Fraunhofer
IGB

FRAUNHOFER INSTITUTE FOR INTERFACIAL ENGINEERING AND BIOTECHNOLOGY IGB

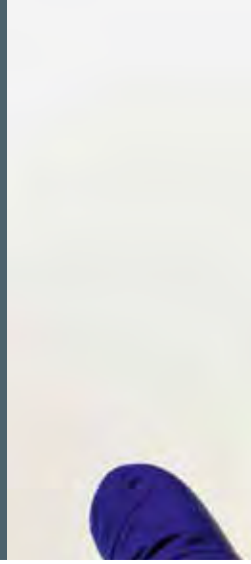
ANNUAL REPORT 2015 | 16

Examination of the culture media during the cell culture used for the formation of the *click*ECM

In the *click*ECM project, researchers from cell biology and material sciences develop a biocompatible and stable coating for medical implants. It consists of the extracellular matrix (ECM) of primary cells, the natural environment of the cells in the tissue. For this purpose, the researchers culture human cells in a cell culture media which contains a sugar modified with a click function. The cells metabolize the click-functionalized sugars during growth and thus incorporate the click function into the glycan structures of their ECM. When the *click*ECM is isolated and brought to a material surface equipped with a complementary click function, both connect via stable covalent bonds (see page 60).

ANNUAL REPORT
2015 | 16

CONTENTS



DEAR READERS,

2015 was an eventful year in many ways. At the end of September, Prof. Thomas Hirth announced his decision to assume a new position on the presidential committee of the Karlsruhe Institute of Technology. Thus, now two new but familiar faces await you at this point in our annual report. Since the beginning of 2016, we have been gladly acting as interim directors to sustain absolute continuity in science and business at our institute. In the customary way, we would like to look back on the past year and look forward to the future of the institute.

Professor Hirth led Fraunhofer IGB for eight years; doubling the number of employees and budget. Hirth greatly increased Fraunhofer IGB's visibility with the research-political and strategically impactful topic of bioeconomy, which the institute had previously pursued in many facets. The formation of three project groups – one in Saxony-Anhalt and two in Bavaria – contributed to the institute's growth. Since the start of 2015, these groups have respectively integrated with neighboring universities' basic research programs as permanent branches and gained access to German state funding programs.

It was also due to Professor Hirth that IGB now plays a leading role in Fraunhofer's lighthouse project "Electricity as a Raw Material", which was launched in 2015. Fraunhofer IGB is one of ten participating institutes and coordinates a part of the project. Related research in the field of electrochemistry will also sustainably strengthen our competence portfolio beyond the project and open up new market segments in the business area of chemistry. A synergy has also arisen with the "Center for Energy Storage" joint project with our Straubing branch BioCat and the Fraunhofer Institute for Environmental, Safety, and Energy Technology UMSICHT in Sulzbach-Rosenberg.

In autumn, 2015, we partnered with the American company OVIVO for the market launching of our ePhos® process – for the recycling of phosphorus from wastewater. Due to amendments in sewage sludge regulations and the rising prices for fertilizer, phosphorus recovery has once again gained interest in the German and European markets.

With the approval of an Attract Group on the topic "Organ-on-a-Chip", we are pursuing new and commercially relevant technologies in the field of health research. In March 2016, Dr. Peter Loskill, a physicist who was successfully recruited from UC Berkeley, will begin new projects in the Department of Cell and Tissue Engineering at Fraunhofer IGB. With the new research training group "3D Infect" at the University of Würzburg, infection research will be strengthened at Fraunhofer IGB. Our Würzburg branch is focusing on the development of three-dimensional human infection tissues models. In addition, we are spinning out two startup companies based on our groundbreaking research in the medicine business area.

The recruitment process is underway to find a successor for Professor Hirth that will assume the position as director of Fraunhofer IGB and of the Institute of Interfacial Process Engineering and Plasma Technology (IGVP) at the University of Stuttgart. The time ahead for us is one of transition and change. We are aware of our responsibility to our employees, business partners and grant donors. We want Fraunhofer IGB to carry on in its path to scientific excellence and economic success. To succeed, we are currently revising our strategic direction to future market and customer requirements.

We thank our customers and partners for the trust-based cooperation in the past year and look forward to the challenges ahead. We wish you pleasant reading and hope that this annual report may inspire ideas that you can include in your work and for further cooperation with Fraunhofer IGB.

We are looking forward to an exciting, successful and productive future with you.

Katja Schenke-Layland

Christian Oehr

FRAUNHOFER IGB IN PROFILE 2015

186 Students

46 Doctoral students

10 Apprentices

483 Employees

47 % Proportion of women

2 Prizes and awards

92 University employees

25 Nationalities

391 Fraunhofer employees

11 BoGy high school students

12 Associate lecturers

73.4 % Own revenues

11.5 million € Non-personnel costs

14.5 million € Personnel costs

27,8 million € Total budget

1.8 million € Investments

3 Branches

2 Fraunhofer Groups

5 Departments

10 Fraunhofer Alliances

21 Members of Advisory Board

PROFILE

BRIEF PROFILE

The Fraunhofer Institute for Interfacial Engineering and Biotechnology 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. Experts in the fields of chemistry, physics, biology, and engineering work effectively together at Fraunhofer IGB, its branches at Leuna, Straubing and Würzburg, and our Stuttgart University IGVP partner institute. 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 in Stuttgart

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

Branches of the institute

- Fraunhofer Center for Chemical-Biotechnological Processes CBP, Leuna branch
- Bio, Electro, and Chemocatalysis BioCat, Straubing branch
- Translational Center "Regenerative Therapies for Oncology and Musculoskeletal Diseases", Würzburg branch

Guiding principles: mission statement and vision

"At 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 FRAUNHOFER IGB

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

Members

Dr. Susanne Arbogast
Roche Diagnostics GmbH

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

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

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

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

Dr.-Ing. Bernd Krause
Gambro Dialysatoren GmbH

Dr. Henk van Liempt
(until August 2015)
Federal Ministry of Education and Research (BMBF)

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

Dr. Christian Naydowski
VOITH Paper Holding GmbH & Co. KG

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

Prof. Dr. Dr. h. c. Ralf Riedel
Dispersive Solid Group, TU Darmstadt

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

Dipl.-Ing. Otmar Schön
HYDAC Technology GmbH

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

MinR Dr. Joachim Wekerle
Ministry of Finance and Economics of the State of Baden-Württemberg

Dr. Günter Wich
Wacker Chemie AG

Prof. Dr. Karl-Heinz Wiesmüller
EMC microcollections GmbH

Dr. Wieland Wolf
ProBioGen AG

Dr. Markus Wolperdinger (Chair)
Linde Engineering Dresden GmbH

Permanent guests

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

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

SERVICES AND INFRASTRUCTURE

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

Infrastructure and laboratory equipment

Fraunhofer IGB has modern laboratories up to BSL2 (biological safety level 2) equipped with the latest technologies. A new pilot plant building is scheduled for completion and commissioning in summer of 2016. Our central storage facilities for chemicals and hazardous substances are shared with the other institutes on the Stuttgart Fraunhofer campus.

Quality management and assurance systems

At Fraunhofer IGB, we ensure by established and standardized processes and procedures that the quality of our services and products meet the respective requirements. A quality management system guarantees that our accredited tests comply with DIN EN ISO/IEC 17025. A quality assurance system makes sure that legal guidelines of Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP) for the respective products or test categories are met.

Accredited testing

The accreditation of reference laboratories and test procedures of our analytics guarantees that our proprietary, in-house test methods and procedures are validated and that the quality of our tests is assured even where no standardized methods are available.

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

- High-performance liquid chromatography (HPLC)
- Ion chromatography (IC)
- Gel permeation chromatography (GPC)
- Gas chromatography (GC, GC/MS)
- Atomic emission spectrometry (ICP-OES)
- Electron spectroscopy for chemical analysis (ESCA/XPS)
- *In vitro* cytotoxicity testing of medical devices
- *In vitro* phototoxicity testing of solutions and substances

Accredited biocompatibility and phototoxicity testing

We perform tests for *in vitro* cytotoxicity of medical devices according to DIN EN ISO 10993-5 using cell lines. Additionally, *in vitro* phototoxicity testing was included in our accreditation system in 2014. With our in-house methods we can investigate solutions and substances with respect to their phototoxic potential. The test method is in accordance with the OECD Guideline 432 and the INVITTOX Protocol no 121. The investigation of the potential photoactive substances is performed on our in-house designed three-dimensional skin model.

Good laboratory practice (GLP) test facility
Several tests are running at our category 9 GLP unit ("Cell-based test systems for the determination of biological parameters"). Within this GLP unit we support research and development projects that investigate different biological parameters of samples/substances using cell-based assays. Examples are testing bioactivity of antiviral compounds or immunogenicity of compounds using immune receptor-based assays, the detection of pyrogens and microbial residues (pathogen-associated microbial patterns, PAMPs) as well as the screening of TLR agonists/antagonists and antimicrobial substances.

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

Special services

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

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

Surface and particle analytics
characterization of chemical, physical, and morphological properties of surfaces, thin layers, powders, and particles

Microbial evaluation
testing of antimicrobial effects and photocatalytic properties of surfaces

Biochemical and biomolecular analytics
diagnostic microarrays, protein expression profiles, protein analysis using MALDI-TOF/TOF mass spectrometry (also quantitative)

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

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

Cell-material interactions
testing of cytotoxicity/biocompatibility of medical devices, assessment of phototoxicity of substances and solutions, evaluation and testing of chemicals (REACH) and nanomaterials

For detailed information on the analytical services we offer, please visit:
www.igb.fraunhofer.de/analytics

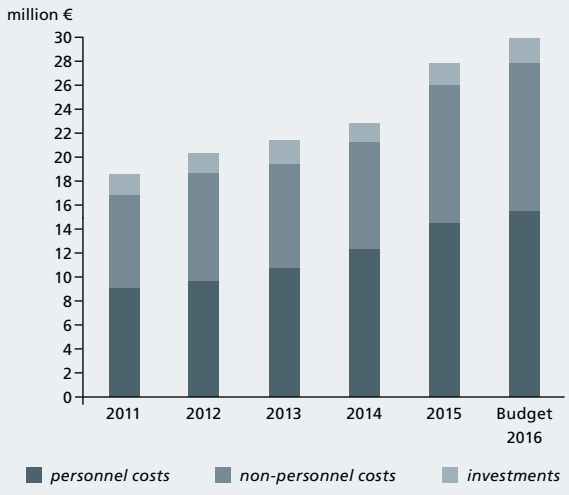
KEY FIGURES

Budget of Fraunhofer IGB

The total budget for 2015 amounted to 27.8 million euros, of which 26.0 million euros were allocated to the operational budget (personnel costs: 14.5 million euros; non-personnel costs: 11.5 million euros). A total of 1.8 million euros was spent on investments.

73.4 percent of the operational budget was financed from Fraunhofer IGB's own revenues generated from contract research projects. 29.3 percent of the institute's revenues came directly from industry.

Development of budget



* incl. CBP (after state government initial financing completed).

Revenue from contract research 2015

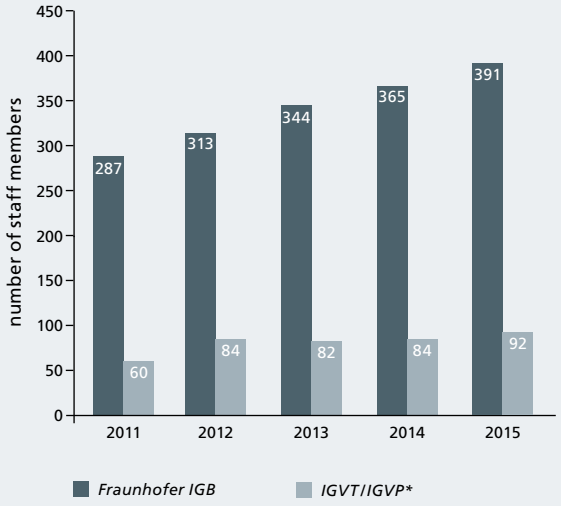
Personnel

At the end of 2015, Fraunhofer IGB (in Stuttgart and its branches in Straubing, Würzburg, and Leuna) had a staff of 391 of which some 90 percent were scientific or technical employees. Women made up 50 percent of the total.

The Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart counted a staff of 92 as of December 31, 2015, predominantly scientists and doctoral students as well as technical staff and student research assistants. Women constituted 33 percent of the total.

The employees of Fraunhofer IGB, of its branches, and of IGVP work together closely and have very culturally diverse backgrounds, with 40 staff members coming from 25 different countries outside Germany.

Development of staff members



* Stuttgart University's Institute for Plasma Research IPF was integrated into the Institute for Interfacial Engineering IGVT in January 2013. Numbers since 2012 refer to the merged Institute of Interfacial Process Engineering and Plasma Technology IGVP.

Staff composition as of December 31, 2015	Fraunhofer IGB	IGVP
Scientists	98	18
Technical staff	99	12
Doctoral students	–	33
Administrative and secretarial staff	36	4
Apprentices	10	4
Scholarship holders	5	10
Work students/Master students/student apprentices	27	(30)*
Student research assistants	116	13
	391	**92**

* Academic theses at IGVP did not count as staff.

ORGANIZATION CHART

Director
(acting, executive)

Prof. Dr. Katja Schenke-Layland
Phone +49 711 970-4082
katja.schenke-layland@
igb.fraunhofer.de

Director
(acting)

Dr. Christian Oehr
Phone +49 711 970-4137
christian.oehr@igb.fraunhofer.de

Deputy Director

apl. Prof. Dr. Steffen Rupp
Phone +49 711 970-4045
steffen.rupp@igb.fraunhofer.de

Assistant to Director

Christine Demmler
Phone +49 711 970-4401
christine.demmler@igb.fraunhofer.de

Assistant to Director

Brigitte Haag
Phone +49 711 970-4402
brigitte.haag@igb.fraunhofer.de

INTERFACIAL ENGINEERING AND MATERIALS SCIENCE

Dr. Christian Oehr
Phone +49 711 970-4137
christian.oehr@igb.fraunhofer.de

Dr. Achim Weber
Phone +49 711 970-4022
achim.weber@igb.fraunhofer.de

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

MOLECULAR BIOTECHNOLOGY

apl. Prof. Dr. Steffen Rupp
Phone +49 711 970-4045
steffen.rupp@igb.fraunhofer.de

Dr. Kai Sohn
Phone +49 711 970-4055
kai.sohn@igb.fraunhofer.de

Dr. Anke Burger-Kentischer
Phone +49 711 970-4023
anke.burger-kentischer@
igb.fraunhofer.de

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

PHYSICAL PROCESS TECHNOLOGY

Dipl.-Ing. Siegfried Egner
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

Dr. Thomas Scherer
Phone +49 711 970-4091
thomas.scherer@igb.fraunhofer.de

Dr. Ana Lucía Vásquez-Caicedo
Phone +49 711 970-3669
analucia.vasquez@igb.fraunhofer.de

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

Administration
Controlling and Finance

Dipl.-Kfm. Michael Bangert
Phone +49 711 970-4019
michael.bangert@igb.fraunhofer.de

Administration
Human Resources and Organization

Katja Rösslein M. A.
Phone +49 711 970-4009
katja.roesslein@igb.fraunhofer.de

Research Strategy and
Business Development

Dipl.-Kffr. Jenny Bräutigam
Phone +49 711 970-4070
jenny.braeutigam@igb.fraunhofer.de

Research Strategy and
Business Development

Dipl.-Agr.-Biol. Sabine Krieg MBA
Phone +49 711 970-4003
sabine.krieg@igb.fraunhofer.de

Research Strategy and
Business Development

Dr. Uwe Vohrer
Phone +49 711 970-4134
uwe.vohrer@igb.fraunhofer.de

Press and Public Relations

Dr. Claudia Vorbeck
Phone +49 711 970-4031
claudia.vorbeck@igb.fraunhofer.de

ENVIRONMENTAL BIOTECHNOLOGY AND BIOPROCESS ENGINEERING

Dr.-Ing. Ursula Schließmann
Phone +49 711 970-4222
ursula.schliessmann@
igb.fraunhofer.de

Prof. Dr. Dieter Bryniok
Phone +49 711 970-4211
dieter.bryniok@igb.fraunhofer.de

Dr. Iris Trick
Phone +49 711 970-4217
iris.trick@igb.fraunhofer.de

- Algal Technology
- Bioprocess Engineering
- Bioenergy
- Integrated Water Management

CELL AND TISSUE ENGINEERING

Prof. Dr. Petra Kluger
Phone +49 711 970-4072
petra.kluger@igb.fraunhofer.de

Prof. Dr. Katja Schenke-Layland
Phone +49 711 970-4082
katja.schenke-layland@
igb.fraunhofer.de

Dr. Svenja Hinderer
Phone +49 711 970-4196
svenja.hinderer@igb.fraunhofer.de

- Test Systems and Implants
- Cardiovascular Systems, Biomaterials and Bioimaging
- Attract Group "Organ-on-a-Chip"

BRANCHES OF THE INSTITUTE

Fraunhofer CBP, Leuna

Dipl.-Chem. (FH) Gerd Unkelbach
Phone +49 3461 43-9101
gerd.unkelbach@cbp.fraunhofer.de

BioCat, Straubing

Prof. Dr. Volker Sieber
Phone +49 9421 187-300
volker.sieber@igb.fraunhofer.de

Translational Center Regenerative Therapies, Würzburg

Prof. Dr. Heike Walles
Phone +49 931 31-88828
heike.walles@igb.fraunhofer.de

FRAUNHOFER IGB'S NETWORKING ACTIVITIES

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

Networking with universities

Basic research is a must for the applications of tomorrow. Thus Fraunhofer IGB maintains close contacts with neighboring universities, both through scientific cooperation and through the professorial and other teaching commitments of Fraunhofer employees. In addition, our branches in Straubing, Würzburg, and Leuna have enabled us to extend our scientific network to locations outside of Stuttgart. Fraunhofer IGB is particularly closely allied to the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart, which until the end of 2015 was chaired by Fraunhofer IGB director Prof. Thomas Hirth.

- Priv.-Doz. Dr. Susanne Bailer
  Private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Dr. Kirsten Borchers
  Associate lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Prof. Dr. Dieter Bryniok
  Professor of Environmental Biotechnology at Hamm-Lippstadt University of Applied Sciences
- Prof. Dr. Thomas Hirth
  Professor, Chair and Director of the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart (until December 2015)
- Prof. Dr. Petra Kluger
  Professor of Tissue Engineering at Reutlingen University, Faculty of Applied Chemistry
- Dr. Christian Oehr
  Associate lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- apl. Prof. Dr. Steffen Rupp
  Außerplanmäßiger professor and private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart
- Prof. Dr. Katja Schenke-Layland
  Professor of Biomaterials in Cardiovascular Regenerative Medicine at the University Hospital for Women of the Eberhard Karls University Tübingen;
  Adjunct associate professor at the Medical Faculty/ Department of Cardiology at the University of California Los Angeles (UCLA), Los Angeles, CA, USA
- Dr.-Ing. Ursula Schließmann
  Teaching activity in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart

- **Prof. Dr. Volker Sieber**
  Professor and chair of Chemistry of Biogenic Resources at the Technische Universität München
- **apl. Prof. Dr. Günter Tovar**
  Außerplanmäßiger professor and private lecturer in the Faculty of Energy Technology, Process Engineering and Biological Engineering at the University of Stuttgart; Director (acting) of the Institute of Interfacial Process Engineering and Plasma Technology IGVP at the University of Stuttgart (since 2016)
- **Prof. Dr. Heike Walles**
  Professor and chair of Tissue Engineering and Regenerative Medicine at the University of Würzburg

Fraunhofer Sustainability Network

Sustainable development is arguably the key political objective of our time. What sustainability means in concrete terms for the Fraunhofer-Gesellschaft was defined early on by the society's Sustainability Network, to which over 20 institutes belong. Fraunhofer IGB was significantly involved in this process, with Prof. Thomas Hirth acting as spokesman of the network until the end of 2015. Thanks to its vanguard role in the German research landscape, Fraunhofer is coordinating a joint project designed to provide a framework for implementing internal sustainability management. Please, read more about these latest developments in the highlights chapter on page 34.
www.nachhaltigkeit.fraunhofer.de

Fraunhofer International Business Development (IBD) Network

International cooperations and joint development activities with globally active partners are of strategic importance for the Fraunhofer-Gesellschaft. Fraunhofer IGB is therefore an active member of the Fraunhofer-Gesellschaft's International Business Development Network, where various Fraunhofer Institutes exchange views on specific issues regarding cooperation with international partners. Best-practice examples serve as the basis for an even more efficient use of resources when initiating and pursuing cooperation projects. The network is in close contact with the International Business Development of the Fraunhofer-Gesellschaft. During the 2015 Annual Network Meeting at Fraunhofer ILT in Aachen, therefore a joint discussion with colleagues from the International Business Development and for the first time also from the Corporate Business Development was held. Highlight of the meeting was a motivational speech of the European Association of Research and Technology Organisations EARTO.

Fraunhofer EU Network

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

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

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

FRAUNHOFER CBP'S NETWORKING ACTIVITIES

Leading-edge Cluster BioEconomy

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

Science Campus Halle – Plant-based Bioeconomy (WCH)

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

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

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

Hydrogen Power Storage & Solutions East Germany (HYPOS)

HYPOS aims to convert excess renewable electricity into the storable chemical energy carrier hydrogen and integrate, by means of an intelligent connection of hydrogen production, with the infrastructure of gas pipelines and gas storage facilities into the energy system. Via the "green" hydrogen, the chemical network, the natural gas supply system, and the electricity supply network in East Germany are connected in an exemplary manner. Within HYPOS, Fraunhofer CBP acts as a research partner mainly in the use of "green" hydrogen.
www.hypos-eastgermany.de

ZIM Cooperation Network Biorefineries (BioRaf)

Within the BioRaf cooperation network, concepts and business opportunities for biorefineries as well as innovative products and processes are especially developed for small and medium-sized enterprises. In addition, synergetic effects should be established in order to tap into the full potential in the field of biorefinery. Fraunhofer CBP is an associate member of the BioRaf network.
www.bioraf-netzwerk.de

FRAUNHOFER GROUPS AND ALLIANCES

Fraunhofer Institutes working in related subject areas cooperate as groups, foster a joint presence on the R&D market and help define the Fraunhofer-Gesellschaft's business policy. Institutes with complementary expertises collaborate in Fraunhofer "Alliances" to offer market solutions along the entire value chain. Fraunhofer IGB is an active member of the Fraunhofer Group for Life Sciences and an associated institute of the Fraunhofer Group for Materials and Components – MATERIALS due to its strong focus on materials science. Furthermore, it is a member of various Fraunhofer Alliances and optimally integrated within the Fraunhofer network.

Fraunhofer Groups

Fraunhofer Group for Life Sciences
www.lifesciences.fraunhofer.de

Fraunhofer Group for Materials and Components – MATERIALS (associated institute)
www.vwb.fraunhofer.de

Fraunhofer Alliances

Fraunhofer Building Innovation Alliance
www.bau.fraunhofer.de

Fraunhofer Big Data Alliance
www.bigdata.fraunhofer.de

Fraunhofer Energy Alliance
www.energie.fraunhofer.de

Fraunhofer Food Chain Management Alliance
www.fcm.fraunhofer.de

Fraunhofer Additive Manufacturing Alliance
www.generativ.fraunhofer.de

Fraunhofer Nanotechnology Alliance
www.nano.fraunhofer.de

Fraunhofer Photocatalysis Alliance
www.photokatalyse.fraunhofer.de

Fraunhofer Polymer Surfaces Alliance POLO®
www.polo.fraunhofer.de

Fraunhofer Cleaning Technology Alliance
www.allianz-reinigungstechnik.de

Fraunhofer Water Systems Alliance (SysWasser)
www.syswasser.de

In addition, Fraunhofer Institutes carry out joint activities within Fraunhofer internal research programs. Examples of IGB involvement are the Fraunhofer lighthouse projects "Theranostic Implants", "Critical Rare Earths", "E3-Production", and "Electricity as a Raw Material".

For further information on our networking activities please visit:
www.igb.fraunhofer.de/network

HIGHLIGHTS 2015

RESEARCH – COLLABORATIONS AND PROJECTS

Expanded Water Check water-testing system 1

Fraunhofer IGB has been analyzing water samples from private households for ten years through a Germany-wide study with Austrian company AQA. "Water Check" is a water-testing system that uses state-of-the-art chemical and physical techniques to analyze 24 important parameters of water including metal content, trace elements, and salts. AQA and Fraunhofer IGB decided last year to expand Water Check to include bacteriological tests. This will enable consumers to have their drinking water investigated for the presence of bacteria like *Escherichia coli*, enterococci, and *Pseudomonas aeruginosa* as well. You can also read the report about this on p. 118.

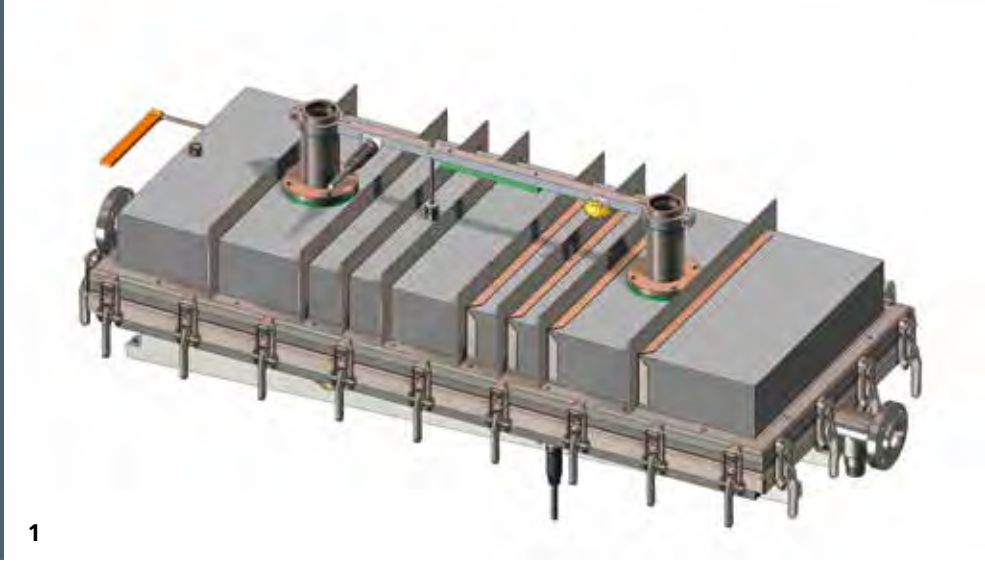
New Fraunhofer lighthouse project: "Electricity as a raw material"

The energy transition and expansion of renewable distributed power generation will make cost-effective, though weather-dependent electricity from wind power and solar installations available in the future. If the excess electricity from these fluctuating sources can be used for electrochemical reactions while at the same time utilizing CO_2 as a source of carbon, then basic industrial chemicals can be sustainably manufactured that previously used petroleum. This is where the Fraunhofer Lighthouse project entitled "Electricity as a Raw Material" comes in, begun at the end of October 2015. Fraunhofer IGB is coordinating the development of a new one-step process in the project with which ethylene will be electrochemically manufactured from CO_2 and water. You can find additional information in the report on page 98.

ePhos® – First licensing agreement in the USA

ePhos®, the electrochemical process for precipitating phosphate from effluent developed and patented by Fraunhofer IGB was successfully introduced to the market in 2015. We have been able to negotiate a licensing agreement with the US company OVIVO, an established supplier of water supply and distribution equipment and systems, covering markets in the USA, Canada, and Mexico.

In the ePhos® process, ammonium (NH_4^+) and phosphate (PO_4^{3-}) are precipitated as struvite through a purely electrochemical approach using a sacrificial magnesium electrode. Due to changes in operating conditions and throughput targets for operators of wastewater treatment plants – caused for example by reduced discharge limits for phosphorus – the need for technologies to eliminate or recover phosphorus from community effluent has grown. Ammonium and phosphate are recovered by the ePhos® process for use as high-quality fertilizer struvite.



1

From proof of feasibility to marketable product

After proof of feasibility and the development of a suitable reactor design, the next priority for successful introduction of the ePhos® process to the market was making sure there was sufficient availability of magnesium consumed by the sacrificial electrodes in electrochemically forming the struvite. We were able to confirm the technical and logistical availability of cast magnesium bar supplies in negotiations with the world's largest supplier of raw magnesium. Due to the rectangular shape of the magnesium bars, however, the design of the original tubular reactor vessel was changed to rectangular geometry. In addition, a great deal of information and numerous requirements mentioned in discussions with potential customers were very helpful during development. Particularly important insights were able to be obtained and incorporated during an initial pilot phase using a wastewater treatment plant in northern Germany that relied on biological elimination of phosphorus (see p. 112).

We presented the process jointly with our licensee at their trade show booth in Chicago during the Water Environment Federation's Annual Technical Exhibition and Conference WEFTEC in October 2015. Again, we were able to pick up important suggestions and requests from interested visitors and potential customers, for example about automation, and take these into account during the development work. The OVIVO company, as our licensee, will build and sell the installations in North America according to our specifications, while Fraunhofer IGB will further develop the technology and be available to the company and its customers for specific application tasks.

The struvite recovered with the ePhos® process is free of biological material and can be immediately employed as high-quality agricultural fertilizer. The experience at the booth in Chicago was surprising in that many of the plant operators from the United States who wished to employ the ePhos® process also wanted to locally market the struvite themselves rather than turning it over to an external purchaser for supra-regional sales.

The motivation for investing in the new phosphorus recovery technology resulted from the new, extremely low discharge limits for phosphorus in the USA. For this reason, the bio-nutrient removal process using anaerobic sludge digestion is increasingly popular there. However, spontaneous precipitation of struvite represents an operational problem associated with considerable costs for them. Current interest has also increased in Germany as a result of the amendment to the German wastewater treatment regulations and the constantly rising prices for fertilizer. As a result, we are talking to industrial partners in order to commence market introduction in Europe during the leading industry trade show IFAT coming up in May 2016.

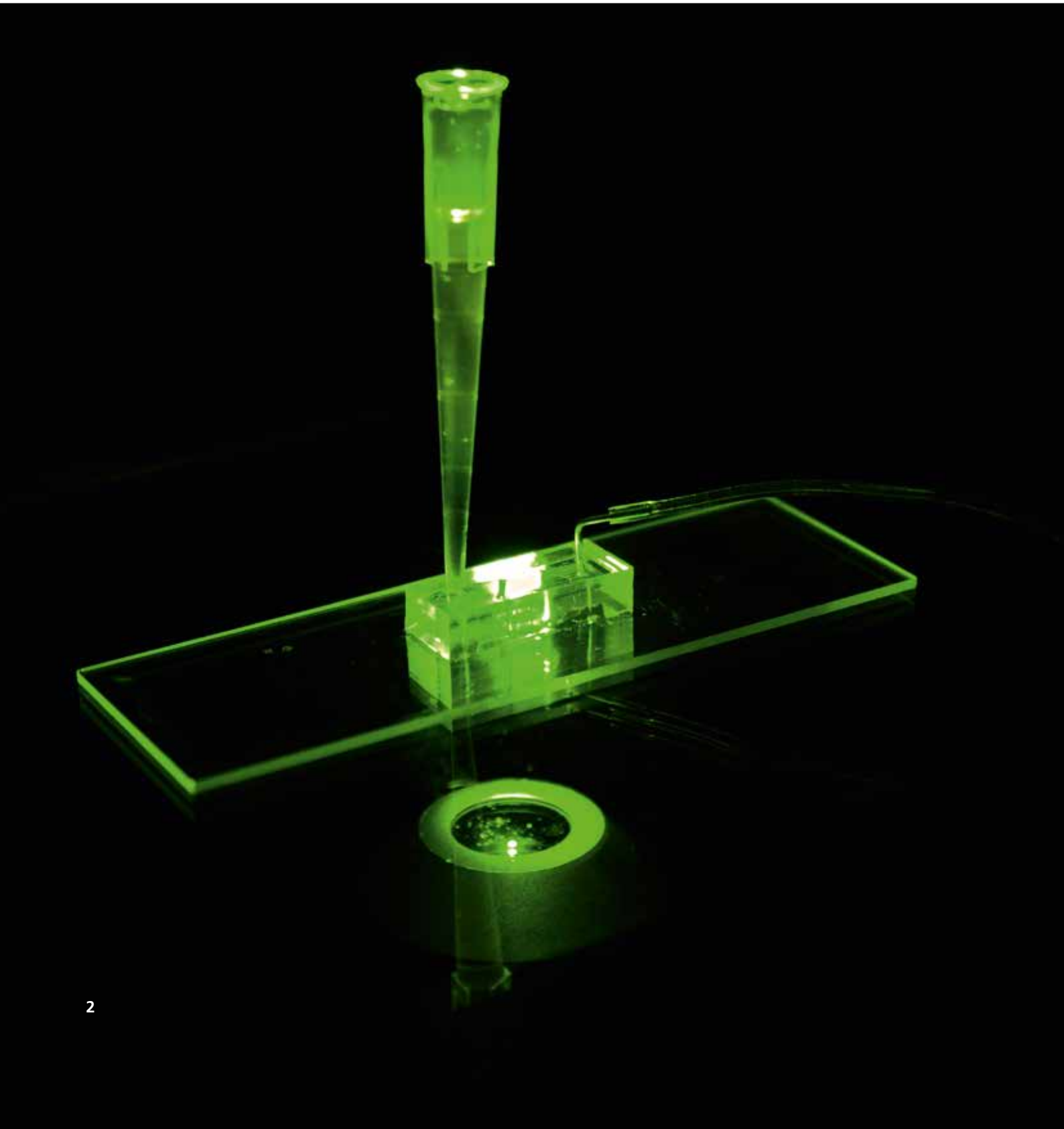
German Research Foundation (DFG) Research Training Group for infection research in Würzburg, Germany

The molecular mechanisms of how microbial pathogens penetrate human beings, multiply, and circumvent attack by the immune system still remain unexplained in many ways. The investigation of these questions is the objective of the "3D Tissue Models for Studying Microbial Infections by Human Pathogens" Research Training Group at the University of Würzburg, approved by German Research Foundation (DFG) in November 2015. Together with the Translational Center, the Würzburg branch of Fraunhofer IGB, three-dimensional tissue models produced from human cells will be optimized for the purpose of studying infection mechanisms under conditions approximating physiological conditions. Traditional entry portals for pathogens such as the epidermis, the mucous membranes of the respiratory tract, and interior lining of the intestinal and urinary tracts will be the focus of the research. The work will commence in April 2016 and be supported by the DFG with a grant of 5 million euros over the next four years.

