Fraunhofer
IGB

FRAUNHOFER INSTITUTE FOR INTERFACIAL ENGINEERING AND BIOTECHNOLOGY IGB

»RESEARCH FOR OUR HEALTH«

ANNUAL REPORT 10|11

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10|11

CONTENT

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RESEARCH AND DEVELOPMENT 2010

"Sustainability and biotechnology – Our contribution to innovation, health, change in the raw materials base and climate protection"

Dear Reader,

Solving global problems such as tackling disease and hunger, as well as securing the supply of water, raw materials and energy for every citizen of the planet, are the big challenges we face in the 21st century. Unrelenting population growth, escalating consumption of resources and rising global warming due to increased CO_2 emissions mean that the development and realization of sustainable processes and products by industry and research is becoming ever more imperative. The German Year of Science 2011 – "Research for Our Health" – and the International Year of Chemistry 2011 under the slogan "Chemistry – our Life, our Future" underline the significance of orienting our actions on the principle of sustainability, a concept which meets the needs of current generations without jeopardizing the options of future generations to satisfy their own needs.

An exceptional role is played here by biotechnology, the key technology of the 21st century. In its many facets it has the potential to make a crucial contribution to securing the supply of raw materials and energy, clean drinking water and safe food, as well as to fighting disease. Therefore, sustainability and biotechnology are core areas of research within all the business areas at the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, whether medicine, pharmacy, chemistry, or the environment and energy. Last year was also marked by a focus on further developing biotechnology as a core competence across all departments of the Fraunhofer IGB. Also at the fore was the setting up and expansion of national and international biotechnology networks. This enabled us to make major progress in the scientific development of our research areas and to secure the economic success of the institute.

Of great significance for the Fraunhofer IGB in 2010 were developments in the field of bioeconomics at national and international levels. Through our collaboration in the federal government's Bio-economy Council, in the SusChem-D technology platform and various European committees, we made contributions to both the "National Research Strategy *BioEconomy 2030*" and to the development of new, bio-based products and processes. Our bioeconomic activities are aimed at achieving the sustainable use of biological resources such as plants, animals and microorganisms, as well targeting all areas of industry and economic sectors which produce, manage or otherwise use biological resources, including biological residual materials. Biotechnology is a key source of innovation here. The sustainable use of natural resources and the development of efficient value chains, processes and products are a central focus of research of the *BioEconomy* strategy – which we progressed significantly last year through our work using biotechnological processes for the sustainable material and energetic use of renewable raw materials. An important specialist field within biotechnology is biocatalysis. In our BioCat Project Group we are working on developing and establishing a "catalysts- and process screening" technology platform which optimally exploits naturally occurring synthesis processes. Two causes for celebration at BioCat in 2010 were first, the receipt of the letter of approval for the start-up financing of the project group, and second, the ground-breaking ceremony for the construction of a new laboratory building in Straubing, the birthplace of our name-giver, Joseph von Fraunhofer.

The speed at which innovative processes can be translated from research to industrial scale is a decisive factor in the realization of a sustainable supply of raw materials and energy based on renewables. At present, there are still problems with the scaling of processes which we are aiming to remedy with the establishment of the Fraunhofer Center for Chemical-Biotechnological

Processes CBP at the chemical site Leuna. Building work on the Fraunhofer CBP commenced at a ground-breaking ceremony in December 2010 and with the handover of the grant letter from the *Land* Saxony-Anhalt. On premises of over 2000 square meters, a process center will be constructed, with a scheduled opening date of the summer of 2012. Here partners from research and industry will be able to jointly develop processes for the material use of renewable raw materials up to technical scale.

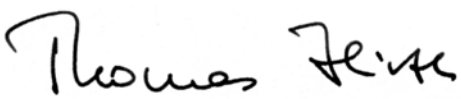
The Fraunhofer IGB is already working on the next generation of biotechnological processes, which are to be based on cell-free systems. Thus last year we were intensively involved in the strategy process "The Next Generation of Biotechnological Processes – Biotechnology 2020+" devised by the German Federal Ministry of Education and Research (BMBF), and together with other institutes in the Fraunhofer Group for Life Sciences we initiated a Fraunhofer pilot project for cell-fee bioproduction.

The business areas medicine and pharmacy were also dominated to a large extent by the institute's biotechnological activities in 2010. The Project Group "Regenerative Technologies for Oncology" at the University of Würzburg has intensified its work in developing human test systems with the goal of establishing tissue-specific, vascularized *in-vitro* tumor models for testing new medicines. These models will make it possible in future to develop and validate new diagnostics, therapeutics and targeted therapeutic processes directly on human tumors *in vitro* without the need for animal testing. To promote medical-biotechnological activities at the Fraunhofer IGB, a cooperation agreement was signed with the University of Tübingen and its associated hospital. A jointly funded professorship for the "Development of Biomaterials for Cardiovascular Tissue Engineering" is intended to permanently strengthen the IGB's "Cardiovascular Tissue Engineering" Attract group.

The strong orientation of our business areas and core competences toward issues of sustainability in key social areas such as health, safety and security, the environment, energy and mobility, meant that the Fraunhofer IGB was able to continue its good performance in 2010 and prepare well for the challenges of the coming years. A particular highlight was Executive Board approval of funding for a project to implement guiding principles for the sustainable development of the Fraunhofer-Gesellschaft. The project will address issues such as research into sustainability, sustainability of Fraunhofer research and establishing sustainable business processes.

Apart from continuing to develop our R&D activities, a focal point last year was sustainable personnel development. This recognizes the fact that our scientific and economic success is predicated on the staff of the Fraunhofer IGB – not forgetting our IGVT colleagues. We were also able to acquire numerous new customers from industry, as well as additional public donors and foundations as sources of commissions for R&D projects.

I hope that this new Fraunhofer IGB annual report stimulates your interest in our R&D activities and in future collaboration with us. Our mission is to shape the future of the region, Germany and Europe in a sustainable way, hand in hand with our partners and customers. Enjoy your read – and I look forward to your suggestions and to working with you.



Yours,
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

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

MinDirig Dipl.-Ing. Peter Fuhrmann
Ministry for the Environment of the State of Baden-Württemberg

MinDirig Dr. Fritz Holzwarth
German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety

Prof. Dr. Dieter Jahn (Chair)
BASF SE

Dr.-Ing. Bernd Krause
Gambro Dialysatoren GmbH

RegDir Dr. Jürgen Ohlhoff
German Federal Ministry of Food, Agriculture and Consumer Protection

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

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

Dipl.-Ing. Otmar Schön
HYDAC Technology GmbH

Dr. Jürgen Stebani
Polymaterials AG

Dr. Thomas Stiefel
biosyn Arzneimittel GmbH

MinR Dr. Joachim Wekerle
Ministry of Economic Affairs of the State of Baden-Württemberg

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Boehringer Ingelheim Pharma GmbH & Co. KG

Dr. Günter Wich
Wacker Chemie AG

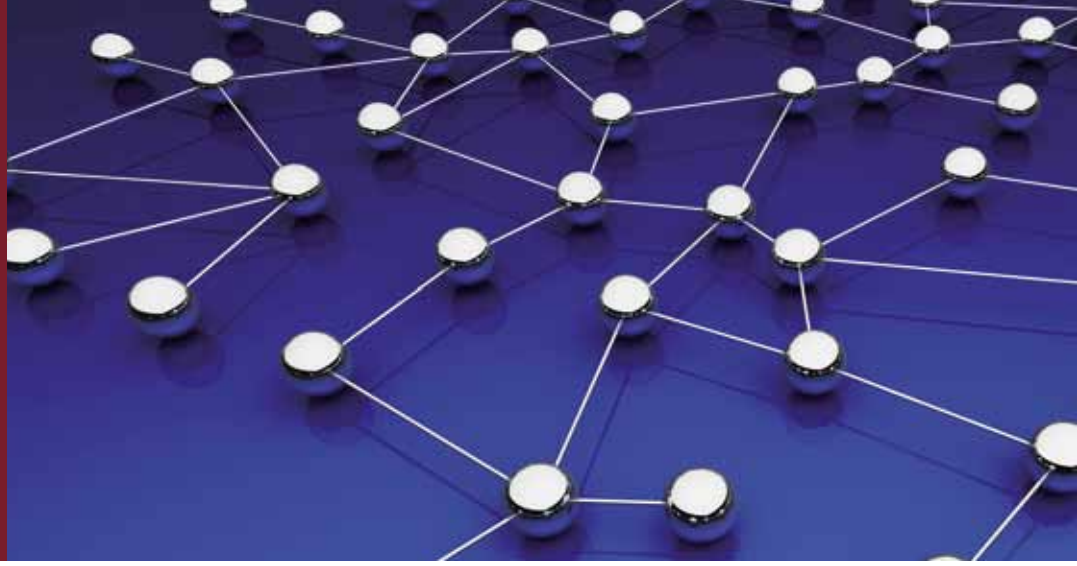
Prof. Dr. Karl-Heinz Wiesmüller
EMC microcollections GmbH

Dr. Wieland Wolf
Laupheim

Permanent guests

Prof. Dr. Herwig Brunner
Former Director of Fraunhofer IGB

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 (Caco2) 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 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 2010, the Fraunhofer IGB had a staff of 268. Some 90 percent were scientific or technical employees. Women made up 56 percent of the total.

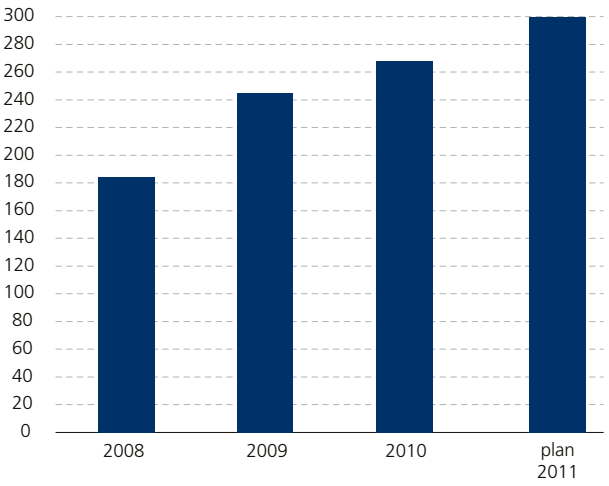
The university institute IGVT counted a staff of 72 effective December 31, 2010, predominantly scientists and Ph.D. students as well as technical staff and student research assistants. Women made up 58 percent of the total.

The Fraunhofer IGB and IGVT staff members come from 21 different nations and work closely together.

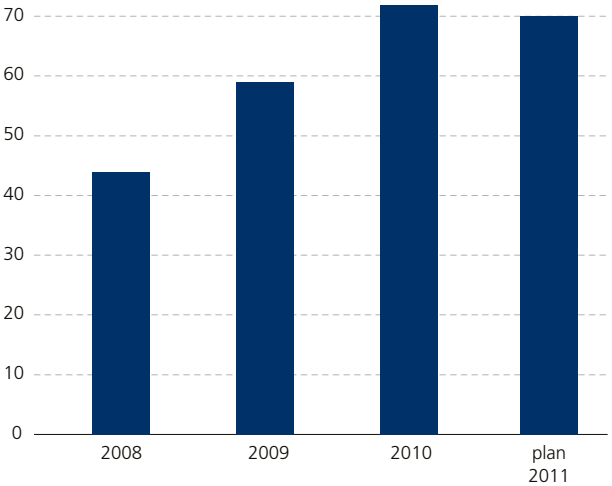
Staff members Fraunhofer IGB	Number
Scientists	68
Technical staff	60
Graduate student research workers	78
Student research assistants	30
Administrative and secretarial staff	24
Trainees	8
Total	**268**

Staff members IGVT	Number
Scientists/Ph.D students	59
Technical staff	4
Student research assistants	9
Total	**72**

number staff members IGB



number staff members IGVT

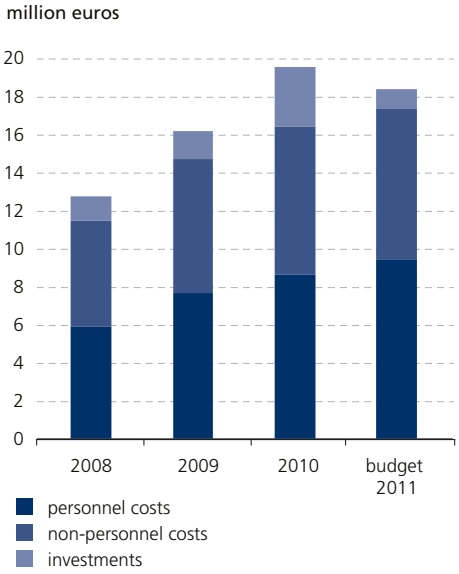


Budget of Fraunhofer IGB

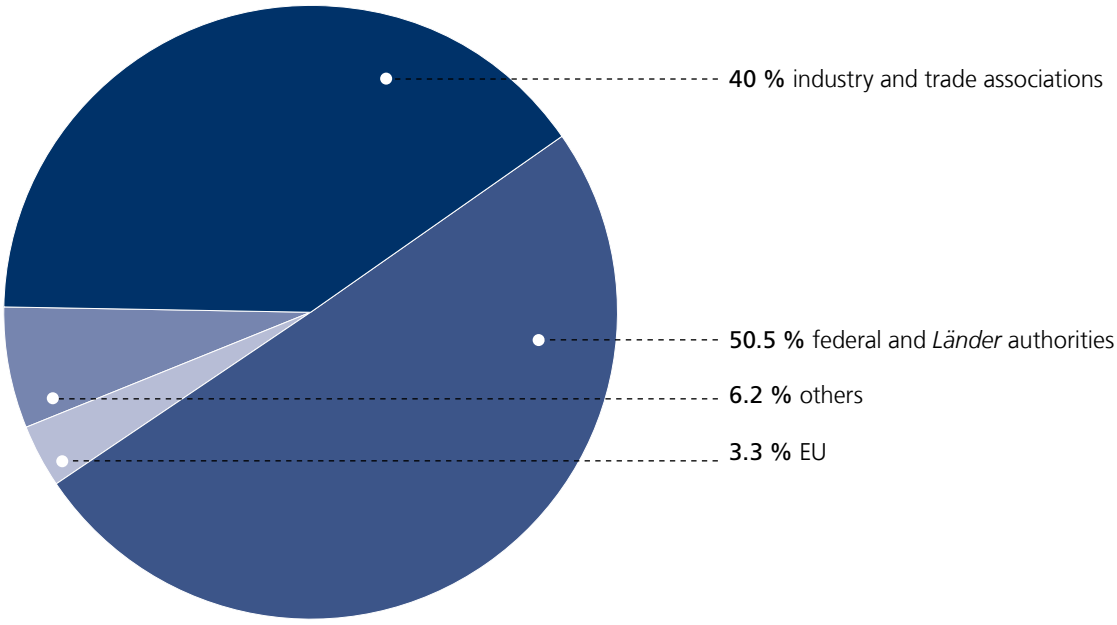
The total budget for 2010 amounted to 19.7 million euros, of which 16.6 million euros was allocated to the operational budget (personnel costs: 8.7 million euros; non-personnel costs: 7.9 million euros). A total of 3.1 million euros was spent on investments.

75 percent of the operational budget was financed from Fraunhofer IGB's own revenues generated from contract research projects, while governmental funding covered the remaining 25 percent. 40 percent of the Institute's revenues came directly from industry.

DEVELOPMENT OF BUDGET



REVENUE FROM CONTRACT RESEARCH



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- Bio-based Raw Materials
- Bio-energy
- Interfacial Biology

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

ATTRACT GROUP

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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 is a must. 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 and Institute for Interfacial Engineering IGVT at the University of Stuttgart
- **Priv.-Doz. Dr. Steffen Rupp**
  Faculty of Chemistry and Faculty of Energy Technology, Process Engineering and Biological Engineering, University of Stuttgart
- **Assistant Professor Dr. Katja Schenke-Layland**
  Department of Cardiology, Medical Faculty, University of California Los Angeles (UCLA), Los Angeles, California, USA
- **Prof. Dr. Volker Sieber**
  Chair of Chemistry of Biogenic Resources, Technische Universität München
- **Priv.-Doz. Dr. Günter Tovar**
  Faculty of Chemistry and Faculty of Energy Technology, Process Engineering and Biological Engineering, 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.

The first sub-project under the management of Prof. Hirth has the objective of developing guiding principles and a strategy for the sustainability of the Fraunhofer-Gesellschaft. In a second sub-project, Fraunhofer staff are developing approaches for designing more sustainable business processes, and also a toolbox to evaluate the sustainability aspects of research projects. In addition, they are tasked with producing guidelines for writing a sustainability report. The Stuttgart campus – common home to five Fraunhofer institutes – is functioning as a pilot site for these activities. The third sub-project focuses on sustainable research topics, synthesizing the expertise of different institutes in order to offer an improved approach to system solutions and to identify new research topics. The Fraunhofer IGB is involved in all three sub-projects.

www.nachhaltigkeit.fraunhofer.de

Fraunhofer International Business Development (IBD) Network

In recent years, international cooperations and joint development activities between globally active partners have increasingly characterized the economy and science. In order to keep a finger on the pulse of time for our customers, we, too, harness the innovation potential of networks for our international business. Three working groups have joined forces in our International Business Development Network with the aim of offering clear perspectives on the latest trends. The Fraunhofer IGB 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. To this end, the Network offers a manual containing fundamental guidelines, documents and checklists relevant to individual project situations, and the possibility of making contacts through personal meetings and through six-monthly workshops with other research funding specialists.

The EU Network is coordinated by Maximilian Steiert from Fraunhofer-Gesellschaft headquarters and Ina Andrees-Ostovan of the Fraunhofer IGB.

Joint EU-IBD Network Meeting in Brussels

50 colleagues from 30 Fraunhofer institutes met in Brussels at the start of November 2010 for the first joint meeting of the EU and IBD networks. The focus was on the exchange of information between the Fraunhofer colleagues as well as with external experts from the European Commission, the Research Executive Agency and other research institutions located in Brussels.

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

Networking and regular exchange of information play a significant contribution to the success of research institutions 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. In February 2010, the Fraunhofer IGB hosted the group's twice-yearly meeting. The participants discussed strategic aspects as well as the applications submission procedure and how to carry out EU projects successfully.

Fraunhofer Symposium "Network Value" 2010

The Fraunhofer symposium "Network Value" which took place on December 7-8, 2010, offered for the first time an internal platform for information exchange and networking. 320 participants, including numerous trustees, had the opportunity to find out about current research activities in a series of parallel lectures. In the gripping "Elevator Pitches" ideas competition, 20 original product ideas competed over two days for the favor of the public. The three winners chosen each day received prize money, while their projects attracted a financial grant for institutes taking up the ideas. Jacqueline Pusch of the Fraunhofer IGB came third on the first day with her idea for a gastro-intestinal wall plaster.

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
EMB, IBMT, IGB, IME, ITEM, IVV, IZI
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, biotechnology, and process, chemical, and herbicide safety, thus bundling numerous IGB key competences.

Fraunhofer Group for Materials and Components – MATERIALS
EMI, IAP, IBP, ICT, IFAM, IGB (guest), IKTS,
ISC, ISE, ISI, ITWM (guest), IWM, IZFP, LBF, WKI
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
EMI, IAO, IBP, ICT, IFAM, IGB, IMS, IRB,
ISC, ISE, IVV, IWM, IZFP, LBF, UMSICHT, WKI
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
CSE, IBP, ICT, IFF, IGB, IIS, IISB, IKTS,
IOSB/AST, IPA, ISC, ISE, ISI, ISIT, IWES, UMSICHT
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.

Fraunhofer Nanotechnology Alliance
ENAS, IAO, IAP, ICT, IFAM, IFF, IGB, IISB, IKTS, ILT
IPA, ISC, ISE, ISI, ITEM, IVV, IWM, IWS, IZFP, LBF
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 actuatoric 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
FEP, ICT, IFAM, IGB, IME, ISC, ISE, IST, IWS
www.photokatalyse.fraunhofer.de
Nine 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
FEP, IAP, IFAM, IGB, IPA, ISC, IVV
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 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
FEP, IFAM, IGB, ILT, IPA, IPK, IST, IWS
www.allianz-reinigungstechnik.de
Cleaning technology has steadily gained significance in the past years and regularly arouses the interest of industry with its applications in buildings, in hygienic production and microsystems technology. By founding this alliance, Fraunhofer is able to offer concentrated competence along the whole process chain and a central point for contact, pooling requests and coordinating projects. Fraunhofer IGB contributes its expertise in the plasma purification of surfaces prior to coating processes and in the electrostatic surface cleaning. Purification success is evaluated by state-of-the art surface analytical methods. The evaluation of microbial contaminations is an additional specialist field of Fraunhofer IGB.

Fraunhofer Water Systems Alliance (SysWasser)
Full members: IGB, IOSB, ISI, IST, UMSICHT, IKTS, ISE, IPK, ILT
Associate members: ITWM, IVI, IZFP
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 catchment, infrastructure, and wastewater treatment and adapt them for use in practical applications on a national and international level, taking into consideration relevant social, economic and environmental aspects. 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.

Furthermore, Fraunhofer IGB is working together with numerous Fraunhofer Institutes in bilateral and joint research projects.

HIGHLIGHTS 2010

APPOINTMENTS, PRIZES AND AWARDS

Heike Walles appointed to the German Ethics Council

In June 2010, Professor Heike Walles was appointed member of the German Ethics Council for a period of four years by the President of the Bundestag, Professor Norbert Lammer. The German Ethics Council pursues ethical, societal, scientific, medical and legal questions as well as the foreseeable consequences for individuals and society that arise in connection with research and development, especially in the area of life sciences and their application to humans. The Ethics Council also draws up opinions and recommendations for political and legislative action.

AAA Morphological Sciences Award for Katja Schenke-Layland

In April 2010, Dr. Katja Schenke-Layland received the prestigious Morphological Sciences Award of the American Association of Anatomists (AAA) at the annual Experimental Biology 2010 conference in Anaheim, California, USA. She was awarded this prize for her work in the area of minimally invasive microscopy of extracellular matrix structures within blood vessels and the heart. Her scientific endeavors open up an important new field of research combining anatomy, stem cell biology and tissue engineering technologies.

Poster prize for Katja Schenke-Layland

Dr. Katja Schenke-Layland was also acclaimed "Poster Competition Winner" at the 5th Cardiovascular Healing Symposium on July 10, 2010 in Würzburg. The award-winning poster featured "Niche Microenvironments as Blueprint for Tissue Engineering Applications."

3rd place for Jacqueline Pusch at Elevator Pitches

In the Elevator Pitches ideas competition at the first "Network Value" Fraunhofer symposium on December 7 to 8, 2010, IGB employee Jacqueline Pusch was placed third out of 320 participants on the first day with her idea "Plaster for Intestinal Walls." The plaster is intended to facilitate employing the new, minimally invasive NOTES surgery technique (natural orifice transluminal endoscopic surgery) for operations in the abdominal cavity via the mouth. This would enable doctors performing surgery on internal organs to switch from the risky laparotomy procedure that involves making an incision in the abdominal wall.

At present it is not possible to gain operative access to the abdominal cavity via the stomach or intestinal wall for two reasons. Firstly, suitable endoscopic instruments do not exist.

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And secondly, there is no safe method by which the incision through the stomach or intestinal wall necessary for the operation can be sealed again. Sealing is vital in order to prevent gastric acid and bacteria escaping into the abdominal cavity and causing fatal infections. The simplest solution would be a plaster that could be applied to the incision directly after surgery from the inside – before the instruments have been completely withdrawn via the mouth. Such a plaster could be made of collagenous proteins such as those present in the intestinal matrix and be produced with the aid of the electrospinning technique.

Medical technology innovation competition – IGVT and Fraunhofer IGB's winning project

In its innovation competition to promote medical technology which the German Federal Ministry of Education and Research (BMBF) organized for the twelfth time in 2010, the project "Fully Integrated Lab-on-a-Chip System for Rapid Identification of Fungal Infections in Immunocompromised Patients" in which the Fraunhofer IGB and the Institute for Interfacial Engineering (IGVT) at the University of Stuttgart are involved, was selected as one of the 15 winning projects.

Mold and yeast infections can be life-threatening for patients whose immune systems are compromised by illness or medications, and must be treated as quickly as possible. The conventional standard procedure for diagnosing these pathogens is very time-consuming and error-prone. What is needed is a fast and reliable verification procedure which simultaneously identifies all relevant fungal pathogens and their potential resistance to medication. Regional partners from science and industry and from Lübeck hope to combine complete identification in a microsystem. Coordinated by the Lübeck-based company Euroimmun, this task is being taken on jointly by physicians under the leadership of Prof. Dr. Cornelius Knabbe of the Ruhr-Universität Bochum, researchers under PD Dr. Steffen Rupp at the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB and Dr. Karin Lemuth from the Institute for Interfacial Engineering at the University of Stuttgart, as well as developers under Dr. Karl-Heinz Boven of Reutlinger Multi Channel Systems MCS GmbH and Dr. Peter Rothacher of Robert Bosch GmbH, Gerlingen.

1 *AAA Morphological Sciences Award for Katja Schenke-Layland.*

2 *From left: Dr. Karin Lemuth (IGVT), Dr. Jan Weile (Ruhr-Universität Bochum), Dr. Ulf Steller (Euroimmun, Lübeck), Dr. Markus Cavalar (Euroimmun, Lübeck), RD Peter Hassenbach (BMBF).*

PROMOTING YOUNG TALENTS | EXHIBITIONS

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

Fraunhofer Talent School

At the Fraunhofer Talent School 2010, which took place at the Stuttgart site for the first time in 2009, Dr. Kai Sohn, deputy head of Molecular Biotechnology, again led the workshop "Who Am I, or The Amazing Journey into the Genome." The aim of the workshop 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 graduates showed great enthusiasm about the opportunity to get insights into the work of a scientist and into exciting research topics. Kai Sohn will hold another workshop in 2011 and once again contribute 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 heavily 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 throw open the doors to laboratories and test areas, offices and workshops, where they use practical examples to demonstrate how interesting their work is. 2010 once again saw well over 100 interested participants in Stuttgart, some of whom visited the "Nature's own chemical plant" and "Here's looking at you, kid" information stations at the Fraunhofer IGB. The next Girls' Day will take place on April 14, 2011.
www.izs.fraunhofer.de/schueler-izs/girls-day/

BOGY – vocational and academic careers orientation at academic high schools

30 high school students completed their "BOGY" internships at the Fraunhofer IGB in 2010. 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 vocational occupations in a research institute, such as technical assistant or laboratory technician. The students were introduced to various working groups in the different 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 docu-

mentation of the test results. The internship gives schoolchildren 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/

Checkpoint Future: open day for university students

On November 29, 2010, over 100 science and engineering students from different 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. With the question "Why not into industry straight away?" the participants were shown the different 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/

MiNe-MINT – bioprocess engineering theme day and life sciences research week

The Fraunhofer IGB is a founder member of MiNe-MINT e.V., a network from the Central Neckar region that aims to awaken the interest of schoolchildren in mathematics, IT, the natural sciences and technology. In June, the Fraunhofer IGB together with the Institute of Bioprocess Engineering (IBVT) of the University of Stuttgart and the companies Visenso and LEWA, hosted a themed bioprocess open day, in which 30 schoolchildren took part. As part of the Life Sciences science and research week at the beginning of the school holidays, the IGB offered the participating schoolchildren an insight into the activities of a research institute for a day.
www.mine-mint.de

Renewable raw materials – teacher training

An elementary building block for promoting school education is the training of teachers, especially when they want to get across complex topics in a graphic way and to keep up with developments. The Schools – Chemical Industry Dialog (DSC), an information and communication venture by Baden-Württemberg's chemical associations, offered practicing, student and trainee teachers of the Stuttgart and Tübingen administrative regions the opportunity to find out about current topics in the chemical industry at the 25th Regional Teacher Congress at the on November 10 in Filderstadt. Professor Thomas Hirth gave a highly topical talk entitled "Renewable Raw Materials – an Issue for Schools, Research and Industry."

nano! Technoseum Mannheim

From March 18 to October 3, 2010, the Technoseum, State Museum for Technology and Work in Mannheim hosted the exhibition "nano! Uses and Visions of a New Technology." The exhibition illustrated the beginnings of nanotechnology in the 1980s, explained the scientific fundamentals and also showed the uses of nanotechnology. The numerous exhibits also included the NANOCYTES® model as a joint loan from the Fraunhofer IGB und IGVT. The model shows how molecularly imprinted nanoparticles can function as tiny receptors to bind the active protein insulin and release it in a targeted fashion.

PROJECTS AND PROJECT GROUPS

Successful project conclusion – DEUS 21 closing event in Knittlingen

A closing event was held in Knittlingen on May 18, 2010, to celebrate the conclusion of the Decentralized Urban Water Infrastructure Systems DEUS 21 project. Around 50 invited guests from industry, politics and local government congregated at Knittlingen's historic "Steinhaus" events venue, where they were greeted by director Professor Thomas Hirth. Undersecretary Wilfried Kraus from the German Federal Ministry of Education and Research (BMBF) gave a speech outlining the funding policy goals of the ministry. Professor Walter Trösch followed with a description of the salient features of the DEUS 21 project, while Dipl.-Ing. Marius Mohr, representing the Fraunhofer IGB, and Dr.-Ing. Thomas Hillenbrand, on behalf of the Fraunhofer ISI, presented selected project results. In finishing, Knittlingen's mayor Heinz-Peter Hopp spoke about the importance of the project for the town.

After a snack, it was off to the "Water House" where the entire technology developed during the project is housed. Here the most recent development, a combustion assembly for thermal utilization of the biogas produced during wastewater treatment, was ceremonially activated. Numerous guests took the opportunity of a tour through the Water House to get a look at the experimental facilities. DEUS 21 was funded in two phases by the BMBF. A demonstration plant for a new form of wastewater treatment was constructed in a development area of Knittlingen. The plant is semi-decentralized and the organic contents of the wastewater are digested in a closed bioreactor to produce biogas, which is then utilized thermally. Assured-quality use of rainwater is also demonstrated. The technology developed can be adapted to the requirements of other sites and realized technically there.

Grant letter handed over to the BioCat Project Group in Straubing

The Fraunhofer IGB BioCat Project Group ("Catalytic processes for a sustainable supply of raw materials and energy on the basis of renewable resources") officially commenced its work on August 1, 2009. On February 2, 2010, the president of the government of Lower Bavaria, Heinz Grunwald, handed over the letter of approval for funding to the tune of 5 million euros from the BayernFIT research, innovation, and technology program to Professor Ulrich Buller, chief scientific officer and Executive Board member at the Fraunhofer-Gesellschaft. The ceremonial handover took place at the Straubing Center of Science, where the project group headed by Professor Volker Sieber currently still has its offices and laboratories. Besides the director of the science center, Professor Martin Faulstich, and the Fraunhofer IGB director, Professor Thomas Hirth, local politicians and Dr. Günter Wich from Wacker Chemie AG expressed their appreciation for the support being given to the BioCat project group.

Ground-breaking ceremony at the BioCat Project Group in Straubing

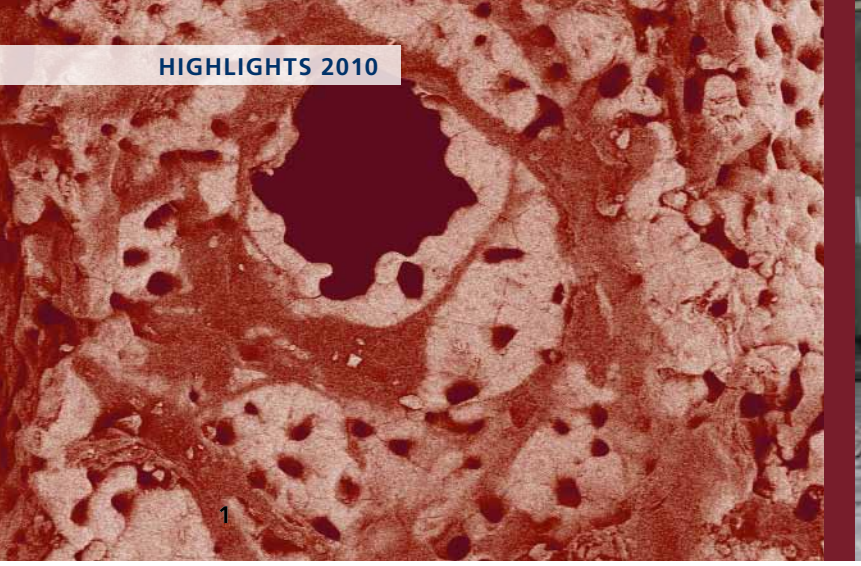
On July 22, 2010, the ground-breaking ceremony took place to mark the construction of a new laboratory building for the BioCat Project Group in Straubing. Just in time for the ceremony, the Chief Mayor of Straubing, Markus Pannermayr, brought the construction permit along. Even the most prominent guest, Bavaria's State Premier Horst Seehofer had a go with a spade himself. Fraunhofer Executive Board member Professor Alfred Gossner was delighted that so many guests from government, science and politics had turned up and with the fact that with the construction of the laboratory building, the Fraunhofer-Gesellschaft is returning to the birth place of Joseph von Fraunhofer, after whom the Fraunhofer-Gesellschaft was named. The lab building will offer space for 12 members of staff and consist of two open-plan labs, one for chemical and one for biological activities. The building is intended to be used for the development of new catalytic processes for the material use of renewable raw materials, which will contribute to securing the supply of basic chemicals to the chemical industry. The scientific activities will be headed by Professor Volker Sieber.

Ground-breaking ceremony at the Fraunhofer CBP in Leuna

A second ground-breaking ceremony took place amid snow and ice on December 8, 2010, in Leuna, initiating construction of the Fraunhofer Center for Chemical-Biotechnological Processes CBP. Professor Thomas Hirth gave a welcome address to some 90 invited guests from politics, industry and research in which he recalled the origins of the concept and discussions with many of the day's participants on the center's financing and realization. He emphasized the future role of the Fraunhofer CBP in closing the gap between laboratory and industrial implementation in the use of renewable raw materials. This represented an important step on the way to a bioeconomy.

The *Land* Saxony-Anhalt, which is providing a major part of the financing of the Fraunhofer CBP, as well as the start-up financing for the project group, was represented by its Finance Minister and Deputy State Premier, Jens Bullerjahn, and its Minister of Employment and Economic Affairs Dr. Reiner Haseloff. The latter handed over the letter of approval to the Fraunhofer Executive Board member Dr. Alfred Gossner and to Professor Thomas Hirth. Further speakers were representatives of the German Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) and the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU), who used their words of greeting to describe the Fraunhofer CBP's prospects and wished it success on its chosen path. Andreas Hiltermann, managing director of the site management company InfraLeuna GmbH, expressed his satisfaction that Leuna is developing into an integrated bio- and petrochemical site.

The cut of the first sod launched the construction of a new building with over 2000 square meters space for plant, pilot plants, laboratories, offices and storage facilities. From the summer of 2012, modular facilities will be available where partners from research and industry can work on developing the material use of renewable feedstocks in industrial scale, culminating in market-ready products.



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 proposals in the area of Health, Environment, Energy, Nanosciences, Nanotechnologies, Materials & New Production Technologies (NMP) plus the Knowledge-based Bio-economy (KBBE), but also the calls specifically targeted at small and medium-sized enterprises (SMEs).

Vascubone

The EU "VascuBone" project commenced in January 2010 under the coordination of Professor Heike Walles. The consortium involving 15 partners from research and industry is developing a toolbox for regenerative therapies for several types of bone defects in the jaw, in long bones or in avascular necrosis of the femoral head. The toolbox will contain a number of biocompatible biomaterials as well as different cell types, approved growth factors, technologies for material modification, simulation processes and analytical processes such as in vivo diagnostics using molecular imaging (MRI and PET/CT) which can be combined according to specific medical need. VascuBone is being funded to the tune of 11.9 million euros for a period of five years as part of the FP7 Health Programme.
www.vascubone.eu

In 2010 once again, the Fraunhofer IGB positioned itself as a competent research partner for small and medium-sized enterprises. In total, seven projects from the EU program "Research for the Benefit of Small and Medium-Sized Enterprises" in which the Fraunhofer IGB is involved were positively evaluated and put forward for funding. The program supports European consortia of innovative SMEs in solving technical problems.

Cleanleachate

Landfill leachate wastewater arises as the result of rainwater seeping through landfill sites where the solid waste decomposes in an uncontrolled manner. The liquid flow contains considerable concentrations of substances that are harmful to health and must therefore be treated before entering the environment. This project is developing an oxidative treatment process (AOP) using a novel electrolysis cell optimized for landfill leachate.
www.cleanleachate.eu

PreserveWine

The Fraunhofer IGB's role in this project is to develop a continuous process for wine stabilization on the basis of pressure change technology (PCT). The objective is to minimize or avoid the addition of chemical preservatives such as sulfur dioxide.
www.preservewine.eu

MicroMilk

The goal of this European consortium project is to improve the nutritional and sensory characteristics of milk and dairy products after processing through quicker and more regular heating. A further objective is improved shelf life of milk; to this end Fraunhofer IGB is developing a novel concept for milk pasteurization based on microwave technology.
www.micromilk.eu

SalinityScan

In this EU project, the Fraunhofer IGB is involved as part of a trans-European consortium in developing a novel flow measuring system. The measuring system is intended to facilitate the exact determination of the volume flows of multi-phase mixtures of oil, water and gas typical of offshore oil production.
www.salinityscan.com

WaterPlasma

Currently available wastewater treatments based on physico-chemical and biological processes are limited, since they are unable to efficiently remove recalcitrant xenobiotic substances. To be able to comply with EU regulations in the future the Waterplasma project aims at developing an innovative decontamination process based on a one atmosphere uniform glow discharge ("OAUGD") plasma reactor that makes it possible to eliminate recalcitrant molecules without the need of chemicals and filters or without resulting in residual materials.
www.waterplasma.eu

FurnitReuse

In this project, old furniture together with plastics from desktop computers, computer screens and peripheral devices is to be recycled by means of an innovative, environmentally sound technology to produce a unique composite material. This composite material can be used, for example, in the transport industry.

DryCheck

This project addresses the development and implementation of a multisensor-based tool to monitor and control the automated drying of sausages. This sensor technology is intended to guarantee consistent quality, homogeneity and consistency of the products. The Fraunhofer IGB is contributing its competence in the field of drying.

SEVENTH FRAMEWORK PROGRAMME

Fraunhofer-Truck in Brussels

Since the 60th anniversary of the Fraunhofer-Gesellschaft in March 2009, the exhibition truck has been touring through Germany and showing which Fraunhofer technologies from the areas of medicine, the environment, safety and security, communications and mobility can be integrated in our daily lives. In April 2010, the truck stopped in Brussels in the vicinity of the European Parliament in order to bring the Fraunhofer world closer to the employees of the various EU organizations – and, of course, all interested visitors. In the field of health, the skin model generated from cultivated human cells shows whether and in what form chemicals have a toxic effect. With regard to the environment, the focus is on the topic of water. Research at the Fraunhofer IGB has identified solutions for developing sources of drinking water that at the same time have a reduced impact on nature.

The president of the Fraunhofer-Gesellschaft, Professor Bullinger, used the opportunity to present the whole spectrum of Fraunhofer research topics to the EU Commissioner for Research, Innovation and Science, Máire Geoghegan-Quinn.

Brazil

In April 2010, at the official launch event of the German-Brazilian Year of Science, Technology and Innovation in São Paolo, the invited guests included scientists from the Fraunhofer IGB. As an emerging power, Brazil was not only at the center of international interest but also once again in the focus of Fraunhofer IGB activities. The year of events is jointly funded by German's Federal Ministry of Education and Research (BMBF) and by Brazil's Ministry of External Relations and its Ministry of Science and Technology.

With the support of the Fraunhofer contact office in São Paulo, the Fraunhofer IGB took part in Brazil's largest science fair for the first time. This fair is organized by the Brazilian Society for the Advancement of the Sciences (Sociedade Brasileira para o Progresso da Ciência, SBPC) and held in Natal, Rio Grande do Norte. At the Baden-Württemberg International joint "Research in Germany" exhibition stand – the only international booth – the institute presented itself to an interested expert audience.

