



Fraunhofer

IGB

FRAUNHOFER INSTITUTE FOR INTERFACIAL ENGINEERING AND BIOTECHNOLOGY IGB

»PROJECT EARTH: OUR FUTURE«

ANNUAL REPORT

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ANNUAL REPORT
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RESEARCH AND
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“Markets Beyond Tomorrow, Sustainability and Bioeconomy” – Fraunhofer IGB’s Contribution

Dear Reader,

the major natural disasters of 2011 in Asia have once again demonstrated the enormity of the challenges we face in the 21st century. Securing supplies of raw materials, energy and water as well as fighting disease and hunger are core tasks in a year committed to the theme of sustainability. At the first Rio Conference in 1992, the international community of states set out Agenda 21 – affirming the common responsibility for sustainable development – and agreed important fundamentals for protecting the environment and resources. Twenty years on, the third successor conference will again take place in Rio de Janeiro. In Germany, the Year of Science 2012 will run under the slogan “Project Earth: Our Future”, with extensive participation from the Fraunhofer-Gesellschaft, the Stuttgart Fraunhofer site and the Fraunhofer IGB in the form of diverse activities and events.

2011 already saw the Fraunhofer IGB dedicate itself intensively to the topic of sustainability, e.g. through its involvement in the Fraunhofer Sustainability Network. In the “Sustainability Strategy” project, commissioned in 2010 by the Fraunhofer-Gesellschaft’s Executive Board, over 20 Fraunhofer institutes, lead-managed by the Fraunhofer IGB, developed a sustainability concept for the Fraunhofer-Gesellschaft comprising guiding principle, strategy and communication. They also identified needs for action in the “Sustainable Research and Business Processes” and “Research for Sustainability” areas at the Fraunhofer-Gesellschaft. The project clearly demonstrated that Fraunhofer is tackling the issues of the future in a responsible way and is using the opportunities that arise from these challenges. Three strategic messages crystallized out of the discussion process with internal and external experts, which we, too, are implementing at the Fraunhofer IGB (see above right).

Another part of the project involved the publication of the first cross-institute sustainability report for the five Stuttgart-based Fraunhofer institutes, coordinated by the Fraunhofer IGB and with the purpose of making the sustainable developments happening at the site more transparent. A particular challenge here was defining sustainability strategies and goals that are mutually valid for each of the five independent institutes with their different organizational structures. Apart from describing strategy and guiding principles, the institutes’ route to sustainable business processes as well as selected research projects with sustainability aspects, the report above all documents the initiatives of the employees, who represent an important pillar of sustainable development in an organization. It thus gives a picture of the organizational culture in practice at the Stuttgart site, offering the best prerequisites for further development of the site in terms of sustainability. The institutes intend to further foster employee engagement through joint activities and events in the Year of Sustainability Research 2012.

The sustainable use of natural resources and the development of efficient value-added chains, processes and products are the main research thrusts of a German bioeconomy strategy. Here we made considerable advances last year with our work on the material and energetic use of renewable raw materials. Of great significance for the Fraunhofer IGB were the developments at national and international levels. Through our involvement in the German government’s Bioeconomy Research and Technology Council (BioEconomyCouncil) and in European committees, we were able to contribute to further development of the “National Research Strategy BioEconomy 2030: Our route towards a bio-based economy” as well as to the development of new bio-based products and processes.

FRAUNHOFER – RESPONSIBLE RESEARCH

Invokes the guiding principle of sustainable development, including all the self-imposed obligations arising from the principle.

FRAUNHOFER – FROM INNOVATION TO TRANSFORMATION

This epitomizes our efforts to assist our customers and partners in achieving more sustainable structures.

FRAUNHOFER – OUT IN THE COMMUNITY

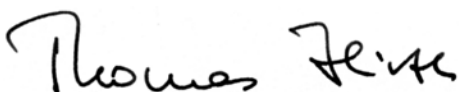
This motto expresses the opening up of our research to all groups of society in order to involve them in innovation processes.

In this context, our participation in the Federal Ministry of Education and Research (BMBF)'s Top Cluster Competition was a particular highlight. Thanks to our presentation on January 19, 2012 in Berlin, our central German BioEconomy cluster beat fellow competitors to come out top as one of five winners of the third round of the competition. Over 80 companies and research bodies from Saxony and Saxony-Anhalt have banded together in this "top" cluster, the core objective of which is the integrated material and energetic use of biomass not going into food production. Applications are the generation of innovative basic materials, chemicals, products from new materials and sources of energy. The BioEconomy cluster is concentrated around the Fraunhofer Center for Chemical-Biotechnological Processes CBP at the chemical site Leuna, which provides the facilities for the development and scaling of processes for the extraction and conversion of renewable raw materials up to industrial scale. From September 2012, a 2000-square-meter process center will be available to partners from research and industry to work together in developing processes for the material use of renewable raw materials up to technical scale.

In order to be able to tackle the challenges of the future, Fraunhofer addresses society's big fields of need such as health, energy, communications, the environment, mobility and security, and in 2011 rolled out its internal "Markets Beyond Tomorrow" program. Based on these global challenges, the Fraunhofer-Gesellschaft went through a cross-institute portfolio process and identified five future-oriented topics that anticipate research-intensive growth markets: low-loss production; the distribution and use of electricity; affordable health; closed loop production; low-emission, reliable mobility in urban areas as well as the identification and management of catastrophes. Together with other institutes the Fraunhofer IGB has attracted two projects which will contribute to developing integrated solution approaches and thus lead to Fraunhofer becoming technology leader within the German and European research landscape. All five departments of the Fraunhofer IGB are involved in the projects "SkinHeal – Healing Skin in the Petri Dish" and "Molecular Sorting – Perfectly Separated for Resource-Efficient Production".

The orientation of our business areas and core competences toward key societal areas of need such as health and food, safety and security, production and the environment, energy and housing, as well as mobility and transport, meant that the Fraunhofer IGB was able to maintain its good performance in 2011, and prepare for the challenges to come. Apart from advancing our R&D activities, we particularly concentrated last year on the issue of sustainable personnel development. The Fraunhofer IGB took a pilot role in the Fraunhofer-wide employee survey, achieving an excellent participation rate of 90 percent. In 2012, we intended to hold various workshops to capture the ideas of our staff and kick off a comprehensive succession process.

Indeed, the staff of the Fraunhofer IGB, supported by their IGVT colleagues, play a pivotal role in the IGB's scientific and commercial success. Last year we once again acquired numerous new commercial customers, as well as public donors and foundations as clients for R&D projects. My colleagues and I hope that the annual report for 2011 sparks your interest in our R&D activities and inspires you to consider working together with us soon. Together with our partners and customers, we aim to shape the future of the region, of Germany and of Europe through innovative, sustainable developments. In this spirit, I wish you an enjoyable read and look forward to your ideas and input.



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 300 experts in the fields of chemistry, physics, biology and engineering work effectively together at Fraunhofer IGB and IGVT. 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 individual Fraunhofer Institutes are advised by Advisory Boards whose members are drawn from industry, public authorities, and the scientific community.

Members

Dr. Manfred Baier
Roche Diagnostics GmbH

Dr. Gerd Eßwein
Freudenberg Forschungsdienste KG

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

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

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BASF SE

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MinR Dr. Joachim Wekerle
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Wacker Chemie AG

Prof. Dr. Karl-Heinz Wiesmüller
EMC microcollections GmbH

Dr. Wieland Wolf
ProBioGen AG

Dr. Markus Wolperdinger
Linde Engineering Dresden GmbH

Permanent guests

Prof. Dr. Herwig Brunner
Former Director of Fraunhofer IGB
Chairman of the Fraunhofer Group for Life Sciences

Prof. Dr. Uwe Heinrich
Fraunhofer Institute for Toxicology and Experimental Medicine ITEM



SERVICES AND INFRASTRUCTURE

Our contract R&D services range from basic research – scientific and technological – to the development of new applications, from laboratory up to 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 specialist areas of expertise. We can train your executives and introduce young people at school or studying to the fascinating world of science and technology.

Infrastructure and laboratory equipment

The Fraunhofer IGB has at its disposal modern laboratories equipped with the latest technology. 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

The Fraunhofer IGB has established a quality management system for the analytics carried out in its reference laboratories, ensuring the highest standards. Accreditation guarantees that

our proprietary, in-house test methods 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)
- Size exclusion chromatography (SEC)
- Gas chromatography (GC, GC/MS)
- Atomic emission spectrometry (ICP-OES)
- Electron spectroscopy for chemical analysis (ESCA/XPS)

Accredited biocompatibility and bioavailability testing

Our biocompatibility testing using cell lines and our 3D skin equivalent are accredited according to DIN EN ISO 10993-5. In December 2009, our two-dimensional intestinal assay (Caco-2) was included in the accreditation audit report. It was certified by the competent body, the Deutsche Gesellschaft für Akkreditierung (DGA), as an in-house method for the classification of substances by their transport characteristics at the intestinal barrier, which enables us, in turn, to certify analysis results.



GMP unit and authorization for the manufacturing of cell-based products

The Fraunhofer IGB has a good manufacturing practice unit for collaborative the development and manufacturing of clinical test material for cell and tissue engineering products (e.g. advanced therapy medicinal products, ATMPs).

Good laboratory practice (GLP) test facility

Our test category 9 GLP test facility ("Cell-based test systems for the determination of biological parameters") is used in research and development projects such as the investigation of the biological activity of type 1 interferons using the antiviral assay (AVA) or the detection of pyrogens.

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

Biochemical and molecular biological analytics:
diagnostic biochips, RNA and protein expression profiles, protein analysis using MALDI-TOF/TOF mass spectrometry (also quantitative)

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

REACH:
evaluation and testing of chemicals

For detailed information,
please order our special brochures or visit:
www.igb.fraunhofer.de

KEY FIGURES

Personnel

At the end of 2011, the Fraunhofer IGB had a staff of 281. Some 90 percent were scientific or technical employees. Women made up 59 percent of the total.

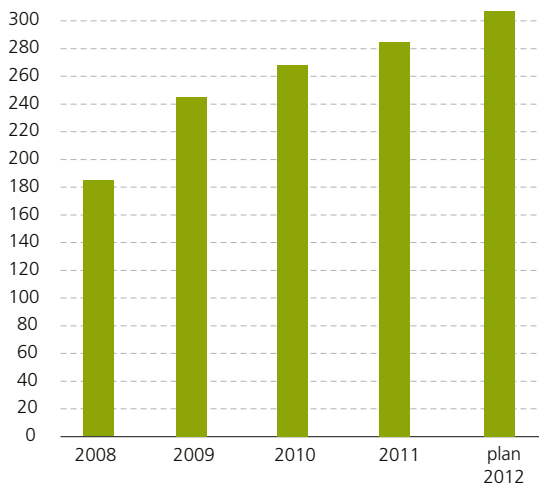
The university institute IGVT counted a staff of 60 effective December 31, 2011, predominantly scientists and Ph.D. students as well as technical staff and student research assistants. Women made up 55 percent of the total.

The Fraunhofer IGB and IGVT staff members, of which 70 persons come from 39 different countries other than Germany all around the world, work closely together.

Staff members Fraunhofer IGB	number
Scientists	66
Technical staff	68
Graduate student research workers	59
Student research assistants	55
Administrative and secretarial staff	24
Trainees	9
Total	281

Staff members IGVT	number
Scientists / Ph.D. students	40
Technical staff	4
Student research assistants	16
Total	60

number staff members Fraunhofer IGB



number staff members IGVT



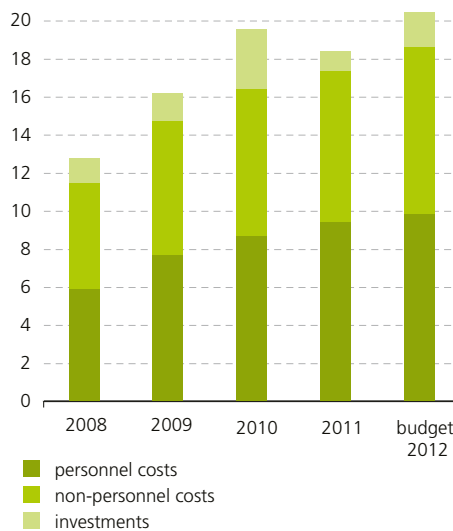
Budget of Fraunhofer IGB

The total budget for 2011 amounted to 18.6 million euros, of which 16.8 million euros was allocated to the operational budget (personnel costs: 9.1 million euros; non-personnel costs: 7.7 million euros). A total of 1.8 million euros was spent on investments.

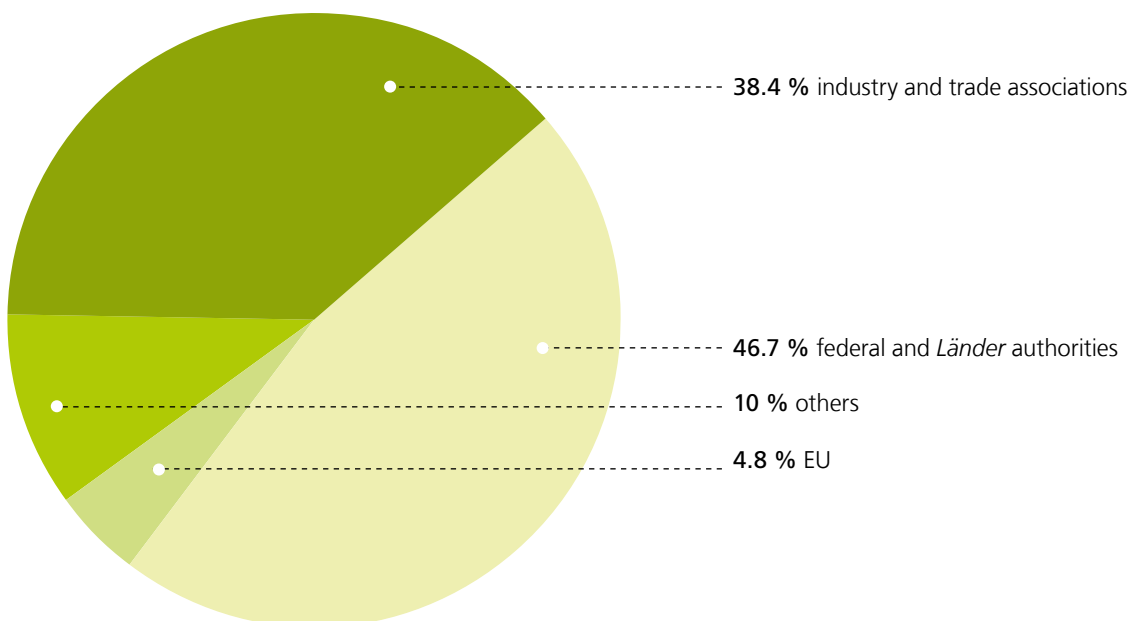
67 percent of the operational budget was financed from Fraunhofer IGB's own revenues generated from contract research projects, while governmental funding covered the remaining 33 percent. 38 percent of the Institute's revenues came directly from industry.

DEVELOPMENT OF BUDGET

in million euros



REVENUE FROM CONTRACT RESEARCH



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

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- Functional Genomics
- Molecular Cell Technologies
- Enzyme, Strain and Process Development for Biotechnology
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- Drying and Extraction
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- Bio-energy
- Interfacial Biology

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- Vascularized Test Systems
- Cells and Biomaterials
- Bioreactors for Tissue Engineering
- GMP Production of Cell-based Products

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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 sustainable standpoints.

Networking with universities

Basic research enables the applications of tomorrow. Therefore the Fraunhofer IGB maintains close contacts with neighboring universities, both through scientific cooperation and through Fraunhofer staff carrying out professorial and other teaching duties. Our project groups in particular have enabled us to extend our scientific network to sites outside of Stuttgart and as far as the USA.

- **Prof. Dr. Dieter Bryniok**
Chair of Environmental Biotechnology,
Hamm-Lippstadt University of Applied Sciences
- **Prof. Dr. Thomas Hirth**
Chair of Interfacial Engineering, University of Stuttgart;
Director of Institute for Interfacial Engineering IGVT at the
University of Stuttgart
- **Dr. Petra Kluger**
Teaching assignment in the Faculty of Energy Technology,
Process Engineering and Biological Engineering, University
of Stuttgart
- **Dr. Christian Oehr**
Teaching assignment in the Faculty of Energy Technology,
Process Engineering and Biological Engineering, University
of Stuttgart
- **Priv.-Doz. Dr. Steffen Rupp**
Lectureship in the Faculty of Chemistry and of the
Faculty of Energy Technology, Process Engineering and
Biological Engineering, University of Stuttgart
- **Prof. Dr. Katja Schenke-Layland**
Chair of Biomaterials in Cardiovascular Regenerative
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ty, Tübingen, and Visiting Assistant Professor at the Depart-
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Los Angeles (UCLA), Los Angeles, California, USA
- **Dr.-Ing. Ursula Schließmann**
Teaching assignment in the Faculty of Energy Technology,
Process Engineering and Biological Engineering, University
of Stuttgart
- **Prof. Dr. Volker Sieber**
Chair of Chemistry of Biogenic Resources,
Technische Universität München



■ **Priv.-Doz. Dr. Günter Tovar**

Lectureship in the Faculty of Chemistry and the Faculty of Energy Technology, Process Engineering and Biological Engineering, University of Stuttgart; Deputy Director of Institute for Interfacial Engineering IGVT at the University of Stuttgart

■ **Prof. Dr. Walter Trösch**

Supernumerary Professor for Biotechnology, University of Hohenheim

■ **Prof. Dr. Heike Walles**

Chair of Tissue Engineering and Regenerative Medicine, University of Würzburg

Fraunhofer Sustainability Network

Sustainable development is arguably the most important key political objective of our time. The guiding principle of sustainable development takes equal account of environmental considerations and social and economic aspects, and also encompasses our intra- and intergenerational responsibilities. What this means in concrete terms for the Fraunhofer-Gesellschaft is expressed in the activities of the 20 institutes that comprises the society's Sustainability Network, chaired by Professor Thomas Hirth (see page 28). The Fraunhofer IGB has been involved in all three sub-projects.

www.nachhaltigkeit.fraunhofer.de

Fraunhofer International Business Development (IBD) Network

International cooperations and joint development activities between globally active partners are of strategic importance for Fraunhofer and its institutes. The Fraunhofer IGB is active member of the Fraunhofer IBD Network and coordinates the International Position Task Force which will illuminate aspects of the internationalization strategy from the viewpoint of the Institute.

Fraunhofer EU Network

The EU Network constitutes a common platform for all Fraunhofer colleagues involved in promotion of European research. The spirit and purpose of the network is the exchange of information and experience regarding both strategic aspects of funding and how to handle application and tendering procedures effectively, as well as how to ensure the smooth implementation of EU financed projects. The EU Network is coordinated by Maximilian Steiert from Fraunhofer-Gesellschaft headquarters and Ina Andrees-Ostovan of the Fraunhofer IGB.

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 on the topic of EU grants for non-university research establishments.

FRAUNHOFER GROUPS AND ALLIANCES

Institutes working in related subject areas cooperate as groups and foster a joint presence on the R&D market. They help to define the Fraunhofer-Gesellschaft's business policy and act to implement the organizational and funding principles of the Fraunhofer model. The Fraunhofer thematic alliances facilitate customer access to the services and research results of the Fraunhofer-Gesellschaft. Common points of contact for the network of institutes active in related fields provide expert advice on complex issues and coordinate the development of appropriate solutions.

Fraunhofer Group for Life Sciences

www.lifesciences.fraunhofer.de

The Group for Life Sciences is a key R&D partner to the pharmaceutical and medical engineering industries and to the fast-growing biotech industry. By pooling complementary areas of expertise, the members are able to offer a broad spectrum of technologies and services. The Group cultivates 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 translation research and biomedical technology, regenerative medicine, healthy foods, industrial biotechnology, and process, chemical, and herbicide safety, thus bundling numerous Fraunhofer IGB key competences.

Fraunhofer Group for Materials and Components – MATERIALS

www.vwb.fraunhofer.de

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 covers 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.

Fraunhofer Building Innovation Alliance

www.bau.fraunhofer.de

The Building Innovation Alliance offers single-source construction expertise by means of integrated systems solutions. It has particular expertise in the systematic assessment of buildings – from materials to structural elements, from rooms and buildings to complete villages. The portfolio also covers the chronological assessment of a building comprising its entire life cycle – from drawing board to construction and finally recycling. Fraunhofer IGB contributes to this alliance with its infrastructure concepts for semi-decentralized energy and water management as well as with its microbiological competences in building-biology.

Fraunhofer Energy Alliance

www.energie.fraunhofer.de

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 and the energy business sector too, benefit from Germany's technology leadership in energy efficiency and renewables. The Fraunhofer IGB contributes its knowledge in the exploitation of the material and energy resources contained in raw, residual and waste organic materials (e.g. for biogas production) as well as membrane technology, particularly for gas purification/reforming and fuel cell applications. Furthermore the Fraunhofer IGB performs research on concepts and technologies for storage and use of energy in the form of heat.



Fraunhofer Nanotechnology Alliance

www.nano.fraunhofer.de

The Fraunhofer Nanotechnology Alliance bundles the competences of nearly one third of the Fraunhofer Institutes, covering almost all aspects of nanotechnology. Activities are focused on three main areas: multifunctional layers e.g. for automotive applications; the design of special nanoparticles as carrier substances for biomedical applications; and the use of carbon nanotubes for actuator applications. The two latter applications are key research fields at the Fraunhofer IGB. Dr. Günter Tovar is the Alliance's deputy spokesman and chief contact person for nanobiotechnology questions.

Fraunhofer Photocatalysis Alliance

www.photokatalyse.fraunhofer.de

Ten Fraunhofer Institutes are involved in this alliance, developing more effective and efficient photocatalysts for applications on glass, ceramics, polymers and metal. 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 new layer, the Fraunhofer Photocatalysis Alliance has developed analysis procedures for chemical-physical as well as microbiological evaluation – the latter being Fraunhofer IGB's remit within the alliance.

Fraunhofer Polymer Surfaces Alliance POLO

www.polo.fraunhofer.de

The Fraunhofer Polymer Surfaces Alliance POLO pools the core competences of seven Fraunhofer Institutes in the development of polymer products with new or significantly enhanced properties by functional surfaces, barrier layers or thin films. POLO was among the first Fraunhofer alliances, and products such as coatings of foil as barrier against oxygen and humidity as well as anti-microbial polymer surfaces have already been developed and marketed conjointly. The Fraunhofer IGB's Dr. Christian Oehr has been a member of the alliance's management since its inception, and has contributed significantly to its success.

Fraunhofer Cleaning Technology Alliance

www.allianz-reinigungstechnik.de

Cleaning technology has increasingly accepted as value-added, e.g. in hygienic production, in microsystems technology, in industrial cleaning of parts or for the pre-treatment of coated surfaces. The alliance covers the entire spectrum of cleaning technology processes including special technologies like laser, plasma or mechanical jets and can provide autonomous and modular turn-key solutions for cleaning systems. Application-specific cleaning devices and equipment are designed and constructed according to process developments. Further competence is the water, process water and wastewater purification combined with energy and material recycling. The Fraunhofer IGB contributes its expertise e.g. in the plasma purification and plasma coating, in the evaluation by surface analytical methods and of microbial contaminations. Further fields of competences are the conditioning and recycling of cleaning and process media as well as construction with respect to cleaning and hygienic design.

Fraunhofer Water Systems Alliance (SysWasser)

www.syswasser.de

Since June 2007, several Fraunhofer Institutes have been pooling their expertise in the development of water systems technologies. SysWasser's mission is to develop sustainable solutions for water treatment, water utilization, water management, and water infrastructure systems and adapt them for use in practical applications on a national and international level, taking into consideration relevant social, economic and environmental aspects. The participating institutes provide a wide range of different technologies which are used by the entire alliance as technology modules for developing optimized system solutions or individual solutions. Its valuable past experience on water infrastructures, systems control and measurement technologies, automation and resource management, enable the alliance to develop skillful master plans and put these into action. Spokesman for the alliance is its founder, Professor Walter Trösch. His objective is an integrated, systemic approach linking water with the energy, waste management and agricultural sectors. Professor Dr. Dieter Bryniok is managing director.

HIGHLIGHTS 2011

PEOPLE AND PRIZES

Department of Environmental Biotechnology and Bioprocess Engineering gets new head

After 35 years of research for Fraunhofer, Professor Walter Trösch was seen off into retirement on May 20, 2011 with a celebratory colloquium attended by colleagues and associates from politics, science and industry. Walter Trösch commenced his career at the Fraunhofer IGB in 1976 as a researcher, subsequently rising to departmental head and deputy head of the institute and making a vital contribution to the institute's scientific development and commercial success. His research activities in the fields of environmental bioprocess engineering and the biotechnology of algae have been trailblazing, and he has been the initiator of multifarious developments such as the two-stage process for the high-load digestion of sewage that has been implemented at several sewage works. With "DEUS 21" and the "Knittlingen Water House" he has created a novel water infrastructure concept that has attracted much international recognition and which was awarded the Joseph-von-Fraunhofer Prize in 2007. Professor Trösch's outstanding contribution has been honored with the Fraunhofer medal presented by Professor Buller of the Fraunhofer-Gesellschaft's Executive Board.

In June 2011, Dr.-Ing. Ursula Schließmann took over as head of the Department of Environmental Biotechnology and Bioprocess Engineering. Having acted as Trösch's deputy for four years, the process engineer is well placed to tackle the challenges of her new post. Schließmann joined the Fraunhofer IGB

in 1995, in the former Department of Membrane and Processing Technology where her initial remit focused on the use of membranes, e.g. for product reprocessing. She deepened this knowledge in her doctoral thesis and for the reprocessing of a food supplement manufactured by fermentation she developed a process combining electro dialysis with different filtration techniques. Schließmann subsequently switched to the Department of Environmental Biotechnology and Bioprocess Engineering, where she concentrated on bioenergy. As head of department she intends to continue with the existing fields of activity and in particular expand the interrelated topics of material and energetic use of biomass. It is of particular concern to her as a process engineer to translate biological processes into ones that can be industrially exploited.

Katja Schenke-Layland accepts professorship at the University Hospital Tübingen

Professor Katja Schenke-Layland, head of the Attract Cardiovascular Systems working group in the Department of Cell and Tissue Engineering at the Fraunhofer IGB, accepted a full professorship at the University Hospital of the Eberhard Karl University in Tübingen on October 1, 2011. Thus in addition to her duties at the Fraunhofer IGB, Schenke-Layland now also leads the working group "Biomaterials in Cardiovascular Regenerative Medicine" at the University Clinic for Thorax- and Cardiovascular Surgery. Schenke-Layland will carry out



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her teaching duties at the Interuniversity Centre for Medical Technologies Stuttgart – Tübingen (IZST), an association of various institutes of the universities of Stuttgart and Tübingen, which are active in the medical engineering research field.

“Skin Factory” is selected “landmark”

The “Production System for Human Skin” which was developed jointly under the leadership of Professor Heike Walles at the Fraunhofer IGB together with the Fraunhofer Institutes for Manufacturing Engineering and Automation IPA, Production Technology IPT and Cell Therapy and Immunology IZI, was one of the prizewinners in the 2011 nationwide innovation competition “365 Landmarks in the Land of Ideas”. On October 26, 2011 the “Skin Factory” – one of 2600 entries submitted – was honored in Stuttgart as a chosen “landmark”, having convinced the independent judging panel. With this first fully automated production system some five thousand postage stamp size skin models can be produced every month and used to test the irritative potential of cosmetics and the toxicity of chemicals realistically, thus reducing the need for animal experiments.

1st place for Christian Schuh at Elevator Pitches

The Fraunhofer IGB’s Dr. Christian Schuh emerged as winner on the second day of the Elevator Pitches ideas competition at the Fraunhofer internal networking symposium “Netzwerk 2011” with 33.6 percent of the participants’ votes. In 90 seconds he sketched out his idea for recovering phosphate used as fertilizer for agricultural purposes and washed out from the soil by water. To this end, he intends to encapsulate populations of phosphate-enriching bacteria in a carrier material, through which the water will stream. If the material is biodegradable, it can be subsequently be re-spread on the fields.

After the success of 2010, the second Fraunhofer “Netzwerk” symposium to foster mutual awareness and cooperation across the institutes, took place late November 2011 with some 350 participants from the Fraunhofer-Gesellschaft, industry and politics. The two-day event showcased ongoing projects as examples of the current Fraunhofer portfolio and served as a communication platform to promote networking.

- 1 *Professor Trösch is being honored with the Fraunhofer medal presented by Professor Buller.*
- 2 *Professor Katja Schenke-Layland.*
- 3 *Dr. Christian Schuh.*



PROJECT GROUPS | JOINT PROJECTS | PROJECTS

BioEconomy cluster wins Leading-Edge Cluster competition

In 2011, the Fraunhofer CBP in Leuna took part in the third round of the Leading-Edge Cluster competition launched by Germany Federal Ministry of Education and Research (BMBF), competing against companies from the sectors of chemical production, the petroleum industry, energy generation, the wood industry and plant engineering, as well as numerous other research institutions. The Fraunhofer CBP's BioEconomy Cluster, under the scientific coordination of Professor Thomas Hirth was named one of five winners in January 2012.

The aim of the cluster is to sustainably increase value creation from native beechwood through using the techniques of coupled production and cascade utilization to produce chemicals, materials and energy. The Fraunhofer CBP will assume a central role in the development, scale-up and industrial realization of production processes here.

The existing industrial structures in the region around the Leuna chemical site will be linked with the Fraunhofer CBP's own external network, comprising the Chemistry/Plastics Cluster of Central Germany (2003), the Rottleberode Wood Cluster (2007) and the Leipzig Energy and Environmental Technology Cluster with its Bioenergy team (2010).

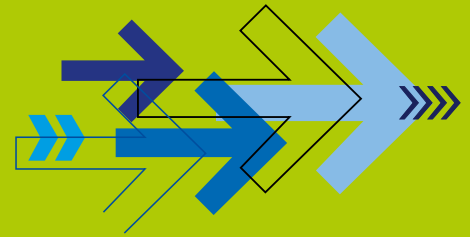
The research side integrates bodies including the Fraunhofer Institute for Mechanics of Materials IWM, Halle, the Fraunhofer pilot plant center (PAZ) for polymer synthesis and polymer processing at Schkopau ValuePark, the Martin-Luther-Universität Halle-Wittenberg, the German Biomass Research Centre, the Helmholtz Centre for Environmental Research and the Leipzig Graduate School of Management (HHL).

Thus the cluster has cross-sector access to numerous specialists for all the various stages of value creation of a biobased economy. Their respective expertise spans the entire complex value creation chains constituting the bioeconomy and creates a nationally and internationally visible beacon for this new paradigm for economic activity.

www.bioeconomy.de

Topping-out ceremony at the Fraunhofer CBP

With the topping-out ceremony on October 6, 2011 celebrating the conclusion of the structural work, the Fraunhofer CBP's new premises are taking shape on an area of over 2000 square meters. The ceremony simultaneously marked the start of interior fitting of the offices and laboratories and the expansion of the process plants. Completion, commissioning and subsequent test operations are planned for summer 2012.



Fraunhofer system research into “cell-free bioproduction”

In order to produce proteins on an industrial scale, biotechnologists have previously harnessed the activities of living cells or microorganisms in bioreactors. With the aid of genetic engineering methods, these organic materials are tweaked to produce the large biomolecules in their three-dimensional form – for chemical reproduction is not possible. This approach does, however, have its drawbacks: toxic proteins kill cells, the membrane proteins of interest for the pharmaceuticals industry can only be manufactured with difficulty, and purification of the proteins is laborious.

The goal of biologists, physicists, mechanical engineers and electronics engineers from the eight institutes in the Fraunhofer Biomolecules from the Production Line Group is to produce proteins on industrial scale using cell-free production methods dispensing with living cells and microorganisms. The Fraunhofer-Gesellschaft is making 6 million euros available for this, as part of its system research. This investment is being supplemented by the Germany Federal Ministry of Education and Research (BMBF) to the tune of 15 million euros for the next three years. The production of proteins is to be divided up into three modules: the actual protein synthesis, subsequent processing, and energy supply.

The Fraunhofer IGB has a central role in this joint project; it is tasked with ensuring the supply of energy to the cell-free compartments. The enzyme ATP synthase, which provides

energy for the cell to use through the synthesis of adenosine triphosphate (ATP), is a peripheral membrane protein. Its integration into technical systems thus represents a particular challenge, including the isolation of ATP synthase, the provision of membrane elements for a reactor structure, and the modeling of the system. This is being jointly worked on by the Fraunhofer IGB departments of Molecular Biotechnology, Interfacial Engineering and Materials Science, and Cell and Tissue Engineering. ATP synthase and the first membrane vesicles have already been successfully isolated and synthesized (see project report page 72).

Markets Beyond Tomorrow

Applied research is always oriented to need, including that of future markets. As part of its strategy process, the Fraunhofer-Gesellschaft has therefore defined which research projects will provide important results for tomorrow and the day after. In the Markets Beyond Tomorrow research program five projects are being funded by up to five million euros. The Fraunhofer IGB is a participant in two of the five projects.

- 1 *Germany's Leading-Edge Cluster.*
- 2 *Topping-out ceremony at the Fraunhofer CBP. © Scherr + Klimke*
- 3 *Membranes can accumulate metals from source streams selectively.*



The “Molecular Sorting for Resource Efficiency” project is focused on consistent recycling and cyclical production following the zero new raw materials approach to manufacturing. This is made possible by the development of new processes for material separation right down to the molecular level, so that residual materials can be reused as secondary raw materials in the production process. The first stage of the project involves developing sample demonstrators for diverse streams of material and transferring these to other technologies.

In the Beyond Tomorrow “SkinHeal” project, researchers are aiming to improve the treatment of chronic wounds. This can be made more effective by enabling patients to check themselves whether an open wound has healed, or whether bacteria have entered the site.

RIBOLUTION – platform for identification of RNA-based diagnostics for personalized medicine

In the “RIBOLUTION” project funded by the Fraunhofer-Zukunftsstiftung (Fraunhofer Future Foundation) and launched in January 2011, Fraunhofer researchers from the institutes IZI (coordination), IGB, IPA, ITEM and FIT are collaborating with partners from clinical practice and the pharmaceuticals industry to develop new diagnostic indicators for diseases such as prostate cancer. The search for biomarkers is focused on the as yet little researched non-protein-coded ribonucleic acids (ncRNAs). When the human genetic code was deciphered

10 years ago, the large areas of our DNA which are not translated into proteins – i.e. seemingly not used – were dismissed as “junk DNA”. However, more recent studies show that their transcripts, the ncRNAs, represent the central level of cell biological control and regulate the transcription and translation of the protein-coding genes. They may therefore play a decisive role in the development of disease – and come into consideration as diagnostic biomarkers. Through the comparison of the ncRNA of sick and healthy individuals, the Fraunhofer IGB researchers are currently screening the entire genome with high throughput next-generation sequencing, allowing up to 10^9 DNA sequence fragments to be detected in parallel (see project report page 62).

Mayor Schuster visits EtaMax facility

“Zero Emission” was the slogan under which the Mayor of Stuttgart, Dr. Wolfgang Schuster, and the head of municipal business development, Ines Aufrecht, visited innovative companies on October 13, 2011. One station was a demonstration plant operated by the Fraunhofer IGB as part of the BMBF-funded “EtaMax” joint research project on the grounds of the EnBW combined heat and power plant in Stuttgart-Gaisburg. Here, organic waste from the wholesale market in Stuttgart will be fermented into biogas. This will be refined by the removal of carbon dioxide, and the resulting biomethane will be used as a fuel for gas-powered vehicles.

1 *Skin test system.*

2 *Mayor Schuster visits EtaMax facility.*



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© C. Flemming/Entdeckungen

EXHIBITIONS

MS Wissenschaft 2011 – New Paths in Medicine May 19 to September 29, 2011

Last year's exhibition on board the MS Wissenschaft ("Science") was entitled "New Paths in Medicine" and was all about research on health issues. The converted river freight barge was underway from May 19 to September 29, departing from Stuttgart. Late September the barge arrived at its final station in central Berlin, after having covered 3640 kilometers in Germany and Austria, visiting 35 cities between Hanover in the north and Vienna on the most southerly leg of the tour. Some 72,000 visitors – including 420 school classes – packed the 600 square-meter exhibition space on board to experience over 30 exhibits on the topics of processes in our body and new developments in the investigation, diagnosis and treatment of illnesses and ailments. Social issues, as well as medical aspects, were addressed.

The Fraunhofer IGB's exhibit showcased artificial tissue models created from human liver and skin cells. Using these models, which have characteristics similar to those of the body's organs, allows researchers in medical engineering and cosmetics, the pharmaceuticals and chemical industries to carry out testing without the need for animal experiments. The visitors were able to compare histological slices of the models under a microscope with those of the natural organs and watch a short film showing them how scientists build the test systems.

"DISCOVERIES 2011: Health" May 20 to September 4, 2011, Island of Mainau, Lake Constance

From May 20 to September 4, 2011, 18 pavilions, an informational tour and an art installation stimulated inquiring minds and the thirst for knowledge from visitors of all ages to the Island of Mainau's "Health Discoveries" exhibition, featuring exhibits to try out and activities to join in. In comprehensible and fun way, the different contributions gave an impression of the innovative power of research in the health sector. Thus, for example, the exhibition showed what successes have been achieved in the prevention and treatment of the "lifestyle" disease diabetes, what diverse applications there are for modern biotechnology, and why sport and healthy diet are still the most effective preventative measures. Further topics were infectious diseases, cancer and rare diseases, and there was an opportunity to learn the basics about the function of the brain.

Seeing, hearing, feeling, tasting, smelling – research focused on the senses was the guiding topic in the Fraunhofer pavilion, where Fraunhofer experts presented selected research projects. In the "feeling" section, Fraunhofer IGB staff explained how scientists cultivate skin in vitro, and, using an accumulation of skin cells, construct skin models that replicate the various layers of skin – no easy task. In the current "Tissue Engineering on Demand" project, the scientists are growing the skin in a small "factory". The artificial skin helps to reduce the number of animal experiments. In future it is hoped to also use it to heal patients with large areas of damaged skin.



SUSTAINABLE RESEARCH – RESEARCH FOR SUSTAINABILITY

Finite resources, social injustice and unstable financial markets are the complex challenges of today's world that we can only tackle through sustainable thinking and acting. The task of research is to contribute to solving this problem with innovative and unconventional developments.

Fraunhofer project "Sustainability Strategy"

In the "Sustainability Strategy" project completed at the end of 2011, the twenty institutes involved in the Fraunhofer Sustainability Network compiled guidelines for the concrete implementation of the sustainability principle within the Fraunhofer-Gesellschaft. The goal is for Fraunhofer to become a trailblazer – both with regard to the implementation of sustainability topics in applied research and the integration of excellence in research with internalized behavior. As spokesman of the network, Professor Thomas Hirth is coordinator of the project, which encompasses the three subprojects "Overall Concept, Strategy and Communication", "Sustainable Research and Business Processes" and "Research for Sustainability". Fraunhofer IGB staff took part in all three subprojects.

Overall concept, strategy and communication

The first subproject, which was led by Professor Thomas Hirth and had a strategic orientation, was concerned with developing a sustainability concept for the Fraunhofer-Gesellschaft. This includes a proposal for a mission statement, both internal

and external spheres of activity, and a catalog of measures. An online survey involved all Fraunhofer staff in the process, and there was also interdisciplinary dialog both at the level of the Sustainability Network and the Fraunhofer headquarters as well as with external experts.

