL REUTILIZATION

Barbara E. Waelkens M.Sc.

Initial situation

Chitin is one of the main components of the exoskeleton of arthropods such as crabs, lobsters and shrimps, and is therefore one of the most commonly occurring biopolymers in the world. Chitin and its derivatives have a large application potential, however this has not yet been implemented in practice. Together with an international team of researchers, the EU-funded ChiBio project is working to further develop the sustainable utilization of crab and shrimp shells. New processes based on the biorefinery concept are being developed to use chitin as the base material for specialty chemicals.

Energetic use of protein-rich waste streams

Besides chitin, the main components of crab shells are mineral substances, such as calcium salts, and proteins [1]. The first step in processing chitin is to extract it. This process can be carried out chemically (acid-base extraction) or enzymatically. The chemical process results in a protein-rich alkaline and a calcium-rich acid solution. Within the biorefinery concept that is virtually wastefree, the protein-rich waste stream can be employed for energy production through an anaerobic digestion. The advantages of anaerobic digestion of organic substances were identified by McCarty [2] as early as 1964: a high degree of stabilization of the organic material, low nutrient requirements, no need for oxygen and the production of biogas, which can serve as a renewable source of energy.

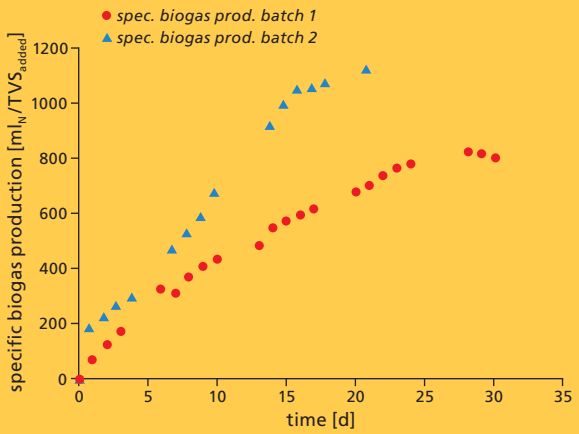
Challenges for biogas production

In principle, almost any type of organic substance can be converted into biogas. In Europe, the production and use of biogas are now widespread in the wastewater treatment as well as in the agriculturural sector. In over 65 countries anaerobic systems are also used in industry and so far more than 1400 plants have been installed by 16 main plant construction companies [3]. One of the challenges in the ChiBio project is the technical implementation of reutilizing the resulting by-products in a sustainable way. For this purpose, the biogas production potential was determined for the by-products obtained from the chemical extraction of chitin of shrimp and crab shells (Fig. 1).

Compared with other substrates, these by-products are characterized by low total volatile solids content, extreme pH values and high salt concentrations. Whereas typical substrates such as sludge from wastewater treatment or liquid manure have a ratio of total volatile solids to total solids (TVS/TS ratio) of 60 percent and 80 percent respectively, the TVS/TS ratio for the byproducts obtained by chitin extraction from crab and shrimp shells is approx. 15 percent and 30 percent respectively.

Potential for biogas production

To determine the biogas production potential, 1-liter laboratory-scale bioreactors (Fig. 2) were feeded with the protein-rich by-product of the chitin extraction of shrimp shells and of two different batches of crab shells (May and July). The experiments were carried out as fed-batches with two feeding cycles. The specific biogas production of the shrimp shell sidestream (Fig. 3) corresponded to 1125 ml_N/g_{TVS} in the first and 830 ml_N/g_{TVS} in the second feeding cycle. The biogas production was higher than the specific biogas yield of the crab shell sidestreams (Fig. 4), for which we measured 305 or 319 ml_N/g_{TVS} in the first and 283 or 391 ml_N/g_{TVS} in the second feeding cycle.



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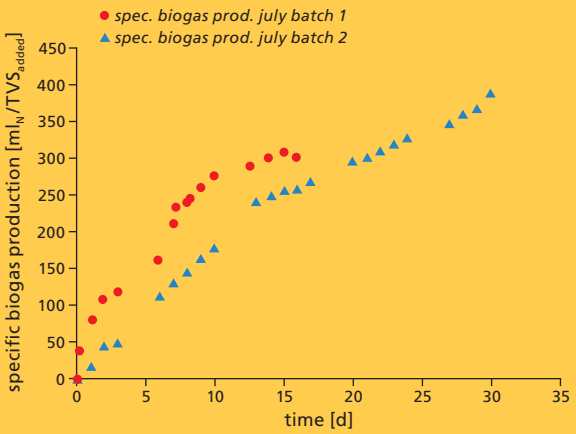

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The specific biogas yield of the processed shrimp shell sidestream was higher than the typical biogas yield for energy crops (approx. 500–700 ml_N/g_{TVS}). This can be explained by the fact that the main component of the latter are carbohydrates, whereas the main components of the shrimp shell sidestream are proteins, which provide a higher specific biogas yield. The specific biogas yield of the processed crab shell sidestreams can be compared with the biogas yield from organic municipal waste (approx. 350 ml_N/g_{TVS}).

The biogas production rates were linear (Figs. 3 and 4), which could indicate a growth limitation of the anaerobic microorganisms. Further investigations into the cause of this growth limitation offer possibilities for improving the anaerobic digestion and thus the specific biogas yield.

Outlook

Further process steps in chitin processing are the biocatalytic splitting of chitin and the purification of the resulting products. Additionally, these processes result in corresponding organic sidestreams, for which the biogas potential will also be determined. At the end of the project it will be possible to make reliable statements about the overall energetic potential that can be drawn from the utilization of these sidestreams.