Philip Riegger, one of our junior researchers, spent three months studying water treatment at UNIMEP (Universidade Metodista de Piracicaba), a long-term university partner of the IGB, where he was under the supervision of Professor Klaus Schützer and Natanael Macedo Jardim. A visit from his German supervisors from the Fraunhofer IGB, Dr. Iris Trick and Birgit Haller, was used as an opportunity to intensify long-standing contacts and renew an existing memorandum of understanding.

As a result of current project work in the city of Americana (funded on the German side by the Federal Environment Ministry, BMU), Dr. Werner Sternad was invited to give lectures on the sustainable use of biogas. The presentations were held, notably, at the 2nd International Congress for Environmental Technology at the FIEMA in Bento Gonçalves and at the Symposium for Renewable Energies and Energy Efficiency which was organized by the German House of Science and Innovation in São Paulo.

For the second half of the bilateral year of science, a joint workshop is planned for March 2011 with the cooperation partner Instituto de Pesquisas Technológicas IPT in São Paulo. This is intended to push cooperation in the areas of nanotechnology and health.

South Korea

The first of both joint expert workshops at the Pusan National University in Busan took place in June. The results of the current project to improve the diagnosis of sepsis were discussed, as were also new ideas for projects. The Fraunhofer IGB research team was accompanied to this workshop by its commercial partner EMC microcollections from Tübingen. The return visit

of a delegation from our Korean partners took place in December, with a follow-up workshop at the IGB. During this intensive workshop future research topics were discussed against the background of bilateral funding calls and further new project applications were sketched out. In addition, a coordination talk took place between the two institute heads Professor Thomas Hirth and Professor An Won Gun. A visit to EMC microcollections rounded off the successful meeting, which was given significant organizational support by the BMBF's international office.

Portugal

As part of our mission to initiate new contacts with industrial and research partners in Europe and to intensify existing ones, the Fraunhofer IGB's business development team recruited Margarida Prado on secondment from the Instituto Gulbenkian de Ciéncia (IGC), where she works on technology transfer. During her 12-month internship the cell biologist will focus on establishing bilateral contacts with mainly Portuguese but also Spanish and French partners. Through her experience in the patents field, she will support the patent strategy process in place at the Fraunhofer IGB. Her placement is financed in part by the Portuguese Fundação para a Ciência e a Tecnologia FCT.

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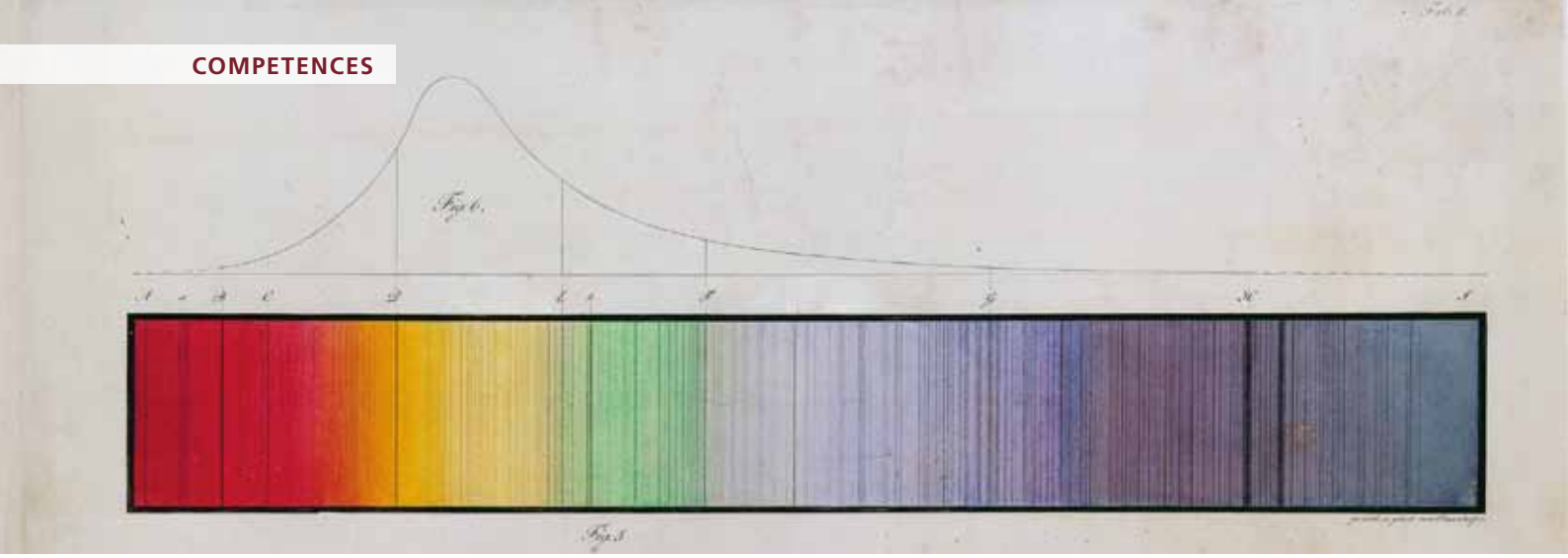


THE FRAUNHOFER-GESELLSCHAFT

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.

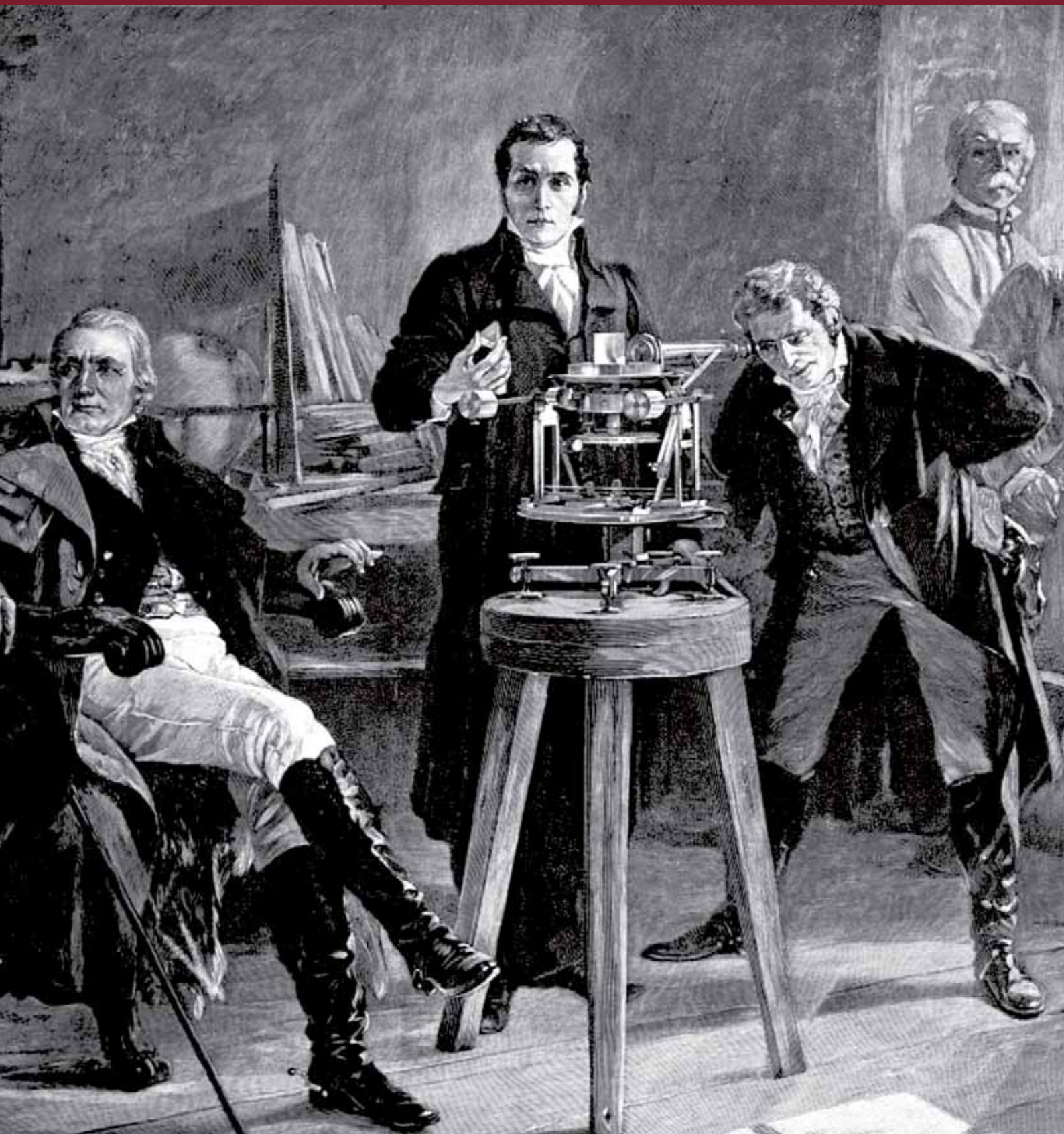
At present, the Fraunhofer-Gesellschaft maintains more than 80 research units in Germany, including 60 Fraunhofer Institutes. The majority of the more than 18,000 staff are qualified scientists and engineers, who work with an annual research budget of €1.65 billion. Of this sum, more than €1.40 billion 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.

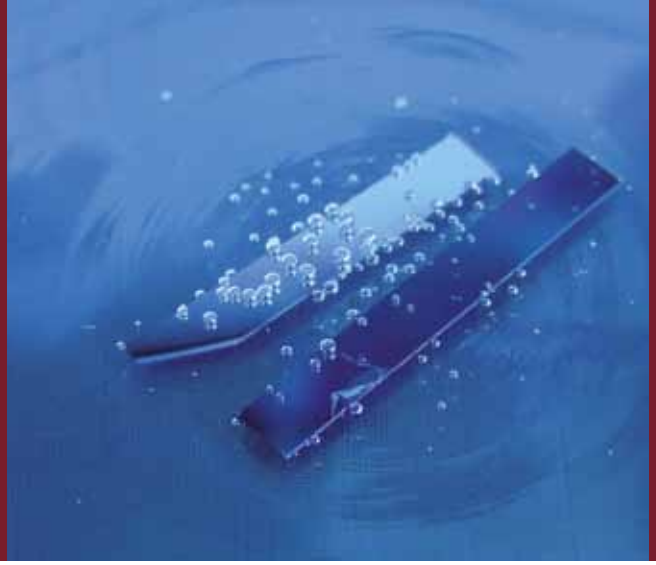
Affiliated international research centers and representative offices provide contact with the regions of greatest importance to present and future scientific progress and economic development.

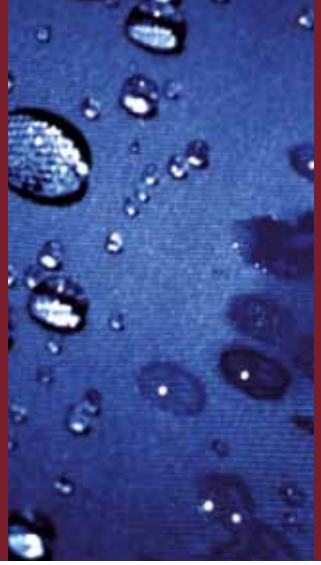
With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits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

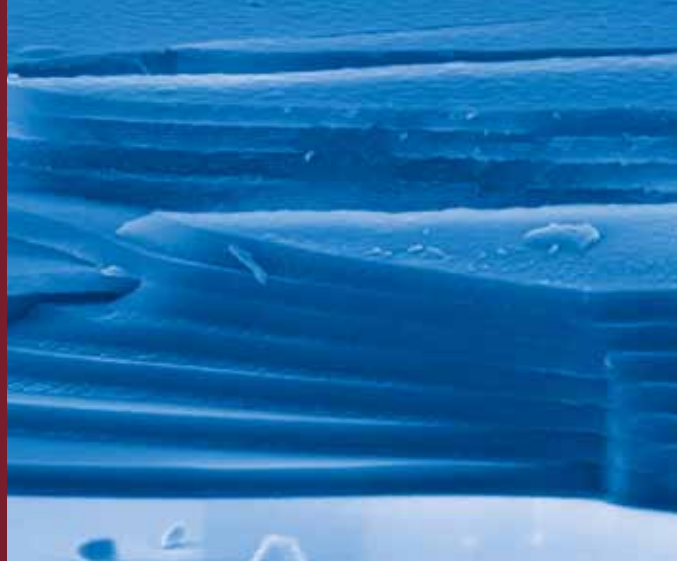
- Deposition of thin films by chemical and physical means, i.e. chemical or physical vapor deposition
- Deposition of nanoparticles using various polymerization methods
- Production of separation membranes by sol-gel processes and consecutive annealing
- Deposition of thin layers by layer-by-layer (LbL) 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 and digital optical 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-SIMS (matrix-assisted laser desorption-ionization time-of-flight mass spectroscopy)
- Determination of elemental composition, using electron spectroscopy, for chemical analyses (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 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
- Development of 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
- Development of 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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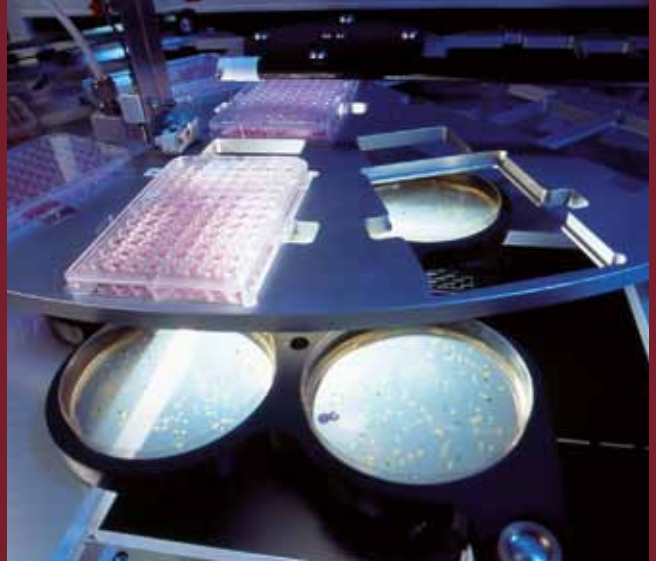
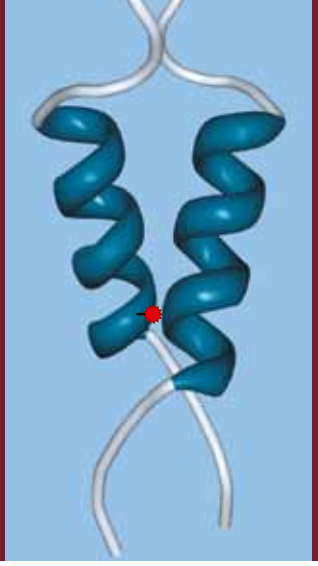


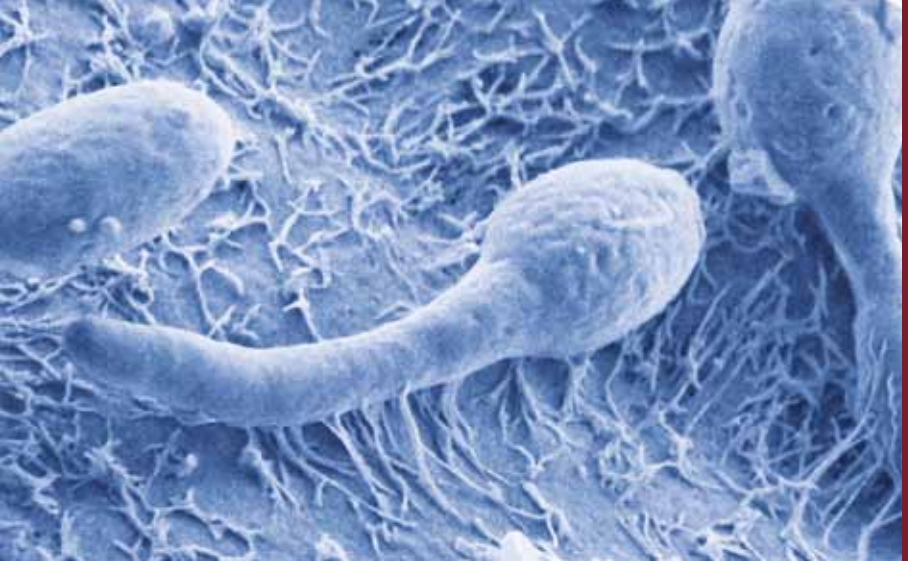


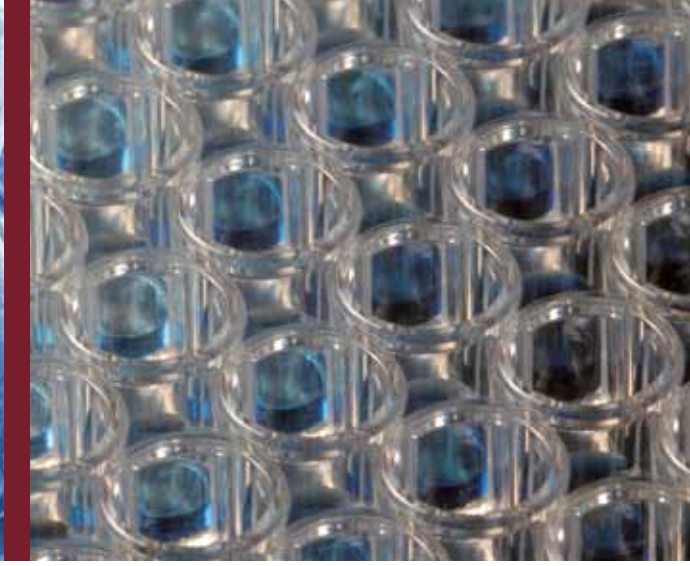
MOLECULAR BIOTECHNOLOGY

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 can be applied as well as personalized medicine may become reality optimized for individual groups of the population. 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 m^3 scale. We also cooperate with the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM on developing processes for manufacturing pharmaceutical proteins, up to GMP-compliant production of biologicals for clinical phases of pharmaceutical development.

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
- 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-GLP)
- 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.

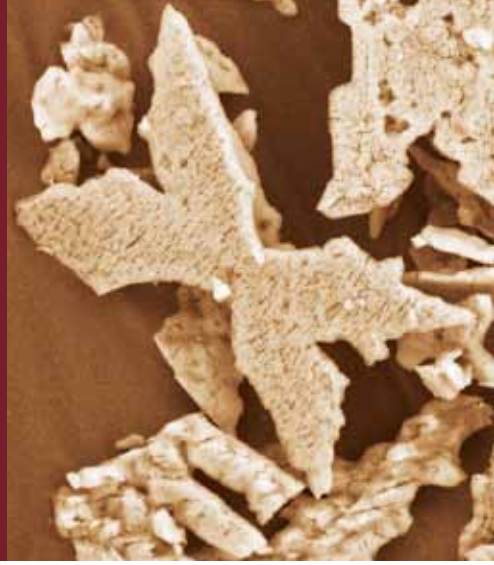
The current main themes of focus are:

- 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 criterion in our R&D activity is sustainability. We define this principally in terms of the minimization or substitution of material flows – 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 heat to be made available for industrial use decoupled in time and space from its source. Potential applications are drying processes in production, the 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), ANSYS 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 flocking and oxidation properties of water
- Pilot plants for advanced oxidation processes (electrophysical precipitation, ozone, hydrogen peroxide, UV radiation, ultrasound, anodal oxidation (direct/indirect), cathode reactions) including disinfection
- 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 2008 SP4.0, CST Microwave Studio 2009, ANSYS Version 11.0: Multiphysics™ and CFX®, COMSOL MultiPhysics® Version 3.5, Design-Expert 7 Workstation, Mechanical Desktop 2004 DX (AutoCAD 2004)

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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 for the sustainable production of organic bulk chemicals and the generation of energy from organic raw materials, residuals and waste products. Ideally, this can be coupled with the recovery of inorganic by-products for reuse as fertilizers, and, where possible, the treatment of intrinsic process water. We generally use anaerobic methods to treat organic residuals such as biodegradable waste or sewage sludge, as these allow commercially viable generation of biogas as a regenerative source of energy. The use of specific anaerobic microorganisms also enables new approaches in communal and industrial wastewater purification, as well as the realization of innovative prototype wastewater purification plants that are both semi-decentralized and sustainable. The 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 algae. Natural and sustainable, it provides a large number of basic chemical materials and an easily digestable biomass.

The core competence of the department is developing robust and ecologically efficient biotechnological processes for the production of basic chemicals for use either as raw materials or as sources of energy (methane, ethanol, methanol).

We understand "robust bioprocesses" as processes that are resistant to contaminations and thus can be operated continuously under aseptic (non-sterile) conditions. The key to these processes is always microbiological fundamentals such as the growth and degradation kinetics of the different organisms concerned. Hereby, 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
- Psychrophilic, mesophilic and thermophilic bioprocesses
- Anaerobic digestion technology for isolating and maintaining new strains
- Cultivation of microalgae in flat-panel airlift photobioreactors
- Microbiological characterization of surfaces using standard processes and application-oriented processes, including development of testing procedures



- Development of real-time processes for monitoring water systems for impurities
- Modeling of processes and simulation of process lines
- Scale-up of stable processes 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 energy, waste, and water management

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 lower water requirements and the possibility of a 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 system concepts for bioenergy management at regional level
- 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 media involved in processing

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 m^3-scale to generate basic engineering data *in situ* for the planning of innovative demonstration plants
- Equipment for handling pathogenic organisms and the corresponding approvals

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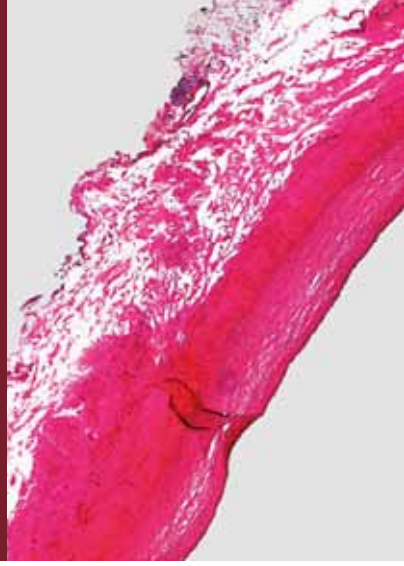

CELL AND TISSUE ENGINEERING

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 in the process of 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 European Union 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, in 2010 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
  - **Bio**logical **vas**cularized **sc**affold, BioVaSc
  - 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 micro-dissection 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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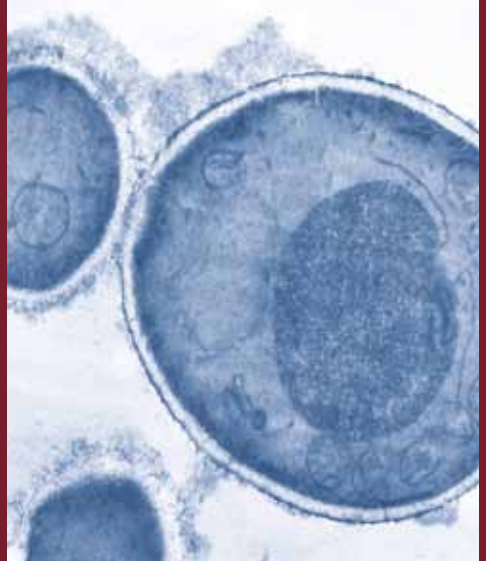
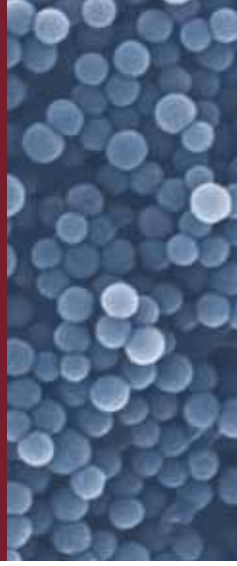




INSTITUTE FOR INTERFACIAL ENGINEERING IGVT

The Institute for Interfacial Engineering IGVT is headed by Professor Thomas Hirth and belongs to the Faculty of Energy Technology, Process Engineering and Biological Engineering of the University of Stuttgart (Faculty 4). At year end the institute had a staff of 72 and an annual research budget of around 2.4 million euros. Most of the institute's activities are currently carried out on the premises of the Fraunhofer IGB, which is a close cooperation partner. The IGVT also uses laboratories, pilot plant facilities, seminary rooms 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 chemical, physical-chemical, physical, biochemical, cell-biological and biotechnological research.

The close cooperation with the various Fraunhofer IGB groups facilitates a continuity of IGVT projects from basic research to application, in the form of research funding received from the German Research Foundation (DFG), the German Federal Ministry of Education and Research (BMBF), the German Federal Foundation for the Environment (DBU), the European Union, the *Land* of Baden-Württemberg, various other foundations and industry. At the IGVT we combine fundamental academic research with application-oriented approaches by incorporating ideas and impulses from the practice.

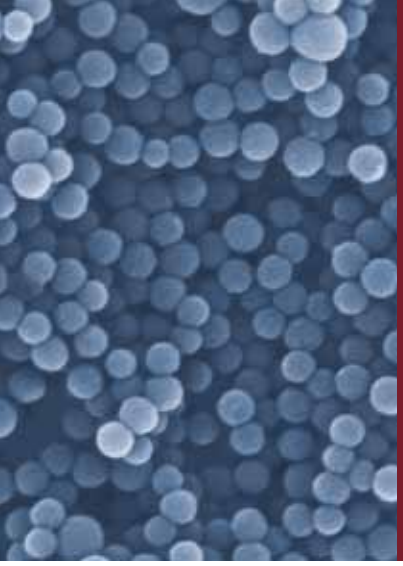
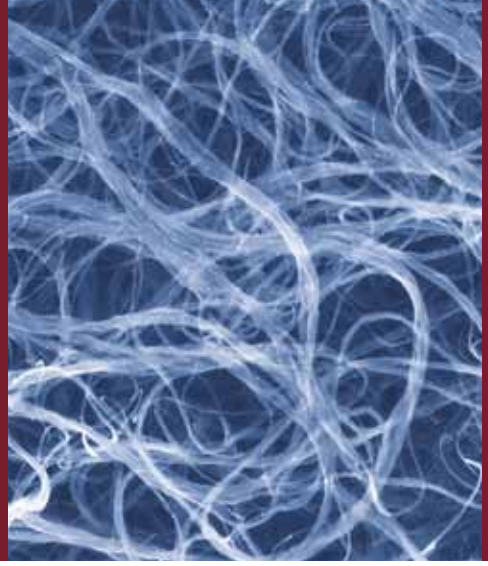
Research and teaching

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 chemical, physical-chemical, biochemical, molecular and cell-biological fundamentals.

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

Biological Interfacial Engineering

- Host-pathogen interactions
- Interactions between microorganisms and surfaces
- Microarray technology for diagnostics and biomedical research
- Screening for enzymes and microorganisms, as well as process development for industrial (white) biotechnology


Chemical Interfacial Engineering

- Biomaterials
- Biomimetic functional layers for medical and bio-technological applications
- Core-shell nano- and microparticles, with a focus on biomimetic shells
- Molecular recognition
- Nano- and microstructured (bio)functional surfaces
- Radical formation and reaction of two-component mixtures in energetic fields

Medical Interfacial Engineering

- Autologous transplants and cell therapies
- Generation of vascularized tissue
- Organoid human test systems as a substitute for animal experiments
- Tissue-specific bioreactors development
- 3-D tissue engineering
- Toxicity studies using organoid tissue models

Physical Interfacial Engineering

- Adsorption/desorption processes for heat storage and dehumidification
- Electrochemically stimulated crystallization in precipitation reactions
- Particle suspensions and emulsions in electric fields
- Plasma diagnostics, interface characterization and physical-chemical modeling building
- Process development for the dispersion of nanomaterials

Environmental Interfacial Engineering

- Characterization of products dried with superheated steam
- Development of dynamic membrane processes for cell retention and water hygienization
- Development of novel membranes and membrane processes for water treatment
- Membranes for gas separation and fuel cells
- Production of valuable products from microalgae in photobioreactors
- Recycling of inorganic nutrients as crystals
- Specific adsorbers for elimination of micro-pollutants from water and exhaust air flows

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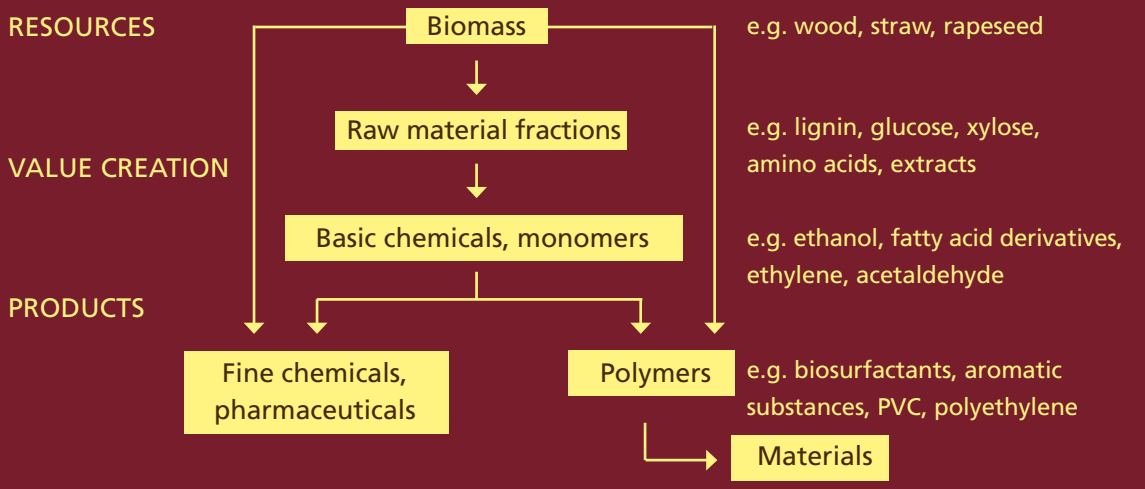
PROJECT GROUP BIOCAT

The focus of the Project Group "Catalytic Processes for a Sustainable Supply of Raw Materials and Energy on the Basis of Renewable Resources" is on developing catalytic processes and new products for a sustainable supply with raw materials and energy. The project group employs key technologies from the fields of chemical catalysis and white biotechnology as well as using a combination of chemical and biocatalysis in the material utilization of biomass and CO_2. These approaches also give rise to new methods for developing (bio)catalysts, which are then utilized here. 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, the aim is to e.g. produce monomers for conductive polymers or, based on plant oils and fatty acids, synthesize functionalized carboxylic acids and bio-based surfactants. Here, the objective is to achieve optimum added value in the transformation of the biomass raw material into the bio-based end product.

Apart from expertise in biotechnology (enzyme technology, fermentations, screening of biocatalysts) and chemistry (organic synthesis, homogeneous catalysis, analytics), the BioCat Project Group, 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.

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 CO_2 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. To this end, the group is dedicated to developing innovative chemical and biocatalytic processes for the material utilization of renewable resources, and above all, to finding ways of combining chemical and biotechnological methods that will allow optimal exploitation of the material variety of plant-derived biomass.

The BioCat Project Group hopes to combine bio- and chemical catalysis in cooperative projects with 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

- Screening of bio- and chemical catalysts
- Optimization of enzymes by enzyme engineering and enzyme immobilization
- 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
- High resolution NMR spectroscopy (400 MHz) for elucidation of molecular structure, reaction kinetics, deep temperature analytics, e.g. 1D ^{1}H-/^{19}F-/^{13}C-/^{31}P-/^{15}N-measurements and 2D applications including development of methods

Infrastructure and technical equipment

- Autoclave unit with 4 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
- Several GC-MS, LC-MS and HPLC modules for analysis
- 400 MHz NMR spectrometer

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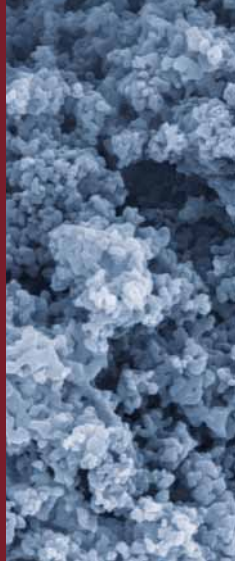


FRAUNHOFER CENTER FOR CHEMICAL-BIOTECHNOLOGICAL PROCESSES CBP

The new Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna, central Germany, will close the gap between the lab and industrial implementation. By making infrastructure and plant (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 will be built under the coordination of the Fraunhofer IGB and ICT at the Leuna chemical site in Saxony-Anhalt, in close cooperation with InfraLeuna GmbH, owner and operator of the infrastructure facilities at the site. The Fraunhofer CBP 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 ground-breaking ceremony took place on December 8, 2010, ushering in the start of construction of the new Fraunhofer center.

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:

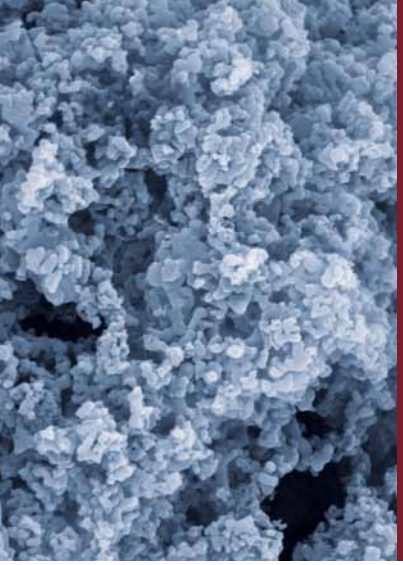
- Functionalization of vegetable oils – epoxidation and ω-functionalization
- Pulping of lignocellulose and separation of its components
- Bio-based alcohols and olefins
- Development of new technical enzymes
- Microalgae as a source for functional ingredients and energy carriers
- Use of residual biomass by means of fermentation

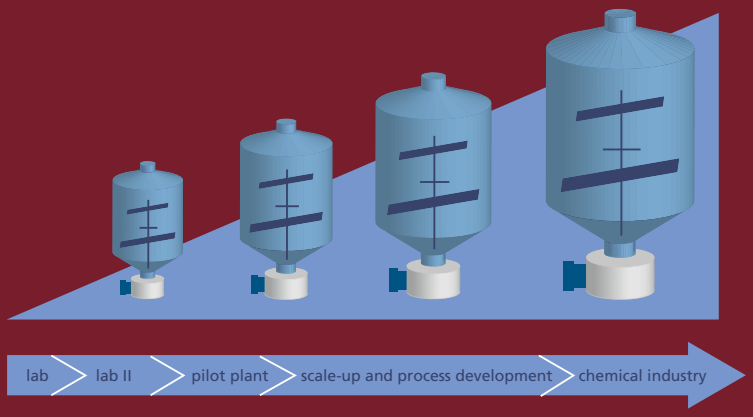
An essential element of the activities of the Fraunhofer CBP will be the focus on the sustainability of processes and procedures along the complete value chain creating products based on renewable resources. The goal is to achieve a cascading material-energetic utilization of as many biomass plant components as possible, on the lines of a "biorefinery".

Thus process development will focus on the following aspects:

- Exploiting the carbon synthesis potential provided by nature
- The energy and resource efficiency of the processes developed
- Minimizing waste streams
- Reducing CO_2 emissions
- Utilization of 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 in particular frequently do not have the independent resources 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 to be commissioned mid 2012, will provide modular process capacities up to 10 m^3 and continuous plants up to 100 l/h, including high pressure processes 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 ranging from 10/100/1000 up to 10 000 l and downstream processing of the fermentation products
- Continuous gas phase reactions of up to 10 l/h
- Continuous liquid phase reactions of up to 100 l/h at temperatures of up to 700 °C and 250 bar
- Mechanical and thermal separation processes
- Pulping and component separation of lignocellulose using organic solvents, with a capacity of 1 metric ton/week
- Containers up to 500 l volume for enzymatic hydrolysis of polysaccharides

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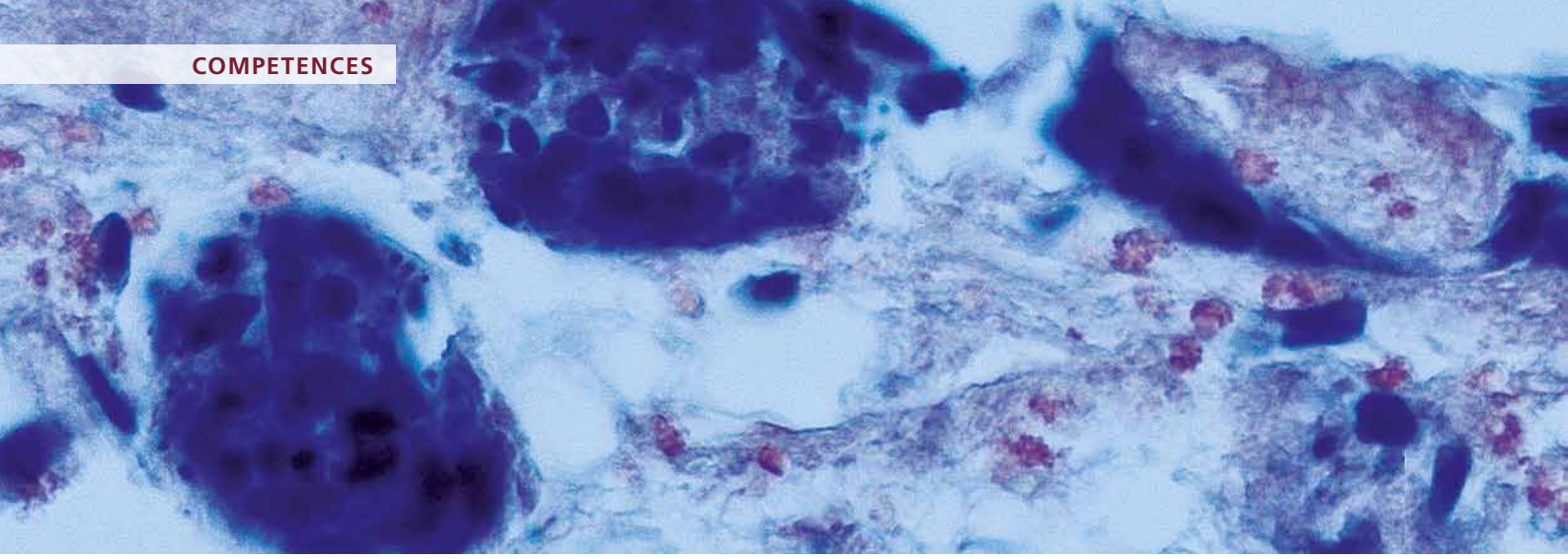


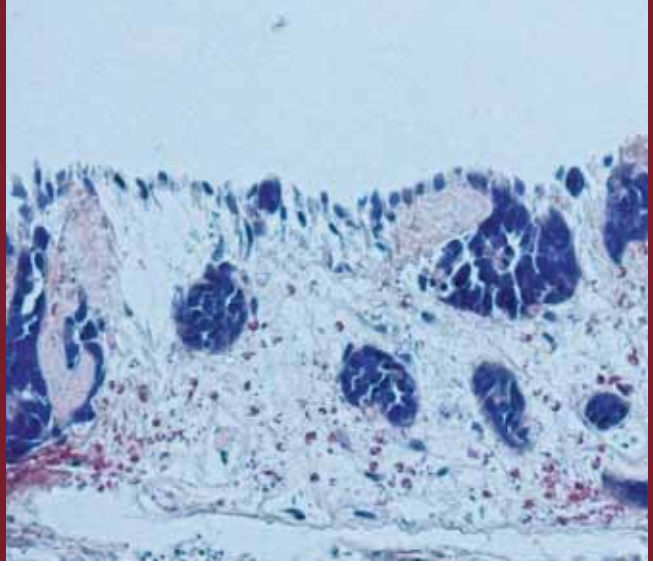
PROJECT GROUP ONCOLOGY

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, microdissection system, Raman spectroscopy

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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 interplay 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 (advanced therapy medicinal products, ATMPs). The Fraunhofer IGB maps the complete value-added chain up to GMP-compliant manufacturing of ATMPs. In 2011 we plan 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 outset up to preclinical tests. To promote the role of regenerative medicine in public health, we are developing a GMP-conform plant for the standardized, automated manufacture of skin by means of an *in vitro* process in a joint Fraunhofer research project financed by the Fraunhofer Future Foundation.