Sustainable research and business processes

The results from the other two subprojects also flowed into the sustainability concept. The spheres of activity in the second subproject are more of internal interest. First, the project team developed the basics for a toolbox for the evaluation of innovative processes which is hoped will lead to an increase in the share of genuine sustainability innovations arising from research. Second, the daily routine decision-making and work processes are to be restructured sustainably. In particular, the areas of personnel, infrastructure, business trips and events were examined and improvements proposed. Communication of what has been achieved and of the planned measures in respect of employees, customers and partners plays an important role here.



Pilot location Stuttgart – sustainability report

The Institutes Center Stuttgart IZS together with the Fraunhofer IGB and four further institutes served as a pilot location for the Fraunhofer's first campus-wide sustainability report. In cross-institute workshops the dimensions of sustainability were translated into four perspectives and corresponding guidelines were compiled as an orientation aid for all staff. The perspectives are: employees, processes, markets and innovation, and society. Selected indicators were evaluated for each of these spheres of activity and best-practice examples presented in order to illustrate change along the lines of sustainable development. Location-based measures for improvement were proposed and will now be implemented on campus in the short or medium term. In addition, the report seeks to showcase outstanding research projects on sustainability topics carried out by individual and cooperating institutes at the Fraunhofer IZS. A follow-up report is to appear every two years. This form of sustainability reporting, which was previously introduced by two institutes (UMSICHT, ICT), serves to highlight the ways to a Fraunhofer-wide sustainability report.

Research for sustainability

The third subproject, which has more of an external dimension, focused on identifying fields of research with promise for the future. The aim was to round off the Fraunhofer-Gesellschaft's portfolio in the field of sustainability with a view to the organization's strategic development. The fields of research include renewable energy, resources, water, and food and agriculture. The research activities of the Fraunhofer IGB are represented in all these areas; moreover, the focus on health research means that the institute is already well positioned with regard to sustainability topics. The strategic considerations in this subproject were also focused on a greater assumption of international responsibility through cooperations in newly industrialized and developing countries. By virtue of its already highly diverse skills base and the high degree of cross-linking in the research landscape, the Fraunhofer IGB is also set to fulfill expectations to contribute to the Fraunhofer-Gesellschaft's striven-for leadership as a system provider in sustainability research.

*www.nachhaltigkeit.fraunhofer.de
www.izs.fraunhofer.de*



PROMOTING YOUNG TALENTS

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

At the Fraunhofer Talent School 2011, which first took place at the Stuttgart site in 2009, Dr. Kai Sohn, deputy head of Molecular Biotechnology, led a workshop on the topic of genetic analysis for the third 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 (DNA). 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 2012, once again contributing to the success of the Fraunhofer Stuttgart Talent School.
www.izs.fraunhofer.de/schueler-izs/fraunhofer-talent-school

Girls' Day at the Fraunhofer campus in Stuttgart

In Germany we currently have the best educated cohort of young women of all times, with girls making up 55.7 percent of high-school graduates alone. 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. 2011 saw once again well over 100 interested participants in Stuttgart, some of whom visited the "Magic liquids and fascinating surfaces" and "Making DNA visible" information stations at the Fraunhofer IGB. The next Girls' Day will take place on April 26, 2012.
www.izs.fraunhofer.de/schueler-izs/girls-day

BOGY – vocational and academic careers orientation at academic high schools

19 high-school students completed their "BOGY" internships at the Fraunhofer IGB in 2011. 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.

www.izs.fraunhofer.de/schueler-izs/schuelerpraktika

Open day for university students

On January 16, 2012, over 100 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 institute’s 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 rising numbers of participants, especially of female students, reflect the success of the event, which has taken place once a year since 2007.

www.izs.fraunhofer.de/studierende

Training at the Fraunhofer IGB

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.

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. www.igb.fraunhofer.de/de/jobs-karriere/ausbildung.html



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FRAUNHOFER IGB'S INTERNATIONAL ACTIVITIES

EU

The 7th Framework Programme for Research and Technological Development (FP7) is the main instrument of European research funding and supports the European Union in its aim of becoming the most dynamic and competitive knowledge-based economy in the world. Of interest to the Fraunhofer IGB is not only the Cooperation program with its calls for research proposals (10 distinct themes including: Health; Environment; Energy; Nanosciences, Nanotechnologies, Materials & New Production Technologies (NMP) plus the knowledge-based bioeconomy (KBBE) under Food, Agriculture and Fisheries, and Biotechnology), but also the calls specifically targeted at small and medium-sized enterprises (SMEs).

ChiBio

In the ChiBio project, the Straubing BioCat Project Group led by Prof. Volker Sieber is collaborating with international partners to develop new methods of producing specialty and fine chemicals from chitin-rich fishing-industry waste. Effectively operating as a biorefinery, ChiBio aims to utilize the residual waste material as efficiently and completely as possible and develop or optimize various material (monomers for polymeric applications) and energetic (biogas production) uses. The consortium comprises research and industrial partners from Norway, Austria, the Czech Republic and Ireland but also Tunisia and Indonesia in order to have access to fisheries waste from African and Asian as well as European sources.

www.chibiofp7.eu

BioConSepT

The BioConSepT project aims to demonstrate the technical feasibility of white biotech processes for the conversion of 2nd generation biomass into platform chemicals. BioConSepT uses lignocellulose and non-edible oils and fats as cheap, abundantly available feedstocks, which cannot be used for the production of food. The main project objectives are:

- To develop robust enzymes and microorganisms suited for 2nd generation feedstocks.
- To reduce costs through the integration of bioconversion and highly selective separation technologies.
- To facilitate easy integration of bioconversion steps into existing production chains by deploying combinations of biological and chemical conversions for bio-based polymers, resins, plasticizers, solvents and surfactants.
- Realization of the first demonstration of integrated production chains from 2nd generation feedstocks to platform chemicals on an industrially relevant scale.

The consortium consists of 15 SMEs (suppliers of equipment, separation technologies and services; bioconversion specialists), 10 large industrial parties (producers, end-users, engineering and consultancy companies) and 5 leading research technology organizations (RTOs) from 11 different countries.

www.bioconsept.eu

H2OCEAN

The aim of the H2OCEAN project is the development of an offshore platform to harvest wind and wave power and use the energy generated locally for multiple applications – including a multi-trophic aquaculture farm. Excess energy will be converted on-site into hydrogen that can be stored and shipped to shore as a “green” energy carrier. In the desalination sub-project,



the IGB's main task will be optimizing reverse osmosis (RO) membranes with low-fouling properties.
www.h2ocean-project.eu

ArtiVasc 3D

The creation of multi-layer tissue structures designed to enable the diffusion of nutrients for surrounding cells is one of the biggest challenges faced by medical research. Under the leadership of the Fraunhofer Institute for Laser Technology ILT, a consortium of 16 European partners from industry and the research community will, over the next four years, combine different technologies from the fields of additive manufacturing and bio-functionalization to develop a process capable of engineering blood vessels in an artificial scaffold system. The vascularized scaffolds will be populated with autologous cells in order to enable the formation of vascularized fatty tissue and, ultimately, artificial skin. This artificial skin will be used as an in vitro test system – for example to reduce the number of animal experiments – and employed directly in skin grafts.
www.artivasc.eu

ConductMem

The EU ConductMem project tackles a central problem of filtration systems and, in particular, of membrane filter plant: biofilms and biofouling. It aims to develop an advanced system that can permanently prevent biofilm formation and surface fouling by the electrolytic production of biocidal oxidizing agents on the membrane surface itself. The trans-European consortium of chiefly small and medium enterprises will demonstrate the technology on membrane bioreactors used for wastewater treatment.
www.conductmem.eu

SolChemStore

The objective of this EU project is the development of a thermo-chemical heat storage technology capable of storing heat at temperatures between 100 and 200 °C, thus increasing

the energy efficiency in industrial processes, in particular in the food industry. Such a technology would also facilitate the use of solar thermal systems like Fresnel collectors. The basic principle here is a reversible, exothermal reaction of two fluids. The project will investigate and evaluate different reaction pairs and system configurations.
www.solchemstore.eu

EcoArtiSnow

Artificial snowmaking is of vital importance to the economy of many regions in the Alps and other mountain areas dominated by small and medium enterprises that have to face warmer winter periods due to climate change. As part of the EcoArtiSnow project, the Fraunhofer IGB is working together with a European consortium of industry and research partners on an integrated approach to significantly improving snowmaking equipment ("snow cannons" or "snow guns", etc.). The objectives are the reduction of energy consumption, improved snow quality, higher production rates and reduced noise emission.
www.ecoartisnow.eu

O4S

As a part of the EU-funded O4S (=Organic for Surfactants) project on organic cosmetics, research is being conducted in collaboration with experienced natural cosmetics manufacturers and experts in biotechnology to obtain biosurfactants from renewable by-products from organic production. In order to guarantee a sustainable and ecologically sound manufacturing process, only gentle conversion and processing methods are allowed. The future-oriented project is intended not only to meet the ever higher standards of consumers, in particular the desire to avoid chemical additives; it also aims to ensure economic viability while at the same time, complying with the strict, controlled biological and ecological principles.
www.organic4surfactants.eu



BRAZIL

Visit of UNIMEP President

The Fraunhofer IGB has long-standing contacts with the Universidade Metodista de Piracicaba (UNIMEP), which were once again deepened in 2011. Professor Clovis Pinto de Castro, the current president of UNIMEP and also director general of the highly respected Instituto Educacional Piracicabano (IEP) visited the Fraunhofer IGB in October and took the opportunity for an official meeting with its director, Professor Thomas Hirth. He also used the occasion to visit the membrane wastewater treatment plant developed in the IGB project DEUS 21 onsite at Heidelberg-Neurott, and followed with interest the field report of the plant operator. During the visit, it was agreed to further deepen the cooperation by the exchange of staff and raising joint project funds.

1st German-Brazilian Workshop on Innovation for Value Creation from Bio-resources, March 16–18, 2011 in São Paulo

The workshop aimed at bringing together major players from industry and research from both countries for the identification of future needs and opportunities in the field of bio-resources. Researchers from the Fraunhofer IGB contributed with lectures, scientific posters and statements in the world café discussions. Their input focused on topics such as bioeconomy, wastewater treatment, recovery of nutrients and the use of residues from ethanol production. The meeting was regarded by both national sides as the starting point for future strategic cooperations.

5th German-Brazilian Symposium on Sustainable Development, July 18–22, 2011 in Stuttgart

The Fraunhofer IGB participated in this event with scientific contributions on biogas production from biosolids and value creation from microalgae. Participants were also able to gain

insights into IGB project results through visiting various technical facilities such as the Heidelberg Municipal Association for Sewage Treatment's South Sewage Plant with its high-load digestion process, the membrane wastewater treatment plant at Heidelberg-Neurott and the new plant for microalgae technology at the factory premises of the IGB's Fair Energy project partner in Reutlingen.

29th German-Brazilian Economy Days, September 18–20, 2011 in Rio de Janeiro

This annual conference is organized by the Federation of German Industry (BDI) and its Brazilian partner Confederação Nacional da Indústria (CNI). Several Fraunhofer institutes collaborated with the Brazilian industrial vocational training initiative SENAI/FIRJAN to present exhibits on the topic "Research for the Future" in a dedicated exhibition space. The Fraunhofer IGB showcased exhibits on the themes sustainable energy and health, which were very well received by the visitors.

SABESP is new cooperation partner

A particular highlight in 2011 was winning SABESP (Companhia de Saneamento Básico do Estado de São Paulo), a major water and wastewater treatment company, as a future cooperation partner in Brazil. In the project "Use of biogas of a municipal waste treatment plant for transportation use" the processing of biogas to biomethane as fuel for a fleet of at least 49 cars is being realized in the town of Franca, São Paulo State. The project is being conducted in the framework of the climate protection initiative funded by the German Federal Ministry for the Environment. Both countries are eagerly awaiting the project's results.



FRANCE

Fraunhofer-Carnot cooperation

Since 2009, researchers from Fraunhofer IGB and the Carnot-Institute CIRIMAT (Centre Inter-universitaire de Recherche et d'Ingénierie des Matériaux) in Toulouse have been collaborating on the bilaterally funded BioCapabili project. The project concerns the antimicrobial effectiveness of biomimetic calcium phosphate. Researchers and technicians from three different IGB departments are working jointly with the CIRIMAT Phosphates, Pharmacotechnics, Biomaterials research group (PPB) headed by Prof. Dr. Christophe Drouet. The mid-term meeting in Paris in February 2011 went successfully, and, thanks to the promising results, profitable discussions with company partners were intensified. Both research groups intend to extend future cooperation and implement their synergistic competences in projects with an international focus.

4th German-French Forum on Research Cooperation, October 12–13, 2011 in Berlin

A roadmap with five core elements was drawn up at this meeting of high-ranking representatives of both countries. Professor Hirth and Professor Schurr from the interdisciplinary research center Forschungszentrum Jülich are coordinating the field of green and white biotechnology on the German side. The goal of the initiative is to strengthen the research capacities of both countries in the context of the bioeconomy.

INDIA

Indian-German Conference on Pathogenic Fungi, August 1–3, 2011 in Bangalore

In order to combine forces in researching human fungal pathogens, Indian and German scientists met in a bilateral workshop at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, to plan future collaborations and to foster the exchange of students and researchers. Thirteen scientists from Germany, including Dr. Steffen Rupp from the Fraunhofer IGB, and 15 scientists from India presented their current work, developed strategies on joint research topics and formed subgroups with the goal of creating a joint research consortium.



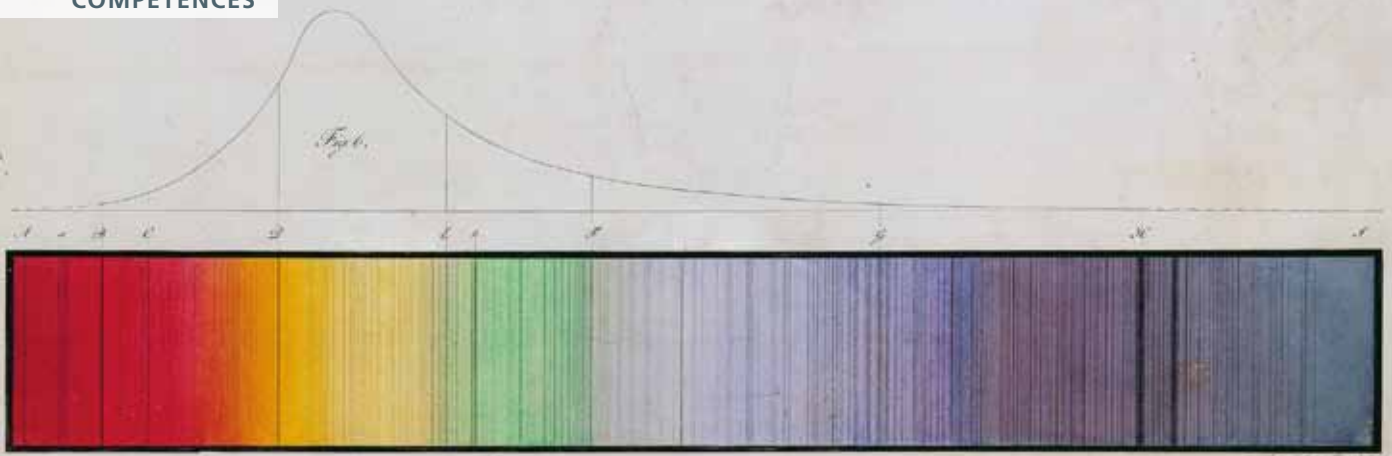
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THE FRAUNHOFER-GESELLSCHAFT

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.

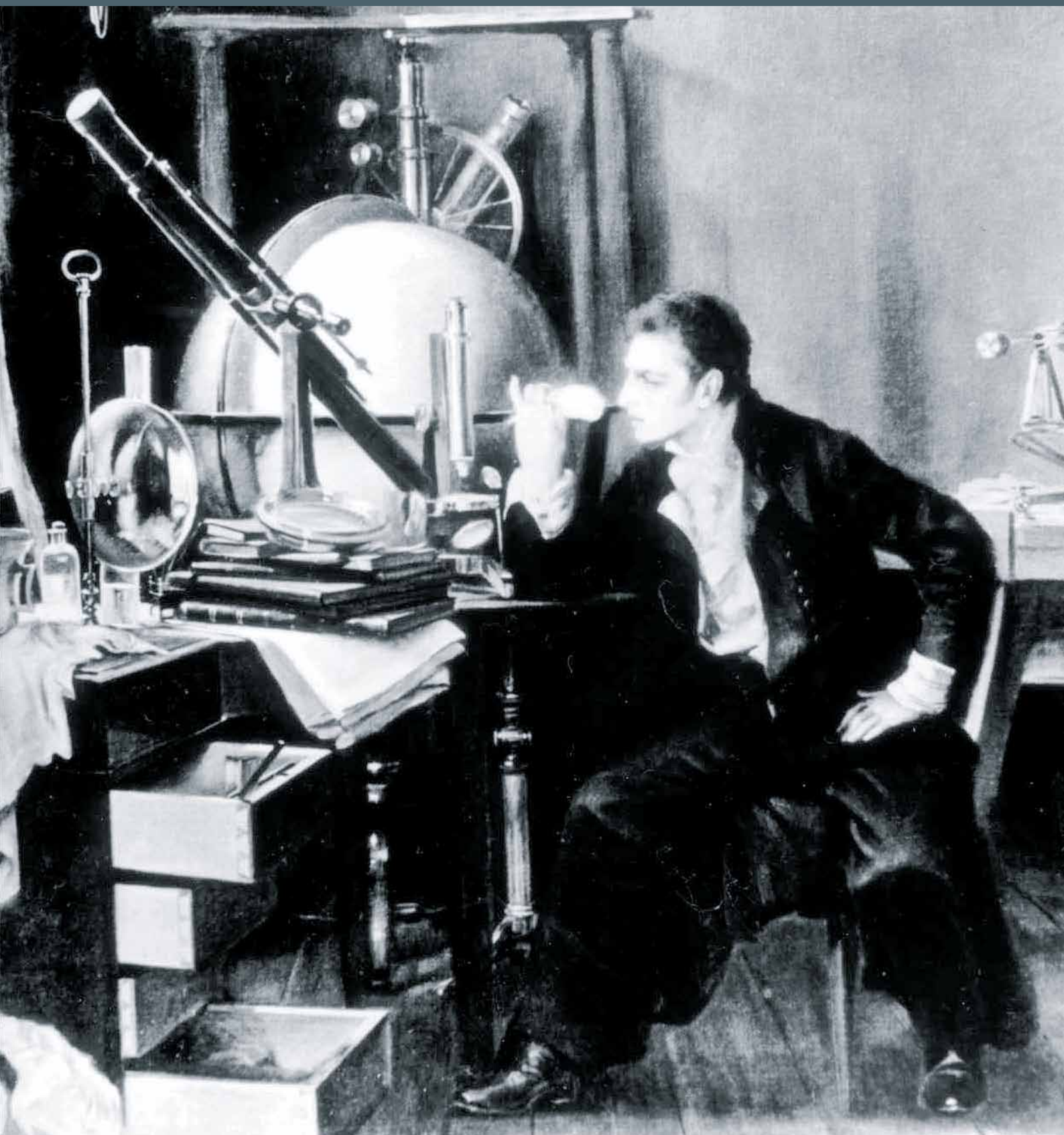
At present, the Fraunhofer-Gesellschaft maintains more than 80 research units in Germany, including 60 Fraunhofer Institutes. The majority of the more than 20,000 staff are qualified scientists and engineers, who work with an annual research budget of €1.8 billion. Of this sum, more than €1.5 billion 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.

Affiliated international research centers and representative offices provide contact with the regions of 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.





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.

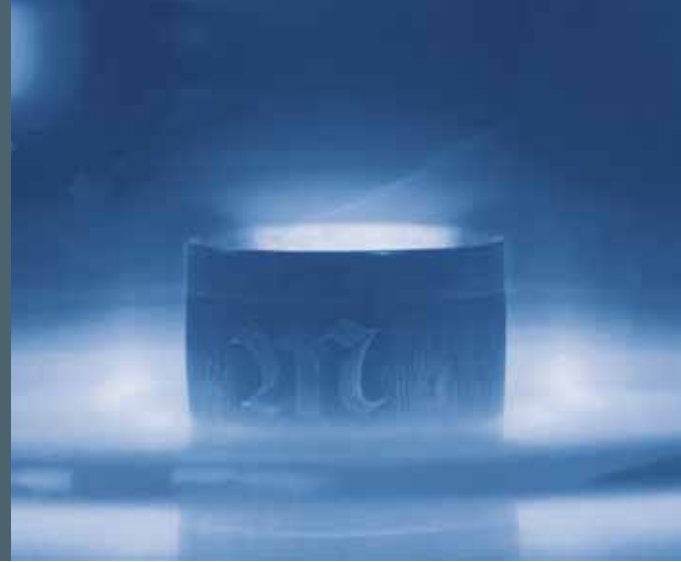
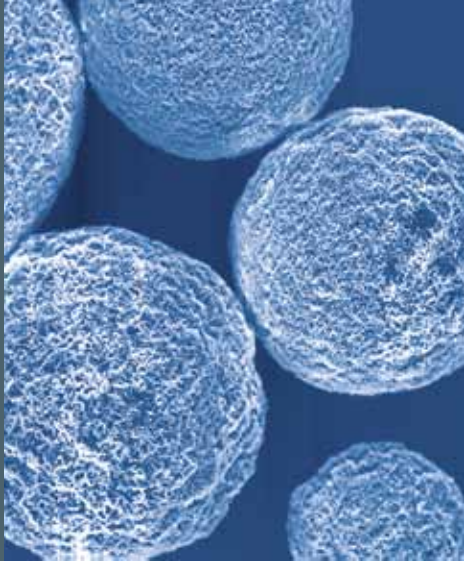
Established preparation methods

- 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 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)
- 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 semiconductors) 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 of plasma-cleaning and plasma-sterilization processes
- 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

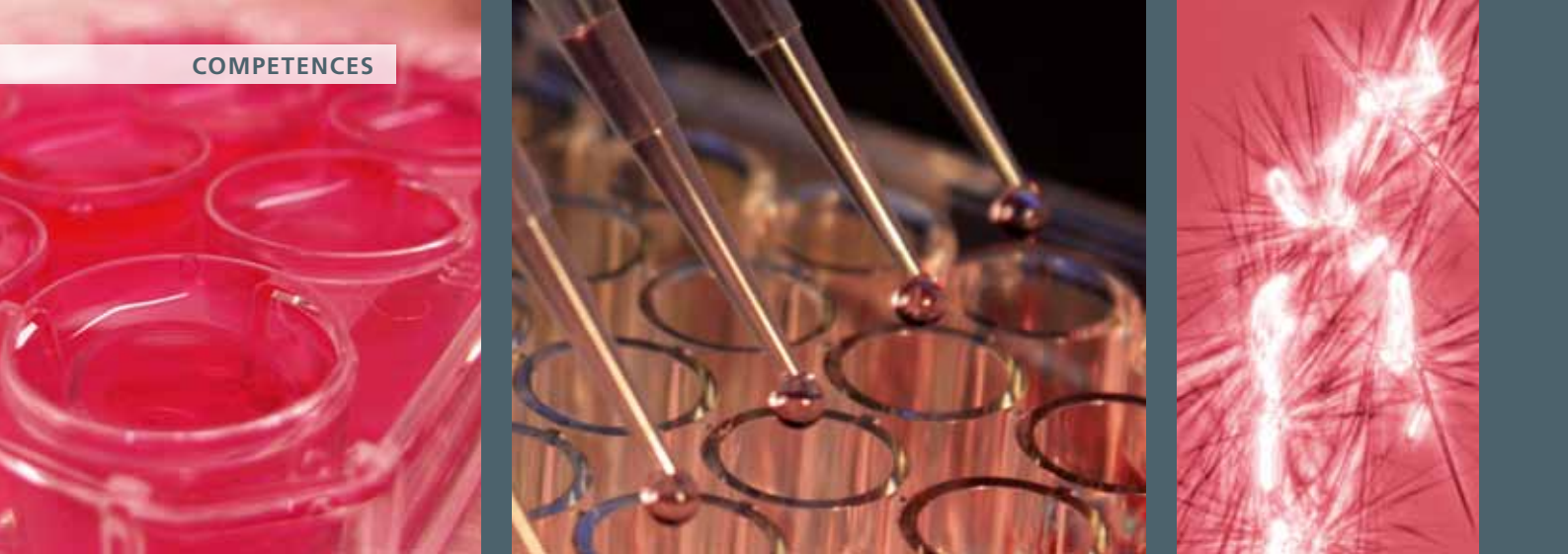
Infrastructure and technical equipment

- 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



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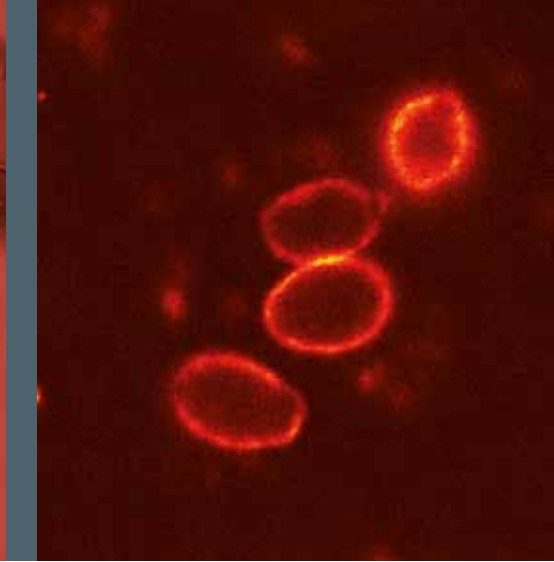
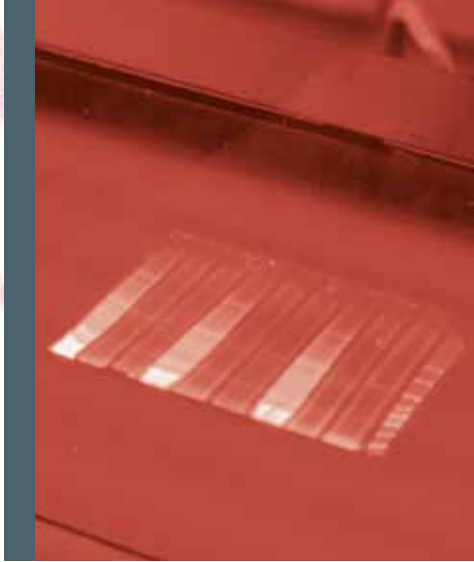
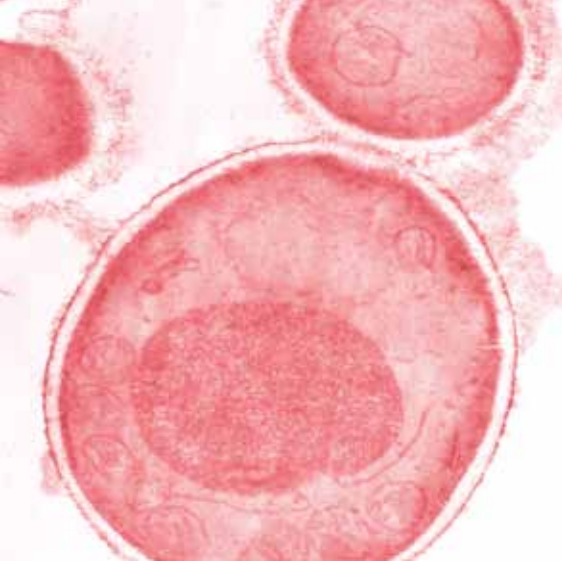
MOLECULAR BIOTECHNOLOGY

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) 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 (e.g. cinnovex, soluferon) 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 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 optimized. 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, chemistry and the environment. In the field of biocatalysis we work closely with the BioCat Project Group based in Straubing, while we collaborate with the project group at Fraunhofer CBP in Leuna to develop our laboratory-scale bioprocesses up to 10 m³ 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.

Range of services

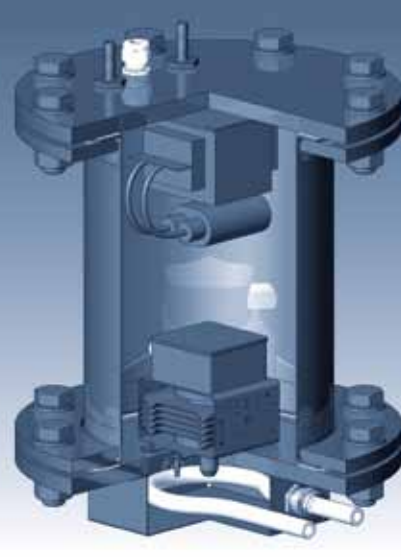
- Screening of targets and active compounds for anti-infectives (2D and LC proteomics, DNA microarrays, parallel sequencing, infection models, screening assays)
- Gene expression analyses for customers
- Development of DNA microarrays: design of probes, production of PCR fragments, contact printing, 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)
- Parallel sequencing facility (Illumina HiSeq GAIIx)
- 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 L (non-GMP)
- Protein purification equipment
- Pulping machines (ball mills, etc.), multi-fermentation bioreactors for bioprocess development, and small bioreactors (up to 30 L) 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



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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 come from sectors such as pulp and paper, metal processing or construction materials manufacturing, and our work for them ranges from the supply of drinking water or energy to integrated treatment, production and recycling processes in industrial production.

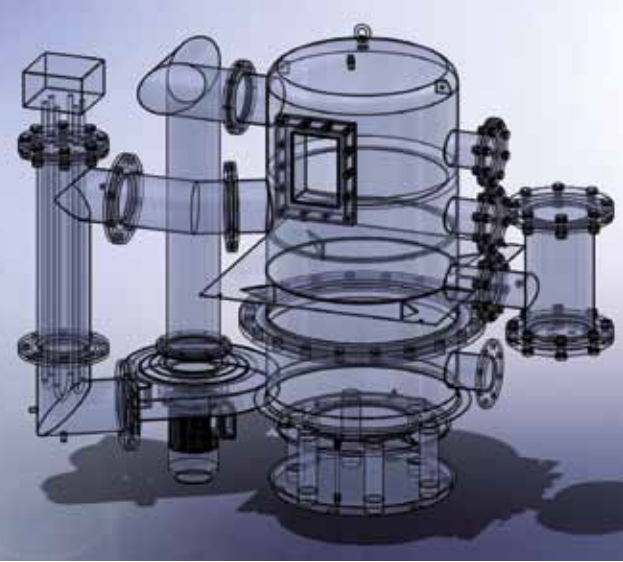
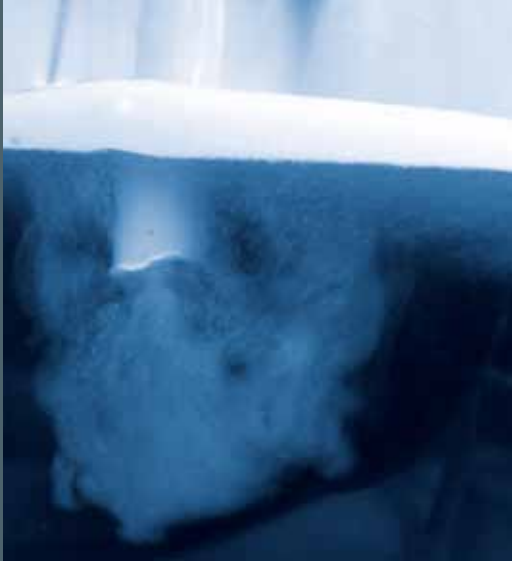
The current main themes of focus are:

- Heat storage using thermo-chemical processes
- Use of sorption systems to remove moisture from gases
- Drying with integrated recovery of volatile materials
- Recycling and management of inorganic nutrients
- Electrophysical processes and oxidative water treatment
- Technical design combined with numeric simulation
- System integration of aseptic processes in the food industry and biotechnology
- Use of high frequency technology in process engineering

The main quality criteria in our R&D activity is sustainability. We define this principally in terms of the minimization or substitution of material consumption – above all of non-renewable sources – and the energy efficiency of processes,

but also in terms of the efficient use of regenerative energy and the materials made available from recycling processes. Recycling and energy saving result directly in improved economic efficiency of processes, meaning that our approach satisfies both ecological and economic demands. One example of this is the development of a process to store thermal energy from waste heat or solar thermics. The intention is to enable availability of heat energy for municipal or industrial use decoupled in time and space from its source. Potential applications are drying processes in production, the temporary heat supply of buildings, or the treatment 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 use 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 (formerly FEMLAB), for theoretical pre-studies 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 for the production of the corresponding electromagnetic waves.



From the knowledge 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

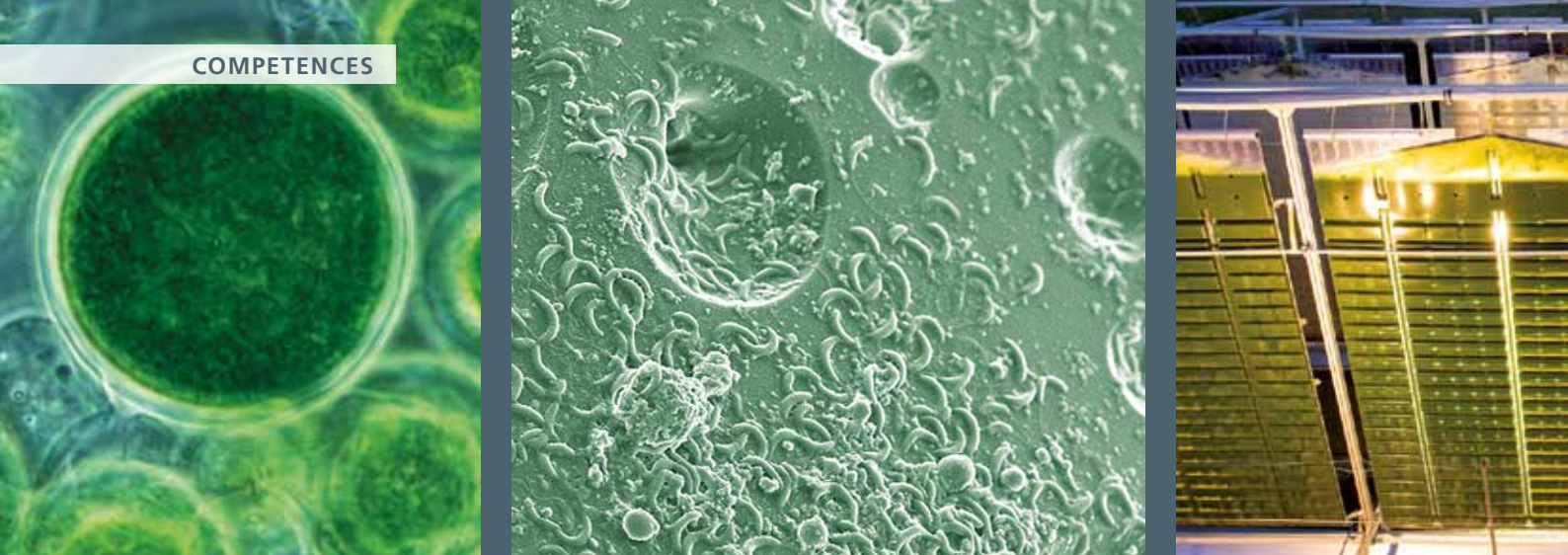
- Process development carried out by an interdisciplinary team drawn from the fields of process engineering, mechanical and chemical engineering
- Engineering specification including characterization of automation algorithms, up to industrial prototypes
- Feasibility studies and preliminary investigations in laboratory and pilot-plant scale

Infrastructure and technical equipment

- Laboratory systems for investigating the floccing and oxidation properties of water
- Pilot plants for advanced oxidation processes (AOP) such as electrochemical precipitation, ozone, hydrogen peroxide, UV radiation, ultrasound, anodal oxidation (direct/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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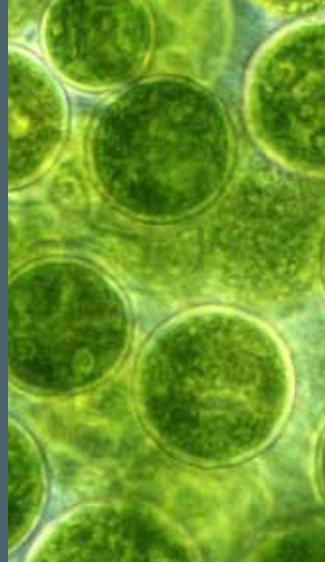
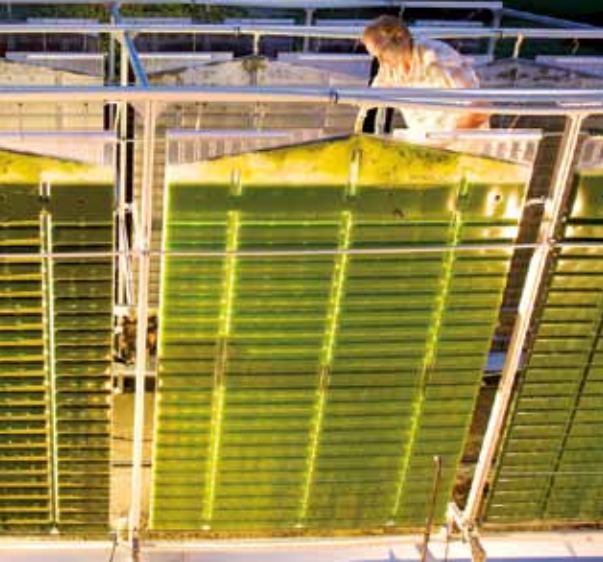
ENVIRONMENTAL BIOTECHNOLOGY AND BIOPROCESS ENGINEERING

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, recyclable materials and sources of energy. These bioconversion processes normally also require the purification of water that serves as a solvent. Ideally, the water treatment is coupled with the recovery of inorganic by-products for reuse as fertilizers. 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 planning, design and construction of innovative semi-decentralized prototype wastewater purification plants. The retention or immobilization of biocatalysts plays a key role here, and we leverage the associated expertise extensively – both for biological surface reactions (biocorrosion, biofilm formation, biomineralization, biofouling, biosensors, 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. Processing throughout is carried out on the basis of microbiological parameters, i.e. the growth and degradation kinetics of the different organisms concerned. Our processing activities extend from the planning, initial operation and optimization of laboratory and pilot plants to the planning, construction, and commissioning of technical demonstration plants together 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 point, 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 sustainable processes or opening up new product lines
- Batch, fed-batch and continuous fermentation processes, including those involving partial or total cell retention
- Cultivation of microalgae in flat-panel airlift 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 contaminations



- Modeling of processes and simulation of process lines
- Scale-up of stable process states and scale-down of unstable process states to help solve problems during technical operation
- Downstream processing technologies such as membrane-based filtration processes, liquid-liquid extraction, and extraction with supercritical media
- Holistic 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 drawback of lower growth rates compared with aerobic organisms can be compensated by process engineering. 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 competence with that of other Fraunhofer IGB departments, we serve the needs of the chemical, energy and environmental business sectors.