New Organ-on-a-Chip Attract Group 2

The Fraunhofer-Gesellschaft approved a new Attract Group in autumn 2015 that began its work at Fraunhofer IGB March 1, 2016. The head of the group is physicist Dr. Peter Loskill, who was conducting interdisciplinary research at the University of California, Berkeley. His objective is to replicate the smallest functional unit of a tissue or organ in the form of a chip with the help of microfluidic systems – in order to be able to test potential pharmacological candidates with high validity at an early stage of their development. In order for the organ-on-a-chip to eventually be employed for high throughput screening, Loskill wants to parallelize and automate the chips. The systems can help minimize animal experiments and reduce the costs of pharmaceutical development.

The initial focus will be on *in vitro* models of myocardial muscle and white adipose tissue obtained from human induced pluripotent stem cells. Since myocardial toxicity is the most frequent cause for pharmaceutical candidates to fail, myocardial tissue plays an important role in the development of medicines. White adipose tissue is especially important not just for purposes of storage, but also in obesity and diabetes, diseases that are occurring with increasing frequency. The Fraunhofer-Gesellschaft is supporting the work with a grant of 2.5 million euros over five years.



1

FRAUNHOFER IGB INTERNATIONAL

New EU projects in "Horizon 2020"

"Horizon 2020" is the European Union's 8th supporting program for research and innovation. With nearly 80 billion euros of funding, it is the world's largest self-sustained funding program for research and innovation over the seven-year period from 2014 to 2020.

It aims to ensure first-class research in Europe, remove barriers to innovation, and open access to innovation in the public and private sectors. "Horizon 2020" aims to establish a society supported by knowledge and innovation and a competitive economy in all of Europe – all the while contributing to a sustainable economy.

The deadlines of the first two-year work program of "Horizon 2020" elapsed in the summer of 2015. Fraunhofer IGB has already achieved positive results, and is delighted to be involved in six new projects and in the coordination of two others.

New projects in Pillar I "Excellent Science"

Amicrex 1

Fraunhofer IGB would like to welcome its first recipient of the Marie Skłodowska-Curie scholarship under "Horizon 2020", Dr. Katalin Solyom. Since May 2015, the Hungarian scientist has been researching in her Amicrex project the development of an integrated process for the production of high-quality, non-polar components from residues of food and agricultural production for use as additives in the food and cosmetic industries.

ERIFORE

Fraunhofer CBP will participate in the project ERIFORE as of January 1, 2016. This is a trans-European network scheme in the area of Circular Forest Bioeconomy.

New projects in Pillar II "Industrial Leadership"

Fraunhofer IGB is involved in the coordination and support action FERTINNOWA in the field of water, which complies with a trans-European networking function in this area. FERTINNOWA started on January 1, 2016. Along with this is the recently announced participation in the "Fast Track to Innovation" project ELSi, which is conducting research in the field of photovoltaic module recycling with strong industry participation. ELSi is scheduled to begin shortly.

New projects in Pillar III "Societal Challenges"

Since August 1, 2015, scientists of Fraunhofer IGB have been involved in the BBI (bio-based industries) public-private partnership project CARBOSURF. In the field of health, we are pleased to be a participant in the project BIO-CHIP, which was launched on November 1, 2015 and is dedicated to innovative treatment options for knee cartilage injuries. In November 2015, we also received funding approval for participation in the area of bio-economy: the project CELBICON has started on March 1, 2016.

Completed projects from the EU's 7th Framework Programme

Some projects of the EU's 7th Framework Programme for Research and Technological Development could be successfully completed in 2015. Among them were the VascuBone, PhosFarm, MCure, Whey2Food, and Noveed projects coordinated by Fraunhofer IGB. For more on the individual projects, kindly consult the respective project sites as well as the homepage of Fraunhofer IGB.

Views EU

In autumn 2015, the second work program of "Horizon 2020" was published for the years 2016 and 2017. Here too, Fraunhofer IGB was able to identify some relevant disclosures, and participate in the first deadlines in December 2015 and January 2016 with exciting project ideas.

For further information on the Fraunhofer IGB EU-funded projects please visit:
www.igb.fraunhofer.de/eu-projects

Visits, Cooperations, Projects

It's all about people – Fraunhofer IGB is internationally active in the EU and beyond. With the aim of expanding our scientific excellence and economic value, Fraunhofer IGB has strategic contacts with Brazil, USA, Israel, China, and Australia. At Fraunhofer IGB, internationalization is led by creative people who collaborate with others to contribute to sustainable development based on excellent research. This is also reflected in the high number of international employees at the institute.

Ireland – Technologies for biomedicine
Meeting with Dublin City University

In July 2015 representatives of Dublin City University and its "Biomedical Diagnostics Institute" (BDI) met with researchers from the Departments Molecular Biotechnology, Interfacial Engineering and Materials Science, and Cell and Tissue Engineering as well as with other experts from the Fraunhofer Group for Life Sciences. Background of the meeting was a first joint competence-mapping and matching for technology development for biomedical applications.

During the meeting – all presentations were held as impulse lectures for subsequent scientific discussions – a number of ideas were generated and tracked for future activities. The meeting was part of a series of informal gatherings with excellent international partners with the common goal of initiating and developing long-term strategic partnership. Key topics such as the development of microfluidic devices, scientist exchange, joint PhD studies and bilateral funding schemes were discussed. A next meeting is planned in the first quarter of the year 2016.

1


2

USA – Cardiac stem cell research
Successful project completion

The collaborative BMBF/CIRM funded (German Federal Ministry of Education and Research and California Institute for Regenerative Medicine) project "Characterization and Engineering of the Cardiac Stem Cell Niche" between Fraunhofer IGB and the University of California in Los Angeles (UCLA) and San Diego (UCSD) was successfully completed in 2015. For the past three years, the groups led by Prof. Katja Schenke-Layland (IGB), Prof. Ali Nsair M.D. (UCLA) and Prof. Shu Chien M.D. (UCSD) have focused on elucidating the composition and function of islet-1 positive microenvironments in the developing human heart. Islet-1 has been described as an identifier of cardiac progenitor cells (CPCs) in the heart.

CPCs are of extreme interest for researchers seeking to discover new therapies for heart attack (myocardial infarction) survivors as these cells have been shown to regenerate the damaged heart post-infarction. Major hurdles in the use of CPCs as a cardiac therapy are the definition of the proper cardiac cell type and the proliferation of these cells in enough number for human therapies. The overall goal of the project was to mimic the microenvironments of islet-1 clusters in a dynamic bioreactor system in order to derive the required amount of CPCs for human therapies. The groups identified different islet-1 clusters within the heart and defined their transcriptional, morphological and protein characteristics, which were then translated into a bioreactor system to differentiate and mature pluripotent-derived cardiac cells. In future studies, the group plans to perform large animals myocardial infarct studies in preparation for phase 1 clinical trials.

China – Semi-decentralized water management 1 + 2
Guest scientist at Fraunhofer IGB

Cooperation with China has been strongly strengthened by the internship of Dr. Liangfei Dong from Changzhou. He stayed and worked at Fraunhofer IGB from October 2014 to September 2015 supporting the Fraunhofer IGB semi-decentralized water management research team. In addition, he represented the IGB at the Congress BAU China 2015 in Bejing and organized the visit of delegates from the Changzhou Science & Technology Bureau September 14th, 2015. On his return visit to Changzhou, in November 2015, IGB scientist Dr.-Ing. Marius Mohr gave a lecture at the university on semi-decentralized water management. Together with Dr. Liangfei Dong, he also visited several companies showing interest in future cooperation. Both Marius Mohr and Liangfei Dong participated in the Water Expo Fair in Bejing, supporting the Baden-Württemberg International booth in cooperation with representatives from the European Network Architecture (e.n.a). He returned with several good contacts and interesting new approaches which will help intensify and strengthen the cooperation with China.

Australia – Heart valve replacement 3
Scientific exchange

For her doctoral thesis "Electrospinning – a suitable method to generate scaffolds for regenerative medicine applications", Dr. Svenja Hinderer was given the German Students Award by the Körber Foundation for her work on a cell-free heart valve replacement, which was performed at Fraunhofer IGB in the Department of Cell and Tissue Engineering. The stable yet elastic scaffold can be sterilized and is biocompatible – making it perfectly suitable for medical applications. The future goal is to develop a cell-free medical device that binds cells after implantation into the patient. The new material will besides other positive effects allow natural remodeling and growth of the valve making it a perfect material for pediatric patients.

3

To further develop the exceptional valve material together with excellent colleagues, the extraordinary scientist travelled halfway around the world. Her goal: adding a second layer of tropoelastin to the material. During her stay from July to September 2015 she developed, with the working group of worldwide leading expert Prof. Tony Weiss at the University of Sydney, a material consisting of an electrospun scaffold coated with tropoelastin silk and at the same time set the course for a long-term scientific partnership. Her stay has been supported by the Fraunhofer TALENTA program and a grant from Deutsche Forschungsgemeinschaft (DFG) for the stimulation of international cooperation.

Russia – Sewage treatment
DBU stipendiary at BioCat in Straubing

As a new research team member of the IGB Straubing branch Bio, Electro, and Chemocatalysis BioCat, the Russian engineer Olesia Dolganova dedicates her work to the application of phyto-technological approaches in sewage purification. A grant of the German Federal Environmental Foundation (DBU) allows her to conduct her research together with her German colleagues at Fraunhofer IGB. Olesia Dolganova received her engineering degree in the field of "Use and protection of water resources" at the University of Kaliningrad, Russia. She holds the UMNIK Award, supporting excellent young scientists at the age of 18–28 in the development of new technologies. The award supports young highly committed researchers in the creation of their own start-up company. At Fraunhofer IGB Straubing branch, Olesia Dolganova continued her project successfully together with her mentor Dr. Tobias Gärtner, manager of the research group "Design and development of chemical catalysts".

Contact

Research Strategy and Business Development

Dipl.-Agr.-Biol. Sabine Krieg MBA
International inquiries, project initiation
Phone +49 711 970-4003
sabine.krieg@igb.fraunhofer.de

Dipl.-Kffr. Jenny Bräutigam
EU projects, project management
Phone +49 711 970-4070
jenny.braeutigam@igb.fraunhofer.de

1

PERSONNEL, PRIZES, AWARDS

Professorship for Dr. Steffen Rupp 1

In May 2015, Dr. Steffen Rupp was appointed *außerplanmäßiger* professor at the Institute of Interfacial Process Engineering and Plasma Technology (IGVP), University of Stuttgart. Prior to this, the Deputy Director of Fraunhofer IGB and Head of the Department Molecular Biotechnology was working there as a private lecturer. With the appointment, the university recognizes the longstanding teaching of the trained chemist. Rupp has been closely linked with the University since the early 1980ies. In 1990, he completed his studies there with a diploma, followed by his doctorate in the field of biochemistry.

Dr. Svenja Hinderer receives German Student's Award 2

Awarded annually, the Körber Foundation's German Student's Award honors the work of the best junior German scientists. The IGB associate Dr. Svenja Hinderer received the award in November 2015 for her doctoral dissertation "Electrospinning – A Suitable Method to Generate Scaffolds for Regenerative Medicine Applications" at the IGVP of the University of Stuttgart. For her doctorate she had researched artificial heart valves under the direction of Professor Katja Schenke-Layland from Fraunhofer IGB. Hinderer is concurrently Group Manager of Cardiovascular Systems, Biomaterials and Bioimaging within the IGB's Department of Cell and Tissue Engineering.

Science4Life founder award for foxySpec mass spectrometer

The founder's initiative Science4Life e.V. honors annually particularly promising business ideas from science, thereby encouraging young academic entrepreneurs. In December 2015, a research team led by the IGB engineers Matthias Stier and Stephan Scherle received one of the founders' awards for the innovative foxySpec mass spectrometer with which one can, for the first time, simultaneously analyze up to 30 different components from both the gaseous and the liquid phase in real time. Through this award, Science4Life e.V. acknowledges the enormous potential of this product development, especially for the process industry.

Change of head of administration

Long-time IGB's Head of Administration, Ulrich Laitenberger, moved to the neighboring Fraunhofer Institute for Manufacturing Engineering and Automation IPA in autumn 2015. The institute's administration subsequently took on a dual leadership consisting of Katja Rösslein and Michael Bangert. Rösslein, director of human resources, assumes the responsibilities of Human Resources and Organization while controller Michael Bangert is responsible for Controlling and Finance.

2

3

apl. Professor Günter Tovar takes on post of acting Director of IGVP 3

At the turn of 2015/16, the University of Stuttgart appointed apl. Prof. Günter Tovar as acting Director of the Institute of Interfacial Process Engineering and Plasma Technology IGVP. Within this role, Tovar assumes, until further notice, the duties of Prof. Thomas Hirth, who served as Director for both the IGB and the University Institute until the end of 2015. Since January 2016, Hirth has been employed at the Presidential Committee of the Karlsruhe Institute of Technology KIT. Tovar previously held the position of Deputy Director of the IGVP.

1

PROMOTING YOUNG TALENTS

An official goal of Fraunhofer IGB is to inspire young people for a future in science. For this reason, Fraunhofer IGB and the other institutes at the Stuttgart Fraunhofer campus are especially involved when it comes to familiarizing students with professions in STEM (Science, Technology, Engineering, and Mathematics) subjects. In addition, Fraunhofer Stuttgart also gives offers to students of science-oriented subjects so that they can affirm their choice of study in order to win them for a career at Fraunhofer.

Fraunhofer Talent School

The Fraunhofer Talent School offers students aged 15+ the opportunity to experience, during a weekend, a comprehensive overview of the research and work at Fraunhofer in Stuttgart. Within this scope, the participating institutes organized workshops in which young people can experience hands-on research and try out interesting projects themselves.

The Department of Molecular Biotechnology was involved with the workshop "CSI Stuttgart" for Fraunhofer IGB. By means of forensics, the ten participants solved a criminal case in the laboratory by isolating DNA and characterizing molecules from saliva samples.
www.stuttgart.fraunhofer.de/talents

Girls' Day

Already for the 15th time the nationwide Girls' Day took place in April, 2015. The German Federal Ministry of Education and Research initiated this day of action to inspire young girls to pursue a career in STEM professions. Although the young girl generation is well-schooled, relatively few girls still opt for a career in these areas. Instead they tend to assume "typically female" occupations.

In 2015, 79 students from grades 7 to 10 came to the Fraunhofer Institute Center Stuttgart for Girls' Day. Four institutes provided eight tours to feature the various professional and research fields at the Stuttgart Fraunhofer campus. In two guided tours, Fraunhofer IGB introduced the participants to the subjects "Tailored tissue from the laboratory" and "Water and raw materials from wastewater and waste" and showed what career paths exist in the institute in the fields of biology, chemistry, and process engineering as well as in interdisciplinary areas.
www.stuttgart.fraunhofer.de/girls-day

BoGy – Career and Study Orientation at Grammar Schools

Once again, in 2015, the Stuttgart-based Fraunhofer Institutes offered numerous weeklong BoGy internships for high school students. Eleven students arrived this year for two weeks in the spring and fall at Fraunhofer IGB. Particularly pleasing was the high proportion of interested female students – eight of the eleven participants were girls. During their internship, the students were given insight into the work and research of the institute. They met and learned about the activities of scientists and graduate students from different disciplines and about typical occupations at such a research institute.
www.stuttgart.fraunhofer.de/bogy

2

Checkpoint Future 1

"Checkpoint Future" is the day for students to visit the Stuttgart Fraunhofer campus. At this year's event, on November 27, 2015, students from different subjects were able to inform themselves about Fraunhofer as an employer and about career opportunities in science. In addition to an introduction to all Stuttgart institutes and a panel discussion on "Career with Fraunhofer", the student day offered participants numerous tours of the institute. They were given insight into the scientific work of Fraunhofer and an overview of its diverse research topics. Fraunhofer IGB participated this year with tours on the subjects "Nature's own chemical plant", "Tissue engineering – tailored tissue from the laboratory", and "Algal technology" .

www.stuttgart.fraunhofer.de/checkpoint

"Your Future in Stuttgart" – 2
Special interest day for international students

On April 18, 2015, the first special interest day for international students was held in the Stuttgart Town Hall. The information session was initiated by the City to inspire students from abroad registered at regional universities to pursue a professional future in Stuttgart, the location of science and business. The Stuttgart-based Fraunhofer Institutes and other business enterprises and research institutions were involved in the information program, and related job fair.

www.stuttgart.de/en/your-future

Dual training at Fraunhofer IGB

In addition to the training and support of students, of importance to Fraunhofer IGB is also the non-university vocational training. Therefore, the institute offers positions in different vocations. In 2015, two new appointments were made. This brings the total number of trainees to eight young women and men.

At Fraunhofer IGB, trainees have the opportunity to work alongside the vocational school in the various work areas of a research institute and thereby acquire the skills necessary for future work in research or industry. If trainees subsequently select the possibility of studying or in-service training, the institute will support them.

The administration offers young people the opportunity to complete training as an administrator for office management. Currently four associates are doing the three-year training. In addition, Fraunhofer IGB trains two IT-specialists for system integration in its IT section. Trainee positions also exist in the research departments. Scientifically interested and talented young people can be instructed to become chemical or biological laboratory assistants at the institute. Currently there are two laboratory assistants in training.

www.igb.fraunhofer.de/ausbildung

For further information
on promotion of young scientists
and training please visit
www.igb.fraunhofer.de/career

RESEARCH IN THE CONTEXT OF SOCIETAL CHALLENGES

The global effects of social imbalances and regional crises were felt to an unusual extent in 2015. At the same time, the United Nations passed new goals for sustainable development (Fig. 1). These address the environment, economy, and society in an equal measure.

Fraunhofer IGB as a trailblazer for sustainability

Fraunhofer IGB goals such as "Global Health", "Water and Sanitation for All", and "Sustainable Energy and Electricity for All" exemplify the relevance of our research topics. In a similar manner, sustainability is an interdisciplinary topic that has an effect on the ways we conduct research. Fraunhofer IGB has been engaged in work beyond its own research remit through the Fraunhofer Sustainability Network since 2007, developing strategies and guidance there for integrating aspects of sustainability into research. Prof. Thomas Hirth, co-founder of the Network and its spokesperson through the end of 2015, has been a trailblazer for professionalizing and strategically anchoring sustainability management practices in the Fraunhofer-Gesellschaft and at Fraunhofer IGB in Stuttgart.

Besides the international debate, the research agenda at the national and European levels also reflects the expectation by society that research and development be oriented more toward the great challenges of our time, not just accompanying our transition to a sustainable society, but shaping this transition as well. The complexity of the problems demands close cooperation between various research institutions, as well as with those who have empirical knowledge and experience, though not scientists. Systematic approaches and user-oriented development of solutions are already being implemented by researchers at Fraunhofer IGB, such as in the "E^3-Production" (see p. 120) and the "Ultra-Efficient Factory" (see p. 114) Lighthouse projects.

Sustainability management practices for research organizations 2 + 3

Criteria such as the degree of interdisciplinary and transdisciplinary work are important features of a responsible research process (Fig. 1), based on the conclusions from the "Guide to Sustainability Management in Non-university Research Institutions/(LeNa)" group project. Coordinated by Fraunhofer, scientists and experts from the administrations and management of 25 institutions of the three participating national German research organizations (Fraunhofer, Leibniz, and Helmholtz) have been working together in the project since 2013 (Fig. 2). The goal is to produce a joint understanding about the contribution of research organizations to sustainable development. A guide is to be developed containing a framework for action with clearly set-out options, practical tips, and inspiring examples of best practice. The guide addresses the trio of topics "socially responsible research", "personnel", and "facilities and operations". These will be treated in greater depth and expanded upon in three further sub-projects by interpreting fundamental principles and management processes based on international sustainability standards in the context of research. A dialog that included external stakeholders as well

2

3

as the participating organizations (Fig. 3) was conducted and clarified the differences between the institutions due to their respective sizes, forms of organization, and organizational culture, as well as areas of conflict and factors contributing to their success. The dialog will be organized and put into a comprehensible format by the end of 2016. The participation of several Fraunhofer Institutes in the project had a positive influence on internal cooperation. The Sustainability Network intends to be more active as an initiator, furnishing a pool of ideas in liaising between research, government policy, and society in the future, and advocating positions on important topics. As an example, the Network took part in the consultative process of the Citizen Science Strategy 2020 project for Germany in 2015.

Fraunhofer-wide dialog for the future

Fraunhofer IGB itself is a stakeholder within the greater Fraunhofer-Gesellschaft. For example, women are strongly represented in management positions at IGB and contribute their experience to corporate social responsibility issues. Following publication of the Sustainability Report in 2014, the further development of sustainable management practices in the Fraunhofer-Gesellschaft was discussed in a dialog held at Fraunhofer headquarters with representatives from science, commerce, government, and society. It was clear here as well that not just pioneering innovation is expected from Fraunhofer, but also that the organization comes to terms with its societal impact in particular. This task is now being incorporated into projects more.

Contact

Dr. rer. nat. Birgit Haller
Phone +49 711 970-4083
birgit.haller@igb.fraunhofer.de

Funding

We would like to thank the German Federal Ministry of Research and Education (BMBF) for funding the project "Leitfaden Nachhaltigkeitsmanagement in außeruniversitären Forschungseinrichtungen (LeNa)", promotional reference 13NKE003A.

Further information

www.lena-projekt.de

1 *UN Sustainable Development Goals.*
2 *LeNa project consortium.*
3 *Transorganizational dialog on guidelines for sustainable management practices.*

Further information on sustainability and research in the Fraunhofer-Gesellschaft:
www.sustainability.fraunhofer.de

COMPETENCES

FRAUNHOFER-GESELLSCHAFT

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

At present, the Fraunhofer-Gesellschaft maintains 67 institutes and research units. The majority of the nearly 24,000 staff are qualified scientists and engineers, who work with an annual research budget of more than 2.1 billion euros. Of this sum, more than 1.8 billion euros is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and *Länder* governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

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

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

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

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

www.fraunhofer.de

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

INTERFACIAL ENGINEERING AND MATERIALS SCIENCE

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

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

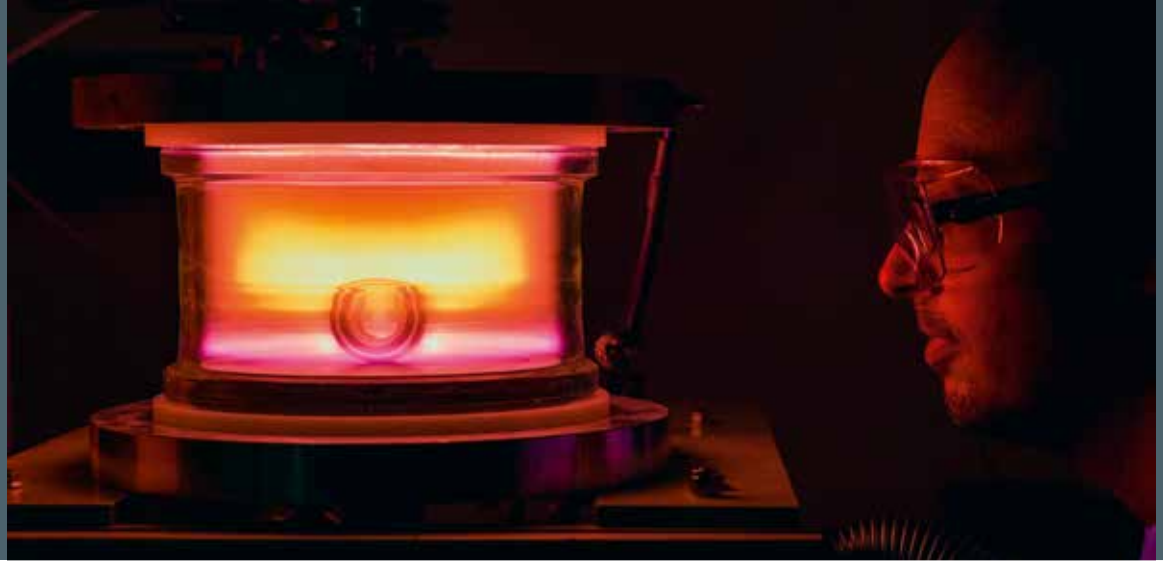
Established preparation methods

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

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

Established characterization and diagnostic processes

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



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

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

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

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

Contact

Dr. rer. nat. Christian Oehr
Head of Department,
Director (acting)
Phone +49 711 970-4137
christian.oehr@igb.fraunhofer.de

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

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

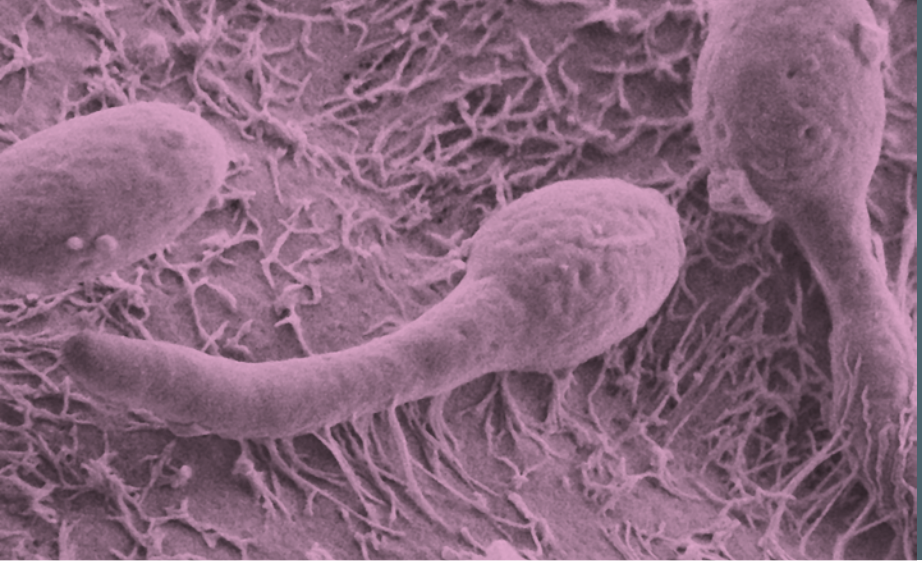
MOLECULAR BIOTECHNOLOGY

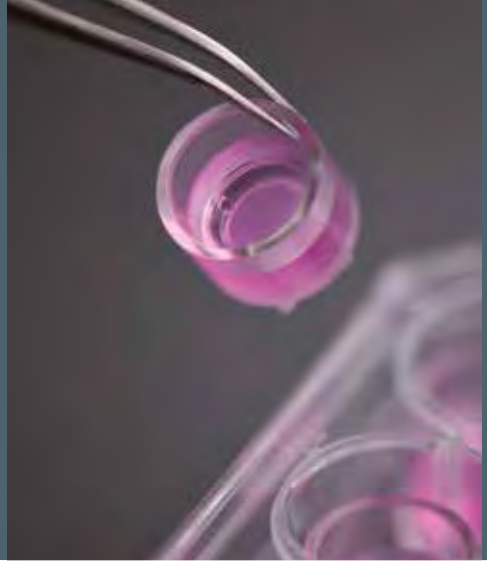
The Department of Molecular Biotechnology is active in the business areas pharmacy, medicine/diagnostics, and chemistry. One focus of the department is on the infection biology of pathogenic microorganisms and viruses. Here we use complex 3D models of infection with components of the immune system to detect the interaction between the host and pathogen and derive new approaches for drug screening and the stimulation of an endogenous defense. We develop new diagnostic methods based on nucleic acid technologies (diagnostic DNA-microarrays, development of biomarkers via DNA-high-throughput sequencing, and next-generation sequencing based diagnostics of nucleic acids circulating in the blood) or by means of cell-based reporter assays, e.g. with an immune receptor-based pyrogen assay. A further focus is the development of cell lines for pharmaceutical biotechnology as well as in strain development for industrial biotechnology. In terms of production processes of pharmaceutical proteins such as interferons and factor VII, we have already developed GMP-compliant processes in laboratory scale. In industrial biotechnology, processes for the microbial production of biosurfactants and the enzymatic synthesis of epoxides up into the 100-liter scale have been developed.

The core competences of the department are in the application of molecular-biological and biotechnological methods for genome, transcriptome, and proteome analysis, and an accredited analytics, which is also suitable for metabolome analysis. To make microbial production as efficient as possible, we use our expertise from the molecular-biological optimization of production strains right up to the development of bioprocesses with integrated, effective downstream processing. In infection biology, the combination of methods of functional genome analysis with our expertise in cell culture technologies lead to a unique expertise in the development of 3D infection models and test systems (e.g. as for the screening of drugs). For targeted drug delivery, we furthermore develop virus-like particles and therapeutic viruses.

Our goal is to understand the processes occurring in nature and to use nature's toolbox and diversity in biotechnological value chains, for example, in the development of biobased chemicals such as biosurfactants or polymer precursors, but also for new diagnostics and therapeutics. The new technologies in genome and proteome analysis enable us to extensively analyze entire microbial communities from the environment or the bioreactor, as well as the interaction between microorganisms and the human individual in the shortest of times. Using this information, products can be tested and validated, measurements for the specific treatment of a disease can be induced, or personalized medicines for different populations can be developed. In industrial biotechnology, the easy availability of genomes and the rapid analysis of cellular regulatory circuits offer the possibility to identify new metabolic pathways, to optimize processes directly in the reactor to use this ideally for the production of chemicals or enzymes.

With our expertise, we provide services, also in collaboration with other departments of Fraunhofer IGB, to different areas of the branches medicine, pharmacy, and chemistry. Thus, in the field of biocatalysis we work closely with the BioCat branch in Straubing. Laboratory-scale bioprocesses of up to 10 m^3 scale can be developed at the Fraunhofer CBP branch in Leuna. In addition, within the Fraunhofer Group for Life Sciences opportunities exist for the process development of pharmaceutical proteins right up to the GMP production of clinical test samples and studies in clinical phase I.