Both bacterial and fungal infectious diseases are again on the increase in industrial nations, making new scientific strategies to combat infections or avoid sepsis essential. Based on its own patents, the Fraunhofer IGB has developed various array technologies and transcriptome analysis methods, as well as human tissue models, and is therefore in a position to research 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 key issue, thanks to the interdisciplinary orientation 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 optimization of technical processes in food manufacturing, e.g. in order to avoid microbial contamination, or through the development of processing techniques and methods that are kind to the product, in order to minimize the loss of valuable nutrients such as vitamins.

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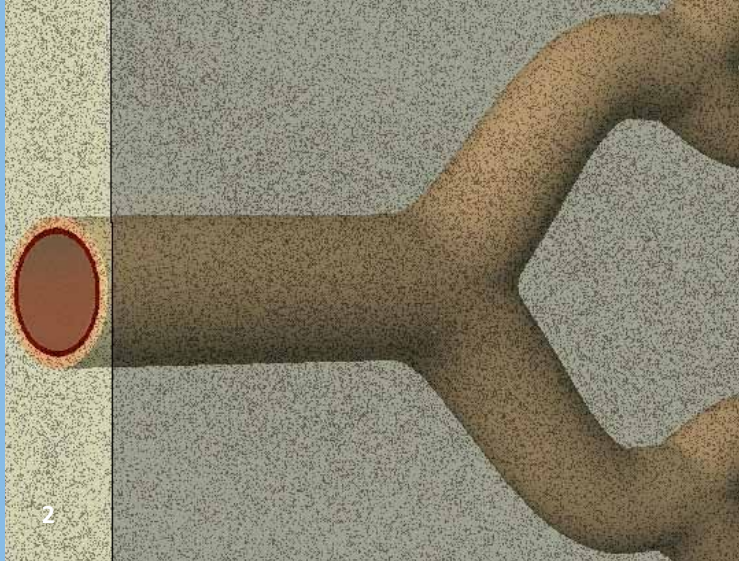


2

ARTIFICIAL BLOOD VESSEL SYSTEMS – THE KEY CHALLENGE OF *IN VITRO* TISSUES

Dr. rer. nat. Petra Kluger, Dr. rer. nat. Kirsten Borchers, Dr. rer. nat. Christian Schuh

The aim in tissue engineering is to create functional tissues and organs *in vitro* and to use them as transplants or *in vitro* test systems. The generation of larger tissue constructs has been limited due to the lack of a proper nutrient supply throughout the tissue via a vascular system. As part of a Fraunhofer research project, a consortium of the five Fraunhofer Institutes IAP, IGB, ILT, IPA and IWM have joined together to accomplish the goal of developing an artificial blood vessel system.

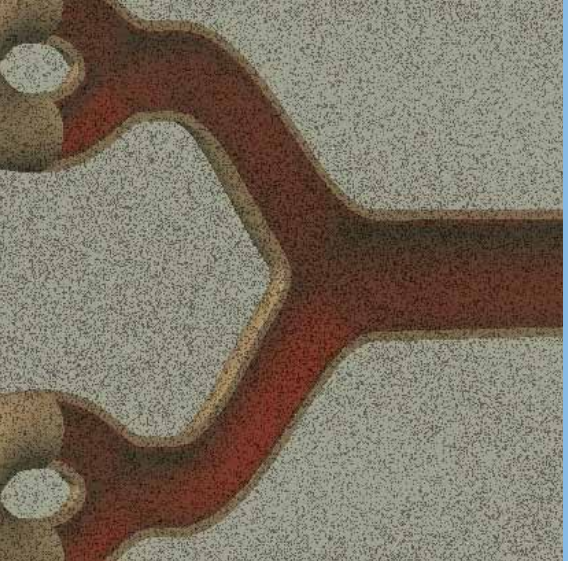
With rapid prototyping and "biologization" to artificial blood vessels

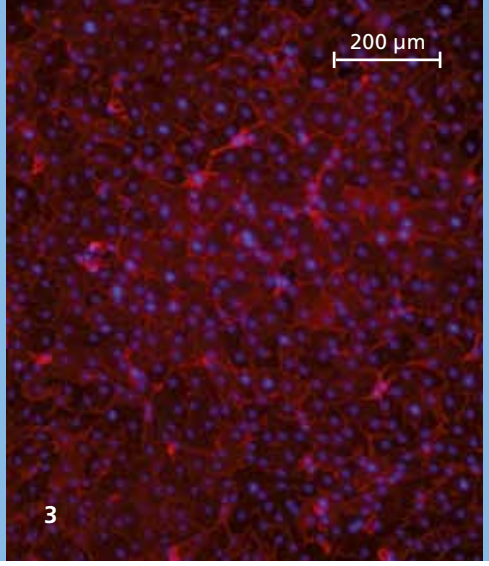
The combination of 3D inkjet printing technology and two-photon polymerization will enable the production of branched vessels smaller than 1 mm in diameter. The combination of the two technologies required the creation of special inks which were developed under the direction of the Fraunhofer IAP. They are based on a modular system utilizing different monomer and polymer components and can be customized for materials and their elastic properties. The focus of the Fraunhofer IGB is the biologization of synthetic tubular structures into biomimetic vascular systems. In order to do this, endothelial cells must be coated onto the synthetic structures in the same manner in which they coat blood vessels in the body. The first step towards this requires the biofunctionalization of the artificial material.

Biofunctionalization of materials

Synthetic surfaces are functionalized with modified biopolymers (such as heparin), growth factors (such as vascular endothelial growth factor, VEGF) and specific anchoring proteins for cells (e.g. the peptide sequence arginine-glycine-aspartic acid, RGD), which allow the colonization of the endothelial cells into the materials. The formation of a confluent cell sheet on the synthetic surface can be achieved by the binding of modified heparin and RGD. Additionally, the thrombogenicity of the synthetic material may be significantly reduced.

As an alternative to the biofunctionalization step, the Fraunhofer IGB is developing hybrid materials from synthetic materials and biological components for a direct, one-step construction of biofunctional artificial vessels. For this purpose, we have modified biopolymers with polymerizable groups allowing their incorporation into the ink-formulation for the rapid-prototyping step. In doing so, the material contains covalently attached biomolecules, which improves an interaction with human cells.





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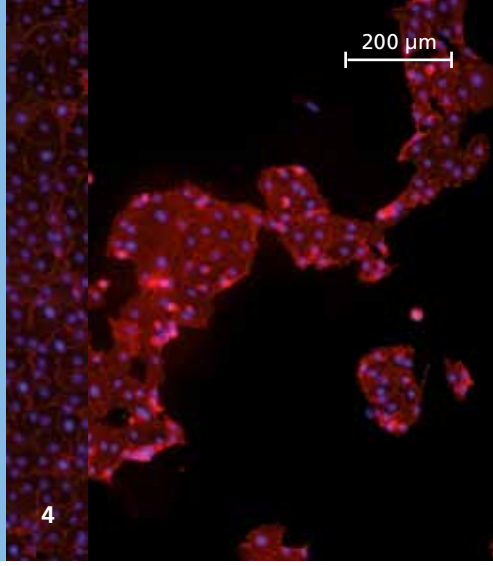

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Perspective: bioreactor for bio functional artificial blood vessels

The formation of a functional endothelium is essential for the biofunctionality of artificial blood vessels. Our goal is to completely cover the inner most layers of the tubes with endothelial cells. An essential step for the culture of functional endothelial cells is the replication of conditions in the body. For this purpose, the Fraunhofer IGB has developed a special bioreactor system in which the artificial vascular structures can be populated with endothelial cells through dynamic culture.

1 *A polymer tube that can be used as an artificial blood vessel or for the supply of in vitro tissue cultures.*

2 *Bio-inspired vascular network in a cell culture matrix for use in tissue engineering (CAD, © Fraunhofer IPA).*

3 *Closed endothelial cell layer on biofunctionalized synthetic material.*

4 *For comparison, the significantly lower cell growth on uncoated polymer.*

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Funding

We would like to thank the Fraunhofer-Gesellschaft for financial support of the project "Establishment of a bio-inspired vascular system for transplants via rapid prototyping utilizing an inkjet printer and multi-photon polymerization (BioRap)" within the MAVO (market-driven prospective research) program.

Project partners

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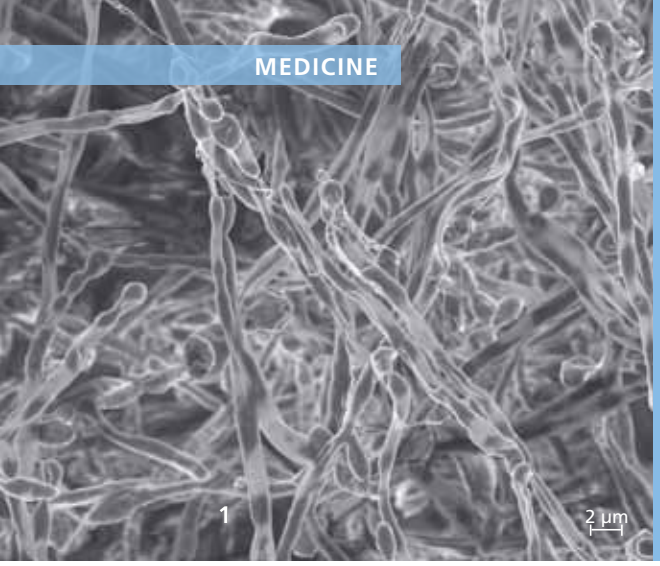
Fraunhofer Institute for Manufacturing Engineering and Automation IPA, Stuttgart, Germany
Fraunhofer Institute for Mechanics of Materials IWM, Freiburg, Germany



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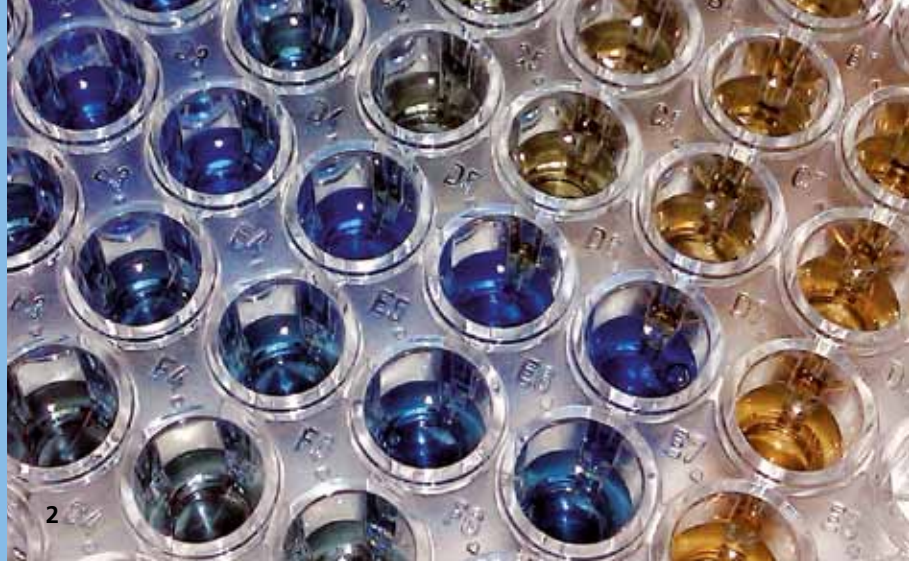

2

QUANTITATIVE PROTEOMICS IN ELUCIDATION OF PATHOGENIC MECHANISMS

Dipl.-Biol. Frauke Purschke, Dr. rer. nat. Ekkehard Hiller

Systemic mycoses, invasive fungal infections, for example with *Candida albicans* (Fig. 1), are frequently occurring infections – particularly in basic haematological-oncological diseases, neutropenia, AIDS, in patients after major surgical interventions, or during chemotherapy or also in preterm neonates. They can often have fatal effects since only limited diagnostic and therapeutic options exist for an effective treatment of the fungal infection to date.

Pathogenic mechanisms

The analysis of the interaction of the fungus with its environment is of particular importance for our understanding of the underlying mechanisms of pathogenicity and the development of new fungicidally active substances. Proteins, which participate in these interactions, are found not only in the cell wall, but can also be secreted by the cells into the external fungal environment. These secreted proteins, as the so-called secretome, represent a section of the organism's proteome, i.e. of the entirety of all the proteins of an organism. They can have direct influences on the host's cells or tissue if, for example, specific proteases are involved in processes such as protein degradation.

Protein identification and quantification

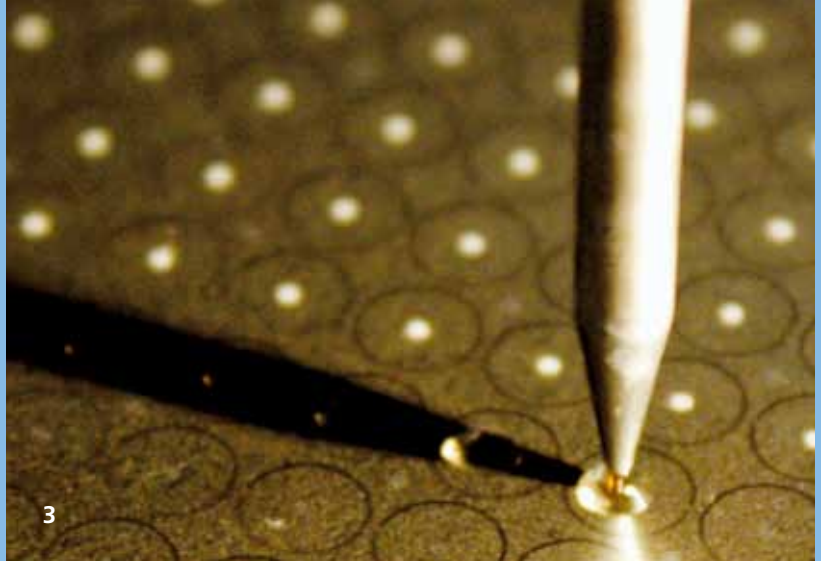
An organism's proteome is subjected to continuous compositional changes. In order to reduce the complexity of a proteome, it is customarily separated into a number of fractions.

In this context, for example two-dimensional gel electrophoresis (2D PAGE) can be used to separate protein extracts of defined concentration (Fig. 2) in accordance with their isoelectric point and the molecular mass. The proteins are then detected by staining and quantified in the gel. The identification of the proteins is subsequently performed using mass spectrometry (MS) (Figs. 3, 4).

Depending on the complexity of the protein mixture, it is possible to quantify the proteins parallel to the mass spectrometric identification. Markers can be used to label the samples individually. Therefore, molecules of characteristic masses are added to the peptides prepared from proteins by proteolytic cleavage. During the MS measurement of numerous samples marked with different molecules, a relative quantification of the peptides from different samples can be performed (Fig. 5). This allows conclusions about the amount of the respective proteins in the samples.

Host-pathogen interaction

The complex biological processes of the host-pathogen interaction of *Candida albicans* are investigated at the Fraunhofer IGB with the aid of differential proteome analyses using 2D PAGE or quantitative mass spectrometry. In this context, we simulate the infection with *Candida albicans* on human epithelial tissues *in vitro*. The differential protein expression analysis of the cytosol shows an adaptive response to nutritional and iron deficiencies as well as to osmotic and oxidative stresses. In addition, there are indications of a restructuring of *C. albicans'* cell surface.



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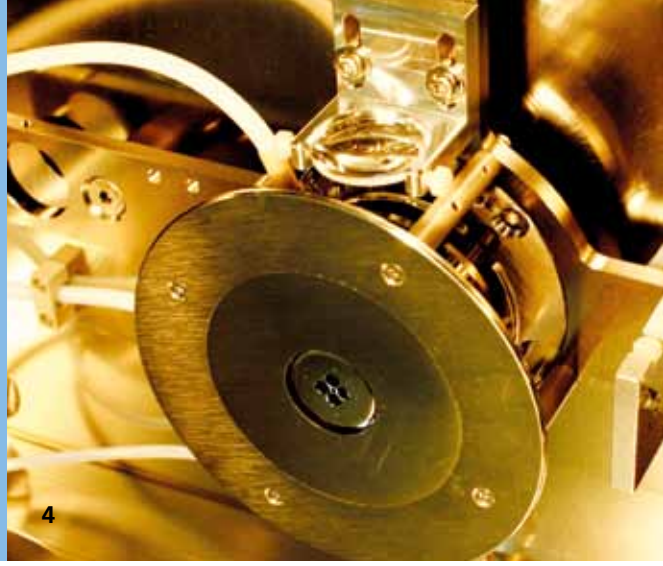

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In previous work we investigated the secretome in different growth forms of *C. albicans* [1]; we are now analyzing the proteins secreted by *Candida* ssp. during contact with an epithelial model. In this process, the proteins which are specifically secreted by the fungus or by the epithelial cells during their contact are to be identified.

Candida as biofilm

Candida ssp. cells growing in a so-called biofilm (Fig. 1) are much more difficult to combat than planktonic cells. To better understand the development of such biofilms, we are analyzing the quantitative composition of the secretome in the temporal course of its formation. The data can also contain indications of the cell-to-cell communication or allow conclusions about the formation of the biofilm's extracellular matrix.

Perspective

The techniques which we have established for the investigation of the proteins secreted by *Candida albicans* represent a basis for quantitative examinations of proteins using mass spectrometry. They can also be used for other organisms or test systems in which the proteins are to be identified and quantified in one step.

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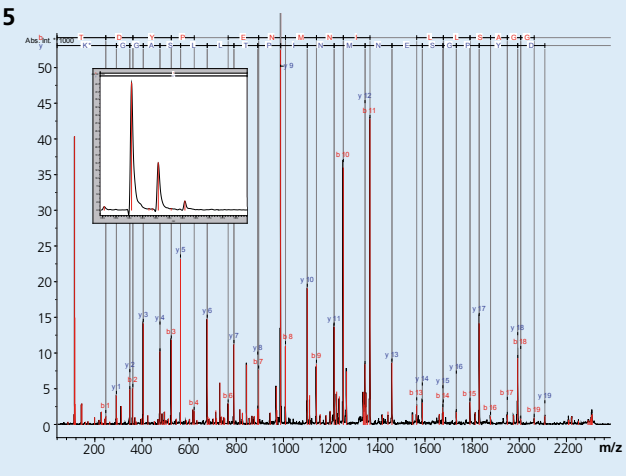

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References

[1] Hiller, E.; Heine, S.; Brunner, H. and Rupp, S. (2007) *Candida albicans* Sun41p, a putative glycosidase, is involved in morphogenesis, cell wall biogenesis, and biofilm formation. Eukaryot Cell 6(11): 2056-65

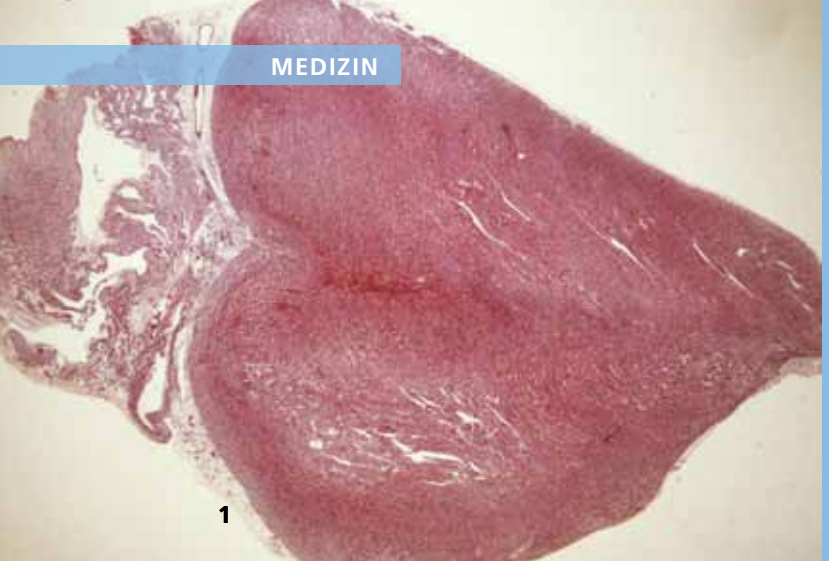
Funding

We would like to thank the German Research Foundation (DFG) for funding the "Identification and characterisation of virulence associated genes during vaginal infections with *Candida albicans*, focusing on the cell wall" research project (GZ:RU 608/4) in priority program 1160 "Colonisation and infection by human pathogenic fungi".

Project partners

www.spp1160.hki-jena.de

1 *Scanning electron microscopic image of a Candida albicans biofilm.*
2 *Determination of protein concentration on microtiter plates.*
3 *Application of separated peptides to a MALDI sample carrier.*
4 *MALDI ion source.*
5 *MS/MS mass spectrum with peaks used for quantification.*



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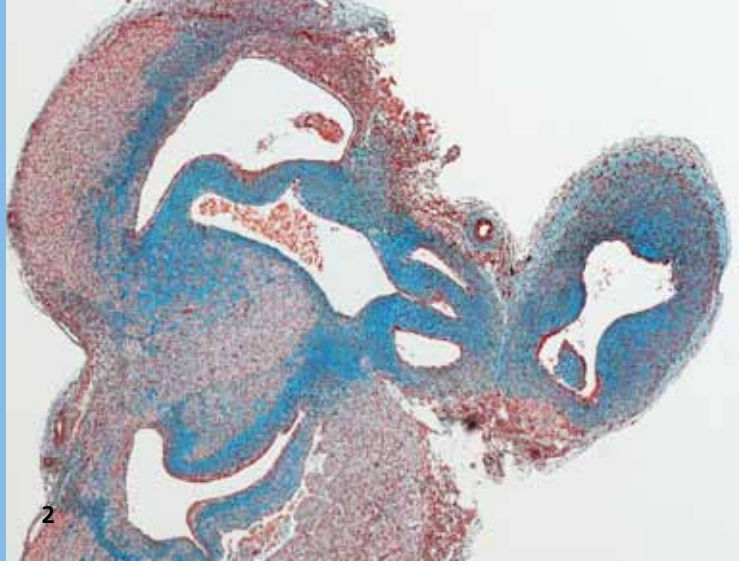


2

DEVELOPMENT OF BIO-INSPIRED STRATEGIES FOR CARDIOVASCULAR REGENERATION

Dr. rer. nat. Katja Schenke-Layland M. Sc.

Heart failure is one of the most common diseases worldwide. There are approximately 10 million people affected in Europe alone. According to the Federal Statistical Office of Germany, heart failure is responsible for almost every other death in Germany [1]. The most common causes of heart failure are due to pathological changes of the heart valves and acute or chronic damage to the heart muscle, known as the myocardium. The currently available, usually surgical replacement procedure for the treatment of damaged myocardium or heart valves is not sustainable. Transplantation of donor valves or the use of artificial heart valves has contributed significantly to the quality of life of many people. However, none of the currently available heart valve models has an adequate long-term potential for growth or self-repair. The design of an optimal heart valve replacement using tissue engineering methods and the design of innovative therapeutic strategies, such as utilizing stem cells for cardiovascular regeneration, are therefore the focus of our research interest.

Challenges and approaches

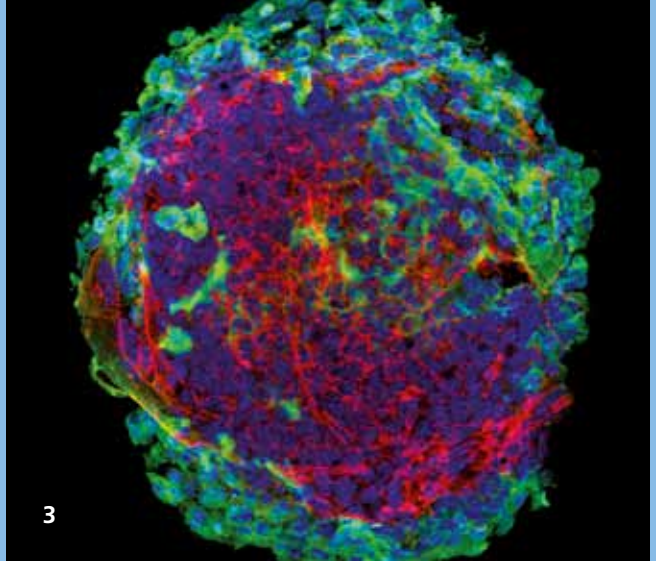
One of the main approaches in cardiovascular tissue engineering is the use of biocompatible substrates that are seeded with the body's own (autologous) cells [2]. To date, the most common carrier substrates are generated using natural or synthetic biomaterials that are either biodegradable or non-biodegradable. Currently, these biomaterial substrates are seeded with cells isolated from either tissue biopsies or adult stem and progenitor cells taken from a variety of organs [3].

Although the results of the first *in vitro* studies were quite promising, long-term *in vivo* results were unsatisfactory. These *in vivo* experiments indicated that the currently pursued approaches of heart valve tissue engineering and myocardial regeneration are still far from a clinical application. Therefore, the Attract Group is identifying developmental processes, cell phenotypes and matrix proteins that control heart valve development. The translation of the gained information to cardiovascular tissue engineering should help generate optimal implants.

Projects and applications

Since over 98 percent of cardiac muscle cells are at their final stage of differentiation, in which they cannot proliferate, the regenerative ability of the heart is extremely limited. A focus of our research is therefore to identify suitable cells that have the potential to replace damaged heart muscle cells in order to restore heart function. Currently, we are testing human pluripotent stem cells as a source of functional heart muscle tissue.

The cell phenotype of the outflow tract valves (pulmonary and aortic valve) is still unknown. The exact identification of the progenitor cell phenotype of these valves and the characterization of the developing extracellular matrix are a critical step in the development of an ideal heart valve replacement. Our group deals with the developmental intra- and extracellular mechanisms that occur during heart valve development (Figs. 1, 2), a process known as valvulogenesis.



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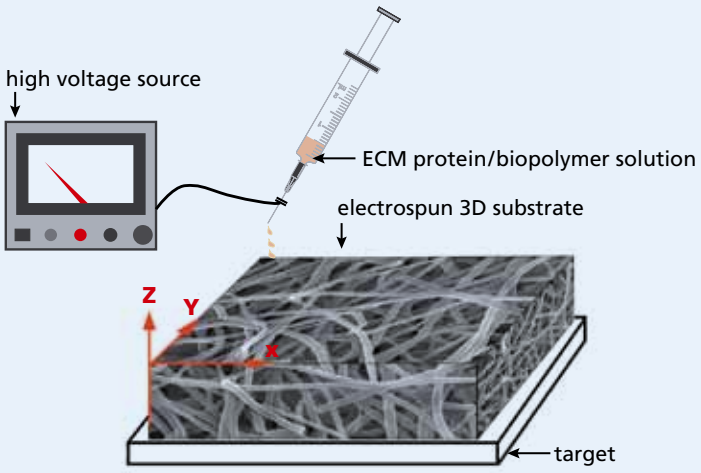

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Another project is the genetic engineering of cell lines used for the permanent *in vitro* production of human extracellular matrix proteins. The *in vitro*-synthesized proteins will be used in the creation of allogeneic biomaterials that serve as optimal hybrid substrates for tissue-engineered myocardium and heart valves. For this process we will employ innovative technologies such as electrospinning.

Skills and technologies

We have extensive and well-published expertise in the establishment of two- and three-dimensional *in vitro* stem cell culture systems using adult and embryonic stem cell technologies [4, 5] (Fig. 3). Other capabilities are the analysis of proteins and structures of the extracellular matrix using minimally-invasive microscopy technologies [6], the development of specific systems for the storage and preservation of tissues and organs [7] and the creation of pluripotent stem cells from patient samples. Another core competence is the design and development of novel biomaterials for the use in regenerative medical research [5, 8] (Fig. 4).

1 *Fetal human heart, 15th week of development, H&E staining.*
2 *Heart valves (blue) in the developing human heart, Movat pentachrome staining.*
3 *In vitro generated embryonic stem cell aggregates (embryoid body). Immunofluorescence staining shows nuclei (blue), cytoskeleton (red) and the ECM protein decorin (green).*
4 *Concept of electrospinning for use in regenerative medical research.*

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University of Southern California (USC), Department of Pharmacology and Pharmaceutical Sciences, Los Angeles, USA
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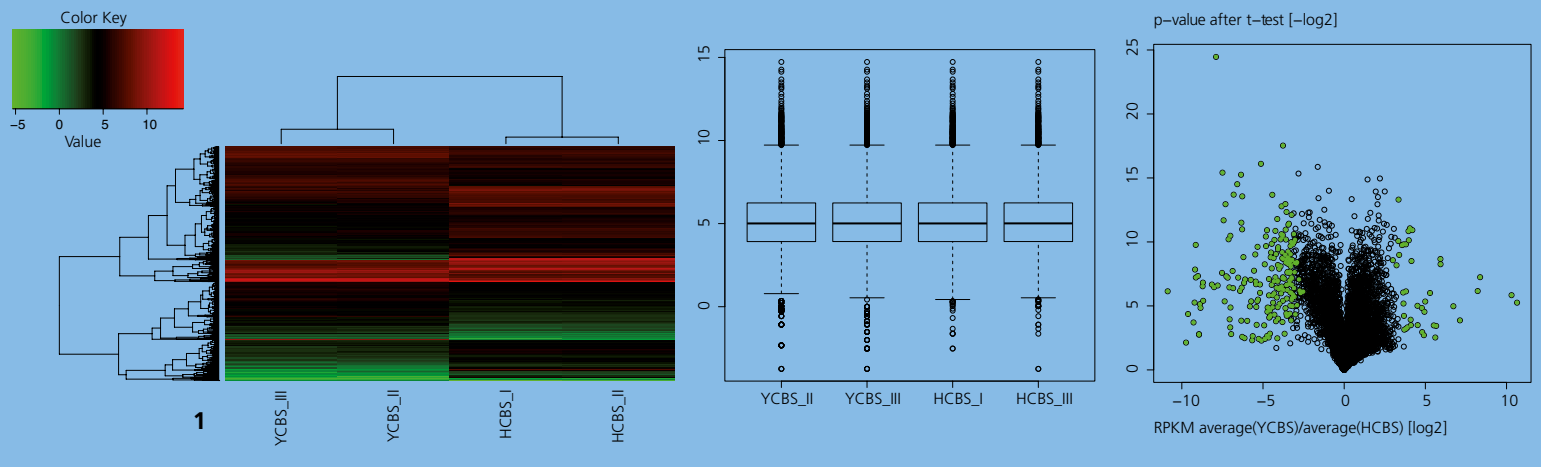
Awards

Morphological Sciences Award of the American Association of Anatomists (AAA) 2010



COUNT BASES – A BIOINFORMATICS PLATFORM FOR THE ANALYSIS OF NEXT GENERATION TRANSCRIPTOME DATA

Stefan Lorenz B. Sc.

Compared with conventional sequencing technologies, new technologies for next generation sequencing (NGS) permit completely new experimental approaches in many fields of biological research [1]. In a single run, 10^6–10^9 DNA fragments with an average sequence length of 30–800 bases are simultaneously sequenced *de novo* [2, 3]. This results in huge amounts of data that require a storage volume of up to 10–100 gigabyte. Intelligent bioinformatic tools have thus become the prerequisite for a meaningful interpretation and organization of the resulting data.

In order to apply next generation DNA sequencing technologies for applications including the analysis of gene expression we have developed a bioinformatics platform called "Count Bases" at the Fraunhofer IGB. This system basically consists of modules that cover sequence analysis (Count Bases – Next-Gen Sequence Assistant), statistics as well as visualization (Count Bases Viewer).

Count Bases – processing of sequence data using the Next-Gen Sequence Assistant

The first module of the bioinformatics platform permits a flexible processing of sequenced raw data. Currently these might comprise up to 30 million and more sequenced DNA fragments per experiment. By means of preprocessing, reads can be processed and allocated efficiently in a few steps using different filter methods. In order to fully exploit the potential of next generation sequencing, we also use barcodes for multiplexing. In this way several samples can be analyzed simultaneously in just one sequencing operation.

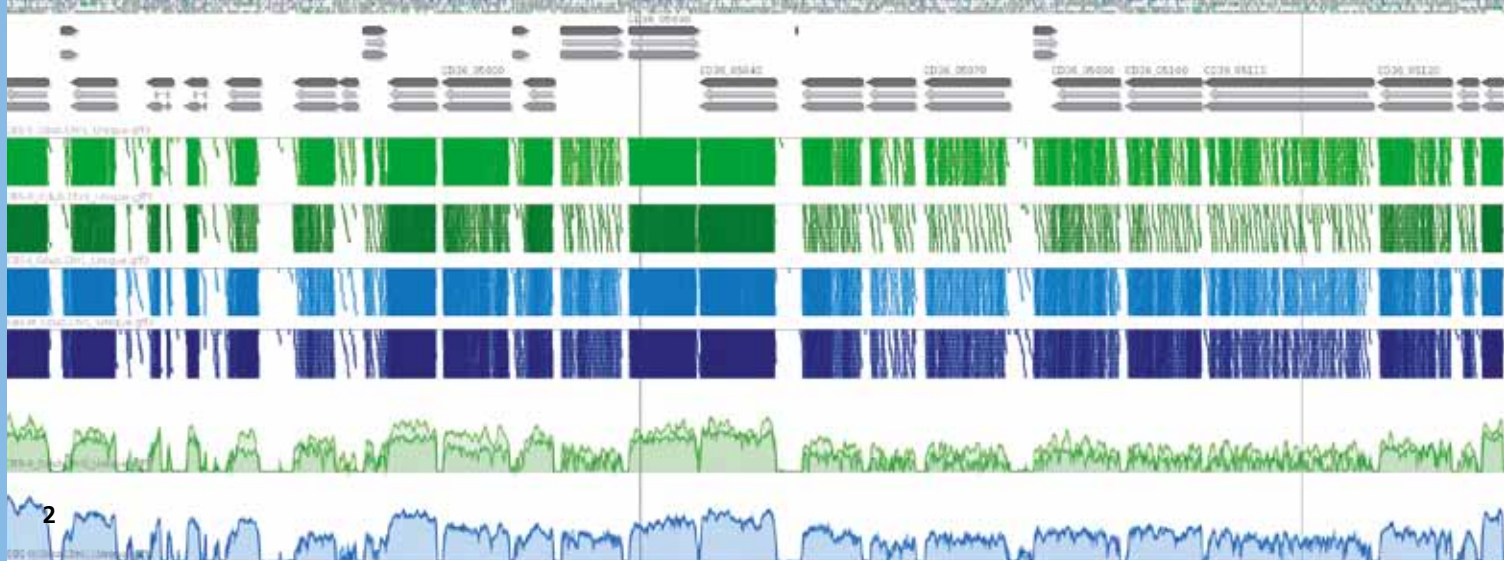
In this context, Count Bases also offers interfaces to various mapping algorithms that permit the mapping of individual reads to the corresponding reference genome [4]. This mapping of sequences to the corresponding gene then provides the basis for quantitative analysis of gene expression. All the functions of the bioinformatics platform can be easily operated via a graphic user interface and allow users reliable interpretations of transcriptomic data.

Gene expression profiles using NGS data

With sequence reads assigned to the reference genome it is possible to generate quantitative expression data. For this purpose this bioinformatics platform provides tools for evaluation that are well established from expression analysis using microarray technologies. In order to identify differentially regulated genes, algorithms based on so-called R scripts are implemented with the necessary statistical evaluation functions [5]. By doing this, MA or volcano plots for example can be generated and relevant lists of genes can be compiled (Fig. 1).

Count Bases Viewer

The interpretation of sequence data is considerably more informative with a clear visual representation. Therefore the Count Bases Viewer – a genome browser that permits an



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interactive and easily adaptable viewing of various data sets was developed at the Fraunhofer IGB (Fig. 2). As a result expression data can be analyzed with various resolutions, either on the genome or, in greater depth of detail, at the sequence level.

In addition, Count Bases Viewer also provides functionalities for the manual re-annotation of transcriptionally active regions by means of an intuitive annotate-by-click principle, which facilitates the generation of new gene models. Other functions such as wiggle plots allow for a quick overview of the expression level of genes under various conditions.

Perspective and application

The platform offers a reliable basis for detailed analyses of next generation transcriptomic data. Count Bases has already been used and optimized at the Fraunhofer IGB for a wide range of data sets, including simple organisms such as yeasts as well as complex human transcriptomes. Count Bases is constantly being upgraded, new mapping tools are being integrated und statistical methods optimized. The implementation of a *de novo* transcriptome assembler, i.e. algorithms that assemble individual sequences, is also planned. Furthermore we also develop database modules to permit the efficient processing and organization of sequence data. In addition to a stand-alone version for local use a basic version of Count Bases is also to be made available to users in future via a Web interface.

1 *Gene expression analysis: heat map, box plots, volcano plot (from left).*

2 *NGS data visualized using the Count Bases Viewer: genes (gray), reads (blocks: green and blue), wiggle plot (curves: green and blue).*

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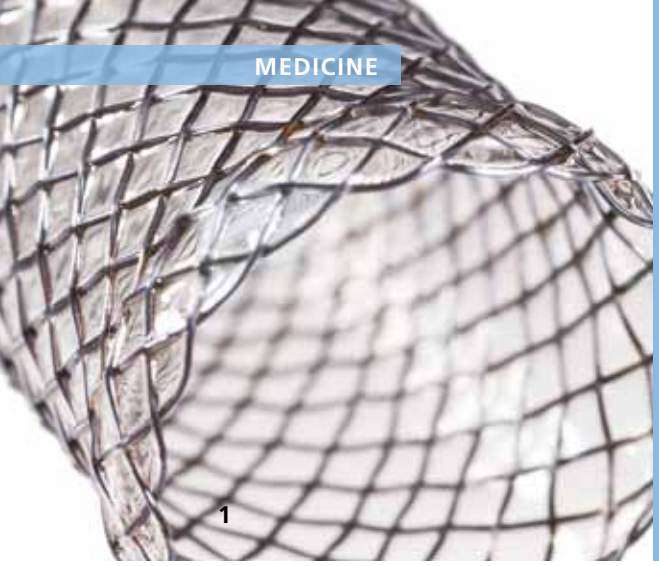

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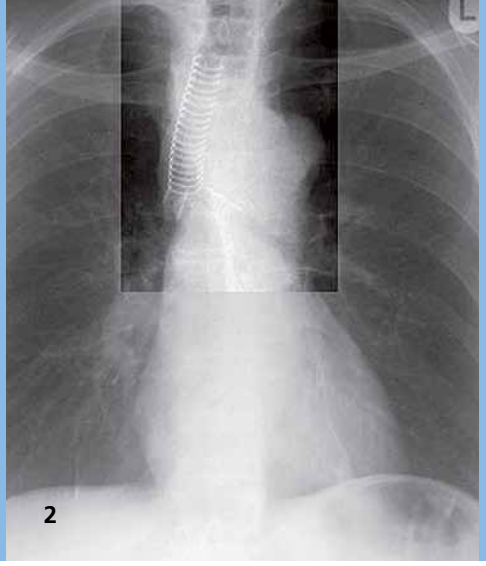

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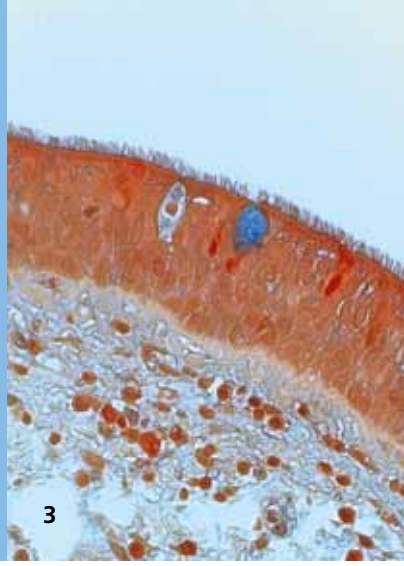


3

OPTIMIZATION OF AIRWAY STENTS VIA BIOACTIVE SURFACE COATINGS

Dr. rer. nat. Martina Hampel, Dr. rer. nat. Steffen Koch

The human trachea (windpipe) forms the first part of the lower respiratory tract and plays an important barrier function against inhalable substances such as particulates, nanoparticles, viral and bacterial pathogens. Critical to this effective barrier is a self-clearing mechanism called mucociliary clearance, which is dependent upon the interaction of different cells of the respiratory tract. An abnormal narrowing of the trachea (stenosis), which for example can be caused by tumors, can be life threatening. Therefore, in respiratory tract stents, small mesh-like tubes are used to stretch the narrowed airways and prevent a build-up. This standard method has been used in vascular surgery as a way to expand narrow blood vessels to increase blood flow, but tends to lead to greater complications in the trachea due to slippage of the stent, which can either partially or complete block the airway. This blockage interferes with the stent surface and function of the respiratory mucosa, and thus the mucociliary clearance, which may lead to a colonization of bacteria and other microorganisms that can cause serious complications such as pneumonia.