Range of services

- New wastewater purification methods
- Biotechnological purification processes for industrial wastewater
- Development of utilization concepts for both organic and inorganic residual materials

- Development of regional-level system concepts for bioenergy management
- Digestion processes to produce biogas from a range of organic substrates
- Development of photoautotrophic processes for microalgae and cyanobacteria in flat-panel airlift 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
- Assessment of microbial contamination on surfaces and in processing media

Infrastructure and technical equipment

- Bioreactors of various types and sizes (laboratory, pilot and technical scale)
- Mobile membrane bioreactors for wastewater treatment
- Pilot plant for environmental and bioprocess engineering applications
- Test plants for different membrane processes (e.g. rotating disk filtration)
- Mobile pilot plants in m³-scale to generate basic engineering data *in situ* for the planning of innovative demonstration plants
- Equipment for handling pathogenic organisms and the corresponding official approvals



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CELL AND TISSUE ENGINEERING

The core competence of the Cell and Tissue Engineering Department is the development of functional 3D tissue models in vitro from isolated primary human cells. With these tissue models, we help solve complex challenges in the areas of regenerative medicine, tissue engineering and the development of cell-based assays for toxicology. We develop biocompatible micro- and nano-structured material surfaces for the effective isolation and culture of primary cells and for optimal cell type-specific culture, in particular of adult stem cells. The physiological culture of our 3D tissue models is made possible by computer-controlled bioreactor systems designed specifically for the cell type in question. Sterility testing and quality control of cell-based transplants is a laborious process which always requires two graft samples – one for testing and one for transplantation. We are therefore establishing a non-invasive reference method based on Raman spectroscopy.

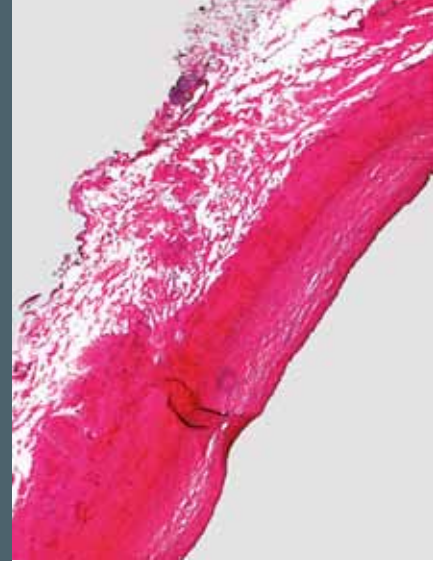
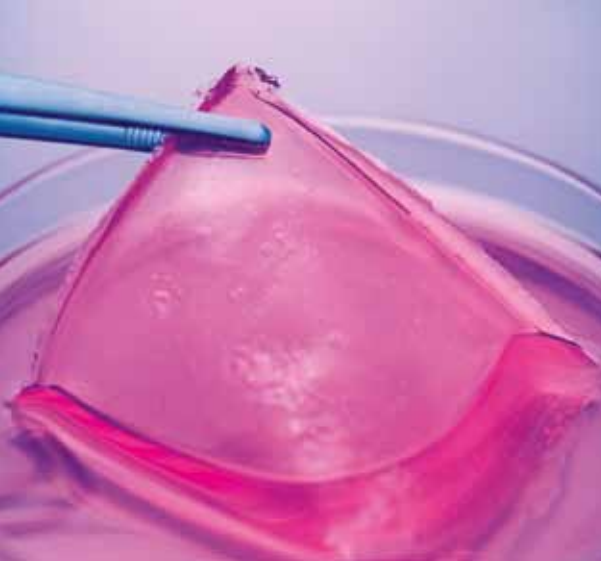
A two-layered human 3D skin equivalent has been patented (EP 1 290 145B1) and accredited for the testing of the biocompatibility of medical devices (DIN ISO 10993-5). The skin model can be extended by further cell types such as melanocytes or tumor cells. It is also suitable – as a preliminary stage to animal testing – in investigations of the penetration and the distribution of test substances, as required by the EU chemicals regulation REACH. The model's scope extends to investigation of differentiation, apoptosis, and also of tumor initiation and graduation. We have recently succeeded in

integrating vascular structures (blood vessel equivalents) into the skin model. In addition, we were able to automate the complete process for manufacturing the avascular skin model.

A further focus is the miniaturization and the characterization of our 3D intestinal testing system. Our accredited two-dimensional intestinal assay based on colon carcinoma cells (2D Caco-2 model) allows validated permeability and transport studies of potential candidate drugs and other substances at the intestinal barrier.

We have also been able to establish GMP conditions for the culture of our vascularized matrix (BioVaSc) in specific bioreactors. This matrix is used to generate complex organ structures. As part of a project funded by the German Federal Ministry of Education and Research (BMBF) we are currently preparing the first clinical study of a trachea transplant based on the BioVaSc.

- Isolation and culture of primary cells from different tissues and species according to GLP or GMP regulations
 - Micro- or nanostructured (bio)material surfaces
 - Skin, liver, intestine, trachea, cardiovascular tissue
- Establishing processes to develop three-dimensional organotypical cell cultures as testing model or for tissue reconstruction
 - BioVaSc (biological vascularized scaffold)
 - Tissue-specific computer-controlled bioreactors
 - Vascularized human liver, intestine and trachea model



- Establishing methods for non-destructive cell and tissue characterization by means of Raman spectroscopy

With the help of these vascularized human test systems, the absorption, distribution, metabolism, excretion and toxicity (ADMET) of substances or medicinal products can be investigated. These parameters are critical in the characterization of the pharmacokinetic and toxicological properties of active substances. Our findings can be extrapolated directly to the human organism, with the consequence that a large number of animal experiments could be replaced.

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, an autologous stem cell transplant and an autologous blood vessel transplant for bypass surgery.

Range of services

- Cell culture technology of primary human cells and of 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), including cell sorting
 - Modern digital image processing techniques such as microdissection and Raman spectroscopy

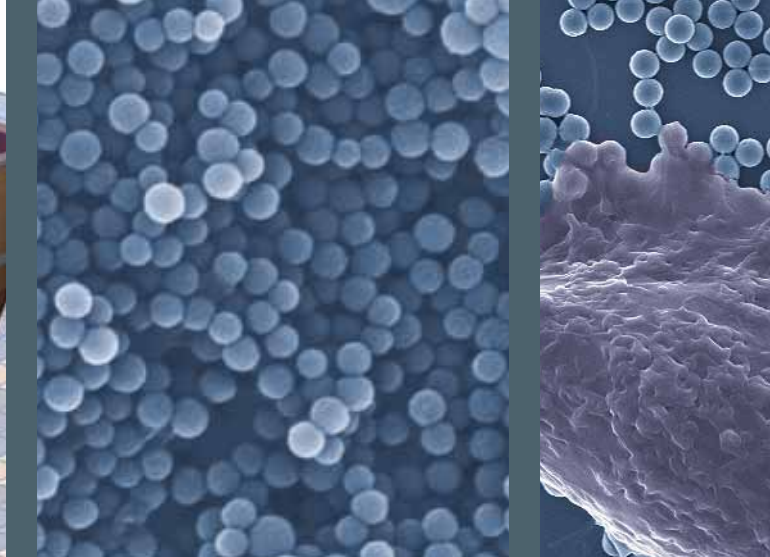
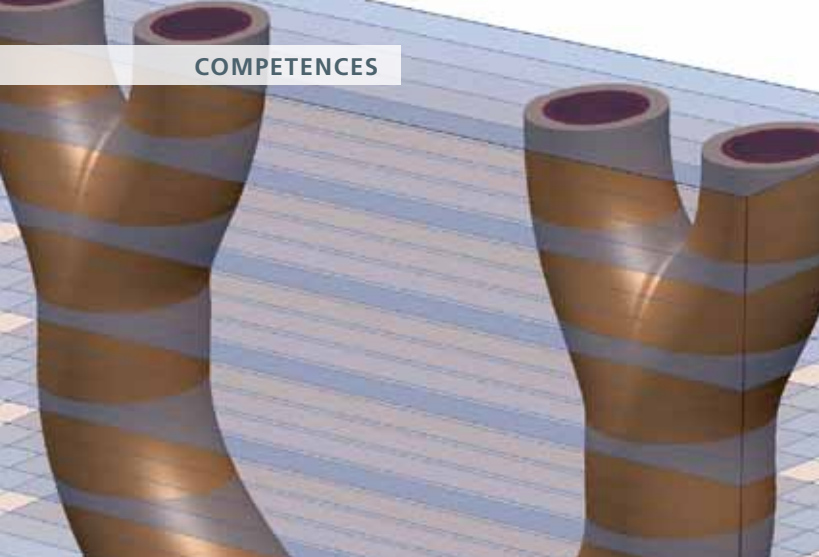
- Establishing of various 3D tissue models
 - Accredited for REACH testing
 - Alternatives to animal testing in cosmetics R&D
 - ADMET testing in substance and drug screening
 - Target screening for new therapeutics and infection biology
- Development of specific computer-controlled bioreactor systems for the cultivation of vascularized 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 like inverse fluorescence microscope, FACS, and microdissection instrumentation
- GMP production unit (cleanrooms, separate quality control area, storage facilities)



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INSTITUTE FOR INTERFACIAL ENGINEERING IGVT

The Institute for Interfacial Engineering IGVT is headed by Professor Thomas Hirth and is part of the University of Stuttgart's Faculty of Energy Technology, Process Engineering and Biological Engineering (Faculty 4). At the end of 2011, the institute had a staff of 60 and a research budget of around 2.7 million euros. Most of the institute's activities are carried out on the premises of the Fraunhofer IGB, which is a close cooperation partner. The IGVT also uses laboratories, pilot plant facilities and offices, at the Allmandring 5b multipurpose facility belonging to Stuttgart University. The institute's working groups have at their disposal sophisticated equipment for interfacial engineering based on biochemical, biotechnological, chemical, cell-biological, nanotechnological, physical and process engineering research.

Close cooperation with the various Fraunhofer IGB departments facilitates a spectrum of IGVT projects ranging from basic research to application. This spread is also reflected in the variety of sources of research funding received by the IGVT, 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. At the IGVT, we combine fundamental academic research with application-oriented approaches by incorporating ideas, incorporating insights and ideas from practice.

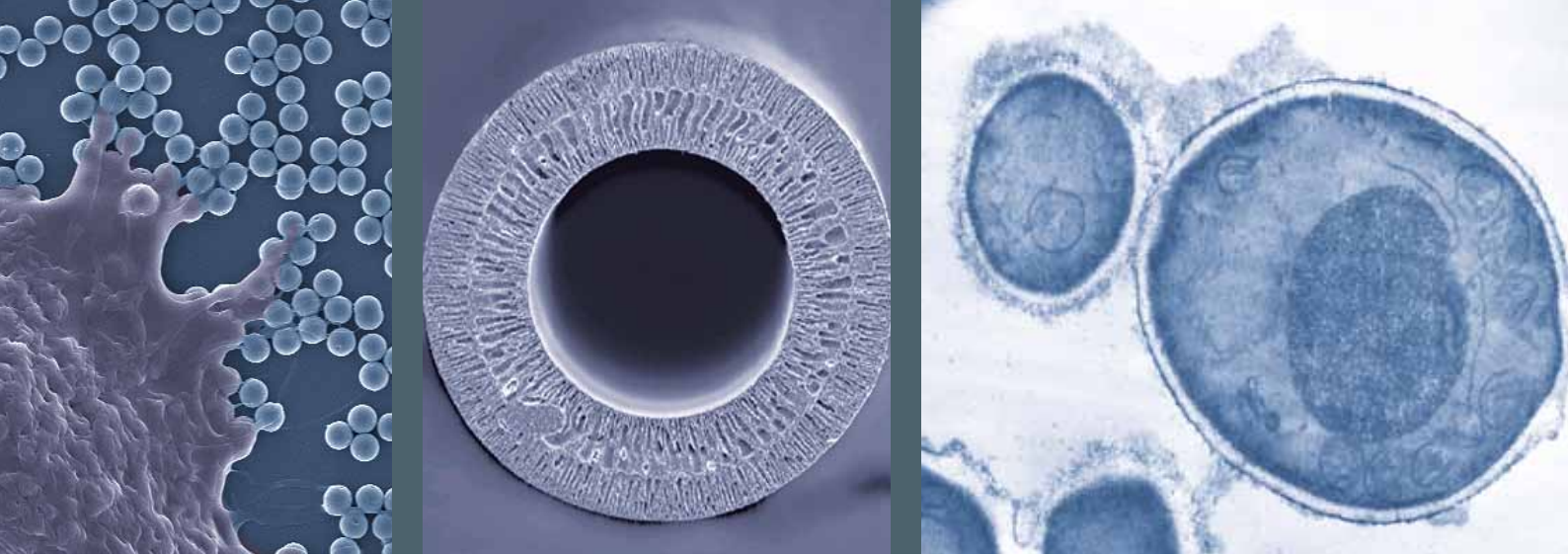
Research and teaching

The IGVT's mission is the characterization, design and functionalization of surfaces of organic, inorganic and biological origin as well as of nano-, bio- and hybrid materials and their interaction. Further activities include the simulation and process engineering of interfacially driven processes in membrane technology and biotechnology, as well as their biochemical, cell-biological, chemical, molecular and physico-chemical fundamentals.

Teaching activities at the institute are focused on the fields of biomaterials, industrial biotechnology, interfacial process engineering and nanotechnology. Credited instruction is also offered in other interdisciplinary fields. Students mostly come from courses in applied materials science, chemistry, mechanical engineering, medical engineering, process engineering, technical biology, technical cybernetics and the WASTE master study program.

Biological Interfacial Engineering

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



Chemical Interfacial Engineering

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

Medical Interfacial Engineering

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

Physical Interfacial Engineering

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

Environmental Interfacial Engineering

- Adsorption/desorption processes for heat storage and dehumidification
- Development of processes for the energetic and material use of biomass
- Drying processes using superheated steam
- Electrochemically stimulated crystallization and recovery of inorganic nutrients
- Membrane processes for water treatment, cell retention and water hygienization
- Membranes for gas separation and fuel cells
- Particle suspensions and emulsions in electric fields
- Production of valuable products from microalgae in photobioreactors

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PROJECT GROUP BIOCAT

The focus of the Project Group BioCat is on developing catalytic processes and new products based on renewable resources to sustainably supply industry and society with raw materials and energy. The project group employs key technologies from the fields of chemical catalysis and white biotechnology including the combination of chemical and biocatalysis in the utilization of biomass and carbon dioxide. Within these approaches also new methods for creating and optimizing (bio) catalysts are developed and utilized. The catalysts can be used, for instance, for the conversion of terpenes – obtained from plants and residual materials in wood processing – into epoxides and monomers for the polymer industry. Starting with lignin, aims are, for example, to produce monomers for conductive polymers or, based on plant oils and fatty acids, synthesize functionalized carboxylic acids and bio-based surfactants.

It is vital that we turn our efforts today, and no later, to developing the next generation of catalysts and processes that instead of crude oil will enable us to use biomass and carbon dioxide as basic sources of raw materials. The project group aims to speed up this trend in “green” or “sustainable” chemistry and make a decisive contribution to the field. However, besides the goal of becoming more sustainable the objective of the work within the group also is to achieve optimum added value in the transformation of biomass waste and raw material into bio-based end products.

Apart from expertise in biotechnology (enzyme technology, fermentations, screening of biocatalysts) and chemistry (organic synthesis, homogeneous catalysis, analytics), the Project Group BioCat, which is composed of biotechnologists, molecular biologists and chemists specialized in catalysis and synthesis, offers sound knowledge 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 also to carry out work in the fields of analysis, research and development of new materials, reactions and catalysts as well as the optimization of catalysts and existing processes in close cooperation with future customers.

The BioCat Project Group combines bio- and chemical catalysis in cooperative projects with the TU München, the Fraunhofer IGB departments and with the Fraunhofer Institute for Chemical Technology ICT. Collaborative projects offer an opportunity to address topics about renewables and set new impulses for the biopolymer industry.



Range of services

- High resolution NMR spectroscopy (400 MHz) for elucidation of molecular structure, reaction kinetics, deep temperature analytics, e.g. 1D ^1H -/ ^{19}F -/ ^{13}C -/ ^{31}P -/ ^{15}N -measurements and 2D applications including development of methods
- Screening of bio- and chemical catalysts
- Optimization of enzymes by enzyme engineering and enzyme immobilization
- Synthesis of fine chemicals
- Design of processes for utilizing waste material
- Design of processes to integrate renewable feedstock into existing processes
- Carrying out of studies in the field of renewable resources

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
- Analytics: GC-MS, LC-MS, HPLC
- 400 MHz NMR spectrometer

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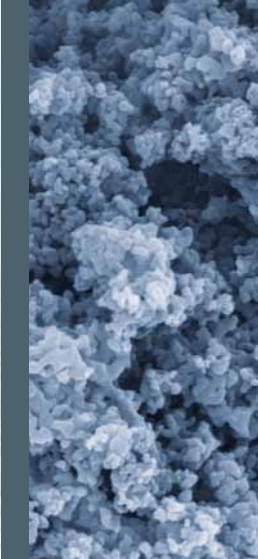


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FRAUNHOFER CENTER FOR CHEMICAL-BIOTECHNOLOGICAL PROCESSES CBP

The Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, central Germany, is intended to close the gap between the lab and industrial implementation. By making infrastructure and plants (pilot scale and miniplant) available, the center will make it possible for cooperation partners from research and industry to develop and scale-up biotechnological and chemical processes, allowing them to utilize renewable raw materials on an industrial scale. The Fraunhofer CBP is being built at the Leuna chemical site, in close cooperation with InfraLeuna GmbH, owner and operator of the site's infrastructure facilities. The center will be jointly run by the Fraunhofer IGB and ICT institutes. It constitutes an important step in Leuna's transformation into an integrated biotechnological and petrochemical site that will play a pioneering role in the industrial use of renewable raw materials. The groundbreaking ceremony in December 2010 has ushered in the start of construction of the new Fraunhofer center. Completion is scheduled for mid 2012.

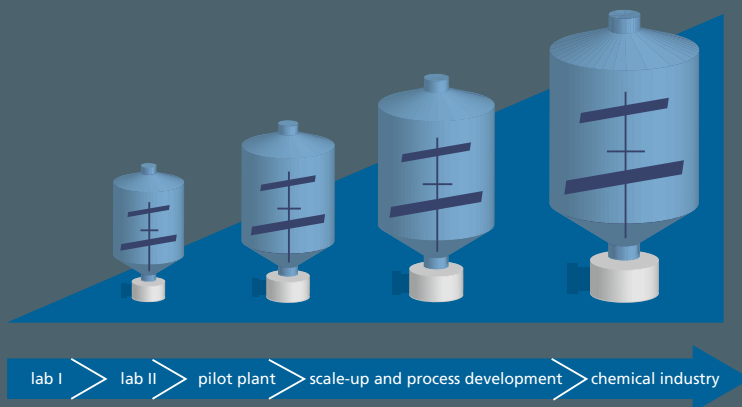
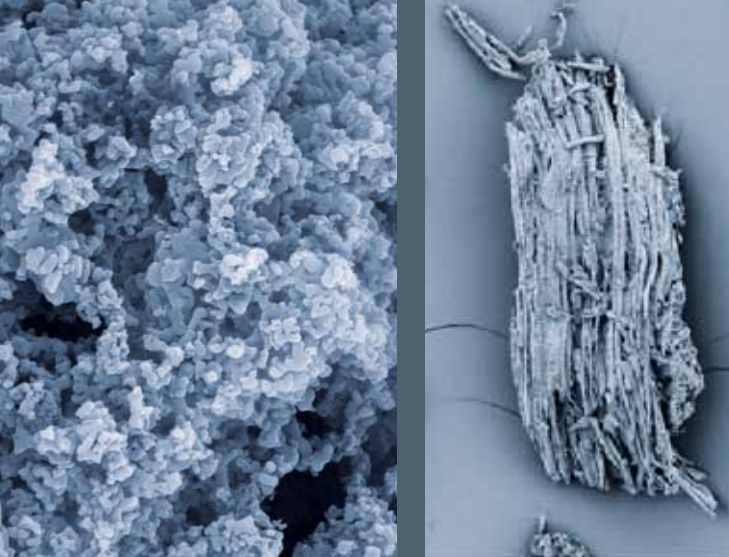
The Fraunhofer CBP represents a hitherto unique platform for developing new processes up to commercially relevant scale, with a direct link to the chemical industry on the one hand, and to Fraunhofer research on the other. Projects will involve affiliated partners from industry, academia and non-university research establishments, and focus on the following specializations:

- Functionalization of vegetable oils – epoxidation and ω -functionalization
- Pulping of lignocellulose and separation of its components
- Manufacturing of bio-based alcohols and olefins
- Development of new technical enzymes
- Production of functional ingredients and energy carriers from microalgae
- Use of residual biomass by means of digestion

The core focus of the Fraunhofer CBP's activities will be the sustainability of processes along the entire value chain involved in creating products based on renewable resources. The goal is to achieve a cascading material-energetic utilization of as many biomass plant components as possible, on the lines of a biorefinery.

Process development will thus concentrate 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 CO₂ emissions
- Utilizing plants that are not suited as either human food or animal feed
- Integration of the processes developed into existing systems, e.g. 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 will make it possible for academic and industrial cooperation partners to develop and scale up biotechnological and chemical processes for utilizing renewable resources right up to industrial scale.

Range of services

The Fraunhofer CBP, which is scheduled for commissioning mid 2012, will provide modular process capacities up to 10 cubic meters and continuous plants capable of high-pressure processing up to 100 liters per hour, plus a wide range of processing, treatment and reconditioning techniques and methods. This versatile "flexible biorefinery" will allow the processing of raw materials such as vegetable oils, cellulose, lignocellulose, starch and sugar, and their conversion into chemical products. Our project group is already available for the preparation and initiation of projects and other customer orders.

Infrastructure and technical equipment

- Fermentation capacity of 10, 100, 1000 and 10,000 L, including downstream processing for fermentation products
- Continuous gas phase reactions of up to 10 L/h
- Discontinuous reactors for liquid phase reactions of up to 500 L
- Mechanical and thermal separation processes
- Pulping and component separation of lignocellulose using organic solvents, with a capacity of 1 metric ton of biomass per week
- Reactors up to 500 L volume for the enzymatic hydrolysis of polysaccharides

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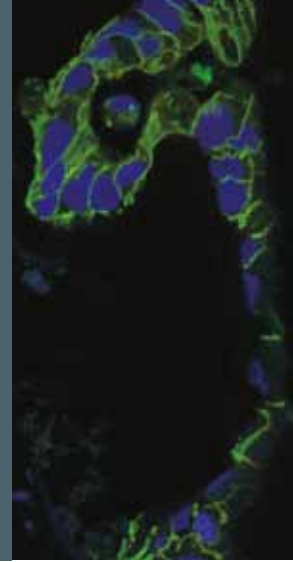
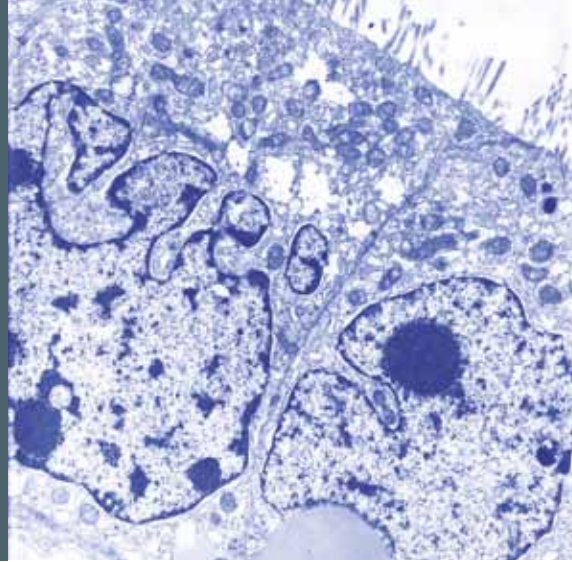
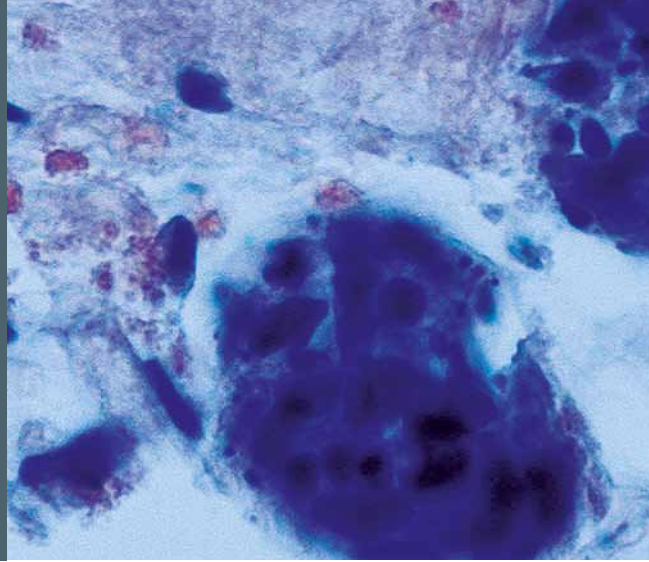
PROJECT GROUP ONCOLOGY

The Project Group “Regenerative Technologies for Oncology” of the Fraunhofer IGB was created in 2009 to coincide with the establishment of the Chair of Tissue Engineering and Regenerative Medicine at the University of Würzburg. The project group benefits from the synergy of leveraging the research of the Fraunhofer IGB and the Medical Faculty of the University of Würzburg.

The focus of the project group is the development of human 3D test systems for the development of cancer drugs. With primary tumor cells, tissue-specific, vascularized in vitro tumor models are established as a test system. The project group will produce human vascularized tumors utilizing the Fraunhofer IGB Cell and Tissue Engineering Department’s methodology of growing human tissue with a functional blood vessel equivalent in vitro. A bioreactor system will support the artificial tumor tissue through blood vessels as in the human body, which will enable the in vitro examination of the molecular mechanisms of angiogenesis (the formation of new blood vessels) and other relevant mechanisms of tumor formation and metastasis. Similarly, by using such tumor models, we can study how new drugs are distributed within the tumor and how they reach their target destination. With the help of these tumor models, we are able to create new cancer diagnostics and therapeutics that will circumvent the need for animal tests and result in validated findings that are directly comparable to human tumors in vitro.

Another focus is the development of 3D in vitro generated tumor stem cell niches. Tumor stem cells are now seen as the cause for the emergence and growth of cancer. Because healthy tissue stem cells divide infrequently, they are resistant to conventional treatments with chemotherapy or radiation. This resistance complicates the treatment of cancer and can lead to relapse, a recurrence of the tumor, or give rise to metastases. There is evidence that tumor stem cells are protected from therapeutic attacks in their specific microenvironments, known as niches. If we can replicate this niche in vitro, targeted therapies could be discovered, which act directly on tumor stem cells.

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 tumors move through the blood or lymphatic system cells to distant organs and form metastases, which can 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.



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), including sorting
- Target screening for new cancer therapeutics

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

- 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 Würzburg for the organization of the clinical phases I-III

Infrastructure and technical equipment

- Cell culture laboratories for work on safety levels S1, S2 GenTSV
- Cell analysis: Fluorescence microscope, FACS, micro-dissection system, Raman spectroscopy

Contact

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MEDICINE

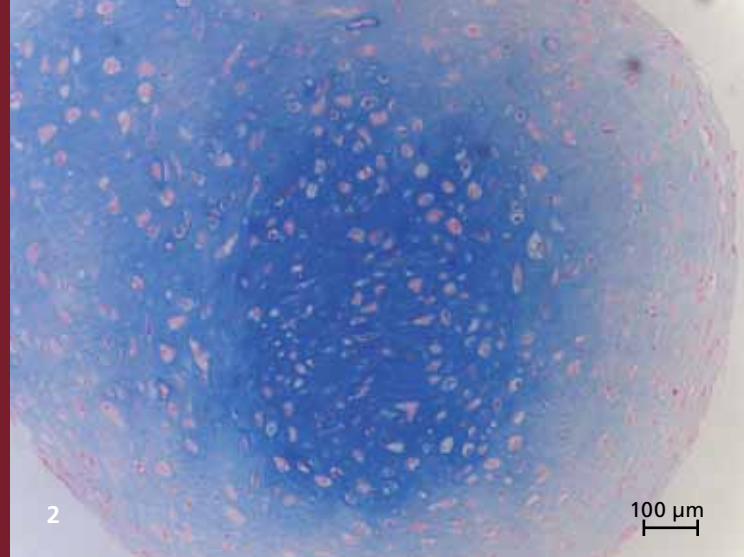
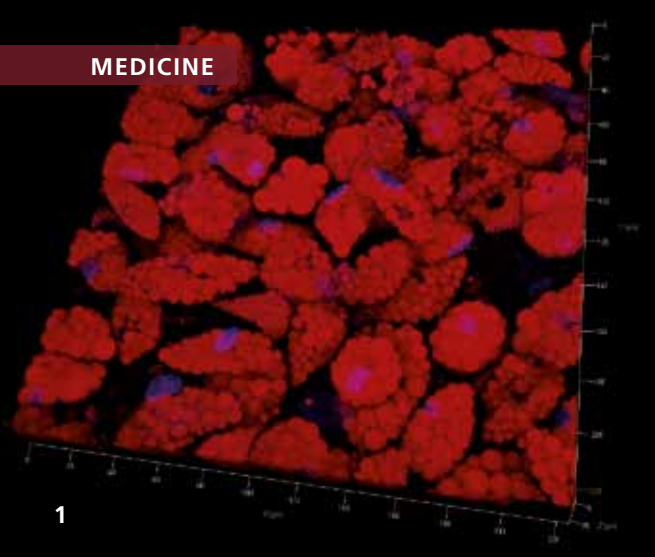
Prof. Dr. Heike Walles

Better cure 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 at the same time can reduce costs. In the medicine business area at the Fraunhofer IGB we frequently work together with medical specialists 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 quality of the food we eat is also critical to human health – which is why improving its production is also a subject of investigation at the Fraunhofer IGB.

The focus of regenerative therapies is on the development of autologous transplants, known as ATMPs (advanced therapy medicinal products). The Fraunhofer IGB maps the complete value-added chain up to GMP-compliant manufacturing of ATMPs. In the last year we started to launch two phase I clinical studies for European registration, together with our network of physicians. The Fraunhofer IGB will make the experience and competence gained through these studies available to small and medium-size enterprises, assuming the role of the mediator from the fundamentals up to the preclinical stage. To promote the role of tissue engineering products in healthcare, we are developing 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 (Future Foundation).

Both bacterial and fungal infectious diseases are again on the increase in industrial nations, making new scientific strategies to combat infection or avoid sepsis a priority. Thanks to the various array technologies and transcriptome analysis methods, 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. Using this know-how, we aim to develop new diagnostics as well as active agents and treatment strategies.

A further focal point, enabled by the interdisciplinary mode of operation of the Fraunhofer IGB, is the optimization of surface properties of established medical devices such as tracheal stents and contact lenses. This is carried out primarily by means of 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. We also make a contribution to preventive healthcare through the development of processing techniques and methods for hygienization and pasteurization that are gentle on the product and thus preserve the product’s original properties.



SYSTEMS BIOLOGY IN TISSUE ENGINEERING – DIFFERENTIATION OF MESENCHYMAL STEM CELLS

Dr.-Ing. Jan Hansmann

Introduction

Mesenchymal stem cells (MSCs) can differentiate into fat, cartilage or bone cells as well as a variety of other cell types [1]. In addition, MSCs are relatively easy to expand in vitro. These two characteristics make MSCs a promising cell source for therapeutic procedures. For the effective use of these cells, for example in the production of tissue engineered biological tissue, a thorough understanding of the relationship between MSC differentiation and the external stimuli that influences their behavior is essential. Experimental methods for the quantitative detection of the dynamics of MSC differentiation and their translation into mathematical models is part of a collaborative project between the Fraunhofer IGB, the IGVT of the University of Stuttgart and other project partners.

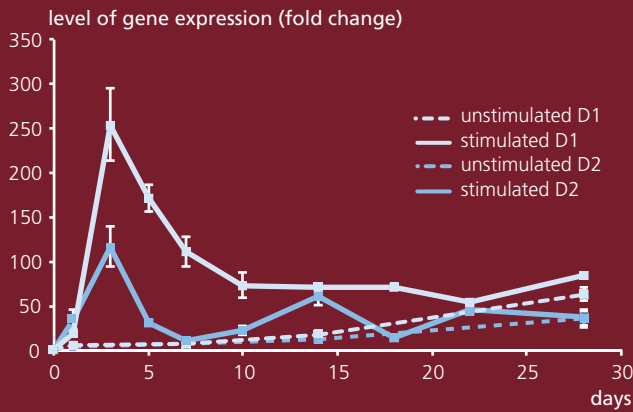
Differentiation studies of mechanical and biochemical signals

The overall focus of the project is the generation of a cell bank of well-characterized cryopreserved human mesenchymal stem cells. A broad study of the differentiation behavior of these cells was conducted (Figs. 1 and 2). The study includes both mechanical stimuli as well as soluble factors that transmit the signals that initiate differentiation down the three pathways of adipogenic (fat), chondrogenic (cartilage) and osteogenic (bone).

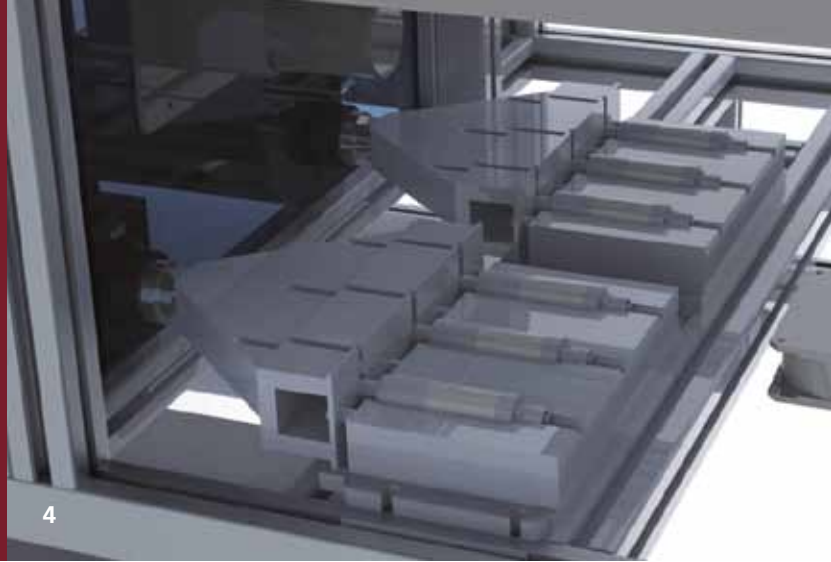
Establishing parameters for mathematical modeling

The high resolution quantitative monitoring of cell state development, for example by molecular biological analysis, or technologies for high-throughput microscopy, is the basis for the mathematical modeling of mesenchymal stem cell differentiation processes. To identify the influence of differentiation-specific stimulation towards all three mesodermal cell types, we measured the temporal evolution of differentiation markers from all three directions (Fig. 3). This data is then used to develop the model, define the process parameters, and for model validation. Here, the mathematical modeling is not limited to the imaging of the soluble factors mediated gene regulation, but also includes the influence of the mechanical deformation of the cytoskeleton and the activation of the mechanically bound receptors.

The mathematical models, developed within the consortium, are complex networks of gene regulating mechanisms. These networks allow the prediction of the cells differentiation pathways. Based on our current data, we have already compared two different strategies for osteogenic differentiation by the addition of soluble biomolecules and we have evaluated these strategies for their long-term results.



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Efficiency through mechanical stimulation

Overall, the integration of mechanical and biochemical stimuli on the differentiation of mesenchymal stem cells opens new opportunities to create optimal differentiation strategies [2]. In comparison to biochemical stimulation, mechanical stimulation has the advantage that no biologically active substances are required, which significantly simplifies the approval process for tissue-engineered products. In addition, biomechanical stimulation is much more cost-effective. The ability to replace certain biochemical stimuli with biomechanics can vastly improve the marketability of a tissue-engineered product.

Bioreactor system

The incorporation of bioreactor systems into cell culture processes is an essential step in the development of successful and marketable tissue engineered products comprised of fully matured tissues [3]. We have already started with the development of a bioreactor system for the generation of bone tissue. Whereby, MSCs are cultured on a synthetic scaffold. During the culture process, the bioreactor supports osteogenic cell differentiation employing bone-specific mechanical stimuli. In a long-term perspective, such in vitro generated bone tissues can be used to treat large bone defects.

- 1 *Fat accumulation (red) in adipogenic differentiated MSCs.*
- 2 *Cartilage-specific proteins (blue) in chondrogenic differentiated MSCs.*
- 3 *Time course of the genetic profile of the transcription factor CEBPA from two donors (D1, D2) during osteogenic differentiation.*
- 4 *Cartridge system for the production of bone tissue.*



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Literature

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- [2] Kahlig, A. et al. (2011) In silico approaches for the identification of optimal culture condition for tissue engineered bone substitutes, Current Analytical Chemistry, accepted
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Funding

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Project partners

Institute for Interfacial Engineering, University of Stuttgart | Institute of Cell Biology and Immunology, University of Stuttgart | Institute for Systems Theory and Automatic Control, University of Stuttgart | Institute of Mechanics, University of Stuttgart | Institute for Automation Engineering, University of Magdeburg | Max Planck Institute for Intelligent Systems, Stuttgart

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

Dr. rer. nat. Karin Lemuth, Dipl.-Biol. Linda Mayer, Priv.-Doz. Dr. rer. nat. Steffen Rupp

Initial situation

Infections by yeasts and mold fungi lead to severe illnesses, especially in immunocompromised patients. With a mortality rate of between 30 to 80 percent, the rapid detection of a pathogen, including 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, clinical studies have shown that phenotypic resistance testing is subject to an error rate of up to 15 percent. Cultivation often fails completely, even when the patient displays clear clinical symptoms. These cases require the initiation of a therapy of suspicion, which cannot be specifically matched to the pathogen.

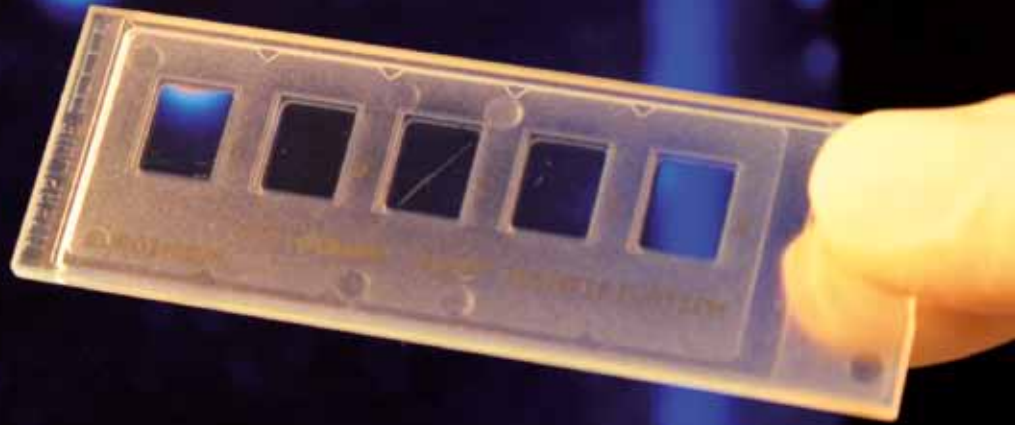
Because of this, molecular biology methods such as sequencing, fluorescence-in-situ-hybridization (FISH), PCR or quantitative real-time PCR (qRT-PCR) are increasingly being used for the identification of pathogens. However, these methods have a limited multiplex capability. This means that only a small number of a large amount commonly occurring pathogens or resistances can be tested for (≤ 10 parameters). This makes numerous cost-intensive tests necessary, reducing the time advantage of the method.