Contact

apl. Prof. Dr. rer. nat. Steffen Rupp
Head of Department
Phone +49 711 970-4045
steffen.rupp@igb.fraunhofer.de

Range of services

- Screening of targets and drugs for anti-infectives (infection models, cell-based screening assays)
- Proteome analyses (2D-/LC proteomics)
- High-throughput sequencing of genomes and transcriptomes
- Next-generation diagnostics of blood samples (circulating nucleic acids in plasma or serum, CNAPS)
- Development of DNA microarrays: probe design, manufacturing of arrays, sample preparation procedures
- Cell-based assays: antiviral assays (GLP), TLR/PRR-based assays/pyrogen detection (GLP), mutagenicity, toxicity
- Development of production cell lines and processes for recombinant production of proteins (biosimilars, protein purification and characterization)
- Cell-free protein synthesis, synthetic biology with non-natural amino acids
- Development of new high-throughput enzyme assays and screening processes
- Strain and parameter screening in multi-fermenter systems
- Development of integrated fermentation processes for industrial biotechnology, including the processing of both 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)
- High-throughput DNA parallel sequencing facility for nucleic acid analysis (Illumina HiSeq2000, Roche Junior)
- Proteomics facility using high-resolution MS technologies (2D gel electrophoresis, nano-LC-MALDI-TOF/TOF, HPLC-ESI-MS/MS)
- Fermentation plant for suspension and adherent cell cultures up to 10 liters of non-GLP
- Plants for protein purification
- Multi-fermentation plants for bioprocess development, and fermenters (up to 40 liters), S2/L2
- Cell disruption equipment (ball mills, high-pressure autoclave, etc.)
- GC-MS/MS, LC-MS/MS, IC, ICP-AES, and ICP-MS, accredited by the Deutsche Akkreditierungsstelle GmbH

PHYSICAL PROCESS TECHNOLOGY

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

Current main themes

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

Apart from our technical competence and specialized expertise, a hallmark of the quality of our R&D activities is our focus on sustainability. Thus, for example, we replace flows of raw materials by recycling in primary quality, upgrading or overhauling processes for the efficient use of regenerative energy and find ways to improve the efficiency of energy use. This also leads to improved economic efficiency of processes, meaning that our approach satisfies both ecological and economic demands at the same time. One example of this is the development of a process of storing heat, which is, for example, provided as waste heat from the conversion of biogas into electricity. The intention is to be able to provide heat energy for industrial use at any time and, thanks to the high energy density, at any location; thus the supply is not directly linked to when and where the energy has been generated. Potential applications are drying processes in production, supplying heat to buildings, or the concentration or thickening of highly contaminated process wastewater with vacuum vaporization.

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

The Physical Process Technology Department is staffed by scientists from various disciplines – such as process engineering, chemical engineering, food chemistry, mechanical and electrical engineering – who work together in multi-disciplinary

project teams. Projects may also involve collaboration with specialists from other Fraunhofer IGB departments, such as microbiologists and bioengineers, or from other Fraunhofer Institutes and affiliated universities, leveraging synergies in expertise to address specific issues.

Range of services

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

Infrastructure and technical equipment

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

Contact

Dipl.-Ing. Siegfried Egner
Head of Department
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

ENVIRONMENTAL BIOTECHNOLOGY AND BIOPROCESS ENGINEERING

The core areas of the Department of Environmental Biotechnology and Bioprocess Engineering are the development of biotechnological processes in the fields of water management, bioenergy, environmental technology, algal technology, product recovery from organic raw materials and waste materials, and interfacial biology.

A focal point are new approaches to the development of system concepts for energy, waste and water management in industry and for communities. Alongside aerobic and anaerobic methods for wastewater purification and water treatment, hybrid methods are being used. We prefer to treat organic waste materials such as biodegradable waste or sewage sludge anaerobically, as this process allows the economical generation of biogas as a renewable energy source. Maximum efficiency is achieved through the integration of several steps to establish short process chains.

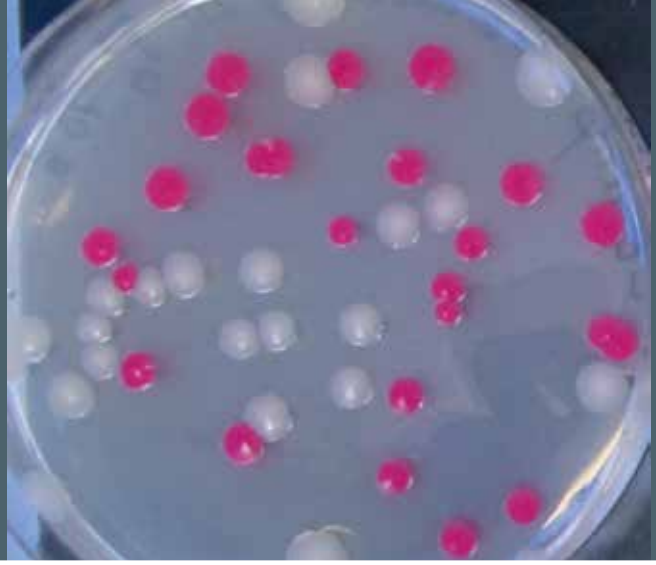
The processes are always designed on the basis of microbiological or process engineering principles such as, for example, the growth and degradation kinetics of the particular organisms, and ranges from the planning, commissioning and optimization of laboratory and pilot plant facilities through to the planning, construction, commissioning and optimization of innovative demonstration plants in cooperation with our industrial partners. In the field of environmental technology, processes and special reactors are available for the purification of industrial wastewater, exhaust air, and contaminated soils. Bioleaching, biosorption, and bioprecipitation are used specifically for the recovery of metals from process waters and wastes.

In algal technology we use microalgae as a natural and sustainable aquatic source of raw materials; these provide a number of valuable substances such as omega-3 fatty acids, pigments, proteins for the food, feedstuff, and cosmetics industries among others. In addition, for energetic utilization, oil and starch can be specifically produced from microalgae. We are developing new biorefinery concepts for the maximum utilization of algal ingredients.

To enable resource-conserving production in companies (ultra-efficient factory) we are developing robust process engineering concepts and methods, among other things for the production of basic chemicals such as, for example, methane, ethanol and methanol, which can be utilized either energetically or materially. In bioprocess development, the retention or immobilization of biocatalysts has an important role. The unique selling point of the department is the intelligent link between the process steps of mechanical, thermal, and chemical technology (incl. downstream processing technology) with bioprocesses using modeling and simulation methods.

In interfacial biology, we characterize microbial contamination on surfaces and in processing media (biofilm formation) and antimicrobial treatments, and develop to this end appropriate test procedures. Biosensors are used for real-time monitoring of water systems in the detection of contaminants.

The Environmental Biotechnology and Bioprocess Engineering Department is thus in a position to take part in solving sociopolitical challenges such as climate change, energy supply and freshwater shortage. By offering sustainable technology options, the department can help industry, communities and



policymakers design a balanced future. Combining our competences with those of other Fraunhofer IGB departments, we serve the needs of the chemical, energy and environmental business areas.

Range of services

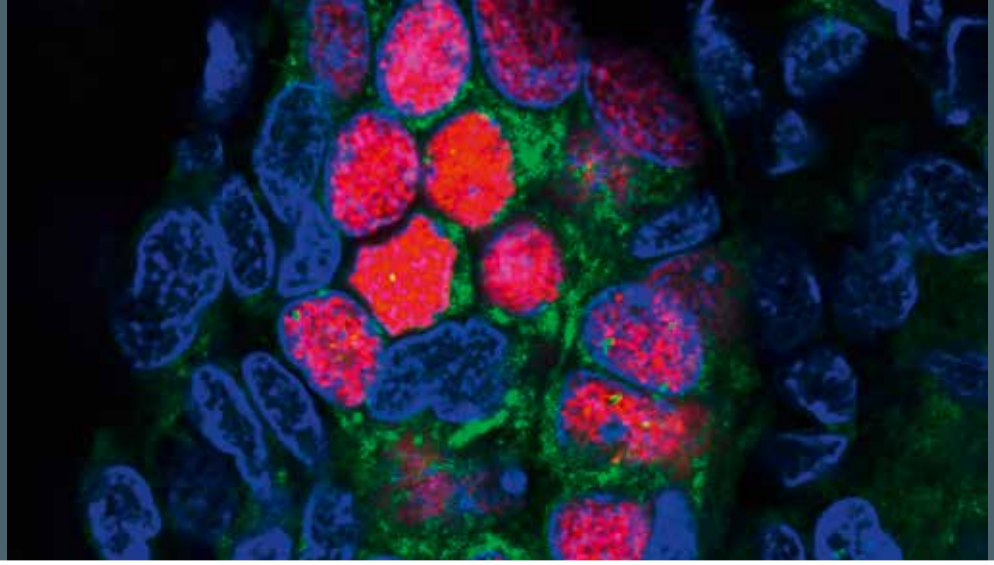
- Development of regional-level system concepts for energy, waste and water management
- Concepts for resource-conserving production in companies – the ultra-efficient factory
- Wastewater and water purification methods for industry and communities
- (Bio-)process engineering processes for water purification
- Development of utilization concepts for both inorganic and organic waste materials
- Digestion processes for producing biogas from a range of organic substrates in different temperature ranges
- Aerobic and anaerobic tests on the degradability of organic residues
- Fermentation tests in line with VDI 4630
- Development of photoautotrophic processes for microalgae and cyanobacteria cultivation in photobioreactors including process control and automation
- Development of heterotrophic processes for microalgae
- Biotransformation of renewable raw materials and industrial waste materials into basic chemicals and energy carriers (methanol, ethanol, etc.)
- Downstream processing technologies such as membrane-based filtration processes, liquid-liquid extraction, and extraction with supercritical media
- Analysis of microbial contamination on surfaces, including development of test procedures
- Development of real-time processes for monitoring water systems for contamination
- Bioleaching, biosorption, bioprecipitation processes for recovery of metals from different types of process water and waste streams using different reactor configurations
- Modeling of processes and simulation of process lines

Contact

Dr.-Ing. Ursula Schließmann
Head of Department
Phone +49 711 970-4222
ursula.schliessmann@igb.fraunhofer.de

Infrastructure and technical equipment

- Pilot plant for environmental and bioprocess engineering applications
- Bioreactors of various sizes (laboratory, pilot and industrial scale) for aqueous substrates, substrates containing a high level of solids, gaseous substrates, including cell retention
- Analytics for substrates and fermentation products, protein analytics, online mass spectrometry
- Mobile pilot plants on a cubic-meter-scale to generate basic engineering data for the planning of demonstration plants
- Demonstration and reference plants for anaerobic and aerobic wastewater treatment, high-load digestion, bioenergy, algal technology
- Demonstration sites for wastewater treatment, bioenergy, and cultivation of algae
- Photobioreactors of various sizes with special control and automation concepts for laboratory, outdoor and greenhouse applications
- Test facilities for different membrane processes (e.g. rotating disk filtration)
- Equipment and official approvals for handling pathogenic organisms
- Special apparatuses for testing antimicrobially finished materials
- Test facilities for cell disruption and extraction with solvents or supercritical fluids
- GIS applications using the ESRI ARC-INFO software; process simulation and automation (MATLAB, Siemens programming)



CELL AND TISSUE ENGINEERING

The focus of the Department of Cell and Tissue Engineering is the development of functional *in vitro* 3D tissue models from isolated primary human cells and pluripotent stem cells under GLP (Good Laboratory Practice) or GMP (Good Manufacturing Practice) guidelines for applications in regenerative medicine, tissue engineering, medical device development and cell-based assays for biocompatibility and stem cell differentiation tests.

We develop synthetic, natural and hybrid biomaterials for the maintenance and differentiation of pluripotent (human embryonic stem (ES) and induced-pluripotent stem (iPS) cells) and adult stem cells. We further design biofunctionalized nano- or micro-structured material surfaces for the isolation of pure cell cultures from human tissues, particularly adult stem cells. The physiological culture of 3D tissue models is achieved with specially developed computer-controlled bioreactor systems which mimic the biomechanical environment of a specific organ or tissue.

The sterility and quality control for cell-based transplants is a complex process, which typically requires multiple transplants for testing. Therefore, we have established non-invasive test methods, Raman microspectroscopy and multiphoton microscopy, for the pre-implantation analysis of tissue-engineered constructs, which drastically reduces production and quality assurance cost, while increasing the safety of the transplanted constructs.

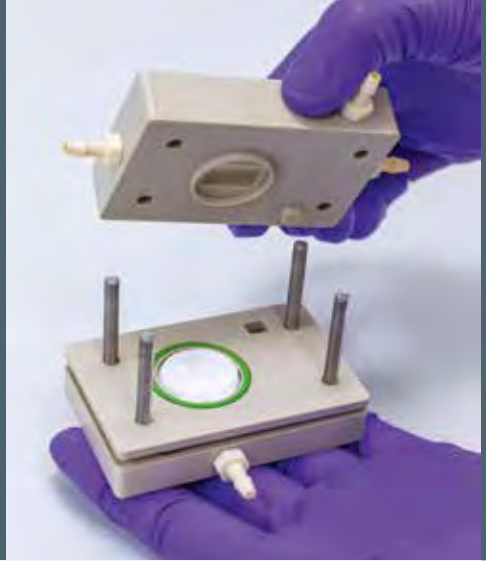
We have developed a two-layer 3D human skin equivalent that has been patented (EP 1 290 145B1). The skin model can be extended to include cell types, such as melanocytes or tumor cells. Furthermore, the skin model is a cost-effective human-based pre-animal test system for penetration and distribution tests of chemicals. Further questions in regard to cell differentiation and death, as well as tumor development and metastasis, can be studied with our model.

Additionally, we are developing methods for the creation of cardiovascular implants, regenerative therapies and *in vitro* 3D test systems. Due to the lack of regenerative potential in the adult cardiovascular system, we primarily work with human ES and iPS cells, as well as complex bioreactor systems. We study our engineered systems *in vivo* in established small and large pre-clinical animal models in close collaboration with the Department of Medicine/Cardiology at the University of California Los Angeles, where we also have access to human GMP-iPS cell lines.

In collaboration with the Department of Women's Health at the University Hospital of the Eberhard Karls University Tübingen we establish novel biofunctional implants, regenerative therapies, medical devices and *in vitro* 3D test systems in the fields of women's health and rare diseases.

Competences

- Isolation and culture of primary cells from different tissues and species in accordance with current GLP or GMP regulations
  - Skin and skin tumors, as well as cardiovascular and urogenital tissues
- Biomaterials design
  - Nano- or micro-structured material surfaces
  - Synthetic materials
  - Tissue-specific human recombinant extracellular matrix proteins
  - Biofunctionalized hybrid approaches



- Derivation of tissue-specific cells from pluripotent and adult stem cells
- Design of tissue-specific, computer-controlled bioreactors
- Establishing methods for the non-destructive characterization of cells and tissues by Raman microspectroscopy and multiphoton microscopy

ADMET (absorption, distribution, metabolism, excretion and toxicity) are pharmacokinetic and toxicological properties that must be tested during drug development. Using our test systems, we are able to test these properties in a more human situation than animal experiments, with the hope to eventually replace animal tests, as required by the 3R's initiative (replacement, refinement, and reduction).

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

Range of services

- Cell culture technology of primary human cells and mammalian cell lines
  - *In vitro* testing of cytotoxicity according to DIN ISO 10993-5
  - *In vitro* testing of phototoxicity according to OECD guideline 432 and INVITTOX protocol no 121
- Cell biology analysis
  - Molecular-biological, histological and immunohistological methods
  - Flow cytometry (FACS)
  - Modern digital image processing techniques such as microdissection
  - Raman microspectroscopy and multiphoton microscopy

Contact

Prof. Dr. rer. nat. Katja Schenke-Layland
Head of Department,
Director (executive, acting)
Phone +49 711 970-4082
katja.schenke-layland@igb.fraunhofer.de

Prof. Dr. rer. nat. Petra Kluger
Head of Department
Phone +49 711 970-4072
petra.kluger@igb.fraunhofer.de

- Establishing of various 3D tissue models
  - Alternatives to animal testing
  - ADMET testing in substance and drug screening
  - Target screening for new therapeutics and infection biology
  - Lab-on-a-chip microfluidics systems
- Development of specific computer-controlled bioreactor systems for the culture of 3D tissue models
- Process development, manufacturing and testing of cell and gene therapeutics as investigational medicinal products or ATMPs (phase I/II clinical studies)

Infrastructure and technical equipment

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

FRAUNHOFER CENTER FOR CHEMICAL-BIOTECHNOLOGICAL PROCESSES CBP

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

With more than 2000 m² of space for plants, technical infrastructure, laboratories, office and storage spaces, a unique platform is available for the development of new processes up to commercially relevant dimensions with a direct connection to the chemical industry on the one hand, and Fraunhofer research on the other. After the five-year start-up period and a successful evaluation in 2014, the project group became a permanent branch of Fraunhofer IGB.

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

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

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

Process development thus concentrates on the following aspects:

- Exploiting the carbon synthesis potential provided by nature
- The energy and resource efficiency of the processes developed
- Minimizing waste streams
- Reducing CO_2 emissions
- Material utilization of plant biomass that is not suited as either human food or animal feed
- Integration of the processes developed into existing systems/infrastructure

Small and medium-sized enterprises frequently do not have the resources of their own to realize the transfer of these new technologies from the laboratory to industrial implementation. The center's pilot scale and miniplant facilities offer these customers an excellent platform for process development. Indeed, this can also be used for the optimization of existing processes.

Range of services

To solve process-technical issues, Fraunhofer CBP provides modular process capacities of up to 10 m^3 reactor volume and continuous plants capable of high-pressure processing up to 20 kg per hour, plus a wide range of processing, treatment, and reconditioning techniques and methods. This versatile, "flexible biorefinery" facilitates the conversion of different raw materials such as: vegetable oils, lignocellulose, starch, sugar, but also petrochemical material flows or residuals, into chemical products.

Infrastructure and technical equipment

- Pulping and component separation of lignocellulose using organic solvents, with a capacity of 1 metric ton of biomass per week
- Fermentation capacities of 10/100/300/1000 and 10,000 liters, equipment for downstream processing of fermentation products
- Automated greenhouse and outdoor microalgae pilot plants, with a total volume of photobioreactors of 11.7 m^3
- Reactors for enzymatic processes up to 1000 liters
- Various process units for chemical reactions under ATEX conditions (continuous up to 20 kg/h or batch up to 100 liters at temperatures up to 500°C and pressures up to 300 bar)
- Mechanical and thermal separation processes (including high-temperature rectification up to 350°C at reduced pressures and extraction with l-propane and sc-CO_2), also under ATEX conditions

Contact

Fraunhofer Center for Chemical-Biotechnological Processes CBP
Am Haupttor | Tor 12, Bau 1251
06237 Leuna | Germany
Fax +49 3461 43-9199 | www.cbp.fraunhofer.de

Dipl.-Chem. (FH) Gerd Unkelbach
Head of Fraunhofer CBP
Phone +49 3461 43-9101
gerd.unkelbach@cbp.fraunhofer.de

Dr.-Ing. Katja Patzsch
Group Manager Biotechnological Processes
Phone +49 3461 43-9104
katja.patzsch@cbp.fraunhofer.de

Dr. rer. nat. Moritz Leschinsky
Group Manager Pre-Treatment and Fractioning of Renewable Raw Materials
Phone +49 3461 43-9102
moritz.leschinsky@cbp.fraunhofer.de

Dr. rer. nat. Daniela Pufky-Heinrich
Group Manager Chemical Processes
Phone +49 3461 43-9103
daniela.pufky-heinrich@cbp.fraunhofer.de

BIO, ELECTRO, AND CHEMOCATALYSIS BIOCAT, STRAUBING BRANCH

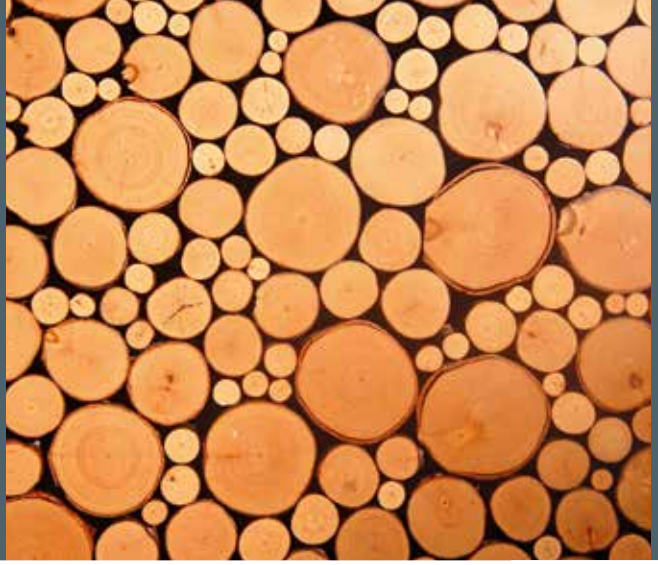
The focus of Fraunhofer IGB's Straubing branch "Bio, Electro, and Chemocatalysis BioCat" is on the development of new chemical catalysts and biocatalysts and their application in technical-synthetic and electrochemical processes. Based on substrates such as biomass, CO_2 and waste streams, the entire spectrum of catalysis is used to develop new sustainable and resource-efficient chemical products. Here, homogeneous and heterogeneous chemical catalysis, enzymatic and whole cell catalysis, electrocatalysis, and especially their combinations are utilized. In the case of using plant biomass, the goal is to achieve the substantial use of the material variety of biobased molecules and to exploit the potential of chemicals and biocatalysis so as to achieve a considerate transformation while obtaining important functionalities. Successful examples of our work include the transformation of terpenes (residual material of wood processing) to biosurfactants, biobased epoxides or monomers, especially impact-resistant, cold-stable polyamides. Other recycled material flows are vegetable oils and fatty acids, lignin and nitrogenous sugar, which are, for example, converted to functionalized carboxylic acids, conductive polymers, and monomers for polyesters and hydrocolloids.

Furthermore, BioCat transfers the expertise of chemical catalysis onto mineral residues to also develop these as a source of secondary raw materials. Even with inorganic residues, the variety of the mostly complex mixtures of different elements constitute an access to new products, where BioCat in this instance, has in view the production of new catalysts and the provision of raw materials for the German industry. The combination of chemistry and biotechnology also offers BioCat the opportunity to develop new energy- and resource-efficient processes in this field.

The group has also developed new methods of managing electrical energy by binding and converting CO_2 in the storage of chemical energy. These products and the corresponding methods are first provided to companies for the production of bulk and fine chemicals. Second, they can be used to store energy in fuels, such as in the form of longer-chain hydrocarbons, and can therefore make a contribution to the success of the energy turnaround. Here, the goal is the best possible utilization converting raw material to the biobased final product.

The BioCat branch unites biotechnologists, molecular biologists, and chemists who, in addition to their respective expertise in biotechnology and chemistry, have in-depth knowledge in the fields of biogenic raw materials, natural materials, and residual streams. By combining these different disciplines, it is possible to offer – apart from professional advice – development work in the areas of (i) new catalysts or catalyst optimization and existing processes, (ii) new materials, and (iii) new reactions which is carried out hand-in-hand with clients. The development work is supported primarily by existing analytical methods such as GC-MS, LC-MS, NMR, and electroanalysis. Thanks to the closely linked expertise in chemical catalysis and biocatalysis, BioCat has already successfully evaluated established processes in the chemical industry and outlined cost-effective and resource-efficient alternatives for the client.

The scarcity of fossil resources and the aspired reduction of CO_2 emissions due to climate change represent a huge scientific challenge for society and science. Since the biomass resource for a change of chemical raw materials is limited, we rely, apart from wastes and residues, mainly on CO_2 as an essential carbon source – and thus combine the need for



CO_2 reduction with material value. Against the backdrop of "sustainable chemistry" the BioCat Group aims to accelerate and decisively shape the development of the new generation of catalysts and processes.

For this, BioCat works closely with the TU München, the departments of Fraunhofer IGB, and the branch Sulzbach-Rosenberg of Fraunhofer UMSICHT. In collaborative projects, topics for the conversion of renewable resources and the use of hydrocarbons to store electrical energy are pursued.

Range of services

- Screening of biocatalysts and chemical catalysts
- Molecular biological and technical optimization of enzymes and enzyme reactions
- Synthesis of fine chemicals
- Development of methods for waste recycling
- Development of methods for integrating the use of renewable resources in existing processes
- Conducting studies in the field of renewable raw materials
- High-resolution NMR analysis (400 MHz) in solution for the purposes of molecular structure elucidation, reaction kinetics, deep temperature analytics, and developing techniques
- Electroanalytical methods (e.g. cyclic voltammetry, chronoamperometry, electrochemical impedance spectroscopy)

Infrastructure and technical equipment

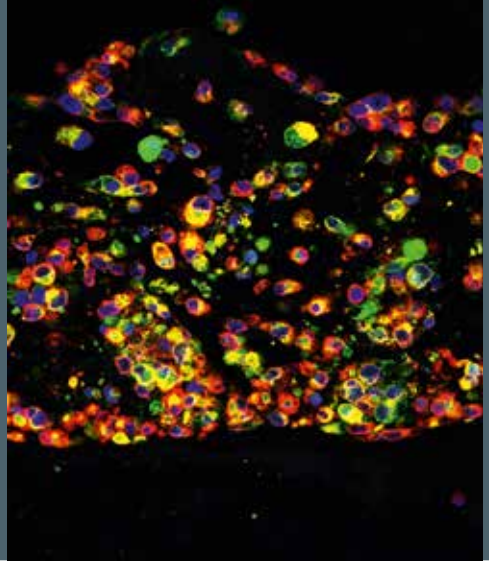
- Autoclave unit with several parallel laboratory-scale reactors (material: Hastelloy C22, volume: 100 mL/reactor; pressure: up to 300 bar, temperature: up to 400°C)
- Various bioreactors up to 40 liters
- Automation platform for high-throughput methods
- Analysis: GC-MS, LC-MS, HPLC, and FT-IR with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

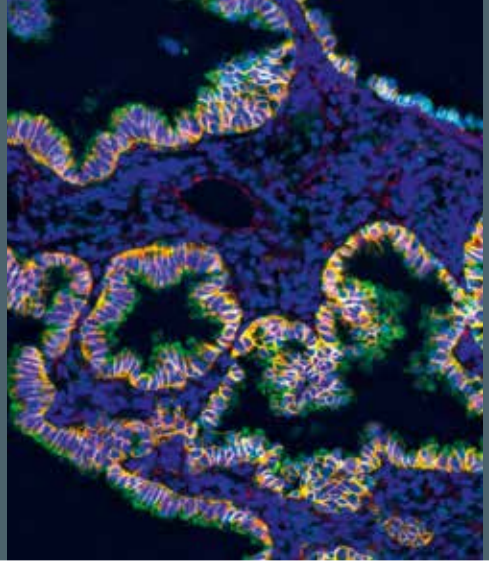
Contact

Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB
Bio, Electro and Chemocatalysis BioCat, Straubing branch
Schulgasse 11a | 94315 Straubing | Germany
Fax +49 9421 187-310 | www.biocat.fraunhofer.de

Prof. Dr. rer. nat. Volker Sieber
Head of BioCat
Phone +49 9421 187-300
volker.sieber@igb.fraunhofer.de

Dr. rer. nat. Michael Hofer
Deputy Head of BioCat
Phone +49 9421 187-354
michael.hofer@igb.fraunhofer.de





TRANSLATIONAL CENTER "REGENERATIVE THERAPIES", WÜRZBURG BRANCH

In the light of increasing life expectancy, a greater health awareness, and growing cost pressure in the health system, regenerative medicine and the development of innovative agents will play a crucial role. The Translational Center Würzburg develops medical products and therapeutic methods on the basis of innovative agents and cell-based therapies. The competence fields of the Translational Center are focused on quickly implementing the transfer of new materials or cell-based regenerative therapies for individualized patient care into medicine.

By establishing an interdisciplinary network in Würzburg, the whole value chain can be covered – from the development of biomaterials and the construction and production of bioreactors to *in vitro* test systems (as an alternative to animal testing), up to therapy accompanying diagnostics (theranostics) and the approval of cell-based implants and (biologized) medical products. Furthermore, there exists a long-standing expertise in admission-relevant animal models as well as the implementation of (pre-)clinical studies.

Innovative products for therapeutical application on human beings are liable to complex regulatory requirements. We advise and support you in the planning and implementation of pre-clinical and clinical studies. Together with the Center for Clinical Research (Zentrale für Klinische Studien, ZKS) at the University Hospital of Würzburg, we are developing strategies which insure the implementation of pre-clinical and clinical inspection in accordance with internationally recognized quality standards (GLP, GCP).

One unique characteristic of the Würzburg IGB team is the vascularized scaffold BioVaSc®, used for the production of implants, which can be connected to the circulatory system during implantation. The complex tissue models were registered as a brand in 2015. This includes models of human skin (SkinVaSc-TERM®), intestines (GutVaSc-TERM®), trachea (TraVaSc-TERM®), and lung (LunVaSc-TERM®). The BioVaSc® technology has been transferred to decellularize other organs such as the lung and the heart to isolate tissue-specific proteins. The ECM proteins obtained can be blended directly with polymers to produce support structures for implants or they can be used for the modification and biologization of implant surfaces.

In the Translational Center Würzburg, we are developing human 3D *in vitro* test systems with methods of tissue engineering, which can be used as an alternative to animal tests, since data of animal studies often do not reflect the conditions of human organisms. In so doing, we focus, among other things, on human barriers such as skin, airways, and the digestive tract, and depict both healthy as well as diseased tissue with our tissue models. With the tissue models, we simulate the interaction of medical products, e.g. stents, with the human body, in order to optimize the surfaces of the implants. Furthermore, the test systems are used for risk assessment of biological substances and synthetic materials in the field of oncology and infection studies, particularly with human obligate pathogens. The new research training group "3D Infect" is being established in cooperation with the Würzburg branch of Fraunhofer IGB and the University of Würzburg.

The main focus of the Department Theranostics is on the development of products enabling a highly efficient and personalized companion *in vitro* diagnostics and even combine diagnosis and therapy *in situ*.

In the Department Bioreactors, a bioreactor platform has been developed for applications in tissue engineering, regenerative medicine, and for the extracorporeal preservation of organs and tissues. A basic specification of our system is that the bioreactor platform is applicable to a large user community in the field of research and development, and within the industry.

Range of services

- Manufacturing and biochemical modification of 3D scaffolds for tissue engineering by means of electrospinning and biofabrication processes – in cooperation with the Department for Functional Materials in Medicine and Dentistry (FMZ) at the University of Würzburg
- Optimization of culture conditions and tissue-specific differentiation of iPS cells
- Tissue models using iPS or primary human cells
- Isolation of primary human stem and tumor cells
- Co-cultures for generating vascularized tissue models, particularly for the human barrier organs
- Disease and infection models based on tissue models
- Co-cultures to generate human solid tumors *in vitro* as tumor test systems
- Specific bioreactors, sensors, and incubators for tissue engineering
- Human vascularized (tumor) tissue for the optimization of medical products, to establish individual diagnostics and personalized therapies, including ATMPs
- Biological cell analysis of tumor tissue: molecular biological, histological, and immuno-histochemical methods, flow cytometry (FACS)
- Target screening for new tumor therapeutics
- *In silico* models for the pharmaceutical industry

Contact

Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB
Translational Center "Regenerative Therapies for Oncology and Musculoskeletal Diseases", Würzburg branch
Röntgenring 11 | 97070 Würzburg | Germany

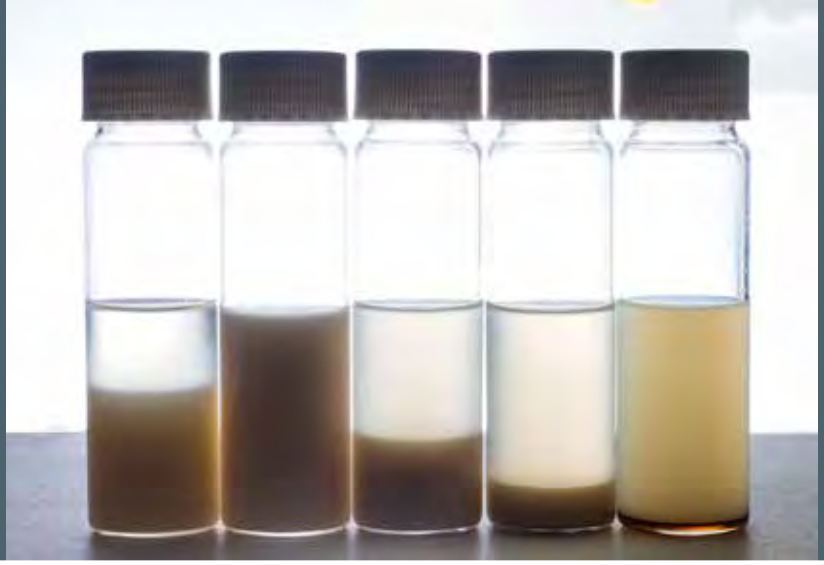
Prof. Dr. hum. biol. Heike Walles
Phone +49 931 31-88828
Fax +49 931 31-81068
heike.walles@igb.fraunhofer.de

Value chain

- Simulation of clinical therapy regimens involving the examination of the active principle and/or the side effects of a new drug candidate using vascularized human tumor and tissue models (disease models)
- Use of the tissue models in the process development to optimize drugs or diagnostic agents
- Implementation and validation of *in vitro* test systems as alternatives to animal testing at the end of pre-clincial development phase
- Studies on the efficacy of new pharmaceutical agents currently undergoing evaluation for clinical use
- Cooperation with the University of Würzburg Medical Faculty in order to organize clinical phases I–III

Infrastructure and technical equipment

- Cell culture laboratory for work on safety levels S1 and S2 GenTSV (German genetic engineering safety regulations)
- Pre-clinical study unit – in cooperation with FMZ, DZHi, and the University Hospital of Würzburg
- Cell analysis: inverse fluorescence microscope, FACS, microdissection system, Raman spectroscopy



INSTITUTE OF INTERFACIAL PROCESS ENGINEERING AND PLASMA TECHNOLOGY IGVP

The Institute of Interfacial Process Engineering and Plasma Technology IGVP is part of the Faculty of Energy Technology, Process Engineering and Biological Engineering of the University of Stuttgart. In 2015, the research budget accounted for 3.22 million euros. At the end of that year, staff of 92 scientific, technical and administrative employees, among them 41 doctoral students, worked at the three IGVP facilities (Pfaffenwaldring 31, Allmandring 5b, and Nobelstrasse 12; see also p. 15) – along with 30 other students researching for their master or bachelor thesis.