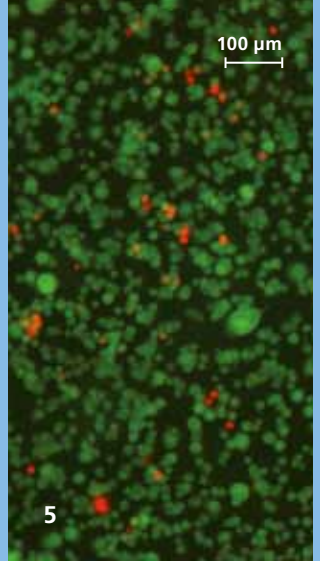
As part of the BMBF-funded joint project "Health regions of the future", the Fraunhofer IGB is involved in the development of surface coatings for airway stents that promote controlled stent in growth while simultaneously preventing the growth of microorganisms.

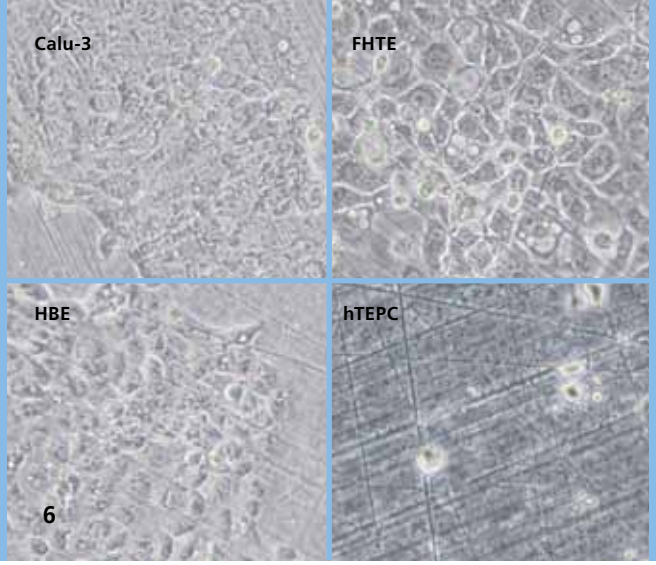
Bioactive surface coating

The tracheal stents designed by the Leufen Medical Company are lined with a polyurethane film. We studied the growth potential of human respiratory cells in this polyurethane (PU) film when incorporated with different artificial and biological surface coatings, including by means of plasma technology. Here, the analysis of cell viability, functionality and the inflammatory reactions was required in order to identify the most suitable surface. In addition, the stent was coated with silver nanoparticles and tested for its antimicrobial properties.

Results

For an initial assessment of the suitability of the polyurethane film's potential for good respiratory cell adhesion and proliferation, three cell lines from different areas of the lower respiratory tract and primary human tracheal epithelial cells were tested. PU films were tested with 11 different coatings as well as with untreated control PU film. We could identify film-cell interaction in regards to adhesion and proliferation. These are two critical factors which determine if a stent graft made of PU films would have the potential to incorporate into the damaged trachea. As expected, differences between primary cells and cell lines were seen in the first experiments on the PU films. Cell lines preferred to grow on untreated, protein-coated and plasma-treated films, whereas primary cells excelled predominantly on fibronectin-coated films (Fig. 5).





Perspective

A dilatation and splinting (stenting) of the lower respiratory tract through the implantation of a tubular airway stent is often the last resort for treating a life-threatening narrowing of the airways with recurrent cancer, metastasis, tracheal injury, congenital malformations, surgical complications or chronic airway inflammation. The creation of a "cell friendly" biocompatible surface design will greatly improve airway stent technology and will minimize the risk to the patient by the fixation of the stent in the trachea. The suppression of biofilm formation on the implanted stent would further decrease the risk of infection for the patient.

If successful, the developed coating method can be utilized in larger implant areas such as dental implants, pacemaker probes, joint implants or implants for bone surgery.

1 *Airway stent of Leufen Medical GmbH.*
2 *X-ray image of an airway stent in the trachea. (Source: www.mevis-research.de)*
3 *Pentachrome staining of the human trachea.*
4 *Human tracheal epithelial cells.*
5 *Live-dead staining (green are living, dead cells are stained red) of primary human tracheal epithelial cells after growth on a fibronectin-coated PU film.*
6 *Growth of different cells on the untreated PU film. All three cell lines (Calu-3, FHTE and HBE) show a growth of the cells. The primary human tracheal epithelial cells (hTEPC), however, cannot grow on the uncoated film.*

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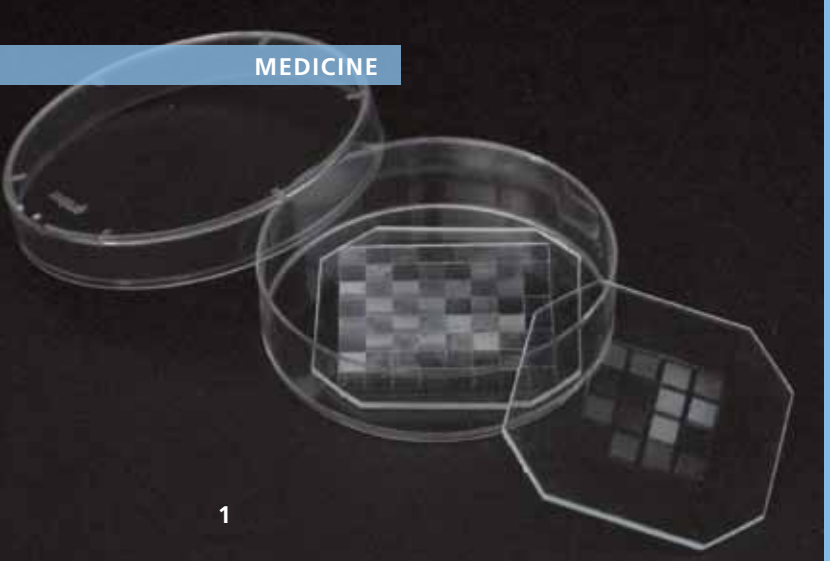

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"MIKROBIOSTRUKT" – CELL CULTURE AND STRUCTURED SURFACES

Dr. rer. nat. Petra Kluger

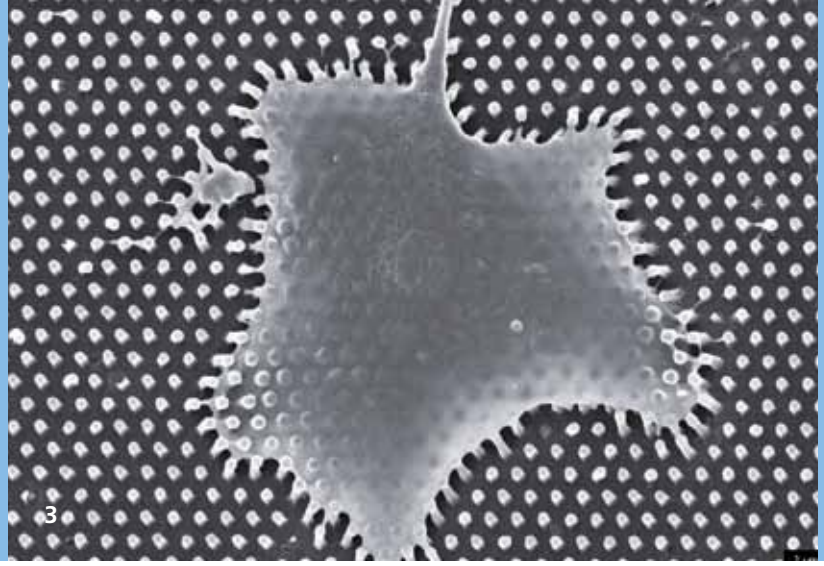
Tissue cells in the body are surrounded by an extracellular matrix (ECM) environment that can vary in composition and behavior between different tissue types. In bone, the ECM is very strong and resilient. However, the ECM of connective tissue is very elastic and capable of swelling [1]. The structures and topographies of ECM are highly tissue-specific and can affect essential cellular functions [2]. A key component of ECM mimicking biomaterial development for cell culture is the reproduction of structured surfaces on nanometer and micrometer levels. In many studies, it has been demonstrated that cell behavior can be modified by these patterned surfaces; this includes changes in adhesion, morphology or differentiation [3-5]. Similarly, surfaces have been developed to ensure that cells do not adhere and proliferate on the surface, for example for use in implants.

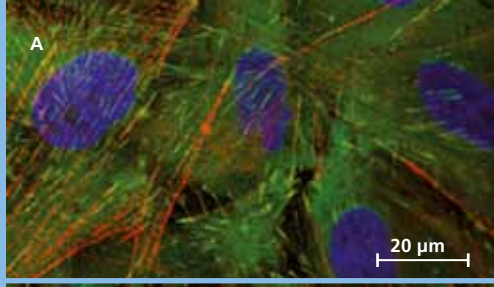
Production of textured cell cultureware

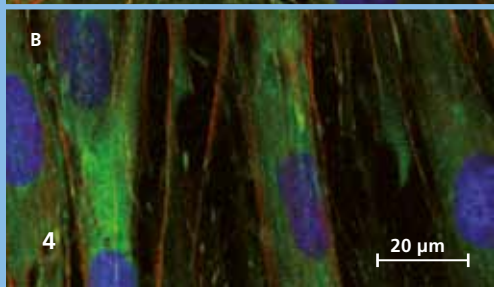
The up-scaled production and testing of micro- and nanometer cell cultureware is quite challenging. Therefore, such substrates have usually only been made at a laboratory scale. For broad scientific use and commercial distribution, an up-scaled cell culture system should be created with sterile disposable components with customizable interfaces. In the interdisciplinary Fraunhofer research project "MikroBioStrukt" an automated process for the mass production of micro- and nano-structured surfaces has been developed and the impact of these surface on different primary cell types has been evaluated. Utilizing the production technology from the Fraunhofer IPT, the reproduction of structures of various shapes and sizes in biocompatible polymers is possible. Specific use of molding and conversion techniques allows not only the topographical modification of routine cell cultureware, it can also be employed for the production of structured surface substrate inserts for petri dishes up to a diameter of 50 mm (Fig. 1) and for 6-, 12- and 24-well plates (Fig. 2). Due to the fact that the inserts are transparent and only up to 1.25 mm thick, routine bright-field microscopical analysis can be preformed.

Screening platform for tissue cells

As part of the project, the response of primary human tissue cells such as epidermal cells, connective tissue cells, endothelial cells, mesenchymal stem cells and cell lines from bone and nerve tissue on various patterned substrates was studied. Significant cell type-specific reactions were observed that are of great interest for tissue engineering. We could identify topographies, which enabled better cell adhesion and proliferation, or structures which did not allow adhesion at all. Scanning electron microscopy showed that human epidermal cells interacted directly with knobs structures (Fig. 3). Groove structures, however, have a greater impact on connective tissue fibroblasts, which are arranged in parallel with grooves in the submicron range. Even intracellular components of the cells, like the actin fibers, aligned to the grooves, whereas this reaction was not observed for fibroblasts on non-structured substrates (Fig. 4).







Perspective

With the Fraunhofer developed assembly chain, the mass production of micro-and nano-structured substrates is now possible. We can manufacture structured cell cultureware or structured inserts for such cultureware. Also, we have acquired important information on the interaction between primary cells and different structuring. In consultation with interested clients, we can quickly and flexibly produce different formats of inserts for structured cultureware, such as structured films for flexible adaptation to their own culture surfaces. We are interested in the future development of this field in collaboration with partners from industry and research.

1 *Petri dish inserts with different structuring. © Fraunhofer IPT*

2 *Micro-structured multi-well plate inserts and direct structured petri dish. © Fraunhofer IPT*

3 *Scanning electron micrograph of a primary keratinocyte on pimples structures. The cell interacts directly with the knobs and anchored firmly to the latter.*

4 *Fluorescence staining of primary fibroblasts. The actin cytoskeleton is stained red, the nucleus blue and the protein vinculin, which is involved in cell adhesion, green. A) Fibroblasts on unstructured substrates have a large cell body with disordered actin fibers. B) This image shows perpendicular nano-grooves. The cells align themselves along the grooves and have a narrow elongated morphology. Very clearly, the orientation of actin fibers along the structure can be seen.*

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Fraunhofer IFAM, Adhesive Bonding Technology and Surfaces, Bremen, Germany
Fraunhofer EMFT, München, Germany

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DEVELOPMENT OF INTEGRATED PRESERVATION PROCESSES

Dr. rer. nat. Ana Lucia Vásquez-Caicedo, Dipl.-Ing. Alexander Lohner

Contaminating microorganisms result in the spoilage of fresh goods. Sometimes they even produce life-threatening toxins. Thus foodstuffs have to be stabilized as effectively as possible and filled or packed under hygienic conditions. Traditional methods of preservation such as heat sterilization have the disadvantage that they destroy valuable heat-sensitive substances contained in the foodstuffs such as vitamins and thus reduce their nutritional value. Also, the addition of chemical preservatives can have negative health effects. Alternatives are therefore sought after.

Physical methods of sterilization

The development of new methods for the microbial stabilization or sterilization of biogenic products such as foodstuffs is the focus of the working group "Aseptic Systems". We are investigating various physical methods, such as microwaves or the pressure change technology, for their ability to reduce microbial load. Simultaneously, their effects on valuable food components are taken into consideration. The focus of our studies is to understand the interaction between the various parameters in the system (temperature, pressure, particle size, viscosity, pH value, etc.) to optimize the process technology for further implementation in a production plant. In cases where we recognize significant technological or energetic advantages, we further develop the processes and optimize them for the application in question.

Example: Preservation of drinks

For example, at the Fraunhofer IGB the pressure change technology (PCT) for the preservation of liquid foodstuffs such as fruit juices or wine is being further developed. In this process, the product is mixed with an inert gas such as nitrogen or argon under pressure followed by an abrupt pressure release. The reduction of microorganisms in fruit juices and other model liquids was successfully demonstrated by cooperation partners using batch and semi-continuously operating process units. Further development to continuous operation and the adaptation of process parameters for several applications are the subject of current and planned projects and scientific studies.

Integrated approach to the process

In order to be able to demonstrate real alternatives, the methods developed have to be adapted in their conception to the requirements of specific food production processes. For this purpose an overall analysis of the product development, production and stabilization including the plant technology and packaging system has to be carried out and validated. In this context, concepts of hygienic design and cleaning in place (CIP) play a central role. We also examine these systems with regard to their energy efficiency.

Example: Automated production of preservative-free choux pastry

Bakery goods such as cream puffs, doughnuts, éclairs, profiteroles or sweet apricot dumplings are baked using choux pastry. Up to now the choux paste had to be produced in a laborious

manual process. After manufacturing, the paste has to be processed very quickly because it is unstable due to its composition. Choux paste is therefore increasingly being replaced by convenience baking powder mixes, which are generally used by large bakeries producing for discounters. These powder mixes contain chemical additives and no longer have the high-quality character of traditional choux pastry products.

In the "ProEclair" project funded by the European Union the Fraunhofer IGB, together with its project partners, has developed an automated process for the production and packing of traditional choux paste under aseptic conditions. The system is especially suited to the central manufacturing and further decentralized utilization of choux paste at various locations, allowing smaller bakeries to produce high-quality pastry goods at competitive prices.

The choux paste is filled directly into sterile closed piping bags, so that the packaged paste can be kept fresh and ready for use for four weeks at a temperature of 4 °C. The baking performance and the sensory properties of the choux paste developed correspond – even after a longer storage period – to those of traditional, freshly prepared choux pastries. A first prototype of the production plant has been set up in a bakery. The system is also equipped for cleaning in place (CIP).

Perspective

The development of processing methods which are gentle to the product and which minimize the loss of valuable components such as vitamins is becoming more and more sought after both for foodstuffs as well as for cosmetics and pharmaceutical production. The further development and technical optimization of alternative processes and their integration into production systems are carried out in compliance with established good manufacturing practices (GMP) standards and hazard analysis and critical control points (HACCP).

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Further information and project partners

www.proeclair.fraunhofer.de

1 *Bakery goods made of choux pastry.*
2 *Preparation for baking.*
3 *Experiments at Zoatec.*

PHARMACY

Priv.-Doz. Dr. Steffen Rupp

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.

1

2

SKIN FROM THE FACTORY – AUTOMATED TISSUE ENGINEERING ON DEMAND

Dr. rer. nat. Michaela Kaufmann

The skin is the first organ that has been grown successfully in the laboratory using tissue engineering methods. This is partly due to the fact that skin biopsies are readily available and skin cells are relatively easy to culture. Besides the goal of developing skin grafts, the use of artificial skin equivalents as *in vitro* test system has begun to move to the forefront. A decisive contribution to this was the 7th Cosmetic Directive, which requires the replacement of cutaneous absorption animal testing and chemical side affect tests with *in vitro* test systems by 2009. Additionally, chemicals have to be tested for toxic side effects as regulated by the EU directive REACH. Toxicity testing has traditionally required a large number of animal tests, which are both costly and time consuming. Laboratory prepared skin equivalents represent a real alternative. Additionally, skin models are also ideal, meaningful, and standardized test systems for the drug screening of chemical or pharmaceutical products.

Currently, the production of an *in vitro* skin test system requires six weeks and must be performed by trained personnel. This process hinders the market availability and cost-effectiveness of an "off-the-shelf" test system. The Fraunhofer Institutes IGB, IPA, IPT and IZI have joined together in a major project to overcome the costly and tedious challenge of the manual preparation of skin test systems by creating a fully automated production system for skin equivalents. Because the patented (Patent No. EP 1 290 145B1) three-dimensional (3D) skin model test system developed at Fraunhofer IGB is a well established system, it was perfectly suited as a standard model for an automated system.

Prerequisite: automated culture processes

The first step in the development of an automated process in tissue engineering was the analysis and understanding of all steps, from the skin biopsy to a 3D skin model, and to be able to translate them into machine processes and environments. The next step was to unify the respective approaches and terminology of natural sciences and engineering to a common language, thereby simplifying the basic issues of automating a tissue engineering system. Within the project, the production of a synthetic collagen replacement of biocompatible and biodegradable polymers was also investigated. Other tasks were the development of a method for tripling the storage time of skin models from five to 15 days as well as a bioreactor for automated cell culture with a functionalized membrane for the expansion of the cells.

Fully automated production of skin models

The fully automated manufacturing system to create a two-layer skin model was completed within the three-year project deadline. The automated process begins with the sterilization of skin biopsies. A gripper arm then transports the biopsies to a different module that separates the dermal cells and enzymes from the epidermal (module B). These two different types of cells are then separated and seeded on cell culture surfaces and then cultured (module C). The culture is monitored until the required numbers of cells have been grown. Once there are enough cells, the two cell types are combined to create a two-layer model. The cells forming the lower flexible dermis are then mixed with collagen (module D).

The model is then stored in a humid incubator set at body temperature for three weeks, after which the one centimeter diameter skin model is complete.

The automated production of the models could be successfully demonstrated. It is important to note that the entire mechanical process is divided into individual modules. This allows the modules to be exchanged in order to meet the requirements of producing different tissue types. This fully automated system can produce 5000 skins models per month at a cost below 50 euros per model.

Perspective

For the first time, the creation of 3D skin equivalents is possible with a fully automated production system. The automation of the manufacturing process ensures reproducible and standardized processes in which the skin models can be produced economically.

The automated system will be in operation and skin models available to customers at the beginning of the third quarter of 2011. Many cooperation opportunities are available for customers in the fields of systems engineering and medical technologies, including the cosmetics, pharmaceutical and chemical industries. Future projects will include expanding the system to flexibly allow the creation of other tissue types.

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Project partners

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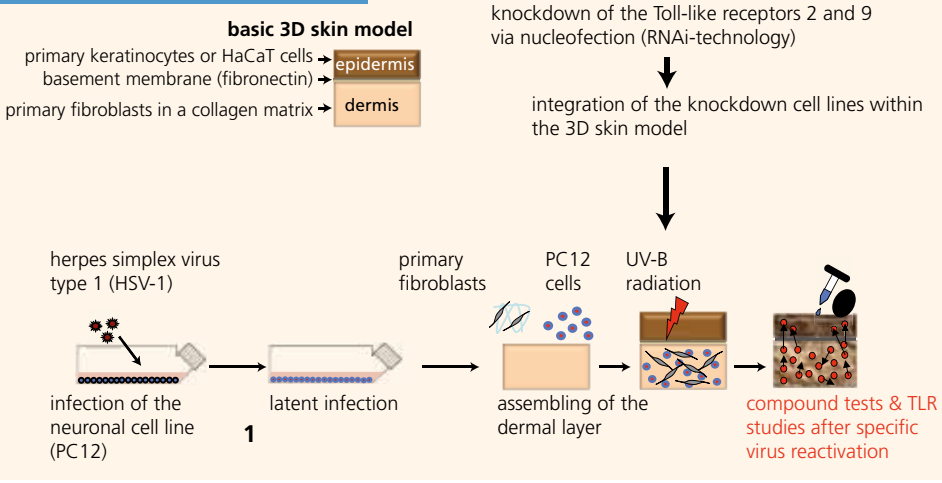
Fraunhofer Institute for Production Technology IPT, Aachen, Germany
Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig, Germany

More information

www.tissue-factory.com

1 *Modular system for the automated production of skin models.*
2 *Rear access to the system.*
3 *Mincing the tissue sample in module B.*
4 *Control before module D.*



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AN *IN VITRO* HERPES INFECTION MODEL FOR NEW ANTIVIRAL THERAPIES

Dipl.-Biol. (t. o.) Ina Hogk

Herpes simplex virus (HSV) infections are among the most common disorders of the skin. More than 90 percent of the total world population is infected with HSV. The most common manifestation of herpes simplex infection is *Herpes labialis* (cold sores), which is usually caused by virus type 1 (HSV-1). In addition to the characteristic skin lesions, HSV can also cause serious diseases in other organs, such as the cornea (*Herpes corneae*) and the central nervous system (*Herpes encephalitis, Herpes meningitis*), which can be fatal. To date, there are no effective cures for the herpes infection. Antivirals, such as nucleoside analogs like acyclovir or its derivatives, are the most often used treatment for HSV. This treatment only alleviates the symptoms and shortens the time of infection, but it does not prevent the reactivation of the virus.

To date, a physiologically adequate *in vitro* model of the HSV-1 infection has not been established yet. Consequently, drug development and studies of infection mechanisms are still performed using animal models. Therefore, the aim of the Fraunhofer IGB is to establish a 3D herpes infection model which accurately reproduces the *in vivo* situation.

Challenge of HSV latency

An important characteristic of all herpes viruses is that it persists in the human body after the treatment of acute symptoms from the first infection. The virus then goes into latency from which it can be reactivated by various factors. After the primary infection of the mucous membrane or skin epithelium, HSV migrates into the cell body of the sensory neurons that innervate the infected region. HSV enters the associated ganglia over the axons of nerve cells and becomes latent within the Ganglion [1, 2]. During the latent phase, there is no virus replication. The viral DNA persists undetected by the immune system of the host, as a circular episome in the nucleus of the ganglion [3]. In order to simulate a herpes infection *in vitro*, a latent with HSV infected neuronal component must be integrated, which ensures that this latency can be formed. Previously described 3D infection models lack this crucial neuronal latency-forming component.

Establishment of a HSV-1 infection model

For the establishment of a functional HSV-1 infection model, the Fraunhofer IGB has extended its patented and accredited human 3D skin equivalent with the neuronal cell line PC12. The PC12 cells were previously infected with the herpes simplex virus type 1 strain and were integrated into the collagen matrix dermal layer of the skin model (Fig. 1). Additionally, the neural cells were differentiated with NGF (nerve growth factor) and cultured over an extended period. Using a cell-based $TCID_{50}$ assay and PCR analysis, viral DNA and cell latency was verified and extracellular virus activity was not found.

Infection model with latently infected neuronal cells

In previous studies, the Fraunhofer IGB has demonstrated the successful development of a functional *in vitro* HSV-1 infection model. For the first time, we were able to integrate a neural component in the form of a cell line.

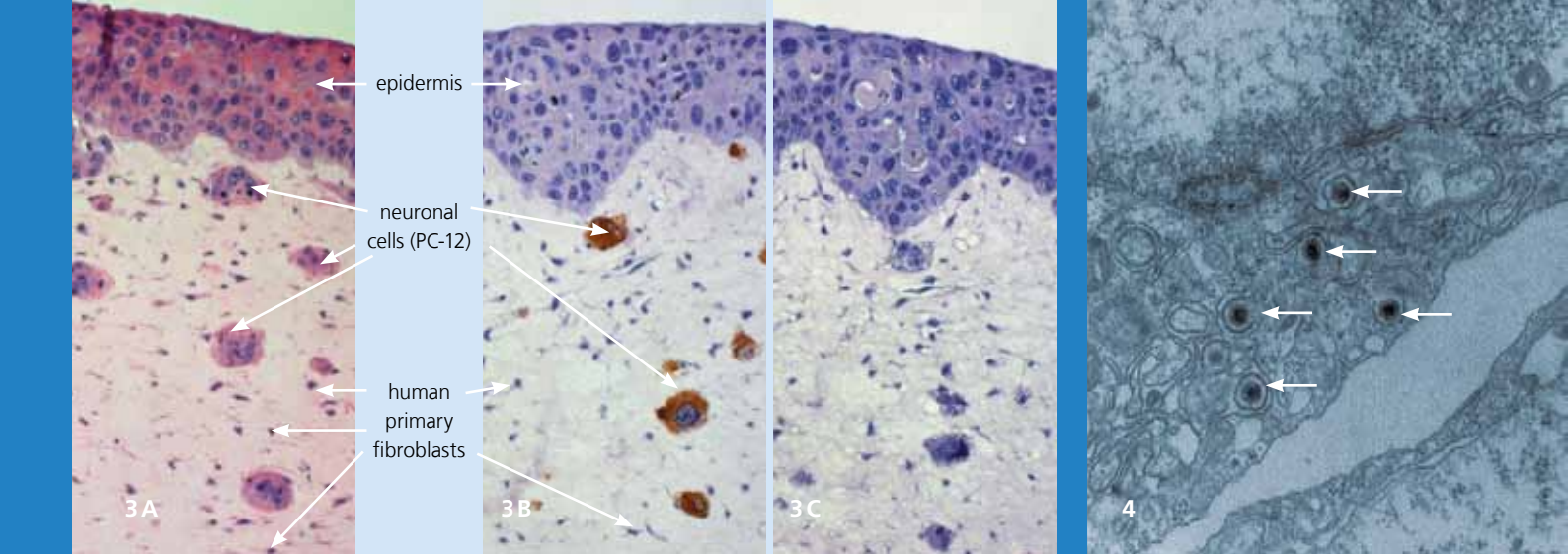

Fig. 3A shows the successful integration of latently infected PC12 cells within the 3D skin equivalent with HSV-1 neuronal cells. The detection of neuronal PC12 cells was performed using a specific antibody (Fig. 3B). Another specific immunohistochemical examination of skin sections showed no virus activity. First promising results indicate that the virus can be reactivated specifically by UV-B radiation. Through this targeted and specific reactivation of infected herpes simplex virus in the infection model, it is possible to accurately simulate the *in vivo* environment.

Perspective

The established and patent pending *in vitro* HSV-1 infection model fulfills an important requirement as a standardized test system for biomedical research in the areas of toxicology, immunology and pharmacology, and particularly for drug screening and studying the mechanisms of infection. In the pharmaceutical industry, new antiviral therapies can be tested or identified with the help of the *in vitro* HSV-1 test system and animal testing during drug development can be reduced.

In future, we will extend the 3D infection model with an immune component designed to better represent the physiological environment of the native skin. With the integration of PRRs (pattern recognition receptors), we want to investigate the role of the immune receptors in an active HSV-1 infection more closely.

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1 *Schematic of the in vitro HSV-1 infection model.*
2 *HSV-1 detection by gel electrophoresis and a TCID50 assay. Infection model during the airlift cultivation.*
3 *A: Structure of the 3D skin model with the neuronal cell line PC12 (H&E staining), B: PC12 staining, C: Isotype control.*
4 *Detection of HSV-1 infection in PC12 cells by transmission electron microscopy.*

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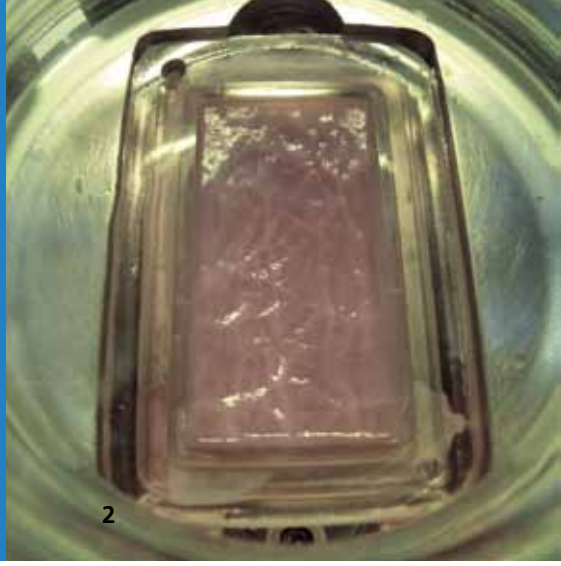


2

DEVELOPMENT OF A VASCULARIZED SKIN MODEL FOR THE STUDY OF MALIGNANT MELANOMA

Dipl.-Biol. Florian Groeber

Malignant melanomas, a highly malignant tumor of melanocytes (pigment cells) of the skin, are among the most common skin diseases in Germany, causing approximately 2000 deaths per year. Previously, the development of new drugs against malignant melanoma had been limited to utilizing two-dimensional cell cultures or animals models. While both methods have been helpful in the development of new drugs, neither is optimal. The drawback of two-dimensional cell cultures is that cells behave differently in cell culture than cells in their natural three-dimensional environment as they are surrounded by and interact with other cells in tissue. Animal models can react differently to drugs in comparison to humans due to species-specific differences in metabolism and tissue-specific architecture [1].

To establish a meaningful model system for the testing of potential skin cancer therapeutics, Fraunhofer IGB has developed an *in-vitro* melanoma model based on a three-dimensional (3D) skin equivalent [2]. The skin equivalent is structurally similar to natural skin and with the addition of melanoma cells can be used to simulate a malignant melanoma. Within our 3D skin equivalent, the melanoma cells form tumor nests which behave naturally according to the origin of the melanoma cells. Currently, we are optimizing our existing 3D melanoma skin equivalent with the addition of a vascular system.

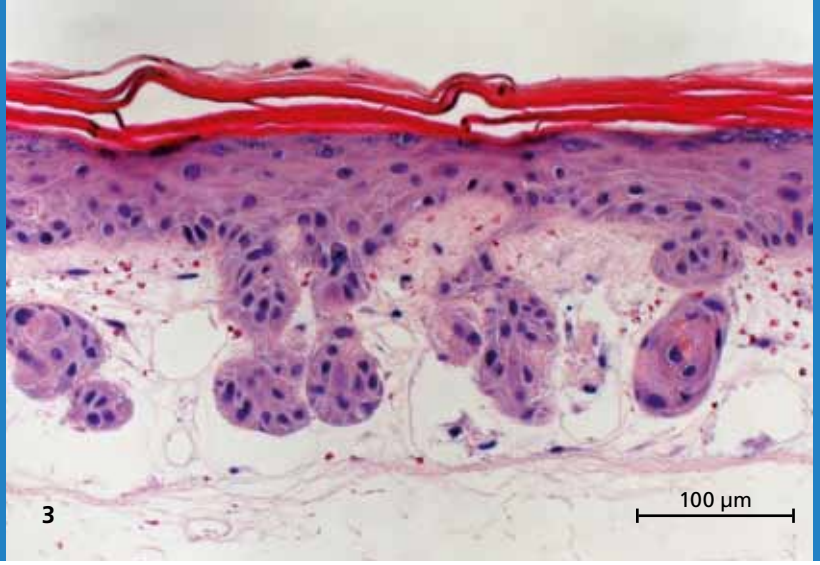
The vascular system in the natural skin is a critical factor in the development of skin tumors. In a process known as "tumor angiogenesis", melanoma recruits existing vascular structures of the patient for its nutrient supply. Additionally, individual melanoma cells can enter the bloodstream through the vessels and thereby form metastases in other parts of the body.

Optimal culture conditions

To generate a vascularized skin equivalent, skin-specific cells, such as keratinocytes and fibroblasts, are seeded into our biological vascularized scaffold, known as BioVaSc. The BioVaSc is then placed in a bioreactor system that is capable of creating optimal culture conditions required for a vascularized skin equivalent.

Vascularized skin model

First experimental studies demonstrated that keratinocytes and fibroblasts could grow and proliferate on the BioVaSc. Histological sections of the vascularized skin equivalent showed the formation of an intact stratum corneum demonstrating the functionality of the keratinocytes. Furthermore, immunohistochemical staining showed the typical layers of the epidermis.



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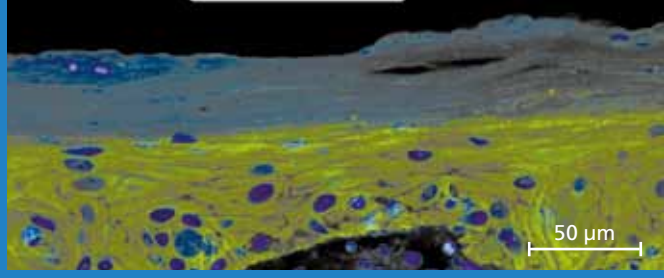

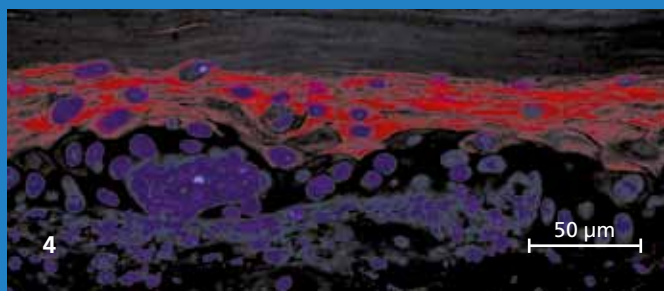

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Bioreactor for vascularized skin model

In parallel to the establishment of the vascularized matrix, the first bioreactor specifically created for a vascularized skin equivalent was developed. The bioreactor is able to supply nutrients to the skin equivalent through the vascular system as in the natural skin. By creating physiological, pulsed pressures, we are able to mimic the natural pressure and shear stress conditions found *in vivo* that are essential for the functionality of endothelial cells [3]. Furthermore, the capillaries allow the optimal delivery of nutrients to the cells.

Perspective

After the successful establishment of a vascularized skin model and the development of a suitable culture bioreactor, we will integrate melanoma cells into the existing vascularized model. A complete vascularized melanoma model will allow the *in vitro* investigation of tumor angiogenesis and the formation of metastasis under standardized conditions, which is essential for the development of new cancer therapeutics.

In collaboration with our partners, a novel therapeutic agent will be tested utilizing the melanoma model. For the first time, the agent will be administered *in vitro* via a vascular system in order to better reflect how it will be administered in a clinical setting.

1 *Bioreactor.*
2 *Biological vascularized scaffold (BioVaSc).*
3 *Vascularized skin equivalent.*
4 *Immunohistological staining of a vascularized skin equivalent against skin-specific surface markers.*

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Project partners

Institute of Cell Biology and Immunology (IZI), University of Stuttgart, Germany

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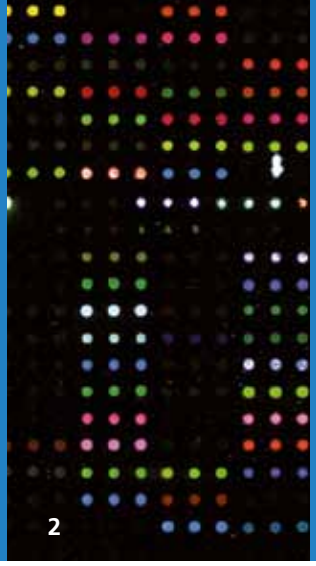

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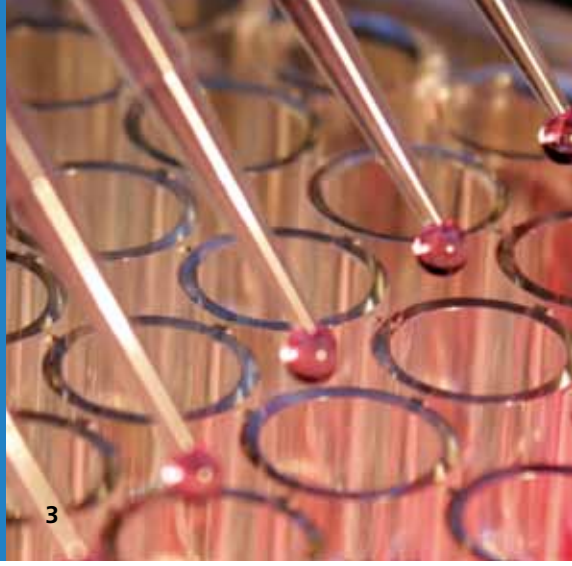


3

FUNGAL INFECTIONS – DIAGNOSTICS AND ACTIVE SUBSTANCE IDENTIFICATION

Dipl.-Biol. (t. o.) Michaela Mai, Dipl.-Agr.-Biol. Petra Keller, Dr. rer. nat. Karin Lemuth

As a result of modern, immunosuppressive therapies as well as a population which is rapidly aging, there is an ever increasing patient population that is susceptible to invasive fungal infections. Fungal infections are linked to a high mortality rate particularly in immunosuppressed patients. Since the standard diagnosis for pathogenic yeast and mold fungi is comparatively protracted and error-prone, prophylactic and expensive administration of antimycotics occurs with increasing frequency in hospitals. In the last several years reports of antimycotic resistances, particularly for *Candida* ssp., have increased steadily.

Conventional clinical tests for the identification of microorganisms and documentation of sensitivity or resistances to antimycotics rely on culture-based procedures (microdilution, Etest®) and can require up to 14 days particularly for molds. However, the culturing of molds from patient samples is frequently unsuccessful even though the patient is definitely clinically suspicious. In these cases a therapy on suspicion, which cannot be specifically adapted to the relevant pathogen, has to be initiated. Furthermore, clinical studies have shown that phenotypical resistance testing contains an error of up to 15 percent.

Precise diagnosis using DNA microarrays

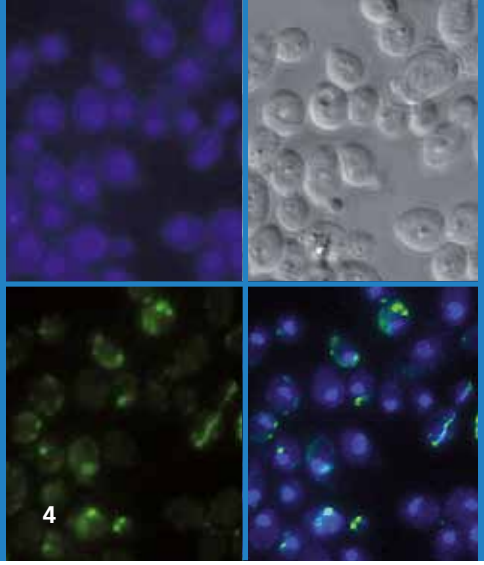
In order to detect human pathogenic fungi and their resistance spectrum quickly and accurately, a DNA microarray (Fig. 1) was developed at Fraunhofer IGB in the scope of the EU-funded joint project EURESFUN (**Eu**ropean **Res**istance **Fu**ngal **N**etwork). Compared to customary culture-based methods, the DNA microarray technology has the advantage that numerous parameters can be concurrently tested.