1 *Substrates: by products resulting from the extraction of chitin from shrimp and crab shells.*
2 *Double-walled 1-liter laboratory biogas reactors.*
3 *Specific biogas production from the sidestream of chitin extraction from shrimp shells.*
4 *Specific biogas production from the sidestream of chitin extraction from crab shells.*

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References

[1] Boßelmann, F.; Romano, P.; Fabritius, H.; Raabe, D.; Epple, M. (2007) The composition of the exoskeleton of two crustacea: The American lobster Homarus americanus and the edible crab Cancer pagurus, Thermochimica Acta, Vol. 463: 65–68

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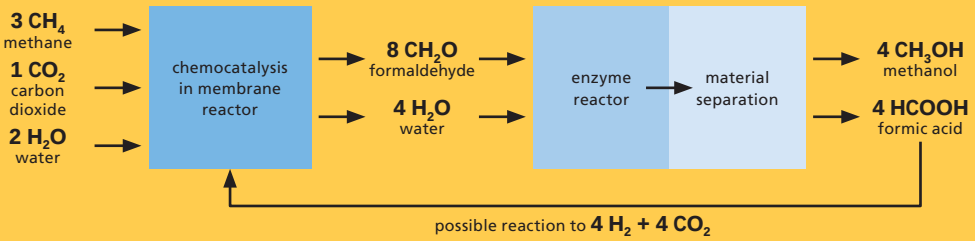
[3] Show, K. Y.; Tay, J. H.; Hung, Y. T. (2010) Global perspective of anaerobic treatment of industrial wastewater, Handbook of Environmental Engineering 11: Environmental Bioengineering

Funding

We would like to thank the European Union for funding the ChiBio research project within the scope of the Seventh Framework Programme (FP7/2007–2013), grant agreement no. 289284.

Project partners and further information

www.chibiofp7.eu



enthalpy of combustion of methane: –890.4 kJ/mole => –2671.2 kJ

enthalpy of combustion of methanol: –726.4 kJ/mole => –2905.6 kJ

1

ENZYME TECHNICAL PRODUCTION OF METHANOL AND FORMIC ACID FROM FORMALDEHYDE

Dipl.-Ing. Matthias Stier, Prof. Dr. rer. nat. Dieter Bryniok

Reutilizing substances from biogas

Currently biogas is used mainly as an energy carrier for the production of heat and electricity. The energetic use of biogas is efficient when the heat is used sensibly all year round. However, this is not the case with all biogas plants. That is why for a long time there has been research into possibilities for reutilizing substances from biogas – which consists of approx. 40 to 75 percent methane, 25 to 55 percent carbon dioxide and 10 percent water – for example for the production of methanol. However, so far neither chemocatalytic nor biotechnological approaches have been very promising.

In the joint project "ECOX – Enzymatic-chemocatalytic oxidation cascades in the gas phase" in cooperation with the Leibniz Institute for Catalysis LIKAT in Rostock and the Martin Luther University in Halle, chemical and biotechnological reaction steps are combined in such a way that biogas can be converted as efficiently as possible to methanol and formic acid (Fig. 1). The aim here is also to lay the foundations for further processes for the conversion of gaseous substrates.

Combination of chemocatalytic and enzymatic conversion

The solution is to be found in the combination of a chemocatalytic conversion of methane to formaldehyde, which is being developed by the project partners, and the subsequent disproportionation of the formaldehyde to methanol and formic acid by means of a formaldehyde dismutase from *Pseudomonas* sp. in an enzyme reactor (Fig. 2). The enzyme technical step is being developed at the Fraunhofer IGB. The formic acid produced in the enzyme reactor can be used as a recoverable substance, returned to the catalytic process or converted to methyl formate. In this process, methyl formate is formed directly from methanol and formic acid in aqueous solution. If the formic acid is returned to the process, the resulting chemical analysis indicates 4 moles of methanol from 3 moles of methane, 1 mole of carbon dioxide and 2 moles of water. In this endothermic process the enthalpy of combustion for 4 moles of methanol is higher than that of the converted biogas with 3 moles of methane.

Enzyme reactor – immobilization of the dismutase

In the studies carried out so far we have succeeded in obtaining the formaldehyde dismutase from both the wild-type strain and from several recombinant strains as a storable enzyme with long-term stability. The enzyme was bound to various carrier materials. This resulted in enzyme activities of 0.0088 – 0.028 micromoles per minute per milligram of the carrier material. The catalytic half-life is 155 days. Enzymes were applied to the carrier with a defined spatial orientation by means of genetic modification, thus increasing the activity one hundred times.

Automated pilot plant for gas phase reactions

To develop the process technology, a fully automated test facility for gas phase reactions was designed and set up (Fig. 2) in which the temperature and the pressure can be precisely controlled. The concentrations of both the substrate formaldehyde and of the products is measured with an online mass spectrometer. By means of a special membrane module it is

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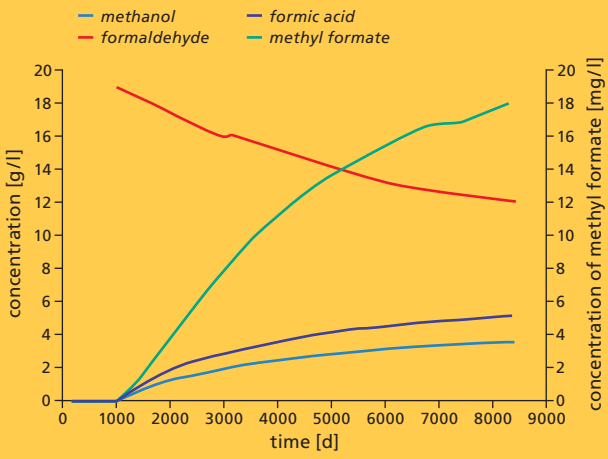

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possible to simultaneously measure all the components of the reaction both in the aqueous phase and in the gas phase with a response time in the seconds range (Fig. 4). Initial tests show that with this method it is possible to provide a complete and reliable analysis of the dismutase reaction.

Outlook

The processing of the formaldehyde dismutase and its immobilization on carrier materials were completed successfully. The immobilized enzyme indicates very high enzyme activities. This and the fully functional test facility with online mass spectrometry are excellent preconditions for the development of an enzyme technical process.

The next step in the research project is the continuous production of methanol and formic acid with the immobilized formaldehyde dismutase in the test facility. In the subsequent project phase the enzyme technical process is coupled with the chemo-catalytic process to produce formaldehyde from biogas.

In addition to this, the technical process for the production of methanol and formic acid from biogas is a model for further enzyme technical processes with gaseous substrates in the gas phase and in combination with chemocatalytic reactions. It therefore represents an important step in the direction of recovering biogenic materials via gaseous intermediate products such as biogas or synthesis gas.