Technically, the institute is organized in the department "Interfacial Process Engineering", headed by apl. Prof. Günter Tovar, and "Plasma and Microwave Technology", which was headed until the end of 2015 by Director Prof. Thomas Hirth, and which is, since the beginning of 2016 also headed by Tovar. Both departments consist of three research groups each. Cooperation of the IGVP with Fraunhofer IGB makes it possible to pursue projects from basic research to application. This approach is reflected in the variety of funding received by the IGVP, including German Federal Ministries (e.g. BMBF), the German Research Foundation (DFG), the German Federal Foundation for the Environment (DBU), the EU, the *Land* of Baden-Württemberg, various foundations and industry. Key partners include the Max-Planck-Institut für Plasmaphysik in Garching, the KIT, and DIFFER in the Netherlands.

Research and teaching

The IGVP focuses on the design, functionalization and characterization of surfaces as well as of bio-, nano- and hybrid materials and their interaction. Special interest lies in the interactions with biological interfaces as, for instance, occurring in infection of human cells with viruses and the formulation of hydrogels and foams to bio-inks for additive manufacturing. Further activities include the simulation and engineering of interfacially driven processes.

On the second part, scientific contributions cover the wide range from fusion oriented high-temperature plasma physics to industrial applications of low-temperature plasmas. A focal point is research on these plasmas for surface activation and deposition of new coatings as well as the development of new plasma sources and processes, as fostered by the synergy between microwave and plasma physics know-how. Research in fusion related plasma physics reaches from fundamental investigations of plasma dynamical processes and simulation of electromagnetic waves to plasma heating with microwaves and development of corresponding transmission systems.

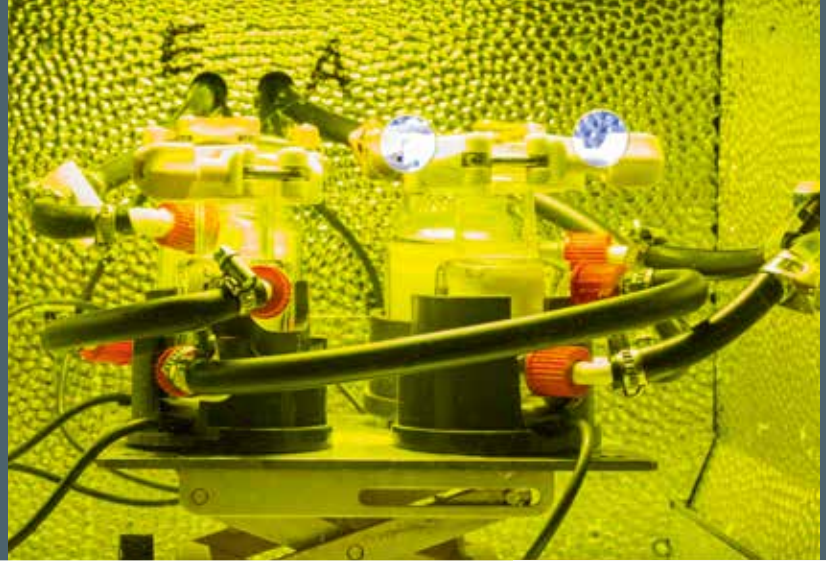
Teaching activities are centered on the subject areas of interfacial process engineering, infection biology, nanotechnology, industrial biotechnology, biomaterials, resource-efficient processes as well as plasma physics and plasma technology.

INTERFACIAL PROCESS ENGINEERING

Biological-Medical Interfaces

Priv.-Doz. Dr. sc. nat. Susanne M. Bailer

- Identification of biomarkers
- Screening for enzymes and microorganisms
- Microarray technologies
- Interactions between microorganisms and surfaces
- Host-pathogen interactions (viruses, bacteria, fungi)
- Virus-based therapies



- Synthetic biology
- Development of cell-based assays and 3D tissue models
- Cell-free protein synthesis

Chemical-Physical Interfaces

Dr. rer. nat. Monika Bach

- Bio- and nanobiomaterials and hydrogels
- Nano- and microstructured (bio-)functional surfaces
- Biomimetic coatings for medicine and biotechnology
- Core-shell nano- and microparticles
- Characterization of interfaces and surfaces
- Bioprinting of artificial tissues

Interfacial Processes

Dipl.-Ing. Matthias Stier

- Process development for industrial biotechnology
- Microalgae production processes in photobioreactors
- Sorption heat storage, superheated steam drying
- Crystallization and recovery of inorganic nutrients
- Particle suspensions and emulsions in electric fields
- Membrane development and membrane processes
- Water treatment

Contact

Institute of Interfacial Process Engineering and Plasma Technology IGVP
University of Stuttgart
Pfaffenwaldring 31 | 70569 Stuttgart | Germany
Fax +49 711 685 6-3102 | www.igvp.uni-stuttgart.de

apl. Prof. Dr. rer. nat. Günter Tovar
Director (acting)
Phone +49 711 970-4109
guenter.tovar@igvp.uni-stuttgart.de

Dr.-Ing. Matthias Walker, Akademischer Oberrat
Head of Administration
Phone +49 711 685-62300
matthias.walker@igvp.uni-stuttgart.de

PLASMA AND MICROWAVE TECHNOLOGY

Plasma Technology

Dr.-Ing. Matthias Walker, Akad. Oberrat

- Plasma source development (low/atmospheric pressure)
- Microplasmas
- Plasma coatings and processes for industrial applications
- Plasma diagnostics and characterization of plasma
- Modeling and simulation of plasma
- Plasma physical and plasma chemical processes

Microwave Technology

Dr.-Ing. Walter Kasparek

- Microwave heating and diagnostics for fusion experiments
- Microwave transmission systems and dedicated antennas
- Mode converters for oversized waveguides
- Millimeter-wave photonic components
- Testing of components in the microwave spectrum
- Reflectometry of millimeter waves in fusion plasmas

Plasma Dynamics and Diagnostics

Dr. rer. nat. Mirko Ramisch

- Magnetic plasma confinement
- Fundamentals of turbulent plasma dynamics
- Probe and imaging diagnostics
- Physics of turbulent transport
- Flow/turbulence interaction
- Wave phenomena and wave type conversion
- Heating mechanisms using microwaves

SELECTED R&D RESULTS 2015

25 Fraunhofer internal projects

164 Projects

4 Fraunhofer lighthouse projects

30 EU projects

13 Projects with universities, municipalities or funded by foundations

47 Industrial projects

7 Projects funded by *Länder*

42 **Projects funded by German *Länder***

MEDICINE

Increased survival rates offered by regenerative medicine, quicker and more accurate diagnostics using molecular-biological approaches, and a coordinated interaction between biologized 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 Fraunhofer IGB, we develop solutions in mostly interdisciplinary projects, based on our competencies in tissue engineering, biomaterials, immunology, and infection biology.

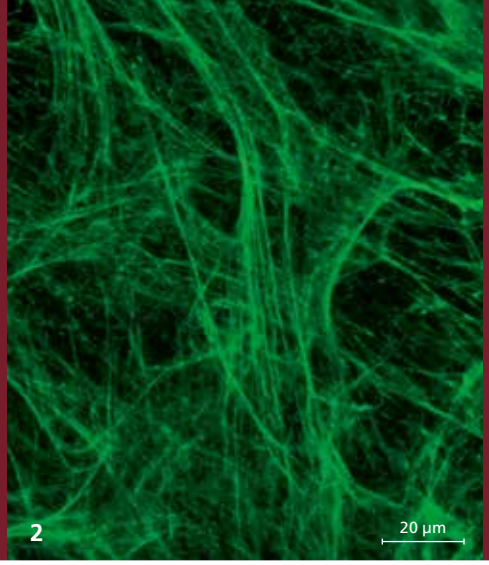
Regenerative medicine – The focus of regenerative therapies is on the development of human cell-based therapeutics, autologous transplants and biologized implants. Fraunhofer IGB and its Würzburg branch, with the Translational Center "Regenerative Therapies", cover the entire value-added chain right up to GMP-compliant manufacturing of cell-based implants (Advanced Therapy Medicinal Products, ATMPs) and – together with a network of physicians – phase I clinical studies. Our quality control systems identify potential contaminants (microorganisms, viruses) by non-destructive means, using spectroscopic, cell-based or molecular methods based on GLP and GMP guidelines. A new approach towards producing dimensionally stable tissue-like structures (e.g. cartilage, fat tissue) is pursued by the 3D printing of human cells on UV-crosslinkable hydrogels.

Diagnostics – New scientific strategies to combat infectious diseases are a high priority. Here, the combination of methods of functional genome analysis with our expertise in cell culture technology and infection biology results in a unique position for the development of infection models and diagnostics. We develop new diagnostic methods based on nucleic acids (diagnostic microarrays, biomarker development using high-throughput DNA sequencing) or by means of cellular reporter systems (cell-based pyrogen assay). This information helps to initiate measures for specific treatments or to develop personalized medicines for different population groups.

Medical engineering – For the optimization of surface properties of established medical devices such as stents we use plasma processes to generate bioactive or antibacterial surfaces; we then test the effectiveness and biocompatibility of these surfaces on *in vitro* tissue models. We also develop biodegradable coatings for bone implants that promote self-healing through cell adhesion. For disinfection and removal of pyrogenic residues we establish plasma sterilization processes for reusable sterile containers in terms of optimum effectiveness and material protection.

As a partner of the Fraunhofer Food Chain Management Alliance, we make a contribution to healthcare through the development of physical hygienization processes that protect the foodstuff's properties. Our medicinal research contributes to the Fraunhofer Group for Life Sciences' competences; in addition we are networked in the Fraunhofer Big Data Alliance.

1



2

clickECM – AN INNOVATIVE BIOLOGICAL COATING FOR IMPLANTS

Sybil Mara Ruff, Silke Keller, Günter Tovar, Monika Bach, Petra Kluger

Optimized biocompatibility for implants

Biomaterials are used in a wide range of applications in medical technology and orthopedics. They are designed to withstand the biomechanical stresses of the body; however, the biocompatibility of many biomaterials still requires optimization [1]. Implants are often coated with biomaterials to improve their biocompatibility and assist in their integration into the body [2]. Conventional biomaterial coatings are attached to implants by a process called physisorption, which is a physical interaction between the implant surface and the material. Despite the advantages of this type of surface coating, the stability requires improvement [2].

The aim of the *click*ECM project was to develop a stable biocompatible and biologically active implant coating with the human extracellular matrix (ECM). The ECM consists of a complex network of biomolecules, such as fibrous proteins, proteoglycans and glycosaminoglycans, as well as electrolytes, water and signaling molecules [3]. The ECM is instrumental in cellular processes such as cell motility, attachment, signal transduction and biomechanical stimuli [3]. Thanks to its unique and tissue-specific composition of biomolecules, the human ECM is the ideal biomaterial for coating implants.

Covalent binding of *click*ECM to surfaces

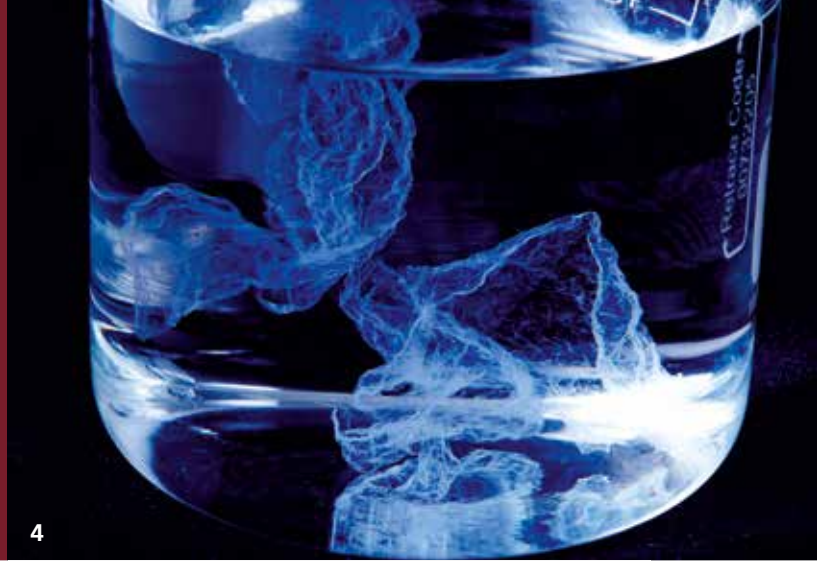
To create a covalent bond, meaning a strong chemical bond, between human ECM and an artificial surface, we developed a process to immobilize ECM via "click" reactions. Click reactions are efficient under physiological conditions, highly biocompatible, specific and selective even in the presence of the wide range of natural functional groups within the surrounding biomolecules.

The first step in equipping ECM with click groups is the generation of human ECM from primary cells. We performed Metabolic Oligosaccharide Engineering (MOE) in order to functionalize the ECM with azide groups during the *in vitro* culture of the cells (Fig. 1). Next, covalent attachment of the "*click*ECM" onto the substrate surfaces was achieved through the complementary click functionalization of the surfaces with an activated alkyne compound (dibenzocyclooctyne, DIBO). Due to the high ring strain of the used cyclooctyne compound, there is no cytotoxic copper catalyst necessary to drive the reaction forward.

Stable and cell proliferation-inducing *click*ECM coating

The successful introduction of the azide groups into the glycan structures of the *click*ECM by the MOE was detected by a reaction with an alkyne-functional dye (Fig. 2). Histological and immunocytochemical staining confirmed that the isolated *click*ECM had a similar biological composition of human skin ECM (Fig. 3). Cell proliferation studies demonstrated that the covalent *click*ECM coating significantly increased cell proliferation when compared to uncoated or DIBO functionalized glass substrates. *click*ECM had a comparable proliferation rate as unmodified ECM, which showed that the azide modification had no effect on cell proliferation. Furthermore, the covalent immobilization of *click*ECM on DIBO functionalized material surfaces had a significantly increased level of coating stability than the conventional physisorbed coatings.

3



4

Outlook

In the future, our *click*EMC coating could promote the integration of implants into their surrounding tissue. The use of autologous cells for the manufacturing of *click*EMC enables the individualized coating of material surfaces. This should significantly improve cell growth on the surface of the implant and reduce inflammation and organ rejection due to the immune system's foreign body response. Furthermore, it is expected that the improved cell adhesion will accelerate the integration of the implant into the patient and the fixed bonding of the coating will considerably increase the long-term stability of the implant.

Another application for *click*ECM is its use as a coating in cell culture dishes. Cell-specific ECM closely mimics the physiological microenvironment of cells, which could positively influence cell proliferation or differentiation, or prevent undesirable changes in the cells.

1 *Cell culture for metabolic oligosaccharide engineering.*
2 *Fluorescence microscopic detection of azide modification (azides: green).*
3 *Proof of collagens (yellow) in the clickECM.*
4 *Isolated ECM after 21 days in vitro culture. (250 mL laboratory glass bottle, 50 µm).*

Contact

Prof. Dr. rer. nat. Petra Kluger
Phone +49 711 970-4072
petra.kluger@igb.fraunhofer.de

Dr. rer. nat. Monika Bach
Phone +49 711 685-68304
monika.bach@igb.fraunhofer.de

Literature

[1] Repenning, D.; Gollwitzer, H (2006) Ossäre Integration, Springer Medizin Verlag Heidelberg

[2] Goodman, S. B.; Yao, Z.; Keeney, M.; Yang, F. (2013) The future of biologic coatings for orthopaedic implants, Biomaterials 34(13): 3174–83

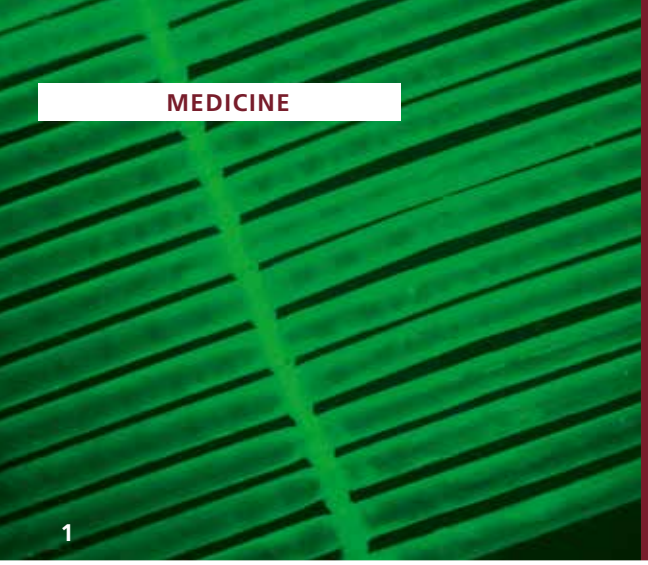
[3] Fitzpatrick, L. E.; McDevitt, T. C. (2014) Cell-derived matrices for tissue engineering and regenerative medicine applications, Biomaterial Science 3: 12–24

Funding

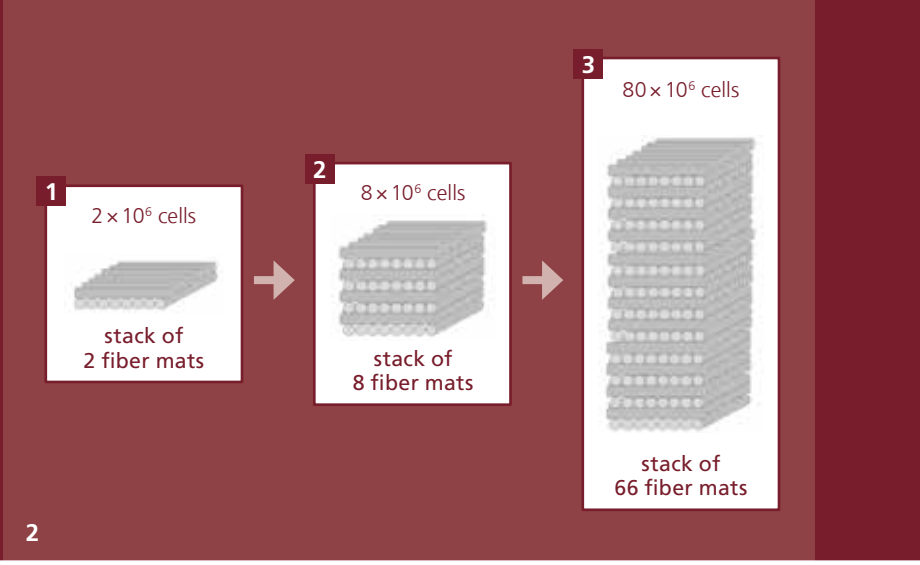
We thank the Fraunhofer-Gesellschaft for supporting the "*click*ECM" project under the "Discover" program. Furthermore, we thank the Baden-Württemberg Stiftung for supporting the project "glycomics/glycobiology".

Project partners

University of Stuttgart, Institute of Interfacial Process Engineering and Plasma Technology IGVP | University of Konstanz, Department of Chemistry, Prof. Dr. Valentin Wittmann and Daniel Wieland



1



2

AMBULUNG – BIOARTIFICIAL LUNG

Annika Wenz, Kirstin Linke, Markus Schandar, Petra Kluger, Kirsten Borchers

Bioartificial lung

We reported last year on the development of a bioartificial lung assist device called "AmbuLung" as part of an EU-funded project. Within the scope of this project, Fraunhofer IGB developed a biological coating for a miniaturized gas exchange module. The coating was designed to mimic the natural interface between blood vessels and blood. Blood vessel cells (endothelial cells) should create a confluent monolayer across the hollow fiber module of the device that will be in constant contact with the patient's blood. The vision is that this cell layer will ensure the blood compatibility of the gas exchanger, which should translate to a module that is functional for several weeks. This is a major improvement over the currently used devices that can only be used for a couple of days and under intensive care due to their low hemocompatibility.

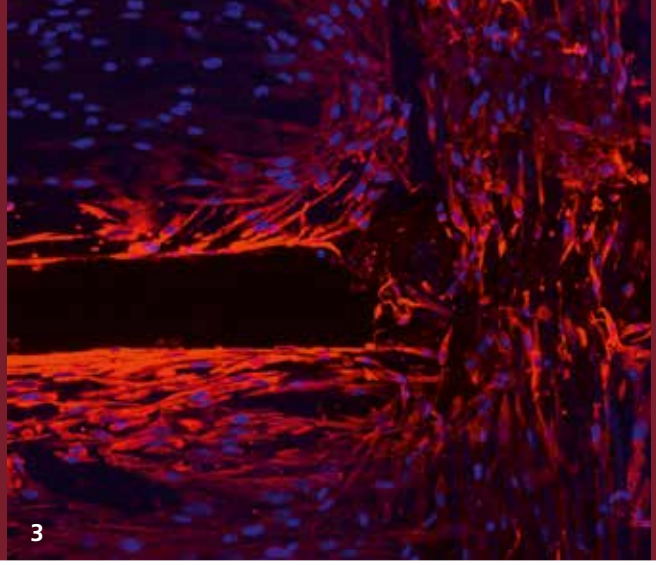
Biofunctionalization of the gas exchange membrane

The overall aim of the work at Fraunhofer IGB was to coat the existing polymethylpentene (PMP) hollow fiber membranes with a hemocompatible and endothelial cell friendly surface and then to seed the membranes with endothelial cells. The aim of the second half of the project was to evaluate the blood compatibility of the coating, to upscale the deployment of endothelial cells and the cell seeding of the entire module. The hemocompatibility evaluation was performed at the University of Tübingen as a Chandler-loop-study of different heparin-containing coatings and it showed that the blood compatibility of the hollow fiber surface was extensively improved by a layer-by-layer coating with albumin and heparin. Coating of PMP with heparin that was chemically coupled via benzophenone-functions did not result in a reduction of blood clotting nor of platelet activation as compared to uncoated PMP. The additional functionalization of the coatings with endothelial cell-specific REDV and EILDPVST peptide sequences had no significant effect on the hemocompatibility of the surfaces.

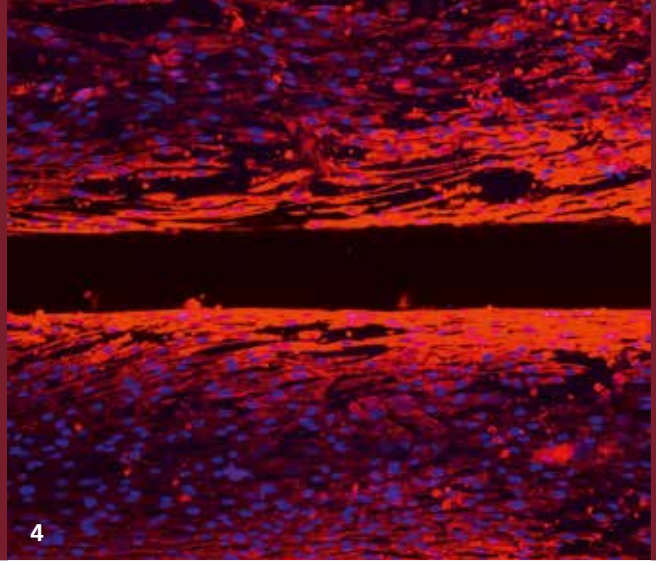
Using the Alcian blue staining technique and fluorescence-labeled peptides, we could demonstrate that the hollow-fiber mats in the AmbuLung prototype could be completely functionalized with heparin, albumin and peptides (Fig. 1).

Seeding the AmbuLung-prototype with endothelial cells

We worked with bioreactors to create dynamic conditions for cell seeding and nutrient supply in the first part of the project (see Fraunhofer IGB Annual Report 2014). The next project goal was the cell seeding of a multilayer membrane stack and the upscaling of the system in a full gas exchanger (Fig. 1). We successfully upscaled the membrane stack to 66 membranes completely seeded with endothelial cells (Fig. 3). After 14 days of dynamic culture, the cells were analyzed for cell morphology and the expression of endothelial cell specific markers such as CD31. The analysis showed that the cells were stably seeded over the entire membrane stack surface and expressed specific endothelial markers (Fig. 4).



3



4

Outlook

The "AmbuLung" should one day serve as a temporary portable artificial lung for patients with chronic obstructive pulmonary disease. This will enable the patients to leave the hospital and regain more independence and mobility, which will significantly improve their health and their quality of life.

1 *Homogeneous peptide functionalization of the hollow fiber "AmbuLung" module (fluorescently labeled REDVGK peptides).*

2 *Upscaling to a stack of 66 mats in "AmbuLung".*

3 *Formation of a complete endothelial monolayer on biofunctionalized polymethylpentene hollow fibers (blue: cell nuclei, red: cell-cell contacts).*

4 *Endothelium on biofunctionalized polymethylpentene hollow fibers after 7 or 14 days of culture.*

Contact

Prof. Dr. rer. nat. Petra Kluger
Phone +49 711 970-4072
petra.kluger@igb.fraunhofer.de

Dr. rer. nat. Kirsten Borchers
Phone +49 711 970-4121
kirsten.borchers@igb.fraunhofer.de

Funding

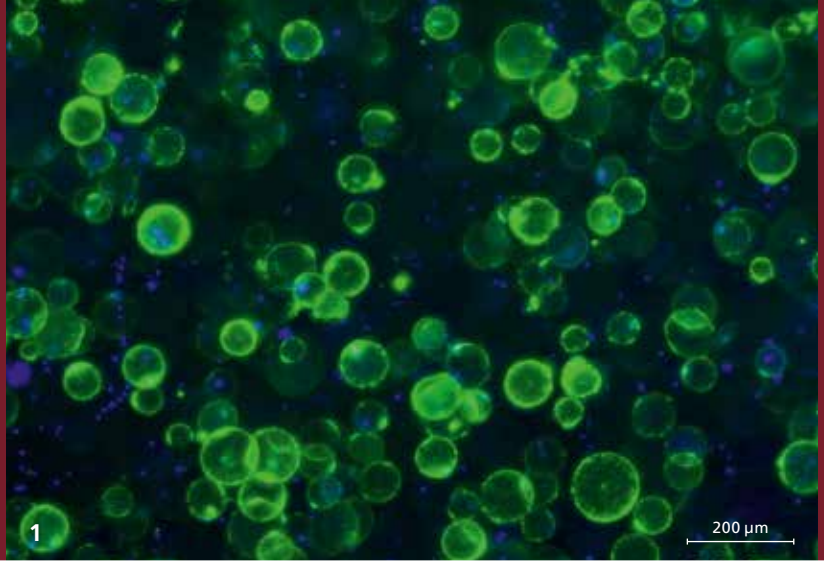
The research project "Ambulatory Bioartificial Lung (AmbuLung)" has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 304932.

Project partners

Novalung GmbH, Heilbronn, Germany | Imperial College of Science, Technology and Medicine, London, UK | Università degli Studi di Firenze, Italy

Further information

www.ambulung.com



DEVELOPMENT OF A FUNCTIONAL THREE-LAYER FULL-SKIN MODEL

Birgit Huber, Kirsten Borchers, Petra J. Kluger

Functional skin for transplants

Patients with extensive burns, open diabetic foot wounds or skin loss due to tumor removal require aesthetic and functional skin replacements. When transplanting a patient's own skin is not possible, there are a number of different skin substitutes on the market that can replace the top two layers of skin, the dermis and the epidermis. However, if the underlying fat tissue is affected, the current products on the market are inadequate. Therefore, tissue models that include the underlying fatty tissue are urgently needed. Researchers now focus on the production of three-layer full-skin models that have the typical appearance and performance of native skin. As part of the EU project "ArtiVasc 3D", Fraunhofer IGB is establishing methods for the construction and characterization of a three-layer full-skin model.

Culture of mature adipocytes

Stem cell derived adipocytes are the gold standard for the production of fat cells. The differentiation process is time consuming and costly. The use of already matured adipocytes has received little attention because they are prone to dedifferentiation when cultured. Approximately 50 percent of adiposed tissue consists of mature adipocytes. Thus they can be abundantly isolated from small amounts of tissue and can be immediately used in a full-thickness skin model. As the body's own cells are not immunogenic and adipocytes have a slow renewal rate of only about 5 percent per year, they may be an interesting cell source for long-term full-skin implants. At Fraunhofer IGB, we have established a culture medium that slows the dedifferentiation of mature adipocytes, enabling their use in the construction of full-thickness skin models [1, 2, 3].

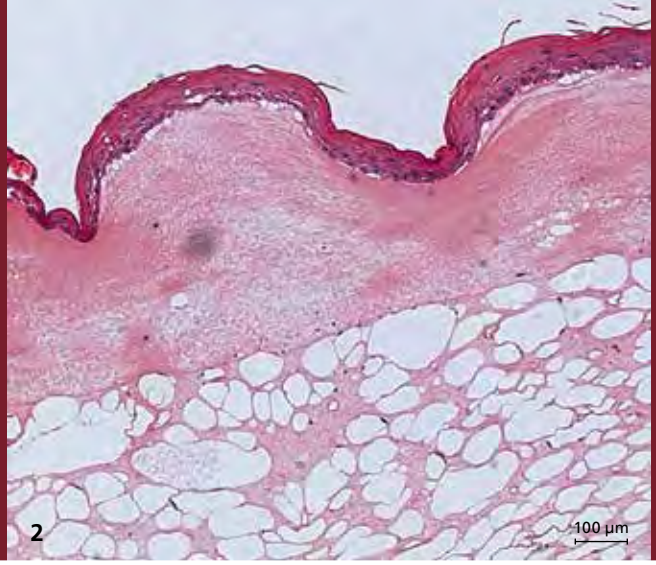
Construction and culturing three-layer skin models

Mature adipocytes are integrated into a collagen type I hydrogel (Fig. 1) to create an adipose layer. A dermal layer made of a collagen type I hydrogel and fibroblasts is placed on top of the model. Finally, a multilayered keratinocyte-containing epidermis with the typical cornified layer is added, resulting in three-dimensional full-skin model (Fig. 2). A suitable culture medium is available at IGB for maintaining the functionality of the mature adipocytes for up to 14 days in the skin model and in parallel allowing the keratinocytes to differentiate and form a multilayer keratinized epidermis (Fig. 3).

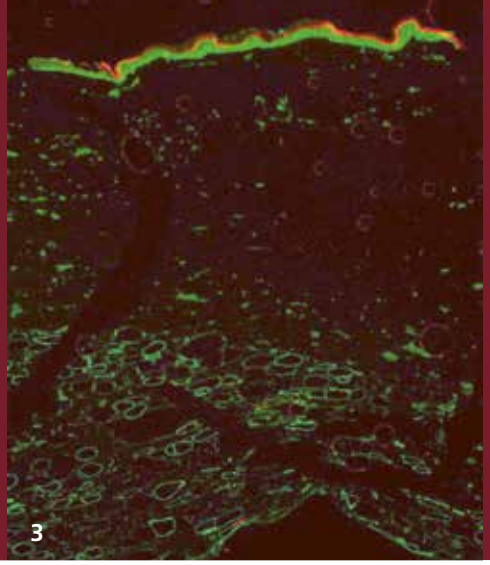
Therapeutic future: Vascularized full-skin models

For the large-scale replacement of full-thickness skin, the proper vascular structures within the skin must be included to transport oxygen and nutrients to the cells. To enable such structures, co-cultures have been developed to integrate vascular cells such as endothelial cells into the mixture of adipocytes, fibroblasts and keratinocytes in the skin model [4]. An optimized medium for the culture of all four cell types is now available at Fraunhofer IGB. In the future, the establishment of a full-skin model should be supplemented with blood vessel-like structures through which the nutrient and oxygen exchange can take place.