DNA microarrays as the diagnostic tool of choice

It is possible to compensate for this diagnostic gap by the use of DNA microarrays, which enable the simultaneous examination of up to several thousand parameters. Such tests were previously rarely used in routine diagnostics due, among other things, to the high experimental and instrument costs of the processing of microarrays. These problems can be minimized by the application of microsystems 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 for Interfacial Engineering IGVT of the University of Stuttgart, in combination with partners from medicine, science and industry and within the BMBF-funded research project "FYI-Chip – Fungi Yeast Identification", are therefore developing a fully integrated lab-on-a-chip system for the rapid identification of fungal infections in respiratory secretions and primarily sterile body fluids in immunocompromised patients. The scientists at the Fraunhofer IGB and IGVT are therefore closely working with the company Euroimmun, based in Lübeck, Germany, with doctors at the Heart and Diabetes Centre NRW, as well as with developers at the Reutlinger Multi Channel Systems MCS GmbH and Robert Bosch GmbH, Gerlingen. The 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

Within the project, the IGVT has developed PCR systems and DNA probes for over 50 relevant fungal pathogens (including *Candida* or *Aspergillus* species.) In order to identify this amount of pathogens PCR systems have been developed for genes that show highly conserved areas, but are also variable enough to enable discrimination between the species. These are currently being tested for their suitability in LOC evaluation models. The Fraunhofer IGB is developing LOC-compatible cell disruption techniques for fungal species. The use of disposable cartridges for the chip makes the system flexible and economical.

Outlook

As a miniature laboratory, the LOC combines sample preparation directly on the chip with highly sensitive and rapid molecular biological diagnostics of yeasts and mold fungi and their resistances. This enables them to support clinicians in their diagnoses and facilitate the rapid and adequate initiation or adjustment of therapy. The LOC system is designed as an open system that might be used for further sample materials, such as biopsy tissues or for the detection of bacterial pathogens and their antibiotic resistance markers in the future.



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Funding

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Project partners

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

- 1 *False color transformation of a DNA microarray.*
- 2 *Rhizopus stolonifer, a dangerous pathogen for immunocompromised patients.*
- 3 *DNA microarray for routine diagnostics.*



RIBOLUTION – PLATFORM FOR THE IDENTIFICATION OF ncRNA-BASED DIAGNOSTICS

Dr. rer. nat. Elena Lindemann, Dr. rer. nat. Kai Sohn

Effective and specific early detection using molecular diagnostics

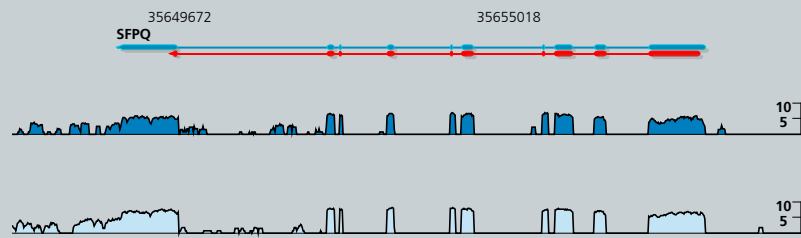
Due to demographic developments our healthcare system faces major challenges. An increasingly aging population also means increasing numbers of oncological, degenerative and chronic inflammatory diseases. This results in rising costs that place an increasing burden on our healthcare system. Effective molecular diagnostics offer a potential solution for this problem. It uses the presence or concentration of specific molecules, so-called biomarkers, as indicators of disease or the response to a particular form of therapy. Improved early detection therefore enables difficult and costly disease progressions to be avoided. In addition, an improved differential diagnosis based on biomarkers enables therapies to be individually adjusted for each patient. Despite a high demand for clinical diagnostics, there is currently a lack of such markers, which show sufficient sensitivity and specificity, for many conditions.

One example is chronic obstructive pulmonary disease (COPD) that, with over 600 million cases and over 2.75 million deaths worldwide per year, represents the fourth most common cause of death. Reliable diagnosis is only possible in advanced stages of the disease, through progressively decreasing lung function, which is usually too late for interfering therapy.

The situation is similar for prostate cancer, one of the most common cancers in men. In this case there is also a lack of reliable biomarkers, which enable the unequivocal diagnosis of the tumor and its subsequent treatment in its early stages.

Non-coding RNAs as biomarkers

The aim of the RIBOLUTION project, where Fraunhofer IGB cooperates with the Fraunhofer institutes IZI (coordination), IPA, FIT, ITEM, as well as numerous clinical partners (Universities of Dresden, Leipzig, Charité Berlin) and the pharmaceutical company GlaxoSmithKline, is the identification of novel diagnostic indicators for diseases such as COPD and prostate cancer. Since January 2011 our project has focused on a new class of molecules, so-called non-(protein)-coding ribonucleic acids (ncRNAs), which are still largely uncharacterized. Previous studies have shown that ncRNAs represent the central level of cellular control in complex organisms and regulate diverse cellular processes, such as transcription, translation, RNA-editing, chromatin structure or epigenetic processes [1, 2]. It is suspected that they play a crucial role in disease development and therefore have great potential as diagnostic biomarkers.



2

Procedure

The first genome-wide identification phase of novel, diagnostically applicable RNA-based biomarkers will be carried out at the Fraunhofer IGB with the aid of high-throughput sequencing technology (Next-Generation Sequencing), which enables up to 10^9 DNA sequence fragments to be sequenced in parallel. This high density of data enables the *denovo* identification of significantly expressed ncRNAs in selected COPD or prostate cancer patient samples. In the second and third phases of the screening process these ribonucleic acids are further screened using specific probes on DNA microarrays (customized arrays) and subsequently validated by quantitative real-time PCR of up to 2000 patient samples.

Results

We are currently establishing suitable procedures for the preparation of ribonucleic acid for sequencing non-coding RNAs from patient samples (e.g. from whole blood in COPD), by Illumina high-throughput sequencing (HiSeq2000). Additionally, we are developing and validating various methods of sample preparation for both strand-specific and non-strand-specific sequencing. All procedures are to be carried out in a GLP-like environment, in order to assure the traceability and secure documentation for later certification or licensing of the diagnostic markers.

Outlook

The high standard of process and quality control will ensure that the identified biomarkers will be valid. It will also be possible to transfer the information and experience gathered throughout the RIBOLUTION project to other relevant diseases. In this context, the project will make major contribution to the field of "personalized medicine".



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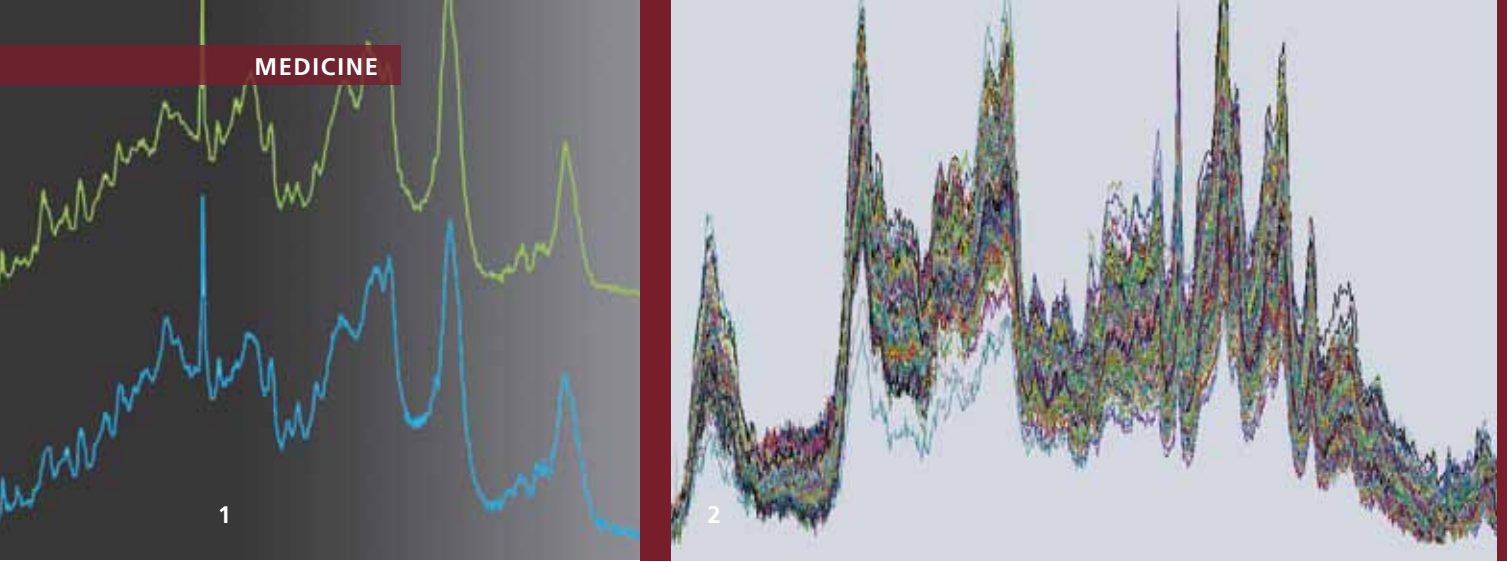
Funding

We would like to thank the Fraunhofer-Zukunftsstiftung (Fraunhofer Future Foundation) for their funding of the project "RIBOLUTION – Integrated platform for the identification and validation of innovative RNA-based biomarkers for personalized medicine".

Project and cooperation partners

Fraunhofer IZI, Leipzig (Coordinator) | Fraunhofer IGB, Stuttgart (lead: biomarker discovery) | Fraunhofer IPA, Stuttgart | Fraunhofer FIT, Sankt Augustin | Fraunhofer ITEM, Hannover | Universitätsklinikum Carl Gustav Carus, Dresden | Universität Leipzig | Charité Universitätsmedizin Berlin | GlaxoSmithKline, London, UK

- 1 Loading the Illumina high-throughput sequencing platform for sequencing.
- 2 Visualization of the sequence data using the GeneScapes viewer, developed at the Fraunhofer IGB.



RAMAN SPECTROSCOPY FOR THE NON-INVASIVE, LABEL-FREE MONITORING OF CELLS AND TISSUE

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

Raman spectroscopy for tissue engineering

Raman spectroscopy is a laser-based optical technology, which is suitable for the characterization and identification of different materials. At the Fraunhofer IGB, Raman spectroscopy is primarily used for the analysis of cells and tissues [1–4]. Simple preparation and non-destructive marker-free analysis, particularly in liquids, are major advantages of this method. Cell identification and quality control monitoring can be performed directly on a sample during cell isolation or the production of tissue transplants. In addition, the method can be used for sterility control as it does not contact the sample and can distinguish between cells and bacteria.

The theory of Raman spectroscopy

In 1923, Brillouin and Smekal first predicted the inelastic scattering of light. It was not until 1928 that Sir C.V. Raman could demonstrate that the inelastic scattering of light could be detected and measured, for which he later won the Nobel Prize. Raman spectroscopy is based on the interaction of electromagnetic radiation and matter. In biology, the effect is created by irradiating a sample with monochromatic light, usually with a strong laser, in the visible or infrared region. The inelastically scattered, red-shifted light is then detected as compared to the excitation-light. In the spectrum itself, several bands are visible, corresponding to the chemical composition of the sample and are referred to as a biochemical

fingerprint. For biological applications, due to the high variability of cells and microorganisms, it is necessary to perform a large number of measurements for device calibration and spectrum references in order to differentiate between different microorganisms. For this reason, multivariate data analysis tools are required to evaluate the large amounts of data. At the Fraunhofer IGB, we use principal component analysis to assess the biological data. This analysis shows similarities of the spectral data by the formation of clusters along the largest variance associated with the principal components. For further data analysis, support vector machines are used for in-depth pattern recognition.

Cell analysis

An important criterion for the quality control of cells in regenerative medicine is the monitoring of the differentiation path of different cell types and the determination of cell viability and differentiation state. While observing these parameters, important steps for the production of tissue-engineered products can be determined. In our studies, we have shown that Raman spectroscopy can be used to categorize a variety of cell types [1, 3, 4]. This gives us the ability to create pure cell cultures. Additionally, the validation of cell viability is an important and recurring parameter in quality control. In this area, we were able to identify spectral regions that allow for the classification of viable, necrotic and apoptotic cells. In our current studies, we established standard protocols to monitor the directed differentiation of pluripotent stem cells.



Tissue analysis

In addition to the analysis of isolated cells, Raman spectroscopy is a suitable method for the analysis of cells within their natural three-dimensional (3D) environment. In previous studies, we successfully identify and characterize skin cells, such as keratinocytes, melanocytes and fibroblasts, within biopsies [3]. In addition, we could analyze cells within a 3D in vitro skin model without the need for histology and immunohistochemistry [3]. Furthermore, we demonstrated that Raman spectroscopy could make a qualitative distinction between native and pathological tissue matrix [4], which will enable the ability to diagnose transplants pre-implantation.

Outlook

Currently, we are optimizing and automating the individual steps of the measurement process, such as image analysis. Additionally and in close collaboration with the University Hospital Tübingen, we are building a spectrum database of the different cells and tissues we have analyzed.

- 1 Raman spectra of different cell types.
- 2 Raman-spectral data of native tissue.
- 3 Microscopic image of cell suspensions in the Fraunhofer IGB Raman spectroscope: Primary trachea epithelial cells (top), HaCaT cell line (bottom).
- 4 The Fraunhofer IGB developed Raman-spectroscopy system.



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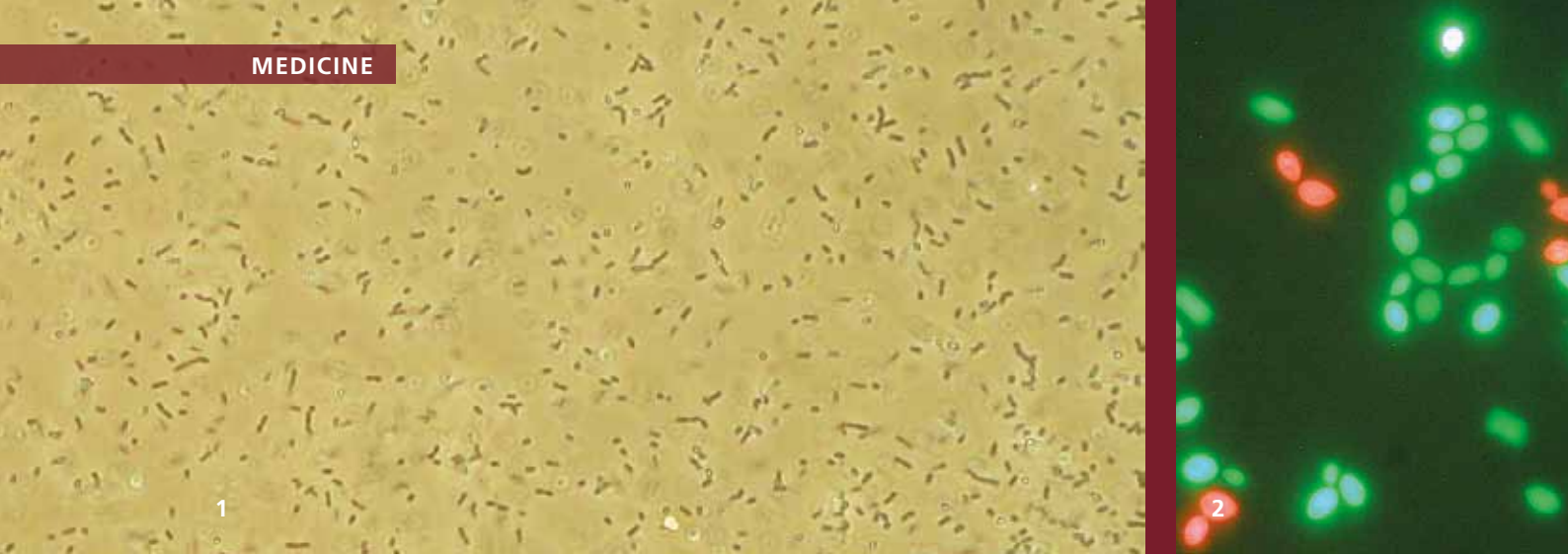
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Funding

We would like to thank the Fraunhofer-Gesellschaft for their support of the project "On-line quality control for accelerating drug development and individualized therapy using Raman spectroscopy" in the program market-driven prospective research (MAVO) and the Attract program, along with the state of Baden-Württemberg for the support of the project "Color-free, chemically selective microscopy for fast cell screening".

Project partners

University Hospital of the Eberhard Karls University Tübingen |
 Institute for Interfacial Engineering, University of Stuttgart |
 Fraunhofer IPM, Freiburg | Beiersdorf AG, Hamburg



PRESSURE CHANGE TECHNOLOGY – STABILIZING LIQUID PRODUCTS WITHOUT PRESERVATIVES

Dr. rer. nat. Ana Lucia Vasquez

Biogenic products such as foodstuffs, and also pharmaceuticals, have to be stabilized for storage or transport by inactivating the microbiological contamination. Well-established processes for preserving foodstuffs such as heat sterilization or pasteurization frequently have the disadvantage that they destroy valuable heat-sensitive substances such as vitamins, thus reducing their nutritional value. Also, the addition of chemical preservatives can have negative effects on the quality of the product and potentially affect consumer's health. Moreover, EU directives (2003/89/EG) regarding the addition of processing aids and other substances with a potential allergenic risk (e.g. sulfur dioxide) in foodstuffs as well as their use in non-alcoholic and alcoholic drinks are becoming ever more stringent. Besides impairing the substances contained in foodstuffs, thermal processes can also inactivate active ingredients in pharmaceutical products. Therefore, there is a need for alternative biological stabilization methods.

Physical methods of biological stabilization

The development of new methods for the biological stabilization and/or sterilization and thus the preservation of foodstuffs, cosmetics and pharmaceutical drugs is one of the main focuses of research at the Fraunhofer IGB. In particular, physical for inactivating contaminating microorganisms, such as pressure change technology (PCT), are being investigated.

One focus of our work is on understanding and describing the inactivation mechanisms of the processes as well as the interaction of the various parameters in the system (temperature, pressure, particle size, viscosity, pH value, etc.) in order to optimize the processes technologically and to be able to implement them in a production process. In this context, we attach great importance to the constituents of the products being treated as gently as possible and that their biological function is not impaired during the treatment.

Pressure change technology

Pressure change technology is a physical, non-thermal process for treating liquids with suspended microbial particles (e.g. Bacteria, yeasts). The product is mixed with an inert gas under pressure and subsequently the pressure is released abruptly. This results in the cell disruption of microorganisms or mechanical damage of their surface, for example of spores or enzymes. The process is preferably used between 5 °C and 40 °C at pressures of up to approx. 50 MPa. The liquid or suspension to be treated as well as the working gas (e.g. argon or nitrogen) are each placed under working pressure and then mixed homogeneously. In the case of microorganisms with cell membranes the gas diffuses through the membrane into the cells until the cytoplasm is saturated with gas. When subsequently the mixture is abruptly brought down to a lower pressure, the gas also immediately resumes its original state of aggregation. This process destroys the cells. Cavitation effects also result in damage of particle surfaces (e.g. erosion of spores).



Preservation of wine

For the preservation of liquid foodstuffs such as fruit juices or wine we are implementing pressure change technology in a continuous process and investigating the impact of the process parameters on various products. In the EU-funded project PreserveWine, pressure change technology is being investigated as an alternative to adding the preservative sulfur dioxide in various process steps during wine making and is being further developed in cooperation with the company Educto GmbH and other European partners. The objectives of the project are the inactivation of microorganisms after the alcoholic and malolactic fermentation and also the protection of the wine against oxidation by means of an inert atmosphere. A batch unit was built for initial tests. Currently, the process is being validated with wine in cooperation with the Institut des Sciences de la Vigne et du Vin in Bordeaux. Here, various parameters such as temperature, retention time and type of gas are being investigated both with regard to wine-relevant yeasts (e.g. *Saccharomyces cerevisiae*) and bacteria (e.g. *Lactobacillus* sp.), and regarding the physical-chemical and sensory characteristics of the product. A continuous plant has been designed for the specific requirements of the wine producers and is currently being built. The process will then be optimized and validated in further trials for use in wine production with red and white wine provided by project partners in Italy and France.

Within the framework of our activities, the entire process from product development, manufacturing, stabilization including process engineering and plant design, is analyzed and validated, implementing the required good manufacturing practice standards (GMP) and risk analysis procedures such as hazard analysis and critical control points (HACCP).



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Funding

We would like to thank the European Union for funding the project "PreserveWine – Non-thermal process to replace use of sulfites and other chemical preservatives in European wines to meet new European Directive" in the Seventh Framework Programme FP7/2007-2013 under grant agreement n° 262507.

Project partners

www.preservewine.fraunhofer.eu/consortium

- 1 *Lactobacillus*, untreated samples. © ADERA (Bordeaux)
- 2 Identification of yeasts, fluorescence microscopy image, untreated sample. Dead yeast cell (red) living yeast cell (green) © ADERA (Bordeaux)
- 3 Batch unit using pressure change technology to treat liquids.
- 4 Barreled red wine in the cellars of our project partner Tenute dei Vallarino, Italy.



PHARMACY

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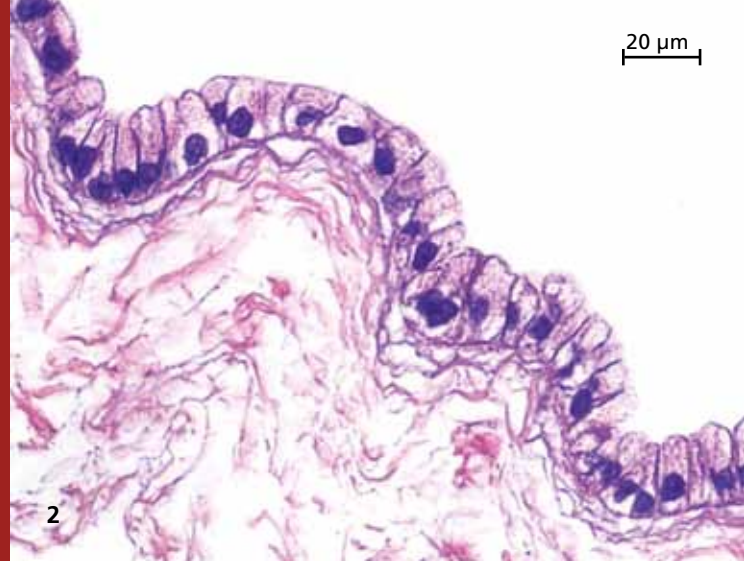
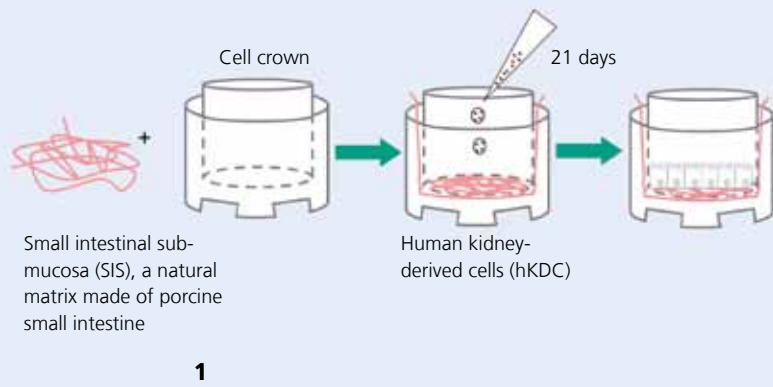
The current challenges faced by the pharmaceutical industry include the accurate diagnosis of diseases and their personalized therapy, the development of new active agents and the enhancement of the effectiveness of new drugs through improved formulations. The pharmacy business area at the Fraunhofer IGB is involved in developing solutions for drug screening, pharmaceutical biotechnology, pharmaceutical chemistry and drug release and formulation.

We identify new drugs by means of the targeted use of cell-based assays, for instance for immunomodulatory substances or anti-infectives. Structure-activity correlations are performed on active hits. Potential active compounds are characterized in vitro by using complex organotypic 3D primary cell models (skin, intestine, lungs, liver) for effectiveness, absorption, distribution in the organ model, metabolization 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 an early, pre-clinical stage.

In the field of pharmaceutical biotechnology we are developing processes to manufacture pharmaceutical proteins. These extend 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 – including by means of molecularly imprinted nanoparticles (NanoMIPs). Cooperation within the Fraunhofer network enables us to supply customers with proteins produced in compliance with GMP (good manufacturing practice) for clinical testing. For the formulation of active agents we develop nanoparticle-based structures which deliver drugs directly to the target location and then release them in a controlled manner.

In addition, we develop cell-based therapeutics and produce samples for clinical trials according to GMP guidelines. Our quality control systems identify potential contaminants (microorganisms, viruses) in a non-destructive way using spectroscopic, cell-based or molecular methods according to the guidelines of good laboratory practice (GLP) or good manufacturing practice (GMP).

Our work in the pharmacy business area is enriched in many ways by the collaboration of different departments at the Fraunhofer IGB. We also contribute to the activities of the Fraunhofer Group for Life Sciences, which cover the development of medicines from screening for active agents to the production of test samples for clinical trials.



AN IN VITRO MODEL OF THE KIDNEY PROXIMAL TUBULE

Anke Hoppensack M. Sc.

The kidneys are responsible for filtering metabolic waste and foreign substances from the blood. During filtration, essential substances such as water and glucose enter the primary urine. In order to prevent their elimination, they are reabsorbed by renal proximal tubular epithelial cells, metabolized if necessary and then released back into the blood. Foreign substances such as pharmaceuticals and toxins can also flow over these transport routes and harm the cells of the epithelium. Large areas of damage in this area can lead to life-threatening impairment of renal function, making the proximal tubular epithelium interesting for pharmacological and toxicological studies, biomedical research and clinical applications.

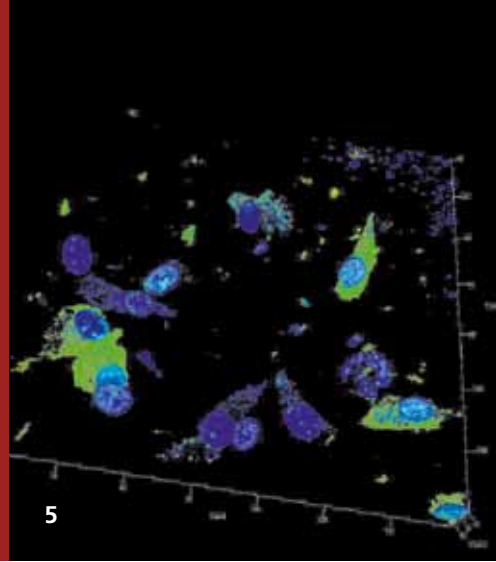
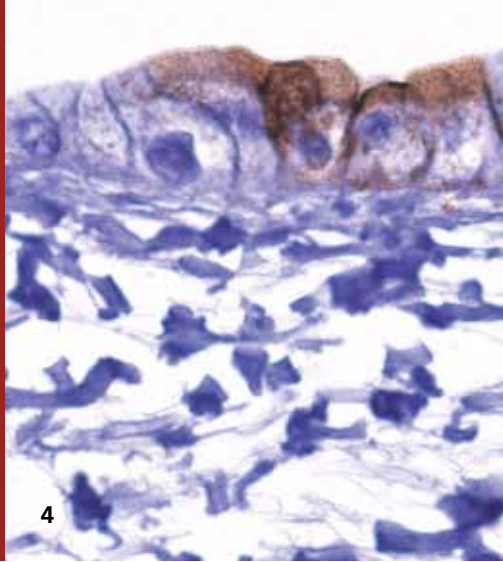
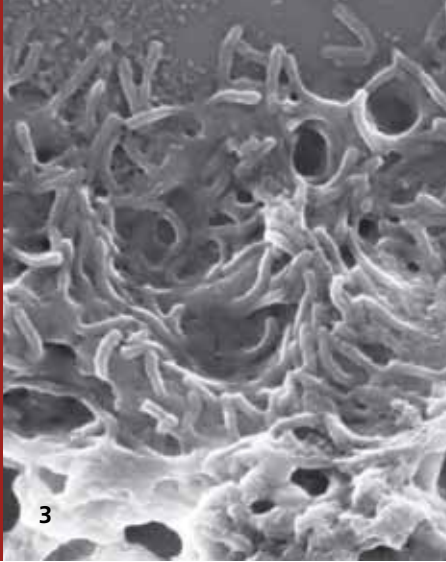
To date, the in vitro simulation of the proximal tubular epithelium of the kidney has been hindered by the lack of a suitable combination of a cell source and culture matrix, which would allow the proper formation and maintenance of an epithelial cell layer. One challenge has been to find a functional human cell source that is available in sufficient quantities. While another challenge has been to find a proper culture substrate that does not lead to a multilayered, atypical epithelium growth, as what can be seen with commonly used synthetic materials with biological coatings.

A natural matrix as a substrate for human kidney cells

Our project partners from ATRM have developed SOPs to isolate an interesting cell population from human kidney tissue (human kidney-derived cells, hKDCs [1]). These cells have properties that resemble renal progenitor cells, they can be easily expanded and safely frozen. We have used these cells in combination with small intestinal submucosa (SIS), which is a clinically approved natural matrix, to create an in vitro model of the kidney proximal tubule. The SIS matrix is made from the decellularized intestinal submucosa from porcine small intestine, leaving an extracellular matrix of connective tissue fibers, growth factors and several other ECM constituents [2]. The in vitro model is constructed by clamping the SIS between two stainless steel rings ("cell crown"), transferring the SIS to a cell culture plate and then seeding it with hKDCs, which is then followed by three weeks of culture.

A cell-matrix construct with the properties of the renal proximal tubule

The culture of hKDCs on the SIS matrix allows for the growth and morphology of tubular epithelial cells. Properties such as contact inhibition, which allows single layer growth, cubic to high prismatic cell morphology and the formation of a brush border on the upper cell membrane, can be realized on the SIS matrix. The brush border cells are essential for creating a cell surface with the high transport rates required for the renal proximal tubule. The hKDCs build a basement membrane on the border of the SIS and become polarized. The polarization



demonstrates the epithelial differentiation of the cells, which ensures the directed transport of substances, and thus the functionality of the cells. Furthermore, immunohistochemical staining identified renal proximal tubular cell markers such as aquaporin-1, a channel protein with which the strong absorption of water is made possible, and N-cadherin, which is a component of cell-cell interactions. Functionality was demonstrated by albumin uptake, which is a specific function of the renal proximal tubule.

Outlook

By using SIS and hKDCs, we have created an in vitro model with a single continuous layer of brush border cells that has many of the important properties of the renal proximal tubule. More studies are required to further characterize the functionality of the model so it may be specialized for specific applications. In addition to basic research and pharmacological studies, the cell-matrix construct is an interesting construct for the development of a bioartificial renal replacement system [3].

- 1 Schematic for the construction of the in vitro model.
- 2 Histological cross-section of the in vitro model.
- 3 Scanning electron microscopy of the brush border.
- 4 Immunohistological staining of aquaporin-1 (brown) in cells.
- 5 Albumin uptake (green) in the cells (nucleus = blue).



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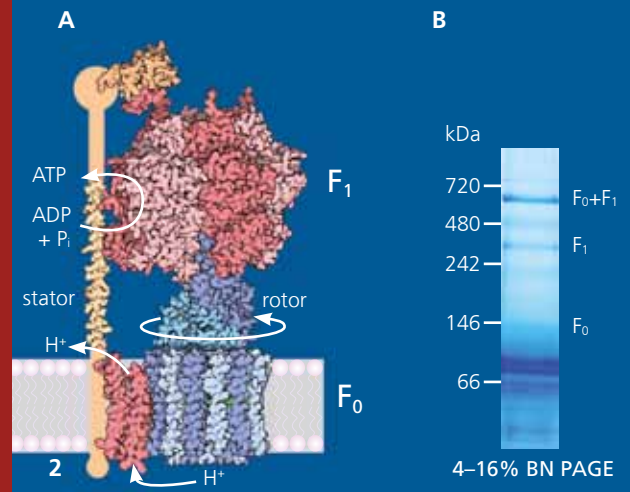
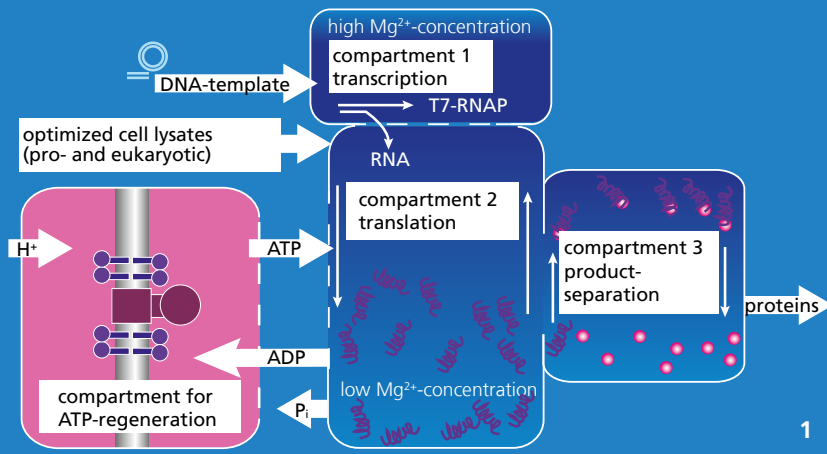
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Project partner

We would like to thank our project partner Advanced Technologies and Regenerative Medicine (ATRM), LLC, Somerville (USA) for their financial support and for the provision of the cells.



CELL-FREE BIOPRODUCTION WITH INTEGRATED ENERGY SUPPLY

Dr. rer. nat. Marcus Thein

Production of biotechnologically relevant proteins

The availability of high-quality, functional biomolecules is a vital foundation of the ability of our modern, developed society to progress. This increases the demand for enzymes, as well as complex peptides, pharma proteins and synthetic molecules for medicine and pharmacy. Peptide-based substances and their production procedures are currently largely developed with the aid of living cells or organisms. Although this technology is now very efficient, there are significant restrictions on numerous levels. For example, the considerable input of materials and energy limits economic efficiency; many end products have a toxic effect on the cells or organisms that produce them, and the steps for the purification of target proteins and separation of all cellular components of the organism are often very difficult and costly.

Cell-free protein synthesis on an industrial scale

Cell-free protein synthesis provides new opportunities here. The specific application of the components from certain organisms needed for this makes it possible to produce efficiently proteins with complex and even totally new properties in adapted reaction compartments. Despite intensive research in cell-free biosynthesis, we are still currently lacking many basics in order to be able to make economically meaningful use of this technology. This is why eight Fraunhofer institutes, within the BMBF-started the Fraunhofer joint project "Biomolecules from the production line", launched in 2011 within the strategic process Biotechnology 2020+, are developing and establishing the elements intended to enable the expansion of the

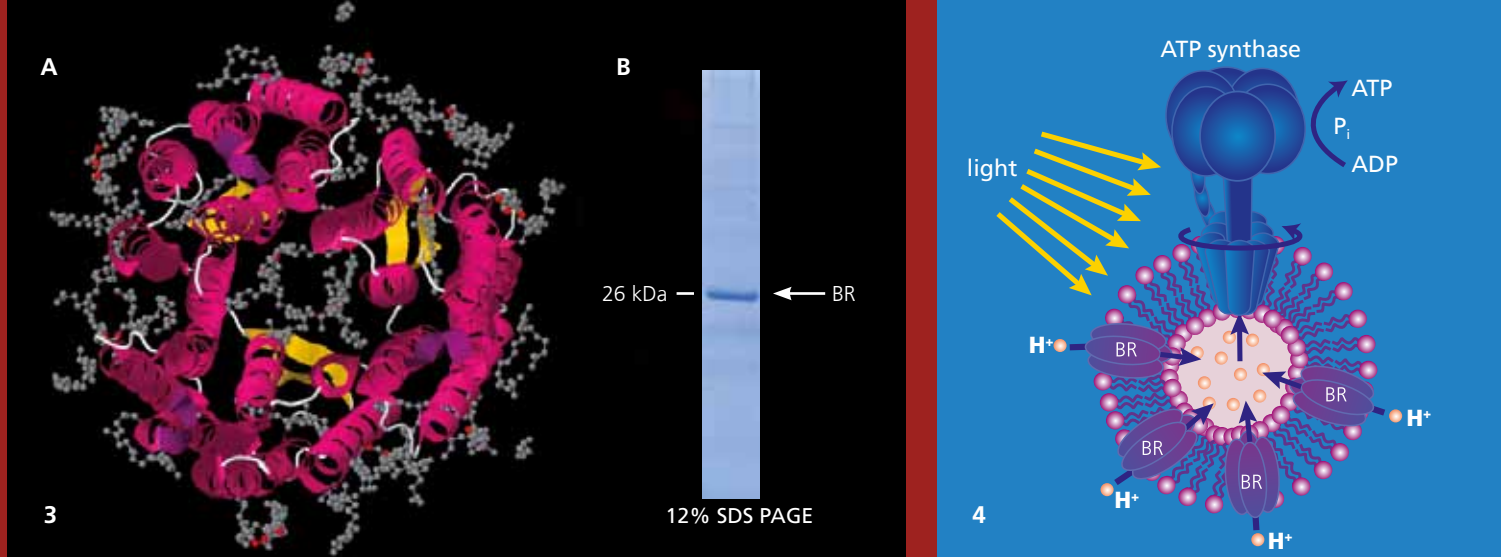
technology to an industrial scale. This should involve the transfer of cell-free protein synthesis technology to efficient, compartmented reactor systems (Fig. 1).

Energy provision as a limiting factor

The production and supply of energy for the system in the form of ATP (adenosine triphosphate) is of crucial importance. ATP is the main, universal form of energy for all energy-dependent cellular processes and therefore equally important for cell-free biosynthesis. In the cell the highly complex, proton-driven protein complex ATP synthase is largely responsible for the regeneration of ATP. The Fraunhofer IGB is, among other things, concerned with using ATP synthase, in a suitable composition, as an energy generation module for cell-free protein synthesis and thereby set new standards in cell-free bioproduction.

Procedure

At the Fraunhofer IGB, ATP synthase, a membrane protein complex consisting of eight subunits, is produced and purified in *E. coli* (Fig. 2). The ATP synthase is subsequently directionally and biologically-actively reconstituted in lipid membranes (vesicles and planar membranes). In order to assure ATP synthase the membrane must be energized via a proton gradient. One possibility for this is the use of the protein bacteriorhodopsin from the halotolerant archaeobacterium *Halobacterium salinarum*, which can generate a proton gradient using light. By the co-reconstitution of ATP synthase and bacteriorhodopsin in lipid vesicles, the irradiation of these vesicles with light can regenerate ATP for cell-free biosynthesis.



Components produced in pure form

All components for an energy generation module in pure form were produced at the Fraunhofer IGB:

- In a first approach, the highly complex ATP synthase was functionally isolated in inverted *E. coli* vesicles. This system previously enabled us to successfully synthesise ATP.
- We also purified ATP synthase by affinity chromatography using a his-tag (Fig. 2B) [2]. This allows the defined and concentrated integration of ATP synthase in lipid vesicles.
- Lipid vesicles with a diameter of 50 nm to 10 µm were produced by membrane extrusion or electroformation.
- We were able to obtain bacteriorhodopsin by osmotic lysis and selective centrifugation from *Halobacterium salinarum* (Fig. 3).

The production of these components in their pure form now enables us to establish the conditions for optimal, stable ATP synthesis.

Outlook

ATP synthase and bacteriorhodopsin are to be directionally co-reconstituted in lipid vesicles or planar lipid membranes (Fig. 4). To this end, suitable conditions are to be found in order to be able to continually regenerate ATP over an appropriate period of time. This energy regeneration module is subsequently integrated into a compartment of the cell-free biosynthesis reactor (see Fig. 1).