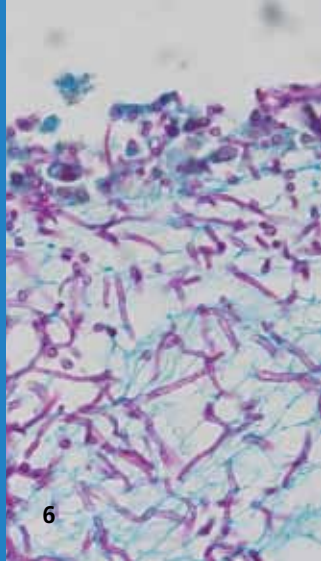
In addition to the identification of the 35 most frequent fungus species, point mutations can be monitored with this microarray that are responsible for the development of a resistance to fluconazole in *C. albicans*. Fluconazole is one of the most frequently administered antimycotics (Fig. 2). The functionality of the developed arrays could be tested and validated with clinical samples.

Identification of new active substances

In order to stay abreast of the resistance development, the search for new antimycotically effective substances is becoming increasingly important. The Fraunhofer IGB identifies and characterizes such new active substances in cooperation with EMC microcollections GmbH (EMC), the Helmholtz Center for Infection Research, and the Tübingen University Hospital.

For this purpose, the Activity Selectivity Assay (AS-HTS), which was developed at our institute, is used for the screening of extensive substance libraries, which are synthesized by our project partner EMC and made available for this work. The AS-HTS imitates the smallest unit of a fungal infection (Fig. 3). In contrast to conventional active substance screening, the human cells are included in the test in this case. They are incubated under addition of the substance to be tested in the presence of the human pathogen, for example *Candida albicans*. A color reaction provides information on the survival of the human cells and concurrently on the antimycotic efficacy of the respective substance being investigated. In this manner, in contrast to conventional active substance screening, the survival of the host cell is directly measured in the presence of the pathogen and the respective test substance.





Thus, the procedure allows immediate elimination of cytotoxic compounds. In contrast to conventional screening, many compounds with antimycotic action which would prove to be incompatible for the host cells in subsequent screenings (generally in animal experiments) are identified by this method.

Characterization of active substances

In order to characterize the antimycotically effective substances and their mode of action more closely, e.g. gene expression studies are performed with total genomic DNA microarrays as well as accredited, complex *in-vitro* infection models at the Fraunhofer IGB. The microarray analyses aid in obtaining insights into mechanism of action, which is then more closely characterized with methods such as immunofluorescence staining (Fig. 4).

The complex infection models built up using human tissue *in vitro* provide information on the penetration, distribution and metabolization of the investigated substances in tissue and help to avoid animal experiments (Fig. 5). Additionally, pharmacological and toxicological properties and the efficacy of the potential active substances can be tested on human tissue (Fig. 6). The tests thus provide evidence of which substances are antimycotically effective and simultaneously harmless for human beings. Only such compounds enter the next test phase.

1 *Printing process of a DNA microarray using 8 pins.*
2 *DNA microarray for the detection of point mutations in pathogenic fungi.*
3 *Screening of substance libraries with the Activity Selectivity Assay (AS-HTS).*
4 *Immunofluorescence images of C. albicans for the elucidation of action mechanisms.*
5 *Structure of an in vitro infection model.*
6 *Cross section of an in vitro infection model: invasion of C. albicans in an epithelial model.*

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Project partners

Euresfun: http://www.chuv.ch/imul/euresfun

Development of new active substances against human pathogenic fungi:

Helmholtz Center for Infection Research, Brunswick, Germany
EMC microcollections GmbH, Tübingen, Germany
Tübingen University Hospital, Tübingen, Germany

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EXTRACTION AND PURIFICATION PROCESS FOR INTERFERON-β-1b

Dr. rer. nat. Hans Weber

Therapeutic proteins continuously acquire higher shares of the pharmaceuticals market. Monoclonal antibodies, for example, show double-digit growth rates and also proteins which have been known for a longer period of time, such as interferon-β (IFN-β) exhibit an annual turnover of three billion US dollars. Treatment with IFN-β is one of the current basic therapies for the most frequent form of multiple sclerosis (MS), relapsing-remitting MS. The costs for IFN-β treatment in Germany amount to 18,000 euros per patient and year with the consequence that the majority of the 2.5 million MS patients worldwide cannot be adequately treated with IFN-β. In this context, the required quantities of active substances at 45 mg per patient and year for IFN-β-1b are very small.

Two forms of IFN-β

There are currently two forms of IFN-β on the market. The recombinant form prepared in animal cells (IFN-β-1a) corresponds to the human form in amino acid sequence and glycosylation. In contrast, the commercially available recombinant variant expressed in *E. coli* is not glycosylated and differs from the natural human form at its N-terminus (methionine is cleaved) and in that at position 17 cysteine has been replaced by serine. The form prepared in *E. coli* is termed IFN-β-1b. The patent protection of the two forms is running out. As a result, the opportunity of making IFN-β available as a biosimilar to a broader group of patients more reasonably and in many parts of the world for the first time ever has arisen.

Criteria for an optimized production process

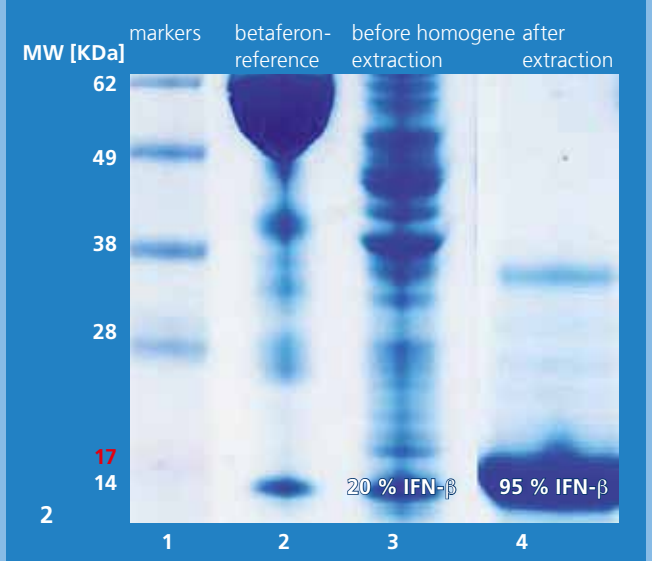
The objective of a current project at Fraunhofer IGB is the development of a procedure for preparing IFN-β-1b on an industrial scale. In this context, the price, the safety of the products, the stability of the processes (ruggedness), and the scalability are of central importance. A high expression rate, low costs for media and fermentation, as well as simple and stable procedures for isolation and purification (downstream processing) are decisive for the economic success and for safe patient care.

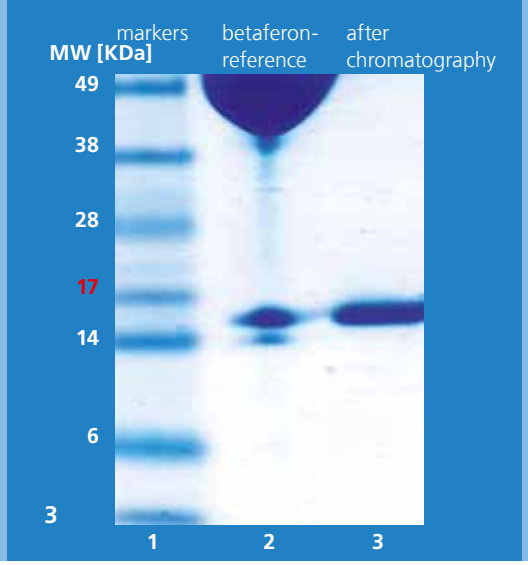
Cloning and expression

Scientists at the Fraunhofer IGB have been able to establish a highly productive clone, which bears an IFN-β-1b gene sequence adapted to *E. coli*. This allows the expression of the desired IFN-β-1b proteins within the cells as inclusion bodies. As a result of high-cell-density fermentation, a stable and high expression rate of at least 20 percent IFN-β-1b in the total cell protein is achieved with this clone.

Scalable purification processes

Isolation, purification, and solubilization of the IFN-β proteins from inclusion bodies have been a technically complex process up to now. The objective was to work out a technically simple and scalable downstream process for IFN-β-1b.





For this, the bacterial cells are disrupted immediately after fermentation with a combined enzymatic-mechanical process. From this cell homogenate, the target protein is obtained with high yield and selectivity in only one extraction step with 2-butanol. The hydrophobic interferon-β moves upward into the upper organic phase (2-butanol) with the aid of surfactants. Bacterial proteins are found concentrated as a solid layer between the lower aqueous and upper organic phase. The lower aqueous phase contains the hydrophilic substances of the cells such as salts and DNA/RNA. Fig. 1 shows the three phases after a phase separation forced by centrifugation. Fig. 2 shows the protein pattern by means of SDS-PAGE before the extraction step (lane 3) and in the organic phase (lane 4). The target protein is present with a fraction of 20 percent before the extraction step; after extraction it has a purity of 95 percent. The following chromatographic steps increase the purity even further (Fig. 3).

Perspective

With the technically simple and scalable purification process for IFN-β-1b established at the Fraunhofer IGB, the majority of the bacterial proteins are separated directly in the first purification step. We can thus avoid the laborious isolation, purification and solubilization of the inclusion bodies, which result in high losses. This process supplies IFN-β-1b in high purity, which can be reasonably manufactured on an industrial scale.

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1 *After centrifugation of the homogenates, three phases form. The IFN-β-1b is located in the upper, organic phase.*
2 *SDS-PAGE gel electrophoresis of the homogenate before extraction (lane 3) and the organic phase with IFN-β-1b (lane 4).*
3 *SDS-PAGE gel electrophoresis of IFN-β-1b after further chromatographic purification.*

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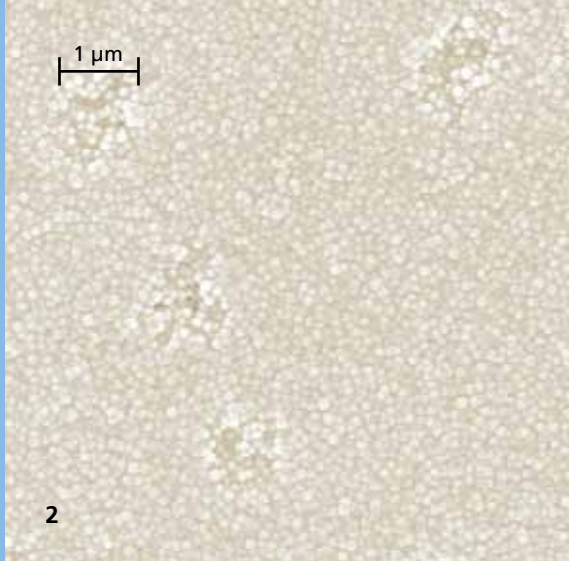


2

FUNCTIONAL INKS FOR INKJET PRINTING

Dr. rer. nat. Kirsten Borchers, Dr. rer. nat. Achim Weber

Inkjet printing is a highly attractive technology with capabilities that, in addition to color printing, are being used increasingly for printing diverse functional structures. Nowadays, for example, electronic printed circuit boards can be produced by means of printing technology. Rapid prototyping also makes use of inkjet printing in order to build complex models or lightweight objects in a layer-by-layer technique. In view of various new application fields, inks with a wide range of new properties are being increasingly needed for these applications.

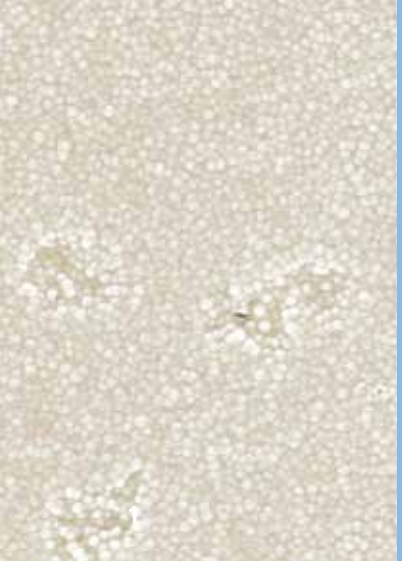
At the Fraunhofer IGB ink formulations are developed for the processing of a variety of functional components. In particular, we produce biofunctional inks, for example to make available biomolecules for the automated production of sensors or medical assays. A further very versatile component for the formulation of functional inks consists of nanoparticles that, depending on their chemical composition, incorporate various properties such as electric charge, conductivity, color or fluorescence in an ink. We produce aqueous or solvent-based inks depending on the requirements. We adapt the additives for adjusting the rheological properties of the inks to the properties of the functional components. A state-of-the-art high-precision printer, the Dimatix Material Printer 3000 (FUJIFILM Dimatix, USA), is available for printing extremely precise thin-film structural elements.

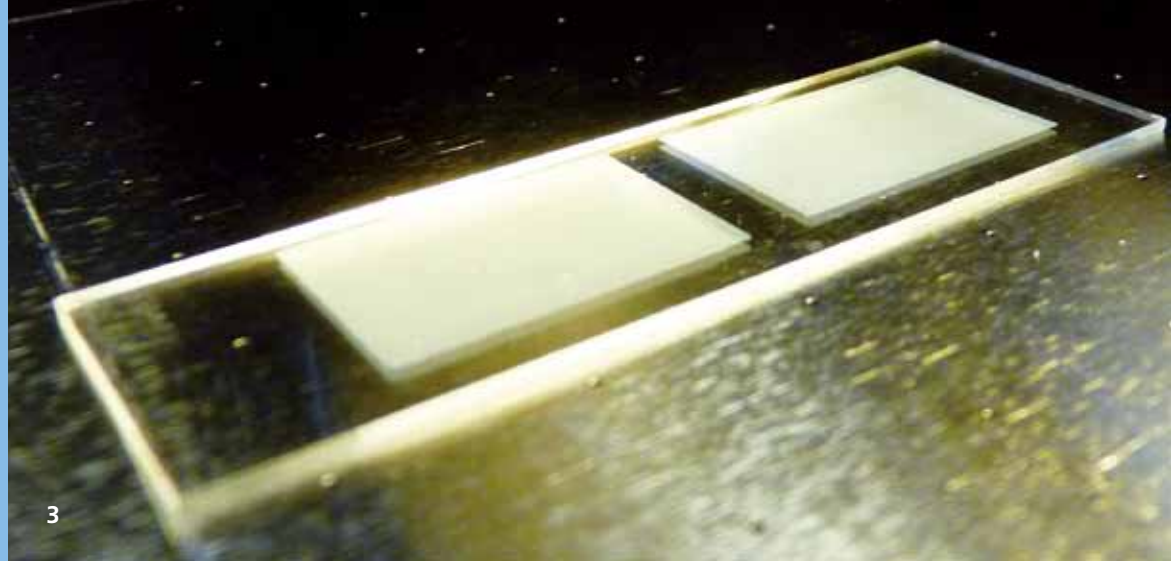
Inks containing nanoparticles

Nanoparticles have the potential for transporting a wide variety of functions. Both the properties of the particle shell as, for example, the provision of certain chemical groups and also loading of the particle core with dyes or active components for subsequent release, can contribute to the systematic design of material properties. Inkjet-suitable formulations are developed at the Fraunhofer IGB for the targeted and structured application of suspensions consisting of functional nanoparticles. To coat surfaces with electrically charged nanoparticles, for example, we have developed a wash-out, water-based ink. Glass carriers printed with a layer of such positively charged nanoparticles, are tested as a substrate for the development of sensitive rapid tests on the basis of nucleic acid microarrays.

Biofunctional inks

In biotechnology too there is a growing need for methods for the reproducible and automatable processing of materials – in particular for the processing of biological and biofunctional materials. At the Fraunhofer IGB an ink formulation has been developed for processing proteins while preserving their native functionality. These can be used, for example, to make certain areas on a substrate attractive for the adhesion of various types of cells. Alternatively, photo-crosslinkable protein inks are developed to be used for building three-dimensional carrier structures for cells. We have used water-soluble and protein-compatible components to adjust the viscosity and the surface tension of the inks (see chart).





Particle-based inks are also used for the development of biomaterials that can be used for cell assays. By adding various-sized particles to the ink we can create fields with differing topographies and investigate their influence on the adhesion of cells.

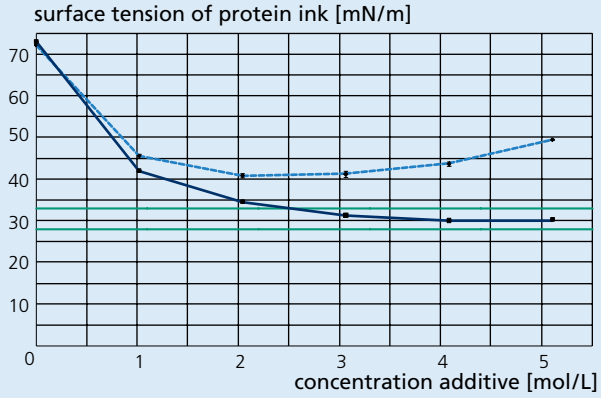
Perspective

Using inkjet technology, the application of expensive and high-quality substances to surfaces succeeds with pinpoint accuracy and practically without loss. Ink formulations from UV-A-crosslinkable biopolymers are currently being developed at the Fraunhofer IGB for use in 3D inkjet printing processes.

Services offered

- Formulation of water- or solvent-based inkjet inks
- Biofunctional inks
- Inks containing nano- or microparticles
- UV-crosslinkable inks
- Conductive and printed circuit board inks
- Printing of high-resolution structures

Adaptation of the surface tension of inkjet inks.



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Project partners

Fraunhofer Institute for Manufacturing Engineering and Automation IPA, Stuttgart, Germany
SCHOTT Technical Glass Solutions GmbH, Jena, Germany
Inomat GmbH, Neunkirchen, Germany

1 *Replaceable cartridge in the high-precision printer Dimatix 3000.*
2 *Printed nanoparticles on a glass surface.*
3 *Printed nanoparticle layers.*

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).

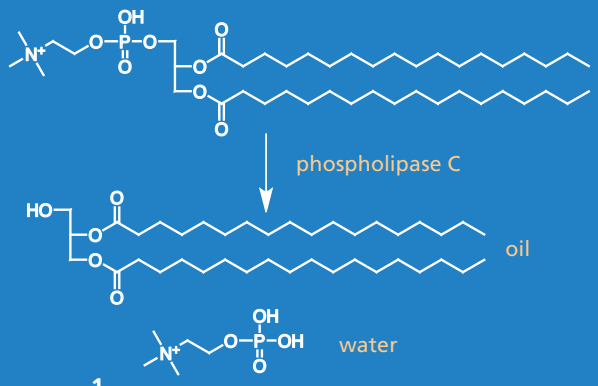
Decoupling of volume and surface properties by means of interfacial process engineering

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 Pfinztal institutes.



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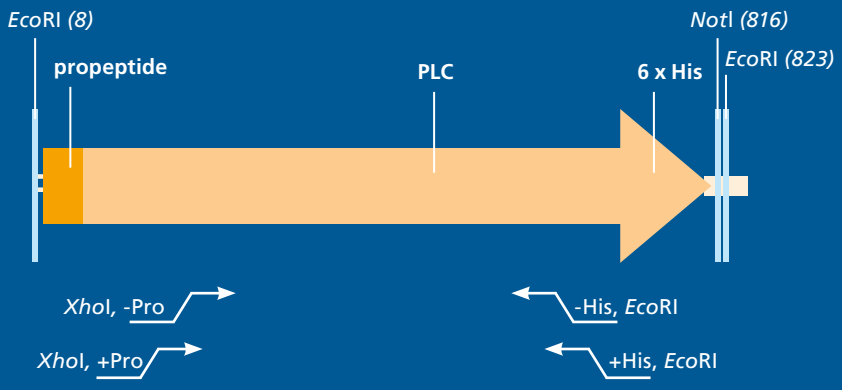


2

EFFICIENT PRODUCTION OF INDUSTRY-RELEVANT ENZYMES

Dr. rer. nat. Sven Krügener, Dipl.-Biol. (t. o.) Dipl.-Ing. (FH) Susanne Zibek

Enzymes are already widely utilized in the food industry, the textile industry, the detergent and the chemical industries as well as in the pharmaceutical sector. With modern methods, research continues to discover further new, industry-relevant enzymes which are scientifically characterized and optimized in terms of their catalytic potential. It is estimated that 10,000 enzymes occur naturally. Of these, 3000 are known, but only around 120 of them are used in industrial applications [1].

Therefore, the Fraunhofer IGB is working with research and industry partners on the joint project "Innozym" with the goal of developing efficient methods for the production and purification of technical enzymes on a scale of up to 10 m^3. This goal will be achieved through the development of appropriate production strains and through the optimization of the bioprocess engineering.

Approach

For the production of industry-relevant hydrolases and oxidoreductases, prokaryotic and eukaryotic expression systems are being evaluated and new expression strains and vectors are being developed. For variants that lead to higher yields at laboratory scale, we are pursuing process development and process optimization up to pilot-plant scale (10 m^3). For upscaling tests, an integrated, multifunctional plant (cascade fermentation and downstream processing apparatuses) will be available for the Fraunhofer IGB and the Fraunhofer Center for Chemical-Biotechnological Processes CBP at the Leuna chemical site next year. Both its conceptual design and construction will be integral to the project.

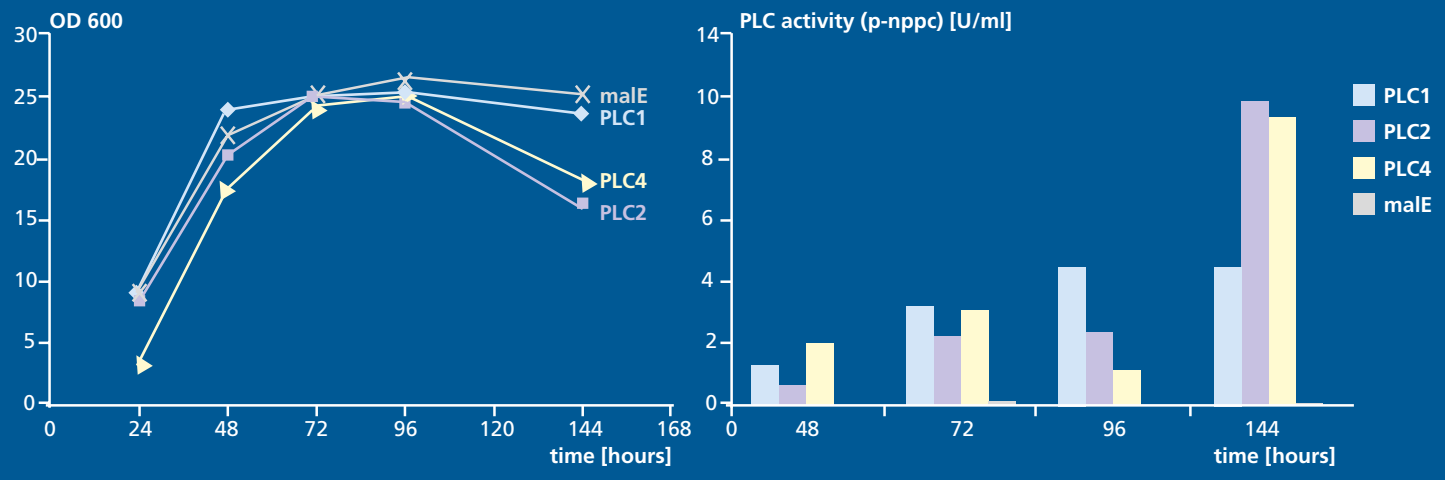
New expression systems

At the Fraunhofer IGB we are currently working on wild-type and protease-deficient strains of *Kluyveromyces lactis* and *Pichia pastoris* as eukaryotic expression strains. *Kluyveromyces lactis*, a non-methylotrophic yeast, can be cultivated and induced with various sugars, such as lactose from whey waste material. With *Pichia pastoris*, a methylotrophic yeast is employed. Methanol is more economical than many conventional culture media and inductors, and the strong promoter of the alcohol oxidase I allows a product yield on recombinant enzymes of up to 30 percent of the cell protein. The strains used are well suited to this application due to their effective secretory pathways, in particular for the production of enzymes that are emitted into the medium. Both production control and downstream processing of the enzymes is hereby significantly simplified.

At the Fraunhofer IGB we are currently developing production strains for the purpose of producing recombinant hydrolases (e.g. phospholipase C, proteases) and oxidoreductases. In the course of the project, extra production strains for the manufacture of cellulases, xylanases and lipases will be developed, which can be utilized in future projects of Fraunhofer IGB and of Fraunhofer CBP.

Example: phospholipase C

Phospholipase C (PLC) catalyzes the hydrolysis of phospholipids in cultures of diacylglycerols and water-soluble phosphorylethanolamine (Fig. 1). PLC is already commercially used in the refinement of plant oils in order to achieve a faster and virtually complete phase separation. Fraunhofer IGB uses



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expression cassettes with different variants of synthetic structural genes with optimized codon usage regarding to optimal transcription and translation on the basis of the PLC sequence of *Bacillus cereus* (Fig. 2). The expression cassettes will be integrated into the genomic DNA of the expression strains.

For the expression system *Klyveromyces lactis*, modified strains can already be identified that carry multiple copy numbers of the corresponding PLC construct in the genome. We have examined enzyme activity of the recombinant PLC variants against the substrate p-nitrophenyl-phosphorylcholine with the help of microtiter plate-based activity tests (Fig. 3). In so doing we could demonstrate that the optimized strains secrete PLC in the culture medium in an active form.

Perspective

Following the molecular-biological strain optimization, it is planned to optimize a high-cell-density cultivation with the utilization of various carbon sources in fed-batch processes. Moreover, we want to evaluate induction strategies with the goal of maximizing yield in terms of both space and time at the Fraunhofer IGB in Stuttgart and to pilot-plant scale at the Fraunhofer CBP in Leuna. Downstream processing should be developed simultaneously, whereby biomass separation methods as well as crystallization and chromatographic processes for product purification and concentration will be focused upon.

1 *Phospholipase-C-catalyzed hydrolysis of phospholipids using the example of lecithin.*

2 *Design of the structural gene for the production of phospholipase C (PLC). Multiple enzyme variants are expressed which can possess a propeptide sequence and histidine residues (His) for purification with affinity chromotagraphy. EcoRI and NotI constitute interfaces for nucleases.*

3 *Left: Chronological process of PLC expression in K. lactis with different constructs. Right: Activity of different phospholipase-C constructs PLC1, PLC2 and PLC4; malE (maltose binding protein) depicts the negative control.*

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Project partners

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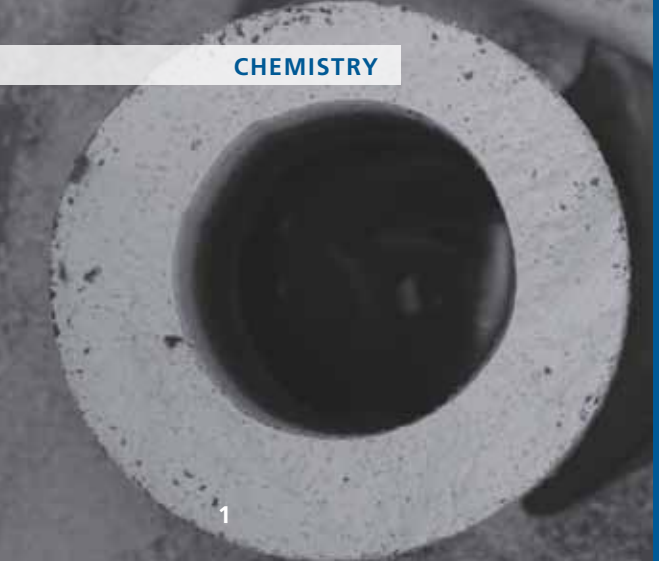
InfraLeuna, Leuna, Germany
Institute for Interfacial Engineering IGVT, University of Stuttgart



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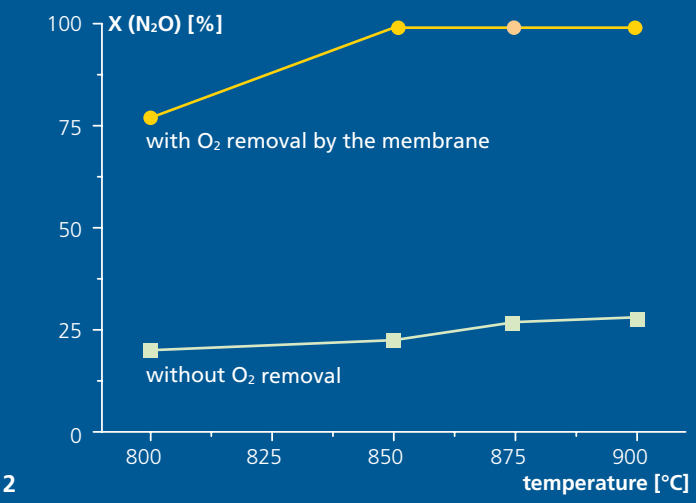

2

MEMBRANE REACTORS BASED ON PEROVSKITE CAPILLARY MEMBRANES

Dr. rer. nat. Thomas Schiestel

The enrichment of oxygen from the air and the separation of oxygen from other gas mixtures are of great importance for a multitude of oxidation reactions and combustion processes. One example is the use of methane contained in natural gas as a base material for the chemical industry. The methane needs to be partially oxidized to synthesis gas, a mixture of carbon monoxide and hydrogen. In recent years mixed conductive perovskites have increasingly come into focus as membrane materials for the selective separation of oxygen from air-gas mixtures. Such membranes can also be used directly as membrane reactors to intensify processes. In membrane reactors separation is coupled with chemical reactions. By doing this reaction products, for example, can be removed from the reaction zone, thus shifting the thermodynamic equilibrium.

Oxygen conducting perovskite capillaries

To combine the special material properties of perovskites with an effective specific membrane surface, at the Fraunhofer IGB we have developed oxygen-conducting perovskite capillary membranes. Compared to conventional geometries (disks, pipes, multi-channel elements) these membranes have the biggest packing density (separation area per volume) and an extremely low material requirement. By means of a wet-spinning process with subsequent sintering, the perovskite capillaries with an outer diameter from 0.5 to 3 mm and wall thicknesses from 0.05 to 0.4 mm are manufactured at pilot plant scale (Fig. 1). Gas-tight capillaries made of the perovskite material $BaCo_xFe_yZr_zO_{3-\delta}$ (BCFZ) show an oxygen flux of 5 $m^3m^{-2}h^{-1}$ and excellent selectivity (separation factor O_2/N_2 > 10,000) [1] at temperatures of 850 °C.

Applications

Together with partners from universities and industry the Fraunhofer IGB tested these membranes for various applications. The capillaries can be used for the manufacture of extremely pure oxygen [2] and for the partial oxidation of methane (POM) [3]. The splitting of water coupled with the POM utilizing these membranes facilitates the simultaneous manufacture of pure hydrogen and syngas [4]. Another application is the splitting of the greenhouse gas nitrous oxide into nitrogen and oxygen (Fig. 2) [5]. The kinetic hindrance is overcome by separating the oxygen through the perovskite membrane.

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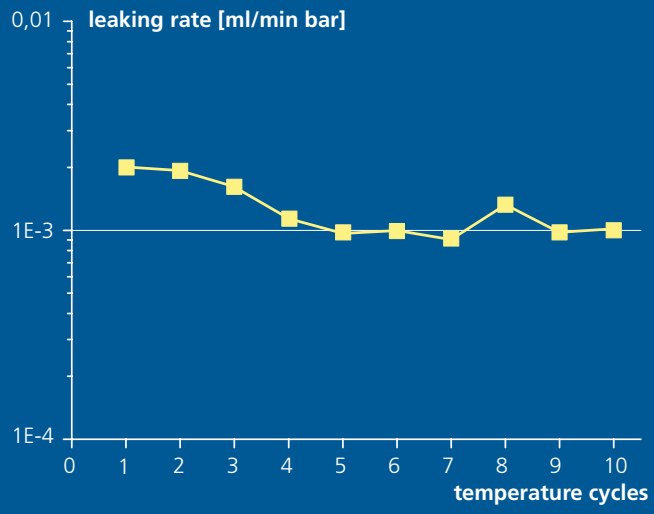

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Perspective

The development of long-term stable membrane modules is necessary (Fig. 3) for large-scale implementation of this technology. One challenge is the development of a high-temperature stable, gas-tight sealing of the membranes in a housing (potting). By optimizing the geometry and sealing materials, the Fraunhofer IGB has made possible the manufacture of sealings that withstand several temperature cycles without losing gas-tightness (Fig. 4).

1 *Typical geometry of a perovskite capillary. Outer diameter: 900 µm, inner diameter: 600 µm, length: 30 cm.*

2 *Conversion of N_2O at different temperatures with or without oxygen removal. Core side: 30 cm^3 min^{-1} (F_{N2O} = 6 cm^3 min^{-1}, F_{He} = 24 cm^3 min^{-1}). Shell side: (A) no oxygen consuming sweep gas applied, and (B) with methane as oxygen consuming sweep gas, 40 cm^3 min^{-1} (F_{CH_4} = 8 cm^3 min^{-1}, F_{Ne} = 12 cm^3 min^{-1} and F_{H2O} = 20 cm^3 min^{-1}). Membrane area: 0.86 cm^2. Amount of Ni-based catalyst on shell side: 1.2 g.*

3 *Floating head membrane module with 12 capillaries. The gas stream turns around inside the floating head.*

4 *Leaking rate of a sealing of a BCFZ capillary membrane and a high temperature stable housing material at 800 °C and 6 bar. The leaking rate is measured by pressure drop. In between measurements the module is cooled to 100 °C with a cooling rate of 1 K/min.*

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Funding

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Project partners

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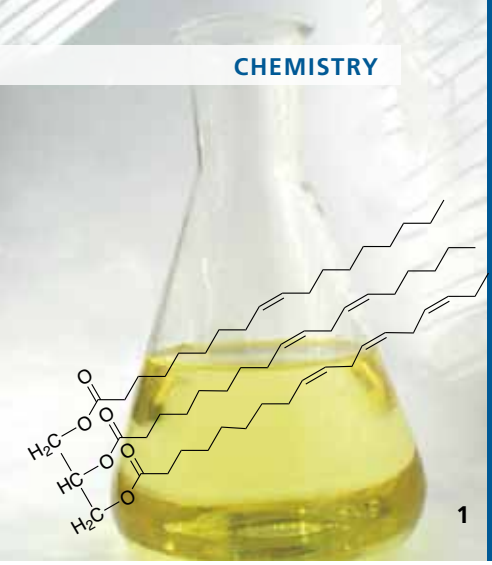
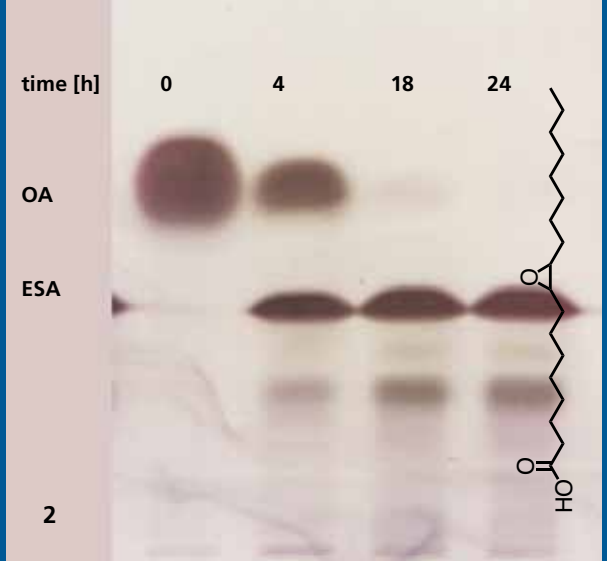
Uhde GmbH, Dortmund, Germany





THE CHEMO-ENZYMATIC PRODUCTION OF EPOXIDES ON THE BASIS OF VEGETABLE OILS

Fabian Haitz M. Sc., Dipl.-Biol. (t. o.) Dipl.-Ing. (FH) Susanne Zibek

Vegetable oils (Fig. 1) consist of triglycerides, glycerol esters, which differ in the composition of the fatty acids. The world market for the most important vegetable oils was approximately 133 million metric tons in 2009. The majority of them was used for human nutrition, approximately 10 percent of these oils was used for chemical-technical products [1, 2]. Compared to this, the worldwide mineral oil consumption in 2009 was about four billion tons. Approximately 50 percent of this was used for the manufacture of liquid fuels; besides this circa 20 percent, for heating, nearly 10 percent, as chemical raw material, and the remaining 20 percent, for various other purposes [3].

Vegetable oils for the chemical industry

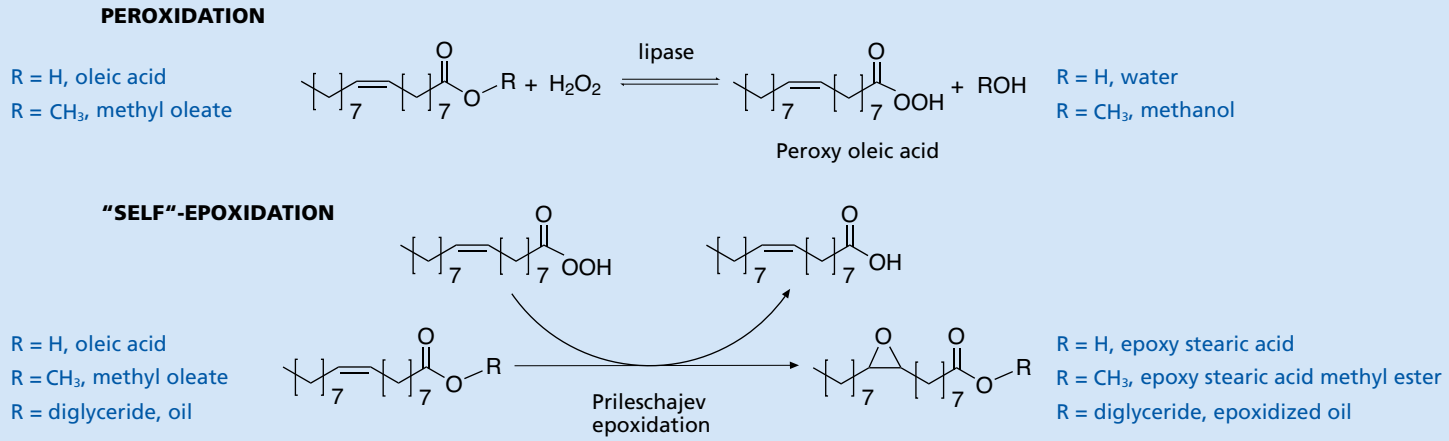
Because of the variable chain distribution, different physical properties, which lead to different application fields, result for the basic products obtained from vegetable oils, such as fatty acids, fatty alcohols, and esters. Fatty alcohols, for example, are used as raw materials for different tensides, primarily fatty alcohol ethoxylates (non-ionic tensides) and fatty alcohol sulphates (anionic tensides) [2]. Branched fatty acid derivates can be synthesized by means of an oligomerization of unsaturated fatty acids with petrochemicals, e.g. short-chain alkenes. In the process, products are obtained, which exhibit a higher thermal stability, a lower solidifying point, and a relatively low viscosity compared to majority of linear parent substances; moreover, they are therefore appropriate for use in lubricants [2].

Application and production of vegetable epoxides

A further possible modification of unsaturated fatty acids and triglycerides is epoxidation, in which products with increased polarity and reactivity are generated. These epoxides can, for example, be used as PVC stabilizers, plasticizers, cross-linkers in powder coatings, in epoxy resins, or as additives in lubricating oils. Normally, epoxides are manufactured from petrochemical base substances. Recently, plant-based epoxides have been obtained on an industrial scale, primarily from soy oil [4]. In this context, the so-called Prileschajew reaction (Fig. 4, bottom) is used, in which the olefinic double bonds of the unsaturated fatty acids are oxidized by peracid to expoxides (oxiranes). The peracid formation takes place via a chemical process, frequently in situ, based on reaction of hydrogen peroxide with acetic or formic acid using stronger mineral acids or ion exchange resins as the catalyst. An alternative to the chemical process is chemo-enzymatic epoxidation, in which the enzyme lipase catalyzes the peracid formation (Fig. 4, top) from fatty acids and hydrogen peroxide [5]. Substantial advantages of the chemo-enzymatic methods are thus the milder process conditions and a higher selectivity of the conversion. The undesired ring-opening reactions, which occur in the chemical methods, can, for example, be avoided to a very great extent in chemo-enzymatic processes.