The development of 3D tissue models is an important stepping-stone in the future of reconstructive medicine. Fraunhofer IGB continues to contribute to this future by developing patient-specific implants to replace functionless tissue.



2



3

1 *Mature adipocytes encapsulated in a collagen type I hydrogel.*

2 *HE staining of a three-layer full-skin model.*

3 *Cytokeratin 10 (red) and Laminin (green) staining of a full-thickness skin model.*

Contact

Prof. Dr. rer. nat. Petra Kluger
Phone +49 711 970-4072
petra.kluger@igb.fraunhofer.de

Dr. rer. nat. Kirsten Borchers
Phone +49 711 970-4121
kirsten.borchers@igb.fraunhofer.de

Literature

[1] Huber, B.; Kluger, P. J. (2015) Decelerating mature adipocyte dedifferentiation by media composition, Tissue Engineering Part C Methods 21(12): 1237–45

[2] Annual Report Fraunhofer IGB 2014

[3] Huber, B.; Borchers, K.; Tovar, G. E. M.; Kluger, P. J. (2015) Methacrylated gelatin and mature adipocytes are promising components for adipose tissue engineering, Journal of Biomaterials Applications 30(6): 699–710

[4] Huber, B.; Volz, A.; Kluger, P. J. (2015) Understanding the cross-talk of mature adipocytes and endothelial cells in physiological fatty tissue for vascularized adipose tissue engineering, Cell and Tissue Research 362(2): 269–79

Funding

The research project "ArtiVasc 3D" has received funding from European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 263416.

Further information and project partners

www.artivasc.eu

1

NEXT-GENERATION DIAGNOSTICS OF SEPSIS

Silke Grumaz, Philip Stevens, Kai Sohn

Sepsis

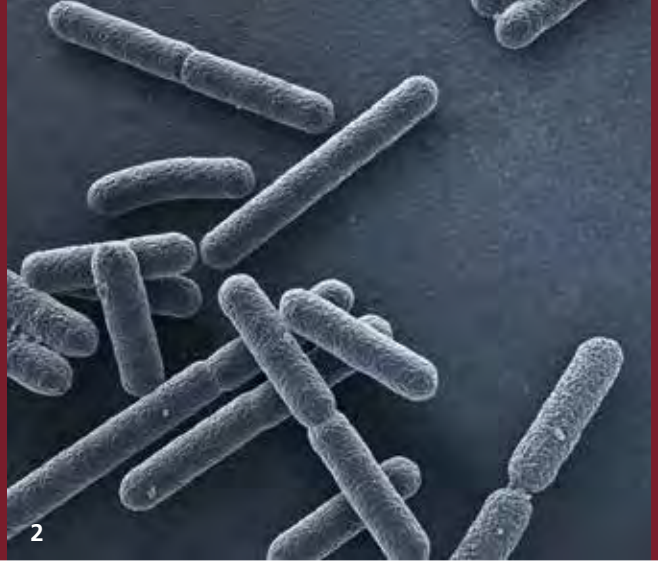
Sepsis (whole-body inflammation due to infection) presents one of the greatest challenges in intensive care medicine because it is associated with a high patient mortality of over 55 percent [1]. Despite medical advances, this figure has remained unchanged for nearly 20 years. One reason for this is the frequent lack of early diagnosis and prompt treatment with effective pathogen-specific antibiotics. However, the use of these kinds of antibiotics requires knowledge of the pathogen. With blood cultures – the current gold standard – microbial diagnostics can take two to five days, yet no pathogen at all is cultured in up to a third of cases [2]. Molecular-level biological techniques offer alternative diagnostic approaches that are not dependent upon prior cultivation of the pathogen, but instead identify it based on its nucleic acids (DNA and RNA). Researchers at Fraunhofer IGB are using the newest advances in the field of high-throughput sequencing in order to develop and make available rapid alternative diagnostic procedures to identify pathogens in under 30 hours.

Circulating nucleic acids – a very promising class of molecules

We use a special class of molecules for this technique at Fraunhofer IGB, known as circulating nucleic acids in plasma and serum (CNAPS). For specific physiological or pathological processes (e.g. with cancer, stroke, or pregnancy), the concentrations of these molecules in the blood are increased due to elevated cell turnover. As a result, this class of molecule has been recently employed for diagnosing various oncological diseases as well as for prenatal diagnostics [3]. In contrast to diagnostic procedures used up to now, this new technique can be carried out non-invasively using a blood sample – and is therefore also called a "liquid biopsy". This works for sepsis patients as well, because bacterial as well as human nucleic acids are present in their plasma, as researchers of Fraunhofer IGB have shown.

New technique for sepsis diagnostics

A novel technique was developed, tested, and validated at Fraunhofer IGB that can be used to search for microbial nucleic acid sequences in the CNAPS. It uses existing high-throughput sequencing with the help of data processing algorithms developed in-house, then matches these sequences to specific pathogens mathematically and quantifies them. This is not trivial and a high level of sensitivity and specificity is required, since over 99 percent of the nucleic acids in this kind of sample are of human origin. In a joint retrospective study with Heidelberg University Hospital, CNAPS were isolated from the plasma of sepsis patients and the newly developed process then validated. Since laboratory results from clinical microbiology were available for the patient samples, a direct comparison between next-generation diagnostics and conventional clinical microbiology was possible. The study showed excellent correlation between next-generation diagnostics and blood cultures, as well as with cultures from localized centers of infection, for example. In comparison to blood cultures, the next-gen diagnostics in some cases provided even more plausible results from a medical point of view – that contaminating pathogens from skin flora are often cultured as well. In addition, simultaneous single-step detection of very different pathogens, such as viruses, bacteria, and fungi, becomes feasible with the new technique. Moreover, researchers at Fraunhofer IGB were able to demonstrate that given a suitably high coverage of the bacterial genome, even detection of the genes responsible for resistance to antibiotics is possible in the same analysis. This is of great importance in the clinical environment, since it facilitates a fast and effective decision by the attending physician on what treatment to employ.



Future prospects

Since the field of sequencing technology is advancing very dynamically, we are working on transporting the technique to various sequencing platforms in order to be able to reduce the time from sample to result even further. With several of these platforms, the diagnosis time will soon be driven down to six or eight hours, offering a crucial advantage for patient management. A larger multi-center validation study in partnership with renowned clinics is also being planned for 2016. The methodology additionally has the potential of being employed with other infectious and difficult-to-diagnose diseases.

1 *Intensive care station.*
2 *Scanning electron micrograph of Escherichia coli.*
3 *Parallel nucleic acid sequencer at Fraunhofer IGB.*

Contact

Dr. rer. nat. Silke Grumaz
Phone +49 711 970-4078
silke.grumaz@igb.fraunhofer.de

Dr. rer. nat. Kai Sohn
Phone +49 711 970-4055
kai.sohn@igb.fraunhofer.de

Literature

[1] Engel, C.; Brunkhorst, F. M.; Bone, H.-G.; Brunkhorst, R.; Gerlach, H.; Grond, S.; Gruendling, M.; Huhle, G.; Jaschinski, U.; John, S.; Mayer, K.; Oppert, M.; Olthoff, D.; Quintel, M.; Ragaller, M.; Rossaint, R.; Stuber, F.; Weiler, N.; Welte, T.; Bogatsch, H.; Hartog, C.; Loeffler, M.; Reinhart, K. (2007) Epidemiology of sepsis in Germany: results from a national prospective multicenter study, Intensive care medicine 33: 606–18

[2] Schmitz, R. P.; Keller, P. M.; Baier, M.; Hagel, S.; Pletz, M. W.; Brunkhorst, F. M. (2013) Quality of blood culture testing – a survey in intensive care units and microbiological laboratories across four European countries, Critical Care 17: R248

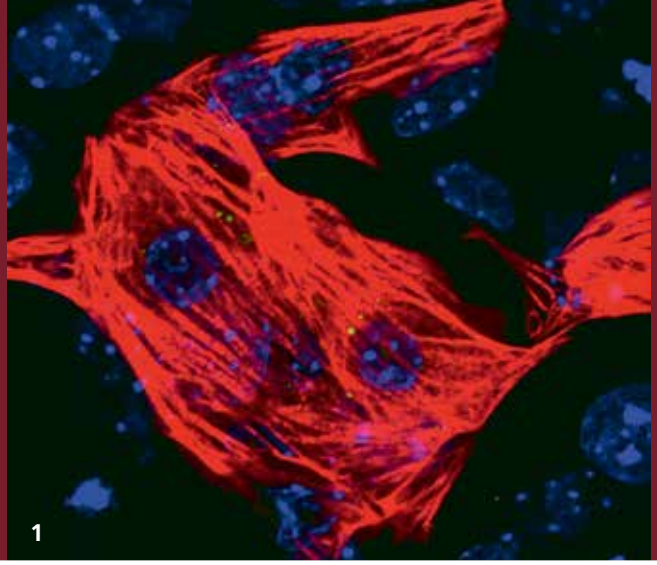
[3] Lo, Y. M.; Chiu, R. W. K. (2011) Plasma nucleic acid analysis by massively parallel sequencing: pathological insights and diagnostic implications, Journal of Pathology 225: 318–323

Funding

We would like to thank the Fraunhofer-Zukunftsstiftung (Fraunhofer Future Foundation) for funding the "Ribolution" project.

Project partner

Heidelberg University Hospital



1

CARDIAC STEM CELL DIFFERENTIATION AND NON-INVASIVE MONITORING

Eva Brauchle, Nian Shen, Shannon Layland, Svenja Hinderer, Katja Schenke-Layland

Challenges in cardiovascular disease

Despite a multitude of newly developed drugs and diagnostics, and significant advances in cardiology and cardiac surgery, diseases of the cardiovascular system are still the number one killer worldwide according to figures from the World Health Organization. Here, heart muscle or heart valves are affected frequently. Damage to these tissues may have different causes; for example, risk factors such as smoking and unhealthy diet can lead to a heart attack. Congenital diseases are also known to be the cause of organ or tissue failure. In adult humans, the heart does not regenerate after damage, which significantly reduces the performance of the heart, and thus the mortality and quality of life of these patients. A number of scientists are working towards restoring heart function through regeneration or developing cardiac test systems, which would enable the *in vitro* testing of new therapies and drugs in a humanized model. Primary isolated beating heart muscle cells cannot be cultured *in vitro*. Therefore, stem cell derived heart muscle cells are required to create a functional heart muscle test system.

Human heart muscle test system from embryonic stem cells

Scientific studies have demonstrated that embryonic stem cells differentiate into functional cardiomyocytes under specific chemical culture conditions. Our strategy is to create a physiological environment that will differentiate and mature cardiomyocytes. We have developed a stretch-flow bioreactor which enables the dynamic culture of embryonic stem cells under defined tensile and continuous medium flow. We have demonstrated that we can differentiate and mature beating cardiomyocytes capable of calcium transport with biomechanical cues from the flow and stretch. The addition of caffeine into the dynamic culture increaes cardiomyocyte stroke rate and influx of calcium ions. The calcium channel blocker Verapamil has the opposite effect when added to the culture. In current studies, a carrier substrate is being used to establish a three-dimensional culture similar to our previous work using electrospun substrates for 3D culture of smooth muscle cells [1] and heart valve cells [2] with the aim of creating a 3D myocard test system.

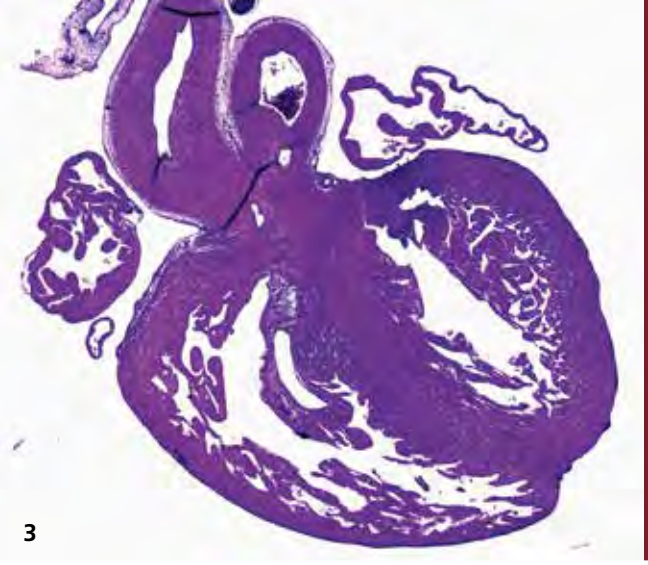
Marker-free monitoring of cardiac stem cell differentiation

The identification of cell differentiating from embryonic stem cells to myocardial cells is an important step in the preparation of a test system. Classically, protein expression is used to identify different stages of embryonic stem cell differentiation. However, this alters the cells making them unsuitable for continuous monitoring of the differentiation.

Raman microspectroscopy

Raman microspectroscopy is an optical technology that can be used for marker-free global analysis of biological cell and tissue samples. It is based on the effect of scattered light, wherein few photons of the incident monochromatic light are shifted by molecular vibration within a sample. Raman spectroscopy detects a molecular fingerprint of an object. As an object changes, its Raman spectra typically changes as well. Thus, cell differentiation processes can be non-invasively monitored and the unique profiles of different cell types and states from a stem cell, or any cell, can be distinguished.

2



3

In our work, we demonstrated that the differentiation path of embryonic stem cells to cardiac progenitor cells and then functional cardiomyocytes can be represented using Raman microspectroscopy [3]. Cell-specific molecular fingerprints of atrial and ventricular murine and human cardiomyocytes can be distinguished, as well as the maturation levels of fetal and adult cardiomyocytes [3]. In recent studies, it was confirmed that Raman microspectroscopy could detect the maturation of cardiomyocytes induced by a stretch-flow bioreactor. We are currently developing a new bioreactor system, which additionally meets the optical requirements for carrying out the continuous microspectroscopy.

1 *Fluorescence image of mature cardiomyocytes in the bioreactor.*
2 *Stretch-flow bioreactor system.*
3 *Histological staining of a human heart.*

Contact

Dr. rer. nat. Eva Brauchle
Phone +49 711 970-4196
eva.brauchle@igb.fraunhofer.de

Dr. rer. nat. Svenja Hinderer
Phone +49 711 970-4196
svenja.hinderer@igb.fraunhofer.de

Literature

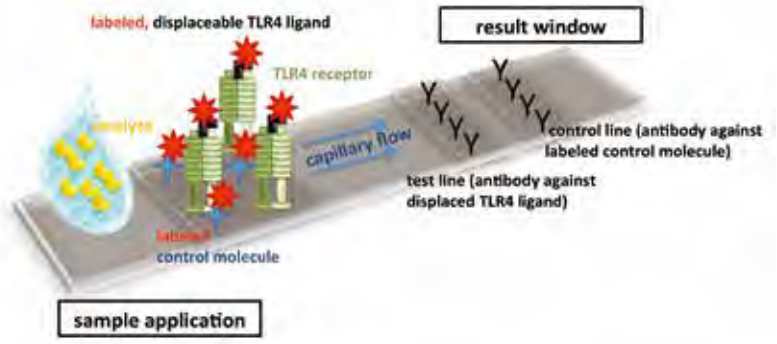
[1] Hinderer, S. et al. (2015) *In vitro* elastogenesis: instructing human vascular smooth muscle cells to generate an elastic fiber-containing extracellular matrix scaffold, Biomed Mater 10: 034102
[2] Hinderer, S. et al. (2014) Bioengineering of a bio-functionalized off-the-shelf heart valve, Biomaterials 35: 2130–2139
[3] Brauchle, E. et al. (2016) Novel non-invasive chamber-specific identification of cardiomyocytes in differentiating pluripotent stem cells. Stem Cell Reports 6: 1–12

Funding

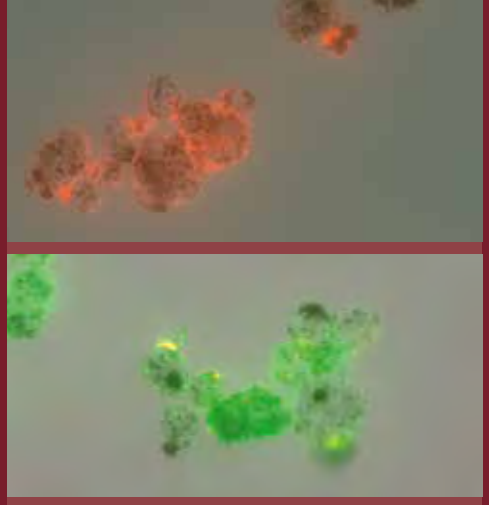
We thank the German Federal Ministry of Education and Research (BMBF) for funding the project "Characterization and Bioengineering of cardiac stem cell niche", promotional reference 1316059, the European Union for supporting the research project "AMCARE", grant agreement no NMP3-SME-2013-604531, and the Fraunhofer-Gesellschaft for supporting the project "Renovatum Therapeutics" under the "Fraunhofer promotes start-ups" program (FFE) and the "OptisCell" project under the market-driven prospective research program (MAVO).

Further information and project partners

www.schenke-layland-lab.com | www.amcare.eu



1



2

IMMUSTICK – THE INNATE IMMUNE SYSTEM ON A TEST STRIP

Christina Kohl, Anke Burger-Kentischer

Pyrogen detection using immunoreceptors

According to global estimates, about 18 million patients die annually from the consequences of sepsis. This complication is caused by pyrogens – bacteria, viruses or fungi or their residues that enter a patient´s blood circulation via contaminated surgical instruments or drugs. The pyrogens, also known as Pathogen-Associated Molecular Patterns (PAMPs) [1], are recognized by receptors of the innate immune system, the Pattern Recognition Receptors (PRRs), which initiate production of fever-inducing messenger substances.

In order to prevent pyrogens from entering the blood via medicinal devices or pharmaceuticals, these must be checked for the presence of pyrogens. EU and FDA regulations currently approve four commercial detection systems [2, 3] but these are either very time-consuming procedures or limited to certain pyrogens.

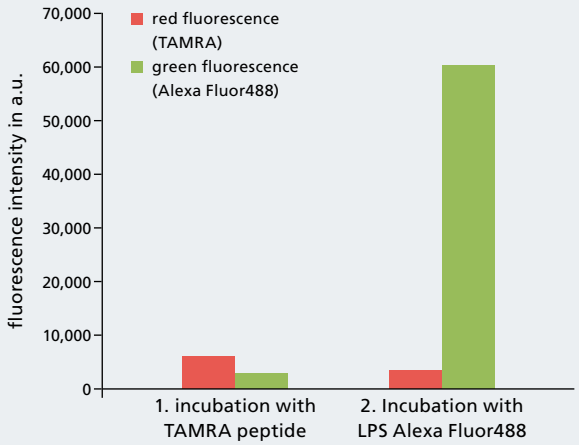
In order to avoid the limitations of conventional tests, for several years Fraunhofer IGB has been developing alternative *in vitro* test systems based on the use of PRRs [4]. The toll-like receptors (TLRs) represent the largest and best known group of PRRs. The PAMP assay patented by Fraunhofer IGB [5, 6] is a sensitive and universally adaptable *in vitro* method suitable for all pyrogens. However, this cell-based test method also requires a well-equipped laboratory with experience in handling cell cultures.

ImmuStick – A “test strip” for pyrogens

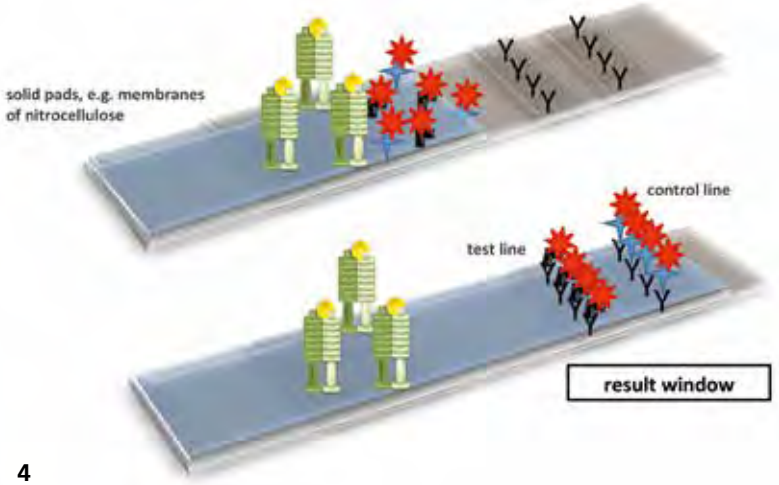
With the ImmuStick, we developed an unconventional, innovative detection system for pyrogens using PRRs as biosensors without the use of animal testing or time-consuming and device-intensive tests. Pyrogens are detected using test strips based on the immunochromatographic principle. Immobilized receptor domains of individual PRRs serve as binding molecules for the corresponding pyrogen. If an applied sample contains the corresponding pyrogen, a color-labeled ligand will be released, indicating the presence of the pyrogen (Fig. 1).

Detection of the pyrogen is based on a classical competitive immunoassay. After the test strips are wetted with the analyte solution, the pyrogen contained in it (TLR4 ligand lipopolysaccharides (LPS); yellow) displaces the weaker binding labeled ligand (black-red) in the biosensor area. Via capillary flow, these migrate together with the control molecules (blue-red) to the result window where specific antigens are immobilized as capture molecules (Y). If the antibodies bind their antigen (the labeled ligand or the control molecule), application of a pyrogen-containing sample solution will result in bi-colored test lines in the result window. The control line appears only after sufficient application of sample solution to the ImmuStick, thus verifying that the test has functioned properly (Fig. 4).

Fig. 2 shows fluorescence microscope images of TLR4 bound to agarose beads. The images show the displacement of a ligand bound weakly to TLR4 (TAMRA, red) by LPS (Alexa Fluor488, green) and the quantitative analysis of this binding study (Fig. 3).



3



4

Fields of application

The ImmuStick is suitable for the legally required proof of the presence of pyrogens in biological products and medical devices (FDA directive). Application in the classification of sepsis pathogens on patients directly is also conceivable. Since some PPRs also recognize specific allergens, the ImmuStick also offers potential for the detection of allergens in cosmetics, medical technology, the pharmaceutical sector and the food industry.

The ImmuStick is the result of further development of an *in vitro* immunoassay into a cost-effective point-of-use test that can even be used by lay persons and which can also be used as on-site system without the need for complex equipment. The use of receptors of the innate human immune system allows all pyrogen classes to be detected.

Application-specific further development

We have demonstrated the basic feasibility of TLR4 for the detection of LPS. The test system has the potential for modular expansion with additional receptors of the innate immune system (TRL, NOD-like receptors, C-type lectins), in order to specifically adapt the pyrogen spectrum. Equipped with different PRRs, the ImmuStick can detect the complete range of PAMPs quickly, easily and directly on-site.

1 *Sample application and result window, biosensor with immobilized TLR4 receptors.*
2 *Competitive displacement of a weaker binding ligand (red) by LPS (green).*
3 *Quantitative analysis of the displacement study (see 2).*
4 *Detection of a sample solution containing pyrogens via test lines in the result window.*

Contact

Dr.-Ing. Christina Kohl
Phone +49 711 970-4183
christina.kohl@igb.fraunhofer.de

Dr. rer. nat. Anke Burger-Kentischer
Phone +49 711 970-4023
anke.burger-kentischer@igb.fraunhofer.de

Literature

[1] Akira, S. et al. (2004) Toll-like receptor signalling, Nat Rev Immunol 4: 499–51

[2] Werner-Felmayer, G. et al. (1995) Detection of bacterial pyrogens on the basis of their effects on gamma interferon-mediated formation of neopterin or nitrite in cultured monocyte cell lines, Clini Diagn Lab Immunol 2(3): 307–313

[3] Jorgensen, J. et al. (1982) Rapid detection of significant bacteriuria by use of an automated Limulus amoebocyte lysat assay, J Clin Microbiol 16(3): 587–589

[4] Lakhani, S. A. et al. (2003) Toll-like receptor signaling in sepsis, Curr Opin Pediatr 15(3): 278–82

[5] Burger-Kentischer, A. et al. (2010) New cell-based innate immune receptor assay for the examination of receptor activity, ligand specificity, signalling pathways and the detection of pyrogens, J Immunol Meth 358: 93–103

[6] Zellbasiertes Testsystem zur Identifizierung und Differenzierung von Keimspektren (2009) DE 10 2006 031 483; EP 2 041 172

Funding

We would like to thank the Fraunhofer-Gesellschaft for funding the project "ImmuStick" under the "Discover" program.


1

SAFE FOODSTUFFS THROUGH PHYSICAL DISINFECTION

Michael Haupt, Bentsian Elkin, Sylvia Schmidt, Iris Trick, Christian Oehr

Egg shells as a cause of *Salmonella* infections

Eggs are used as a source of protein for human nutrition worldwide. Average annual consumption is 215 eggs per person, but varies quite strongly from country to country. According to the World Health Organization (WHO), *Salmonella* infections afflict more than 85,000 people in European countries annually [1]. The number of those afflicted no doubt has been declining the past years due to various measures. However, illness from *Salmonella* in Europe overall remains the second most common communicable animal-borne disease [2]. Poultry farms are the cause of *Salmonella* outbreaks in many cases. Undetected *Salmonella* infections occur in nearly 30 percent of German laying hen operations according to the German Federal Institute for Risk Assessment (BfR) [3]. Consumption of meat or eggs can result in its spread among the population and lead to infections. Salmonellosis is one of the diseases that must be reported.

Need for disinfection techniques

Current European legislation prohibits all hygienic treatment of foodstuffs, such as chemical disinfection or ionizing radiation, with the exception of ultraviolet radiation (UV). Conventional UV lamps contain many times the environmentally safe level of mercury and require longer exposure times. Most egg producers do not use the technology though, because the hygienic effectiveness is low and the maintenance costs high. The objective of the EU-funded project named OVOSHINE is to develop a cost-effective, safe, and fast physical method for disinfecting eggs in order to reduce the number of cases of illness caused by either raw eggs or insufficiently heated foodstuffs containing eggs, and increase food safety and security.

New excimer lamps for UV treatment

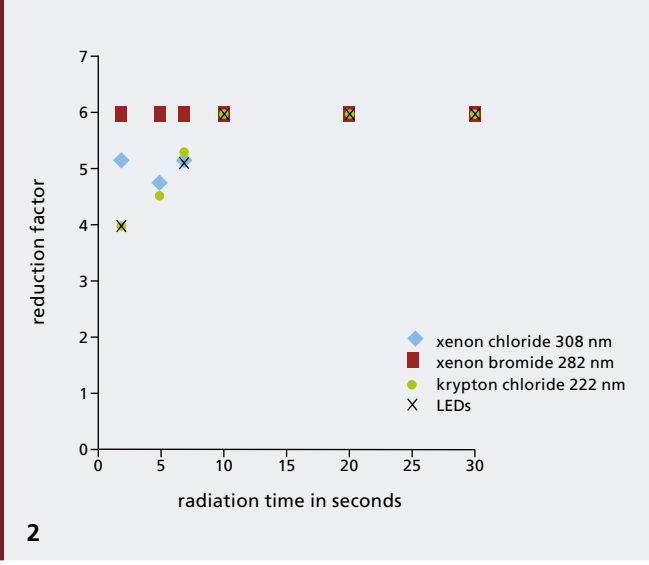
UV treatment of surfaces has long been known as a process for minimizing the number of organisms able to divide and multiply. Specialized excimer plasma lamps were designed at Fraunhofer IGB and their radiant output vs. distance, spectral distribution, and electrical power consumption tested in the lab for selected specimens. The inactivation effect of the radiation was checked for several species of bacteria using microbiological techniques. In addition, novel UVC LEDs were employed for emitting light at wavelengths considerably below 300 nm.

Inactivation of vegetative cells

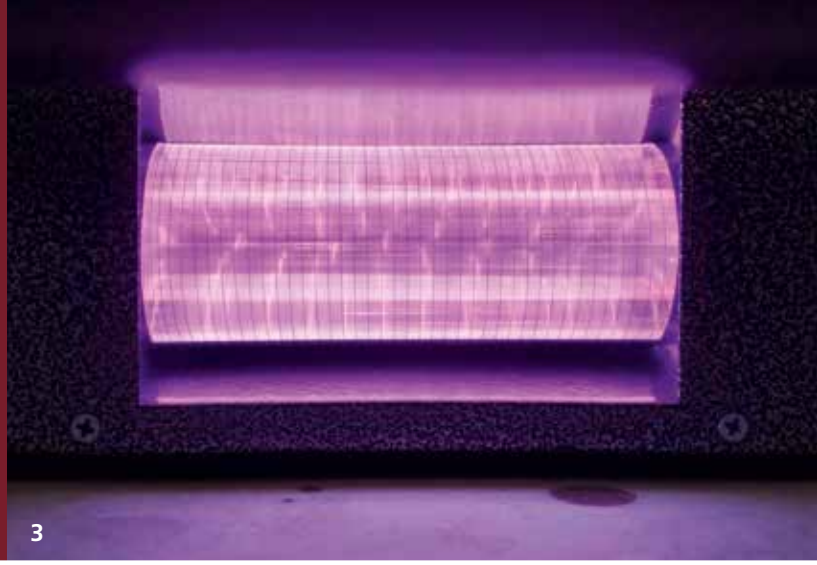
Excimer lamps and LEDs with different wavelengths (172 nm, 222 nm, 282 nm, 285 nm, and 308 nm) were investigated. The objective was to reduce the bacterial cell count by a reduction factor[1] of at least $R_F = 4$ in just 2 – 10 seconds, indicating a reduction of cell counts by a factor of 10^5. Reduction factors of at least $R_F = 6$ within 10 seconds could be demonstrated for vegetative cells in a test system generating reproducible irradiation at various wavelengths and radiation intensities. A reduction factor of $R_F = 4$ was attained without problem for two-second irradiation durations. These values are in reference to investigations using strains of *Escherichia coli* and *Salmonella enteritidis* that play a role in contamination of eggs.

Inactivation of endospores

In addition, it was also useful to investigate the extent to which endospores of *Bacillus* strains could be inactivated using this process, despite the relatively short treatment durations. Although forms of endospores with relatively high natural



2



3

resistance to radiation were involved, a reduction factor of R_F = 4 could be demonstrated with as little as 60 seconds of irradiation. The results obtained with spores of *Bacillus atrophaeus* thus far are very promising and open up further application areas for the highly effective excimer plasma lamps.

Prospects

We were able to show that radiation from excimer plasma lamps can be very effective against bacteria and even spores. The UV irradiation system developed by Fraunhofer IGB is a technologically simple and cost-effective alternative to other disinfection or sterilization techniques – one that can be adapted to numerous applications such as in the pharmaceutical and medical fields. There are also applications for sterilizing plastic packaging materials used with foodstuffs.

In addition, the lamps can also be utilized for activating the surfaces of adhesives, paint, or printed matter. We would be happy to advise you on the selection of radiation sources for your specialized application and provide assistance in implementation.

Contact

Dr. rer. nat. Michael Haupt
Phone +49 711 970-4028
michael.haupt@igb.fraunhofer.de

Dr. rer. nat. Iris Trick
Phone +49 711 970-4217
iris.trick@igb.fraunhofer.de

Literature

[1] Weltgesundheitsorganisation Europa (2015) Salmonellen in der Europäischen Union, www.euro.who.int/whd2015 (accessed on November 17, 2015)

[2] Hugas, M.; Beloeil, P. A. (2014) Controlling *Salmonella* along the food chain in the European Union – progress over the last ten years

[3] BfR (2006) Krankmachende Salmonellen in knapp 30 Prozent der großen Legehennenbetriebe nachgewiesen, 18/2006, 29.06.2006

Funding

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 605309.

Further information and project partners

www.ovoshine.eu

[1] The reduction factor R_F is calculated from the starting cell count used and the re-cultivable cells (R_F=log (starting cell count) – log (number of re-cultivable cells). A R_F of 5 for example indicates a cell count reduction by a factor of 10^5.