- 1 *Diagram of a compartmented production unit for cell-free bioproduction.*
- 2 *ATP synthase: (A) model [1]; (B) purified ATP synthase subunits in a gel.*
- 3 *Bacteriorhodopsin: (A) model (source: PDB); (B) purified BR in a gel.*
- 4 *Diagram of a vesicle for light-driven ATP synthesis (source: [3]).*



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Literature

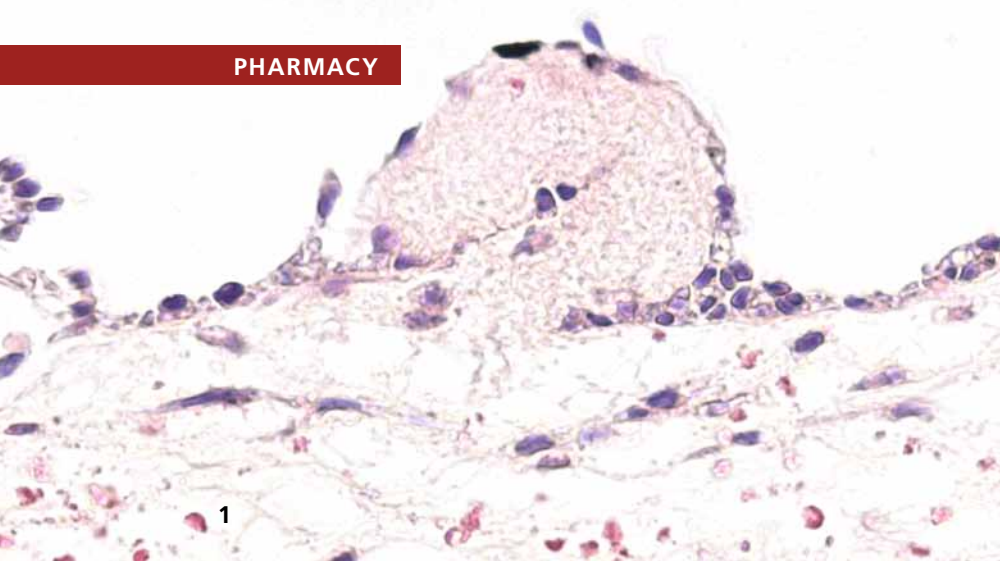
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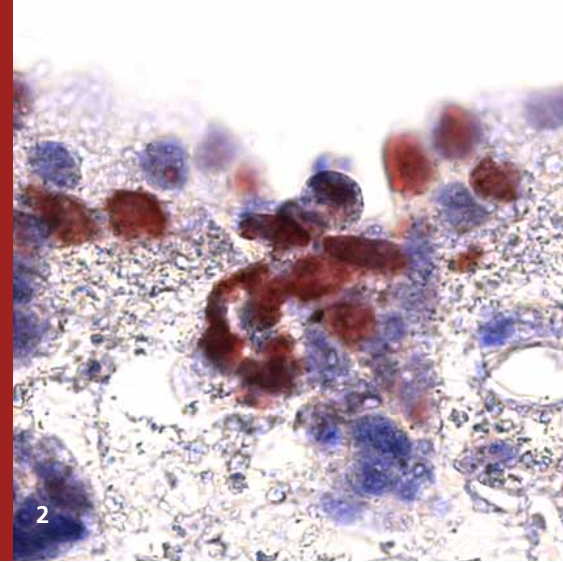
We would like to thank the German Federal Ministry of Education and Research (BMBF) for their funding of the joint project "Biomolecules from the production line", within the Biotechnology 2020+ programme and the Fraunhofer-Gesellschaft for funding of the joint project "Basic module for cell-free bioproduction – The industrial cell", as part of the Fraunhofer system research.

Project partners

Fraunhofer IBMT, Berlin | Fraunhofer ISIT, Itzehoe | Fraunhofer IZM, Berlin | Fraunhofer IPA, Stuttgart | Fraunhofer IPK, Berlin | Fraunhofer IME, Aachen | Fraunhofer ISI, Karlsruhe



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2

DEVELOPMENT OF A 3D IN VITRO TUMOR TEST SYSTEM FOR NERVE SHEATH TUMORS

Dipl.-Biol. Corinna Moll

Hereditary nerve sheath tumors

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder affecting one in 3500 individuals worldwide. NF1 patients carry a germline mutation in the tumor suppressor gene *Nf1*, leaving only one functional copy of the gene coding for neurofibromin. Loss of the remaining *Nf1*-allele due to a somatic mutation in Schwann cells may lead to the formation of what are initially benign tumors. With a 10 percent risk, benign plexiform neurofibroma undergoes a malignant transformation, giving rise to malignant peripheral nerve sheath tumors (MPNST). The complete surgical removal of these highly aggressive neoplasms is often unsuccessful. Since chemotherapy and radiation are ineffective treatments, there is an urgent need for the establishment of new therapeutic strategies. Drug testing is prevalently performed in two-dimensional culture systems, which do not adequately reflect the physiological conditions in the human body. Therefore, the establishment of three-dimensional (3D) models is important to simulate a tumor's complexity in vitro.

A common strategy in tissue engineering

A common strategy in tissue engineering is the seeding of cells onto biodegradable scaffolds for generating 3D tissue models. Such bioartificial scaffolds mimic the extracellular matrix and allow the formation of functional contacts between the cells and their surroundings, thereby making 3D tissue models highly attractive for tumor research.

Establishing a tumor test system

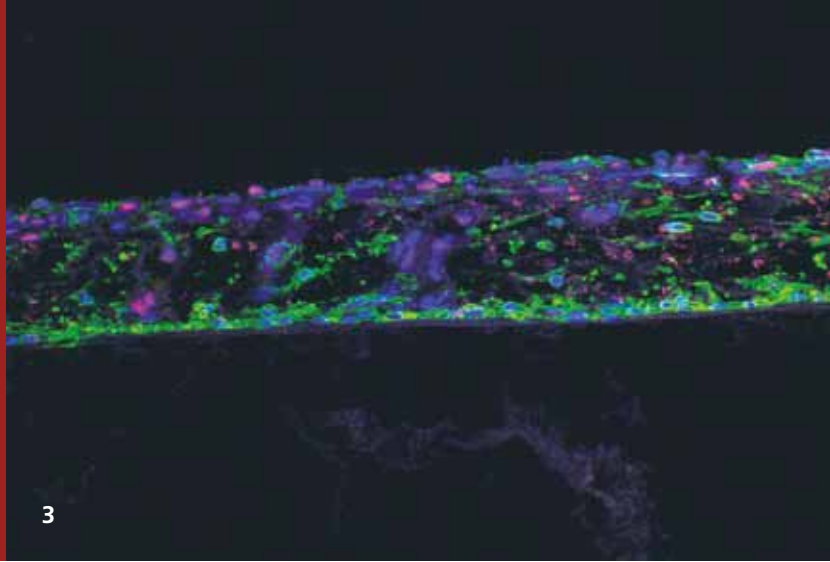
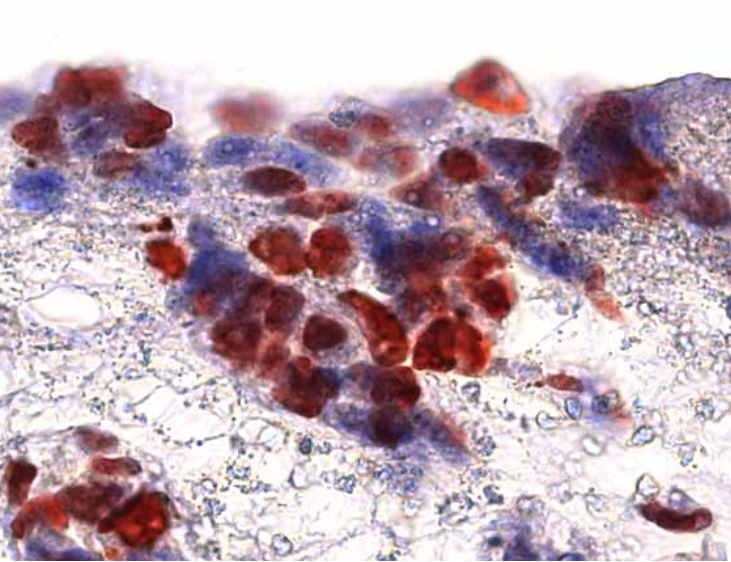
For establishing a 3D test system, two MPNST cell lines (NSF-1 and S462) are cultured statically on a biological scaffold (BioVaSc) derived from an acellularized porcine jejunal segment. The porous collagen scaffold allows the tumor cells to colonize the matrix according to their invasive properties.

Co-cultures for simulating tumor stroma

In order to study the interaction between tumor cells and tumor stroma, primary dermal fibroblasts and microvascular endothelial cells can be added to the tumor cell monoculture. Furthermore, the introduction of primary fibroblasts derived from NF1 patients (*Nf1*^{+/+}) allows the adaptation of the model to the physiological situation in NF1 patients.

3D matrix and co-cultures allow invasive growth

The MPNST cell lines showed individual and characteristic growth patterns. The NSF-1 cell line adhered to the matrix surface and only migrated into pre-existing cavities, whereas the S462 cell line infiltrated deeper regions of the scaffold. The S462 cells' invasive growth correlates with their expression of matrix-degrading enzymes, matrix metalloproteases [1].



3

In contrast to rigid two-dimensional surfaces, the 3D biological scaffold allows for the proper growth of tumor cells in a more physiological relevant environment. Overall, we observed a strong influence of the culture conditions on the tumor cells' differentiation state, suggesting that 3D culture with tumor-associated stroma cells more accurately mimics the tumors' physiology.

Outlook

Reconstructing a tumor on a biological scaffold allows the extensive study of tissue organization and differentiation. Not only are these culture conditions essential for the investigation of the mechanisms that contribute to tumor growth, 3D tumor models are also expected to become relevant for in vitro validation of therapeutic agents, possibly reducing the number of animal experiments to a minimum.

The future further development of the system will include the use of primary tumor cells to create patient-specific, personalized models that can be used for testing therapeutic strategies in vitro. Additionally, constructing the tumor model on a vascularized BioVaSc using patient-specific endothelial cells will enable the study of tumor angiogenesis.



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Project partner

Charité Universitätsmedizin Berlin

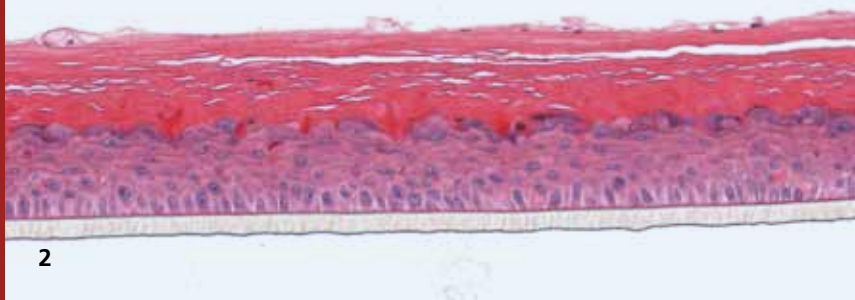
Further information

www.term.uk-wuerzburg.de

- 1 *Monoculture of MPNST cell line NSF-1 on the BioVaSc (H&E staining, 200x).*
- 2 *MPNST cell line S462 on the BioVaSc (staining of proliferation marker Ki67, 200x).*
- 3 *Fluorescent double staining of tumor cells (red) and fibroblasts (green).*



MANUAL



SKIN TEST SYSTEMS FROM AN AUTOMATED SYSTEM – VALID PREDICTIONS WITHOUT ANIMAL EXPERIMENTS

Dr. rer. nat. Martin Funk, Dr. rer. nat. Michaela Kaufmann

The skin is the first organ to be successfully grown in a lab using the methods of tissue engineering. Recently, a fully automated system for the production of skin was developed by four Fraunhofer institutes, coordinated by the Fraunhofer IGB. The development of in vitro skin equivalents will play a key role in the replacement of animal test systems. The significance of such in vitro test systems stems from the 7th Amendment to the Cosmetic Directive (76/768/EEC) that bans animal tests for raw materials used in the cosmetics industry. Furthermore, the REACH directives for chemical testing require the submission of chemical-physical data and toxicological in vitro data for newly developed chemicals. Together, these new regulations make the creation of a large volume of valid, meaningful in vitro test systems particularly important. In order for an in vitro test system to be accepted by the European Centre for the Validation of Alternative Methods (ECVAM), it must be shown that the test system is sufficiently sensitive, specific and reproducible to describe the toxicological properties of the tested substance.

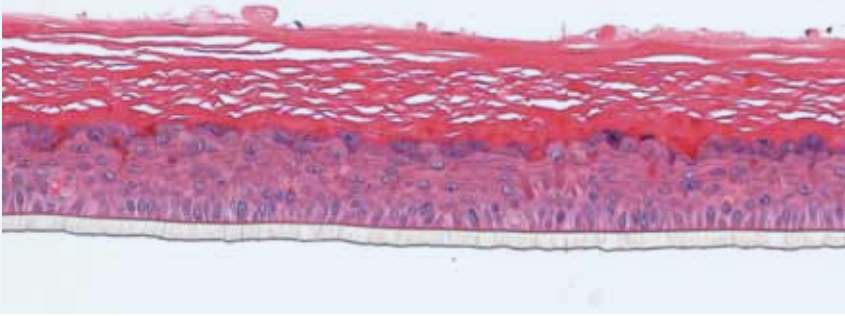
Automated, upscaled production of high-quality human epidermis

Within a few months, the Fraunhofer project consortium was able to establish the process for producing a human epidermis model for skin in an automated system. In this process, dermal cells (keratinocytes) are isolated, expanded and then cultured in specially designed and patented culture vessels to establish a properly structured epidermis. The system creates reproducible epidermis test models in large quantities that cannot be morphologically distinguished from manually prepared test models and we are currently investigating the physiological comparability between the two systems.

In vitro irritation tests with automatically produced epidermis models

Epidermis models are particularly suitable for assessing the irritation effect of test compounds. Manually produced epidermis models are currently being used in accordance with ECVAM guidelines as validated tests to replace animal experiments. For these tests, the samples to be examined are tested directly on the surface of the epidermis model. This allows the rapid, reproducible, and specific quantification of cell damage. This simple but efficient test system allows for

AUTOMATED



the high-throughput analysis of any kind of substance for its irritation potential. In ongoing studies, we are now using a number of officially prescribed substances with known irritation potential as control substances for the automation produced epidermis models in comparison to the already validated manually created skin models.

In collaboration with the authorities towards a validated test system

The main objective is the validation of the first in vitro irritation skin test system created from a fully automated system while working in close consultation with the ECVAM. Accordingly, we are developing a validation concept in close contact with the chemical substance authorities. We are benefitting from the existing data from previous validation studies and the existing experiences of the ECVAM with this test system. This should allow us to validate the test system within the shortest possible time period while preparing the models for commercial use.



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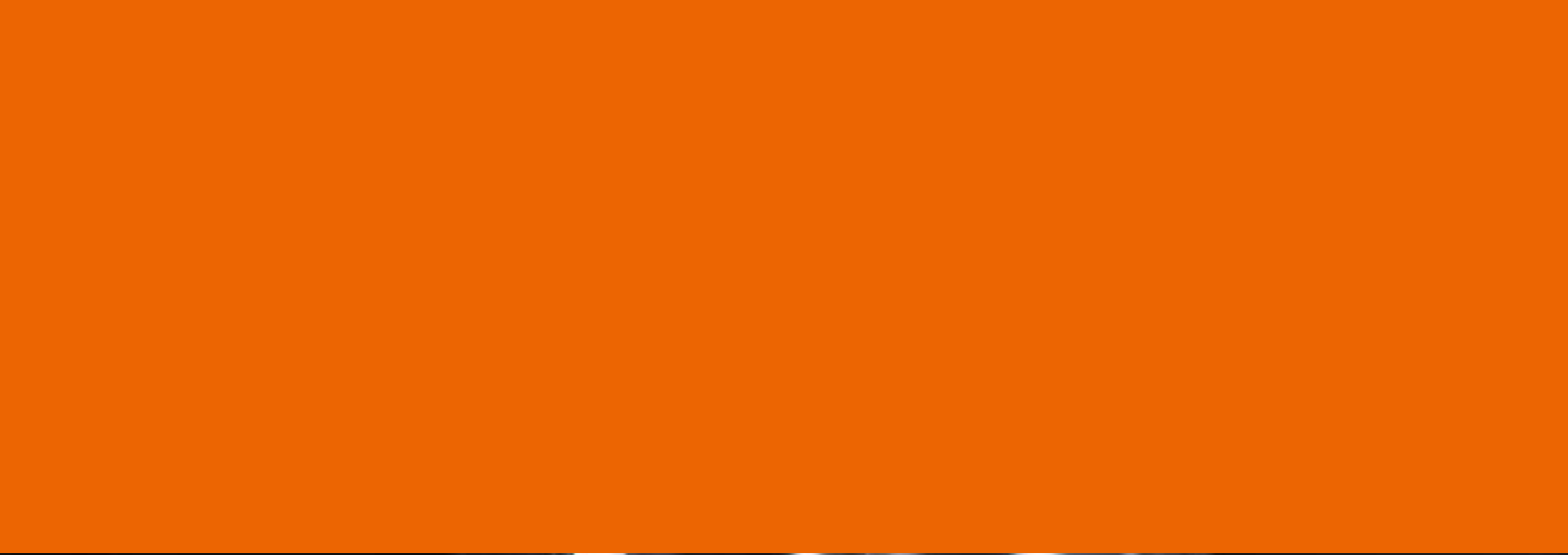
Project partners

Fraunhofer IPA, Stuttgart | Fraunhofer IPT, Aachen |
Fraunhofer IZI, Leipzig

Further information

www.tissue-factory.com

- 1 Irritation test on epidermis model.
- 2 Comparison of the histology of manual (left) and automated (right) produced epidermis models.
- 3 System for the automated production of skin models.



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 resources

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).

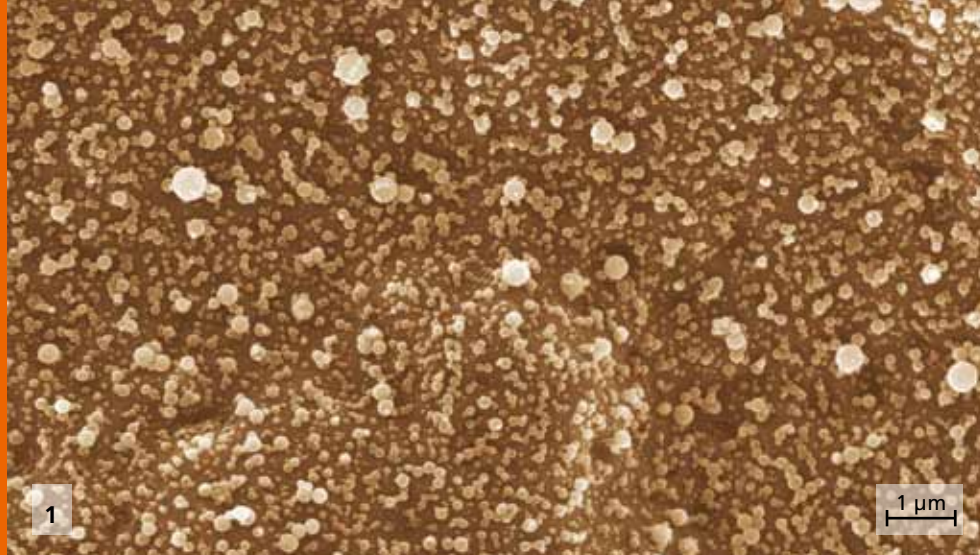
Decoupling of volume and surface properties by means of interfacial process engineering

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 resources to industrial scale will also be given by the Fraunhofer Center for Chemical-Biotechnological Processes in Leuna, which is being jointly built and operated by the Fraunhofer IGB and ICT institutes.



BIOACTIVE MINOR COMPONENTS FROM VEGETABLE OILS

Dr. rer. nat. Carmen Gruber-Traub, Dr. rer. nat. Achim Weber

Obtaining valuable materials

Renewable resources used in the production of biofuel are increasingly gaining importance. The vegetable oils involved, for example from rape seed or soy, contain various minor components (valuable materials and contaminants). On the one hand, biodiesel contains contaminants which can negatively affect the quality of the fuel. On the other hand, smaller amounts of important valuable materials such as bioactive Vitamin E (α -tocopherol) can also be found. To date, when biodiesel is burned, these valuable materials are normally burned along with it.

Due to its antioxidant properties tocopherol plays an important role in the human body, where it protects cells from the damaging effects of oxygen. Natural tocopherol-containing extracts are separated from the seeds of oil-containing plants, especially from wheat, corn, soy, cotton and rice, and then enriched. On an industrial scale, synthetic vitamin E is produced as a racemic mixture. Since synthetic tocopherol is relatively unstable, it is normally bound to an acetyl group. Through this process it loses all antioxidant properties. Up to 50 percent of the absorbed synthetic tocopherol can, however, be converted to natural vitamin E by the body.

The goal of this project was to develop an adsorptive process at pilot plant scale in which valuable bioactive minor components could be extracted as additional, value-added products in plant processing. To this purpose, we included polymeric nanoscale adsorber particles in a new process concept for the separation of substances.

The production of nanoscopic polymeric adsorber particles

For the separation of bioactive α -tocopherol from vegetable oils nanoscopic-sized polymeric particles with free binding sites on the particle surfaces were developed. In the patented NANOCYTES® process from the Fraunhofer IGB we mixed suitable monomers with so-called cross-linkers. By using the miniemulsion polymerization process we obtained nanoscopic-sized polymeric adsorber particles ranging from 200 to 300 nanometers in one step [1, 2]. Through the addition of suitable imprinting molecules and the subsequent extraction of these molecules, chemical negative imprints on the particle surfaces are created (Fig. 1).

The polymeric adsorber particles were then attached to polymeric packing materials and fixed into place. The coated packing materials were integrated into a technical process and a demonstration plant (Fig. 2) was developed at the Fraunhofer IGB.



The adsorption of tocopherol

In this project we were successful in producing polymeric adsorber particles for the separation of α -tocopherol from vegetable oils. To this purpose we optimized the polymer composition of the adsorber particles to achieve the maximum adsorption of α -tocopherol [3]. Up to 24 μg of tocopherol adsorb onto 1 mg of specific particle material.

Adsorption columns with particle-loaded packing materials

In order to enlarge the adsorption surface, the polymeric adsorber particles were then attached to polymeric packing materials as carrier structures and integrated into an adsorption column. For the optimal adsorption of tocopherol onto the polymeric particles, their concentration in the column should be in the area of up to 30 $\mu\text{g}/\text{ml}$. By contrast, untreated packing materials displayed only very limited adsorption capacities. By changing the solvent, the tocopherol can be completely separated from the adsorber column via extraction. The columns are then again available for further cycles.

Consequently, a demonstration plant is now available for research and development projects focusing on the separation of various minor components from vegetable oils, plant-extracts and biodiesel. After reconditioning the oilseeds, the plant can be utilized directly on site at the oil mill, in the plant-processing industry or by biofuel producers.

Outlook

By adapting the polymeric adsorber material, the demonstration plant developed here for the separation of valuable materials and contaminants from vegetable oils can be applied to other separation tasks for bio-based oils and plant-extracts. In order to increase the adsorption surface, packing materials with low packing densities and thus low free volumes can also be used in the future.



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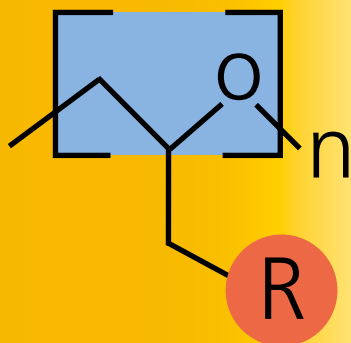
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Funding

We would like to thank the Fraunhofer-Gesellschaft for funding the project "Obtaining bioactive minor components from plants" within the scope of its program for small and medium-sized enterprises (MEF).

- 1 *Image of polymeric adsorber particles on packing materials taken by a scanning electron microscope.*
- 2 *Packing materials coated with adsorber particles.*
- 3 *Demonstration plant for the separation of minor components from vegetable oil.*



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2



MULTI-FUNCTIONAL PEGS – NEW MATERIALS FOR THE LIFE SCIENCES

Dr. rer. nat. Michaela Müller, Dr. rer. nat. Christian Schuh, Dipl.-Chem. Alexander Southan

PEG – a biocompatible all-round talent

Polyethylene glycol, PEG, is non-toxic, not immunogenic, hydrophilic and highly elastic. Due to these qualities the polymer is a much sought after ingredient in medical products, pharmaceuticals, the chemical and cosmetic industries as well as in tissue engineering. Its application normally requires that PEG be linked to a matrix or cross-linked. This process involves adjusting the cross-link density by means of the chain length of PEG since the functional groups are located at the end of the chain. Such end-group functionalized PEG is commercially available; however, the choice of chain lengths is extremely limited.

Multi-functional PEGs via side chain functionalization

To bypass these limitations, we at the Fraunhofer IGB, in cooperation with the Institute for Interfacial Engineering IGVT at the University of Stuttgart, have developed polymer-analogous and monomer-based synthesis strategies for novel multifunctional PEGs in which the chemically reactive functional groups are found in side chains of PEG (Fig. 1). The following are examples of possible reactive functions:

- thiol
- amine (primary, secondary)
- carboxyl
- photoactive groups

The amount of side groups and, accordingly, the distance between two functional side groups can be adjusted. It is also possible to produce copolymers with the respective functionalized PEGs.

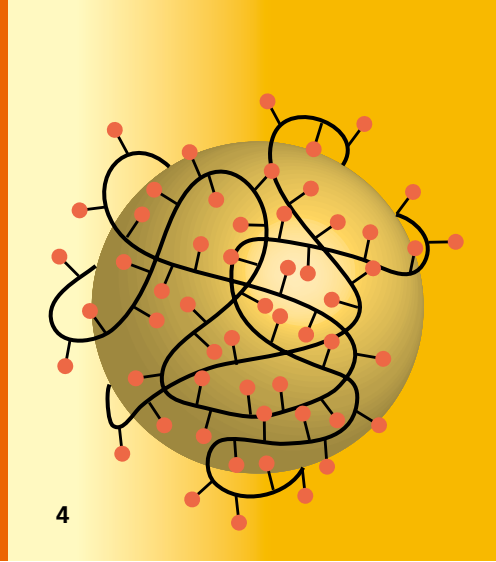
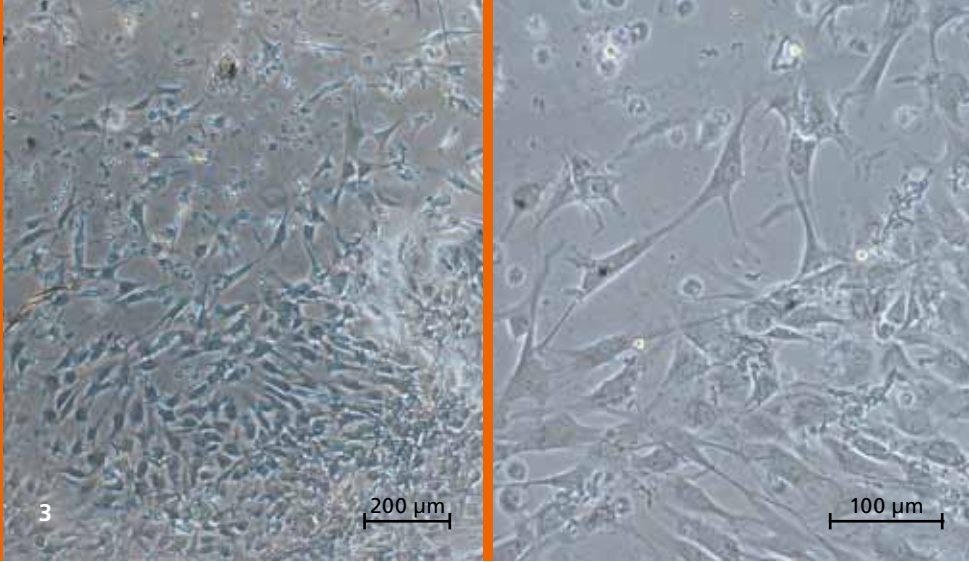
An example: thiol-PEG

In the past years the thiol-En-Michael-addition has established itself in the field of tissue engineering as a biocompatible reaction without by-products for the development of cross-linked hydrogel matrix materials. At the Fraunhofer IGB a novel PEG derivative was synthesized which carries this biocompatible thiol group on each repeating unit. This multifunctional thiol-PEG for which a patent application has been filed is now available for use in the life sciences [1]. Together with Michael acceptors such as PEG-700-bisacrylate hydrogels form within seconds (Fig. 2).

In contrast to conventional systems that are based on end-functionalized PEG systems, the qualities of these materials can be precisely adjusted, simply by altering reagent ratios. This is demonstrated with regard to swelling capacities, for instance, which we were able to precisely adapt within a wide range of 10 to 60 percent while constantly maintaining high gel yields (figure to the right).

Biofunctionality

Initial studies, in which modified PEG-based hydrogels were seeded with human fibroblasts, indicate good biocompatibility. Unlike non-functionalized PEG our new hydrogels also appear to be biofunctional. Images taken under the light micro-



scope reveal a high number of adherent cells on the hydrogel after a colonization time of 48 hours (Fig. 3).

Outlook

By means of controlled variations in the reaction process any number of thiol groups can be attached to PEG, providing a wide spectrum of multi-functional PEGs for the construction of hydrogels. Other areas of application, especially of thiol-PEG, are the PEGylation of gold surfaces (Fig. 4) or of acrylic group-carrying surfaces. A further possible use could consist of using multi-functional PEGs as a biocompatible matrix in drug-delivery systems with custom-made qualities.



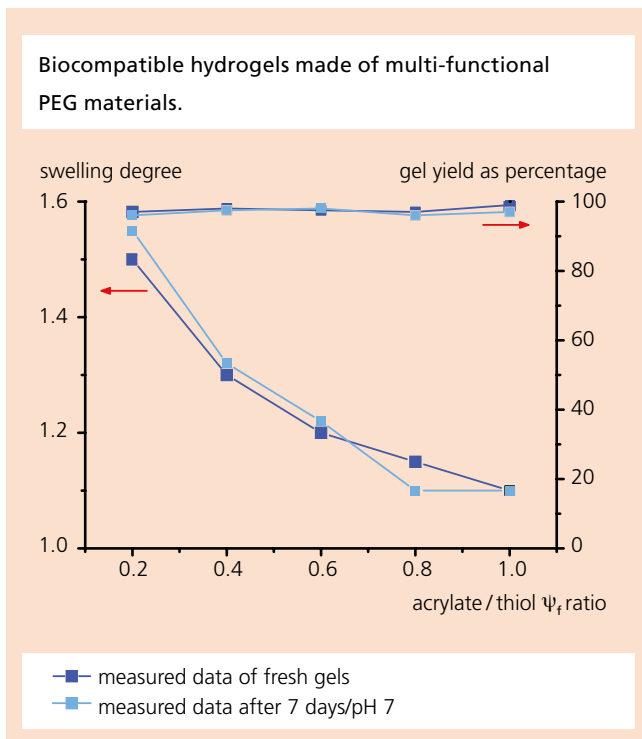
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Funding

We would like to thank the Peter and Traudl Engelhorn Foundation for funding this research with a post-doc scholarship and the Ministry of Science, Research and the Arts Baden-Württemberg for funding the project "SynElast – desmosin mimetics for the development of a synthetic elastin replacement", promotional reference 720.830-5-10a.

Project partner

Institute for Interfacial Engineering IGVT, University of Stuttgart

Further information

www.igvt.uni-stuttgart.de/forschung/projekte-cgvt/synelast.html

- 1 Chemical structure of multi-functional PEGs.
- 2 Biocompatible hydrogels made of multi-functional PEG materials, developed at Fraunhofer IGB.
- 3 Human fibroblasts on multi-functional PEG hydrogels.
- 4 Application example: PEGylation of gold particles to improve biocompatibility.

IONIC LIQUIDS IN GAS ABSORPTION

Dipl.-Ing. Jessica Blath, Dr. rer. nat. Thomas Schiestel

New materials with extraordinary properties

Ionic liquids are a new kind of materials and exhibit extraordinary properties which offer a high application potential in industry. Properties such as a negligible vapor pressure, a broad temperature range in the liquids phase, a low melting temperature and high chemical and thermal stability and also a high electrical conductivity are typical for ionic liquids. Manifold possibilities of combining anions and cations permit tailoring to specific applications. Therefore, ionic liquids are called "designer solvents".

In the literature [1] it was found that the absorption of gases varies in ionic liquids. Nitrogen and hydrogen were dissolved only slightly while carbon dioxide showed a high absorption. This difference can be used for the selective separation of individual gases from mixtures. A future application can be seen in the flue gas treatment of coal-fired power plants, where amine solutions can be replaced with ionic liquids.

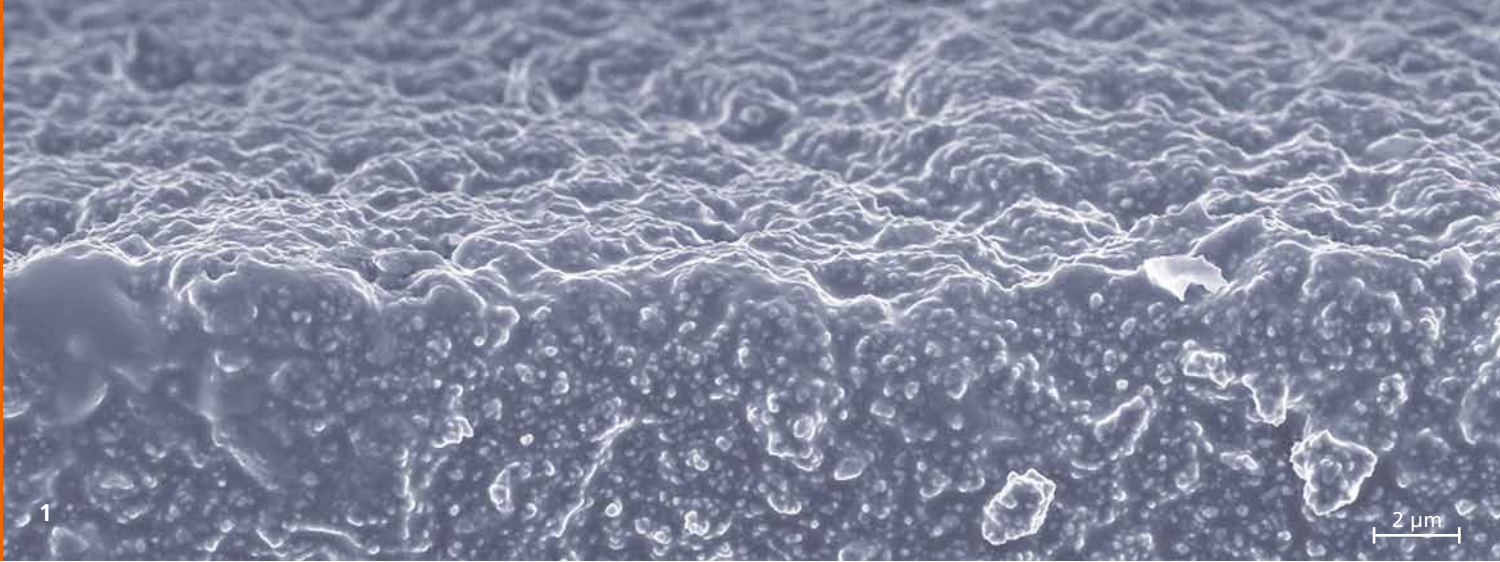
Procedure

To evaluate the properties of the ionic liquids, a wide range of anion and cation combinations was tested. Subsequently, the relationship between the chemical structure and the absorption capacity was investigated. A pressure drop method was used to examine the absorption of carbon dioxide, nitrogen, methane, and carbon monoxide in various ionic liquids.

High gas absorption for carbon dioxide

The highest gas absorption in all ionic liquids was found for carbon dioxide. Methane was absorbed less, while nitrogen and carbon monoxide were only dissolved marginally. For physical absorption a linear correlation was discovered between the Henry's law constant and the reciprocal molar mass. Here, a low Henry's law constant represents a high absorption ability per mol ionic liquid. The figure to the right shows the results for carbon dioxide at 60 °C by physisorption in ionic liquids.

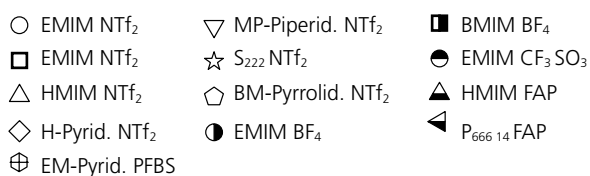
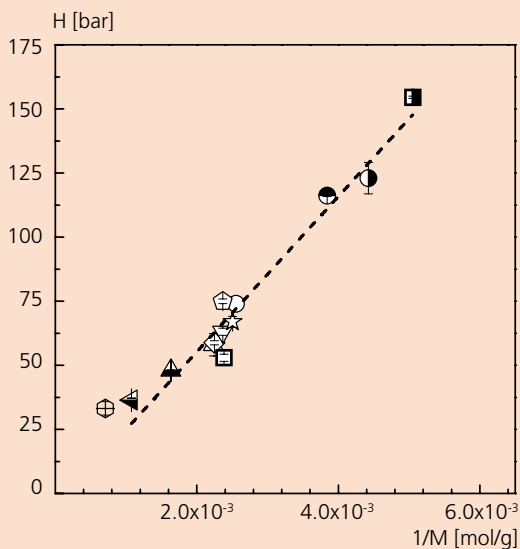
Chemical absorption of carbon dioxide was found in imidazolium-based ionic liquids with a basic anion. In such systems the absorption capacity was considerably higher [3]. The basicity of the anions strongly influences the absorption capacity. Low pK_B values tend to cause low Henry's law constants and accordingly high absorption capacities (up to 75 g CO₂ per kg ionic liquid). The investigated ionic liquids with chemisorption character are in a similar range of carbon dioxide loading compared to commonly used amine solutions for flue gas treatments and have the advantage of a negligible vapor pressure.



Outlook

The results show a high potential for ionic liquids in gas separation technologies by means of selective carbon dioxide absorption. In addition, ionic liquids can be immobilized in porous structures by capillary forces and can then be used as a liquid membrane. These supported ionic liquid membranes are stable in the long term due to the negligible vapor pressure.

A linear correlation between the Henry's law constant of CO₂ in ionic liquids and the reciprocal molar mass [2].



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We would like to thank the Fraunhofer-Gesellschaft for financial support of the project "IL-ECHEM" within the market-driven prospective research program (MAVO).