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Funding

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Project partners

Leibniz Institute for Catalysis at the University of Rostock LIKAT, Rostock | Martin Luther University Halle-Wittenberg, Institute of Pharmacy, Working Group Processing of Biotechnical Products, Halle

1 *Combined chemocatalytic-enzymatic process for the production of methanol and formic acid from biogas.*
2 *Online mass spectrometer.*
3 *Pressure enzyme reactor.*
4 *Simultaneous measurement of the educt (formaldehyde) and of the products (methanol, formic acid, methyl formate) in the dismutase-catalyzed reaction.*

APPENDIX

PATENTS GRANTED IN 2013

In the year 2013 seven patents were granted. These patents are assigned to our business areas as follows:

Medicine

Process for production of a regioselective membrane
EP 1 497 017,
granted January 9, 2013

Hyphae-specific cell wall proteins of *Candida*
DE 10 2004 013 826,
granted May 29, 2013

Arrangement and method for analysis of biological samples
JP 5328663,
granted August 2, 2013

Simultanous detection of microRNA biogenesis forms
DE 10 2012 215 925,
granted September 19, 2013

Pharmacy

Cellular pyrogen test
EP 2 041 172,
granted November 27, 2013

Chemistry

Process for producing gas-tight and temperature-stable modules with ceramic hollow-fibre or capillary membranes
EP 1 858 632,
granted March 13, 2013

Method of producing functional surface areas on a flat substrate
EP 2 051 147,
granted May 22, 2013

TRADE FAIRS AND EVENTS 2013

Trade fairs and exhibitions

BAU
World´s Leading Trade Fair for Architecture, Materials, Systems
Fraunhofer Building Innovation and Photocatalysis Alliances
January 14 – 19, 2013,
Munich, Germany

International Green Week
Fair for food, agriculture and horticulture
Joint Fraunhofer booth
January 18 – 27, 2013,
Berlin, Germany

8th International Congress "Forum Life Sciences"
Fraunhofer Group for Life Sciences
March 13 – 14, 2013,
TU Munich, Germany

Ideas 2020 – A Tour of Tomorrow's World
Exhibition of the Helmholtz Association
since March 14, 2013,
Germany-wide

Energy Storage
International Summit for the Storage of Renewable Energies
Fraunhofer Energy Alliance
March 18 – 19, 2013,
Düsseldorf, Germany

Hannover Messe Energy
Leading Trade Fair for Renewable and Conventional Power Generation, Power Supply, Transmission, Distribution and Storage
Fraunhofer Energy Alliance
April 8 – 12, 2013, Hanover, Germany

Hannover Messe Surface Technology
Leading Trade Fair for Surface Technology
Joint Fraunhofer booth
April 8 – 12, 2013, Hanover, Germany

Metropolitan Solutions
Innovations for Urban Infrastructures
Fraunhofer Building Innovation and Water Systems (SysWasser) Alliances
April 8 – 12, 2013, Hanover, Germany

Wasser Berlin
Trade Fair and Congress for Water and Wastewater
April 23 – 26, 2013, Berlin, Germany

Deutsche Biotechnologietage 2013 (German days of biotechnology 2013)
May 14 – 15, 2013, Stuttgart, Germany

9th Nationale Branchenkonferenz Gesundheitswirtschaft (National industry conference for the healthcare sector)
Fraunhofer Group for Life Sciences
Juli 10 – 11, 2013, Rostock-Warnemünde, Germany

Biotechnica
Europe's Event for Biotechnology, Life Sciences and Lab Technology
Fraunhofer Group for Life Sciences
October 8 – 10, 2013,
Hanover, Germany

Messe K
Joint Fraunhofer booth
October 16 – 23, 2013,
Düsseldorf, Germany

parts2clean
11th Leading International Trade Fair for Industrial Parts and Surface Cleaning
Fraunhofer Cleaning Technology Alliance
October 22 – 24, 2013,
Stuttgart, Germany

World Conference on Regenerative Medicine
Fraunhofer Group for Life Sciences
October 23 – 25, 2013,
Leipzig, Germany

Events

Checkpoint Zukunft (Checkpoint Future)
Day for students at Fraunhofer
February 4, 2013, Fraunhofer Institutes Center Stuttgart, Germany

Annual meeting of the German Society for Matrix Biology
March 7 – 9, 2013,
University Hospital, University of Tübingen, Germany

Fraunhofer Talent School
March 15 – 17, 2013,
Fraunhofer Institutes Center Stuttgart, Germany

DECHEMA colloquium
"Effiziente Herstellung industrieller Enzyme"
March 21, 2013, Frankfurt am Main, Germany

Girls' Day
Future Prospects for Girls
April 25, 2013, Fraunhofer Institute Center Stuttgart, Germany

DECHEMA status workshop
"Biosurfactants – Challenges and perspectives"
May 16 – 17, 2013, Frankfurt am Main, Germany

5th FEBS Advanced Lecture Course Human Fungal Pathogens
May 25 – 31, 2013, La Colle sur Loup, France

Tag der Wissenschaft (Day of Science)
June 22, 2013, University of Stuttgart, Germany

Gordon Research Seminar and Gordon Research Conference (GRS / GRC) Elastin, Elastic Fibers & Microfibrils
July 20 – 26, 2013, University of New England, Biddeford, ME, USA

47th Scientific Conference of the Deutschsprachige Mykologische Gesellschaft e. V.
September 5 – 6, 2013, Tübingen, Germany

Anniversary Symposium **"60 Jahre Fraunhofer IGB"**
September 25, 2013, Fraunhofer IGB, Stuttgart, Germany

Checkpoint Zukunft (Checkpoint Future)
Day for students at Fraunhofer
November 4, 2013, Fraunhofer Institute Center Stuttgart, Germany

ProcessNet Annual Meeting of the section SuPER **"Integrierte stoffliche und energetische Nutzung von Biomasse"**
November 5 – 6, 2013, Frankfurt am Main, Germany

TERMIS-Americas
Annual Conference of the Tissue Engineering & Regenerative Medicine International Society
November 10 – 13, 2013, Atlanta, GA, USA

Congress "Ressourceneffizienz- und Kreislaufwirtschaftskongress Baden-Württemberg 2013"
November 12 – 13, 2013, Stuttgart, Germany

unitag (University Day)
November 20, 2013, University of Stuttgart, Germany

bone-tec
International Bone-Tissue-Engineering Congresses
December 16 – 19, 2013, Singapore

TRADE FAIRS AND EVENTS, PREVIEW 2014

International Green Week
Fair for food, agriculture and horticulture
Joint Fraunhofer booth
January 17 – 26, 2014, Berlin, Germany