1 *Dangerous Salmonella can reside on egg shells.*

2 *Measurement results following irradiation of Salmonella spec. on test specimens using various lamps.*

3 *Excimer plasma lamp that emits UV radiation at 282 nm.*

PHARMACY

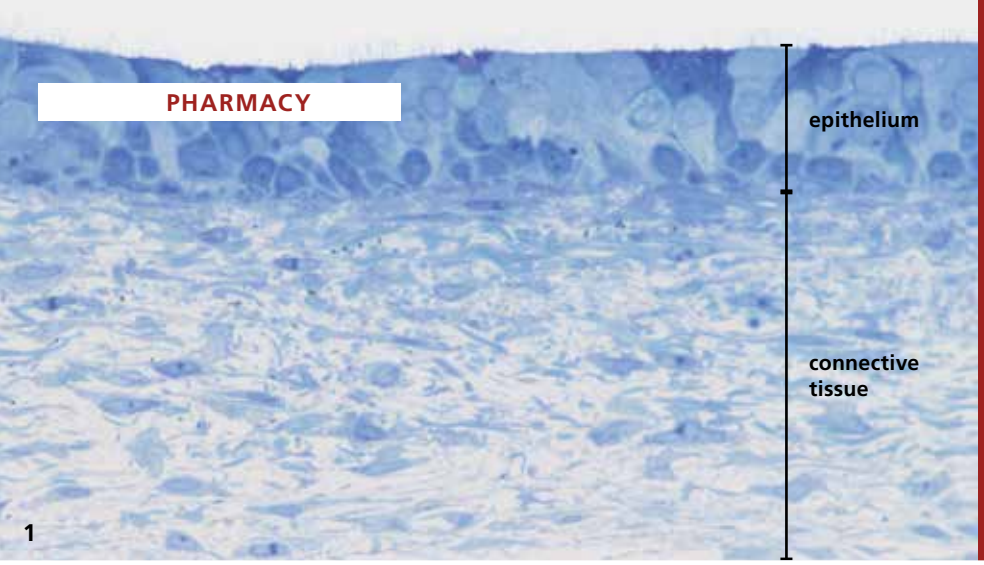
Current challenges faced by the pharmaceutical industry include improving personalized therapy, the development of new active agents, and the enhancement of the effectiveness of drugs through improved formulations. In the pharmacy business area, Fraunhofer IGB develops solutions for target and drug screening, pharmaceutical biotechnology and chemistry, including for the formulation and targeted delivery and release of drugs.

Screening and validation of drugs – Based on its own patents Fraunhofer IGB has developed various array technologies, high-throughput sequencing methods and human tissue models and is therefore able to elucidate host-pathogen interactions and make available targets for new anti-infectives. By targeted use of cell-based assays, we identify new drugs, e.g. for immunomodulatory substances or anti-infectives, on the basis of structure-activity correlations. Using complex organotypic 3D complex tissue models – both "healthy" and "diseased" tissues – we characterize potential active compounds *in vitro*. In particular, models of the human barriere tissues, i.e. skin, intestine, respiratory tract and the blood-brain barrier, are constructed as tissue models from primary or iPS cells, to investigate the absorption, distribution in organ models, toxicity and effectiveness of new drugs. In these tissue models we simulate clinical regimens to identify new prognostic markers, mechanisms of resistance and effectiveness by molecular methods such as gene expression and proteome analysis as well as by histology and confocal Raman spectroscopy.

Manufacturing and processing – We develop processes for the production of pharmaceutical proteins ranging from the establishment of new expression vectors, the strain development in microorganisms and mammalian cells, and the optimization of fermentation processes to the purification of the pharmaceuticals. We offer the production of clinical IMPs in compliance with GMP (Good Manufacturing Practice) regulations via internal Fraunhofer cooperation. Increasingly, we are also implementing cell-free biotechnological methods, which allow for the fast optimization of pharmaceutical proteins, produced in milligram amounts, that can be characterized while using the cell-based systems. Likewise, other highly efficient "cell-free" applications are the introduction of non-canonical amino acids or the coupling of drug and targeting molecules.

Formulation – With regard to the formulation of active agents, we are developing nanoparticulate structures that deliver drugs directly to the target location and then release them in a controlled manner. Virus-like particles represent a novel approach for the packaging and intravenous targeting of drugs.

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



1

2

HUMAN 3D IN VITRO TEST SYSTEMS FOR INFECTION STUDIES

Florian Groeber, Marco Metzger, Heike Walles, Maria Steinke

Initial situation

Humans are the only natural hosts for numerous pathogens. Because of this fact a large amount of data obtained from animal tests does not correlate with the infection mechanisms in the human organism. Thus, many aspects of corresponding diseases are still speculative and the development of new therapy processes and vaccines is possible only under complicated conditions. In order to research the interactions between human obligate pathogens and the host tissue, corresponding 3D *in vitro* tissue models similar to the physiologic circumstances of the human body are necessary. In the Translational Center "Regenerative Therapies for Oncology and Musculoskeletal Diseases", the Würzburg branch of Fraunhofer IGB, the manufacture of 3D *in vitro* test systems is based on the BioVaSc-TERM®, a biological scaffold gained from pig gut.

3D *in vitro* test system for infection studies with *Bordetella pertussis*

The bacterium *Bordetella pertussis* that elicits whooping cough attacks the human airways and is primarily located at the cilia of the airway mucosa. We successfully generated a 3D *in vitro* test system of the human airway mucosa with a high *in vitro*/*in vivo* correlation, equipped with functional cilia (Fig. 1) [1]. After an infection with sterile-filtered culture supernatant of *Bordetella pertussis*, we note for example the complete destruction of airway epithelial cells, which considerably affects the protective function of the airway mucosa.

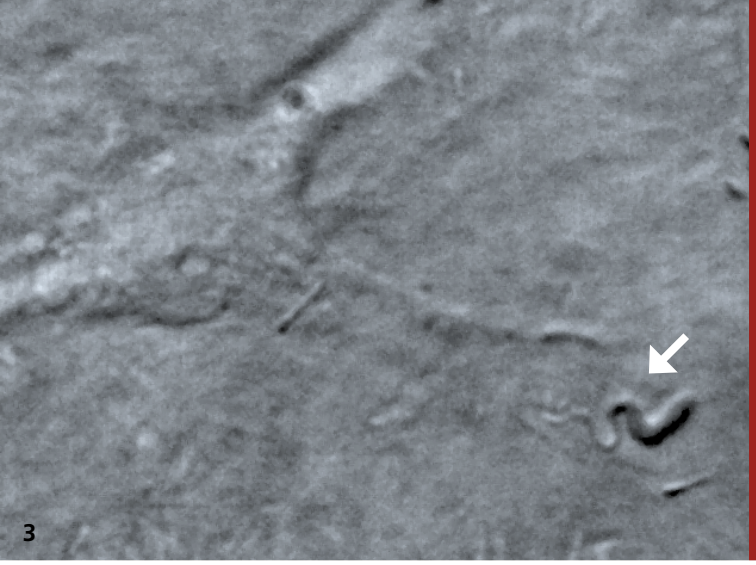
3D *in vitro* test system for the examination of human sleeping sickness

Human sleeping sickness is a dangerous tropical disease caused by the eukaryotic pathogen *Trypanosoma brucei* and transmitted via the tsetse fly [2]. As soon as the pathogen spreads in the body, the treatment of this disease becomes very difficult. Therefore, novel therapies aim to fight the pathogen already in the skin. In order to recapitulate this step, we used *in vitro* skin models with a high similarity to human skin that can be used as an alternative method to animal testing.

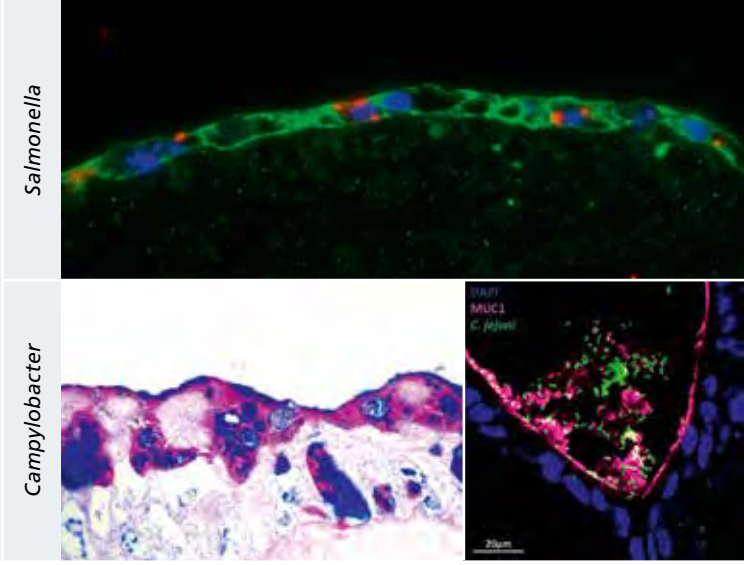
In the first step, the natural infection path through the tse tse fly was established *in vitro* demonstrating that the fly accepts the skin model as a host (Fig. 2). Moreover, we were able to show that the sting leads to the transmission of trypanosomes. The trypanosomes were active inside the model for a long period, which verified the applicability of the *in vitro* skin models for infection studies with *Trypanosoma brucei*.

Infection studies of intestine test systems with *Salmonella* and *Campylobacter*

Human intestine pathogens such as *Salmonella typhi* and *Campylobacter jejuni* are the reason for numerous, serious gastrointestinal diseases. Existing bowel tissue models were further developed in the Translational Center by means of the BioVaSc-TERM® technology and the dynamic tissue culture. Thus, a more physiological enzyme and transport activity as well as cell morphology were shown. On this basis and in cooperation with the Institute for Molecular Infection Biology Würzburg (IMIB, Prof. Dr. Jörg Vogel's workgroup), a human triple culture model was established which depicts the human



3



4

intestinal epithelium (Caco-2), the blood barrier (endothelial cells), and the components of the immune system (Peripheral Blood Mononuclear Cells, PBMCs). By means of *Salmonellae* marked with fluorescence (Fig. 4), the transmigration was examined through flow cytometry. As a result, a time-dependent increase of infected epithelial cells was shown while the endothelium was not affected. Moreover, the infection led to the release of IL-8 into the vascular compartment and an activation of monozytes (CD14+) and NK-cells (CD56+).

In a second cooperation project (ZINF, Dr. Cynthia Sharma's workgroup), we were able to integrate the mucigeneous cell line E12 (HT29-MTX-E12, Fig. 4 below). After the infection with *Campylobacter* it was shown that the mucosa represents an additional barrier with respect to colonization, transmigration, and destruction of the epithelial conglomerate.

Overview

Understanding important steps of a natural infection forms the basis for developing new preventive and therapeutic strategies for the fight against infectious diseases. Our 3D *in vitro* test systems are suitable to further investigate these infection mechanisms and can support the (further) development of therapy strategies and vaccines in the long run.

1 *3D test system of the human airway mucosa.*
2 *Tsetse fly during the infection of an in vitro skin model.*
3 *Pathogen of sleeping sickness beside a human cell.*
4 *Infections with Salmonella or Campylobacter spec. on Caco-2 resp. E12 intestine models.*

Contact

Dr. sc. hum. Marco Metzger
Phone +49 931 31-86686
marco.metzger@igb.fraunhofer.de

Dr. rer. nat Maria Steinke
Phone +49 931 31-80720
maria.steinke@igb.fraunhofer.de

Literature

[1] Steinke, M.; Gross, R.; Walles, H.; Gangnus, R.; Schütze, K.; Walles, T. (2014) An engineered 3D human airway mucosa model based on an SIS scaffold Biomaterials 35: 7355–62
[2] WHO Factsheet N°259; http://www.who.int/mediacentre/factsheets/fs259/en/

Funding

We would like to thank the Free State of Bavaria (BayernFIT-Programm) and the Interdisciplinary Center for Clinical Research IZKF of the medical faculty of the University of Würzburg for funding our work.

Project partners

Prof. Dr. Thorsten Walles, Department of Thoracic and Cardiovascular Surgery, University Hospital of Würzburg | Prof. Dr. Roy Gross, Chair of Microbiology, University of Würzburg | Prof. Dr. Markus Engstler, Chair of Cell and Development Biology, University of Würzburg | Dr. Cynthia Sharma, Research Center for Infectious Diseases, University of Würzburg | Prof. Dr. Jörg Vogel, Institute for Molecular Infection Biology, University of Würzburg

1

PRODUCTION OF VIRUS-LIKE PARTICLES FOR PHARMACEUTICAL APPLICATIONS

Susanne M. Bailer

Initial situation

For medical applications, active substances require transport vehicles with surfaces presenting high valence target structures available in combined form. Effective vaccines can also be developed in this way. Furthermore, such vehicles can embed drugs and direct them to their site of action. This greatly reduces the adverse effects of drugs and even makes the use of some new active substances possible in the first place.

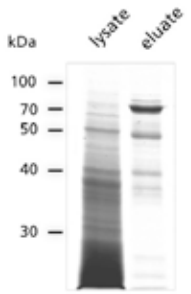
Potential of virus-like particles

Virus-like particles (VLPs) are biobased protein capsules that imitate virus capsids but are not infectious. Due to their stability, size and the large number of surface functions, VLPs are perfectly suitable as the basis for vaccines. Thus, they can be used instead of viruses that are difficult or impossible to culture *in vitro*. Alternatively, VLP basic structures can be used to present unrelated antigens on their surface. In addition, VLPs can be used as biocontainers for drug delivery and have great potential in intravenous administration of active substances. VLPs, in particular those that originate from RNA viruses, are ideal vehicles for embedding therapeutic RNAs and thus for protected target control of RNAs toward their target cells.

Standardized production process as a solution

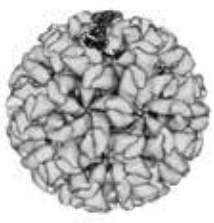
The potential of VLPs has not been fully exploited yet by any means, especially because there are no standardized processes for their production. Expression and purification procedures are generally developed on an individual basis and optimized for each protein or VLP. However, this empirical and individually tailored approach is time- and cost-intensive and thus represents a challenge for industrial production. Processes for VLP production can be considerably simplified and standardized using basic structures that can be adapted for numerous applications in a modular manner.

The goal of this project is to develop a modular system for the production of VLPs. A basic module with an inner capsular structure will be genetically equipped with a functionally variable protein surface that serves either for targeted control of VLPs (drug delivery) or vaccine development. Since the basic module always remains unaltered and only the protein surface is specific, production of VLPs can be standardized compared to current systems and thus can be carried out in a reproducible, cost- and time-effective manner.



analysis

structure



assembly

Efficient and cost-effective VLP platform technology

As the basis for a VLP platform technology, non-enveloped viruses of the *Caliciviridae* family were chosen. To synthesize the VLPs in Baker´s yeast, plasmids were developed coding for the virus protein variants. Baker´s yeast is particularly well suited for the production of VPLs, because proteins for pharmaceutical applications can be produced with minimal side effects and in a cost-effective manner in this organism. In this way, a VLP basic structure could already be developed and characterized with success. Thus, a system is available for the expression and isolation of native caliciviral VLPs, so that a downstream processing can now be established. The aim is to establish an efficient and cost-effective process based on these VLPs that will make it possible to produce such biocontainers in great quantities and with high purity and homogeneity.

Outlook

A modular system and an accordingly standardized process have a wide range of applications and the demand on the market is high. In addition to multinational corporations, SMEs in particular are sharing the pharmaceutical market for drug delivery and vaccine development.

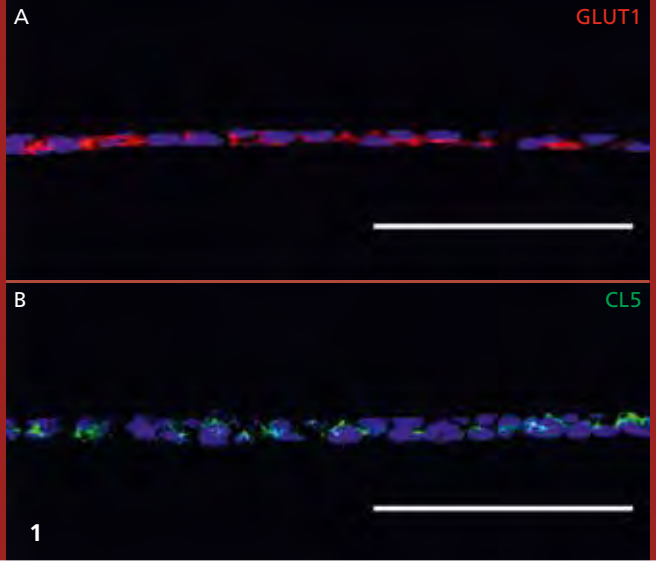
Contact

Priv.-Doz. Dr. sc. nat Susanne Bailer
Phone +49 711 970-4180
susanne.bailer@igb.fraunhofer.de

Funding

We would like to thank the Fraunhofer-Gesellschaft for funding the project "Vari-VLP" in the SME-oriented internal research program.

1 *Standardized production of VLPs.*



HUMAN IN VITRO BLOOD-BRAIN-BARRIER MODELS FOR DRUG DEVELOPMENT

Antje Appelt-Menzel, Alevtina Cubukova, Heike Walles, Marco Metzger

Dense barriers between blood and brain

The blood-brain barrier (BBB) presents one of the densest and most important barriers between the blood circulation and the central nervous system (CNS). The BBB consists of specialized microvascular endothelial cells, which coat the cerebral capillaries and are connected through very tight junctions. Together with pericytes, astrocytes, neurons, microglial cells, and the extracellular matrix of the basal membrane of the brain capillaries, they form a dynamic and complex regulatory system – the so-called neurovascular unit [1]. The main function of the BBB can be divided into three subgroups: the physical, metabolic, and transport barrier. The BBB serves principally to maintain the homeostasis of the CNS and for protection against neurotoxical substances and pathogens such as germs and viruses.

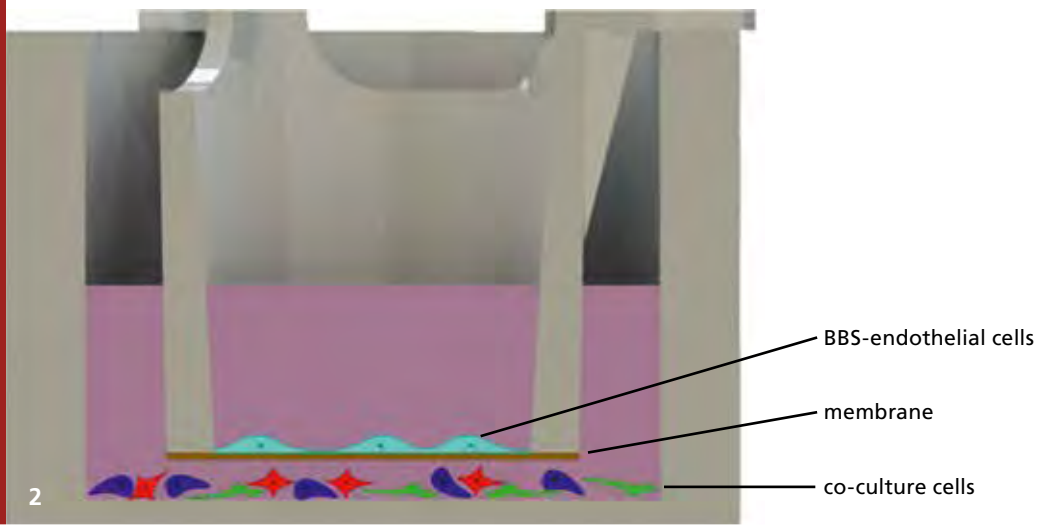
Demand for BBB models for drug development

For the development of drugs applied for the treatment of neurodegenerative diseases such as Alzheimer's, Parkinson's disease, and multiple sclerosis or even brain tumors, the denseness of the BBB models towards substances and the high metabolic activity of the endothelial cells poses a problem. Numerous medications/drugs cannot overcome the BBB in sufficient concentration to reach the target location or they are metabolized before transportation and thus become less effective. Due to the high demand for test systems in basic and preclinical research of medication/drug development and infection studies, a range of different BBB models have been developed.

Besides the *in silico*, acellular *in vitro*, and *in vivo* models, numerous cell-based BBB models have been developed. However, standardized models based on immortalized cell lines show only inhomogeneous tight-junction expression and possess low barrier integrity which is detected through transendothelial electric resistance (TEER) below 150 Ω*cm^2 [2]. In comparison, the TEER values in animal tests reached more than 150 Ω*cm^2 in the blood-brain barrier [3, 4]. The availability of human primary BBB cells is extremely limited. Moreover, using human primary BBB cells is an very serious matter not only in respect of ethical aspects. Human brain cells can, for instance, be isolated from biopsy or autopsy material obtained from patients suffering epilepsy or brain cancer. However, the risk remains that the isolated cells are contaminated with cells that are changed due to diseases, which may significantly change the features of the BBB models.

Novel models from induced pluripotent stem cells

In order to provide human BBB models, an innovative alternative to avoid such problems is the application of human induced pluripotent stem cells (hiPSC). We are able to differentiate hiPSC *in vitro* – under reproducible methods and with established and reproducible methods – into endothelial cells of the blood-brain barrier [5, 6] and to use them for establishing models. The endothelial cells were examined for the existence of endothelial-specific markers, tight-junctions markers as well as specific transporters (Fig. 1) by means of protein- and gene-based detection methods. The establishment of the BBB models includes using transwell inserts as quadrupel culture with pericytes, astrocytes, and neural cells, which can also be differentiated from hiPSC (Fig. 2). The barrier integrity, detected through TEER measurements, is



2

improved due to co-culture cells with the result that we reach between 1000 Ω*cm² and 2500 Ω*cm² depending on the culture conditions.

Outlook

The application of stem cells has great potential for developing regenerative therapies. Thus, patient-specific hiPSC was used to establish *in vitro* disease models such as have been described earlier. Therefore, the hiPSC are differentiated into the above-mentioned cells that are affected by the disease but are difficult to access, in order to establish a sufficient number of models for the drug/medication tests.

The pharmaceutical industry is searching for standardized and predictive model systems, since during the process of approval for drugs/medication many substances fail – due to toxicity and insufficient efficacy [7], even though they were previously tested in animal tests or cell lines [8].

1 *Staining of GLUT1⁺ transporter (A) and CL5⁺ tight junctions (B) in blood-brain barrier models.*

2 *Schematic depiction of the composition of in vitro blood-brain barrier models.*

Contact

Dipl.-Ing. (FH) Antje Appelt-Menzel
Phone +49 931 31-80771
antje.appelt-menzel@igb.fraunhofer.de

Dr. sc. hum. Marco Metzger
Phone +49 931 31-86686
marco.metzger@igb.fraunhofer.de

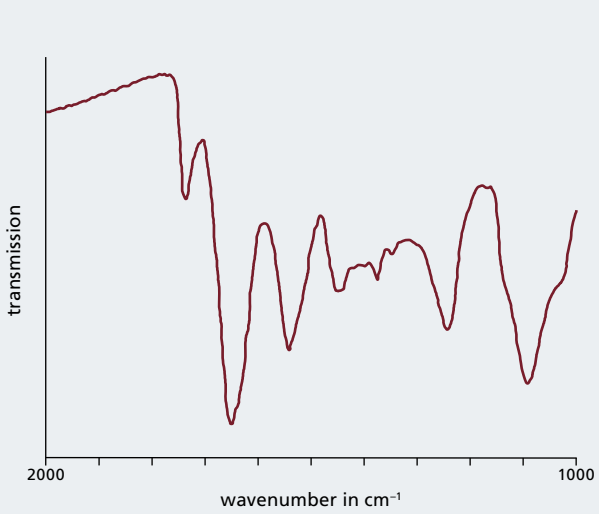
Literature

[1] Hawkins, B. T. et al. (2005) Pharmacological Reviews 57(2): 173–185
[2] Deli, M. A. et al. (2005) Cell Mol Neurobiol 25(1): 59–127
[3] Butt, A. M. et al. (1990) J Physiol 429: 47–62
[4] Crone, C. et al. (1982) Brain Res 241(1): 49–55
[5] Lippmann, E. S. et al. (2012) Nat Biotechnol 30(8): 783–791
[6] Lippmann, E. S. et al. (2014) Sci Rep 4: 4160
[7] Kola, I. et al. (2004) Nat Rev Drug Discov 3(8): 711–715.
[8] Lippmann, E. S. et al. (2013) Fluids Barriers CNS 10(1): 2

Funding

We would like to thank the German Federal Ministry of Education and Research (BMBF) for funding the project "BioTransporter – Effizienter Wirkstofftransport in biologischen Systemen: Cyclodextrin-Komplexe zur Beschleunigung des Transportes lipophiler Wirkstoffe (LipoTrans)", promotional reference 13N11803.

1



2

ANALYSIS OF PARTICLE DISTRIBUTION IN TISSUE MODELS USING IR MICROSCOPY

Michaela Müller, Monika Riedl

Label-free analysis for formulations of active ingredients

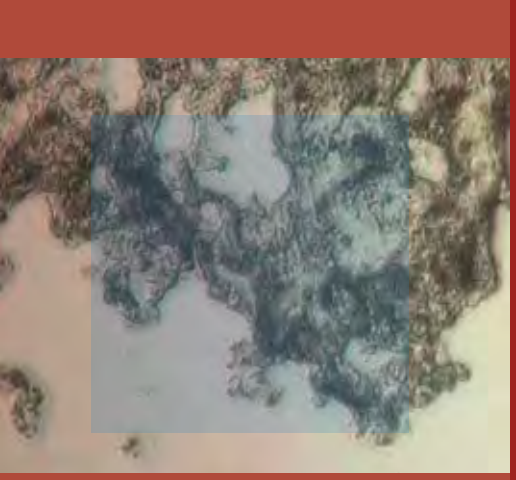
One important aspect in the development of medicinal products is the uptake of the formulated active ingredients via the mucous membranes, for example in the gastrointestinal tract. Laser scanning confocal fluorescence microscopy is the standard method used to investigate these ingredients in dissected cross-sections of tissue. Prior labelling of the components in the formulation with fluorescent molecules is generally required for this purpose. These dyes can significantly change the transport properties of the formulation through the tissue compared with the actual, non-labelled formulation. There is thus great demand for label-free analytical methods. At Fraunhofer IGB, confocal Raman microscopy and infrared microscopy are used as spectroscopic methods with a high spatial resolution that require no molecular probes.

The research project "Platform for efficient epithelial transport for pharmaceutical applications using innovative particulate carrier systems" (PeTrA), funded by the German Federal Ministry of Education and Research, has conducted transport studies with newly developed active ingredient formulations in a variety of *in vitro* tissue models. The distribution of the polymer nanoparticles in these models has then been investigated with methods including infrared microscopy.

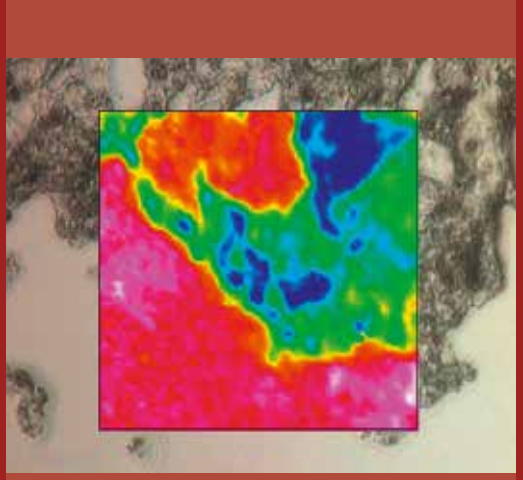
Measurement techniques and sample preparation

Sample preparation is particularly important for the successful conduct of measurement, in addition to the selection of suitable equipment and measurement techniques (transmission, reflection or attenuated total reflection (ATR)). Analyses were carried out using the infrared microscope Hyperion 3000 (Bruker) in the example described here. An FPA (focal plane array) detector with 64 x 64 "pixels" was used to produce the images. Each pixel that is recorded contains a full infrared spectrum, with each image therefore containing 4096 individual spectra.

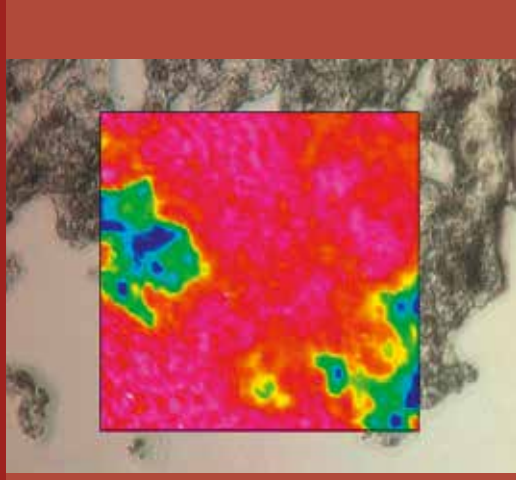
The biological samples are intestinal tissue models, based on Caco-2 cells on a biological collagen matrix perfused with the polymer particle formulation in a bioreactor. Cross-sections of 20 µm were prepared using a cryomicrotome and transferred to a calcium fluoride window that is permeable for infrared. Tissue models and cross-sections were produced by Prof. Dr. Heike Walles' research group at the Institute of Tissue Engineering and Regenerative Medicine, University of Würzburg. Infrared spectra were recorded in transmission on an area measuring approx. 170 x 170 µm² using the FPA detector, resulting in a theoretical lateral resolution of approx. 2.7 µm.



3



4



5

Specific infrared bands

Infrared spectra of the tissue model and the particle formulation show that the particles have a specific absorption band at 1760 cm^{-1} and can therefore be distinguished from the surrounding tissue matrix. The matrix is composed mainly of collagen and exhibits typical absorption bands at approx. 1650 cm^{-1} and 1550 cm^{-1} (amide bands). The infrared images were then analyzed such that the intensity distribution of the relevant integrated absorption bands is illustrated in the ranges of 1800–1700 cm^{-1} and 1700–1500 cm^{-1}.

A comparison between the optical IR microscope image (Fig. 3) and the two images that were analyzed (Figs. 4 and 5) clearly shows the regions with larger accumulations of particles. The formulation investigated here accumulated in the apical portion of the tissue model. Results were confirmed using alternative methods. Based on this example, we were able to demonstrate that detection of accumulations of non-labelled active ingredient particles in cross-sections of the intestinal tissue model is possible using IR microscopy.

Perspectives

Infrared microscopy on biological samples is an option whenever spatially resolved chemical information in the range of approx. > 3 µm is required. For example, it is also suitable for the identification of particles in tissue from implants that have been produced by abrasion or for the identification of optically visible deposits in tissue as a result of protein denaturation or mineralization.

Contact

Dr. rer. nat. Michaela Müller
Phone +49 711 970-4140
michaela.mueller@igb.fraunhofer.de

Dr. rer. nat. Christian Oehr
Phone +49 711 970-4137
christian.oehr@igb.fraunhofer.de

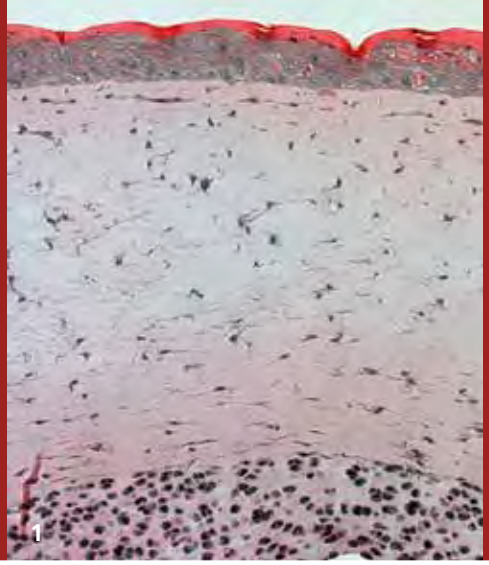
Funding

We would like to thank the German Federal Ministry of Education and Research (BMBF) for funding the project "PeTrA", promotional reference 13N11457.

Project partners

Evonik Industries AG, Darmstadt, Germany | Merck KGaA, Darmstadt, Germany | EMC microcollections GmbH, Tübingen, Germany | Helmholtz Centre for Infection Research (HZI), Braunschweig, Germany

1 *Light microscopy of a tissue model with dyed Caco-2 cells.*
2 *Infrared spectrum in the range of 2000–1000 cm^{-1}.*
3 *Optical image of the sample site subjected to analysis.*
4 *FPA imaging in the range of 1700–1500 cm^{-1}; blue/green: tissue.*
5 *FPA imaging in the range of 1800–1700 cm^{-1}; blue/green: particles.*



IN VITRO INFECTION MODELS WITH IMMUNOCOMPETENCE

Andreas Kühbacher, Anke Burger-Kentischer, Kai Sohn, Steffen Rupp

In vitro models for infection research

In infection research, *in vitro* models are well suited for studying initial processes in the colonization of epithelial surfaces by pathogens. In particular, adhesion and invasion processes can be studied and analyzed very well using human infection models, as already shown many times by us and others. In addition, these models can be used effectively for screening for new active substances [1]. In this way, effects on human cells can be recorded and thus an initial assessment of the toxic and protective effects of the potential drug can be made at the same time.