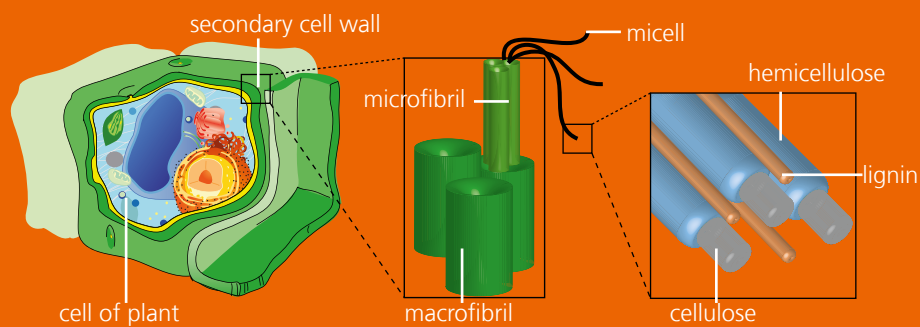
Project partners

Fraunhofer ICT, Pfinztal | Fraunhofer IFAM, Bremen

Further information

www.il-echem.fraunhofer.de

1 Scanning electron micrograph of porous aluminium oxide structures with ionic liquids as liquid membrane.



1



2

ROBUST CELLULASES AND XYLANASES FOR THE SACCHARIFICATION OF LIGNOCELLULOSE IN IONIC LIQUIDS

Björn Vater B. Sc., Dipl.-Ing. (FH) Nadine Staiger M. Sc., Dipl.-Biol. (t.o.) Dipl.-Ing. (FH) Susanne Zibek

Lignocellulose – nature's building block

Lignocellulose is one of the most important renewable resources in a biobased economy. It consists mainly of cellulose, hemicellulose and lignin. Through its design it protects plants against decay caused by microorganisms or enzymes. As a result, the sugars from lignocellulose are less accessible than those from starches from, for example, potatoes, corn or grain. Cellulose, the main component of lignocellulose, consists of β -1,4 glycosidically bonded glucose molecules. The second sugar polymer of Lignocellulose is hemicellulose which, unlike cellulose, is a heterogeneous, branched polymer. It is made up of various C6 and C5 sugars (e.g. xylose); its composition varies from plant to plant. Lignin itself is a highly cross-linked, phenol-containing polymer in which the phenylpropane units are composed at random [2, 3].

Digestion of lignocellulose

For the bioconversion of lignocellulose to high-quality products the substance must first be broken up, after which its sugar polymers must be broken down into their molecules (C6 and C5 sugars). These sugars can then be used for fermentation or for chemical conversion. The necessary first step is the so-called pretreatment. The methods used here aim to break down the lignocellulose composite and make the cellulose available for enzymatic hydrolysis. Various methods are described, such as steam-explosion or organosolv processes. Their advantage is the comparatively fast digestion rate. However, they also require large amounts of energy and often produce by-products such as furfural or hydroxymethylfurfural. These often impair fermentation which leads to lower yields.

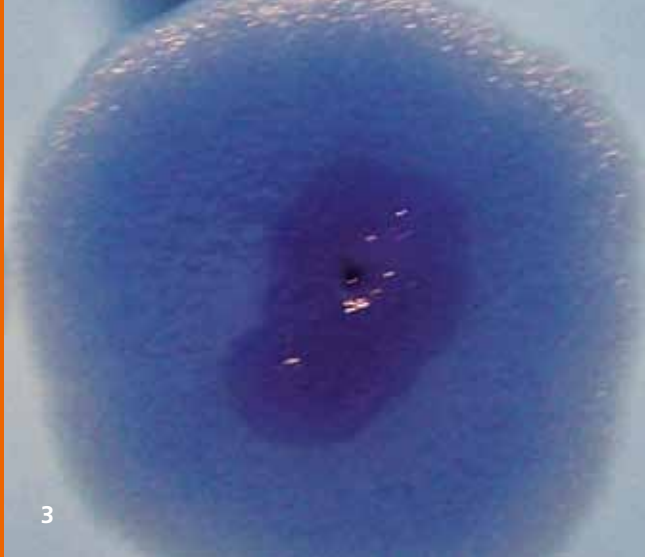
An alternative method for the digestion of lignocellulose without creating by-products could be the use of ionic liquids as solvents. These are able to dissolve Lignocellulose even at moderate temperatures [4].

Properties of ionic liquids

Ionic liquids are salts whose melting point lies below 100 °C. Due to the considerable size of the ions and little symmetry amongst the cations, the crystal lattice energy is reduced and the salts remain liquid below 100 °C [5]. Ionic liquids are also known as designer solvents since their properties can be varied by altering the anion/cation pairs [5, 6]. Thus, the melting point, viscosity, density and hydrophobicity can be adjusted by changing the structure of the ions [5]. Furthermore, they are not flammable, chemically and thermally stable and permit enzyme stability to the likes of those in apolar, organic solvents. They belong to the Green Solvents. Through selection of the correct ion pairs high product yields can be achieved whilst reducing waste volumes. Furthermore, ionic liquids can be recycled, which reduces the costs of the entire process [5, 6].

Robust cellulases and xylanases

The conversion of lignocellulose in ionic liquids can be accomplished in two different ways. Firstly, lignocellulose can be dissolved in the ionic liquid and subsequently precipitated with an antisolvent. The precipitate is then hydrolyzed ex situ with the help of enzymes. The in situ variation prescribes dissolving lignocellulose and simultaneously hydrolyzing it with enzymes. In both cases enzymes are needed that tolerate ionic liquids.



3



4

Due to the high salt concentrations, the denaturing of enzymes is, as a rule, reversible. For this reason, we examined the activity of 14 commercial enzymes (cellulases and xylanases) in five different ionic liquids with varying concentrations (0–100 percent). We discovered six xylanases and three cellulases which displayed a high tolerance of an ionic liquid with a concentration of 40 percent. The stability of the xylanases was higher than that of the cellulases.

New cellulolytic and xylanolytic enzymes from halophilic microorganisms

To find stable enzymes which show activity in even higher concentrated ionic liquids, we are looking for new cellulolytic and xylanolytic enzymes from halophilic microorganisms. These microorganisms live in extremely saline environments with salt concentrations of up to 30 percent. For screening purposes the halophilic bacteria were cultured in the laboratory (Fig. 2). We were able to detect xylanase activities in the ionic liquid [Emim][Ac] (1-ethyl-3-methyl-imidazolium acetate). Gene banks with the DNA of these active strains are currently being examined for enzymatic activity by using special agar plate assays in high-throughput screening (Fig. 3). We aim to recombinantly produce those enzymes displaying the desired properties and use these for biotechnical processes.

- 1 Schematic construction of lignocellulose in the secondary cell wall of plants.
- 2 Culture of a halophilic microorganism.
- 3 Agar plate assay for the detection of cellulolytic activities by means of halo formation.
- 4 Ionic liquids as solvents for lignocellulose.



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Funding

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Project partners

Fraunhofer IAP, Golm | Fraunhofer ISI, Karlsruhe | Fraunhofer UMSICHT, Oberhausen | Fraunhofer WKL, Braunschweig

THE BARRIER EFFECT AND ENHANCED EMPTYING BEHAVIOR OF PLASTIC CONTAINERS

Dr. rer. nat. Jakob Barz

The resource-efficiency factor

In numerous technical fields resource and energy efficiency is playing an increasingly important role. Optimization of resource usage and energy consumption has a great impact on production processes as, alongside cost-efficiency, environmental aspects need to be taken into account more and more. A prime example of this is the replacement of glass with plastics which is aimed at for two reasons. For one, plastic packaging is lighter and thus contributes to a reduction of fuel costs during transportation. Furthermore, it is not susceptible to breakage. One disadvantage, however, is the poor barrier effect of such packaging. The latter can be augmented in a resource-efficient process by coating the plastic surface by using plasma technology.

Enhanced properties through plasma coating

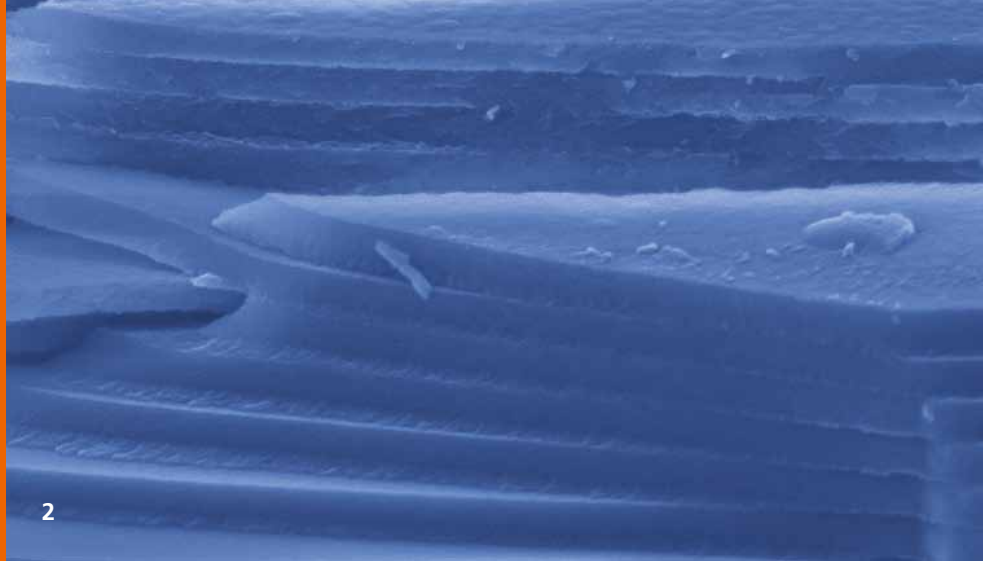
When attempting to improve the properties of plastic containers, coating and co-extrusion processes come into question. Considering coating processes, plasma technology is particularly promising and even environmentally friendly: with this technology it is possible to precisely attain a large variation of surface properties by varying the coating process parameters. This allows, for example, for a reduction of the permeation of substances and the adjustment of surface wetting. Plasma processes require only a minimal amount of coating substances since these are transformed into a coating in the plasma in a highly efficient manner. At the Fraunhofer IGB coatings distinctive for their excellent barrier effect against gasses and liquids and simultaneously displaying optimized drain behavior properties were developed for various materials and applications.

Plasma coating

In the plasma processes for the production of functional coatings (plasma polymerization) the necessary low molecular parent compounds are first partly fragmented by the energy input in the plasma. These fragments (radicals) subsequently react with the surface of the material to be treated and create a stably bound coating. In contrast to wet chemical processes plasma technology is advantageous because the coating steps can be carried out in direct succession – that is, without intermediate steps for drying or washing. Coatings which serve as barriers or conducive to better emptying behavior are, for example, fluorocarbon-based [1], methyl-based [2], high-density glass-like diffusion barriers [3] as well as adapted multilayer systems.

Effective barriers against water vapor and oxygen

At the Fraunhofer IGB barrier coatings were produced which raised the barrier effect of the plastic polyethylene terephthalate (PET) against water vapor and oxygen by a factor of more than 1000 compared to untreated materials. In comparison to commercially available coatings based on ethylene vinyl alcohol copolymer (EVOH), this coating retains oxygen five times and water vapor even 50 times better.



Enhanced drain behavior

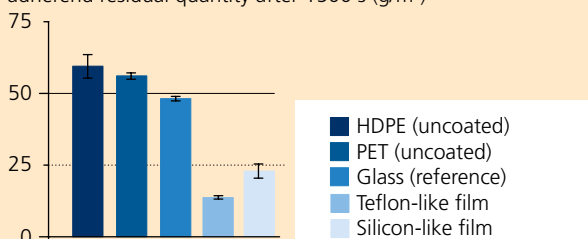
If an additional coating is applied in a subsequent step of the process, it is possible to adapt the surface to suit other needs relating, for example, to chemical and wetting properties. Oil and water-resistant fluorocarbon coatings, for example, create a Teflon-like surface. Test fluids drain remarkably better from such surfaces than from untreated ones. The improvement is noticeable not only for laboratory testing media such as water and oil but also for common industrial bulk goods like glues, varnishes, and paints. To give an example: it was possible to improve the emptying behavior of treated HDPE canisters for oil-containing bulk goods by 10 percent compared to untreated canisters. The multifunctional coatings have already successfully been applied to various flat materials as well as to moldings such as canisters and tanks.

Outlook

The coatings are suited to many applications, for example, containers for packaging and storage as well as for displays and inspection windows in damp rooms. Creating multifunctional layers or layer systems using plasma technology is particularly appealing since these can be designed to display a variety of chemical and physical material properties, and match the desired property profile while using only a single process.

Draining behavior of a test oil on untreated and plasma-coated polymer surfaces.

adherent residual quantity after 1500 s (g/m^2)



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Funding

We would like to thank the German Federal Ministry of Education and Research (BMBF) for funding the project "Innofunk", promotional reference O33R045A.

- 1 *In a special plasma reactor the reactive plasma gas is created directly inside the canister and thus coats its inner walls.*
- 2 *Multilayer film as a barrier against oxygen and steam.*

TARGETED MODIFICATION OF LIPIDS THROUGH INTEGRATED EMULSIFICATION AND ENZYME REACTIONS

Dr. rer. nat. Hans Weber

Production of synthesis components from renewable raw materials

In view of our finite fossil energy resources and increasing demands for fuel, the use of renewable raw materials is even now becoming more relevant. In order to enhance their application we at the Fraunhofer IGB, together with our project partners in the BMELV funded joint project "Integrated bio-production", are developing a novel chemo-biotechnological production process for the production of synthesis components from renewable raw materials based on the example of vegetable oils. We are focusing on native vegetable oils that, like mustard oil, are not in competition to foods, in order to produce bio-based lubricants and lubricant components, i.e. base oils and additives of the polyolester class (NPG-, TMP-, PE-Ester) or estolides.

Application of enzymes

The use of biocatalysis enables the chemo-, regio- and stereo-selective modification of oils, mono- or diglycerides and fatty acids under mild reaction conditions. At the Fraunhofer IGB lipases are used for the biotechnological conversion of triglycerides. Aside from the hydrolysis and transesterification reactions at the ester group, lipases also catalyse epoxylation reactions on double bonds. Some lipases show distinct fatty

acid selectivity and catalyze hydrolysis or transesterification reactions under kinetic control, depending on the chain length or other steric properties, such as the position and number of double bonds with varying reaction speeds. If such lipases are used in enzymatic transesterification reactions, long chain poly-unsaturated fatty acids (LCPUFAs) are enriched in a targeted way and thereby influence the product properties and melting points of triglycerides.

Analysis

For the characterization of the ingredients, testing of the technical suitability of the raw materials and examination of the resulting synthesis components, procedures for the determination of the iodine, peroxide and acid values, fatty acid analysis using gas chromatography (GC), and gas-liquid chromatography (LC and DC) for the separation of the tri-, di- and monoglycerides, as well as the free fatty acids, were established and validated. We took part in round robin tests organized by the Fraunhofer ICT in order to ensure external quality control.

Process-integrated emulsion production without emulsifiers

In order for a lipid to be enzymatically or chemically transposed, it must first be emulsified in a watery solution. We were able to establish two different procedures for the process-integrated production of O/W and W/O emulsions: One is a two-step procedure with mechanical pre-emulsification and fine emulsification using high-pressure homogenizers



or ultrasound procedures. The second is a one-step membrane technique with ceramic tube modules, which are superficially modified for the production of W/O emulsions. Our studies on the stability of emulsions and distribution of the droplets have shown that both procedures enabled stable emulsions, which are suitable for enzymatic and chemical transformations, to be created for several hours. This membrane variant is distinguished by smaller droplet sizes and a more narrow size distribution.

For process-integrated use the addition of emulsifiers is expendable in both processes. The emulsions produced in the course of the project up till now have been produced without the addition of emulsifiers.

Examination of lipases for fatty acid selectivity

Fatty acid selectivity is a valuable tool for the targeted enrichment and production of fatty acids, mono- and diglycerides. A method for the examination of lipases for fatty acid selectivity has been developed, in which the liquid chromatography separation of the products of hydrolysis (triglycerides, diglycerides, monoglycerides and free fatty acids) was coupled to quantitative gas chromatography fatty acid analysis. Lipases from our project partner EUCODIS were examined with mustard seed oil, which features a broader distribution of fatty acids up to C24. A discrimination of long-chain, polyunsaturated fatty acids was found, enabling the application of lipases for the enrichment of mono- and diglycerides with LCPUFAs. This makes replacement products made of cost-effective vegetable oils, which resemble cocoa butter in their melting behaviour, accessible.



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Project partners

Addinol Lube Oil GmbH, Leuna | DHW Deutsche Hydrierwerke GmbH Rodleben, Dessau-Roßlau | Dracosa AG, Bitterfeld-Wolfen | EUCODIS Bioscience GmbH, Wien | Fraunhofer Institute for Chemical Technology ICT, Pfinztal | InfraLeuna GmbH, Leuna | Martin-Luther-Universität, Halle-Wittenberg | Taminco Germany GmbH, Leuna | Umicore AG & Co. KG, Hanau-Wolfgang | Karlsruhe Institute for Technology (KIT) | University of Stuttgart, Institute for Interfacial Engineering IGVT

- 1 W/O emulsion of mustard seed oil; emulsion was mechanical.
- 2 O/W emulsion of mustard seed oil, membrane emulsion.
- 3 Separation of mono-, di-, and triglycerides, as well as fatty acids, using thin-layer chromatography.



ENVIRONMENT

Dipl.-Ing. Siegfried Egner

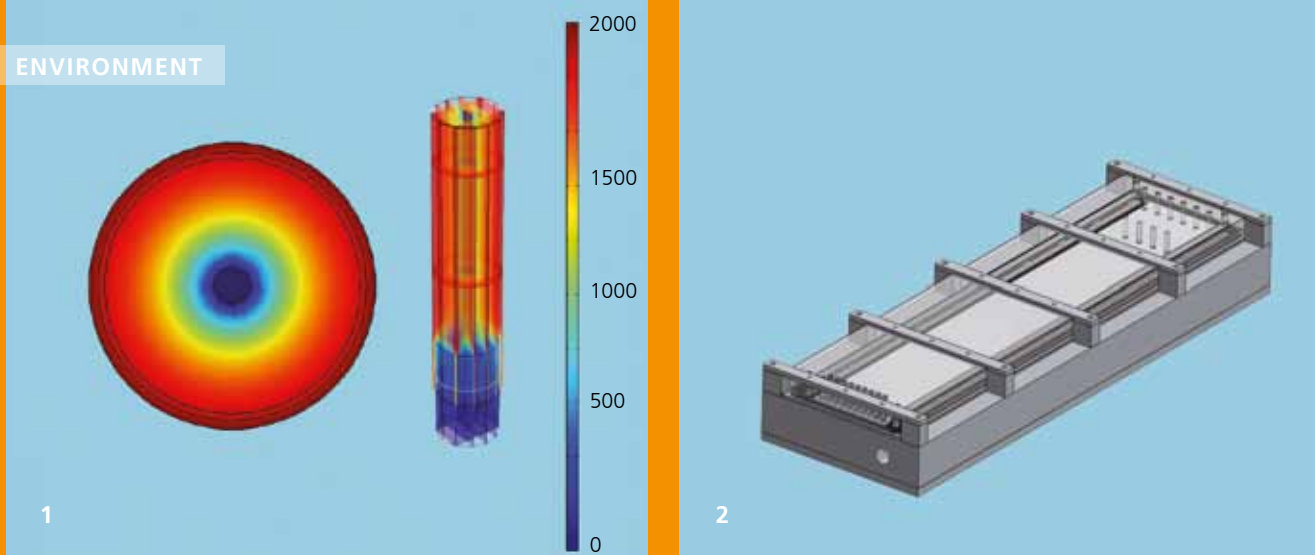
Against the background of worldwide discussions concerning the greenhouse effect and the shortage of resources, resource-efficient economic management and environmental protection are further gaining in importance. Resource-conserving industrial activities and protection of the environment are interdisciplinary tasks requiring extensive research and development. In this context, the environment business area at the Fraunhofer IGB stands for technological developments which contribute towards avoiding negative environmental impacts and ensuring technological progress – above all by interweaving ecological and economic sustainability. Typically, tasks and approaches in the environment business area are often directly linked with topics in the energy and chemistry business areas.

In the framework of a number of joint European and national projects with partners from research and industry, Fraunhofer IGB is developing processes and system components which help to save resources such as raw materials, water and energy, are climate-friendly, improve material recycling and in general contribute to improving the use of renewable resources. An example is the innovative DEUS 21 infrastructure concept for semi-decentralized energy and water management. This is being further developed to allow its use in urban redevelopment. Another example is research on how to avoid the emission of particulate or dissolved, persistent or endocrine micro-pollutants.

Approaches to minimizing the demand for finite resources include the substitution of chemical solvents with dry physical processes, for instance in the industrial cleaning of structural components, the service life extension of metal-working lubricants, the recovery of substances from agro-industrial process water as high-quality fertilizers or the generation of algae biomass for material and energetic utilization.

A common additional feature of our research projects is proof of the sustainability of the products and processes developed. This involves the systematic analysis of all environmental impacts of a product during its life cycle – from production via use to its disposal or recycling – from a holistic perspective which takes into account both economical and ecological aspects. We perform this analysis called life cycle assessment together with various specialized partners.

Comprehensive, complex projects in the Environment business area are carried out by interdisciplinary teams drawn from the natural sciences and engineering. Access to further technical competence and opportunities for collaboration on projects arises through the Fraunhofer IGB's participation in the Fraunhofer Cleaning Technology, Water Systems (SysWater) and Energy Alliances, as well as in the national technology platform SusChem Deutschland. Moreover, the Fraunhofer IGB has excellent international networks, particularly within Europe.



THE USE OF ELECTRIC FIELDS IN PROCESS ENGINEERING FOR THE EFFICIENT SEPARATION OF DISPERSIONS

Alexander Karos M. Sc.

In numerous process engineering steps such as downstream processing after biological process stages, material conversion processes in the production of resources as well as in environmental technology, a number of individual process steps have to be carried out in order to obtain products in the desired concentration, purity or activity. In order to increase the efficiency of the process chain, the various unit operations have to be intensified, optimized and equipped with further functionalities. For this purpose, processes are developed to make use of more than one specific substance parameter, for example the molecular weight and the charge.

Electric fields as a process engineering instrument for the separation of dispersions

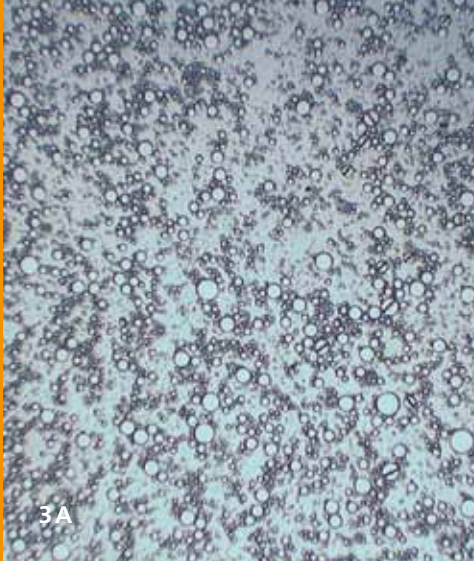
The Fraunhofer IGB is working on processes in which electric fields with different characteristics such as form, strength and density are used, thus opening up new design possibilities in process engineering. For example, the use of the electric fields creates an additional degree of freedom, that influences the kinetics, selectivity, process yield and hence the overall efficiency of the separation process. The processes of electrocoalescence, electrophoresis, electrofiltration and crystallization under the influence of electric fields are being investigated, further developed and made usable for new applications within the framework of national and international research projects.

Electrocoalescence – separation of water from emulsions

Within the scope of the EU project SalinityScan, a process and the corresponding reactor design among other things are being developed, enabling the efficient separation of water from water-in-oil emulsions, as occurs in oil production. The process is based on dielectrophoresis effects in inhomogeneous, alternating electric fields. Under the influence of an electric field a polarization of the dispersed particles as well as a formation and deformation of electric double layers on the molecular level take place. The dispersed particles align themselves along the electric flux lines in accordance with the induced dipole moment within the liquid. This results in coalescence into larger formations, which can then be separated mechanically. With a prototype plant developed at the Fraunhofer IGB it is possible to break down a 30-percent water-in-oil (crude oil) emulsion with a mean droplet diameter of 30 μm almost completely within two 2 hours. Gravity separation under the same boundary conditions takes 144 hours and achieves a maximum separation of 71 percent.

Free-flow electrophoresis – fractionation of metal ions and organic molecules

A further process that has a great potential for the selective separation of mixtures of substances is electrophoresis. Especially with mixtures in which the individual substances are chemically and physically very similar, good separation results can be achieved with electrophoresis. Within the scope of the Fraunhofer Beyond Tomorrow Project called "Molecular Sorting" the Fraunhofer IGB is working on the development of a free-flow electrophoresis process for the concentration and fractionation of mixtures of metal ions for industrial use.



The main separation feature is the relationship between the molecular size and molecular charge, by which the speed of migration in the electric field and thus the selective separation are defined. With the help of free-flow electrophoresis, solutions can be continuously separated and the various fractions delivered for further processing. Using the prototype plant at the Fraunhofer IGB, with a throughput of 1 L/h up to 19 fractions can be separated from a mixture of substances. A further field of application for this technology is the separation of mixtures of bio-based polymers in downstream processes.

Electrofiltration

Besides the processes in which electric fields are the main mechanisms, the Fraunhofer IGB is developing processes in which electric fields are used to improve existing methods and to increase the product yield. In electrofiltration, a filtration is overlaid by an electric field. The charged solid particles experience a force and can be selectively influenced in their movement. As a result, the building up of a surface layer on the filter is substantially reduced and the efficiency of the filtration increased. The Fraunhofer IGB is working on electrofiltration processes for process water treatment as well as the processing of substances in the field of biotechnology.



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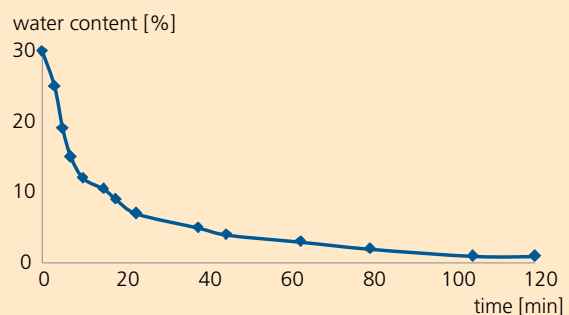
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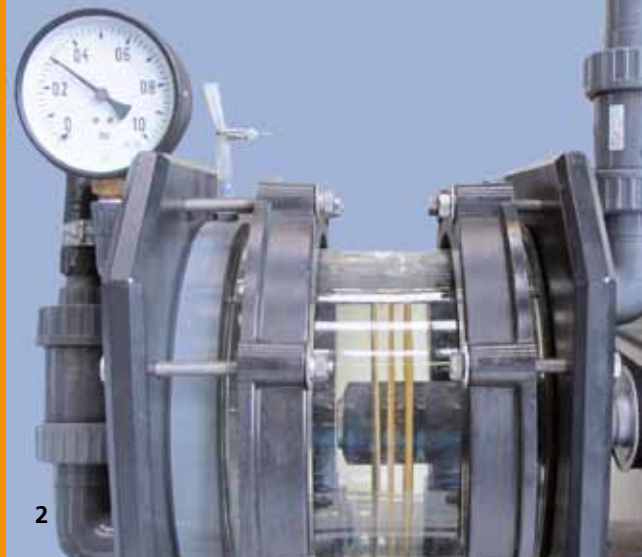
Funding

We would like to thank the European Union for funding the research project "SalinityScan" in the Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 262646, and the Fraunhofer-Gesellschaft for funding the project "Molecular Sorting" in the "Markets Beyond Tomorrow" research program.

- 1 Computer simulation of the electric field strength in a cylindrical coalescence reactor.
- 2 Free-flow electrophoresis – prototype plant at the Fraunhofer IGB.
- 3 Separation of a 30-percent water-in-oil emulsion: A after 1 min, B after 10 min and C after 80 min.

Time sequence of the separation of a 30-percent water-in-oil emulsion.





FURTHER DEVELOPMENT OF THE ROTATING DISK FILTER FOR ANAEROBIC WASTEWATER TREATMENT

Dr.-Ing. Marius Mohr

The challenge: Filtration of anaerobic sludges

Micro- and ultrafiltration for the separation of solids from liquids is state of the art in wastewater treatment and has great advantages because of the almost germ-free and solids-free effluent. The relatively high costs and the energy consumption are disadvantages of this technology. Both also depend on the achievable flux, the specific flow rate, which is limited by the fouling of the membrane. This applies in particular to the filtration of anaerobic sludges, which is why the large-scale implementation of membrane plants has in most cases remained restricted to aerobic systems. As a result of the further development of the rotating disk filter, a unit is to be created that will make the purification of urban and industrial wastewater cost-effective. This unit will use the anaerobic membrane bioreactor process (AnMBR process) developed and patented by the Fraunhofer IGB (EP 1968 900 Anaerobic Purification of Wastewater).

Rotating disk filter used at pilot-plant scale

The rotating disk filters available up till now were designed for use in the context of sewage sludge digestion and are already in operation for this purpose at several sewage treatment plants. As part of the research project DEUS 21 (funded by the Federal Ministry of Education and Research) a plant for the treatment of municipal wastewater using the AnMBR process without heating was operated in Knittlingen at technical scale. This demonstration plant showed that the anaerobic purification of wastewater works without any technical problems [1]. Depending on the temperature during continuous operation, net fluxes of 12 to 14 L/(m²·h) were achieved

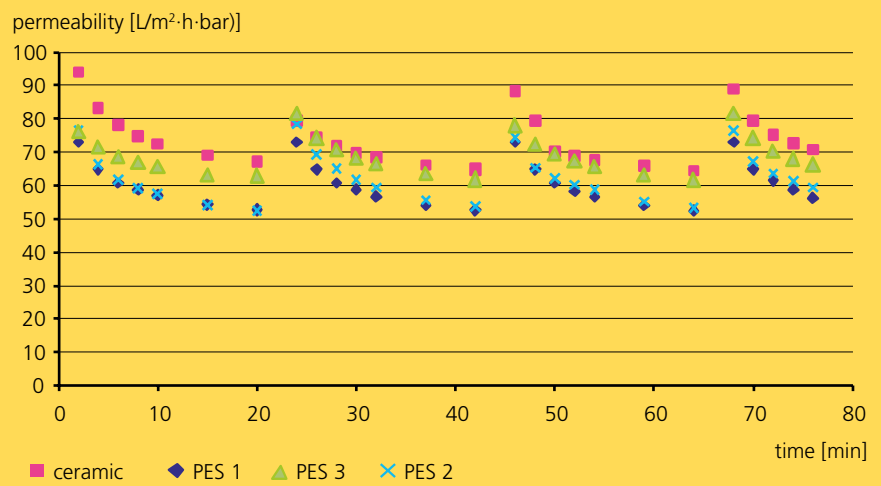
in the filtration without any process optimization. That this process is also suitable for the treatment of industrial organic wastewater (e.g. from breweries, dairies, in the production of fruit juice, etc.), was already demonstrated in pilot-plant experiments [2]. However, in order to be able to use the rotating disk filter economically for a wide range of applications, the operating costs and the investment costs have to be reduced.

Vertical shaft increases cost-effectiveness

Within the scope of a ZIM project funded by the Federal Ministry of Economics and Technology the firms Eisenmann AG and Pflüger Präzision GmbH, in cooperation with the Fraunhofer IGB, are developing a new type of rotating disk filter. Here, the shaft on which the disks are positioned is no longer arranged horizontally but vertically. This reduces the need for seals. Also as a result of this, the filter can be disassembled more easily on site, which makes maintenance much simpler. Due to the smaller number of seals and the circumstance that one motor drives several shafts, the specific energy consumption is reduced. The specific investment costs are also lowered, on the one hand because of the reduced number of seals, on the other because the size of the modules that are driven by each motor was increased.

Successful test operation

A first prototype with 18 m² filter area was operated for several months in the summer of 2011 at the Knittlingen plant under real operating conditions (Fig. 1). A higher flux was achieved than with the previously used filter. After the initial



teething troubles, the quality of the filtrate was always excellent, both as regards the visual impression and also the CSB concentrations, which were measured once or twice a week in the filtrate of the different filter modules.

Polymer instead of ceramic membranes

In order to reduce the investment costs even further, the replacement of ceramic membranes by less expensive polymer membranes made of polyether sulfone (PES) was investigated. In pilot-scale experiments we established whether, as a matter of principle, PES disks are suitable for use in the rotating disk filter, whether the manufacturing quality guarantees reliable filtration and which fluxes are to be expected using this material. For this purpose we used four different sets of disks on a filter successively at pilot-plant scale (Fig. 2) in order to filter the anaerobic sludge used at the Knittlingen plant. The reference chosen was the ceramic membrane also used in Knittlingen; additionally, three different PES membranes were tested. The permeabilities when using the various membranes are shown in Fig. 3. Here the PES membranes achieved only slightly lower values than the ceramic membranes. The quality of the filtrate in all the PES membranes was at least as good as with the ceramic membrane. Thus the general suitability of this polymer for use in the rotating disk filter was clearly demonstrated.

Outlook

In the next step a prototype with the PES disks is to be tested in continuous operation in the Knittlingen demonstration plant. Additionally, applications of the rotating disk filter for purifying special industrial wastewater will be investigated and implemented.



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Project partners

Eisenmann AG, Holzgerlingen | Pflüger Präzision GmbH, Enzweihingen

- 1 A shaft being removed from the prototype of the new rotating disk filter in Knittlingen. © Pflüger Präzision.
- 2 Pilot-plant filter with PES membranes.
- 3 Permeabilities of various membranes in pilot-plant experiments with anaerobic sludge.



1



2

PHOSPHORUS RECOVERY FROM WASTEWATER BY ELECTROCHEMICAL STRUVITE PRECIPITATION

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

Background

The expansion of a bio-based economy accompanied by a worldwide growing need for food is resulting in an increasing demand for fertilizers. However, the supply of fertilizers is restricted by limited phosphorus reserves and the high primary consumption of energy required for the production of synthetic nitrogen fertilizer. The only way out of this development in terms of sustainability is the recycling of the essential nutrients phosphorus (P) and nitrogen (N). Thus, these nutrients must be recovered from the production material cycles, the consumption of foodstuffs, the bioenergetic recovery or the processing of renewable resources (including the production of bioethanol). Solid residues and wastewater generated in different production processes are suitable for P recovery. One of the most advantageous approaches to recover P from wastewater is the crystallization of P, N and Magnesium (Mg) as struvite (magnesium-ammonium phosphate: $\text{MgNH}_4\text{PO}_4 \cdot 6 \text{H}_2\text{O}$) [1]. Struvite can be used directly in agriculture as a high-quality, slow releasing fertilizer [2] (Figs. 1, 2).

State-of-the-art technology

Since the limiting reactant in the struvite precipitation reaction is generally magnesium, this ion must be added for the precipitation. In established processes MgCl_2 , $\text{Mg}(\text{OH})_2$ or MgO are added in a liquid phase [1].

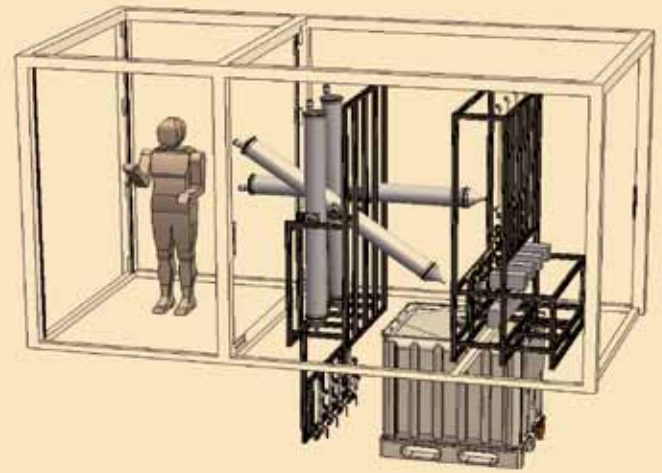
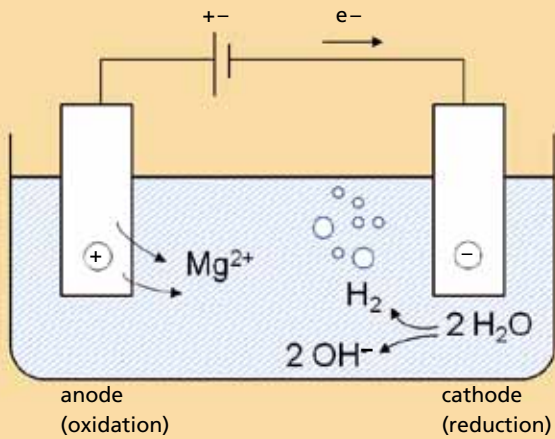
The disadvantages of this method are:

- Dilution of the water to be treated, since the chemicals are supplied as a solution or suspension (max. concentration 32 % MgCl_2)
- Incomplete struvite precipitation, as $\text{Mg}(\text{OH})_2$ and MgO have a very low solubility
- Overdosage of the Mg salts ($\text{Mg:P} = 1.2$ to $2:1$ [3]) and, in connection with this, unnecessary costs for chemicals

For optimum struvite precipitation the pH value has to be raised to a range between 8.5 and 9.5. In state-of-the-art technologies, a base such as sodium hydroxide (NaOH) is used for this purpose [1], which further increases the cost of the process.

New electrochemical process

In order to overcome the above-mentioned disadvantages, the aim of the project was to implement the recovery of phosphorus from wastewater as struvite using a novel electrochemical process. For this, batch and continuous experiments were carried out with an electrolytic cell, consisting of an inert cathode and a sacrificial magnesium anode (Fig. 3). Water-cleavage takes place as a result of the cathodic reduction. OH^- ions are formed, while hydrogen (H_2) is released. A process for the recovery of this gas is currently being developed. Oxidation takes place on the anode. Magnesium ions are released into the solution and react with the P and N in the water to form struvite. Here, magnesium is the limiting reactant. Both in the laboratory and in pilot-plant scale, experiments were carried out with various ion concentrations (20-500 mg/L $\text{PO}_4\text{-P}$ and 100-1500 mg/L $\text{NH}_4\text{-N}$). A pilot plant with a volume flow of 1 m^3/h wastewater is currently in the test phase (Fig. 4).



Results

Long-term trials in a laboratory plant showed very promising results concerning the recovery of struvite from wastewater. With the technology developed at the Fraunhofer IGB, it was possible to lower the phosphorus concentrations by 99.7 percent to under 2 mg/L. Thus, the P discharge concentration complied with the limits of the German Wastewater Regulations for plants up to 100,000 population equivalents (2 mg/L). As a result of the electrolytic water-splitting at the cathode, the pH value of the wastewater increased and remained constant at pH 9. This had the advantage that no base had to be added for the struvite precipitation process. Another advantage of the process was its low energy consumption, which in spite of the electrolytic magnesium release, was only 70 Wh/m³ of wastewater. This process was tested with municipal wastewater. However, it is also suitable for other sectors such as the food industry where the wastewaters are rich in ammonium and phosphate.

Outlook

This new development demonstrated that electrolytic struvite precipitation is possible. On the one hand, the discharge limits of the wastewater regulations regarding phosphate elimination were fully achieved. On the other hand, a simple, efficient and flexible technology is available for recycling a high-quality fertilizer. The demonstration plant will be tested after completion of the trials at various locations with different substrates. With these results, the plant will be made ready for series production by the industrial consortium.