Science conference of the Federal Ministry of Defence (BMVg) and the Studiengesellschaft der Deutschen Gesellschaft für Wehrtechnik mbH (DWT)
February 3 – 5, 2014, Berlin, Germany

BIOFACH
Trade Fair for Organic Food
February 12 – 15, 2014, Nuremberg, Germany

Cooperation forum "Technologien für zellbasierte Therapien",
Fraunhofer Group for Life Sciences
March 12, 2014, Erlangen, Germany

Energy Storage
International Summit for the Storage of Renewable Energies
Fraunhofer Energy Alliance
March 25 – 27, 2014, Düsseldorf, Germany

Girls' Day
Future Prospects for Girls
March 27, 2014, Fraunhofer Institutes Center Stuttgart, Germany

Hannover Messe Energy
Leading Trade Fair for Renewable and Conventional Power Generation, Power Supply, Transmission, Distribution and Storage
Fraunhofer Energy Alliance
April 7 – 11, 2014, Hanover, Germany

Hannover Messe IndustrialGreenTec
Leading Trade Fair for Environmental Technology
Fraunhofer Building Innovation and Photocatalysis Alliances
April 7 – 11, 2014, Hanover, Germany

Fraunhofer Talent School
April 11 – 13, 2014, Fraunhofer Institutes Center Stuttgart, Germany

IFAT
World's Leading Trade Fair for Water, Sewage, Waste and Raw Materials Management
Fraunhofer Water Systems Alliance (SysWasser)
May 5 – 9, 2014, Munich, Germany

BIO International Convention
Fraunhofer Group for Life Sciences
June 23 – 26, 2014, San Diego, USA

parts2clean
12th Leading International Trade Fair for Industrial Parts and Surface Cleaning
Fraunhofer Cleaning Technology Alliance
June 24–26, 2014, Stuttgart, Germany

Tag der Wissenschaft (Day of Science)
July 12, 2014, University of Stuttgart, Germany

PSE 2014
14th International Conference on Plasma Surface Engineering
September 15–19, 2014, Garmisch-Partenkirchen, Germany

unitag (University Day)
November 19, 2014, University of Stuttgart, Germany

Checkpoint Zukunft (Checkpoint Future)
Day for students at Fraunhofer
December 5, 2014, Fraunhofer Institutes Center Stuttgart, Germany

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German Federal Ministry of Education and Research (BMBF), reviewer

German Research Foundation (DFG), review board "Process Engineering, Technical Chemistry", member subject area "Biological Process Engineering"; reviewer

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Fraunhofer Group for Life Sciences, group chairman

Gesellschaft für Umweltsimulation e. V. (GUS, Society for Environmental Engineering), member

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Institute of Textile Technology and Process Engineering Denkendorf (ITV), member of advisory board

Max Planck Institute for Intelligent Systems, member of advisory board

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Schenke-Layland, K.

L'Agence nationale de la recherche (ANR), reviewer for single application procedure

American Association of Anatomists, member Scientific Affairs Committee; member PostDoc Fellowship Committee; reviewer for Young Investigator Awards

Arthritis Research UK, reviewer for single application procedure

European Society for Biomaterials (ESB), member

German Research Foundation (DFG), reviewer for research fellowships and single application procedure

German Society for Matrix Biology, member

International Society for Stem Cell Research (ISSCR), member

Katholieke Universiteit Leuven (Catholic University of Leuven), Research Council, reviewer for single application procedure

Schiestel, T.

Deutsche Gesellschaft für Materialkunde e. V. (DGM, German Association for Materials Science), community committee "Hochleistungskeramik", member working group "Keramische Membranen"

Schließmann, U.

DECHEMA (Society for Chemical engineering and Biotechnology), member

ProcessNet – an Initiative of DECHEMA and VDI-GVC, section "Fluid Dynamics and Separation", member subject division "Membrane Technology"

Schmid-Staiger, U.

aireg – Aviation Initiative for Renewable Energy in Germany e. V., member working group "Rohstoffbereitstellung"

European Algae Biomass Association (EABA), member

Sieber, V.

DECHEMA (Society for Chemical engineering and Biotechnology), section "Biotechnologie", member subject divisions "Biotechnologie Nachwachsende Rohstoffe", "Chemische Biologie", "Biotransformationen", "Systembiologie und Synthetische Biologie" and temporary working group "Neue Bioproduktionssysteme"

German Chemical Society (GDCh), member

German Federal Ministry of Education and Research (BMBF), reviewer

German Research Foundation (DFG), reviewer

German Society for Biochemistry and Molecular e. V. (GBM), member

Research Center for Industrial Biotechnology at the TUM, member of directorate

Straubing Center of Science, member of directorate

Sternad, W.

HACH LANGE GmbH, consumer advisory board, member

Tovar, G. E. M.

Colloid Society, member

Deutsche Gesellschaft für Materialkunde e. V. (DGM, German Association for Materials Science), expert committee "Biomaterialien", head of working group "Biomimetische Biomaterialien"

German Bunsen Society for Physical Chemistry (DBG), member

DECHEMA (Society for Chemical Engineering and Biotechnology), member

Fraunhofer Nanotechnology Alliance, spokesman; member of steering committee

German Chemical Society (GDCh), member

NanoMAT, member

ProcessNet – an Initiative of DECHEMA and VDI-GVC, section "Chemical Reaction Technology", member of advisory board subject division "Nanotechnology"

Trösch, W.

German Water Partnership e. V., member of executive board

Unkelbach, G.

American Chemical Society (ACS), member "Division of Cellulose and Renewable Materials", "Division of Biochemical Technology" and "Division of Catalysis Science and Technology"

DECHEMA (Society for Chemical Engineering and Biotechnology), member

Vohrer, U.

Deutsche Physikalische Gesellschaft (DPG, German Physical Society), member

Expert forum "Reinigung und Vorbehandlung vor der Beschichtung" of Ostbayerischens Technologie-Transfer-Institut e. V. (OTTI), conference advisory board/specialist manager

Fraunhofer Cleaning Technology Alliance, founding member

German Bunsen Society for Physical Chemistry (DBG), member

German Chemical Society (GDCh), member

Research Alliance Cultural Heritage, founding member

Scientific and Technical Council of the Fraunhofer-Gesellschaft, member

Standing committee of the Fraunhofer-Gesellschaft, member

The Association of German Engineers (VDI), member

Walles, H.