To date, however, further investigations, in particular on the interaction between pathogens and the immune system, have only been inadequately possible. Here, we are working under the framework of the Marie Curie Initial Training Network "ImResFun" to establish a skin model which not only consists of epidermal and dermal components but also contains immune cells. The focus is on understanding how human epithelial and immune cells respond to infection and how they communicate in the defense against pathogens. For this purpose, in this study the novel skin models supplemented with defined immune cell types are infected with the most frequent human fungal pathogens of the species *Candida*. The aim of the network ImResFun, which consists of 12 partners from nine European countries, is to find new means for fighting *Candida* infections.

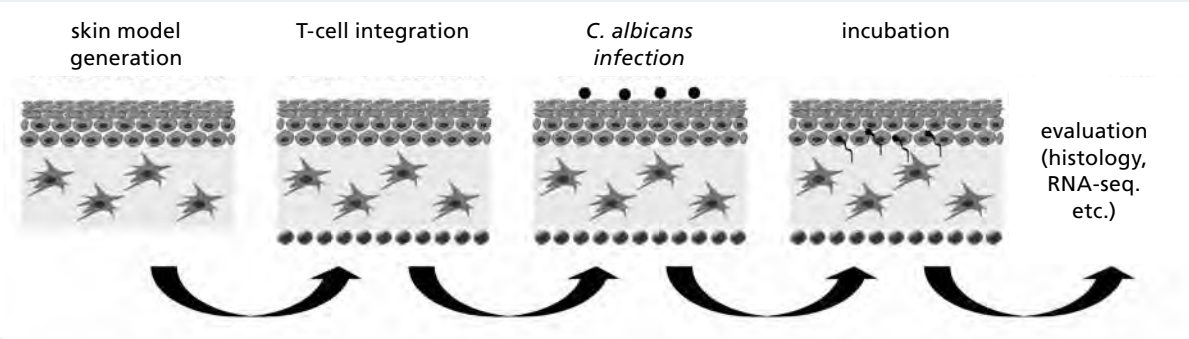
Immunocompetence by integration of immune cells in 3D skin models

In healthy humans, the skin is resistant to symptomatic infections by microorganisms that, like *Candida albicans*, naturally colonize the skin. Skin infections in general occurring rarely are primarily superficial. Deeper invasion into subepithelial tissue that would allow *C. albicans* to access the blood stream leading to systemic spread doesn't normally occur in humans with intact skin.

However, *in vitro* skin models consisting of keratinocytes as an epidermal layer and fibroblasts embedded in collagen as a dermal layer are penetrated and destroyed very quickly by *C. albicans* [2]. This is not surprising since these skin models do not contain any components of the immune system. Hence, we developed skin models that also include immune cells. In order to design reproducible skin models that are independent of donor-based differences in primary cells, we built them from immortalized keratinocytes and fibroblasts. Cells known as T cells (T-lymphocytes) that provide immune response to *C. albicans* in humans as well (Fig. 1) were integrated into the models as immune cells. In the presence of T cells, invasion of *C. albicans* is significantly reduced and even stopped during the observation period. This means that the system shows at least partial immunocompetence *in vitro*.

Immune response in a test tube

Using next-generation sequencing, this partial immunocompetent system was comprehensively studied in dual RNA sequence analyses in the presence and absence of *C. albicans*. We discovered that none of the individual cell types alone achieved an effective defense against *C. albicans* infection. Instead, cytokine-mediated communication between the different cell types seems to be necessary to trigger an effective antimicrobial response. One of the key molecules identified by us in these analyses is the immune receptor TLR2 required



2

for recognition of the pathogen. This receptor induces a signal cascade that finally stops the fungal invasion.

Immune receptors – signal transducers of the immune system

These results underscore the role of immune receptors as important sensors and regulators of the immune system that help the body to decide when and how the body's own defense mechanisms must be activated. In the framework of ImResFun, we are therefore also looking for immunomodulatory substances for immune receptors. Screening systems developed by Fraunhofer IGB [3] were used to find immunomodulators that can support a non-sufficient immune response or control an exaggerated immune response. With this approach, the body's own arsenal against pathogens can be involved more efficiently in therapeutic approaches and hence more rapid deactivation of infectious diseases and improved protection against infections can be achieved.

Future prospects

We will further expand these promising approaches for developing partial immunocompetent *in vitro* models in order to better understand the molecular mechanisms of the body's own defenses in epithelial tissue and to develop new active substances for the treatment of infectious diseases based on this understanding.

1 *Histological section of an in vitro skin model consisting of keratinocytes (upper layer), fibroblasts (middle layer) and T cells (lower layer).*

2 *Procedure during investigation of Candida infections using immunosupplemented skin models.*

Contact

Dr. Andreas Kühbacher
Phone +49 711 970-4166
andreas.kuehbacher@
igb.fraunhofer.de

Prof. Dr. rer. nat. Steffen Rupp
Phone +49 711 970-4045
steffen.rupp@igb.fraunhofer.de

Literature

[1] Burger-Kentischer, A. et al. (2011) A screening assay based on host-pathogen interaction models identifies a set of novel antifungal benzimidazole derivatives, Antimicrobial agents and chemotherapy 55 (10): 4789–4801. doi:10.1128/AAC.01657-10

[2] Dieterich, C. et al. (2002) *In vitro* reconstructed human epithelia reveal contributions of *Candida albicans* EFG1 and CPH1 to adhesion and invasion, Microbiology 148 (Pt 2): 497–506

[3] Burger-Kentischer, A. et al. (2010) A new cell-based innate immune receptor assay for the examination of receptor activity, ligand specificity, signalling pathways and the detection of pyrogens, Journal of immunological methods 358 (1–2): 93–103. doi:10.1016/j.jim.2010.03.020

Funding

The "ImResFun" Marie Curie Initial Training Network has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no MC-ITN-2013-606786.

Further information and project partners

www.imresfun.org

CHEMISTRY

The chemical industry is one of the most important and research-intensive economic sectors in Germany. Many innovations in other sectors, such as in the automotive, electrical and electronic, construction and packaging industries, would not be possible without the contributions of chemistry. Resource- and energy-intensive processes characterize the chemical industry. The dependence on the import of raw materials, the limited availability of fossil resources worldwide – even in competition with energy use – and the need to consider the impact on both the climate and the environment mean that at the foreground of our work are also initiatives to make the use of fossil resources more efficient or create substitutes for them.

Biobased chemicals and materials – Our activities are aimed at the development of biotechnological (fermentative or biocatalytic) processes for the production of chemicals and fuels from renewable resources, biogenic residues or microalgae, and the coupling of these with chemical processes. The Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna offers new ways of transferring the use of renewable raw materials to an industrial scale.

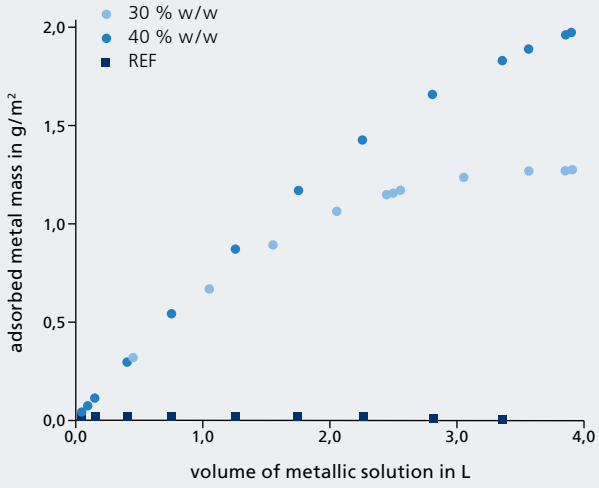
Process intensification and integration – Substance separation is a key step in many sectors of the chemical industry, since both raw materials and synthesis or fermentation products are often present as mixtures. Our focus is on the development of methods for upstream and downstream processing for a more efficient use of raw materials and energy, with the effective separation of material flows occurring by means of membranes or other separation techniques. The integrated recirculation of material flows and the recovery of valuable materials (recycling) as part of a sustainable waste management represent here the current fields of action. An increase in efficiency through better conversion rates is achieved, for example, through an intensive energy input using microwaves.

Functional surfaces and materials – By the decoupling of volume and surface properties of materials through interfacial process engineering, e.g. in the form of customized coatings, which are, in turn, procedurally geared towards efficient use of resources, new possibilities result as to the base materials of workpieces and thus for new products based on a selection of sustainable raw materials.

We also examine chemicals for their potential risk (e.g. within the scope of REACH). The diversity of our research and development work shows how we are meeting 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.

particle	chemical function		possible targets
–COO^-	carboxyl	weak cation-IEX	(heavy) metals
–SO_3^-	sulfate	strong cation-IEX	(heavy) metals
–NH_2	amine	weak anion-IEX	arsenate, diclofenac-Na
–NMe_3^+	quaternary ammonium	strong anion-IEX	Penicillin G K salt
–PO_3H^-	phosphonate	complex-forming	rare earth materials, iron, aluminium
–$NHSNH_2$	thiourea	affinity	noble metals
–⬡	heteroaromatic	hydrophobic adsorption	bisphenol A
–⬡	aromatic	hydrophobic adsorption	carbamazepine

1



2

FRAUNHOFER LIGHTHOUSE PROJECT "CRITICAL RARE EARTHS"

Uwe Vohrer, Thomas Schiestel, Klaus Niedergall, Christopher Hänel, Thomas Scherer, Max Kotzur, Lea König, Gabriele Beck-Schwadorf, Susanne Größchen, Hedwig Pilgram, Iris Trick

Recycling magnet material

Under the Fraunhofer Lighthouse Project entitled "Critical Rare Earths", Fraunhofer IGB has been responsible for Work Package 7 entitled "Recovery of Rare Earth Metals from Permanent Magnets and Industrial Waste". It has set itself three goals to be met by the Midterm Meeting with its project partners. Firstly, sintered magnets from used electric motors should be recycled in such a way that the reprocessed granulate can supplement primary magnet production by at least ten percent without having an impact on the properties of the new magnets produced. Secondly, the extent to which this recycled granulate can be utilized for manufacturing composite magnets comprising granulate with a polymer binder should be tested and proven. And finally, magnets and/or particulate material arising from production should be physically processed in such a way that metal oxides or metals are recovered, which can then be re-introduced as recycled industrial feedstock in a production process.

Physical processing

All milestones and objectives were successfully reached. Fraunhofer IGB's priority in the research project was to focus on the area of physical processing. The most important results from the three technologies investigated and developed are presented below.

Bioleaching

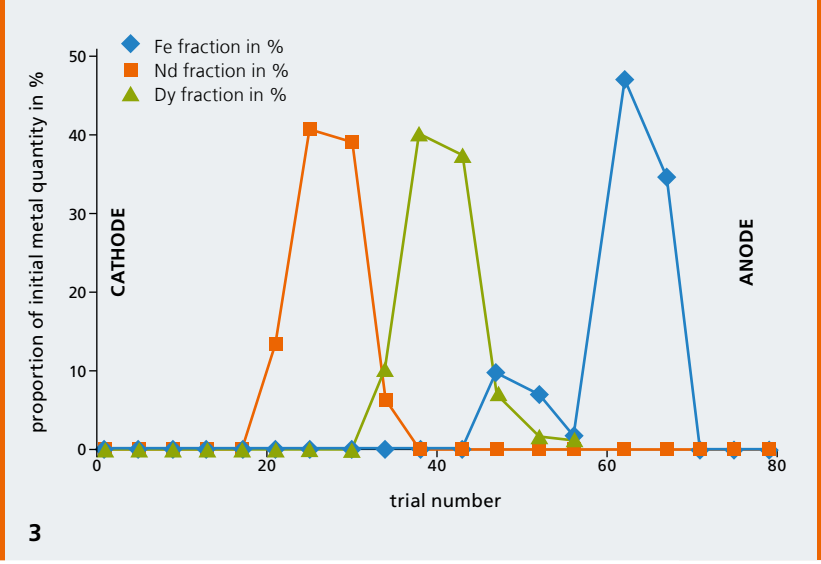
Bioleaching involves processes that have been known for thousands of years in metal mining and can be employed for processing tailings that contain metals using contemporary biotechnology. Prior to commencement of the project, however, little was known about suitable strains of microorganisms that might be employed for processing used magnets and ideally for leaching out neodymium specifically.

The research group therefore investigated known bacterial strains as well as organisms isolated from soil samples and evaluated them with regard to their ability to liberate and accumulate neodymium at the laboratory scale. Both stirred and fixed-bed bioreaction vessels were employed for this. A suitable mixed population of various aerobic soil bacteria was enriched and isolated from the soil samples, characterized and visualized by scanning electron microscopy. In an aerobic process at laboratory scale we could show the microbial population liberating neodymium from used magnets.

Summary: An aerobic process using a suitable heterogeneous microorganism population was set up and demonstrated that this is capable of specifically liberating and accumulating neodymium.

Membrane adsorption

Membrane adsorbers were able to be produced in the form of both film membranes and membranes constructed of hollow fibers. The active adsorber layer was introduced in the form of modified particles. Fig. 3 shows SEM images of a film membrane with particle loading of 40 percent by weight. The membrane thickness is 107 ± 9 µm. Different particles were tested as adsorber materials. Fig. 1 shows a selection of the chemically functionalized particles employed.



3


4

The neodymium adsorptive capacity of a membrane loaded with phosphonate particles at 30 percent and 40 percent by weight, respectively, compared to an unloaded reference membrane is shown in Fig. 2.

Summary: It was shown that functionalized membrane adsorbers can be used to concentrate dilute neodymium solutions by a factor of 100. The membrane adsorption is completely reversible. A certain selectivity in separating neodymium and dysprosium can be achieved with desorption.

Free-flow electrophoresis (FFE)

Ions can be deflected and separated by an electric field in free-flow electrophoresis. Fig. 3 shows successful separation of a neodymium-dysprosium-iron mixture. An eluate from the membrane adsorption process served as the sample. EDTA was used as the complex ligand in a ratio of one-to-one with dysprosium and iron. HCl and KCl in a 3.25 mM acetate buffer was employed as the separation medium. The field strength was 139.5 V/cm and the residence time 90 seconds. Moreover, a three-fold increase of the lab-scale reactor was able to be implemented (Fig. 4).

Summary: It was shown that rare earth metals as well can be separated from one another by means of optimized free-flow electrophoresis. In addition to proof of concept, a scale-up of the facility by a factor of three was successfully implemented.

Contact

Dr. rer. nat. Uwe Vohrer
Phone + 49 711 970-4134
uwe.vohrer@igb.fraunhofer.de

Dr. rer. nat. Thomas Schiestel
Phone + 49 711 970-4164
thomas.schiestel@igb.fraunhofer.de

Funding

The Fraunhofer-Gesellschaft intends to strengthen Germany as a center for commerce by rapidly transforming original scientific ideas into marketable products through the Lighthouse Project initiative.

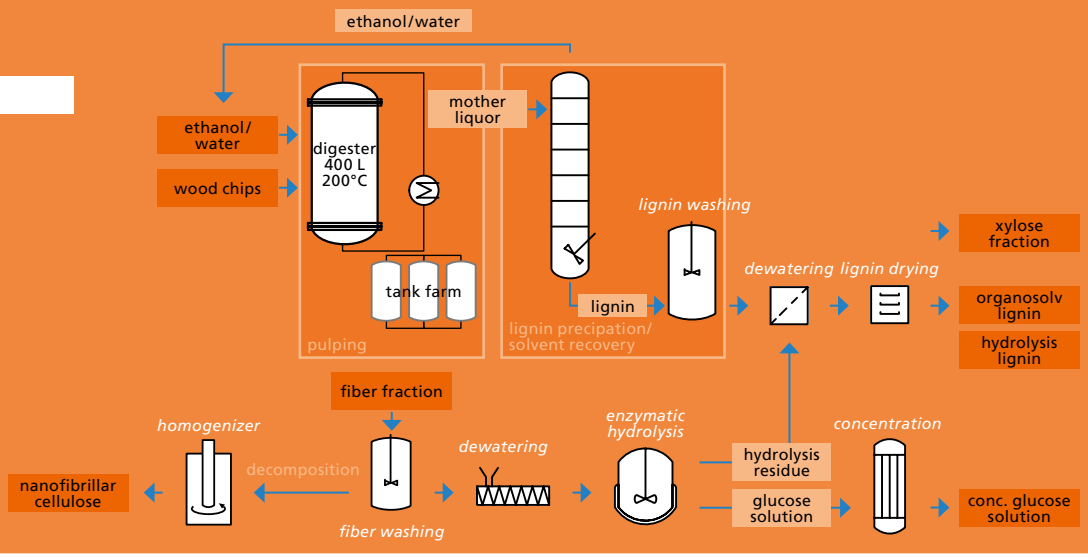
Project partners

Fraunhofer institutes IMWS, IWM, IWU, IWKS, IGB, IFAM, ISI, LBF

Further information

www.seltene-erden.fraunhofer.de

1 *Particles with differing functional groups were employed in the membrane adsorbers.*
2 *Adsorption of neodymium by particles with PO_3H^- functional groups.*
3 *Separation of Fe, Nd, and Dy from eluate of membrane adsorption by means of FFE.*
4 *Free-flow electrophoresis prototype.*



1

NANOFIBRILLAR CELLULOSE

Carmen Gruber-Traub, Achim Weber

Biobased raw material for new applications

Cellulose is the main component in plants and is of great technological and economic importance. In our latitudes, it is obtained mainly from wood or straw. The largest quantities of cellulose are converted in the paper and textile industries. The current interest focuses on three new forms of cellulose: nanofibrillar cellulose (NFC), nanocrystalline cellulose (NCC), and bacterial nanocellulose (BNC). These are summarized by the umbrella term nanocellulose. However, nanocellulose is not yet commercially available. It is currently only being produced in pilot plants.

Nanocellulose produced from residual biomass from lignocellulose biorefineries

Nanocellulose is produced at Fraunhofer IGB using, as yet, unexploited residual biomass from the Fraunhofer CBP lignocellulose biorefinery as the raw material. This process initially involves breaking down the wood, followed by separation into its chemical constituents for the conversion of wood or lignocellulose into platform chemicals for a chemistry of the future. Nanofibrillar cellulose (NFC) was successfully produced from the, as yet, unexploited residual biomass containing lignocellulose (Fig. 1). The focus is on the development and optimization of process engineering parameters through exposure to shear forces during treatment in the high-pressure homogenizer or the use of ultrasound. Likewise, the relevant purification and bleaching processes are being optimized.

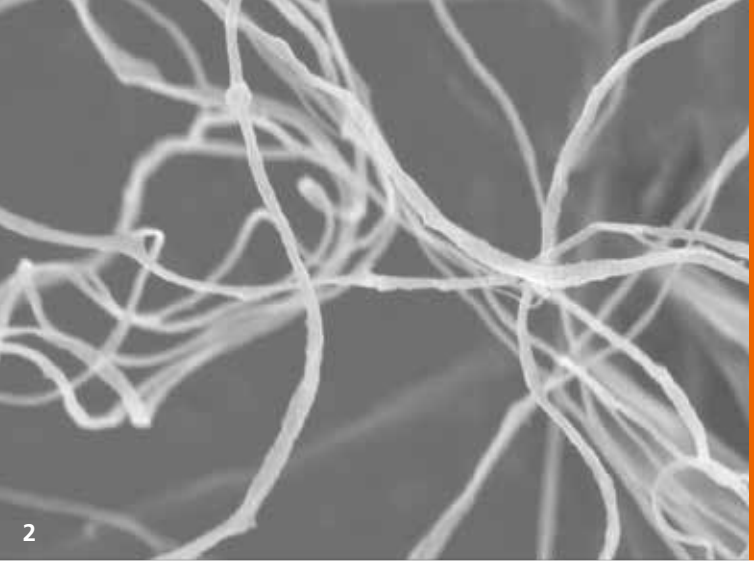
Novel NFC manufacturing procedure through combining different processes

The overall process for the manufacture of NFC is divided into three steps: purification, bleaching and extraction. Purification (step 1) consists of a swelling process to increase surface area and ethanolic purification of the fibers, with subsequent alkaline treatment. Bleaching (step 2) removes residual lignin and other undesirable components. NFC extraction (step 3) is realized through exposure to high shear forces. In this step, a variety of process steps were investigated under laboratory conditions at Fraunhofer IGB, such as ultrasonication, rotor-stator homogenization and the use of high-pressure homogenization, and a suitable overall procedure was developed through combining different processes. NFC (Fig. 2) can currently be produced at the institute at the scale of grams and upscaling of the process is viable.

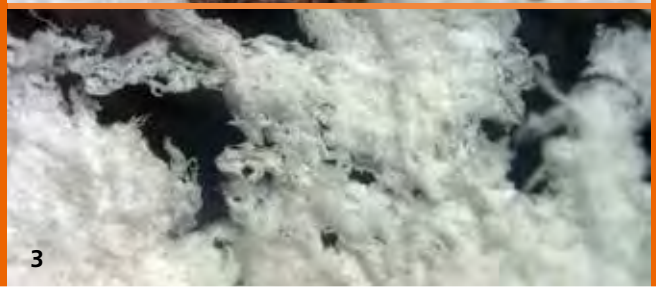
Cellulose as the basis for novel materials

The demand for fiber-reinforced composites, for example fiberglass-reinforced or carbon-fiber-reinforced polymers, is on the rise in a variety of industrial sectors. The use of nanocellulose would constitute a true biobased alternative to the materials that have been used until now for many of these applications. The advantages of cellulose are its biodegradability, CO_2 neutrality, high availability, and low price. Furthermore, cellulose is characterized by high tensile strength and low density. In comparison, carbon fibers and carbon nanotubes (CNT) have an elastic modulus ranging from 270 GPa to 950 GPa, with a tensile strength of 30 GPa [1]. However, their production costs are very high. This is where the opportunity lies for nanocellulose, which has the potential for being far cheaper to produce. Given an elastic modulus of 150 GPa and tensile strength of 10 GPa – equating to 8 times that for steel – and the lowest density of the materials used for comparison here, composite materials are possible that could reduce weight and costs many times over, at the same tensile strength and loading [2].

Fraunhofer IGB is currently investigating the incorporation of nanocellulose into polylactide and polyethylene (Fig. 3). The



2



3

challenge here is to achieve dispersion of the NFC in the polymer matrix that is as homogenous as possible. Our development offers a sustainable alternative to companies that wish to convert their residues containing cellulose into higher-end products. For example, novel sources of raw material, such as cotton, could be exploited for the production of nanocellulose. In collaboration with industrial partners, we therefore intend to work on follow-up projects to fully exploit material in residual biomass for the production of nanocellulose and on upscaling of the overall procedure.

Perspectives

The coming years will reveal whether nanocellulose can win through against competing materials (e.g. carbon fibers or graphene), both with reference to the cost and applications.

Contact

Dr. rer. nat. Carmen Gruber-Traub
Phone +49 711 970-4034
carmen.gruber-traub@
igb.fraunhofer.de

Dr. rer. nat. Achim Weber
Phone +49 711 970-4022
achim.weber@igb.fraunhofer.de

Literature

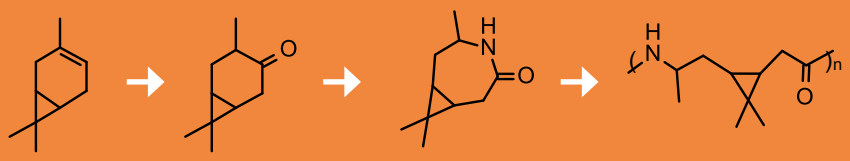
[1] Yu, M.; Lourie, O.; Dyer, M.; Moloni, K.; Kelly, T.; Ruoff, R. (2000) Strength and Breaking Mechanism of Multiwalled Carbon Nanotubes under Tensile Load, Science Magazine 287: 637–640

[2] Crotogino, R. (2012) The economic impact of Nanocellulose; ArboraNano – International Symposium on Assessing the Economic Impact of Nanotechnology, Washington DC, 27.03.2012

1 *Lignocellulose biorefinery with decomposition to produce NFC.*

2 *NFC produced from residual biomass from the Fraunhofer CBP lignocellulose biorefinery.*

3 *Fiber fraction from residual biomass (top) and composite material (NFC/polylactide, bottom).*



3-carene carane lactam polyamide based on 3-carene

1

DEVELOPMENT OF TRANSPARENT HIGH-PERFORMANCE POLYAMIDES FROM WOOD INDUSTRY WASTE PRODUCTS

Harald Strittmatter, Dominik Pastötter, Paul Stockmann, Volker Sieber

Background and aims of project

Large quantities of terpenes are a by-product of the production of cellulose. To date, these substituted cyclic or bicyclic, partially functionalized hydrocarbons are still mainly thermally utilized. The aim of the research described here was to continue the development of the use of terpene lactams as building blocks for biobased polyamides, as presented in the 2014 Annual Report. In addition to camphor, which can be converted into a monomer in only one synthetic step thanks to the carbonyl group that is already present in the molecule, we also investigated 3-carene, one of the main constituents in turpentine oil.

Synthesis of carane lactam

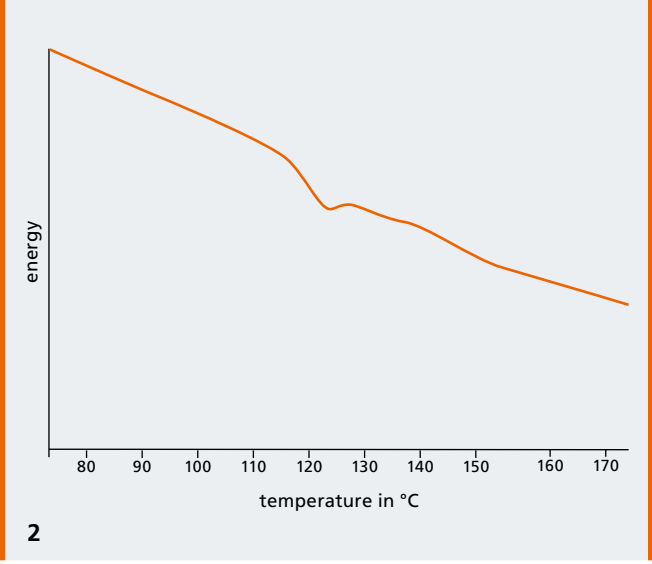
3-carene is also a bicyclic terpene. However, the carbonyl group that is required for the synthesis of a lactam must first be produced through oxidation of the double bond in the molecule. In contrast to camphor lactam, the lactam that is derived from 3-carene (carane lactam) would appear to be simpler to polymerize as the second cycle is at a longer distance from the functional group required for polymerization. This ensures lower steric hindrance which is, however, still adequate for the expected properties of the polymer, as is indicated by DSC analysis (differential scanning calorimetry).

Polymerization of carane lactam

The conversion of the lactam can be carried out by anionic polymerization, analogous to the production of polyamide 6 (reaction in mold, RIM). In contrast to the hydrolytic polymerization where the lactams are opened in a first step to aminocarbonicacids in the anionic case the chain formation proceeds directly from the monomer in the presence of a catalyst and an activator. Carane lactam polymerizes within a few minutes at temperatures of approx. 220°C. We can hereby obtain a transparent polymer that has no melting point based on differential scanning calorimetry (DSC) (Fig. 2). This indicates that only minimal crystalline regions remain.

Advantages of the new polyamides

Most biopolymers are produced from sugar and starch and are thus in direct competition with the food supply. Conversely, the current case involves utilizing waste products. Based on the sterically complex substituted cycle between the amide bonds – in contrast to typical partially crystalline standard polymers – we obtain materials that mainly have amorphous properties and enable new applications due to their transparency, for example, for the manufacture of ski goggles.



2


3

Further research

Further research aims to develop an optimized synthetic process for carane lactam and the corresponding polymer that allows economically competitive production of kilogram quantities of the polymer. The mechanical properties of the new material and potential applications are to be identified after the production of test specimens.

Contact

Dr. phil. Harald Strittmatter
Phone +49 9421 187-350
harald.strittmatter@igb.fraunhofer.de

Prof. Dr. rer. nat. Volker Sieber
Phone +49 9421 187-300
volker.sieber@igb.fraunhofer.de

Funding

We would like to thank the Bavarian State Ministry of Economics, Infrastructure, Transport and Technology for funding this project.

1 *Polyamide produced from carane lactam.*
2 *Differential scanning calorimetry (DSC) of the new polyamide.*
3 *The biobased amorphous polyamides are also suitable for transparent applications.*

1

PROCESS UPSCALING FOR THE PRODUCTION OF BIOAROMATIC COMPOUNDS FROM LIGNIN

Daniela Pufky-Heinrich, Björn Rößiger, Robert Röver, Gerd Unkelbach

Lignin as a biobased raw material

Current research is focusing on plant biomass that is not used as food, in food production or as animal feed and is available at competitive prices as a raw material for the production of platform chemicals. Herein, lignocellulosic biomass from wood is an important feedstock. In addition to cellulose, the other main constituent in wood is lignin. It is incorporated into plant cell walls and is responsible for the rigidity of wood. However, current processes for the production of chemical products from raw materials containing lignocellulose are generally designed to produce wood pulp and not to exploit all components in their entirety [1]. The wood pulp industry produces about 50 million metric tons of lignin as a by-product, mainly in the form of so-called kraft lignin. To date, the bulk of this lignin has mainly been used in energy production and burned directly in the pulping plants [2].

Small quantities of lignin in which the polymeric structure has been preserved are used in applications such as bonding agents, additives in cement or rubber. Moreover, due to its basic aromatic structure, it possesses enormous potential as a raw material for the production of aromatic building blocks for syntheses.

Cleavage of lignin into aromatic structures

Cleavage of the phenolic macromolecule lignin enables the production of mixtures of aromatic building blocks for synthesis. These can be used directly as raw material, e.g. for phenol formaldehyde resins, polyurethanes or in epoxides, or can be converted into the classic aromatic compounds, benzene, toluene, xylene or phenol, after further separation and defunctionalization. A variety of methods are suitable for this, such as hydrolysis, oxidative and reductive cleavage or enzymatic conversion. On an industrial scale, only the oxidative cleavage of lignosulfonates to vanillin has been realized. No other industrial processes have been described to date for other applications [3].

The process of base-catalyzed depolymerization (BCD) of lignin results in hydrolysis of the ether bonds in the lignin macromolecule and thereby in the production of monomers, dimeric and oligomeric alkyl-functionalized aromatic compounds. The BCD process is carried out in aqueous or alcoholic solution at temperatures of up to 350°C and at 250 bar. Intensive research both on organosolv lignin and on technical lignin containing sulfur has been performed at the laboratory scale at Fraunhofer ICT and the process has been optimized. BCD of lignin is highly selective and results in high yields of aromatic cleavage products [4].

Piloting of the process at Fraunhofer CBP

Scaling of this process at the pilot scale was carried out successfully at Fraunhofer CBP. We investigated and optimized the continuous process of chemical cleavage of lignin and the subsequent separation and purification of the aromatic fractions using a multi-stage process design. The alkaline solution was processed at a capacity of up to 20 kg/h. After depolymerization, the aromatic lignin fragments are processed by acidification of the reaction solution and separated into a liquid oil fraction (BCD oil) rich in monomers and a solid fraction rich in phenolic oligomers (BCD oligomers) during subsequent separation and purification using mechanical and thermal techniques. For this, a variety of filtration units and centrifuges are available at Fraunhofer CBP. BCD oil extraction

2

3

is carried out in a continuous counterflow extraction plant with a maximum throughput of 85 kg/h. Distillation units with a capacity of up to 60 L/h are used to recover the solvent from the extract.

The BCD oil yield rises with increasing process intensity (temperature, pressure and standing time), with a concomitant increase in monomer content. The degree of depolymerization increases, simultaneously resulting in a decrease in the molar mass of BCD oligomers. Oligomers with a mean molar mass of 609 g/mol and a yield of 58.8 mass percent were obtained from the conversion of kraft lignin (Mn_{lignin} = 1488 g/mol).

Perspectives

Optimization of the process with reference to a process design that is material- and energy-efficient and product optimization will follow on from the demonstration of the principal feasibility of upscaling the BCD process. In addition to the preparation of sample quantities for following processes, this will mainly focus on evaluation of the integration of base-catalyzed depolymerization as a technology module in a biorefinery.