Chemo-enzymatic epoxidation of Dragon head oil

The Fraunhofer IGB focuses on the optimization of chemo-enzymatic epoxidation of different vegetable oils and fatty acids, which are not in competition with the food industry. In this context, the oil of the annual, herbaceous Iberian dragon's



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head, for example, is used (Fig. 3). Using commercially available enzymes, e.g., an immobilized lipase from *Candida antarctica* (Novozym® 435, Fig. 4), we optimized the manufacturing process. In this context, for example, the influence of substrate concentration, hydrogen peroxide addition, the quantity of lipase used, and the temperature on the turnover of different substrates was investigated. As a result of the optimization of different process parameters, the different unsaturated fatty acids and oils could be converted into the corresponding epoxides with an efficiency of 100 percent using Novozym® 435 (Fig. 2). The produced epoxides are currently being investigated with regard to their technical utilization, and the manufacturing process is also being further optimized with regard to the product properties. On the basis of these results, a process design for the manufacture of epoxides on a technical scale should be prepared and assessed with regard to its cost-effectiveness.

New enzymes for chemo-enzymatic epoxidation

Beyond this, we also have screened for appropriate new enzymes. In this context, we have succeeded in identifying new, not commercially-available enzymes, which also catalyze peracid formation and thus in a subsequent step the expoxidation of unsaturated fatty acids. The newly identified enzymes are to be produced in large quantities, immobilized and investigated in terms of their turnover performance in an epoxidation.

1 *Vegetable oils as renewable raw materials for the production of epoxides.*

2 *Thin-layer chromatographic analysis of the lipase-catalyzed conversion of oleic acid (OA) to epoxy stearic acid (ESA).*

3 *Oil of Dragon's head is an alternative to edible oils.*

4 *Simplified reaction diagram of a chemo-enzymatic epoxidation [6] and reaction of an immobilized lipase (Novozym® 435).*

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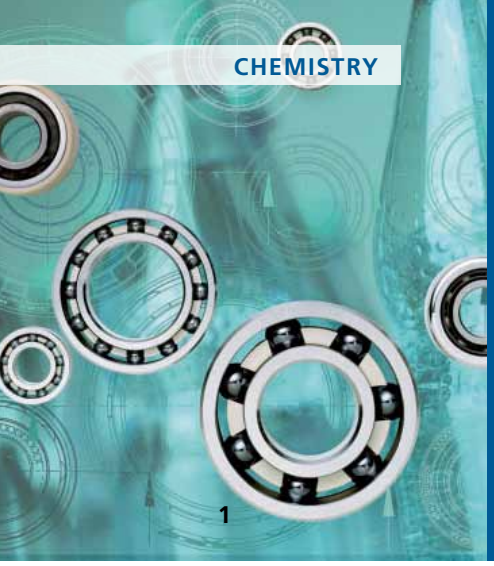

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REDUCED FRICTION AND ICE ADHESION – OPTIMIZATION BY MEANS OF PLASMA TECHNOLOGY

Dr. rer. nat. Michael Haupt

According to estimates, losses equal to five percent of the gross national product occur in the industrialized countries due to friction and wear on the surfaces of machines, for example in roller bearings. These losses can be substantially reduced; there are large potentials for reduction via directed change in the physical-chemical properties of the material surfaces. By reducing friction and wear, energy which would otherwise be lost as heat can be saved. In this context, a very promising approach is to change the wetting behavior of surfaces with regard to media – such as lubricants or also atmospheric humidity, water and cleaning agents – by means of a plasma modification.

Additionally, the adhesion of ice to wings or external sensors on airplanes and helicopters is influenced by the wetting behavior of the surfaces. By means of plasma functionalization, ice formation can be delayed and the adhesion of ice to the surfaces can be prevented. Expensive de-icing of planes, consumption of large quantities of de-icer, but above all consumption of up to 30 percent aviation gasoline and thus substantial CO_2 emissions could thus be avoided. Beyond this, anti-icing surface functionalization would make a considerable contribution to aviation and building safety.

NANODYN joint project

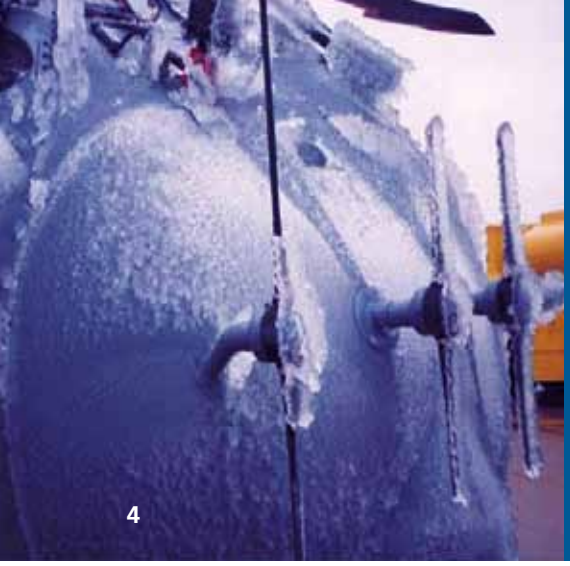
With the objective of developing microscale and nanoscale structured layers in order to control the wetting behaviors of surfaces, two research institutes and four industrial enterprises have teamed up in the NANODYN joint project. The University of Bremen is concerned with the simulation of structured wetting and dewetting surfaces, whereas the Fraunhofer IGB supports the project via the development of new plasma coatings, the creation of surface structuring as well as selective analysis of the structures generated.

Structured surfaces by means of plasma

Micro- and nanostructured surfaces exhibit ordered structures up to a size range of only a few nanometers. In addition to the chemical properties, structuring of the surfaces influences the wetting properties. Both the chemistry of the surface and the topography can be specifically adapted to the application via a plasma coating. By means of a special mask technology, the structures can also be applied to plastic foils, which are available as rolled goods. The ice adhesion to the modified surfaces is investigated in an ice chamber by studying ice formation (icing) and de-icing. In the chamber the temperature and atmospheric humidity can be selectively adjusted.

Application fields for plasma structuring

The diversity of application fields in which the new technology is to be used can be easily read off the list of participating companies. For example, the bearing manufacturer Cerobear hopes to increase resource efficiency in production and the service lives of roller bearings in applications. For ROWO Coating, efficiency increases, which could be achieved by coating film materials, are of interest. EADS Surface Technology, which expects a minimization of ice formation on airplane wings, comes from a completely different field.



The incorporation of PINK Thermosysteme, a manufacturer of plasma reactors, ensures that the new coating technology can also really be implemented on an industrial production scale.

Results

Friction can be reduced by up to 30 percent in coated roller bearings by means of a plasma surface coating. On textiles and plastic films we could selectively adjust the wetting properties from hydrophilic to super-hydrophobic. This allows us to incorporate novel sensors, for example, for atmospheric humidity, temperature, or voltage into the coated textiles. Without functionalization of the textiles, the sensors would be very slow or would not function long enough. For the aviation industry, we have developed plasma-functionalized nanostructured PU films. Compared to uncoated films, the ice adhesion could be reduced by more than 90 percent on plasma-coated PU films.

Perspective

The developed surface functionalizations will be used in a large number of products, such as in roller bearings for the food industry or wetting and dewetting sensor textiles. Plasma functionalized plastic films with modified wetting properties can be glued to airplane wings to reduce or eliminate hazardous surface icing. Additionally, they are also appropriate for wind turbines, on solar panels and on buildings whose surface is to be kept free of snow and ice.

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Project partners

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Cerobear GmbH, Herzogenrath, Germany
ROWO Coating Gesellschaft für Beschichtung mbH, Herbolzheim, Germany
PINK Thermosysteme, Wertheim-Bestenheid, Germany
EADS, Munich, Germany

Further information

www.nanodyn.de

1 *Plasma-functionalized roller bearings for the food industry.*
2 *Precision bearings.*
3 *Ice formation on an untreated airplane wing in wind tunnel test.*
4 *Ice-covered helicopter sensors.*

1

LIGNIN AS NATURAL RESOURCE FOR THE CHEMICAL INDUSTRY

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The renewable raw material lignin (Fig. 1) is the most frequently occurring natural source of aromatic compounds [1]. Together with cellulose and hemicellulose, lignin forms so-called lignocellulose, a polymer, which is responsible for the stabilization of plant cell walls. Every year large quantities of ligneous materials in the form of straw and wood wastes accrue; they can be used as a source of lignin. There is a great potential in the utilization of lignin structures up to lignin monomers as aromatic base materials for chemical syntheses or for use in biomaterials and adhesives. In order to effectively use lignin, the development of new biocatalytic and chemocatalytic depolymerization processes is required.

Such processes are at the focus of current research work at the Fraunhofer IGB. At the Stuttgart site, the identification, characterization, optimization and provision of ligninolytic enzymes of prokaryotic and eukaryotic origin are being studied. The BioCat Project Group in Straubing develops chemical-physical processes for the exploitation of lignin. The development of chemical-biotechnical processes should allow the material use of ligneous, renewable raw materials in the context of a biorefinery.

Utilization of lignocellulose

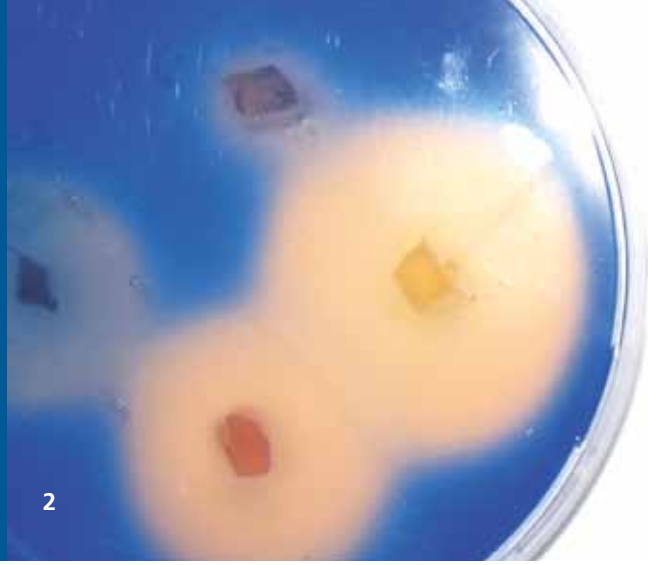
During the pulping of lignocellulose, two material streams occur: on the one hand, fibers containing cellulose, which can be enzymatically transformed into glucose; on the other hand, the pulping solution, which contains the dissolved hemicellose sugars as well as dissolved lignin itself. After precipitating the lignin and enzymatic cleavage of the sugar oligomers contained in it, the latter can be used for fermentation by microorganisms. In this context, the fermentability of the pulping solution is distinctly increased by an enzymatic detoxification with laccase [2]. The scale-up of the enzymatic lignocellulose disintegration up to a scale of 1 m^3 is being performed in the scope of the "Lignocellulose Biorefinery II" joint project at the Fraunhofer CBP in Leuna.

Ligninolytic enzymes from fungi

In the "Innozyme" joint project, the Fraunhofer IGB focuses on the identification, characterization and provision of extracellular, ligninolytic enzymes from certain basideomycetes, the so-called white rot fungi. Appropriate strains and co-cultures have already been identified (Fig. 2). The expression of lignin-cleaving enzymes such as laccases and peroxidases could be optimized by means of different media composition and inductors. Secreted enzymes are characterized by means of 2D gel electrophoresis and mass spectrometric detection, and then chromatographically purified. Finally, they are investigated and assessed biochemically. The enzymes are produced in submerse or emerse culture systems, respectively, and used in cell-free, enzymatic lignin disintegration, for example in the scope of the "Lignocellulose Biorefinery II" joint project.

New ligninolytic enzymes from bacteria

In addition to white rot fungi, some xylophagous insects are able to use ligneous plant material as a source of food. This ability of termites and the larvae of some beetle and butterfly



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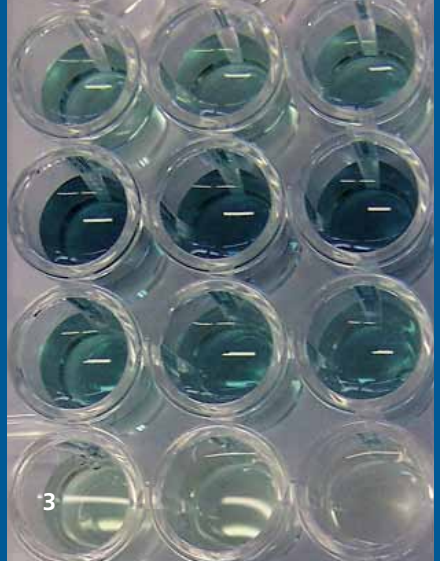

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species is based on a symbiotic mode of life with bacteria and fungi. In the "Lignocellulose Biorefinery II" joint project, the spectrum of the available biocatalysts for lignin degradation is to be extended at the Fraunhofer IGB in Stuttgart by concentrating and isolating symbiotic microorganisms from the digestive tract of the larvae of xylophagous insects. Parallel to this, culture-independent technologies (metagenomic screening) are used to identify ligninolytic enzymes of symbiotic origin. Beyond this, commercially available ligninolytic bacterial strains are being investigated with regard to their suitability for lignin depolymerization (Fig. 3). Appropriate enzymes are recombinantly produced and used for cell-free biotechnical processes.

Chemical-physical procedures

The oxidative cleavage of lignin provides better selectivity than its reductive degradation. Vanillin (4-hydroxy-3-methoxybenzaldehyde) can be obtained from *black liquor,* the secondary product stream in the manufacture of paper from wood, with a crude yield of 20 percent [3]. Depending on the source of lignin, additionally varying amounts of 4-hydroxy-benzaldehyde or syringaldehyde (3,5-dimethoxy-4-hydroxy-benzaldehyde) are formed. The objective of the work being performed in the BioCat Project Group at Fraunhofer IGB is to use selective oxidative cleavage to obtain a source of aromatic compounds from renewable raw materials. By developing secondary products, a bio-based product tree is to be established from the three above-mentioned platform chemicals and raw vanillin is to be transformed into marketable compounds with technically feasible processes.

1 *Proposed structure of lignin.*
2 *Oxidation of a model substance (blue) by a ligninolytic enzyme.*
3 *Activity determination of ligninolytic enzymes by means of oxidation of a model substance.*

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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 business area.

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 decentralized energy and water management. This is being further developed to allow its use in urban redevelopment. A further example is research being conducted into 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 algal 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 and Water Systems (SysWater) Alliances, as well as in the national technology platform SusChem Deutschland. Moreover, the Fraunhofer IGB has excellent international networks, particularly within Europe.

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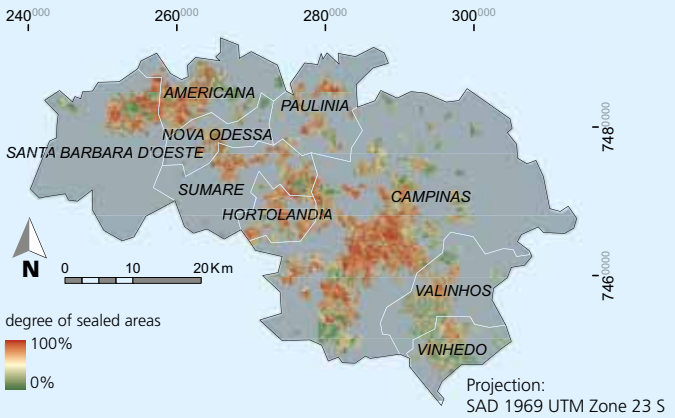


2

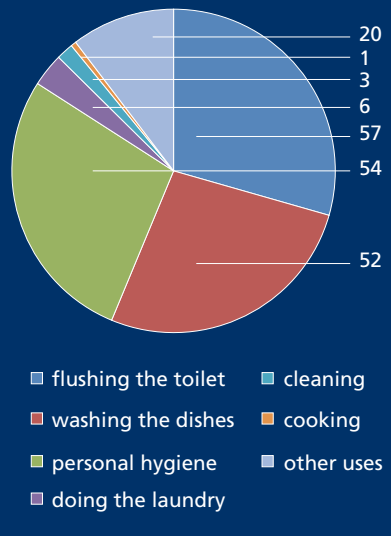
REGIONAL POTENTIAL ANALYSIS FOR RAINWATER UTILIZATION IN CAMPINAS, BRAZIL

Dipl.-Geoökol. Birgit Haller, Dr. rer. nat. Iris Trick

The south-east of Brazil, particularly São Paulo and its surrounding area, is marked by strong industrial and demographic growth. Therefore, environmental problems such as water pollution and scarcity of resources are increasing. For almost ten years scientists of the Fraunhofer IGB have been maintaining project partnerships with academic institutions and the relevant authorities of the Campinas region in the State of São Paulo to jointly develop innovative and sustainable water management solutions. Here, a special mention should be given to the Methodist University Piracicaba (UNIMEP). The exploitation of rainwater offers great potential. On the one hand, the precipitation intensity and the large areas of sealed soil (Fig. 1) within the cities often cause localized flooding. On the other hand, the demand for drinking water has strongly increased over the past years, resulting in temporary supply bottlenecks. A helpful alternative to current municipal water management could be provided by means of customized storage, processing and utilization of the harvested rainwater. To assess the potential rainwater yield and demand at regional level the Fraunhofer IGB in co-operation with the IGVT of the University of Stuttgart are utilizing and progressing spatial planning methods which build on geographical information systems (GIS). Their German partner is the Institute of Geography of Tübingen University which is providing planning details for the conceptual water and wastewater management.

Combination of geographic satellite data with regional precipitation maps

At regional level satellite data with medium spatial resolution, such as can be obtained from the Landsat system, provide a solid basis for the derivation of various planning parameters for rainwater utilization. For the Campinas region the degree of sealed soil in settlement areas was calculated pixel-based with the help of the software application *Impervious Surface Analyst* of Würzburg University [1] (Fig. 2). Through combination with regional precipitation maps it was possible to estimate the potential yield and the spatially distributed amount of rainwater available annually. In addition, the sealed soil map provides a basis for assessing various requirement values which could be compared with local yield values. As a first step we have estimated the population density spatially distributed over the individual regions based on the assumption that the density of development correlates with the population density [2]. For certain domestic uses, such as toilet flushes per capita, it was possible to include figures from local statistics to determine requirements (Fig. 3). Demand for watering public green spaces and gardens as well as for other uses (washing the car, external cleaning) varies depending on the development density. It was possible to determine four different requirement classes (Fig. 4) for irrigation by means of regression analysis using some high-resolution satellite data (Worldview 2).



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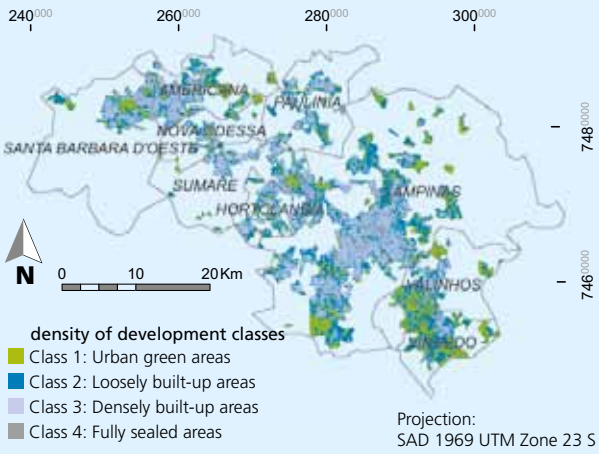

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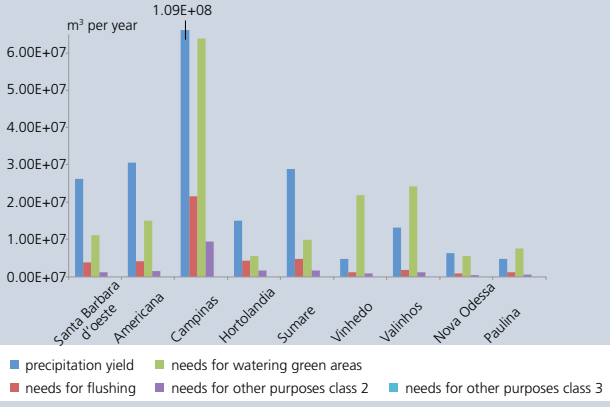
Potential yield and result

As a result it is now possible to compare the potential yield with various requirement scenarios for rainwater utilization for individual municipalities. The diagram below shows that as an annual total amount sufficient rainwater is available in the cities of the Campinas region to meet various requirements. Demand for the watering green areas is estimated as very high as fallow land is also included in the evaluation. Further detailed planning is necessary for implementation purposes.

Perspective

The GIS-supported approach provides the possibility to evaluate the yield and demand situation relating to individual areas. In terms of the local level this means that, for instance, semi-decentralized rainwater utilization units can be determined. The suitability of the basic data plays a decisive role here, with satellite data ensuring independence from national authorities. The method is based on standard software systems. The aim is to support regional planners and the planning of municipal water management operations.

Comparison of rainwater yield and various requirement scenarios for municipalities in Campinas.



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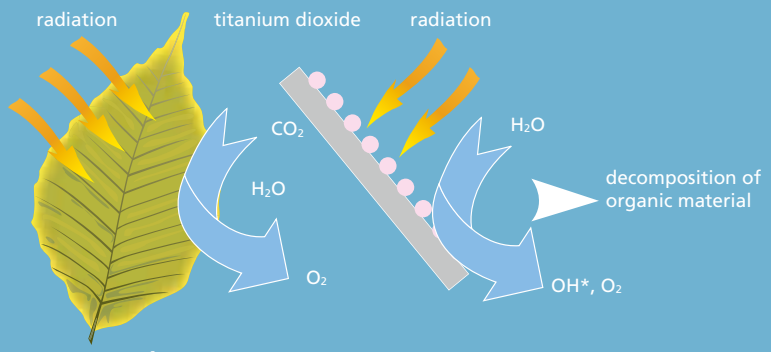
1 *High degree of sealed soil in the center of Piracicaba, in the Campinas region.*

2 *Sealed soil areas in the cities based on Landsat satellite data.*

3 *Domestic water consumption in l/cap/d for South Brazil; total consumption 173 l/cap/d.*

4 *Classes of different development densities as the basis for the rainwater requirements assessment.*



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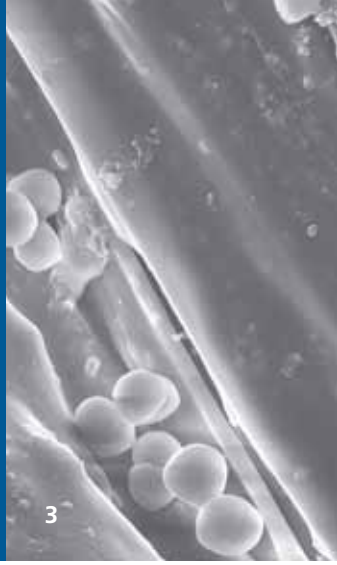


3

PHOTOCATALYTIC COATINGS TO COUNTERACT MICROORGANISMS ON SURFACES

Dr. rer. nat. Iris Trick

An innovative approach to achieving an antimicrobial effect completely without the use of biocidal or other chemical-synthetic agents is the equipment of surfaces with photocatalytically active coatings or nanoparticles (Fig. 1). The aim of a joint research project funded by the German Federal Ministry of Education and Research (BMBF) was the representation of such practice-oriented, highly effective coatings with self-cleaning and self-disinfectant properties based on photocatalytically active titanium dioxide components. These coatings can be used for a large number of products with a wide range of applications.

Procedure

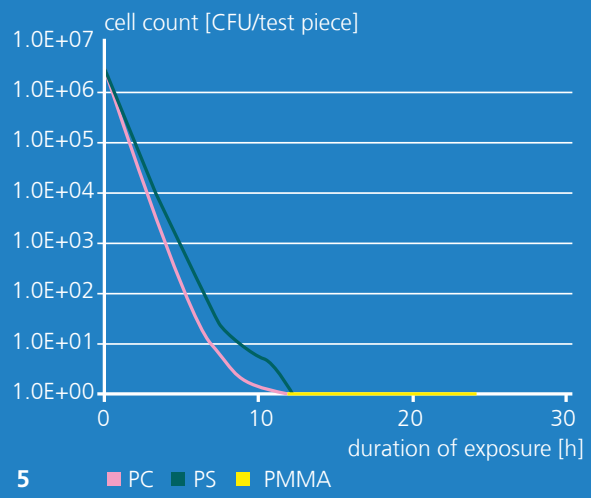
The material to be examined was made available by project partners and evaluated microbiologically at the Fraunhofer IGB. In all, more than 50 different surface modifications of polypropylene, polyvinyl chloride, polycarbonate, ceramic, glass and cellulose (filter material) as well as corresponding non-modified control samples were investigated. Gram-positive and Gram-negative bacterial strains were used as test organisms. These were applied to the surfaces in a defined cell count in accordance with standardized cultivation and using a spray technique. The photoactivation of the surfaces coated with titanium dioxide was carried out with a Philips Actinic BL-TL 20 W/10 low-pressure mercury vapor discharge lamp at a relative humidity of 93 percent and a temperature of 20 °C.

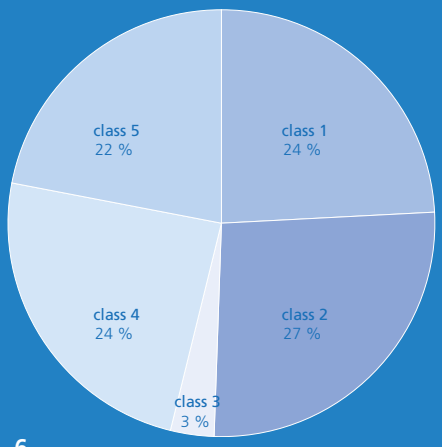
Results

The samples consisting of various materials were produced using spray techniques, sol-gel processing, by compounding, PVD methods, spray pyrolysis or plasma sputtering. Of great interest from the microbiological viewpoint were the influence of the material properties, the method of coating and/or the equipment of the specimens as well as the impact of various proportions of photocatalyst on the inactivation of the various test organisms (Fig. 3). Fig. 5 shows an example in which three synthetic materials were examined. Here, with the test organism *Sarcina lutea* a distinct 5-6-log reduction of the cell count was achieved depending on the time. This corresponded to an inactivation of 99.999 to > 99.9999 percent.

For all the measurement series carried out during the joint research project with the aim of characterizing the various surfaces, materials and thus the coating processes with regard to their antimicrobial properties, the endeavor was to achieve a quantification of the so-called reduction factor. The evaluation included all the results that were available from the characterization of the glass or synthetic material samples. In order to achieve a better comparability, the results available after a 12-hour exposure and with the Gram-positive bacterial standard test strain *Sarcina lutea* were taken as a basis. The resulting classification of the samples examined is shown in Table 1. As the initial cell count was generally set at 10^6, for example a reduction factor of 6 corresponds to the maximum achievable reduction of the microbial contamination under experimental conditions and thus to class 1.

Fig. 6 shows that about 50 percent of the photocatalytic surfaces examined with an observation time of 12 hours exposure come under classes 1 and 2. This means that at least 99.999 percent of the organisms used in each case on the samples examined are inactivated. In a further almost 30 per-





cent of the coatings a reduction of the microbial contamination by 99.99 to 99.999 percent was still achieved. An inactivation based on photocatalytic activity could be detected both on glass and on various synthetic materials. The advantage for an industrial implementation can be seen in the fact that, adapted to the requirements, all the above-mentioned coating processes are suitable, thus opening up a wide range of applications for photocatalytic finishes. The precondition is a relatively uniform distribution of the particles constituting the photocatalyst. A complete decomposition of cell structures was not observed with the length of treatment examined (Fig. 4). There is a need for further research here, especially regarding the degradation of fungal hyphae on surfaces.

Perspective

The Fraunhofer IGB plans to continue investigating from the scientific point of view the influencing factors and mechanisms of photocatalysis, to make available to industrial partners in bilateral cooperation schemes the practical experience gained while carrying out effectivity tests and to further develop the verification procedures.

Table 1: Classification of the results for comparison of the photocatalytic properties of the samples.

Length of exposure (hours)	Reduction factor Rf Reduction of log units	Reduction of the cell count in %	Class
12	6	> 99.9999	1
12	5	99.999	2
12	4	99.99	3
12	n. q.*		4
12	No reaction		5

*n. q. = Inactivation: Yes, not quantifiable

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Project partners

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Fraunhofer Institute for Chemical Technology ICT, Pfinztal
Fraunhofer Institute for Surface Engineering and Thin Films IST, Braunschweig | MRC Systems GmbH, Heidelberg
University of Heidelberg, Institute of Hygiene, Heidelberg
University of Heidelberg, Institute of Applied Physical Chemistry, Heidelberg | Laserzentrum Hannover e. V., Hannover
GXC-Coatings GmbH, Goslar | Sartorius AG, Göttingen
NTTF Coatings GmbH, Rheinbreitbach

1 *Diagram showing the photocatalytic reaction.*
2 *Photoactivation in test rig.*
3 *SEM image of test organisms on a synthetic material surface.*
4 *Structural changes of bacterial cells.*
5 *Inactivation of S. lutea on a photocatalytic synthetic material surface.*
6 *Percentage representation of classified surfaces.*

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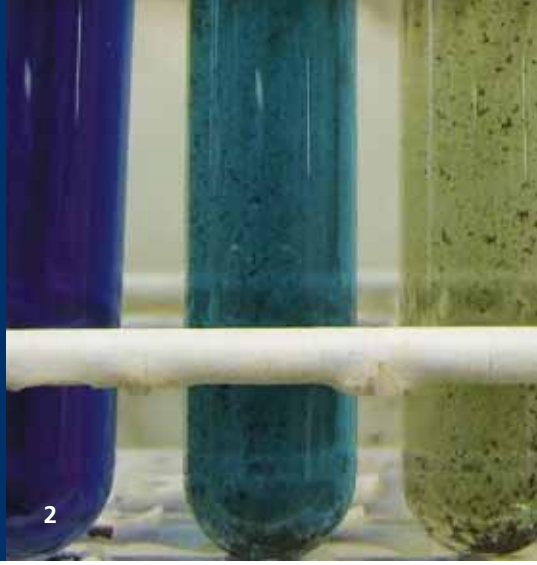

2

THE DEVELOPMENT OF OXIDATIVE TREATMENT METHODS FOR WASTEWATER PURIFICATION AND PROCESS WATER TREATMENT

Dipl.-Ing. Christiane Chaumette, Alexander Karos M. Sc.

Water is used in numerous industrial production processes as a solvent or means of conveyance, as cooling water or washing water. Rising costs for treatment and disposal as well as stricter maximum permissible discharge levels have resulted in process water being recirculated several times and the use of selective contaminant removal strategies. With the continuous improvement and change of products and materials as well as by introducing new production methods, new challenges are constantly arising in process water treatment.

Here, oxidative processes for water treatment offer effective and sustainable treatment options. The term advanced oxidation processes (AOPs) covers processes in which hydroxyl radicals are formed. These hydroxyl radicals are highly reactive and oxidize organic substances that are difficult to degrade chemically or biologically. The formation of hydroxyl radicals can be achieved by dosing oxidative substances such as ozone or hydrogen peroxide, by energy input in the form of UV irradiation, ultrasound or electric current, or combinations of these methods. At the Fraunhofer IGB, photo- and electrochemical processes, ozone treatment and plasma processes as well as combinations of these processes are currently being investigated for water treatment.

AOP research facility

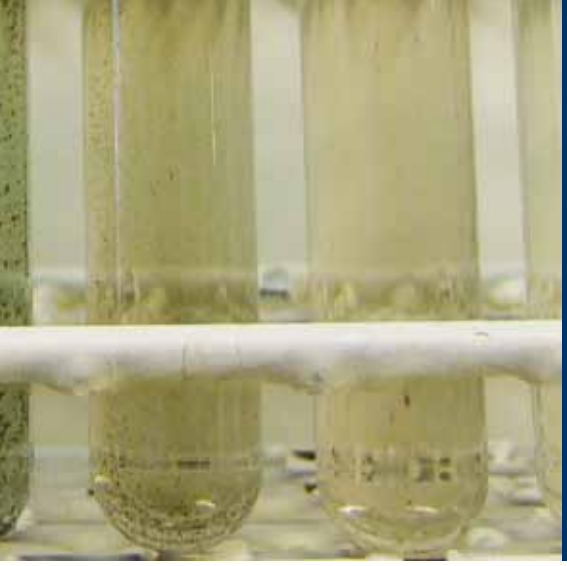
The Fraunhofer IGB has a pilot plant for the development of oxidative processes for wastewater treatment (Fig. 1). This facility offers an ozone generator (up to 4 g ozone/h) and an ozone reactor, a UV reactor (2 kW medium-pressure mercury lamp), ultrasonic units (25 kHz and 40 kHz; 1.7 kW) and an electrolysis cell (up to 50 A and 10 V) with separate anolyte und catholyte circuits (electrode surface 180 cm² each). These modular units can be freely combined. If required, further unit processes such as filtration and biological treatment can be incorporated in the process.

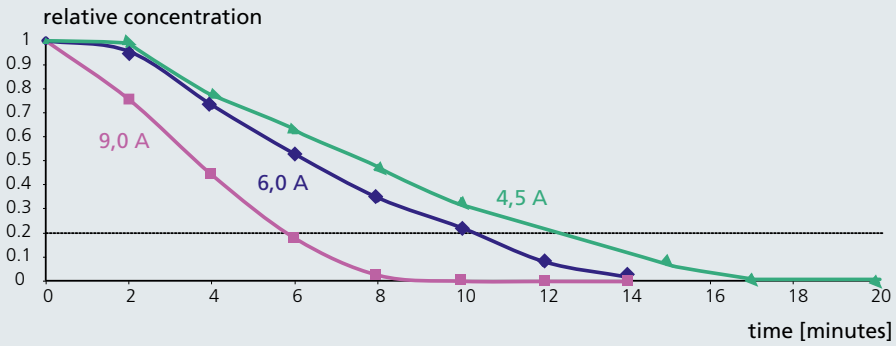
The facility is equipped with an online TOC analyzer, continuously measuring dissolved organic carbon and volatile organic carbon both in the intake and in the discharge during a test run. The facility is suitable for trials on the semi-industrial scale with a volume flow of up to 500 l/h.

In addition to the continuous improvement of processes for oxidative water treatment we typically use the facility to test run wastewater samples with selected AOP processes on behalf of industrial clients. Thus effective treatment strategies can be tested inexpensively on pilot plant scale and developed for industrial use. Here the specific energy input is of primary interest.

Example: methylene blue degradation

A problem in the field of oxidative wastewater treatment is the formation of degradation by-products, some of which are hazardous or are not sufficiently evaluated toxicologically. However, the formation of toxic by-products can be avoided in almost all cases by choosing suitable process parameters. In order to quantify the reaction mechanisms and degradation





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products of various AOP methods in the AOP research facility, tests with the model substance methylene blue ($C_{16}H_{18}ClN_3S$) were carried out. Figs. 2 and 3 show the oxidative degradation of the dye by indirect anodic oxidation. In addition to the decoloration (measurement at 664 nm), the formation of by-products was observed using HPLC, coupled with UV and mass spectrometry. In a comparison of anodic oxidation, ozone treatment und UV treatment, the ozone treatment turned out to be the best method for this wastewater model.

Further applications

At present the focus is on industry-oriented studies of landfill leachate and textile effluents. The aim here is to meet the discharge criteria of the communal treatment plants in a cost-effective way. In other projects currently under way we are developing new technical solutions for UV treatment and anodic oxidation together with our industrial partners. These projects aim to make the solutions ready for market launch.

Perspective

By reducing the use of chemicals, electrolytic and oxidative processes offer economically attractive and sustainable solutions for the purification of industrial, process water and wastewater polluted by substances which are not broken down in biological treatment. The energy required to operate the process can also be made available as electric current regeneratively provided by photovoltaics or wind power plants.

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1 *Pilot plant at Fraunhofer IGB for the development of advanced oxidation processes (AOPs).*

2|3 *AOP method: anodic oxidation; decoloration of a model solution (Nb/BDD anode, 25 mg/l methylene blue in 0.5 M salt solution, 25 °C)*

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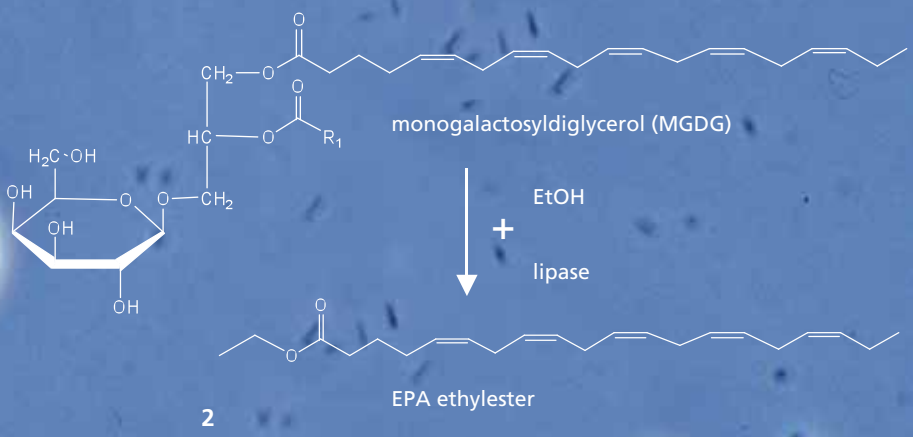

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EXTRACTION OF EPA ETHYL ESTERS FROM MICROALGAE WITH SUPERCRITICAL FLUIDS

Dipl.-Ing. Andrea Seibert, Dr. rer. nat. Ulrike Schmid-Staiger

Algae produce a multitude of chemical base materials with high added value potential, such as carotenoids, fatty acids and proteins (Table 1). The long-chain omega-3 fatty acid eicosapentaenoic acid (EPA, 20:5) is most often utilized as a dietary supplement. Thus far, EPA has been predominantly extracted from fish oil, where it exists in composite form with DHA (docosahexaenoic acid, 22:6). Further refinement to obtain pure EPA is a complex and expensive process. Due to the various effects of both of these fatty acids on the human body, only pure fatty acids are capable of a precise and definite application. In comparison to fish oil, many microalgae hold only EPA (ca. 5 percent by weight) along with shorter-chain fatty acids and no DHA.

The goal of an ongoing project at the Institute for Interfacial Engineering IGVT at the University of Stuttgart is therefore to establish an integrated process for the production of EPA from the microalgae *Phaeodactylum tricornutum* as a cost-effective alternative to EPA production from fish oil.

Conditions of EPA production

The algal cells (Fig. 1) are cultivated with sunlight, mineral salts, and CO_2 in closed photobioreactors that are developed at the Fraunhofer IGB. EPA is produced in the chloroplast membrane of the microalgae as monogalactosyldiglycerol. For extraction of the monogalactosyldiglycerols from the chloroplast membrane, different organic solvents such as ethanol have been tested. Additionally, continuous extraction via supercritical fluids has been tested. This would afford the advantage of extracting the product without potentially health-harming solvents. In order for EPA to be utilized as a dietary supplement, it must also be processed in the form of ethyl ester (Fig. 2).