DECHEMA (Society for Chemical Engineering and Biotechnology), section "Biotechnologie", member subject division "Medizinische Biotechnologie"

DIN, the German Institute for Standardization, standards committee "Feinmechanik und Optik NAFuO", collaboration on working committee "Medizinische Produkte auf Basis des Tissue Engineering"

European Union, reviewer for Seventh Framework Programme for Research

German Academic Exchange Service (DAAD), reviewer for special program "Moderne Anwendungen in der Biotechnologie"

German Federal Ministry of Education and Research (BMBF), reviewer

German National Academic Foundation, person of confidence

German Pharmaceutical Industry Association (BPI), member working group "Tissue Engineering"

German Research Foundation (DFG), reviewer for SFB/Transregio, doctorate program, single application procedure

German Society for Regenerative Medicine, member of academic advisory board

Gesundheitsforschungsrat des BMBF (Health research council) of the German Federal Ministry of Education and Research (BMBF), member of medical technical committee

VDI Society Materials Engineering (VDI-GME), technical division "Nanoscale Engineering", member expert committee "Nanotechnik in der Medizintechnik"

Weber, A.

DECHEMA (Society for Chemical Engineering and Biotechnology), section "Biotechnologie", member subject divisions "Biotechnologie Nachwachsender Rohstoffe", "Medizinische Biologie" and "Mikrobielle Materialzerstörung und Materialschutz"

GMM VDE/VDI-Society Microelectronics, Microsystems and Precision Engineering, expert committee 4.7 "Mikro-Nano-Integration", reviewer of program committee

Materials Research Society (MRS), member

Zibek, S.

DECHEMA (Society for Chemical Engineering and Biotechnology), section "Biotechnologie", member subject division "Chemische Biologie"

Furtwangen University, Faculty Medical and Life Sciences, academic advisory board, expert committee "Biotechnologie/Verfahrenstechnik"

The Association of German Engineers (VDI), member

SCIENTIFIC COOPERATIONS

With universities

Aalto University, Helsinki, Finland

Anhalt University of Applied Sciences, Köthen, Germany

Aristotle University of Thessaloniki, Greece

Biberach University of Applied Sciences, Germany

Catholic University of Leuven, Belgium

Charles University, Prague, Czech Republic

Cranfield University, UK

Eberhard Karls University of Tübingen, Germany

Eindhoven University of Technology, Eindhoven, the Netherlands

Energy Institute at the Johannes Kepler University Linz, Austria

ESADE Foundation, Barcelona, Spain

Escola de Engenharia de Piracicaba (EEP), Brazil

Esslingen University of Applied Sciences, Germany

Georgia Institute of Technology (Georgia Tech), Atlanta, USA

Gottfried Wilhelm Leibniz University of Hannover, Hanover, Germany

Hamm-Lippstadt University of Applied Sciences, Germany

Hannover Medical School (MHH), Hanover, Germany

Hebrew University of Jerusalem, Israel

Helmut Schmidt University, University of the Federal Armed Forces Hamburg, Germany

Hochschule Merseburg – University of Applied Sciences, Germany

Innsbruck Medical University, Austria

Julius Maximilian University of Würzburg, Germany

Letterkenny Institute of Technology (LYIT), Ireland

Linnaeus University, Kalmar, Sweden

Ludwig Maximilians University of Munich (LMU), Germany

Luiz de Queiroz College of Agriculture, Piracicaba, Brazil

Lund University, Lund, Sweden

Martin-Luther-University, Halle-Wittenberg, Germany

McGill University, Montreal, Canada

National University of Ireland, Galway, Ireland

Newcastle University, UK

Norwegian University of Life Sciences (NMBU), Ås, Norway

Queensland University of Technology (QUT), Brisbane, Australia

Reutlingen University, Germany

Royal College of Surgeons Ireland (RCSI), Dublin, Ireland

Royal Institute of Technology (KTH), Stockholm, Sweden

RWTH Aachen University, Germany

Sheffield Hallam University, UK

Stanford University, USA

Stichting Dienst Landbouwkundig Onderzoek, Wageningen, the Netherlands

Stockholm University, Sweden

Technische Universität München (TUM), Munich, Germany

Trinity College Dublin, Ireland

Umeå University, Sweden

Universidad Politécnica de Cartagena (UPCT), Spain

Universidade Metodista de Piracicaba (UNIMEP), Brazil

Universitat Politècnica de Catalunya (UPC), Barcelona, Spain

Université Paul Sabatier Toulouse III, France

University of Bari Aldo Moro, Italy

University of Bergen, Norway

University of California Los Angeles (UCLA), USA

University of Greifswald, Germany

University of Hamburg, Germany

University of Heidelberg, Germany

University of Hohenheim, Stuttgart, Germany

University of Innsbruck, Austria

University of Kaiserslautern (TU Kaiserslautern), Germany

University of Konstanz, Germany

University of Leipzig, Germany

University of Milano-Bicocca, Milan, Italy

University of Novi Sad, Serbia

University of Seville, Spain

University of Southern California (USC), Los Angeles, USA

University of Stuttgart, Germany

University of Sydney, Australia

University of Veterinary Medicine Hannover, Foundation, Hanover, Germany

University of Vienna, Austria

University of West Hungary, Sopron, Hungary

Univerza v Mariboru, Maribor, Slovenia

Uppsala University, Sweden

With other research organizations

AIT Austrian Institute of Technology, Vienna, Austria

Association pour la Recherche et le Developpement des Methodes et Processus Industriels – ARMINES, Paris, France

Ateknea Solutions, Barcelona, Spain

BAM Federal Institute for Materials Research and Testing, Berlin, Germany

Centre for Process Innovation (CPI), Wilton, Redcar, UK

Centro de Investigación Cientifico Technológico para la Mineria (CICITEM), Antofagasta, Chile

Centro technológica CARTIF, Valladolid, Spain

Centro Tecnologico Agrario y Agroalimentario Asociacion – ITAGRA, Palencia, Spain

Chemical Process Engineering Research Institute (CPERI), Thessaloniki, Greece

CiS Forschungsinstitut für Mikrosensorik und Photovoltaik GmbH, Erfurt, Germany

Deutsches Zentrum für Biomaterialien und Organersatz Stuttgart-Tübingen, Germany

Dr. Margarete Fischer-Bosch-Institut für Klinische Pharmakologie (IPK), Stuttgart, Germany