- 1 *Precipitated struvite crystals, SEM micrographs.*
- 2 *Recovered struvite that can be used directly as a fertilizer.*
- 3 *The principle of the electrochemical struvite precipitation process.*
- 4 *Diagram of the pilot plant.*



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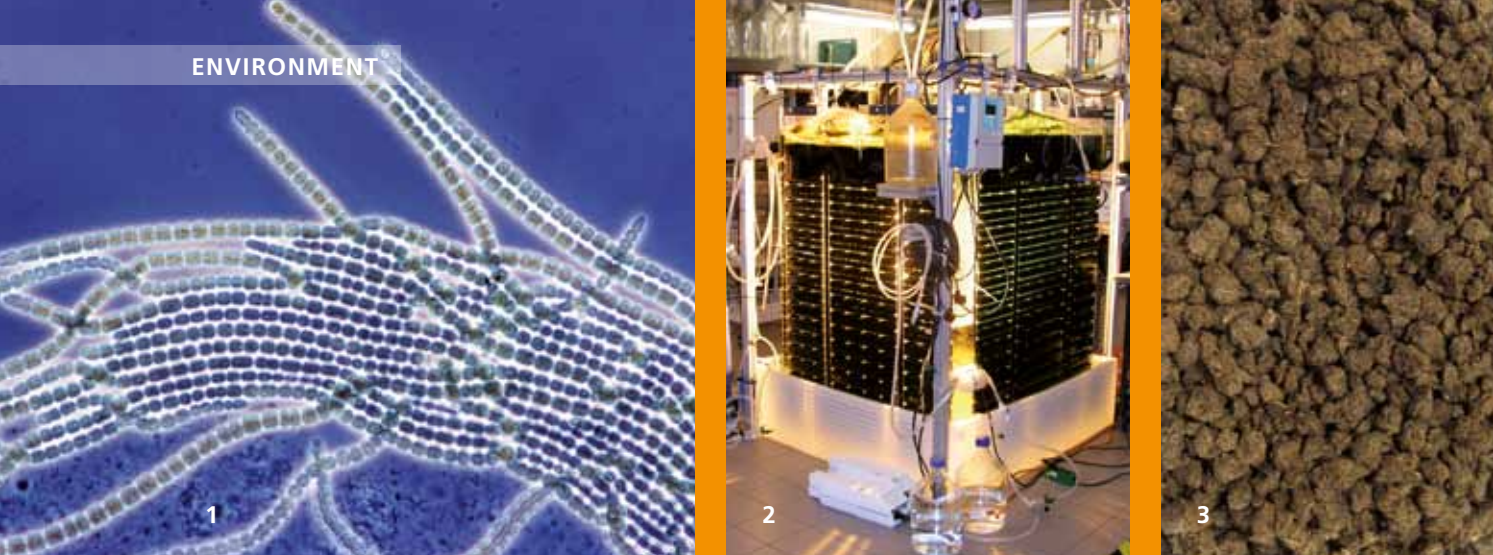
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Funding

We would like to thank the German Federal Ministry of Economics and Technology (BMWi) for funding the project "Development, construction, production and trials of a system for the effective treatment of process wastewater by means of an electrochemical precipitation process to produce a high-quality fertilizer (magnesium-ammonium phosphate MAP)", promotional reference KF 2143101 RH8.

Project partners

Bamo IER GmbH, Mannheim | EC-Tec GmbH & Co. KG, Kellmünz | E.R.S Steuerungstechnik GmbH & Co. KG, Osterburken | Geltz Umwelttechnologie GmbH, Niefern-Öschelbronn



FERTILIZER PELLETS FOR ORGANIC FARMING WITH INSECT REPELLENT ACTIVITY

Dr. rer. nat. Ulrike Schmid-Staiger, Dr.-Ing. Maria Soledad Stoll

EU project EcoBug

Organic farming means refraining from the use of chemically synthesized pesticides and fertilizers. As a result, organically-grown cabbage or rape seed are often plagued by the cabbage root fly, the common enemy of such plants, causing great damages in crop yield.

Digestates contain valuable plant nutrients such as nitrogen, phosphorus and potassium, which are essential for plant growth. In addition there is a number of cyanobacteria, especially filamentous cyanobacteria from the Oscillatoriales family which display proven repellent activity against the cabbage root fly. By preventing it from depositing its eggs, the fly can no longer threaten the plant. This gave rise to the idea and goal of the EcoBug project of developing a new, combined product for organic farming: digestates were to be processed to fertilizer pellets together with cyanobacteria which act as a repellent against the cabbage root fly.

Cultivating cyanobacteria

In flat-panel airlift (FPA) reactors developed by the Fraunhofer IGB even highly shear-sensitive microalgae can be cultivated photoautotrophically by simply using light, CO₂ and mineral nutrients. In this project, processes for the repeated fed-batch as well as the continuous culture in FPA reactors were developed for the various filamentous cyanobacteria with proven

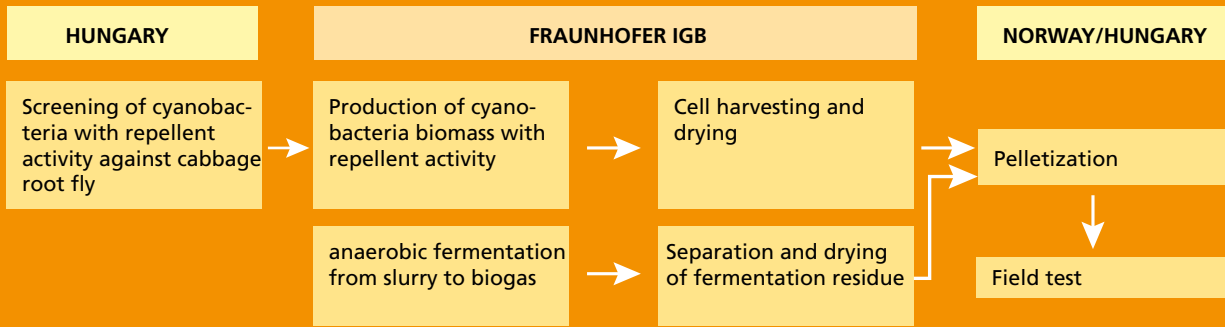
repellent activity against the cabbage root fly. For the first time filamentous shear sensitive cyanobacteria were cultivated in FPA reactors and both growth rates and the achievable biomass concentration were optimized. The most important cultivation parameter in this process is the ratio of light input by way of the reactor surface to the cell concentration in the reactor.

The digestion of cow manure and nutrient recovery

The fertilizer pellets were made with digestates from the digestion of cattle manure collected from selected organic farms. The anaerobic digestion of cattle manure to biogas was optimized in a two-step gas-lift reactor with a reactor volume of 2 x 100 liters. With only 14-day hydraulic retention time a biogas production of approx. 300 liters per kg of organic dry mass was achieved. The digestate was dried and the fertilizing qualities of the dried digestate were examined and confirmed in pot experiments with German ryegrass at the Fraunhofer IME. The advantage of ryegrass is that fructification pruning can be carried out three times within a short, three-month period. This way a high level of nutrient depletion by the plant can be attained.

Drying and pelletization

Through cultivating the cyanobacteria in the FPA reactors, we were able to produce a sufficient amount of biomass for two selected strains. These were then dried and combined with the dried manure digestate before pelletization. The cyanobacterial mass and digestate were dried with



4

superheated steam (superheated steam dryer, SHS), developed by the Fraunhofer IGB, to form stable cyanobacterial flakes and digestate under atmospheric pressure (working temperature 120–160 °C, retention time 20–30 min). The use of superheated steam for drying provides excellent possibilities to optimize the drying process regarding drying time, energy consumption and other parameters such as product quality.

Combined fertilizer-pesticide pellets in field trials

This way we were able to create combined fertilizer-pesticide pellets with two different cyanobacteria contents. The fertilizing effects and repellent activity of the pellets were subsequently tested in field trials on cabbage fields in Hungary and Spain. Our project partners in both countries reached highly satisfying results: kohlrabi and white cabbage plants which were fertilized with the combined pellets grew significantly better than non-fertilized plants. None of the plants fertilized with the combined pellets in the field trials were infested with the cabbage root fly.

Outlook

The positive outcome of the cabbage-growing field trials on repellent activity and fertilizing effects in Hungary and Spain has shown that now an excellent product, EcoBug-Pellets, for battling this pest is available for effective cabbage root fly control in organic farming. However, future endeavors will have to involve optimizing the various process steps in order to reduce production costs and offer the pellets at competitive prices. The fertilizer-pellet principle can also be applied to other digestates from the digestion of agricultural waste to make use of further organic residues as fertilizer pellets.



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Funding

We would like to thank the European Union for funding the research project "Development of an innovative industrial bioreacting and fermentation process producing an organic insect-repellent-fertilizer for ecological farming" in the Seventh Framework Programme under grant agreement n° 218467-2.

Project partners

Organic agricultural associations from Germany, Norway, Spain and Lithuania | SMEs from Norway, Great Britain and Germany | Research institutions: Nor-Tek, Oslo, Norway (coordinator) and the University of West Hungary, Mosonmagyaróvár, Hungary

- 1 *Anabaena spec. MACC 797, a cyanobacterium with repellent activity against the cabbage root fly.*
- 2 *Cultivating cyanobacteria in the 30-liter flat-panel airlift reactor.*
- 3 *EcoBug pellets made of digestate from cattle manure plus 0.1 % cyanobacteria.*
- 4 *EcoBug project diagram.*



ENERGY

Dr.-Ing. Ursula Schließmann

The fossil energy carriers coal, mineral oil, and natural gas are the residues of biomasses created during the pre-Carboniferous period by means of photosynthesis and laid down during the Carboniferous period. During this period, the earth's net energy content increased steadily. Today, as a result of the anthropogenic utilization of these fossils and the reduction of the overall photosynthesis capacity, this net energy content is steadily on the decrease. The result is rising atmospheric CO₂ – and consequently, climate change.

Making the transition to sustainable energy is thus a key challenge of the 21st century. The Fraunhofer IGB is tackling this challenge in many ways. We have contributed toward: expanding photosynthesis capacity by developing an algae photobioreactor; the exploitation of regenerative energy sources by means of highly innovative membrane technology (fuel cells, osmosis power plants); improved energy efficiency by producing biogas from organic waste (by-products of the food industry and primary agricultural products), and energy savings through process optimization in wastewater treatment technology and anaerobic wastewater treatment as well as in industrial processes such as drying with superheated steam at ambient pressure. Additionally, the Fraunhofer IGB is working on process technologies and systems for long-term, stable storage of thermal energy and for the purification of biogas for CNG (compressed natural gas) vehicles.

A further field of activity is devising integrated material flow and energy concepts at both local and regional level, replacing the current historically grown solutions with systematic approaches using state-of-the-art technologies. This is why the Fraunhofer IGB is a very active partner in the Fraunhofer Energy, Building Innovation and Water Systems (SysWasser) Alliances (see pages 20–21).



BRAZILIAN VEHICLE FLEET DRIVES ON BIO-METHANE FROM THE SEWAGE PLANT

Dr.-Ing. Werner Sternad, Barbara Waelkens M. Eng.

Great potential for the use of sludge gas for mobility in Brazil

The wastewater treatment situation in Brazil differs greatly from that of Germany. Although the majority of the population in industrialized areas such as the state of São Paulo (SP) is connected to the sewer system, a large amount of untreated sewage nevertheless flows into receiving waters. Due to Brazil's Growth Acceleration Programs, wastewater treatment technology will undergo further development in the future. At present, the sludge gas produced in Brazilian sewage plants is not, as a rule, systematically used, but rather burned in open flares.

According to the IANGV (International Association for Natural Gas Vehicles) Brazil owns one of the world's largest natural gas vehicle fleets along with a huge network of natural gas fuel stations. In 2009, its 1.6 million vehicles enabled the country to come in fourth behind Pakistan, Argentina, and Iran. With regards to its 1704 natural gas fuel stations, Brazil even took third place. As early as in 2003 flexible fuel vehicles were introduced into the Brazilian market and currently constitute 87 percent of all new registrations. These vehicles can be run on gasoline, methane, ethanol and also a mixture of these fuels. Converting the tanks of such vehicles also enables the use of natural gas as a fuel source. The Brazilian market already has a factory-converted Tetrafuel vehicle which runs on pure gasoline, Brazilian gasoline (with 20 percent ethanol), ethanol and compressed natural gas.

Exploiting sludge gases from Franca's sewage plant

As a part of international efforts geared towards climate protection, the BMU supports selected projects in partner countries, which contribute to the reduction of greenhouse gas emissions. Such is the case with the project of the Fraunhofer IGB with the Brazilian water provider and sewage disposal company SABESP. The project aim is to gather the sludge gases produced in the city of Franca's sewage plant, operated by SABESP, and purifying it until it reaches the quality of natural gas (bio-methane). This product, considered today to be one of most environmentally sound fuels in existence, shall in turn be made available to a fleet of vehicles. The benefits of this fuel are truly great due to its balanced carbon footprint – its combustion creates virtually no new greenhouse gases.

Approach

In order to reduce the bureaucratic hurdles involved in such an endeavor, the project was registered under the German-Brazilian Framework Agreement on Technical Cooperation. Project implementation can be subdivided into categories such as process selection, determination of required design data, determination of exact location, basic and detail engineering, machine assembly and operation, vehicle conversion and staff training.



Results

The sewage plant in the city of Franca is run by using the activated sludge process and operates with two sludge digestors (Fig. 1). These produce an average of 2700 m³/d of sludge gas which is burned in two open flares (Fig. 2). Based on our analysis, methane levels rise somewhat higher than 60 percent. With a methane content of 60 percent and a calorific value of 10 kWh/m³, approximately 1600 L/d of gasoline can be replaced. SABESP plans on having 49 vehicles converted to have them run on bio-methane. It is expected that the city of Franca will add some of their own to that total. Since the ferrous sludge from the waterworks is also processed in the digestion process, the concentration of H₂S is very low. This simplifies the purification of the sludge gases. Conceived and designed by our own team, the concept for purifying the sludge gases and exploiting the resulting bio-methane is currently being installed at the existing sewage plant. The latter is in turn being expanded to include a double-membrane gas tank, a pressure swing adsorption in a container used for gas purification and generation of bio-methane as well as a bio-methane gas station with high-pressure tanks for fuelling converted vehicles. By summer 2012 the plant will begin operations and be run by the sewage plant staff. The general appearance of the plant can be seen in the diagram in Fig. 3.

Outlook

Both the reduction of methane emissions from the sewage plant as well as the replacement of fossil fuels with bio-methane will serve to reduce greenhouse gas emissions. Should the project prove a success, SABESP plans to equip more plants with similar technologies. We furthermore expect this project to convince other operators of sewage plants and disposal sites and communities in Brazil to choose the path of sustainability and use bio-methane as a fuel source.



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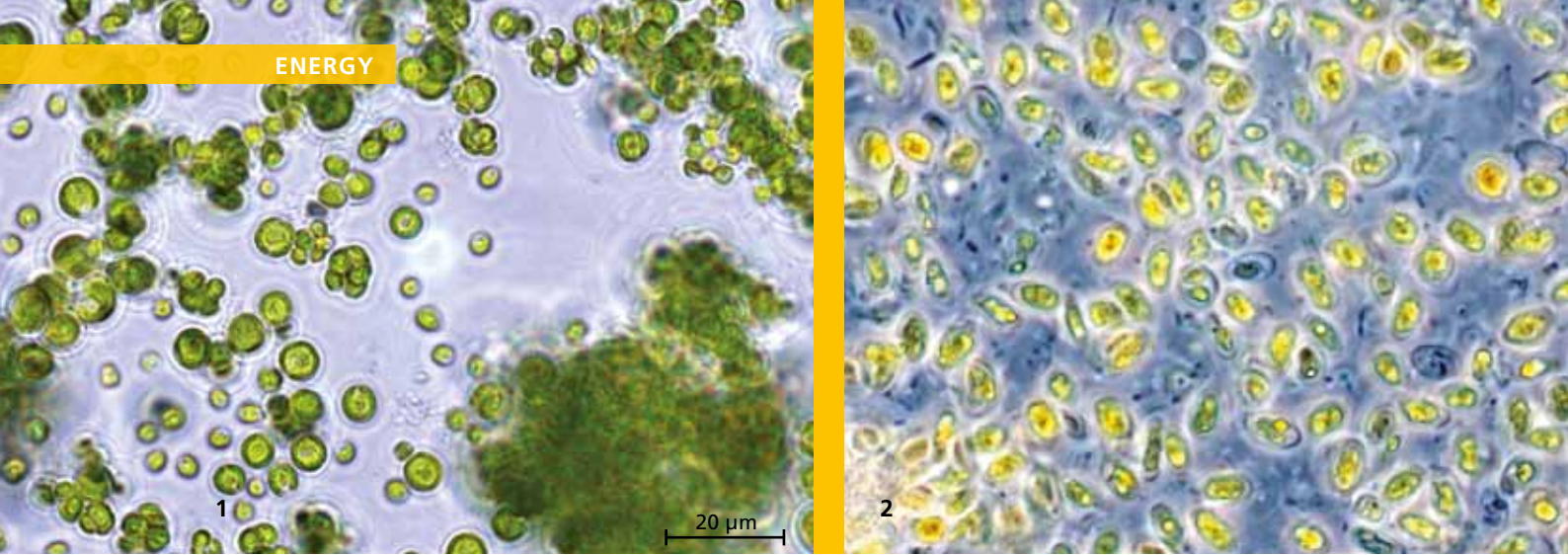
Funding

We would like to thank the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) for funding the project "Use of sludge gas of a municipal wastewater treatment plant for transportation purposes in Americana, SP, Brazil", promotional reference IKI 09_I_029.

Project partner

Companhia de Saneamento Básico do Estado de São Paulo – SABESP, São Paulo and Franca

- 1 *Digestors at the Franca sewage plant.*
- 2 *Open flares at the Franca sewage plant.*
- 3 *Diagram of the device on the Franca sewage plant.*



OPTIMIZED DIGESTION OF ALGAE BIOMASS BY MODELING AND SIMULATION

Dr. rer. nat. Yasemin Sterr

Initial situation

A worldwide increase in demand for electrical energy by approximately 70 percent is expected in the next two decades. Additional power plant resources are necessary to meet this growing demand for electricity. Moreover, the challenges of worldwide climate protection can only be realized with a sustainable energy supply. In order to achieve these aims, the increased and efficient use of biomass for the production of electricity and heat is essential. Coupling a thermal gasifier or a biogas reactor to a micro gas turbine provides a feasible solution. Depending on the process, algae, wood, sludges, peat, waste, grape marc and other organic residues can be used as input materials.

Objectives

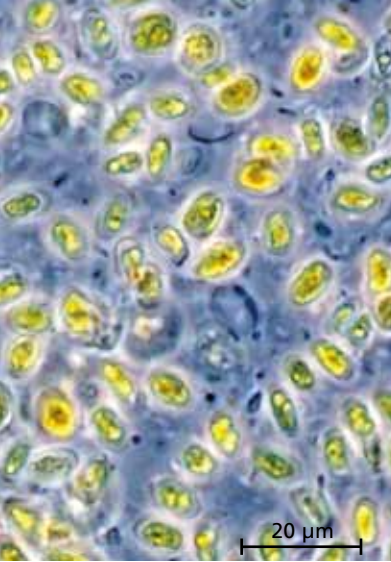
Mathematical models for the design of decentralized biomass power plant concepts are being developed as part of the research project DeDeBio. To generate biogas, both a thermal wood gasification process (DLR) and also a biological process, with algae as the source material, are to be examined. Besides the development of tools for CFD-based (computational fluid dynamics) combustor design, the focus is on the modeling of the biogas reactor and the wood gasifier. These numerical models are then to be used for the simulation of the product gas composition and, in combination with micro gas turbine models, for the design and assessment of various plant and operating concepts.

Anaerobic digestion of algae biomass

In a biogas reactor the substrates used are converted in several reaction steps into biogas, consisting mainly of the components CH_4 and CO_2 . The gas yields and gas compositions obtained in this way depend on various factors such as the process control, the preparation of the substrate and the composition of the substrate. The biogas yield of plants is generally limited by the greater or lesser proportion of lignocellulose, which is difficult to recycle. However, the use of microalgae with a low lignocellulose content, for example *Chlorella vulgaris* (Fig. 1), *Phaeodactylum tricornutum* (Fig. 2) and *Spirulina platensis* (Fig. 3), permits an almost complete utilization of the organic substance. Thus in the real process, after the previous extraction of recyclable substances from the algae, the residual materials can be converted into biogas in a continuous two-phase gas-lift reactor under mesophilic conditions (see diagram). The types of algae used were digested with varying degrees of success. Both the composition of the biogas and the yield varied depending on the cell contents, the cell wall components and the stability of the cell wall. In particular the protein content of the cell plays a decisive role. Depending on the type of algae, the biogas yield was between 280 and 400 L/kg total volatile solids (TVS).

Modeling of the bioreactor

The Fraunhofer IGB has developed a black box model for the biogas reactor using Buswell and Boyle's stoichiometric calculations. This model expresses the composition of the biogas depending on the input material on the basis of stoichiometric compositions. If, using a correction factor, one allows for the incomplete stoichiometric conversion of the charged biomass



into biogas in the real process (part of the charged biomass enters into the growth of the bacteria) as well as the limited availability of the organic substances (possibly non-digested cell components), both the product gas yield and the product gas composition can be calculated at the reactor outlet with the help of the model. In this way alterations in the process parameters or of the plant configuration can be simulated and the iteration steps in designing the plants for generating product gas can be reduced in the future.

Outlook

The mathematical models generated in this way for the simulation of the biogas plants operated with algae residues can be used for the further development and optimization of biological reactors. The model generated can thus assist with the calculation of the target-oriented optimization and also the scaling-up of the plants. The results obtained within the scope of the project and the models developed will for the first time permit a comprehensive modeling of these plant concepts and of the plant components – and will help decentralized, gas-turbine-based biomass power plants to attain market maturity more quickly.



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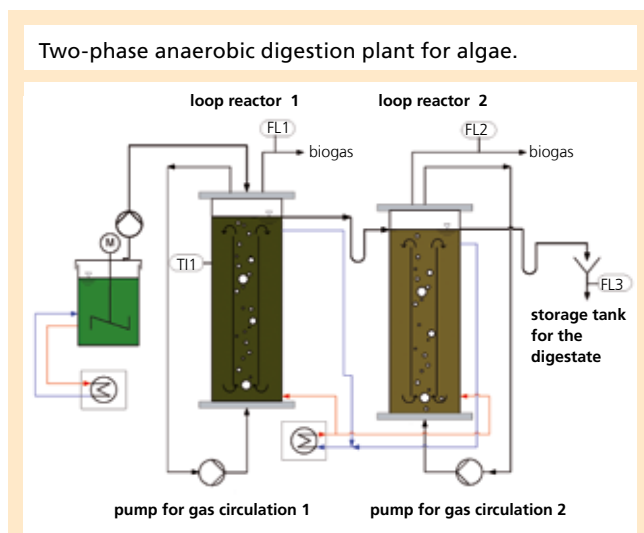
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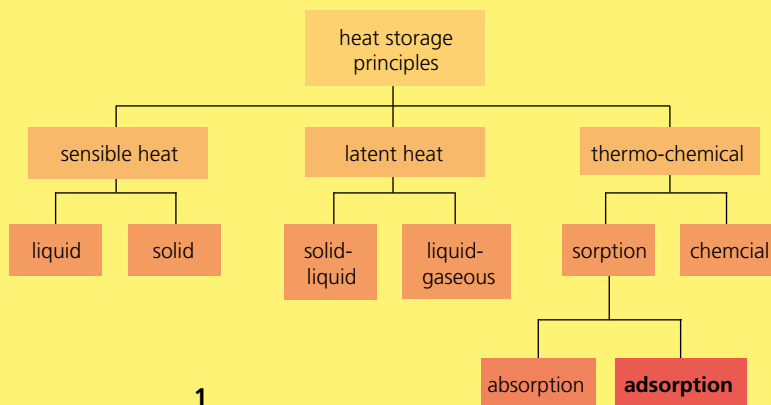
We would like to thank the Foundation "Energieforschung Baden-Württemberg" (Energy Research Baden-Württemberg) for funding the project "Development and validation of design tools for design of decentralized biomass power plant concepts for combined heat and power generation – DeDeBio".

Project partner

Deutsches Zentrum für Luft- und Raumfahrt (DLR), Stuttgart



- 1 *Microalgae Chlorella vulgaris*, magnified 1000 times.
- 2 *Microalgae Phaeodactylum tricornutum*, magnified 1000 times.
- 3 *Microalgae Spirulina platensis*, magnified 1000 times.



HEATSAVER – SORPTIVE THERMAL ENERGY STORAGE FOR INDUSTRIAL PROCESSES

Dipl.-Ing. Mike Blicker

An important contribution to the achievement of the climate protection targets and the desired changes in energy policies is an improved utilization for both fossil and renewable primary energy sources. This is done by secondary usage of energy which was not used during its first application. A case in point is the utilization of waste heat created by combustion engines during the generation of power from (bio)gas: the waste heat produced typically makes up over 50 percent of the energy content of the fuel used. In addition, there are many more commercial, industrial, and electricity generating processes which release large amounts of waste heat. However, this cannot necessarily be utilized simultaneously or directly in another application. Considering the fact that approximately 50 percent of the final EU energy requirements¹ are needed for heat production, it becomes apparent that there is great potential for optimizing energy use.

For the efficient use of heat and waste heat there is a need for compact and flexible storage systems to temporally and, if necessary, spatially decouple or compensate the supply and demand for heat. Currently available industrially manufactured thermal storage systems regularly only store sensible heat. They usually use water as a storage medium, thus restraining the storage density and limiting the storage temperature level to 100 °C at the most. Latent heat storage units which may achieve slightly better storage density values regularly lack the required flexibility due to their defined operating temperature. The disadvantage of both systems is their permanent heat loss to the environment which over time leads to self-discharging, despite insulation.

Sorptive thermal energy storage – an alternative with great potential

Sorptive heat storage systems which are counted as thermo-chemical storage systems (Fig. 1), are relatively new, promising technology approaches with considerable benefits compared to both sensible and latent heat storage systems. Storage densities can be many times higher, which allows for more compact storage. The energy stored here is bound physico-chemically and not by sensible means. Thermal loss is eliminated since during storage no temperature gradient between the medium and the environment exists. Further important advantages arise through more flexible working temperatures and loss-free storage over a lengthy time period. In connection with the EU-funded project HeatSaver, the Fraunhofer IGB, together with European partners in industry and research, has declared it a goal to exploit the potential of this technology and implement it.

From laboratory to pilot scale systems

The basis for developmental work has been established in laboratory experiments together with our project partner ZeoSys. Firstly, various adsorbent agents were examined in an experimental reactor with a capacity of 1.5 liters. In particular, various zeolites were characterized according to their properties and particle sizes. A pilot plant was then developed and constructed in which various heat exchanger configurations and process conditions can be examined on a 15-liter scale (Fig. 2). Due to the fact that good heat and mass transport in the storage reactor highly influences the storage efficiency, intensive tests

¹ EUREC (Europe and Renewable Energy Research Centres) Agency, 2009



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	Specific heat storage capacity	Specific heat storage capacity	Specific discharge power
	Wh/kg	kWh/m ³	W/kg
Material (TG DSC)	300–380	–	–
Laboratory 1.5-liter reactor	160–220	109–150	100–240 fluctuating
Laboratory 15-liter reactor	180–240	122 – 163	45–67
Container 750-liter-reactor*	(150–220)	(102–150)	(19–50)

(Material zeolite NaX / particles 2.5–3.5 mm or powder in the case of TG DSC)
 *The results for the 750-liter reactor are estimations based on initial experiments.

were carried out at this stage. The results served as a basis for a further scale-up of the technology to a storage volume of 750 liters. This plant was integrated into a transportable 10-foot container housing all the necessary additional components. As a result, the technology can be tested under realistic conditions at various locations (Fig. 3).

Results

In the course of the project it was possible to successfully develop a novel heat storage technology based on a closed, adsorptive heat storage process and translate it to different scales (1.5 to 750 liters). A heat exchanger design for adsorbent bulk which can easily be scaled-up was created to improve heat input and output. The specific energy storage densities that were attained range from 150 to 240 Wh/kg of storage material (Fig. 4). This corresponds to an increase by a factor of 2 to 3.5 in comparison to water-based sensible heat storages with a working temperature range of 60 Kelvin.

Outlook

A transportable test storage unit is now available which should be improved further and tested at various industrial locations. In subsequent projects this technology will be further developed and demonstrated. The goal is to offer industrially relevant solutions. With these solutions e.g. biogas-based power plants can be operated as fully-fledged combined heat and power plants by efficiently using the waste heat.



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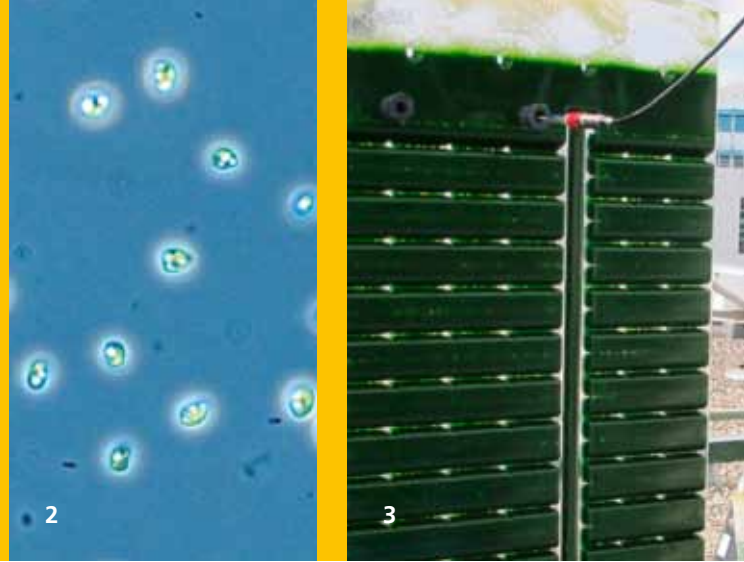
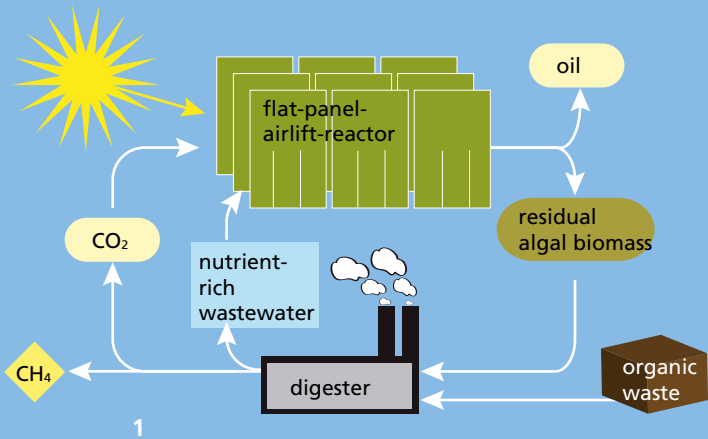
Funding

We would like to thank the European Union for funding the research project "HeatSaver – Thermo-chemical heat storage system to save energy costs across a wide area of industrial applications" in the Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 222116 / FP7-SME-2007-1.

Project partners

ZEOSYS GmbH, Berlin | B&O Gebäudetechnik GmbH, Berlin | Giordano Industries, Aubagne, France | Dvigatel Regital, Tallinn, Estonia | BTB GmbH, Berlin | UK ISRI, Melton Mowbray, England

- 1 Possibilities for thermal energy storage.
- 2 Zeolite packed bed in an experimental reactor.
- 3 Pilot storage unit with a volume of 750 liters in a transportable container.
- 4 Comparison of results with varying reactor sizes.



LIPID-RICH ALGAE BIOMASS AS A REGENERATIVE ENERGY SOURCE – OUTDOOR PRODUCTION

Dipl.-Ing. Ronja Münkkel, Dr. rer. nat. Ulrike Schmid-Staiger

Currently, biofuels are mainly produced from plant-based raw materials, for example biodiesel from rapeseed or palm oil. In Germany the arable land will no longer be available for food production; in Southeast Asia rainforests are being cleared for oil palm plantations. The high water consumption during the cultivation of land plants for the production of biofuels is also viewed critically. Moreover, the current production capacity and area available for this purpose cannot meet the demand for renewable resources for biofuels.

Biodiesel from microalgae represents an alternative to present-day biofuels. Compared with cultivating higher plants, the cultivation of microalgae has a considerable number of advantages. These include a higher productivity, reduced water consumption and the possibility of cultivating algae on land that is not suitable for agricultural purposes. At present we are examining a concept for the sustainable energetic use of microalgae within the framework of the research project EtaMax. Integrated in a cycle of materials and energy streams, algae biomass is produced from flue gas and wastewater streams (Fig. 1). Microalgae are cultivated autotrophically, solely by using sunlight. Oil produced from algae can be used as energy source and the resulting exhaust gas is returned to the process. The remaining biomass is fermented to produce biogas. This process permits high-quality biomass to be created from waste streams and the complete energy recovery of the biomass.

Requirements for the biomass and production process

The prerequisite for the economical use and an efficient downstream process of the algae biomass is a high lipid content. Furthermore, the spectrum of fatty acids should have a high proportion of saturated and monounsaturated fatty acids, as polyunsaturated fatty acids reduce the storage stability of the algae oil. The enrichment of fatty acids in the form of triglycerides can be induced by a nitrogen limitation of the microalgae culture. The triglycerides are deposited inside the cells as storage molecules (Fig. 2). In laboratory experiments at the Fraunhofer IGB we were able to achieve lipid contents of up to 70 percent [w/w] under permanent artificial light.

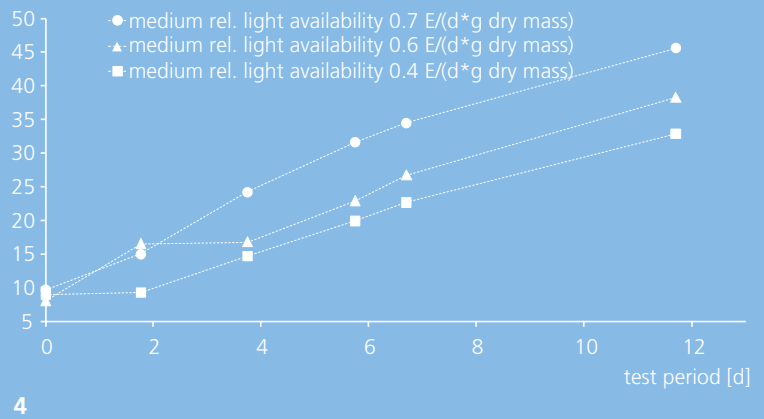
When producing algae as energy source, it is necessary to transfer this process into an outdoor cultivation process. Here the challenge is to establish a process that runs well and remains stable under varying outdoor conditions, and also generates biomass with a high lipid content. It has to be taken into account that the recurrent day-night rhythm and changing weather conditions result in a variable process temperature and different light intensities.

Outdoor plant for lipid production

In 2010 and 2011 we operated an outdoor pilot plant with five south-facing 30-liter flat-panel airlift reactors to characterize the lipid production process with the microalgae *Chlorella vulgaris* (Fig. 3). A two-stage batch process was established. Biomass was produced in a first growth phase from four to seven days with an optimum supply of nutrients. This was followed by the lipid production phase, in which the algae cells enriched lipids by means of nitrogen and phosphate



lipid content in % [w/w]



limitation. The focus of the investigation was to maximize the lipid content of the algae and to determine a quantitative correlation between the relative light intensity and the biomass concentration in the reactor. The relative light intensity describes the ratio of light input to biomass concentration in the reactor and is specified as Einstein (1 mole of photons) per gram of dry mass and day.

Factors influencing the lipid content

We succeeded in establishing a stable process under outdoor conditions, permitting the production of algae biomass with a very high lipid content. Thus with *Chlorella vulgaris* we were able to achieve a maximum lipid productivity of 0.3 g fatty acids/(L*d) in the outdoor pilot plant. It became clear that the flat-panel airlift reactor used here, which was developed several years ago at the Fraunhofer IGB, is ideal for this process. From the literature it is known, for example, that the cultivation of microalgae in photobioreactors developed and operated in Italy leads to a maximum lipid productivity of only 0.2 g fatty acids/(L*d) [1].

We determined the influence of the relative light intensity on the lipid content of the biomass by the parallel operation of flat-panel airlift reactors, each with different biomass concentrations. We were able to show that high lipid contents of over 45 percent [w/w] are achieved with a low dry mass concentration and related high relative light intensities (Fig. 4).

Outlook

Making use of the results generated under outdoor conditions, the high lipid content of the biomass can be selectively adjusted by means of process management. A defined, consistent quality of the biomass with high lipid content provides the ideal basis for the development of a downstream process to obtain biodiesel from algae. Working on the basis of these experiments the aim is to make the production process viable at the industrial scale and to further reduce the production costs.



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Literature

[1] Rodolfi, L. et al. (2009) *Biotechnology and Bioengineering* 102(1): 100-12

Funding

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Project partners

Daimler AG | EnBW Baden-Württemberg AG | FairEnergie GmbH | Fraunhofer IVV | Karlsruher Institut für Technologie (KIT) | Netzsch Mohnopumpen GmbH | Paul Scherrer Institut PSI | Stadt Stuttgart | Stulz Wasser- und Prozesstechnik GmbH

- 1 Cycle diagram of the outdoor cultivation of microalgae.
- 2 *Chlorella vulgaris* with deposited storage lipids.
- 3 Outdoor plant with five 30-liter flat-panel airlift reactors.
- 4 Lipid content of a nitrogen-limited outdoor culture of *Chlorella vulgaris* with different light availabilities.