The integrated downstream processing for the production of EPA from microalgae can be broken down into multiple steps:

- Cell disruption of the algal cells
- Extraction of the monogalactosyldiglycerols from the microalgae
- Transesterification of the monogalactosyldiglycerols to EPA ethyl esters
- Further steps of purification

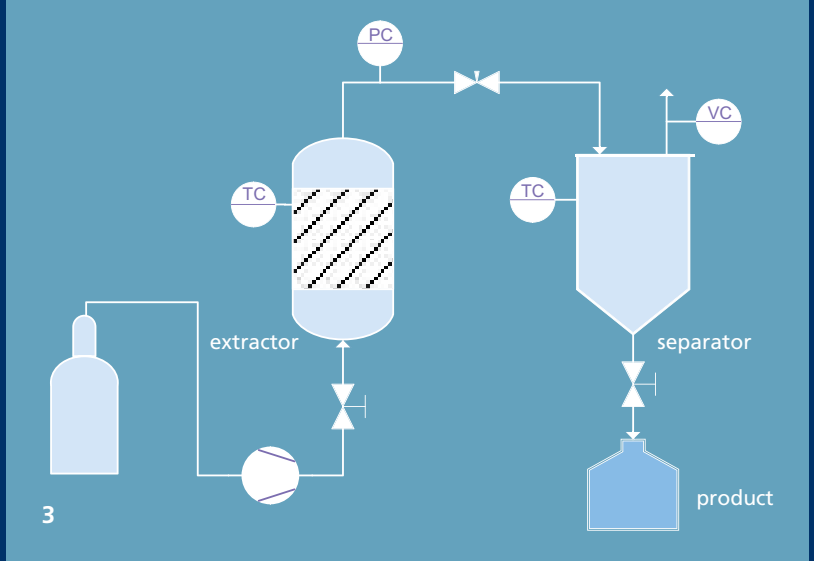
Mechanical cell disruption

Because EPA is found in the chloroplast membrane of the algal cells, cell disintegration is necessary to reduce the diffusion barrier effect of the cell membrane. Here two possibilities have been tested: pressing the algal biomass with up to 2000 bar to the point of disintegrating using a high-pressure homogenizer, and using a stirred ball mill, where the cell membrane is ground up and consequently the entire cell structure is destroyed and disintegrated.

Extraction of the galactolipids with supercritical CO_2

In addition to organic solvents like ethanol, we have also employed supercritical CO_2 ($scCO_2$) for the extraction of the galactolipids from the algal cells (Fig. 4). In the extractor, the biomass acts as a packed bed through which the $scCO_2$ flows. The extract is subsequently isolated from the CO_2 in the separator and collected (Fig. 3).

Because of the polarity of the galactolipids, the yield rate of the extraction process with $scCO_2$ can be increased through the use of ethanol as a co-solvent. The effects of the high-



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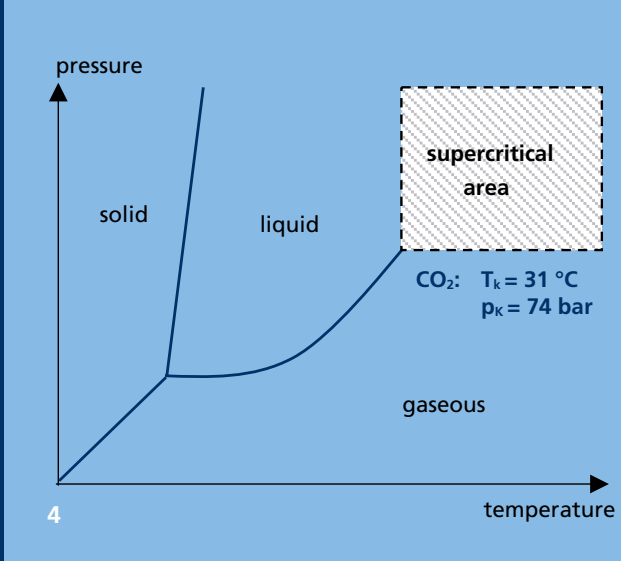

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pressure homogenizer versus stirred ball mill on the extraction results were also tested. It was shown here that extraction of the disintegrated biomass using the stirred ball mill method exhibited the highest yield rate of up to 85 percent.

Transesterification of the galactolipids to EPA ethyl esters

In the production of EPA ethyl ester for application as a dietary supplement, it is necessary to split the EPA from extracted galactolipids and to esterify it enzymatically with ethanol (Fig. 2). For this purpose, another solvent in addition to ethanol is required in order to maintain the enzyme activity, such as $scCO_2$. Enzymes for the transesterification are immobilized and employed as an enzyme packed bed. An ethanol extract with galactolipids is added to the continuous flow of $scCO_2$ over the enzyme packed bed. Contingent upon the concentration of galactolipids in the ethanol extract, the residence time for complete transesterification must be adjusted correspondingly.

Further steps of purification and perspective

For the extraction of pure EPA ethyl esters further purification steps are required: The separation of the ethanol using rectification, polar residual components using $scCO_2$ and the short chain fatty acid ethyl esters using $scCO_2$-chromatography still need to be developed.

To establish sustainable, resource-efficient and environmentally-friendly processes for the algal biomass material and energy potential utilization in the future, first valuable products should be extracted from the algae and fractionated using supercritical fluids and the residual biomass could then be used for energy production, according to the principles of a biorefinery.

1 *Microscopic image of Phaeodactylum tricornutum.*
2 *Conversion of monogalactosyldiglycerol and omega-3 fatty acid EPA to EPA ethyl esters with ethanol.*
3 *Flowchart of the plant for the extraction with supercritical fluids.*
4 *Phases diagram of supercritical fluids using the example of CO_2.*

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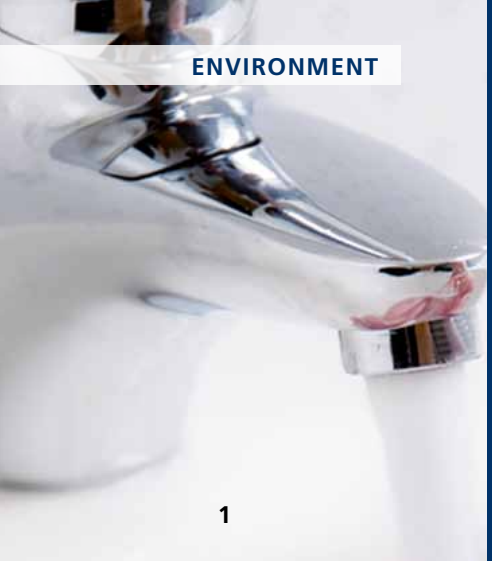
Table 1: Useable algae components

Pigments / Carotenoids	β-carotene, astaxanthin, lutein, zeaxanthin, canthaxanthin, chlorophyll, phycocyanin, phycoerythrin, fucoxanthin
Polyunsaturated fatty acids (PUFAs)	DHA (C22:6), EPA (C20:5), ARA (C20:4), GAL (C18:3)
Antioxidants	catalases, polyphenols, superoxid dismutase, tocopherols
Vitamins	A, B1, B6, B12, C, E, biotin, riboflavin, nicotinic acid, pantothenate, folic acid
Other	antifungal, antimicrobial and antiviral agents, toxins, amino acids, proteins, sterols, MAAs for light protection

MAA: Mycosporine-like Amino Acid (absorbs UV).



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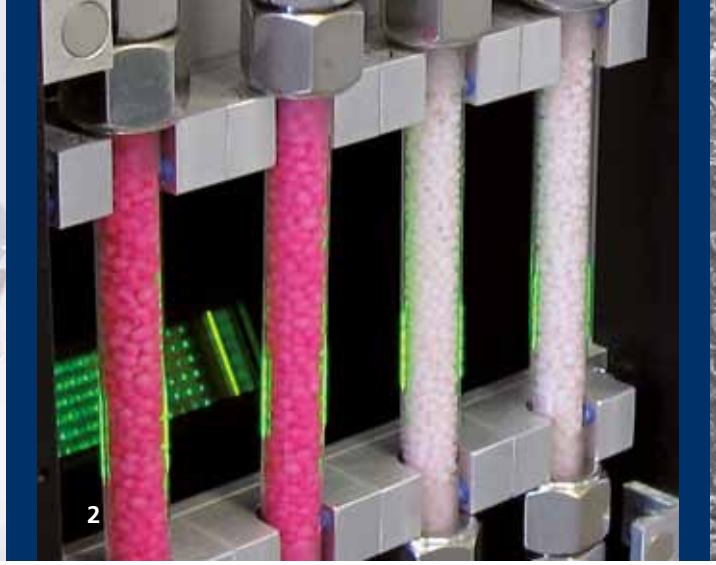

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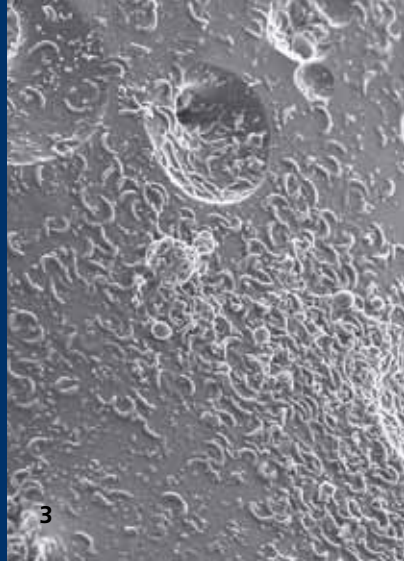

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BIOLOGICAL TOXINS IN WATER – DETECTION WITH BIOSENSORS

Dipl.-Ing. (FH) Tanja Maucher, Dr. rer. nat. Iris Trick

Hormones in baby food, antibiotics in meat and dioxins in eggs – toxins in food are a legitimate cause for serious consumer concern. In Germany, water is a consistently available consumable (Fig. 1) that is indispensible and therefore monitored with particular diligence. Suppliers of drinking water are aware of their immense responsibility and strive for ever better monitoring of their distribution systems.

First and foremost suited for this purpose are measuring principles that allow for *in situ* detection of toxic substances and which immediately indicate an alert. With the help of newly developed microbial sensors developed at Fraunhofer IGB, the presence of inorganic poisons such as cyanide or azide in the drinking water can promptly be identified. The next step was to focus on tests proving the presence of biological toxins produced by plants, fungi or bacteria. These also contain to some extent an enormous toxic potential. Even in low concentrations it can already present a life-threat to their consumer [1]. It is therefore of utmost importance to recognize their presence immediately.

Biological toxins

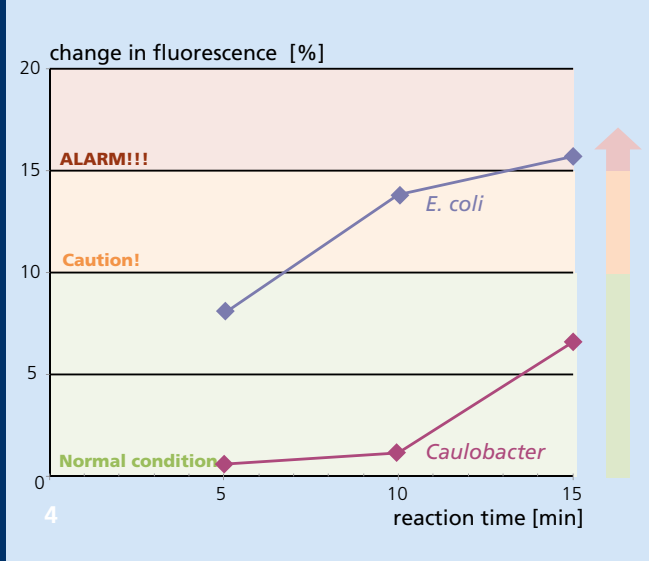
Some biological toxins are alkaloids, others are built from lipopolysaccharides, peptides or proteins. The toxic effect can manifest itself through a disruption of the cell protein synthesis, blocking the nerve receptors, a disruption of the cellular respiration or through overstimulation of the immune system. The toxin ricin, for example, a complex protein, is one of the most toxic known substances. Large amounts accumulate in the process of caster oil production, and it can easily be purified using simple methods [2]. With the two characteristics of easy access and serious impact, ricin is classified as a potential biological weapon of war. In addition, like many other biological poisons, it is highly water-soluble. Alongside ricin *Staphylococcus* enterotoxin F and other biological toxins were utilized in the biosensor system.

Principle of biosensor system

The biosensor system developed by the Fraunhofer IGB consists of three different cell types (two bacteria cultures and one mammalian cell line) genetically engineered in such a way that they build a red fluorescence protein (RFP). The cells are first immobilized and made available in a closed system (Figs. 2 and 3). In cases of alarm the intensity of the fluorescence changes, which can be detected using a probe (made by bbe Moldaenke) or a newly developed 2D sensor (Fraunhofer IOSB).

Reaction of biosensors to biological toxins

The goal was to develop a broadband detector as sensitive as possible in the detection of biological contaminants. Fig. 4 shows the reactions of the bacterial cell systems (*Caulobacter crescentus* RFP und *Escherichia coli* RFP) to the addition of a relevant amount of ricin i.e. at a potentially lethal concentration against the reaction time of the bacterial system. After only a few minutes a significant change in the fluorescence can be observed. The mammalian cell system (cell line HEK 293) reacts more slowly compared to the bacterial cells, but, regardless of the completely different cell constitution, with



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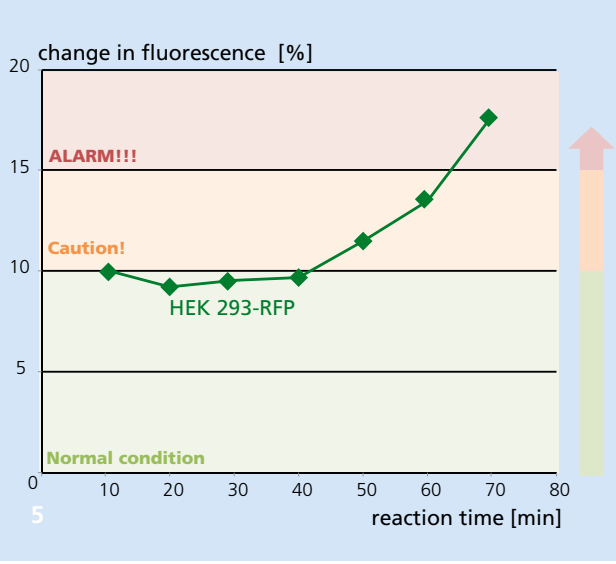

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an equally significant signal (Fig. 5). Consequently, it emphasizes the significance of the biosensors and allows the operator to distinguish between a false and genuine case of alarm.

Perspective

The novel biosensors used react to the biological toxins with a clearly visible change in fluorescence. The Fraunhofer IGB is working on implementing the process jointly with users and industry partners as a marketable product. Furthermore, we plan to adapt the reaction principle for additional applications in the food and environment sectors and to develop the biosensor accordingly.

In collaboration with the Institute for Interfacial Engineering IGVT at the University of Stuttgart, we are researching the interaction of the applied cells with possible toxins in order to illuminate the molecular mechanisms.

1 *Water as continually available consumable direct from the tap.*
2 *Bioreactors with microbial sensors for the monitoring of drinking water supplies. Contact with toxins results in a change in fluorescence of biosensors integrated in a demonstrator (co-operation partner Fraunhofer IOSB), and an alarm is activated.*
3 *Scanning electron microscopic image of Caulobacter crescentus, immobilized on a substrate.*
4 *Reaction of the bacterial cells of the biosensor to the addition of ricin.*
5 *Reaction of the mammalian cell line HEK 293-RFP to the addition of ricin.*

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Funding

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Project partners

Berliner Wasserbetriebe (Coordinator), Germany
bbe Moldaenke GmbH, Kiel-Kronshagen, Germany
Fraunhofer Institute for Optronics, System Technologies and Image Exploitation IOSB, Karlsruhe, Germany

ENERGY

Prof. Dr. Walter Trösch

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 CO_2 – 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 super-heated 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.

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2

RESIDUES OF OLIVE OIL PRODUCTION – FROM AN ENVIRONMENTAL PROBLEM TO BIOGAS PRODUCTION

Dr. rer. nat. Yasemin Sterr, Jennifer Bilbao M. Sc., Prof. Dr. Dieter Bryniok

With an annual production of nearly 2.2 million metric tons, olive oil production in Europe constitutes one of the most important sectors of the foodstuffs industry [1]. During its production (Figs. 2, 3) in Mediterranean countries like Spain, Greece and Italy large quantities of liquid and solid residues are generated in a short space of time during a two-or three-phase separation process. Due to the high content of phenols, fatty acids and organic substances the discharge of liquid waste into rivers creates a phytotoxic effect in bodies of water. In some regions the residues are collected in storage ponds (Fig. 4), which may also lead to damage to the environment.

Despite the fact that research into a cost-efficient, technically feasible and environmentally sound solution for the disposal of these residues has been going on for over 50 years, it has not yet been possible to find a satisfactory answer which can be comprehensively transferred to industrial applications. Together with nine European partners from research, industry and various associations the Fraunhofer IGB is developing a combined process during which organic substances present in high concentrations, such as polyphenols, are first extracted and reused as natural antioxidants. The residual biomass is then digested for the generation of biogas.

Digestion of residual biomass

Anaerobic digestion is a well-established method for the treatment of highly polluted wastewater or sewage sludge. Various microorganisms turn organic carbon compounds in several stages into biogas under the exclusion of oxygen. The biogas acts as a precious energy carrier [2]. Olive oil residues are characterized by a high concentration of potassium, organic and sulfur compounds and a low nitrogen concentration. Therefore, these residues constitute a special challenge for anaerobic microorganisms [3]. For this reason the experiments were carried out on a large number of solid and liquid waste batches which had been generated during olive oil production using different production methods in Spain, Italy and Greece. First the organic residues which accrued after extraction were tested in batch experiments in a two-stage anaerobic digestion unit in double-wall 1-l bioreactors (Fig. 5).

Biogas as a product

In these tests it was possible to reduce the proportion of organic compounds in the liquid waste by 75–90 percent. In the solid waste the organic dry matter could be reduced by 78–90 percent. Biogas production from solid waste came up to between 150 and 720 ml/g of total volatile solids (TVS) within 20–30 days. From liquid waste 680–980 ml/g TVS biogas were produced within 8–10 days. The methane content in biogas from solid waste was between 44 and 70 percent; the methane proportion in biogas from liquid waste was between 60 and 69 percent. The biogas yield increased after improved adaptation of the methanogenic mixed culture. Potential interruptions of biogas production, e.g. through inhibitory substances in the waste substrates, are currently being evaluated in continuous anaerobic digestion experiments at both a 1- and 100-liter scale.

Currently anaerobic digestion experiments are being carried out at pilot plant level. The results at laboratory scale already permit initial assessments of the energy balance: depending on the waste fraction approximately 300–3600 kWh per metric ton of solid matter; and due to the small proportion of organic substances, approximately 45-540 kWh per metric ton of liquid waste, can be generated. Additionally, the amount of waste could be considerably reduced in the process.

Fertilizers from digestion residues

Digestion residues will continue to be processed into organic fertilizers. Therefore the remaining solid matter is separated from the biogas plant and the liquid phase may be used for irrigation. Additionally the nutrients can be precipitated from the liquid phase and processed into fertilizer salts. Analyses of dried digestion residues show that the residues are highly suitable for the production of organic fertilizers.

Perspective

In order to embark upon an overall environmentally friendly and economically attractive course for residue recycling in the olive oil industry it is necessary also to consider logistical factors, the extraction of reusable materials and the heat utilization of the combined heat and power unit. This is the subject of current work and is being evaluated together with the project consortium.

1 *Black olives after harvest.*
2 *First washing stage of olives delivered for olive oil production.*
3 *Raw olive oil after separation in clarifying decanter in olive oil production.*
4 *Storage ponds for residues after olive oil production in Spain.*
5 *Double-wall bioreactors for anaerobic digestion of solid and liquid waste.*

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Funding

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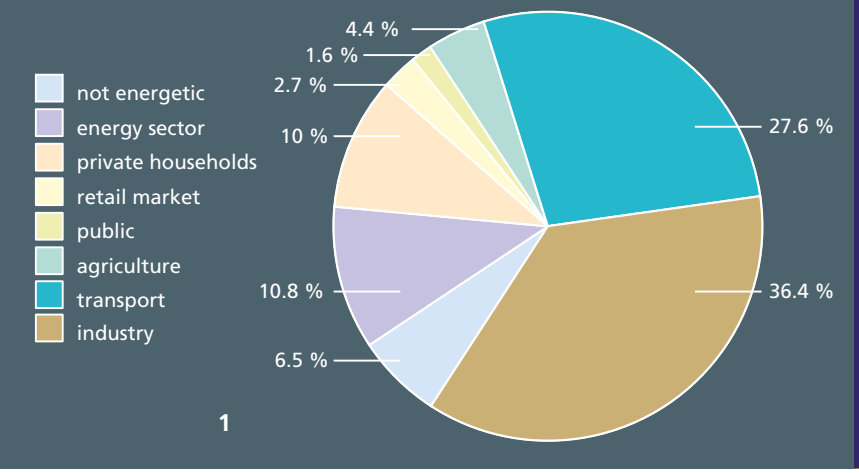

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POTENTIAL AND USAGE OF BIOGAS ILLUSTRATED THROUGH THE EXAMPLE OF BRAZIL

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

Brazil is the fifth largest country in the world with a population of approximately 190 million people. With a gross domestic product of $1573 billion (2009) [1], it constitutes the largest economy in Latin America. Brazil's energy consumption in 2008 is illustrated in Fig. 1 [2]. The two sectors with the highest energy consumption are industry (36 percent) and transportation (28 percent). The majority of energy use in transportation is expended through heavy load transport. Recently, converting buses and trucks to run on natural gas has begun to be discussed and taken into consideration [3]. Even in Europe this significant step towards environmental conservation has only been partially implemented. Natural gas can be directly substituted by bio-methane, derived from biogas – an important step towards employing more sustainable and renewable energy sources. In Europe, some regional bus fleets have already been converted to run on bio-methane.

Biogas is produced from organic matter by anaerobic digestion. Typical sources are agricultural products or residues, municipal organic waste, and industrial and municipal wastewater as well as sewage sludge. In many European countries biogas produced in wastewater treatment plants (WWTP) is already utilized in the production of electricity and heat (CHP) or as fuel. Although the biogas originating in the WWTP and landfills of newly industrializing countries like Brazil is principally burned, interest in renewable energy sources is very high and the search for economical and reasonable applications continues to grow.

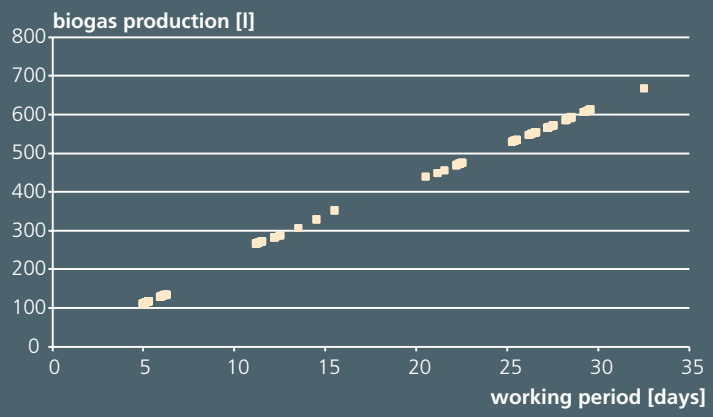
The Fraunhofer IGB, in partnership with two Brazilian WWTP operators, has explored the potential of biogas production from their treatment facilities in line with the International Climate Initiative of the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety.

Approach

One of the evaluated treatment plants is equipped with the activated sludge treatment process without specific removal of nutrients. It has the capacity of serving a population equivalent (PE) of around 350,000. The other WWTP operates a trickling filter process with a capacity of serving a PE of around 170,000 (Fig. 2). To assess the level of biogas production, experiments with raw sludge from the treatment plants were carried out in an automated, thermostatic pilot plant.

Biogas production potential

Fig. 3 illustrates a representative sequence of biogas production in the pilot plant operated with raw sludge from a Brazilian WWTP. The slope of the line depicts the mean of daily gas production. Fig. 4 shows the specific biogas production obtained per unit of influent total solids. In both German and Brazilian treatment plants, specific biogas production depends on the quality of the raw sludge and the operation of the digestor. Strikingly, the biogas produced in the pilot digestor operated with raw sludge from the Brazilian treatment plants was in the range of that produced by the German treatment plants. This means that in Brazil there exists good potential with regard to further biogas capacity development.



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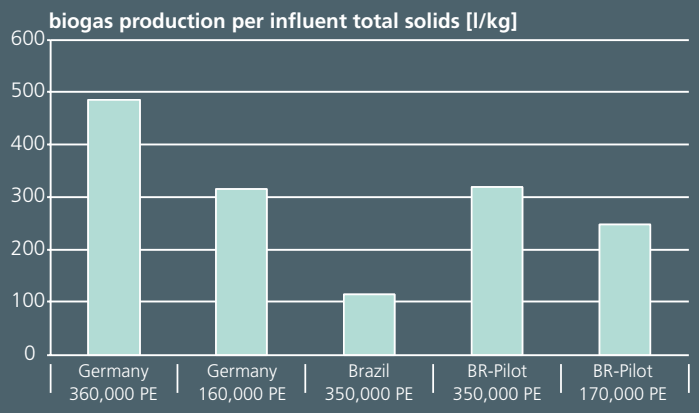

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There were also differences in the composition of the sludge gas. While the sludge gas from German treatment plants typically exhibits concentrations of H_2S of less than 200 ppm, that in the Brazilian plants exhibits concentrations up to more than 2000 ppm. Therefore, before any further usage, the sludge gas must be purified. For use as fuel according to the quality standards of natural gas, purification and compression costs range from R$0.2 to 0.3 per m^3 of bio-methane (1 euro = R$2.29, Jan. 31, 2011). At a price of about R$1.5 to 1.7 at natural gas filling stations, the economic feasibility of this application becomes clear. From the sludge gas of a WWTP with the capacity to serve a population equivalent to approximately 150,000 people, a daily supply of bio-methane equal to around 1500 liters of fuel could be produced. Much of current municipal transportation needs could be met with this supply.

Perspective

Brazil is rich in natural resources that can be used to produce biogas, and the government has begun to set up the requisite framework (e.g. growth acceleration programs PAC I and II). Brazilian urban waste, consisting typically of around 65 percent organic waste, ends up in landfills. A study regarding potential biogas generation at pig production farms in the state of Rio Grande do Sul established that the achievable magnitude of biogas production could substitute approximately 8 percent of natural gas needs of that state [4]. Organic waste materials of the agricultural as well as bio-ethanol and bio-diesel industry hold further potential for the generation of biogas.

The utilization of biogas in Brazil remains yet in its early stages. The example of the well-functioning pilot plant described demonstrates that the generation and usage of biogas from organic waste sources is not only environmentally sensible, but can also offer economic benefits. The Fraunhofer IGB, working with German companies and Brazilian partners, supports the technological development and sustainability of these processes.

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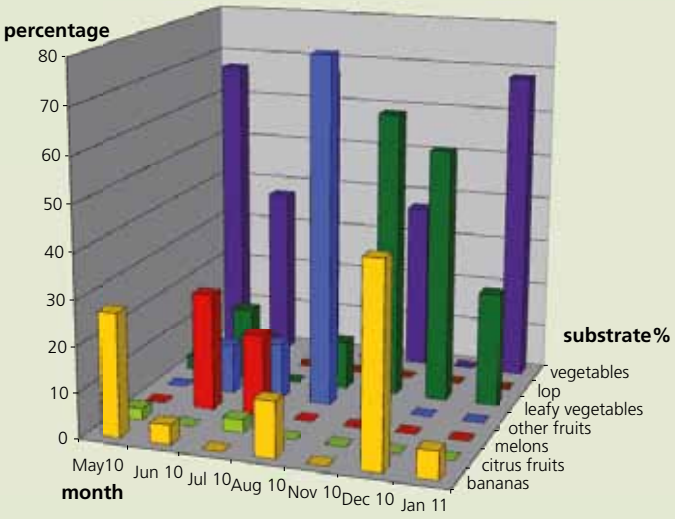
[4] Deutsche Energie Agentur – dena (2010) Biogas potential in Rio Grande do Sul, Brazil – an examination of the potential for biogas from pig production

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.

1 *Energy usage in Brazil by sector in 2008 [1].*
2 *Digestors at a Brazilian wastewater treatment plant.*
3 *Sequence of biogas generation (pilot plant).*
4 *Biogas production per unit of influent total solids.*



1

BIO-METHANE AS A FUEL – BASIC DATA FOR THE ETA-MAX DEMONSTRATION PLANT HAVE BEEN OBTAINED

Dr.-Ing. Ursula Schließmann

The utilization of vegetable biomass for the recovery of bio-energy – power, heat or fuels – plays an exceptional role as a sustainable alternative to conventional energy carriers. Biogas, a mix of energetically usable methane and carbon dioxide, is created during the anaerobic digestion of organic matter. In conjunction with the combined heat and power generation, biogas generation is considered a technology with a high net energy yield and a high CO_2 avoidance potential.

The project consortium linking partners from research, energy management and industry has therefore focused its activities on easily fermentable, low-in-lignocellulose, wet biomass – low-cost biowaste and residual algal biomass which constitute no competition for the production of foodstuffs – with a combined, modular process under maximum energy recovery. The aim is the complete conversion into biogas and the simultaneous closing of all materials cycles. The main focus is on the regional creation and utilization of regenerative methane (bio-methane). To do so the biogas is to be purified by separation of the carbon dioxide so that the bio-methane can be used as fuel for vehicles, which are operated on compressed natural gas (CNG).

Key technical components

In a high-load digestion process developed by the Fraunhofer IGB which has already been technically implemented several times, the solid matter biowaste fractions which are low in lignocellulose are almost completely converted into biogas within the space of only a few days.

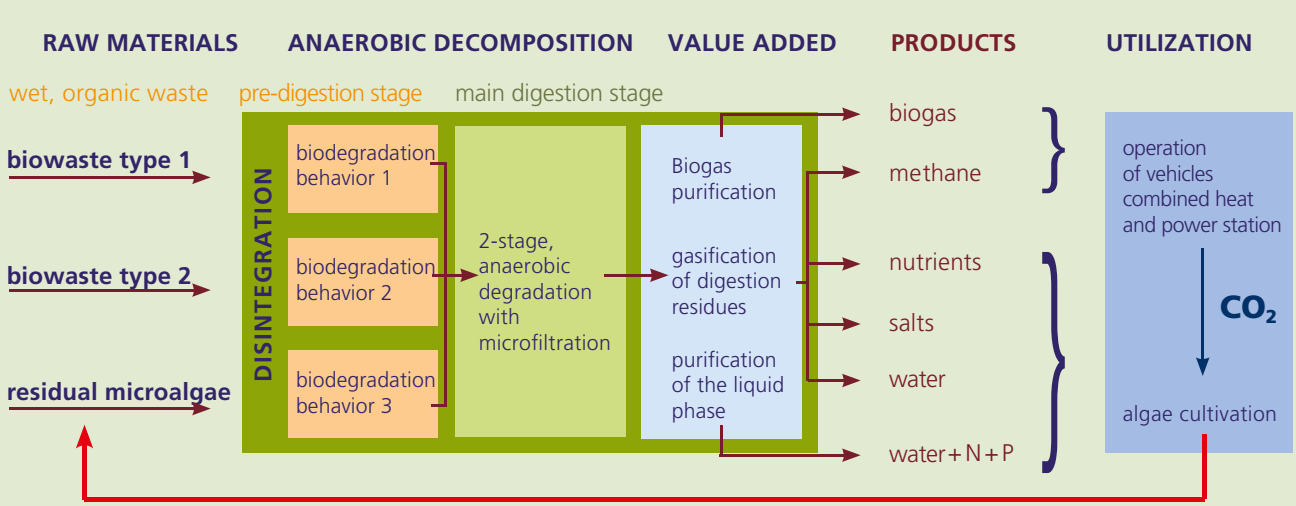
To ensure that a digestion plant can convert the different substrates as efficiently as possible into biogas, the process technology for the individual substrates is specifically adapted by means of a flexible multi-substrate high-load digestion plant. Only by doing so can the substrate be converted into methane with the maximum degree of efficiency.

Additional wet, low-lignocellulose biomass for multi-substrate high-load digestion is contributed by means of residual algal biomass. Energy recovery from algal biomass is already possible in a highly efficient manner today thanks to a photobio-reactor platform developed by the Fraunhofer IGB. The algae in the reactors grow to high cell densities using only sunlight as an energy source and carbon dioxide as a carbon source plus inorganic nitrogen and phosphate.

For small amounts of digestion residues which cannot be further decomposed in an anaerobic environment, the catalyst-supported hydrothermal gasification under high pressure and high temperature is examined. Here the same products are created as during the digestion process: carbon dioxide and methane.

Results

During the first year the process parameters were determined in a digestion plant at pilot plant scale (2 x 30-l reactors) at the Fraunhofer IGB for transfer to demonstration plant scale (2 x 3.5 m³). The two-stage pilot plant produced 850 l of biogas from central market waste per total volatile solids (TVS). In terms of the existing reactor volume this equates to an average of 190 l biogas per day at a volume load of 7 g TVS/ld.



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During the investigations unsorted market waste from the Stuttgart central market was provided, disintegrated and digested. The digestion of this unsorted waste constitutes a major challenge for the microorganisms. Our investigations showed that the fluctuations in the composition of the substrate could only be compensated by means of intelligent process control: by adding substrate portions of different digestion stages via several pre-digestion tanks, we can ensure a continuous biogas production with few variations despite the great fluctuations in the substrates.

The investigations in the pilot plant enabled us to successfully determine permissible values such as the minimum detention period and maximum volume load and parameters for the ideal feed of different substrate compositions which are key to the transfer to a larger scale.

EtaMax utilizes carbon dioxide, which is generated as a co-product during the digestion process and during the combustion of biogas as a source for the cultivation of algae. Current investigations have shown that the inorganic nutrients necessary for growth are contained in sufficient quantities in the filtrate of the digestion plant and can be used for the cultivation of algae. Expensive nutrients will therefore not be necessary.

Perspective

The joint factor of all individual components to be utilized is the minimum energy input for the implementation of the individual tasks. In the spring of 2011 the findings determined at pilot plant scale will be converted to a demonstration plant on the site of the EnBW combined heat and power station in Stuttgart-Gaisburg where they will be tested. The biogas generated in this way is purified utilizing a membrane system before it is used as fuel for vehicles. In addition, the environmental protection authorities will survey the biowaste potential which could be available in Stuttgart in the mid- or long term for large digestion plants.

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Funding

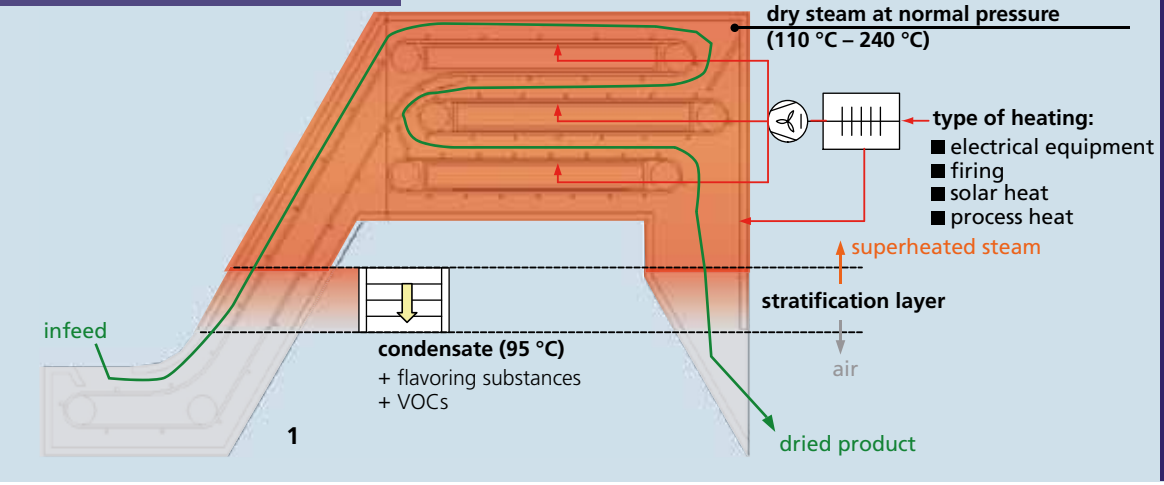
We would like to thank the German Federal Ministry of Education and Research (BMBF) for funding the joint research project "EtaMax – more biogas from waste and residual microalgae biomass through combined bio/hydrothermal gasification", promotional reference 03SF0350A within the scope of the program "BioEnergie 2021".

Project partner

Fraunhofer Institute for Process Engineering and Packaging IVV
Karlsruhe Institute of Technology (KIT)
Paul Scherrer Institute PSI
Daimler AG
EnBW Energie Baden-Württemberg AG
FairEnergie GmbH
Netzsch Mohnopumpen GmbH
Stulz Wasser- und Prozesstechnik GmbH
Subitec GmbH
The city of Stuttgart

1 *Easily digestible waste from the central market such as lettuce, fruit and vegetable accumulates in different amounts (random checks).*

2 *EtaMax: process and value chain.*



ENERGY-EFFICIENT DRYING THAT IS GENTLE ON THE PRODUCT AND ECOFRIENDLY

Sukhanes Laopeamthong M. Sc., Dipl.-Ing. Siegfried Egner

In the treatment and production of solids, drying frequently is considered an important process step. The amount of energy consumed by drying in many cases represents one of the largest parts of the overall processing chain. It is estimated that approximately 12 percent of the energy consumption for worldwide industrial application is used for drying purposes [1]. Nowadays, the industry is urged to reduce the energy required for drying. Thus, an energy-efficient drying technology capable of saving energy and nevertheless maintaining a consistently high and sustainable product quality becomes necessary. Conventional drying processes work with hot air.

Possibilities using superheated steam for drying

Due to its superior heat transfer properties to hot air, higher drying rates are achievable with superheated steam. Thus, drying with superheated steam is acquiring special importance with respect to the high potential for energy saving. In addition, oxidation processes on the material to be dried, which can result in quality deterioration and explosion risks, are considerably minimized due to the absence of oxygen from the air. Furthermore, condensable organic substances such as aromatic essences or other highly volatile components can be recovered from the exhaust stream and reused as value-added products [2]. At the same time this helps to avoid odor nuisances.

Principle of superheated steam at atmospheric pressure

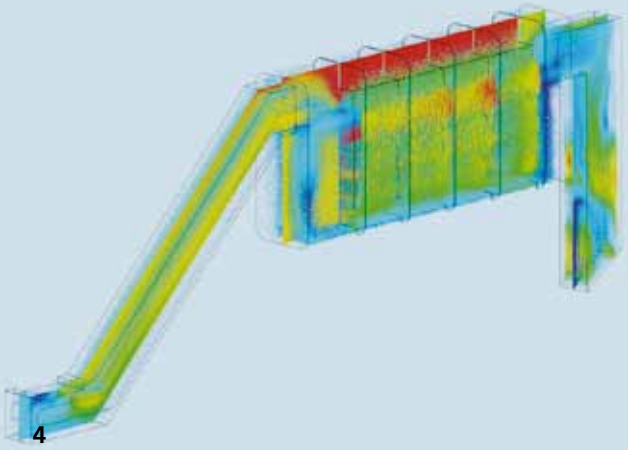
The material to be dried is introduced to the superheated steam atmosphere where it is heated up convectively and its moisture evaporates. This heat transfer process is effectively enhanced, since superheated steam has on the one hand a high heat capacity and thermal conductivity; on the other hand due to its low viscosity, fast penetration into the material is facilitated. As a consequence, this drying principle is especially effective for materials with a porous structure and results in a short residence time in the drying process. As the evaporation heat is supplied to the material from superheated steam, the steam atmosphere is cooled down. The moisture that is carried off vaporizes and becomes excess steam, which is discharged from the drying room in order to regulate the stratification layer. The superheated steam is recirculated and reheated in a closed loop. In this way, the temperature can be kept at the necessary level.

By exploiting the substantial difference in density between air and steam as well as proper handling of the material to be dried, any conveying technology can be applied for drying with superheated steam.

Continuously operating plant

To demonstrate the drying technology we have developed a continuously operating plant for drying with superheated steam at atmospheric pressure (Figs. 3, 4) and set it up in the pilot plant of the Fraunhofer IGB (Fig. 2). This has an evaporative capacity of 50 kg/h at a working temperature of up to 250 °C and is designed in accordance with the standards of the food industry. The system is closed upwards, however downwards it is atmospherically open. Excess steam can flow to the lower section due to the higher density, which at the same time prevents the infiltration of ambient air. By means

3



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of a targeted deposition of the excess steam, the phase boundary layer between the superheated steam and the air is controlled (Fig. 1). The plant has four chambers in which the drying temperature and the flow rate can be adjusted individually.

Results and advantages

At the Fraunhofer IGB, we have already completed various projects dealing with superheated steam drying at atmospheric pressure. We have also successfully dried a wide range of products such as mineral resources, building materials, biomasses as well as foodstuffs and animal feeds.