Flanders Institute for Biotechnology (VIB), Gent, Belgium

German Cancer Research Center (DKFZ), Heidelberg, Germany

Helmholtz-Zentrum Dresden-Rossendorf, Helmholtz Institute Freiberg for Resource Technology, Germany

Institut Carnot CIRIMAT, Toulouse, France

Institut Dr. Schrader Creachem GmbH, Holzminden, Germany

Institut National des Sciences et Technologies de la Mer, Salammbo, Tunesia

Institut Pasteur, Paris, France

Institute of Textile Chemistry and Chemical Fibers (ITCF), Denkendorf, Germany

Institute of Textile Technology and Process Engineering (ITV), Denkendorf, Germany

Institute on Membrane Technology, Italian National Research Council, ITM-CNR, Rome, Italy

Instituto Nazionale di Economia Agraria (INEA), Rome, Italy

Inter-American Institute for Global Change Research IAI, São Jose dos Campos, Brazil

IVL Swedish Environmental Research Institute Ltd., Stockholm, Sweden

Julius Kühn-Institut (JKI), Federal Research Centre for Cultivated Plants, Quedlinburg, Germany

Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

Laboratoire Phenobio SAS, Martillac, France

Leibniz Institute for Catalysis (LIKAT), Rostock, Germany

Leibniz Institute for Plasma Science and Technology (INP), Greifswald, Germany

LEITAT Technological Center (Asociación Acondicionamiento Tarrasense), Barcelona, Spain

Max Planck Institute of Colloids and Interfaces, Potsdam-Golm, Germany

Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany

Max Planck Institute for Infection Biology, Berlin, Germany

Max Planck Institute for Intelligent Systems, Stuttgart, Germany

Max Planck Institute for Plant Breeding Research, Cologne, Germany

Max Planck Institute for Polymer Research, Mainz, Germany

Max Planck Institute for Solid State Research, Stuttgart, Germany

Methodology Centre for Environment Assessment (METCENAS), Prague, Czech Republic

National Institute of Laser, Plasma and Radiation Physics, Magurele-Bucharest, Romania

Nederlandse Organisatie voor toegepast natuurwetenschappelijk onderzoek TNO, Delft, the Netherlands

Norwegian Institute of Food, Fisheries and Aquaculture Research Nofima, Oslo, Norway

Optimizacion Orientada a la Sostenibilidad S.L. (IDENER), Seville, Spain

PROFACTOR GmbH, Steyr-Gleink, Austria

Research & Development centre Re/genT, Helmond, the Netherlands

Robert-Koch-Institute, Berlin, Germany

Teknologisk Institutt (TI), Oslo, Norway

VITO – Flemish Institute for Technological Research NV, Mol, Belgium

VTT Technical Research Centre of Finland, Finland

With hospitals

Charité – Universitätsmedizin Berlin, Germany

Haukeland University Hospital, Bergen, Norway

Heart and Diabetes Center North Rhine-Westphalia University Hospital of the Ruhr University of Bochum, Bad Oeynhausen, Germany

Hospital Charlottenhaus, Stuttgart, Germany

Hospital Schillerhöhe, Gerlingen, Germany

Karl Olga Hospital, Stuttgart, Germany

Robert Bosch Hospital, Stuttgart, Germany

Sana Herzchirurgie Stuttgart, Germany

University Hospital Frankfurt, Frankfurt am Main, Germany

University Hospital Innsbruck, Germany

University Hospital Tübingen, Germany

University Hospital Ulm, Germany

University Hospital of Würzburg, Germany

With museums

Bavarian State Archives, Munich, Germany

Deutsches Bergbaumuseum, Bochum, Germany

Deutsches Museum, Munich, Germany

Deutsches Schifffahrtsmuseum, Bremerhaven, Germany

Germanisches Nationalmuseum, Nuremberg, Germany

Landesmuseum Württemberg, Stuttgart, Germany

Stiftung Preußischer Kulturbesitz, Rathgen-Forschungslabor, Berlin, Germany

Zentrum für Bucherhaltung, Leipzig, Germany

LECTURES AND SEMINARS

Esslingen University of Applied Sciences

Winter semester 2013 / 14

Weber, A.
Lecture
"Physikalische Chemie – Thermodynamik und Reaktionskinetik"
Faculty Natural Sciences, BSc Chemical Engineering/ Colour and Coatings, BSc Biotechnology, 4 SH

Hamm-Lippstadt University of Applied Sciences

Summer semester 2013

Bryniok, D.
Lecture
"Bioenergie I"
Study course Energy Engineering and Resource Optimisation, 1 SH

Bryniok, D.
Lecture
"Technische Mechanik II"
Study course Energy Engineering and Resource Optimisation, 1 SH

Bryniok, D.
Exercises for lecture "Technische Mechanik II"
Study course Energy Engineering and Resource Optimisation, 4 SH

Bryniok, D.
Lecture
"Energie und Wasser"
Study course Energy Engineering and Resource Optimisation, 1 SH

Bryniok, D.
Seminar
"Energie und Wasser"
Study course Energy Engineering and Resource Optimisation, 1 SH

Winter semester 2013 / 14

Bryniok, D.
Lecture
"Technische Mechanik I"
Study course Energy Engineering and Resource Optimisation, 2 SH

Bryniok, D.
Exercises for lecture "Technische Mechanik I"
Study course Energy Engineering and Resource Optimisation, 4 SH

Bryniok, D.
Practical course
"Bioenergie"
Study course Energy Engineering and Resource Optimisation, 2 SH

Bryniok, D.
Mentoring practical semesters, project and bachelor theses
Study course Energy Engineering and Resource Optimisation

Heidelberg University Biochemistry Center

Summer semester 2013

Sohn, K.
Parts of seminar and practical course "Proteine/Nervensystem"
Medical Faculty, study course Biochemistry

Winter semester 2013 / 14

Sohn, K.
Parts of seminar and practical course "Blut und Eisenstoffwechsel"
Medical Faculty, study course Biochemistry

University of Hohenheim

Summer semester 2013

Kluger, P. J.; Hansmann, J.; Kleinhans, C.; Groeber, F.; Hoppensack, A.
Lecture
"Tissue Engineering"
Faculty of Science, BSc Nutritional Science, BSc Food Science and Biotechnology, 2 SH