APPENDIX

Patents granted 2011

In the year 2011 ten patents were granted.
These patents are assigned to our business areas as follows:

MEDICINE

Automated separation of tissue layers
DE 10 2009 022 349,
granted February 3, 2011

Automated separation of fatty tissue
DE 10 2009 022 346,
granted May 19, 2011

Isolated nature-identical Collagen
US 8,013,121,
granted September 6, 2011

Three-dimensional biocompatible skeleton structure containing nanoparticles
DE 10 2007 020 302,
granted November 10, 2011

Pipette head with filter and flushing means
DE 10 2009 022 350,
granted November 3, 2011

PHARMACY

Three-dimensional skin modell
JP 4751005,
granted May 27, 2011

Structured-functional bonding matrices for biomolecules
EP 1 461 619,
granted April 27, 2011

CHEMISTRY

Method for gaining fatty associated materials from fuel and use of this method
EP 2 072 102,
granted June 29, 2011

ENVIRONMENT

Anaerobic purification of wastewater
EP 1 968 900,
granted June 8, 2011

Verfahren zur Rückgewinnung von Phosphatsalzen aus einer Flüssigkeit
DE 10 2010 050 691,
granted November 9, 2011

Trade fairs and events 2011

Trade fairs and exhibitions**International Green Week
Fair for food, agriculture and
horticulture**

January 21-30, 2011, Berlin,
Germany

**Forum Life Sciences
"Pharma Development,
Food and Nutrition, Industrial
Biotechnology"****7th international Congress
with exhibition**

Fraunhofer Group for Life Sciences
March 23-24, 2011, Technische
Universität München-Garching,
Germany

**Hannover Fair Energy
Leading Trade Fair for Re-
newable and Conventional
Power Generation, Power sup-
ply, Transmission, Distribution
and Storage**

Fraunhofer Energy Alliance
April 4-8, 2011, Hannover,
Germany

**Euro BioMat
European Symposium on Bio-
materials and Related Areas**

April 13-14, 2011, Jena, Germany

**Location Fair
"Leuna – Dialog 2011"**

May 5, 2011, Kulturhaus Leuna,
Germany

**MS Wissenschaft (MS Science)
Exhibition "Neue Wege
in der Medizin"**

May 19 - September 29, 2011

**Exhibition "Entdeckungen
2011: Gesundheit" (Discover-
ies 2011: Health)**

May 20 - September 4, 2011,
Insel Mainau, Germany

Nanotech

Fraunhofer Nanotechnology
Alliance
June 13-16, 2011, Boston, USA

BIO International Convention
Fraunhofer Group for Life Sciences
June 27-30, 2011,
Washington D. C., USA

**German-Brazilian
Economic Days**

September 18-20, 2011,
Rio de Janeiro, Brazil

**BIOTECHNICA
Europe's No. 1 Event for Bio-
technology and Life sciences**
October 11-13, 2011, Hannover,
Germany

**parts2clean
9th Leading International Trade
Fair for Industrial Parts and
Surface Cleaning**

Fraunhofer Cleaning Technology
Alliance
October 25-27, 2011, Stuttgart,
Germany

**World Conference on
Regenerative Medicine**
November 2-4, 2011, Leipzig,
Germany

**Workshops, seminars,
events**

**Workshop with Co-operation
partner Instituto de Pesquisas
Tecnológicas IPT as part of Ger-
man-Brazilian Year of Science,
supported by the BMBF (IB)**

March 22-23, 2011,
São Paulo, Brazil

**Fraunhofer Talent School
Workshop "CSI Stuttgart – vom
genetischen Fingerabdruck zur
Täteridentifizierung"**

April 1-3, 2011, Fraunhofer
Institutes Center Stuttgart,
Germany

**15. colloquium of municipal
wastewater and waste
treatment**

"Technologie mit Zukunft"
April 13, 2011, Fraunhofer IGB,
Stuttgart, Germany

**Girls' Day
Future Day for Girls**

April 14, 2011, Fraunhofer
Institutes Center Stuttgart,
Germany

**IHK Technologie-Akademie
für den Mittelstand
(Technology Academy for
SMEs)**

"Oberflächen charakter-
isieren, modifizieren und
reinigen"
April 20, 2011, Fraunhofer IGB,
Stuttgart, Germany

**4th FEBS Advanced Lecture
Course Human Fungal
Pathogens:**

**Molecular Mechanisms of
Host-Pathogen Interactions
and Virulence**
May 7-13, 2011,
La Colle sur Loup, France

**OTTI symposium
"Reinigen und Vorbehandeln
vor der Beschichtung"**
May 18-19, 2011, Neu-Ulm,
Germany

**Tag der Wissenschaft
(Day of Science)**
July 2, 2011, University of
Stuttgart, Germany

**"Skin Factory" – prizewinner
in the nationwide innovation
competition
"365 Orte im Land der Ideen"**
October 26, 2011, Fraunhofer
Institutes Center Stuttgart,
Germany

**Tag der technischen Biologie
(Day of technical biology)**

November 5, 2011,
Zentrum für Bioverfahrenstechnik,
University of Stuttgart, Germany

unitag (University Day)
November 16-17, 2011,
University of Stuttgart, Germany

Visit of Green Talents
December 6, 2011, Fraunhofer
IGB, Stuttgart, Germany

**Science Tour 2011:
Health Research in Germany
German Academic Exchange
Service (DAAD)**
December 8, 2011, Fraunhofer
IGB, Stuttgart, Germany

Preview 2012

**Checkpoint Zukunft
(Checkpoint Future)**

Day for students at Fraunhofer
January 16, 2012, Fraunhofer
Institutes Center Stuttgart,
Germany

**BMBF-Statusseminar
"BioEnergie 2021"**

February 14-15, 2012, Fraun-
hofer IGB, Stuttgart, Germany

**16th colloquium of municipal
wastewater and waste
treatment**

"Technologie mit Zukunft"
February 16, 2012, Fraunhofer
IGB, Stuttgart, Germany

Energy Storage**International Summit for the
Storage of Renewable Energies**

Fraunhofer Energy Alliance
March 13-14, 2012, Düsseldorf,
Germany

Anuga FoodTec**International trade fair for
food and drink technology**

Fraunhofer Food Chain
Management Alliance
March 27-30, 2012, Köln,
Germany

**Workshop of DGM, BioRegio
STERN and BIO Deutschland**

"Neue Biomaterialien
und Technologien für die
Regenerative Medizin"
March 29, 2012, Stuttgart,
Germany

Hannover Fair**Research & Technology
Leading Trade Fair for R&D
and Technology Transfer**

Fraunhofer joint booth
April 23-27, 2012, Hannover

Hannover Fair Energy**Leading Trade Fair for Re-
newable and Conventional
Power Generation, Power
supply, Transmission, Distribu-
tion and Storage**

Fraunhofer Energy Alliance
April 23-27, 2012, Hannover,
Germany

**Hannover Fair Metropolitan
Solutions & IndustrialGreenTec****Leading Trade Fair for Envi-
ronmental Technology**

Fraunhofer Building Innovation
Alliance
April 23-27, 2012, Hannover,
Germany

Girls' Day**Future Day for Girls**

April 26, 2012, Fraunhofer
Institutes Center Stuttgart,
Germany

BIOPRO-**10th Anniversary event****"Biotechnologie zum
Anfassen"**

May 2, 2012, Fraunhofer IGB,
Stuttgart, Germany

**Spring meeting of Plasma
Germany**

May 7-8, 2012, Fraunhofer IGB,
Stuttgart, Germany

IFAT Entsorga**World's Leading Trade Fair
for Water, Sewage and Raw
Materials Management**

Fraunhofer Water Systems
Alliance
May 7-11, 2012, München,
Germany

Workshop**"BioRap – 3D-strukturiertes
Biomaterial mittels Rapid
Prototyping"**

May 16, 2012, Fraunhofer IGB,

Stuttgart, Germany

**3rd International Conference
Strategies in****Tissue Engineering**

Fraunhofer Group for Life Sciences
May 23-25, 2012, Würzburg,
Germany

MS Wissenschaft (MS Science)

Exhibition "Auf der Suche
nach der Welt von morgen"
May 30 until mid-October 2012

ACHEMA**World forum of the process
industry and the trend-
setting technology summit for
chemical engineering, envi-
ronmental protection and
biotechnology**

Fraunhofer joint booth
June 18-22, 2012,
Frankfurt am Main, Germany

BIO International Convention

Fraunhofer Group for Life Sciences
June 18-21, 2012, Boston, USA

LOPE-C**4th International Conference
and Exhibition for the Organic
and Printed Electronics Industry**

Fraunhofer Alliance for Polymer
Surfaces POLO
June 19-21, 2012, München,
Germany

Day of Sustainability

June 29, 2012, Fraunhofer
Institutes Center Stuttgart,
Germany

**Tag der Wissenschaft
(Day of Science)**

June 30, 2011,
University of Stuttgart, Germany

13th Wörlitzer Workshop**"Membrantechnologien
und Modifizierung von
Membranen"**

July 4, 2012, Wörlitz, Germany

**IHK Technologie-Akademie
für den Mittelstand****(Technology Academy for
SMEs)**

"Wirtschaftlichkeit durch
Ressourceneffizienz – vom
Wärmespeicher bis zum
Wasserrecycling"

July 18, 2012, Fraunhofer IGB,
Stuttgart, Germany

**Open house at Leuna
chemical site**

September 1, 2012, Leuna,
Germany

PSE 2012**13th International Conference
on Plasma Surface Engineering**

September 10-14, 2012,
Garmisch-Partenkirchen, Germany

parts2clean**10th Leading International
Trade Fair for Industrial Parts
and Surface Cleaning**

Fraunhofer Cleaning Technology
Alliance
October 23-25, 2012, Stuttgart,
Germany

unitag (University Day)

November 21, 2012,
University of Stuttgart, Germany

Details may be subject to
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Get further information here:
www.igb.fraunhofer.de

Committee memberships

Anadere, I.

Bundesverband der Pharmazeutischen Industrie e. V. (BPI),
Work group "Advanced Therapies", Member

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Subject divisions "Biotechnologie" and "Chemische Biologie", Member

Fraunhofer Water Systems Alliance SysWasser,
Managing director

German Water Partnership,
Regional Section Croatia, Member

Ingenieurtechnischer Verband Altlasten e. V. (ITVA),
Member

Verein Deutscher Ingenieure e. V. (VDI),
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Member

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Specialist Manager

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Deutscher Ethikrat, Member

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Europäische Union EU, Evaluator for 7th Framework Programme for Research

Gesundheitsforschungsrat des BMBF, Member of medical-technical committee

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GMM VDE/VDI-Gesellschaft Mikroelektronik, Mikrosystem- und Feinwerktechnik, Expert committee 4.7 (Mikro-Nano-Integration), Evaluator in program committee

Lectures and Seminars

Baden-Württemberg Cooperative State University Karlsruhe**Summer semester 2011**

Unkelbach, G.
Lecture "Organische Chemie"
Degree program paper technology, 2 SWS

Hamm-Lippstadt University of Applied Sciences**Summer semester 2011**

Bryniok, D.
Lecture "Bioenergie I"
Energy Engineering and Resource Optimization, 1 SWS

Bryniok, D.
Lecture "Technische Mechanik II"
Energy Engineering and Resource Optimization, 1 SWS

Bryniok, D.
Exercises for lecture "Technische Mechanik II"
Energy Engineering and Resource Optimization, 3 SWS

Bryniok, D.
Lecture "Umwelttechnik"
Energy Engineering and Resource Optimization, 1 SWS

Winter semester 2011/2012

Bryniok, D.
Lecture "Technische Mechanik I"
Energy Engineering and Resource Optimization, 2 SWS

Bryniok, D.
Exercises for lecture "Technische Mechanik I"
Energy Engineering and Resource Optimization, 4 SWS

Bryniok, D.
"Betreuung Praxissemester"
Energy Engineering and Resource Optimization

University of Applied Science, Offenburg**Winter semester 2011/12**

Kluger, P. J.
Lecture "Werkstoffe in der Medizintechnik – Biologische Aspekte"
Fakultät Elektrotechnik und Informationstechnik, Bachelor Medizintechnik, 1 SWS

University of Stuttgart**Summer semester 2011**

Bach, M.; Hirth, T.; Tovar, G. E. M.
Lecture "Komplexe Fluide"
Faculty of Energy Technology, Process Engineering and Biological Engineering, Process Engineering M. Sc., 2 SWS

Hirth, T.; Rupp, S.
Lecture "Biomaterialien – Herstellung, Struktur und Eigenschaften von biobasierten Materialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering, Technical Biology B. Sc., 2 SWS

Hirth, T.; Tovar, G. E. M.
Lecture "Grenzflächenverfahrenstechnik I – Chemie und Physik der Grenzflächen"
Faculty of Energy Technology, Process Engineering and Biological Engineering, Process Engineering M. Sc., *Vertiefungsfach*, 2 SWS

Hirth, T.; Tovar, G. E. M.
(with Masuch, K.)
Lecture "Grundlagen der Verfahrenstechnik I"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Technical Biology B. Sc.,
2 SWS

Hirth, T.
Lecture "Nachhaltige Rohstoffversorgung – Von der Erdölraffinerie zur Bio-raffinerie"
Fachübergreifende Schlüsselqualifikation, 2 SWS

Hirth, T.; Tovar, G. E. M.; Kluger, P. (with Doser, M. and Planck, H.)
Lecture "Medizinische Verfahrenstechnik I"
Faculty of Energy Technology,
Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering,
Process Engineering Diploma and M. Sc., Mechanical Engineering Diploma, 2 SWS

Kluger, P.; Tovar, G. E. M.
Lecture "Biomaterialien – Biokompatible Materialien"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Technical Biology B. Sc.,
2 SWS

Rupp, S.
"Ausgewählte Kapitel der modernen Biochemie"
Faculty of Chemistry, Study program Biochemistry, 1 SWS

Rupp, S.
Parts of lecture "Moderne Methoden in der Biochemie"
Faculty of Chemistry, Study program Biochemistry, 1 SWS

Rupp, S.
Parts of Lecture "Biochemischen Forschungspraktikum für Diplom-Chemiker"
Faculty of Chemistry, Study program Biochemistry, 8 SWS

Tovar, G. E. M.; Hirth, T.
Lecture "Nanotechnologie I – Chemie und Physik der Nanomaterialien"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, Technical Biology Diploma, 2 SWS

Tovar, G. E. M.
Lecture "Produktgestaltung mit Nano-, Bio- und Hybridmaterialien"
Faculty of Chemistry,
Chemistry Diploma, 3 SWS

Tovar, G. E. M., Hirth, T.
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Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, Technical Biology Diploma, 2 SWS

Winter semester 2011 / 12

Hirth, T.; Tovar, G. E. M.; Schiestel, T.
Lecture "Grenzflächenverfahrenstechnik II – Technische Prozesse"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, 2 SWS
Hirth, T.; Tovar, G. E. M.

Lecture "Grundlagen der Grenzflächenverfahrenstechnik"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, 2 SWS

Hirth, T.; Tovar, G. E. M.
(with Masuch, K.)
Lecture "Grundlagen der Verfahrenstechnik II"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Technical Biology B. Sc.,
2 SWS

Hirth, T.; Rupp, S.; Tovar, G. E. M.; Kluger P. (with Doser, M. and Planck, H.)
Lecture "Medizinische Verfahrenstechnik II"
Faculty of Energy Technology,
Process Engineering and Biological Engineering
Process Engineering Diploma and M. Sc., Mechanical Engineering Diploma, 2 SWS

Hirth, T.
Lecture "Nachhaltige Rohstoffversorgung und Produktionsprozesse"
Process Engineering M. Sc.,
2 SWS

Hirth, T.
Lecture "Sustainable Production Processes"
WASTE M. Sc., 2 SWS

Lemuth, K.; Hampel, M.; Tovar, G. E. M.
"Praktikum Medizinische Verfahrenstechnik"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Process Engineering M. Sc., Technical Biology Diploma, once only

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

Rupp, S.
Parts of "Biochemisches Praktikum für Technische Biologen"
Faculty of Chemistry, Study program Biochemistry, 8 SWS

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

Tovar, G. E. M.
Lecture "Biofunktionale Oberflächen – Chemie, Struktur und Funktion"
Faculty of Chemistry,
Chemistry Diploma, 2 SWS

Tovar, G. E. M.; Hirth, T.
Lecture "Nanotechnologie II – Technische Prozesse und Anwendungen für Nanomaterialien"
Faculty of Energy Technology,
Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, Technical Biology Diploma, 2 SWS

Summer semester 2011 and Winter semester 2011 / 12

Hirth, T.; Tovar, G. E. M.
"Mitarbeiterseminar für DoktorandInnen und DiplomandInnen"
Study program Process Engineering, Chemistry, Technical Biology,
1 SWS

Lectures and Seminars

Hirth, T.
»Anleitung zu wissenschaftlichem Arbeiten«
Study program Process Engineering, Chemistry, Technical Biology

Hirth, T.; Tovar, G. E. M.
"Grenzflächenverfahrenstechnisches Kolloquium"
Fachübergreifende Veranstaltung, 1 SWS

Hirth, T.; Tovar, G. E. M.
"Exkursion Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc.,
Vertiefungsfach, 2 SWS

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

Tovar, G. E. M. and others
"Arbeitstechniken und Projektarbeit (Übung)"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering B. Sc.,
2 SWS

Technische Universität München, Germany

Summer semester 2011

Sieber, V.
"Einführung in die Weiße Biotechnologie"
Study Program *Nachwachsende Rohstoffe*, 2 SWS

Sieber, V.
"Technische Biokatalyse"
Study Program *Industrielle Biotechnologie*, 2 SWS

Sieber, V.
Parts of lecture
"Technologie und Verwertung sonstiger biogener Rohstoffe"
Study Program *Forstwirtschaft*,
5 SWS

Winter Semester 2011 / 12

Sieber, V.
"Enzymengineering"
Study Program *Industrielle Biotechnologie*, 2 SWS

Sieber, V.
"Grundstoffe und Werkstoffe aus der Natur"
Study Program *Nachwachsende Rohstoffe*, 2 SWS

Sieber, V.
Parts of lecture
"Biokunststoffe und ihre Herstellung"
Study Program *Nachwachsende Rohstoffe*, 4 SWS

Sieber, V.
Parts of lecture
"Bioraffinerie und Naturstofftechnologien"
Study Program *Nachwachsende Rohstoffe*, 4 SWS

Sieber, V.
Parts of lecture "Grundlagen Chemie"
Study Program *Nachwachsende Rohstoffe*, 2 SWS

Sieber, V.
Parts of lecture
"Spezielle Biotechnologie"
Study Program *Nachwachsende Rohstoffe*, 2 SWS

Heidelberg University Biochemistry Center

Summer semester 2011

Sohn, K.
Parts of seminar and practical course "Nervensystem: Biochemische Analyse neuronaler Proteine und Lipide"
Medical Faculty,
Study program Biochemistry,
Seminar: 2 SWS,
Practical course: 6 SWS

Winter semester 2011 / 12

Sohn, K.
Parts of seminar and practical course "Leber und Harnstoff"
Medical Faculty,
Study program Biochemistry,
Seminar: 2 SWS,
Practical course: 6 SWS

University of Hohenheim, Stuttgart

Summer semester 2011

Kluger, P. J.
Lecture
"Tissue Engineering"
Faculty of Science, Food Science B. Sc., Biology B. Sc., Technology of Life Science B. Sc., 2 SWS

Winter semester 2011 / 2012

Schließmann, U.
"Mikroalgen – Rohstoffquelle zwischen Vision und Wirklichkeit"
Faculty of Natural Science,
Study Program Food Science and Biotechnology, one-time

Trösch, W.
Parts of Lecture
"Wasser-, Abwasser- und Abfallbehandlung"
Faculty of Natural Science,
Study Program Food Science and Biotechnology, 2 SWS

Trösch, W.
Parts of lecture "Allgemeine Biotechnologie"
Faculty of Natural Science,
Study Program Food Science and Biotechnology, 2 SWS

Trösch, W.
Parts of lecture
»Biochemie für Technologen«
Faculty of Natural Science,
Study Program Food Science and Biotechnology, 2 SWS

University of Tübingen

Winter semester 2011/2012

Schenke-Layland, K.
"Medizintechnik"
Medical Faculty, B. Sc., 2 SWS

University of Würzburg

Walles, H.
Lecture "Grundlagen des Tissue Engineering"
Technologie der Funktionswerkstoffe M. Sc.

Walles, H.
Lecture/Exercise "Mikrosysteme für biologische und medizinische Anwendungen"
Technologie der Funktionswerkstoffe M. Sc.

Walles, H.
Lecture
"Tissue Engineering"
Biomedizin M. Sc.

Walles, H.
Practical course
"Modellorganismen"
Biomedizin M. Sc.

Walles, H.
"Stammzellen"
Integriertes Seminar für Studenten der Medizin

Scientific cooperations

With universities

	McGill University, Montreal, Canada	Universität Wien, Austria	Centro tecnológica CARTIF, Valladolid, Spain
Aristotle University of Thessaloniki, Greece	Medizinische Hochschule Hannover MHH, Germany	Université Paul Sabatier Toulouse III, Toulouse, France	Chemical Process Engineering Research Institute (CPERI), Thessaloniki, Greece
Charles University, Prag, Czech Republic	Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Germany	Universitetet for Miljo og Biovitenskap, Aas, Norway	Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany
Comenius University, Bratislava, Slovakia	Ruhr-Universität Bochum, Germany	Universitetet i Bergen, Bergen, Norway	Deutsches Zentrum für Biomaterialien und Organersatz, Stuttgart-Tübingen, Germany
Cranfield University, Cranfield, UK	Stanford University, USA	University of California Los Angeles (UCLA), Los Angeles, USA	
Eberhard Karls Universität Tübingen, Germany	Stockholms Universitet, Sweden	University of Novi Sad, Novi Sad, Serbia	Dr. Margarete Fischer-Bosch-Institut für Klinische Pharmakologie (IPK), Stuttgart, Germany
Energieinstitut an der Johannes Kepler Universität Linz GmbH, Austria	Technische Universität Darmstadt, Germany	University of Southern California (USC), Los Angeles, USA	European Molecular Biology Laboratory EMBL, Heidelberg, Germany
Ernst-Moritz-Arndt-Universität Greifswald, Germany	Technische Universität Dortmund, Germany	University of West Hungary, Sopron, Hungary	Flanders Institute for Biotechnology (VIB), Gent, Belgium
Escola de Engenharia de Piracicaba (EEP), Brazil	Technische Universität Kaiserslautern, Germany	Univerza v Mariboru, Maribor, Slovenia	Institut Dr. Schrader Creachem GmbH, Holzminden, Germany
Escola Superior de Agricultura „Luiz de Queiroz“ (ESALQ), Piracicaba, Brazil	Technische Universität München, Germany	Uppsala Universitet, Uppsala, Sweden	Institut für Textilchemie und Chemiefasern ITCF, Denkendorf, Germany
Hochschule Hamm-Lippstadt, Germany	Technische Universiteit Eindhoven, The Netherlands	VTT Technical Research Centre of Finland, Finland	Institut für Textil- und Verfahrenstechnik ITV, Denkendorf, Germany
Julius-Maximilians-Universität Würzburg, Germany	Tierärztliche Hochschule Hannover, Germany		Institut National des Sciences et Technologies de la Mer, Salammbou, Tunisia
Katholieke Universiteit Leuven, Belgium	Trinity College Dublin, Ireland	With other research organizations	Institut Pasteur, Paris, France
Georgia Institute of Technology, Atlanta, USA	Universidad de Sevilla, Spain	Acondicionamiento tarrasense asociación, LEITAT, Terrassa (Barcelona), Spain	Johann Heinrich von Thünen-Institut, Braunschweig, Germany
Gottfried Wilhelm Leibniz Universität Hannover, Germany	Universidade Metodista de Piracicaba (UNIMEP), Brasilien	AIT – Austrian Institute of Technology, Wien, Austria	Johann Heinrich von Thünen-Institut, Hamburg, Germany
Letterkenny Institute of Technology, Letterkenny, Irland	Universita degli Studi di Bari, Italy	Bundesanstalt für Materialforschung und -prüfung (BAM), Berlin, Germany	Karlsruher Institut für Technologie (KIT), Karlsruhe, Germany
Linnéuniversitetet, Kalmar, Sweden	Universita degli Studi di Milano-Bicocca, Italy	Carnot institute CIRIMAT, Toulouse, France	Leibniz-Institut für Katalyse e. V. (LIKAT), Rostock, Germany
Ludwig-Maximilians-Universität München, Germany	Universität Hamburg, Germany	Centre de Recerca i Investigació de Catalunya CRIC, Barcelona, Spain	Leibniz-Institut für Plasmaforschung und Technologie e. V. (INP), Greifswald, Germany
Lunds Universitet, Lund, Sweden	Universität Heidelberg, Germany	Centre for Process Innovation CPI, Wilton, Redcar, UK	
Martin-Luther-Universität Halle-Wittenberg, Germany	Universität Hohenheim, Germany		
	Universität Innsbruck, Austria		
	Universität Konstanz, Germany		
	Universität Stuttgart, Germany		

Scientific cooperations

Ludwig Institute for Cancer Research, Stockholm, Sweden	Klinik Charlottenhaus, Stuttgart, Germany
Max-Planck-Institut für Festkörperforschung, Stuttgart, Germany	Klinik Schillerhöhe, Gerlingen, Germany
Max-Planck-Institut für Intelligente Systeme, Stuttgart, Germany	Robert-Bosch-Krankenhaus, Stuttgart, Germany
Max-Planck-Institut für Kolloid- und Grenzflächenforschung, Golm, Germany	Universitätsklinikum Innsbruck, Austria
Max-Planck-Institut für Polymerforschung, Mainz, Germany	Universitätsklinikum Lübeck, Germany
National Institute of Laser, Plasma and Radiation Physics, Magurele-Bucharest, Romania	Universitätsklinikum Frankfurt am Main, Germany
Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek TNO, The Netherlands	Universitätsklinikum Tübingen, Germany
Norwegian Institute of Food, Fisheries and Aquaculture Research Nofima, Oslo, Norway	Universitätsklinikum Würzburg, Germany
PROFACTOR GMBH, Steyr-Gleink, Austria	University Hospital Lausanne, Switzerland
Research & Development centre Re/genT, Helmond, The Netherlands	-----
Robert-Koch-Institut, Berlin, Germany	With museums
Teknologisk Institutt (TI), Oslo, Norway	Bayerisches Hauptstaatsarchiv, München, Germany
Vlaamse Instelling Voor Technologisch Onderzoek N.V (VITO), Mol, Belgium	Deutsches Bergbaumuseum, Bochum, Germany
-----	Deutsches Museum, München, Germany
With hospitals	Deutsches Schiffahrtsmuseum, Bremerhaven, Germany
Haukeland University Hospital, Bergen, Norway	Germanisches Nationalmuseum, Nürnberg, Germany
Herz- und Diabeteszentrum Nordrhein-Westfalen der Universitätsklinik der Ruhr-Universität Bochum, Germany	Landesmuseum Württemberg, Stuttgart, Germany
	Stiftung Preußischer Kulturbesitz, Rathgen-Forschungslabor, Berlin, Germany
	Zentrum für Bucherhaltung, Leipzig, Germany

Academic theses

Ph. D. theses

Brachhold, M. Lokalisation von Tsa1p, einem thioispezifischen Antioxidant-ähnlichen Protein aus <i>Candida albicans</i> und dessen Einfluss auf die Wirt-Pathogen-Interaktion, Universität Stuttgart Fraunhofer Verlag, ISBN 978-3-8396-0287-4	Fischer, A. Charakterisierung primärer humaner Endothelzellen auf Thiolheparin- und RGD-funktionalisierten Polymer-substraten, Universität Stuttgart
Lindemann, E. Identifizierung und vergleichende Charakterisierung eines zentralen Regulationsfaktors der Morphogenese und des Stickstoffmetabolismus in humanpathogenen Pilzen, Universität Stuttgart	Groeger, C. Gewinnung von Omega-3-EPA aus Mikroalgen – Untersuchung des Zellaufschlusses und der Extraktion, Universität Braunschweig
Mohr, M. Betrieb eines anaeroben Membranbioreaktors vor dem Hintergrund der Zielstellung des vollständigen Recyclings kommunalen Abwassers und seiner Inhaltsstoffe, Technische Universität Darmstadt, Fraunhofer Verlag, ISBN 978-3-8396-0336-9	Kahlig, A. Definition physikalischer Parameter zur Entwicklung eines Bioreaktors zur Herstellung von vaskularisiertem Knochengewebe, Universität Stuttgart
Schmidt, M. C. Untersuchung und Verbesserung des Entleerungsverhaltens von Füllgut-Verpackungssystemen, Universität Stuttgart	Klechowitz, N. Adhäsion und Proliferation humaner primärer Endothelzellen auf heparinisierten und RGD-funktionalisierten Polymeroberflächen, Hochschule Niederrhein
-----	Kotzan, J. Title protected, Universität Hohenheim
Diploma theses	Kotzur, M. Title protected, Universität Stuttgart
Brückner, M. Elektrische Anforderungen zur Zündbarkeit von Plasmen in Lumen von langen Hohlkörpern, Westsächsische Hochschule Zwickau	Kraft, B. Wirkung von UV-Strahlung als Hauptkomponente in Plasmen auf zelluläre Signalkaskaden in Hautzellen und in einem <i>In-vitro</i> -Hautmodell, Universität Hohenheim
Bublinski, M. Title protected, Universität Stuttgart	Liedke, A. Charakterisierung einer kontinuierlichen Prozessstrategie zur Lipidproduktion mit <i>Chlorella vulgaris</i> im FPA Reaktor, Universität Stuttgart

Mattmer, E.-M.
Hydrogele durch Aza-Michael-Reaktion-Darstellung, Charakterisierung, Stabilität,
Hochschule Isny

Michalowski, A.
Eine Methode zur Kreuzvernetzung interagierender Proteine *in vivo*,
Universität Stuttgart

Schuster, J.
**Anodische Oxidation zur Abwasserbehandlung im Hinblick auf die Anwendung zur Depo-
niesickerwasseraufbereitung,**
Universität Stuttgart

Schwarzkopf, P.
Title protected,
Technische Universität Clausthal

Schweinlin, M.
Isolation, Kultivierung und Charakterisierung jejunaler porciner Epithelzellen,
Universität Hohenheim

Master theses

Cerces, D.-M.
Title protected,
Universität Stuttgart

Chaudhari, V. N.
Title protected,
Universität Stuttgart

Czelejewska, W.
Title protected,
Technische Universität
Hamburg-Harburg

Dominas, F.
Title protected,
Hochschule Mannheim und EN-
SIC Nancy (Frankreich)

Fukohani, S.
Title protected,
Hochschule Bremerhaven

Haro de la Pena, R.
Title protected,
Universität Stuttgart

Jong, W. N.
Study of heat transfer and the effect of process parameters on the efficiency of a closed sorption thermal storage unit,
Universität Stuttgart

Morawietz, T.
Title protected,
Hochschule Esslingen

Priyanka, P.
Title protected,
Hochschule für Wirtschaft
und Recht Berlin

Rentea, B.
Title protected,
Universität Stuttgart

Rottenfuß, S.
Title protected,
Hochschule für Angewandte
Wissenschaften Hamburg

Simon Legorreta, N.
Title protected,
Universität Stuttgart

Stillhammer, M.
Title protected,
Universität Stuttgart

Terán Camarena, F. M.
Title protected,
Universität Stuttgart

Toro Santamaria, J. M.
Title protected,
Universität Stuttgart

Zhang, C.
Oberflächenfunktionalisierung von Kunststofffolien zur Verminderung der Eisbildung und Eishaftung („Anti-Icing“),
Hochschule Reutlingen

Bachelor theses

Baum, M.-D.
Untersuchung der Proteinadsorption auf plasmabehandeltem Polyethersulfon,
Universität Stuttgart

Berio, D. A. C.
Non-invasive Raman spectroscopy of cardiovascular matrix,
Hochschule Bremerhaven

Bitz, A.
Title protected,
Hochschule Furtwangen

Bladocha, J.
Title protected,
Hochschule Esslingen

Blaschke, L.
Title protected,
Hochschule Furtwangen

Brüderle, K.
Experimentelle Untersuchungen zur Biogasproduktion aus Mikroalgen,
Universität Hohenheim

Egger, S.
Entwicklung eines Messsystems zur automatisierten Beurteilung von Epidermismodellen mittels Impedanzspektroskopie,
Universität Stuttgart

Frisenborg, L.
Fluor-Kohlenstoff-Plasma-beschichtungen von Hybrid-Wälzlagern zur Minimierung der Reibung und deren Charakterisierung hinsichtlich deren Eignung für den Einsatz in der Lebensmittelproduktion,
Universität Stuttgart

Gretzinger, S.
Herstellung Chitosan-basierter partikulärer Protein-formulierungen mittels Sprühtrocknung,
Hochschule Biberach

Hamm, J.
Title protected,
Hochschule Reutlingen

Jesswein, I.
Strukturierung der Oberflächen von Polyurethan- und Polytetrafluorethylen-Folien durch kombinierte Plasma- und Materialdruckverfahren für Anti-Eis-Eigenschaften,
Universität Stuttgart

Kayser, M.
Design of enabling tools for the engineering of elastin structures for application in cardiovascular regenerative medicine,
Universität Stuttgart

Knopf, A.
Nutzung der Raman-Spektroskopie zur nicht-invasiven Charakterisierung des Differenzierungszustandes von pluripotenten Stammzellen,
Fachhochschule Frankfurt
am Main

Kunz, H.
Title protected,
Hochschule Fulda

Löder, J.
Title protected,
Hochschule Esslingen

Mächler, S.
Title protected,
Hochschule Heilbronn

Minarik, W.-C.
Title protected,
Fachhochschule Aachen

Prinz, S.
Entwicklung von quantitativen und qualitativen Messtechniken für Eis-abweisend funktionalisierte Oberflächen in Bezug auf die Eisbildung,
Universität Stuttgart

Queck, S.
Title protected,
Universität Stuttgart

Academic theses

Raible, M.
Inbetriebnahme einer Ammoniumsonde zur kontinuierlichen Messung des Ammoniumgehalts in Mikroalgenkulturen, Universität Hohenheim

Schäfer, T.
Phenoladsorption aus Filtraten sowie Aufkonzentrierung von Algenbiomasse und Schlämmen mittels Rotationscheibenfilter, Fachhochschule Furtwangen

Schmid, F. F.
Title protected, Hochschule Esslingen

Schneider, S. K.
Evaluierung der osteogenen Differenzierung von humanen mesenchymalen Stammzellen auf plasmamodifizierten Oberflächen, Hochschule Biberach

Schrade, D.
Abscheidung von Schichten aus Silizium- und Titandioxid in einem induktiv gekoppelten Plasma, Universität Stuttgart

Steuer, K.
Untersuchung eines Azol-resistenten klinischen *Candida albicans*-Isolats, Hochschule Furtwangen

Weiss, C.
Niederdruckplasmaprozess zur Herstellung von TiO₂-Schichten und deren Charakterisierung, Universität Stuttgart

Winter-Emden, C.
Entwicklung einer Sensorzelle für Bioreaktoren im Tissue Engineering, Hochschule Ulm

Werner, A.
Charakterisierung und Optimierung des Lipidproduktionsprozesses mit der Mikroalge *Chlorella vulgaris* hinsichtlich Kohlenstoffdioxidverfügbarkeit und Begasungsrate, Universität Stuttgart

Student research studies

Hamm, J.
Evaluierung der Zellzahl und Morphologie primärer humaner mikrovaskulärer Endothelzellen in Abhängigkeit der Spender- und Biopsatvariabilität, Hochschule Reutlingen

Jando, J.
Title protected, Universität Stuttgart

Runaf, S.
Comparison of electrode materials in the treatment of leachate model solution, Universität Stuttgart

Schneider, S. K.
Evaluierung der Biokompatibilität von Polymeren zum Aufbau eines synthetischen Hydrogels nach dem Vorbild des natürlichen Elastins, Hochschule Biberach

Internship reports

Blaschke, L.
Title protected, Hochschule Mannheim

Held, T.
Validierung der SNP-Detektion in DLBCL mittels ZIP-Code-Array, Hochschule Furtwangen

Jückstock, J.
Versuche zu Parylenbeschichtungen und zur Plasmareinigung, Technische Universität München

Knopp, S.
Partikelherstellung im Nanometerbereich mittels Rotor/Stator und mittels Sprühtrocknung, Hochschule Furtwangen

Kotljaraova, O.
Title protected, Technische Hochschule Mittelhessen

Kotzan, J.
Title protected, Universität Hohenheim

Kroner, J.
Title protected, Hochschule Furtwangen

Möbeler, J.
Synthese von Cyclodextrin-Monomeren und Herstellung molekular geprägter Nanopartikel, Georg Simon Ohm Hochschule Nürnberg

Schneider, V.
Title protected, Hochschule Esslingen

Schneidt, V.
Title protected, Hochschule Esslingen

Weisser, S.
Title protected, Hochschule Furtwangen

Semester works

Baum, M.-D.
Verminderung von Membranfouling durch plasmamodifizierte Oberflächen, Universität Stuttgart

Prinz, S.
Oberflächenfunktionalisierung von Kunststofffolien zur Verminderung der Eisbildung und Eishaftung, Universität Stuttgart

Publications 2011

Journal papers

- Barz, J. (2011)
Barriere mit Wirkung,
Journal für Oberflächentechnik
JOT 51 (7): 56-57
- Barz, J. (2011)
**Fraunhofer-Beschichtung
verringert Permeation,**
Gefährliche Ladung 7: 22
- Barz, J.; Oehr, C.; Lunk, A. (2011)
**Analysis and modeling
of gas-phase processes in a
CHF₃/Ar discharge,**
Plasma Processes and
Polymers 8 (5): 409-423
- Bauer, J.; Kinast, S.; Burger-
Kentischer, A.; Finkelmeier, D.;
Kleymann, G.; Rayyan, W. A.;
Schroppel, K.; Singh, A.; Jung,
G.; Wiesmüller, K. H.; Rupp, S.;
Eickhoff, H. (2011)
**High-throughput-screening-
based identification and
structure-activity relationship
characterization defined
(S)-2-(1-aminoisobutyl)-1-(3-
chlorobenzyl)benzimidazole
as a highly antimycotic agent
nontoxic to cell lines,**
Journal of Medicinal Chemistry
54 (19): 6993-6997
- Blath, J.; Christ, M.; Deubler, N.;
Hirth, T.; Schiestel, T. (2011)
**Gas solubilities in room
temperature ionic liquids –
Correlation between
RTIL-molar mass and Henry's
law constant,**
Chemical Engineering Journal
172 (1): 167-176
- Borchers, K.; Schönhaar, V.;
Hirth, T.; Tovar, G. E. M.;
Weber, A. (2011)
**Ink formulation for inkjet
printing of Streptavidin and
Streptavidin functionalized
nanoparticles,**
Journal of Dispersion Science and
Technology 32 (12): 1759-1764
- Brockbank, K. G. M.;
Heacox, A. E.;
Schenke-Layland, K. (2011)
**Guidance for removal of fetal
bovine serum from cryopre-
served heart valve processing,**
Cells Tissues Organs 193 (4):
264-273
- Brockbank, K. G. M.;
Wright, G. J.; Yao, H.;
Greene, E. D.; Chen, Z. Z.;
Schenke-Layland, K. (2011)
**Allogeneic heart valve storage
above the glass transition at
-80 °C,**
The Annals of Thoracic Surgery
91 (6): 1829-1835
- Burger-Kentischer, A. (2011)
**Human immune system in a
microtiter plate: Innate immu-
ne assay for the examination
of receptor activity,**
G.I.T. Laboratory Journal Europe
3-4: 2
- Burger-Kentischer, A.;
Finkelmeier, D.; Keller, P.;
Bauer, J.; Eickhoff, H.;
Kleymann, G.; Rayyan, W. A.;
Singh, A.; Schroppel, K.;
Lemuth, K.; Wiesmüller, K.-H.;
Rupp, S. (2011)
**A screening assay based on
host-pathogen interaction
models identifies a set of
novel antifungal benzimid-
azole derivatives,**
Antimicrobial Agents and Che-
motherapy 55 (10): 4789-4801
- Dally, I.; Schandar, M.; Linke,
K.; Pusch, J.; Walles, T.;
Walles, H. (2011)
**In vitro development of a
vascularized tracheal patch
to restore airway defects after
resection,**
Tissue Engineering
Part A 17 (3-4): 578
- Engelhardt, S.; Hoch, E.;
Borchers, K.; Meyer, W.;
Krüger, H.; Tovar, G.;
Gillner, A. (2011)
**Fabrication of 2D protein
microstructures and 3D
polymer-protein hybrid mi-
crostructures by two-photon
polymerization,**
Biofabrication 3 (2): 025003
- Genov, S.; Riester, D.; Hirth, T.;
Tovar, G.; Borchers, K.; Weber, A.
(2011)
**Preparation and characterisa-
tion of dry thin native protein
trehalose films on titanium-
coated cyclo-olefinpolymer
(COP) foil generated by spin-
coating/drying process and
applied for protein transfer by
Laser-Induced-Forward Trans-
fer (LIFT),**
Chemical Engineering and
Processing 50 (5-6): 558-564
- Göhler, S.; Pusch, J.;
Sawodny, B.; Walles, H.;
Hirth, T. (2011)
**Development of a dynamic
intestinal tissue equivalent
that enables the analysis of
new drug candidates *in vitro*,**
Tissue Engineering
Part A 17 (3-4): 562-563
- Groeber, F. K.; Hansmann, J.;
Kaufmann, M.; Walles, H. (2011)
**Development of a vascularized
skin equivalent,**
Tissue Engineering
Part A 17 (3-4): 556
- Groeber, F. K.; Holeiter, M.;
Hampel, M.; Hinderer, S.;
Schenke-Layland, K. (2011)
**Skin tissue engineering – *In
vivo* and *in vitro* applications,**
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Weber, C.; Burger-Kentischer, A.; Müller, M.; Trick, I.; Hirth, T.

Preparation and characterization of PEG-based hydrogels as antibiofilm agent delivery systems

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