Superheated steam drying at atmospheric pressure offers the following advantages:

- No airlocks and sluices necessary
- 50 percent lower energy consumption and up to 80 percent reduction in drying time compared with hot-air drying
- 90 percent of the supplied latent heat can be recovered
- Compact plant and lower investment costs

For sensitive products such as foodstuffs, drying with superheated steam achieves good results in spite of the high temperature required. Due to the short drying phase, a degradation of the substances in the foodstuffs or browning as a result of enzymatic reaction can be observed to a small extent. At the same time, superheated steam drying at temperatures over 120 °C results in a hygienization of the products.

Perspective

In the plant set up at the Fraunhofer IGB, we can investigate the drying of diverse materials and characterize the product-specific process as well as the dried products. Implementation and construction of drying units is followed up by our partner from the industrial sector of machinery and plant manufacturing.

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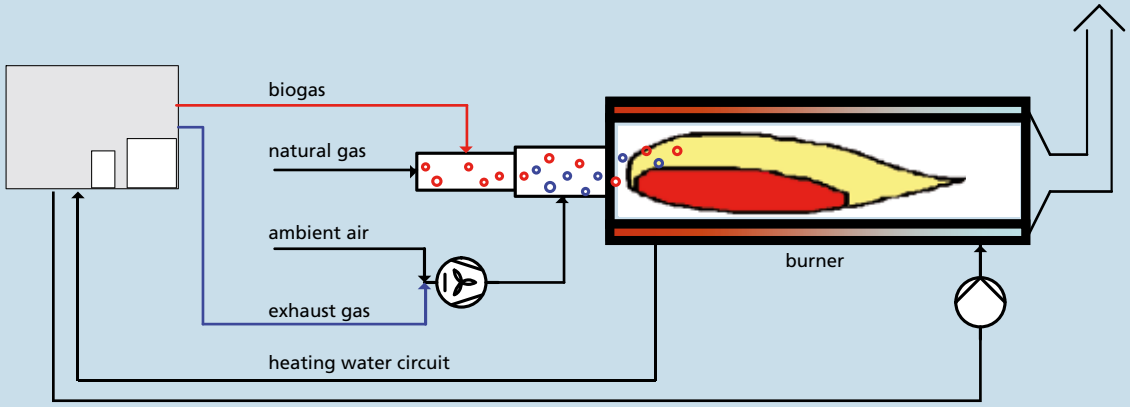
References

[1] Strumillo, C.; Jones, P.; Zylla, R. (1995) Energy Aspects in Drying, Handbook of Industrial Drying, 2nd Ed.; Mujumdar, A.S., Ed.; Marcel Dekker: N.Y.

[2] Mujumdar, A. S. (1990) Superheated Steam Drying – Principles, Practice and Potential for Use of Electricity. Canadian Electrical Association Report 817 U 671: Montreal

1 *Diagram of the continuous belt dryer.*
2 *Continuous belt dryer at the Fraunhofer IGB.*
3 *Three-dimensional CAD model.*
4 *CFD simulation of the continuous belt dryer.*



1

DIRECT UTILIZATION OF BIOGAS WITHOUT STORAGE

Dipl.-Ing. Marius Mohr, Dipl.-Ing. (FH) Stephan Scherle

Within the framework of the project DEUS 21 funded by the BMBF the Fraunhofer IGB is operating a semi-centralized plant for the anaerobic purification of water with integrated membrane filtration in Knittlingen. The plant generates biogas from the organic compounds contained in the wastewater and kitchen waste from approximately 170 households added via a vacuum system. The quantities of biogas achieved per day range between 8000 and 10,000 liters. As the methane content in this biogas lies between 60–70 percent, it constitutes a valuable energy source the utilization of which can reduce the demand from fossil energy carriers.

The biogas quantities generated in conventional biogas plants are considerably larger than the biogas generated at the Knittlingen plant. Plants for the utilization of relatively small amounts of biogas have therefore not been available on the market. Similarly small plants for the utilization of natural gas can not be utilized for biogas due to the different composition and the lack of accreditation. To be able to utilize the biogas with a larger aggregate, it would have to be stored in a reservoir. This is critical for explosion prevention reasons and because of its location in a residential area. In addition, for pressure storage it would be necessary to process the biogas. Therefore the Fraunhofer IGB has developed an aggregate together with C-deg GmbH in Kiel which allows for the energetic utilization of small quantities of unpurified biogas.

Biogas combustion with heat recovery

As biogas can not safely be provided at all times due to the small size of the wastewater plant as well as potential variations in the filling level in the reactors, combustion is handled by means of a support flame which is fed with natural gas (Fig. 1). Moreover, combustion is fed with an exhaust air flow from the filtrate ventilation of the wastewater treatment plant. This air flow also contains 2–3 percent methane which escapes the wastewater treatment plant dissolved in the filtrate. Yet, due to the high greenhouse effect potential the methane must be prevented from escaping into the atmosphere. At the same time the exhaust air flow transports oxygen and substances causing an odor nuisance such as hydrogen sulphide and ammonia, for combustion. A controlled combustion process ensures that the best possible conversion rate for these pollutants is achieved. Therefore, the flow of supply air varies depending on the amount of oxygen required, which in turn depends on the biogas amounts added. The exhaust gas generated by the combustion process is fed to a heat exchanger in which the heat energy of the incinerated gas is transferred to the heating circuit of the wastewater purification plant to heat the mesophilic digestion of the solid matter and the regenerate stream of the plant for nitrogen recovery.

Advantages

The main advantage of the incineration of the biogas and the process air is the elimination of the greenhouse gas methane and the reduction of pollutants such as hydrogen sulphide and ammonia. The plant also shows that even small quantities of biogas can be used in a useful way for the generation of heat. The addition of biogas can occur under atmospheric pressure. The biogas is converted in the time and the quantity in which it is created. There will therefore be no need for compressors, gas processing plants and gas tanks. The biogas plant will also not have any problems with negative pressure as is the case with active biogas suction. These advantages facilitate the easy and cost-efficient connection to various biogas plants.

Technical data

- Controlled combustion depending on biogas supply, nominal capacity: 6 kW
- Efficiency of heat exchanger: 60–70 percent
- Temperature combustion chamber: 1000–1200 °C

Perspective

Within the scope of the project presented here it was possible to develop a reliable prototype which can be further optimized during future implementation. If necessary, the technical design allows for a modification of the heat exchanger. In this way, aggregates such as a Stirling engine can be used to generate additional electricity. It is also possible to utilize heat exchangers with an increased efficiency. The heat output of the burner can be adapted to meet the relevant requirements. In the case of biogas plants which continually produce biogas in sufficient quantities a natural gas flare may not be necessary.

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Funding

We would like to thank the German Federal Ministry of Education and Research (BMBF) for funding the project "Decentralized Urban Infrastructure Systems DEUS 21", promotional reference 02WD0850.

Project partners

Fraunhofer Institute for Systems and Innovation Research ISI, Karlsruhe, Germany
City of Knittlingen, Germany
Eisenmann Maschinenbau KG, Holzgerlingen, Germany
EnBW Energie Baden-Württemberg AG, Karlsruhe, Germany
Kerafol GmbH, Eschenbach, Germany

Further information

www.deus21.de

1 *Diagram of the burner for biogas utilization.*
2 *Photograph of the burner unit.*
3 *Container, next to the "Knittlingen water house", in which the burner operates.*

APPENDIX

Patents granted in 2010

In the year 2010 six patents were granted. These patents are assigned to our business areas as follows:

MEDICINE

Improved electrophoretic separation method for analyzing gene expression
AU 2005291445,
granted October 7, 2010

Isolated nature-identical collagen
EP 2 029 186,
granted December 1, 2010

PHARMACY

Variants of human recombinant Interferon-Gamma with increased thermal stability
CA 2,232,264,
granted April 13, 2010

Superpotent calcitonin analogs having greatly increased hypocalcemic action *in vivo*
CA 2,245,379,
granted April 27, 2010

ENVIRONMENT

Anaerobe Reinigung von Abwasser
DE 10 2005 063 228,
granted January 7, 2010

Water treatment unit
BR PI0108021,
granted September 8, 2010

Trade fairs and events 2010

Trade fairs and exhibitions

Analytica
22nd International Trade Fair for Instrumental Analysis, Laboratory Technology and Biotechnology and Analytica Conference
Fraunhofer joint booth
March 23-26, 2010, München, Germany

GLOBE
March 24-26, 2010, Vancouver, Canada

Hannover Fair Energy
Leading Trade Fair for Renewable and Conventional Power Generation, Transmission and Distribution
Fraunhofer Energy Alliance
April 19-23, 2010, Hannover, Germany

BIO International Convention
Fraunhofer Group for Life Sciences
May 3-6, 2010, Chicago, IL, USA

Nanotech
Fraunhofer Nanotechnology Alliance
June 21-24, 2010,
Anaheim, CA, USA

IFAT Entsorga
World's Leading Trade Fair for Water, Sewage, Waste and Raw Materials Management
Fraunhofer Water Systems Alliance (SysWasser)
September 13-17, 2010,
München, Germany

12th International Conference on Plasma Surface Engineering PSE
September 13-17, 2010, Garmisch-Partenkirchen, Germany

BIOTECHNICA
Europe's No. 1 Event for Biotechnology and Life Sciences
Fraunhofer Group for Life Sciences
October 5-7, 2010, Hannover, Germany

parts2clean
8th Leading International Trade Fair for Cleaning in Production and Maintenance Processes
Fraunhofer Cleaning Technology Alliance
October 12-14, 2010, Stuttgart, Germany

Südback
Trade Fair for the bakery and confectionery trades
October 16-19, 2010, Stuttgart, Germany

K – International Trade Fair for Plastics and Rubber
Fraunhofer joint booth
October 27 - November 3, 2010, Düsseldorf, Germany

Bayern Innovativ-Cooperation Forum
"Biopolymers – Perspectives – Technologies – Markets"
November 11, 2010, Straubing, Germany

Workshops, seminars, events

Grant letter handed over to the BioCat Project Group, Straubing
February 2, 2010, Straubing Center of Science, Germany

Information session
Automated Tissue Engineering on Demand
February 26, 2010, Fraunhofer Institutes Center Stuttgart, Germany

Fraunhofer-Technologiezirkel (Fraunhofer Technology Circle)
Technologietrends – Perspektiven für die Märkte von Übermorgen
March 10-11, 2010, Fraunhofer Institutes Center Stuttgart, Germany

Fraunhofer Talent School Workshop »Wer bin ich oder die phantastische Reise ins Genom«
March 12-14, 2010, Fraunhofer Institutes Center Stuttgart, Germany

Girls' Day
Future Day for Girls
April 22, 2010, Fraunhofer Institutes Center Stuttgart, Germany

Students day
"Talente für das Land" as part of Robert Bosch Stiftung
May 8, 2010, Stuttgart, Germany

Finissage DEUS 21
May 18, 2010, Knittlingen, Germany

Basic seminar Cleaning technology "Reinigung in der Produktion"
Fraunhofer Cleaning Technology Alliance
June 16-18, 2010, Dresden, Germany

OTTI forum
"Produktgestaltung mit Funktionsschichten – Möglichkeiten und Perspektiven der Oberflächenbeschichtung"
June 21-22, 2010, Regensburg, Germany

Tag der Wissenschaft (Day of science)
"Entdecken – Forschen – Faszinieren"
June 26, 2010, University of Stuttgart, Germany

MiNe-MINT – Day of bioprocess engineering for high school students
"Wii leuchtet die Zelle?"
June 30, 2010, University of Stuttgart and Fraunhofer IGB, Germany

62ª Reunião Anual da Sociedade Brasileira para o Progresso da Ciência (SBPC)
Joint booth "Research in Germany" of Baden-Württemberg International
July 25-30, 2010, Natal, Brazil

Ground-breaking ceremony
Project Group BioCat, Straubing
July 22, 2010, Straubing, Germany

BioStar 2010,
Science in Exchange
4th Congress on Regenerative Biology and Medicine
October 13-15, 2010, Stuttgart, Germany

Meeting of the Fraunhofer senate in Stuttgart
October 19, 2010, Fraunhofer Institutes Center Stuttgart, Germany

Unitag (University Day)
November 17-18, 2010,
University of Stuttgart, Germany

Checkpoint Zukunft (Checkpoint Future)
Day for students at Fraunhofer
November 29, 2010, Fraunhofer Institutes Center Stuttgart, Germany

OTTI forum
»Carbon Nanotubes – Auf dem Weg aus der Forschung in die Anwendung«
December 6-7, 2010,
Regensburg, Germany

Ground-breaking ceremony
Fraunhofer CBP, Leuna
December 8, 2010, Leuna, Germany

Preview 2011

International Green Week
World's biggest fair for food, agriculture and horticulture
January 21-30, 2011, Berlin, Germany

Workshop with Co-operation partner Instituto de Pesquisas Tecnológicas IPT as part of German-Brazilian Year of Science, supported by the BMBF (IB)
March 22-23, 2011, São Paulo, Brazil

Forum Life Sciences
"Pharma Development, Food and Nutrition, Industrial Biotechnology"
7th International Congress and Exhibition
Fraunhofer Group for Life Sciences
March 23-24, 2011, Technische Universität München, Germany

Fraunhofer Talent School
Workshop "CSI-Stuttgart – Vom genetischen Fingerabdruck zur Täteridentifizierung"
April 1-3, 2011, Fraunhofer Institutes Center Stuttgart, Germany

Hannover Fair Energy
Leading Trade Fair for Renewable and Conventional Power Generation, Transmission and Distribution
Fraunhofer Energy Alliance
April 4-8, 2011, Hannover

15. Kolloquium zur kommunalen Abwasser- und Abfallentsorgung
"Technologie mit Zukunft"
April 13, 2011, Fraunhofer IGB, Stuttgart, Germany

Girls' Day
Future Day for Girls
April 14, 2011, Fraunhofer Institutes Center Stuttgart, Germany

Technologie-Akademie für den Mittelstand (Technology academy for SMEs)
"Auf die Oberfläche kommt es an – Oberflächen charakterisieren und modifizieren"
April 20, 2011, Fraunhofer IGB, Stuttgart, Germany

Location fair "Leuna – Dialog 2011"
May 5, 2011, Kulturhaus Leuna, 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

MedTech & Pharma Partnering
June 8, 2011, Garching, Germany

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

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

BIOTECHNICA
Europe's No. 1 Event for Biotechnology and Life Sciences
October 11-13, 2011, Hannover, Germany

parts2clean
9th International Trade Fair for Industrial Parts and Surface Cleaning
October 25-27, 2011, Stuttgart, Germany

MiNe-MINT –
Research Week Life Sciences
November 3, 2011, Fraunhofer IGB, Stuttgart, Germany

Unitag (University Day)
November 2011, University of Stuttgart, Germany

Checkpoint Zukunft (Checkpoint Future)
Day for students at Fraunhofer
December 5, 2011, Fraunhofer Institutes Center Stuttgart, Germany

Exhibitions in the Year of Science 2011 "Research for Our Health"

"Entdeckungen 2011: Gesundheit" Insel Mainau
May till September 2011

MS Wissenschaft 2011
"Neue Wege in der Medizin"
May till September 2011

www.wissenschaft-im-dialog.de

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

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VDI-Fachausschuss "Nanotechnologie für die Medizintechnik",
Vice Chairman

Verein Deutscher Ingenieure e. V. (VDI),
Steering Committee »Qualitätssicherung bei der Vakuumbeschichtung von Kunststoffen«, Member

Pusch, J.

Verein Deutscher Ingenieure e. V. (VDI),
Steering Committee "Technische GMP", Member

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

Rupp, S.

Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM),
Expert group "Eukaryontische Krankheitserreger", Executive Board

Deutschsprachige Mykologische Gesellschaft e. V. (DMykG),
Member

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

Gesellschaft für Biochemie und Molekularbiologie e. V. (GBM),
Member

Schenke-Layland, K.

Deutsche Forschungsgemeinschaft DFG,
Expert evaluator for research fellowships and single application procedure

American Association of Anatomists,
Evaluator for Young Investigator Awards

L'Agence nationale de la recherché-ANR,
Expert evaluator for single application procedure

Research Council – Katholieke Universiteit Leuven,
Expert evaluator for single application procedure

Arthritis Research UK,
Expert evaluator for single application procedure

Schiestel, T.

Deutsche Gesellschaft für Materialkunde e. V. (DGM),
Community committee "Hochleistungskeramik", Working committee "Keramische Membranen", Member

---

Sieber, V.

Bundesministerium für Bildung und Forschung (BMBF),
Expert evaluator

Deutsche Gesellschaft für Chemische Technik und Biotechnologie e. V. (DECHEMA),
Member

Gesellschaft Deutscher Chemiker (GDCh),
Member

Gesellschaft für Biochemie und Molekularbiologie e. V. (GBM),
Member

Sternad, W.

HACH LANGE GmbH,
Consumer Advisory Board, Member

Tovar, G. E. M.

Deutsche Bunsen-Gesellschaft für Physikalische Chemie (DBG),
Member

Deutsche Gesellschaft für Chemische Technik und Biotechnologie e. V. (DECHEMA),
Subject divisions „Nanotechnologie"

Deutsche Gesellschaft für Materialkunde e. V. (DGM),
Expert committee "Biomaterialien", Leader of *Querschnittsarbeitskreis* "Biomimetische Biomaterialien"

Kolloid-Gesellschaft,
Member

Fraunhofer-Allianz Nanotechnologie,
Second Speaker;
Steering Committee

Fraunhofer-Zukunftsthema Biofunktionale Oberflächen,
Coordinator

Gesellschaft Deutscher Chemiker (GDCh),
Member

NanoMAT,
Member

Strategiekreis »Nanowelten«, Forschungsunion Wirtschaft-Wissenschaft,
Member

Trösch, W.

Rumänisch-deutsche Stiftung "Aquademica",
Member

Deutsche Gesellschaft für Chemische Technik und Biotechnologie e. V. (DECHEMA),
Subject division "Biotechnologie"

European Network Architecture ENA,
Member

Fachverband Biogas,
Member

Fraunhofer-Allianz SysWasser,
Speaker

German Water Partnership,
Executive Board

Vohrer, U.

Deutsche Bunsengesellschaft (DBG),
Member

Gesellschaft Deutscher Chemiker (GDCh),
Member

Deutsche Physikalische Gesellschaft (DPG),
Member

Fachtagung »Reinigung und Vorbehandlung vor der Beschichtung« des Ostbayerischen Technologie-Transfer-Institut e. V. (OTTI),
Conference Advisory Board/ Specialist Manager

Forschungs-Allianz Kulturerbe (FALKE),
Founding Member

Fraunhofer-Allianz Reinigungstechnik,
Founding Member

Hauptkommission der Fraunhofer-Gesellschaft,
Member

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

Wissenschaftlich-Technischer Rat der Fraunhofer-Gesellschaft (WTR),
Member

Committee memberships

Walles, H.

Bundesministerium für Bildung und Forschung (BMBF),
Expert evaluator

Bundesverband der Pharmazeutischen Industrie e. V. (BPI),
Member of committee "Zulassung", Working committee "Tissue Engineering"

Deutscher Akademischer Austausch Dienst (DAAD),
Expert evaluator for special program "Moderne Anwendungen in der Biotechnologie"

Deutscher Ethikrat,
Member

Deutsche Forschungsgemeinschaft DFG,
Expert evaluator for SFB (TransRegio), Research training group, Single application procedure

Deutsche Gesellschaft für Chemische Technik und Biotechnologie e. V. (DECHEMA),
Working committee "Medizinische Biotechnologie"

Deutsche Gesellschaft für Regenerative Medizin e. V.,
Working committee "Regenerative Medizin", Member, Advisory Board

DIN Deutsches Institut für Normung e. V., Normenausschuss Feinmechanik und Optik NAFuO,
Collaboration on working committee "Medizinische Produkte auf Basis des Tissue Engineering"

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

Gesundheitsforschungsrat des BMBF,
Member of medical-technical committee

VDI-Fachausschuss "Nanotechnologie für die Medizintechnik",
Member

Weber, A.

Deutsche Gesellschaft für Chemische Technik und Biotechnologie e. V. (DECHEMA),
Member

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

Lectures and seminars

University of Stuttgart, Germany

Hansmann, J.; Elter, T.; Gröber, F.; Ludwig, D.; Seibert, A.; Tovar, G. E. M; Biehler, S.
"Arbeitstechniken und Projektarbeit (Übungen)"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc.
SS 2010 and WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M; Oehr, C.
"Grundlagen der Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M
"Grenzflächenverfahrenstechnik I – Chemie und Physik der Grenzflächen"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*, SS 2010, 2 SWS

Hirth, T.; Tovar, G. E. M
"Grenzflächenverfahrenstechnik II – Technische Prozesse"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M
"Theoretische Grundlagen der Verfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Technical Biology B. Sc.
SS 2010, 2 SWS

Hirth, T.
"Nachhaltige Rohstoffversorgung – Von der Erdölraffinerie zur Bioraffinerie"
Fachübergreifende Schlüsselqualifikation, Process Engineering M. Sc.
SS 2010, 2 SWS

Hirth, T.
"Nachhaltige Rohstoffversorgung und Produktionsprozesse"
Process Engineering M. Sc.
WS 2010/11, 2 SWS

Hirth, T.
"Sustainable Production Processes"
Master WASTE
WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M
"Medizinische Verfahrenstechnik I"
Faculty of Energy Technology, Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering,
Process Engineering M. Sc. and Diploma, *Maschinenbau* Diploma
SS 2010, 2 SWS

Hirth, T.; Rupp, S.; Tovar, G. E. M
"Medizinische Verfahrenstechnik II"
Faculty of Energy Technology, Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering,
Process Engineering M. Sc. and Diploma, *Maschinenbau* Diploma
WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M
"Praktikum zur Medizinischen Verfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering and Faculty of Engineering Design, Production Engineering and Automotive Engineering,
Process Engineering M. Sc. and Diploma, Maschinenbau Diploma
SS 2010, 2 SWS

Hirth, T.; Tovar, G. E. M
"Exkursion Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
SS 2010 and WS 2010/11, 2 SWS

Hirth, T.; Tovar, G. E. M
"Praktikum Grenzflächenverfahrenstechnik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
SS 2010, 2 SWS

Hirth, T.; Tovar, G. E. M
"Grenzflächenverfahrenstechnisches Kolloquium"
Fachübergreifende Veranstaltung
SS 2010 and WS 2010/11, 1 SWS

Hirth, T.; Tovar, G. E. M
"Anleitung zu wissenschaftlichem Arbeiten"
Study program Process Engineering, Chemistry, Technical Biology
SS 2010 and WS 2010/11

Hirth, T.; Tovar, G. E. M
"Mitarbeiter-Seminar für DoktorandInnen und DiplomandInnen"
Study program Process Engineering, Chemistry, Technical Biology
SS 2010 and WS 2010/11, 1 SWS

Oehr, C.
"Plasmaverfahren für die Dünnschicht-Technik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc.
SS 2010 and WS 2010/11, 2 SWS

Rupp, S.
Beiträge zum "Biochemischen Praktikum für Technische Biologen"
Faculty of Chemistry,
Study program Biochemistry
WS 2010/11, 8 SWS

Rupp, S.
Beiträge zum **"Biochemischen Forschungspraktikum für Diplom-Chemiker"**
Faculty of Chemistry,
Study program Biochemistry
WS 2010/11, 8 SWS

Rupp, S.
Beiträge zur Vorlesung "Moderne Methoden in der Biochemie"
Faculty of Chemistry,
Study program Biochemistry
SS 2010, 1 SWS

Rupp, S.
"Ausgewählte Kapitel der modernen Biochemie"
Faculty of Chemistry,
Study program Biochemistry
SS 2010, 1 SWS

Rupp, S.
"Medizinische und molekulare Diagnostik"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Study program Biochemistry
WS 2010/11, 1 SWS

Tovar, G. E. M; Hirth, T.
"Nanotechnologie I – Chemie und Physik der Nanomaterialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
SS 2010, 2 SWS

Tovar, G. E. M; Hirth, T.
"Nanotechnologie II – Technische Prozesse und Anwendungen für Nanomaterialien"
Faculty of Energy Technology, Process Engineering and Biological Engineering,
Process Engineering M. Sc., *Vertiefungsfach*
WS 2010/11, 2 SWS

Tovar, G. E. M
"Produktgestaltung mit Nano-, Bio- und Hybridmaterialien"
Faculty of Chemistry, Chemistry Diploma, SS 2010, 3 SWS

Tovar, G. E. M
"Biofunktionale Oberflächen – Chemie, Struktur und Funktionen"
Faculty of Chemistry, Chemistry Diploma, WS 2010/11, 2 SWS

Hamm-Lippstadt University of Applied Science, Germany

Bryniok, D.
Lecture **"Technische Mechanik I"**
Energy Engineering and Resource Optimisation
WS 2010/11, 2 SWS

Bryniok, D.
Exercises to lecture **"Technische Mechanik I"**
Energy Engineering and Resource Optimisation
WS 2010/11, 2 SWS

Bryniok, D.
Lecture **"Projektmanagement"**
Energy Engineering and Resource Optimisation
WS 2010/11, 1 SWS

Technische Universität München

Sieber, V.
"Grundstoffe und Werkstoffe aus der Natur"
Study program *Nachwachsende Rohstoffe*
WS 2010/11, 2 SWS

Sieber, V.
Parts of lecture "Bioraffinerie und Naturstofftechnologien"
Study program *Nachwachsende Rohstoffe*
WS 2010/11, 4 SWS

Sieber, V.
Parts of lecture "Biokunststoffe und ihre Herstellung"
Study program *Nachwachsende Rohstoffe*
WS 2010/11, 4 SWS

Sieber, V.
Parts of lecture "Grundlagen Chemie"
Study program *Nachwachsende Rohstoffe*
WS 2010/11, 2 SWS

Sieber, V.
Parts of lecture "Spezielle Biotechnologie"
Study program *Nachwachsende Rohstoffe*
WS 2010/11, 2 SWS

Lectures and seminars

Sieber, V.
"Einführung in die Weiße Biotechnologie"
Study program *Nachwachsende Rohstoffe*; SS 2010, 2 SWS

Sieber, V.
Parts of lecture "Technologie und Verwertung sonstiger biogener Rohstoffe"
Study program *Forstwirtschaft*
SS 2010, 5 SWS

Heidelberg University Biochemistry Center

Sohn, K.
Parts of seminar and practical course "Nervensystem: Biochemische Analyse neuronaler Proteine und Lipide"
Medical Faculty,
Study program Biochemistry
SS 2010, Seminar: 2 SWS, Practical course: 6 SWS

Sohn, K.
Parts of Seminar and practical course "Leber und Harnstoff"
Medical Faculty,
Study program Biochemistry
WS 2010/11, Seminar: 2 SWS, Practical course: 6 SWS

University of Hohenheim, Stuttgart

Kluger, P.J.
Lecture "Tissue Engineering"
Faculty of Natural Sciences,
Ernährungswissenschaft B. Sc., Biology B. Sc.,Technologie der Life Science B. Sc.
SS 2010, 2 SWS

Kluger, P.J.
Practical course "Tissue Engineering"
Faculty of Natural Sciences,
Ernährungswissenschaft B. Sc., Biology B. Sc., *Technologie der Life Science* B. Sc.
SS 2010, 2 SWS

Trösch, W.
Parts of lecture "Wasser-, Abwasser- und Abfallbehandlung"
Faculty of Natural Sciences,
Study program Food Science and Biotechnology
WS 2010/2011, 2 SWS

Trösch, W.
"Angewandte Bioverfahrenstechnik: Energie – Grundlagen und technische Beispiele"
Faculty of Natural Sciences,
Study program Food Science and Biotechnology
SS 2010, 1 SWS

Trösch, W.
Parts of lecture "Allgemeine Biotechnologie"
Faculty of Natural Sciences,
Study program Food Science and Biotechnology
WS 2010/2011, 2 SWS

Trösch, W.
Parts of lecture "Biochemie für Technologen"
Faculty of Natural Sciences,
Study program Food Science and Biotechnology
WS 2010/2011, 2 SWS

University of Tübingen

Walles, H.
Ringvorlesung "Aspekte der Regenerationsbiologie und -medizin"
Study program Medicine

University of Würzburg

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

Scientific cooperations

With universities

Aristotle University of Thessaloniki, Greece

Charles University, Prague, Czech Republic

Comenius University, Bratislava, Slowakia

Cranfield University, Cranfield, UK

Eberhard Karls Universität Tübingen, Germany

Ernst-Moritz-Arndt-Universität Greifswald, Germany

Escola de Engenharia de Piracicaba (EEP), Brazil

Escola Superior de Agricultura »Luiz de Queiroz« (ESALQ), Brazil

Katholieke Universiteit Leuven, Belgium

Kyoto University, Japan

Gottfried Wilhelm Leibniz Universität Hannover, Germany

Hochschule Hamm-Lippstadt, Germany

Julius-Maximilians-Universität Würzburg, Germany

Linnéuniversitetet, Kalmar, Sweden

Ludwig-Maximilians-Universität München, Germany

Lunds Universitet, Lund, Sweden

McGill University, Montreal, Canada

Medizinische Hochschule Hannover MHH, Germany

Ruhr-Universität Bochum, Germany

Stanford University, USA

Stockholms Universitet, Stockholm, Sweden

Technische Universität Darmstadt, Germany

Technische Universität Dortmund, Germany

Technische Universität Kaiserslautern, Germany

Technische Universität München, Germany

Technische Universiteit Eindhoven, The Netherlands

Tierärztliche Hochschule Hannover, Germany

Trinity College Dublin, Irland

Universidad Complutense de Madrid, Spain

Universidad de Sevilla, Spain

Universidade Metodista de Piracicaba (UNIMEP), Brazil

Universita degli Studi di Bari, Italy

Universita degli Studi di Milano, Italy

Universita degli Studi di Milano-Bicocca, Italy

Universität Bremen, Germany

Martin-Luther-Universität Halle-Wittenberg, Germany

Universität Hamburg, Germany

Universität Heidelberg, Germany

Universität Hohenheim, Germany

Universität Innsbruck, Austria

Universität Stuttgart, Germany

Universität Wien, Austria

Université Paul Sabatier Toulouse III, Toulouse, France

Universitetet i Bergen, Bergen, Norway

University of California Los Angeles (UCLA), Los Angeles, USA

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

University of Manchester, UK

University of Novi Sad, Novi Sad, Serbia

University of West Hungary, Sopron, Hungary

Univerza v Mariboru, Maribor, Slowenia

Uppsala Universitet, Uppsala, Sweden

With other research organizations

AIT – Austrian Institute of Technology, Wien, Austria

Bundesanstalt für Materialforschung und -prüfung (BAM), Berlin, Germany

Carnot institute CIRIMAT, Toulouse, France

Centre de Recerca i Investigació de Catalunya CRIC, Barcelona, Spain

Centre for Process Innovation CPI, Wilton, Redcar, UK

Centro technológica CARTIF, Valladolid, Spain

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

Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany

Deutsches Zentrum für Biomaterialien und Organersatz, Stuttgart-Tübingen, Germany

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

European Molecular Biology Laboratory EMBL, Heidelberg, Germany

Flanders Institute for Biotechnology (VIB), Belgium

Institut für Textilchemie und Chemiefasern ITCF, Denkendorf, Germany

Institut für Textil- und Verfahrenstechnik ITV, Denkendorf, Germany

Institut Pasteur, Paris, France

Johann Heinrich von Thünen-Institut, Braunschweig, Germany

Karlsruher Institut für Technologie (KIT), Karlsruhe, Germany

Leibniz-Institut für Katalyse e. V. (LIKAT), Rostock, Germany

Leibniz-Institut für Plasmaforschung und Technologie e. V. (INP), Greifswald, Germany

Ludwig Institute for Cancer Research, Stockholm, Sweden

Max-Planck-Institut für Festkörperforschung, Stuttgart, Germany

Max-Planck-Institut für Kolloid- und Grenzflächenforschung, Golm, Germany

Max-Planck-Institut für Metallforschung, Stuttgart, Germany

Max-Planck-Institut für Polymerforschung, Mainz, Germany

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

Nor-Tek Teknologisenter, Oslo, Norway

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

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

Robert-Koch-Institut, Berlin, Germany

Teknologisk Institutt (TI), Oslo, Norway

With hospitals

Blutspendezentrale, Katharinenhospital, Stuttgart, Germany

Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinik der Ruhr-Universität Bochum, Germany

Katharinenhospital, Stuttgart, Germany

Klinik Charlottenhaus, Stuttgart, Germany

Klinik Schillerhöhe, Gerlingen, Germany

Klinikum Ludwigsburg, Germany

Olgahospital, Stuttgart, Germany

Robert-Bosch-Krankenhaus, Stuttgart, Germany

University Hospital Lausanne, Switzerland

Haukeland University Hospital, Norway

Universitätsklinikum Innsbruck, Austria

Universitätsklinikum der RWTH Aachen, Germany

Universitätsklinikum Lübeck, Germany

Universitätsklinikum Tübingen, Germany

Universitätsklinikum Würzburg, Germany

With museums

Bayerisches Hauptstaatsarchiv, München, Germany

Deutsches Bergbaumuseum, Bochum, Germany

Deutsches Museum, München, Germany

Deutsches Schifffahrtsmuseum, Bremerhaven, Germany

Germanisches Nationalmuseum, Nürnberg, Germany

Stiftung Preußischer Kulturbesitz, Rathgen-Forschungslabor, Berlin, Germany

Zentrum für Bucherhaltung, Leipzig, Germany

Academic theses

Ph. D. theses

Barz, J. P.
Particle dynamics simulation and diagnostics of the PECVD processes in fluorocarbon rf discharges
Universität Stuttgart
Verlag Dr. Hut,
ISBN: 978-3-86853-467-2

Hansmann, J.
Induktion von Angiogenese *in vitro* durch modellbasierte Bioreaktortechnologie,
Universität Stuttgart
Fraunhofer Verlag,
ISBN: 978-3-8396-0113-6

Koch, S.
Evaluierung der Raman Spektroskopie für die marker- und zerstörungsfreie Qualitätskontrolle im Tissue Engineering,
Universität Stuttgart
Fraunhofer Verlag,
ISBN: 978-3-8396-0112-9

Röhm, M.
Charakterisierung einer Familie von Pry-Proteinen in *Candida albicans*,
Universität Stuttgart
Fraunhofer Verlag,
ISBN: 978-3-8396-0216-4

Roelofs, K. S.
Sulfonated poly(ether ether ketone) based membranes for direct ethanol fuel cells,
Universität Stuttgart
Fraunhofer Verlag,
ISBN: 978-3-8396-0122-8

Zavrel, M.
Characterization of *Candida albicans* genes involved in cell wall biogenesis and infection,
Universität Stuttgart

Zschoerper, P. N.
Oberflächenmodifizierung von Carbon Nanotubes mittels technischer Niederdruckplasmen
Universität Stuttgart
Verlag Dr. Hut,
ISBN: 978-3-86853-685-0

State examination theses

Alle, M.
Parametrisierung mikroskaliger Niederschlag-Abflussmodelle mit hochauflösenden Fernerkundungsdaten,
Universität Tübingen

Diploma theses

Falkner, V.
Amino- und Carboxyfunktionalisierung von Membranen mittels Niederdruckplasma und Einfluss der Oberflächenfunktionalisierung auf die Kultivierung primärer Keratinozyten und Fibroblasten,
Hochschule Mannheim

Fink, M.
Title protected
Fachhochschule Stralsund

Göhler, S.
Charakterisierung und Evaluierung eines 3D Darmgewebemodells für die Anwendung von Resorptionsstudien an der intestinalen Barriere,
Fachhochschule
Gießen-Friedberg

Holzäpfel, T.
Extrazelluläre Metabolitanalyse und Untersuchungen zur RNA-Stabilisierung für die Expressionsanalyse von *Candida albicans* während der Wirt-Pathogen-Interaktion,
Universität Hohenheim

Kuhnt, A.
Entwicklung molekular geprägter Polymerpartikel gegen Substanzen mit endokriner Wirkung – am Beispiel von Bisphenol A,
Hochschule Aalen

Leitz, D.
Nährstoffrückgewinnung aus Abwasser – Betrieb und Parametrisierung eines kontinuierlichen Kristallisationsreaktors zur Gewinnung von Struvit als Düngemittel,
Naturwissenschaftlich-Technische Akademie Prof. Dr. Grübler gemeinnützige GmbH, Isny

Mehne, F. M. P.
Klonierung AP1- und IRF-induzierbarer Reportergenplasmide und deren Analyse in einem zellbasierten PAMP-Testsystem,
Hochschule Darmstadt

Möller, Y.
Etablierung eines zellbasierten Reportergenassays zum Nachweis von Mikroorganismen,
Universität Stuttgart

Müller, L.
Elektrophoretische Abscheidung und Spin-Coating von Hydroxylapatit auf Gold- und Titan-Quarzmikrowaagen (QCM)-Sensoren
Universität Stuttgart

Neumüller, N.
Anaerobe biologische Behandlung von Reststoffen aus der Olivenölproduktion in einem Gaslift-Schlaufenreaktor
Hochschule Mannheim

Ranghieri, J.
Bestimmung von Einflussgrößen auf Magnesium- und Phosphatkonzentration bei kontinuierlicher Kristallisation von Magnesium-Ammonium-Phosphat (MAP),
Universität Stuttgart

Schobess, M.
Title protected
Technische Universität Clausthal

Staudenmeyer, V. M.
Wassergewinnung aus Luftfeuchtigkeit – Planung, Aufbau und Inbetriebnahme einer Versuchsanlage,
Universität Stuttgart

Szczawinski, D.
Wirtsabwehrmechanismen während *Candida*-Infektionen,
Hochschule Darmstadt

Uhl, W.
Aufbau und Inbetriebnahme eines Versuchsaufbaus zu Wärmetransport und Speicherung mittels Zeolithen,
Hochschule Augsburg

Volkwein, W.
Title protected
Naturwissenschaftlich-Technische Akademie Prof. Dr. Grübler gemeinnützige GmbH, Isny

Vörös, C.
Herstellung synthetischer Hydrogele zum Aufbau dreidimensionaler Gewebeschichten,
Naturwissenschaftlich-Technische Akademie Prof. Dr. Grübler gemeinnützige GmbH, Isny

Weihmüller, J.
Entwicklung eines Bioreaktors zur automatisierten Zellkultur,
Universität Stuttgart

Wurster, S.
Einfluss von Oberflächenchemie und Topographie auf primäre humane mikrovaskuläre Endothelzellen,
Hochschule Mannheim

Wutzke, R.
Bestimmung von physikalischen Parametern zur Kryokonservierung von dreidimensionalen humanen Hautäquivalenten,
Universität Stuttgart

Master theses

Haitz, F.
Prozessentwicklung zur Produktion von C5- und C6-Zuckern als biobasierte Plattformchemikalien aus Lignocellulose,
Hochschule Offenburg

Haitz, T.
Anaerobe Behandlung von Reststoffen aus der Olivenölproduktion in einem Gaslift-Schlaufenreaktor
Hochschule Offenburg

Hinderer, S.
Standardisierung und Charakterisierung eines Systems zur Untersuchung von Angiogenese,
Universität Reutlingen

Kranzioch, I.
Title protected
Hochschule Offenburg

Kußmaul, E.
Polyglycidolbasierte, synthetische Polymere zum Aufbau von biokompatiblen Hydrogelen,
Hochschule Reutlingen

Miao, Y.
Title protected
Technische Universität Hamburg-Harburg

Ong, Y. Y.
Evaluation of process parameters for anodic oxidation of a selected model subtance in water treatment,
Universität Stuttgart

Parajuly, K.
UV and UV/H_2O_2 treatment of aqueous solution of organic model compounds for the evaluation of wastewater treatment options,
Universität Stuttgart

Riegger, P.
Title protected
Hochschule für Wirtschaft und Umwelt Nürtingen-Geislingen

Schönhaar, V.
Untersuchung der Thiol-En-Reaktion PEG-basierter Polymere zum Aufbau biokompatibler Hydrogele,
Hochschule Reutlingen

Bachelor theses

Briem, M.
Derivatisierung von Heparin zur Biofunktionalisierung von Implantatoberflächen,
Hochschule Aalen

Franz, M.
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