Technische Universität München (TUM), Munich

Summer semester 2013

Sieber, V.
Lecture
"Enzymengineering"
Study course Renewable Resources, 2 SH

Sieber, V.
Parts of Lecture
"Technologie und Verwertung von sonstigen biogenen Rohstoffen"
Study course Forestry, 4 SH

Sieber, V.
Lecture
"Biokatalyse und Proteintechnologie"
Study course Chemistry, 1 SH

Sieber, V.
Lecture
"Industrielle Biokatalyse für NaWaRo"
Study course Renewable Resources, 3 SH

Winter semester 2013 / 14

Sieber, V.
Lecture
"Technische Biokatalyse"
Study course Renewable Resources, 2 SH

Sieber, V.
Lecture
"Einführung in die Stoffliche Nutzung"
Study course Renewable Resources, 2 SH

Offenburg University of Applied Sciences

Winter semester 2013 / 14

Kluger, P. J.
Lecture
"Werkstoffe in der Medizintechnik – Biologische Aspekte"
Faculty Electrical Engineering and Information Technology, BSc Medical Engineering, 1 SH

University of Stuttgart

Summer semester 2013

Bach, M.; Hirth, T.; Rupp, S.; Tovar, G. E. M.
Lecture
"Komplexe Fluide"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, 2 SH

Bailer, S. M. (et al.)
Lecture
"Wissenschaftliche Praxis – Ringveranstaltung"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 2 SH

Hansmann, J.; Rupp, S.; Tovar, G. E. M.; Hirth, T. (with Doser, M.)
Lecture
"Medizinische Verfahrenstechnik I"
Faculty of Energy Technology, Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering, MSc Process Engineering, MSc Mechanical Engineering, MSc Technical Biology, 2 SH

Hansmann, J.; Kluger, P. J.; Bailer, S. M.
Lecture
"Zellkulturtechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 2 SH

Hansmann, J.; Kluger, P. J.; Bailer, S. M.
Practical course
"Zellkulturtechnik, Dreidimensionale Gewebekultur und Bioreaktortechnologie"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 2 SH

Hirth, T.; Schließmann, U.
Lecture
"Biologische und chemische Verfahren zur industriellen Nutzung von Biomasse (Energieträger und Chemierohstoffe)"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Energy Technology, MSc Environmental Engineering, MSc Technical Biology, 2 SH

Hirth, T.; Rupp, S.
Lecture
"Biomaterialien – Biobasierte Materialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering, BSc Technical Biology, 2 SH

Hirth, T.; Tovar, G. E. M.
Lecture
"Grenzflächenverfahrenstechnik I – Chemie und Physik der Grenzflächen"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, 2 SH

Hirth, T.; Tovar, G. E. M. (with Groß, J.)
Lecture
"Grundlagen der Verfahrenstechnik I"
Faculty of Energy Technology, Process Engineering and Biological Engineering, BSc Technical Biology, 2 SH

Hirth, T.
Lecture
"Nachhaltige Rohstoffversorgung – Von der Erdölraffinerie zur Bioraffinerie"
Faculty of Energy Technology, Process Engineering and Biological Engineering, Interdisciplinary key qualification, 2 SH

Tovar, G. E. M.; Borchers, K.
Lecture
"Biomaterialien – Biokompatible Materialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering, BSc Technical Biology, 2 SH

Tovar, G. E. M.; Hirth, T.
Lecture
"Nanotechnologie I – Chemie und Physik der Nanomaterialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, MSc Technical Biology, MSc Materials Science, 2 SH

Tovar, G. E. M.; Borchers, K.; Kluger, P. J.
Exercises
"Biomaterialien und Nanotechnologie"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 4 SH

Tovar, G. E. M.; Hirth, T.
Exercises
"Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, MSc Technical Biology, 2 SH

Tovar, G. E. M.; Hirth, T. (with Doser, M.)
Exercises
"Medizinische Verfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, MSc Technical Biology

Tovar, G. E. M.; Hirth, T.
Exercises
"Nanotechnologie"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, MSc Technical Biology, BSc Medical Engineering, 2 SH

Tovar, G. E. M.; Hirth, T.
Exercises
"Verfahrenstechnik"
Study courses of Mechanical Engineering, 2 SH

Winter semester 2013 / 14

Hirth, T.; Oehr, C.; Tovar, G. E. M.
Lecture
"Grenzflächenverfahrenstechnik II – Technische Prozesse"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, 2 SH

Hirth, T.; Tovar, G. E. M.
Lecture
"Grundlagen der Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, 2 SH

Hirth, T.; Tovar, G. E. M. (with Groß, J.)
Lecture
"Grundlagen der Verfahrenstechnik II"
Faculty of Energy Technology, Process Engineering and Biological Engineering, BSc Technical Biology, 2 SH

Hirth, T.; Kluger, P. J.; Tovar, G. E. M. (with Doser, M.)
Lecture
"Medizinische Verfahrenstechnik II"
Faculty of Energy Technology, Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering, MSc Process Engineering , MSc Mechanical Engineering, 2 SH

Hirth, T.
Lecture
"Nachhaltige Rohstoffversorgung und Produktionsprozesse"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, 2 SH

Hirth, T.
Lecture
"Sustainable Production Processes"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc WASTE, 2 SH

Kluger, P. J.; Hirth, T.
Lecture
"3D-Gewebekultur"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 2 SH

Oehr, C.
Lecture
"Plasmaverfahren für die Dünnschicht-Technik"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, 2 SH

Tovar, G. E. M.; Borchers, K.; Kleinhans, C. (with Brümmer, F.)
Lecture
"Biomaterialien – Herstellung, Charakterisierung und Anwendungen"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Technical Biology, 2 SH

Tovar, G. E. M.; Hirth, T.
Lecture
"Nanotechnologie II – Technische Prozesse und Anwendungen für Nanomaterialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering, MSc Process Engineering, specialization subject, BSc Medical Engineering, MSc Materials Science, MSc Technical Biology, 2 SH

Tovar, G. E. M.
Seminar
"Aktuelle Methoden der Nanotechnologie und Grenzflächenverfahrenstechnik in der Medizintechnik"
BSc Medical Engineering, 2 SH

Summer semester 2013 and winter semester 2013 / 14

Haitz, T.; Kahlig, A.; Stier, M.; Tovar, G. E. M. (et al.)
"Arbeitstechniken und Projektarbeit"
Faculty of Energy Technology, Process Engineering and Biological Engineering, BSc Process Engineering, 2 SH

Hirth, T.
"Anleitung zu wissenschaftlichem Arbeiten"
Study courses Process Engineering, Technical Biology, WASTE

Rupp, S.
"Anleitung zu wissenschaftlichem Arbeiten"
Study courses Process Engineering, Chemistry, Technical Biology

Tovar, G. E. M.; Hirth, T.
"Mitarbeiterseminar für DoktorandInnen und DiplomandInnen"
Interdisciplinary course, 1 SH

Tovar, G. E. M. ; Hirth, T.
"Grenzflächenverfahrenstechnisches Kolloquium"
Interdisciplinary course, 1 SH

Tovar, G. E. M.
"Anleitung zu wissenschaftlichem Arbeiten"
Study courses Process Engineering, Technical Biology, Medical Engineering

University of Tübingen

Winter semester 2013 / 14

Schenke-Layland, K.
Lecture, seminar and practical course
"Vitale Implantate"
Faculty of Medicine, BSc Medical Technologies

Schenke-Layland, K.
Lecture, seminar and practical course
"Implantology"
Faculty of Medicine, MSc Biomedical Technologies

University of Natural Resources and Life Sciences, Vienna

Summer semester 2013

Walles, H.
Visiting professor/lecture
"Grundlagen des Tissue Engineering von komplexen Geweben"
MSc Biotechnology, 1 week full-time

University of Würzburg

Summer semester 2013

Walles, H.
Lecture
"Grundlagen des Tissue Engineering II"
Faculty of Chemistry and Pharmacy, MSc Functional Materials, 5 SH

Walles, H.
Exercise
"Mikrosysteme für biologische und medizinische Anwendungen"
Faculty of Chemistry and Pharmacy, MSc Functional Materials, 5 SH

Winter semester 2013 / 14

Walles, H.
Lecture
"Grundlagen des Tissue Engineering"
Faculty of Chemistry and Pharmacy, BSc Functional Materials, 5 SH

Walles, H.
Lecture and exercises
"Mikrosysteme für biologische und medizinische Anwendungen"
Faculty of Chemistry and Pharmacy, MSc Functional Materials, 5 SH

Walles, H.
Lecture
"Tissue Engineering"
Graduate School of Life Sciences, International Research Training Group 1522 "HIV/AIDS and associated infectious diseases in Southern Africa"

Walles, H.
Lecture
"Werkstoffe für Biosensoren, Tissue Engineering und Geweberegeneration"
Faculty of Chemistry and Pharmacy, MSc Functional Materials, 5 SH

Walles, H.
Practical course
"Grundlagen des Tissue Engineering"
Faculty of Chemistry and Pharmacy, BSc Functional Materials, 1 week full-time

Summer semester 2013 and winter semester 2013 / 14

Walles, H.
Lecture
"Tissue Engineering"
Faculties of Biology and Medicine, MSc Biomedicine, 2 SH

Walles, H.
Practical course
"Modellorganismen"
Faculties of Biology and Medicine, MSc Biomedicine, 1 week full-time

Walles, H.
"Stammzellen"
Faculty of Medicine, integrated seminar for students of medicine, 2 SH

Walles, H.
Seminar and Journal Club for doctorate students,
Faculty of Medicine, 4 SH

Walles, H.
"Anleitung zum selbstständigen wissenschaftlichen Arbeiten",
doctorate students and students of Faculty of Medicine, 3 SH

Stated are the total semester hours (SH) of the particular lecture or course.

ACADEMIC THESES

Dissertations

Berg, M.
Etablierung von Methoden zur Studie von molekularen Wechselwirkungen in *S. cerevisiae* basierend auf dem erweiterten genetischen Code, Universität Stuttgart

Bilbao, J.
Phosphorus recovery from wastewater filtrates through a novel electrochemical struvite precipitation process, Universität Hohenheim

Frank, D.
Experimentelle Untersuchung und Modellierung der Fällung von Kalium-Magnesium-Phosphat, Universität Stuttgart

Gronen, A.
Identifizierung geeigneter Milchsäurebakterien zur Milchsäureproduktion aus Weizenstroh-Hydrolysat – Stammisolierung, Charakterisierung und Stoffwechselanalyse, Universität Stuttgart

Haller, B.
Entwicklung eines global übertragbaren raumbezogenen Planungsinstruments für das integrierte urbane Wassermanagement, Universität Stuttgart, Fraunhofer Verlag, ISBN 978-3-8396-0663-6

Hartmann, S. C.
Entwicklung eines DNA-Mikroarrays zur Identifizierung und Resistenzcharakterisierung Sepsis-assoziierter humanpathogener Mikroorganismen unter Anwendung der Receiver Operating Characteristic (ROC)-Analyse, Universität Stuttgart, Fraunhofer Verlag, ISBN 978-3-8396-0601-8

Hoch, E.
Hydrogelsysteme auf Basis UV-polymerisierbarer Biopolymere für den Aufbau von Gewebemimetika mittels Inkjet-Bioprinting am Beispiel von hyalinem Knorpel, Universität Stuttgart

Hoppensack, A.
Entwicklung eines humanen In-vitro-Modells des renalen proximalen Tubulus, Julius-Maximilians-Universität Würzburg

Kühnle, S.
Charakterisierung von Niederdruckmikroplasmen und ihre Anwendung zur Oberflächenmodifizierung von porösen, polymeren Hohlfasermembranen, Universität Stuttgart, Fraunhofer Verlag, ISBN 978-3-8396-0616-2

Ludwig, D.
Entwicklung von Verfahren und Prozessmodellen zur Fraktionierung von Lignocellulose, Universität Stuttgart

Moller, B.
Herstellung, Charakterisierung und Weiterverarbeitung von Carbon Nanotube Dispersionen, Universität Stuttgart

Moß, K. S.
Neue Mikroorganismen und Enzyme zur Herstellung von N-Acetylglukosamin und Chitobiose, Universität Stuttgart, Fraunhofer Verlag, ISBN 978-3-8396-0522-6

Pudlas, M.
Nicht invasive Diagnostik in der Regenerativen Medizin mittels Raman-Spektroskopie, Universität Stuttgart, Fraunhofer Verlag, ISBN 978-3-8396-0396-3

Schreiber, T.
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