1 *BCD oil and BCD oligomers as products of lignin depolymerization.*
2 *Pilot-plant for base-catalyzed depolymerization of lignin.*
3 *BCD cleavage product solution.*

Contact

Dr. rer. nat. Daniela Pufky-Heinrich
Phone +49 711 970-9103
daniela.pufky-heinrich@
cbp.fraunhofer.de

Dipl.-Chem. (FH) Gerd Unkelbach
Phone +49 711 970-9101
gerd.unkelbach@cbp.fraunhofer.de

Literature

[1] Raschka, A.; Carus, M. (2012) Stoffliche Nutzung von Biomasse. Basisdaten für Deutschland, Europa und die Welt, Nova-Institut für Ökologie und Innovation GmbH, Hürth

[2] Nachwachsende Rohstoffe (2009), FCI –Fonds der Chemischen Industrie im Verband der Chemischen Industrie e.V.

[3] Pufky-Heinrich, D.; Unkelbach, G. (2014) Herstellung biobasierter umweltfreundlicher Klebstoffe. Aromatische Molekülbausteine aus Lignin; adhäsion, Seite 16–19

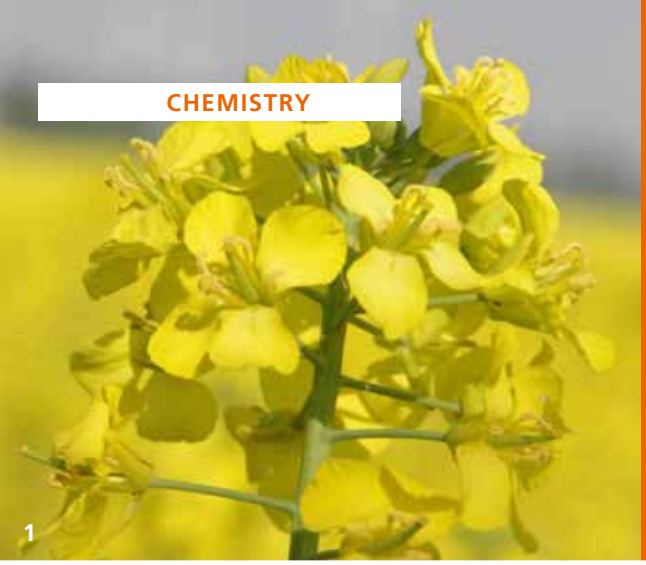
[4] Schmiedl, D.; Endisch, S.; Pindel, E.; Rückert, D.; Reinhardt, S.; Unkelbach, G.; Schweppe, R. (2012) Base catalyzed degradation of lignin for the generation of oxy-aromatic compounds – possibilities and challenges, Erdöl Erdgas Kohle 128 (10): 357–363

Funding

We would like to thank the German Federal Ministry of Food and Agriculture (BMEL) and the Agency for Renewable Resources (FNR) for funding the project "Lignoplast", promotional reference 22014212.

Project partner

Fraunhofer ICT, Pfinztal, Germany



RAPESEED BIOREFINERY – VALUABLE MATERIALS FROM RAPESEED

Marcus Zang, Sandra Franke, Daniela Pufky-Heinrich

Conventional rapeseed processing

Processing of rapeseed in Europe is currently done in conventional oil mills and consists of press cycles and post-extraction processing of the press cake using n-hexane to increase the oil yield. Rapeseed oil is the primary product of value in this process. The technologies that have been optimized over the past decades facilitate maximal extraction of the oil. The solid residue from the extraction process, i.e. the press cake, is a byproduct marketed as conventional animal feed. Valuable biologically active constituents contained in rapeseed, such as sinapinic acid, phytic acid, and tocopherol, go unutilized since they cannot be extracted natively using the conventional method. As a result, there is hardly any potential with conventional oil mills to realize any increased value. Nevertheless, development of the technology to hull the seeds in recent years has achieved the means to minimize the proportion of anti-nutritive compounds, coloring agents, bittering agents, and fibrous components, so that the quality of the oil as well as the press cake can be improved [1]. Conventional pressing processes using a traditional oil mill are not able to be used with the hulled rapeseed due to its commensurately low proportion of hulls, though.

Oil seed processing for industry

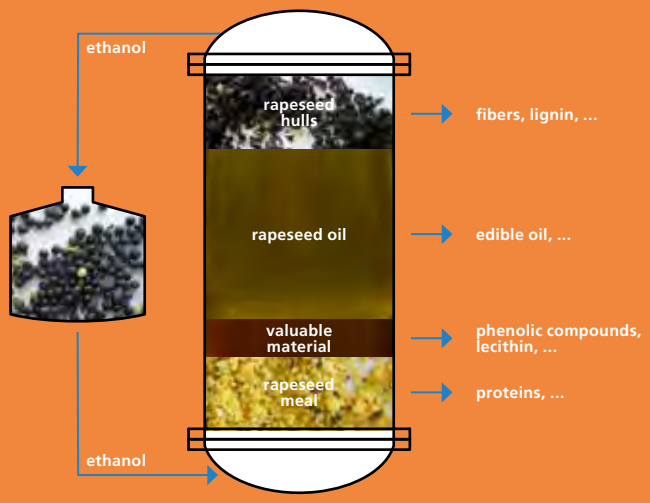
Having set the goal of utilizing domestic resources more effectively, such specialized rapeseed meal and protein as well as other valuable constituents should be transformed into value-added products and lead to diversification of the product palette into higher-priced market segments. As a result of this situation, there is considerable market potential in the oil seed processing industry. The extraction of new potential value, as it were, can lead to a reduction in the dependence of the branch on biodiesel production and open up new markets in the chemical, pharmaceutical, and cosmetics industries.

Native pulping and extraction process

Beginning with hulled rapeseeds, a pulping and extraction process was developed using ethanol as a mild extraction agent with which the constituents could be recovered. Cellular breakdown of the seed was accomplished using a rotor-stator system in order to achieve as complete an extraction of oil as possible during the subsequent multiple extraction cycles. The advantage of the process lies in the fact that the expressed oil can be phase-separated by means of energy-efficient cooling in the ethanol rather than having to recover it through distillation. Rapeseed meal as well as an extract mixture containing secondary constituents can be recovered as additional products.

Comprehensive commercialization of rapeseed

The rapeseed oil recovered corresponds in quality to pre-refined oil. Complete refining in order to introduce it as an edible oil is accordingly not absolutely necessary. The de-oiled rapeseed concentrate is nearly colorless and contains more than 50 percent protein. In addition, the tiny proportions of sinapinic acid and glucosinolates permit it to be processed further into high-quality animal feed and rapeseed protein products. Sinapinic acid, phospholipids, oligosaccharides, phenolic compounds as well as glucosinolates were able to be concentrated from the extract isolate mix of the oil and ethanol. The rapeseed hulls are rich in lignin (about 30 percent) that is available for further commercial utilization of the material. The research results are of great interest to the oil seed and processing industries. A joint process patent ("Verfahren



3

zur ganzheitlichen Verwertung von Ölsaaten") has been filed together with our project partner B+B Engineering GmbH as part of the research.

Prospects

The product quality of rapeseed oil and rapeseed meal concentrate as well as the enrichment of secondary constituents in the extract mixture achieve the prerequisites for complete utilization of rapeseed as a raw material. Ideas for utilizing the rapeseed hull material are being evaluated. A pilot plant at Fraunhofer CBP will be constructed under a group project planned by the German Agency for Renewable Resources (Fachagentur Nachwachsende Rohstoffe, FNR), in conjunction with partners from industry and research in order to prepare for introducing the process into industry. The following goals will be pursued over a period of three years:

- Optimization of the process and procedural parameters
- Evaluation of the products for employment in the food and feed industries
- Technological, ecological, and economic evaluation of the individual process steps as well as of the entire process
- Development of strategy for introducing the process to industry and marketing the technology

1 *Rape flower.*
2 *Rapeseed, kernels, and hulls.*
3 *Fractionating products from the rapeseed biorefinery.*

Contact

Marcus Zang M. Eng.
Phone +49 3461 43-9115
marcus.zang@igb.fraunhofer.de

Dr. rer. nat. Daniela Pufky-Heinrich
Phone +49 3461 43-9103
daniela.pufky-heinrich@
igb.fraunhofer.de

Literature

[1] Börner, M.; Peglow, M.; Henneberg, M.; Ihlow, M. (2012) Dehulling of canola seed in a fluid bed application; 103rd AOCS Conference; Long Beach, CA

Funding

We would like to thank the Ministry for Science and Industry of the State of Saxony-Anhalt and the Saxony-Anhalt Investment Bank for funding the project "Entwicklung von Aufschlussverfahren zur Gewinnung hochwertiger Produkte aus Raps" (Development of pulping process for recovery of high-quality products from rapeseed), promotional reference no 1304/00101. We would also like to thank the German Federal Ministry of Food and Agriculture (BMEL) and the Fachagentur Nachwachsende Rohstoffe e. V. (Agency for Renewable Resources) for funding the project "Vorstudie für die Pilotierung zur ethanolischen nativen Extraktion geschälter Rapssaat" (Pilot study for ethanol-based native extraction of hulled rapeseed), promotional reference no 22035614.

Project partner

B+B Engineering GmbH, Magdeburg, Germany

THE FRAUNHOFER LIGHTHOUSE PROJECT "ELECTRICITY AS A RAW MATERIAL"

Uwe Vohrer, Thomas Schiestel, Klaus Niedergall, Thomas Scherer, Tobias Gärtner

Excess electrical power for energy-intensive manufacturing

The energy transition in Germany is in full swing. Renewable energy sources contributed 24 percent of the 630 TWh of electrical power generated in 2013. Their proportion is estimated to climb to 80 percent by 2050, while at the same time greenhouse gas emissions are expected to fall to 80 percent of the comparative 1990 figures. The associated expansion of wind power and photovoltaics will result in a considerably increasing rise of power available from fluctuating energy sources. As an industrialized country, Germany is confronting the pressing question of whether and how the expected excess in the electrical grid can be coupled cost-effectively to energy-intensive manufacturing operations.

The goal: power to chemicals

The Fraunhofer-Gesellschaft views the energy transition and the cost-effective excess electrical power it will increasingly generate as an opportunity for electricity-intensive manufacturing. The goal of the Fraunhofer Lighthouse Project "Electricity as a Raw Material" is to develop new electrochemical processes in order to utilize excess electrical power for manufacturing chemicals. For subsequent pilot production and system integration, it means the processes must be modularized and distributed, and electrochemical production at existing Fraunhofer Group facilities made more adaptive. New technologies and scientific expertise are being developed for future "Power-to-Chemicals" industrial processes that will subsequently be marketed as part of long-established value-added chains. This should lay the scientific and technological foundations for manufacturing products using an increasingly CO_2-free mix of electrical power sources.

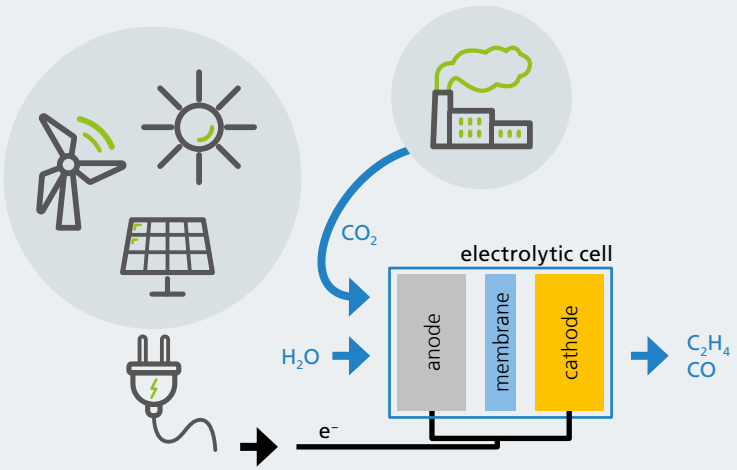
Synthesis pathways – hydrogen peroxide or CO_2 conversion

The technological focus of the Fraunhofer Lighthouse Project is to develop new electrochemical processes, concentrating on two synthesis pathways.

- One pathway is oriented toward electrochemical manufacture of hydrogen peroxide (H_2O_2) from oxygen and hydrogen, with prototype demonstrations of the process in a distributed facility. H_2O_2 is employed as an environmentally friendly oxidant for diverse applications in the chemical, paper, and textile industries. Responsibility for this subproject lies with the Fraunhofer Institute for Chemical Technology ICT.
- The second pathway's goal is to electrochemically or electrocatalytically convert CO_2 for manufacturing fundamental hydrocarbon compounds like alkenes and alcohols, demonstrating the technology at the pilot-plant scale. Development of a demonstration setup for one-step electrosynthesis of ethylene from CO_2 by means of gas diffusion electrodes is being led by Fraunhofer IGB. Another setup for one-step electrosynthesis of C1–C4 alcohols from CO_2 using high-pressure techniques is being led by the Fraunhofer Institute for Environmental, Safety and Energy Technology UMSICHT, while a third setup using two-step activation of CO_2 by H_2 for synthesizing C4–C20 alcohols is being led by the Fraunhofer Institute for Ceramic Technologies and Systems IKTS.

All of these development projects are being paralleled by process simulations (at the Fraunhofer Institute for Industrial Mathematics ITWM) as well as by joint development of electrochemical components and process analysis systems by

1



2

Fraunhofer ISC, IST, and IAP. A work package for system analysis and sustainability considerations carried out by Fraunhofer IGB and UMSICHT rounds out the project.

Electrochemical generation of ethylene

Fraunhofer IGB is coordinating the sub-project entitled "Development of a new one-step electrochemical process with which alkenes, mainly ethylene, will be electrochemically produced from CO_2 and water". The primary innovation in this sub-project consists of producing ethylene or other alkenes through direct reduction of CO_2 in just a one-step process. The goalpost for the process is to demonstrate ethylene production on a scale of one kilogram per day.

A total of four departments at Fraunhofer IGB are working together on this project. The BioCat group in Straubing is looking after the development of the catalysts, optimizing reaction of the electrodes, and characterizing the materials. The research focus of the Department of Interfacial Engineering and Materials Science is developing and characterizing charge-carrying materials (membranes and gas diffusion electrodes) as well as characterizing and optimizing interface phenomena at triple-point phase changes. The Department of Physical Process Technology is looking after the electrode configuration, system integration and setup, and the testing and optimizing of the pilot plant. The necessary measurement, monitoring, and control engineering is being contributed by the Department of Environmental Biotechnology and Bioprocess Engineering.

The development is being carried out in close cooperation with the parallel work packages for process simulation (Fraunhofer ITWM) and component development & process analysis (ISC, IST and IAP).

Contact

Dr. rer. nat. Uwe Vohrer
Phone + 49 711 970-4134
uwe.vohrer@igb.fraunhofer.de

Dr. rer. nat. Thomas Schiestel
Phone + 49 711 970-4164
thomas.schiestel@igb.fraunhofer.de

Funding

The Fraunhofer-Gesellschaft intends to strengthen Germany as a center for commerce by rapidly transforming original scientific ideas into marketable products through the Lighthouse Project initiative.

Project partners

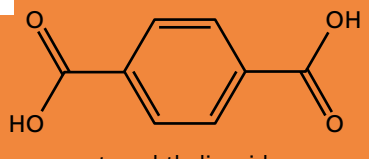
Fraunhofer institutes IAP, ICT, IGB, IKTS, ISC, IST, ITWM, IVV (advisory role), UMSICHT, WKI

Further information

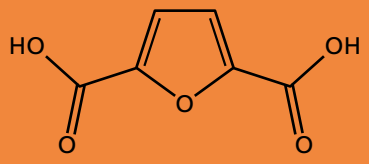
www.strom-als-rohstoff.fraunhofer.de

1 *If electricity generation is expanded by weather-dependent energy sources like wind and solar, excess electrical power will become available for use in electrochemical processes.*

2 *Principle behind electrochemical manufacture of ethylene from CO_2.*

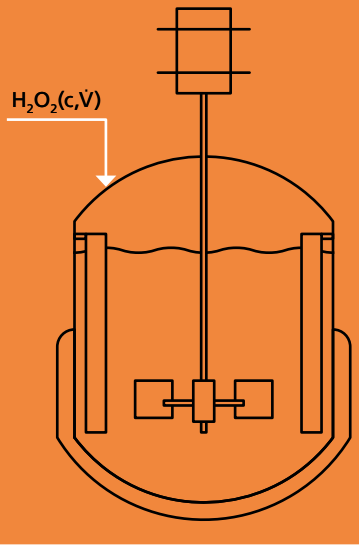


terephthalic acid



2,5-furandicarboxylic acid

1



2

BIOBASED MONOMERS FOR POLYMER CHEMISTRY – FROM LAB TO PILOT PLANT

Fabian Haitz, Björn Vater, Nicole Werner, Susanne Zibek

Polymers from renewable resources

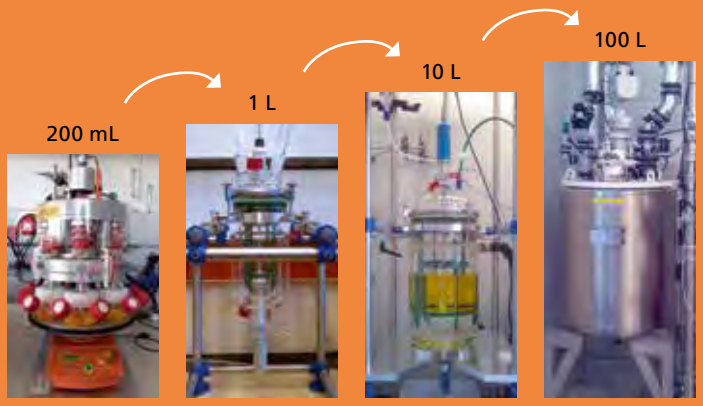
Experts as well as laypeople associate the terms "polymer" and "plastic" with chemistry in its early form. Actually, petroleum-based monomers are constituted through chemical synthesis and subsequently combined catalytically with the help of macromolecular chemistry into long chains – the polymers. Thus, polymer chemistry is strongly bound up with reagents derived from petrochemicals. This leads to a strong dependence on petroleum supply. The utilization of locally available renewable raw materials would reduce this dependence on oil-exporting nations and additionally could make manufacturing more sustainable.

The European BioConSepT project has taken this into account in its approach and is working to bridge biology and chemistry. The 29 project partners from throughout Europe have pursued development of a variety of important industrial feedstock compounds from a starting point of second-generation renewable raw materials such as lignocellulose and oils not used in the foodstuffs sector. They have worked jointly to "biologize" production of these compounds. The task of Fraunhofer IGB in the consortium has been to develop biotech-based production of plant oil-based epoxides, 2,5-furandicarboxylic acid (FDCA) and long-chain dicarboxylic acid (DCA), and to optimize their manufacture at the lab-scale in order to subsequently transfer these processes to the pilot-plant scale. Modeling experiments for this scale-up were carried out in the lab using scalable reaction vessels and fermenter. Using certain dimensionless scaling factors that had been derived from these experiments, the IGB group was then able to design the processes for the proportionately larger pilot plant. Chemo-enzymatic production of the epoxides using enzymes was able to be carried out successfully at pilot-plant scale to demonstrate the potential of the biotechnical processes.

2,5-furandicarboxylic acids and long-chain dicarboxylic acids

FDCA and DCA are important building blocks in chemical synthesis due to their bifunctionality. In the case of FDCA, the big potential comes from its high degree of homology with terephthalic acid (PTA). The research group was able to successfully develop and demonstrate whole-cell catalysis using *Pseudomonas putida* through the addition of hydroxymethylfurfural from biomass containing lignocelluloses. A yield of more than 80 percent with concentrations of up to 20 g/L of FDCA was able to be achieved through carefully guiding the reaction in the laboratory.

Similarly, dicarboxylic acids were synthesized using a whole-cell catalytic process to convert long-chain monocarboxylic acids (MCA). A microorganism named *Candida viswanathii* carries out this task with very high selectivity; concentrations of up to 100 g/L of 1,18-octadecenoic acid have been achieved. In addition, monocarboxylic acids with varying lengths of carbon chains (C9, C16–C22) were successfully converted to their corresponding dicarboxylic acids.



3

4

Epoxides from plant-based oils and waste products

The utilization of specific enzymes for manufacturing epoxides from oils was also pursued within the project. Epoxides possess a sterically strained reaction group that can be linked to other molecules through ring-opening polymerization reactions (ROP). Epoxides are normally constituted from hydroperoxides under extreme chemical conditions. In contrast, epoxidation of oils using enzymes offers an avenue of producing a functional monomer from renewable natural resources as well as from waste streams with the help of a lipase under gentle conditions. In addition, the renewable raw material does not compete for agricultural land with the production of foodstuffs.

A process was developed in the BioConSepT project that employs immobilized lipases for manufacturing epoxides. This results in lower effort and expense in separating the epoxide reaction products and in the reusability of the enzyme. Fraunhofer IGB optimized the process at the 10-liter scale, carried out dimensional analyses for understanding the mechanisms of the process, implemented a 100-liter scale-up in the pilot plant at Fraunhofer CBP, and evaluated the results. The process was carried out five times in a row at repeated epoxide yields of over 80 percent while re-using the same enzyme charge, demonstrating the recyclability of the enzyme. The resultant epoxide was separated by chemistry companies, refined, and tested for use as a softening agent in PVC.

Contact

Fabian Haitz M. Sc.
Phone +49 711 970-4213
fabian.haitz@igb.fraunhofer.de

Dr.-Ing. Susanne Zibek
Phone +49 711 970-4167
susanne.zibek@igb.fraunhofer.de

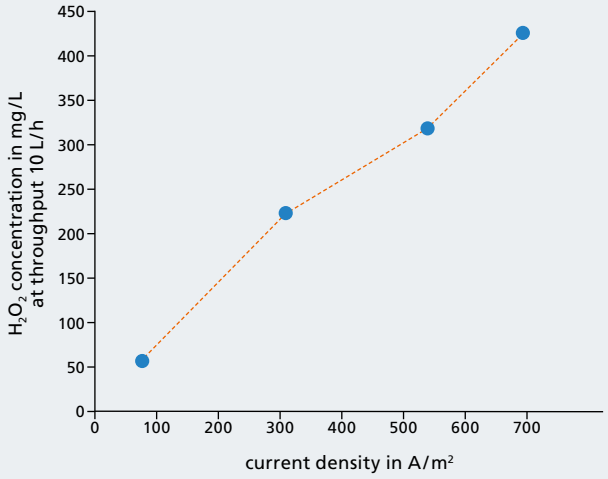
Funding

The research project "BioConSepT" has received funding from the European Union's Seventh Framework Programme for research, technological development, and demonstration under grant agreement no 289194.

Further information and project partners

www.bioconsept.eu

1 *Structural comparison of petroleum-based terephthalic acid with FDCA manufactured using renewable raw materials.*
2 *Schematic representation of a stirred reaction vessel that can be scaled thanks to its standardized geometric relationships.*
3 *Sequence from lab scale to 100-liter stirred vessel.*
4 *Fractions of vegetable oils not used in the food industry as sources for biobased monomers.*



1

ELECTROLYTIC GENERATION OF HYDROGEN PEROXIDE

Christiane Chaumette, Carsten Pietzka, Behnam Parwizi, Thomas Scherer

Decentralized production of H_2O_2

Hydrogen peroxide, which is a platform chemical with a wide range of applications, is produced commercially in centralized chemical plants today. Areas of application are, for example, pulp and paper processing and water treatment, as well as applications with smaller consumption volumes such as plant and surface disinfection in food processing facilities and hospitals. When hydrogen peroxide is transported it is classified as a hazardous good, so transportation is cost-intensive, which will burden its use in future. That is why, together with industrial partners, Fraunhofer IGB has developed a concept for producing hydrogen peroxide on-site and by using electric power and an electrochemical cell.

The decentralized production of hydrogen peroxide in concentrations and volumes below the explosion threshold is attractive for two reasons. On the one hand, this option reduces the risk and cost of transportation, storage and handling; on the other, electrolytic generation from electricity allows for a flexible operation of the production process. This will be especially cost-effective in future when surplus electricity could be used to balance out peaks of power supply to the grid as a consequence of intermittent, regenerative power generation.

The electrolytic generation of hydrogen peroxide for water treatment was demonstrated with landfill leachate in the research project "Oxfloc – Integrated water treatment in a one-stage oxidative-adsorptive process to degrade and remove harmful substances", which is funded by the European Union. In this project a treatment process was developed that accomplishes oxidative and adsorptive removal of pollutants from landfill leachate in one treatment step by combining two electrolytic processes. For demonstration, power from solar cells was used in the demonstration plant for the treatment of the leachate.

Electrolytic cell for various applications

The electrolytic cell developed at IGB has a controlled flow across the area of the electrodes (Fig. 2). Oxidation reactions occur at the anode and the pH value decreases while, cathodically, at a gas diffusion electrode converting oxygen and protonated water molecules, a hydrogen peroxide solution is produced and oxygen as well as protons are consumed.

In initial trial runs with the addition of oxygen, concentrations of > 400 mg/L hydrogen peroxide (Fig. 1) were achieved in sodium sulfate solution (50 mM). With air supplied, H_2O_2 concentrations of 50 mg/L were attained with an energy requirement of 10 kWh/kg H_2O_2. The cell is operating with a continuous flow; there is no recirculation of the solution. Modular designed systems incorporating these cells can be flexibly adjusted to the customer's individual need for hydrogen peroxide.

The pH value and the concentration of the solution can be adjusted by selecting the process conditions (divided/undivided electrolytic cell, volume flow and composition of the solution, current density and temperature) and of the electrode material. This allows for an energy-optimized treatment of the water flow and enables it to be reutilized within the framework of the integrated water management of industrial processes.

Outlook

In future we will investigate and evaluate further gas diffusion electrodes for electrosynthesis in order to produce chemicals on site and to offset power peaks caused by fluctuating regenerative electricity supply, by converting flexibly the electric energy into basic chemicals. To develop the process, scalable and adaptable continuous flow cells are available that enable a wide range of development tests by changing the gas diffusion layer.

Also, the flat cells with an electrode area of 90 – 140 cm^2 are suitable for benchmarking various gas diffusion electrodes and their catalysts, as well as for stability tests and feasibility studies in real-life process solutions and wastewater.

Applications

Besides the treatment of wastewater directly at the point of origin, initially applications will be developed with smaller consumption volumes, in areas such as the hygienization of plants and machines in the food industry or surface disinfection in hospitals. The production of chemicals on an industrial scale is a medium-term objective.

1 *Generation of hydrogen peroxide with oxygen in saline solution.*

2 *Electrolytic cell with 130 cm^2 anode area in its quick-action clamping device.*

Contact

Dr. rer. nat. Thomas Scherer
Phone +49 711 970-4091
thomas.scherer@igb.fraunhofer.de

Dipl.-Ing. Siegfried Egner
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

Funding

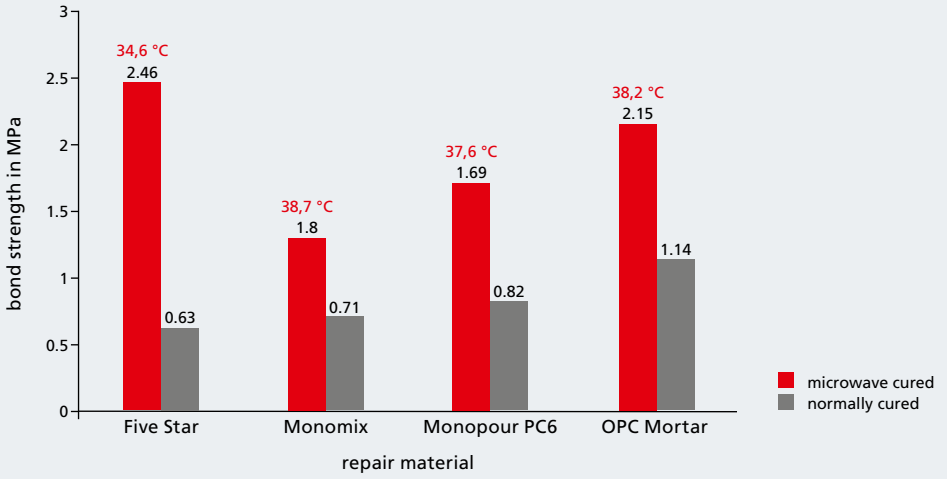
The project "Oxfloc" has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 606216. The above report is based partially on results from this Oxfloc research.

Project partners

Magneto Special Anodes BV, Schiedam, Netherlands | Bamo Mesures SAS, Argenteuil, France | Eilenburger Elektrolyse- und Umwelttechnik GmbH, Eilenburg, Germany | E.R.S. Steuerungstechnik GmbH & Co. KG, Osterburken, Germany | ASIO spol. s r.o., Brno, Czech Republic | Acondicionamiento Tarrasense Associacion, Terrassa, Spain

Further information

www.oxfloc.eu



1

MCure – ADVANCED TECHNOLOGY FOR EFFICIENT REPAIR OF CONCRETE STRUCTURES

Chen Zhao, Ali Imran Javaid, Simone Mack, Siegfried Egner

Concrete repair and curing

Large numbers of concrete structures such as bridges, tunnels, dams, and harbors have reached a state, or will do in the long term, where repair is necessary. This is due to a variety of disintegration mechanisms in the concrete, excessive loads or poor workmanship. According to CON REP NET, over 50 percent of Europe's annual construction budget is spent on rehabilitation and refurbishment projects, in particular for the repair of damaged concrete structures [1]. This has generated a requirement for technology that will result in more durable and effective repairs to concrete structures. In addition to concrete repairs, efficient curing of concrete is also important in the production of finished parts.

The curing of concrete is strongly dependent on the course of the process temperature and thereby on the ambient temperature. This limits work in colder climates on a seasonal basis. Therefore, the "MCure" project has developed a scientifically novel system for the stimulation of the curing process that is independent of the outside ambient temperature. It is based on the use of microwaves and is characterized by low energy consumption and high temporal efficiency.

Curing process

Optimized curing of concrete and achievement of the desired strength requires the maintenance of a specific moisture content and corresponding temperature profile in the concrete for a period of time after placement and surface finishing. The combined effect of heat, or the internal changes in temperature, and duration of curing on the development of strength is referred to as "maturity". This increases rapidly over the first 24 hours of the curing process, after which it slows down significantly and lasts for an indefinite period.

Optimum strength is achieved in concrete with high temperature curing. The magnitude of the increase in temperature and its duration requires precise control over a specific cycle. Such a rapid rise in temperature can only be achieved through the use of an external energy source, e.g. microwaves, and requires precise sensor technology, controlled by operating algorithms. Reliable processing of concrete under unfavorable weather conditions is currently only possible for precast concrete parts with the use of steam heating.

Curing fresh concrete with microwaves

The curing process can be accelerated with the use of microwaves, that mainly interact with the moisture in the concrete. The moisture contents in the concrete are highly polar due to the high electronegative nature of oxygen and the electropositive nature of hydrogen. The electric field produced by the microwaves induces oscillations whilst travelling through the materials with a bipolar molecular structure. During this process, the moisture is vaporized and migrates to the surface of the material via diffusion. The curing process starts with the direct interaction between the water molecules and microwaves and partly also with the heat generated inside the concrete. This results in the development of a more rapid effect during the first phase of curing.

When curing concrete, the priority is not to achieve maximum speed of vaporization, but to generate temperatures that are sufficiently high (relative to ambient temperature) to promote

2

diffusion and evaporation, such that more accelerated curing is made possible. The substrate interface is the most critical zone in a portion of concrete requiring repair and this is usually where problems occur in relation to adhesion. Thanks to the deep penetration of microwaves into the material, the repair substrate interface is also acted on effectively.

Field trials with a prototype

Field trials have been carried out on samples with a variety of volumes using microwave powers of varying intensities, based on which optimum process parameters were defined. The results demonstrate the ability of the MCure system to outperform the current standard concrete curing techniques.

Advantages of the MCure system

The system can be used throughout the year, independent of climatic conditions, for rapid, durable and high quality repairs and refurbishments. It makes more efficient use of resources, especially in harsh winter conditions, due to the robustness of the system and the effectiveness of the technology in all kinds of weather. This technology improves both the durability and strength of the repaired concrete. Furthermore, this novel curing technique makes a contribution toward advancements in the fields of remote moisture sensing and concrete compressive strength.

Outlook

MCure was shown to enhance the quality of the concrete curing process in a demonstrator. A mobile and – through robotics – flexible system will now be developed jointly with industrial partners and will be tested in a follow-up project on a construction site. The system will then be licensed and made available on the market.

Contact

Dipl.-Ing. Siegfried Egner
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

Literature

[1] Vimmr, V. (2004) Future performance discussion on industry response to owners' aspirations, CON REP NET Network Newsletter No. 4

Funding

The research project "MCure" has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 605664.

Project partners

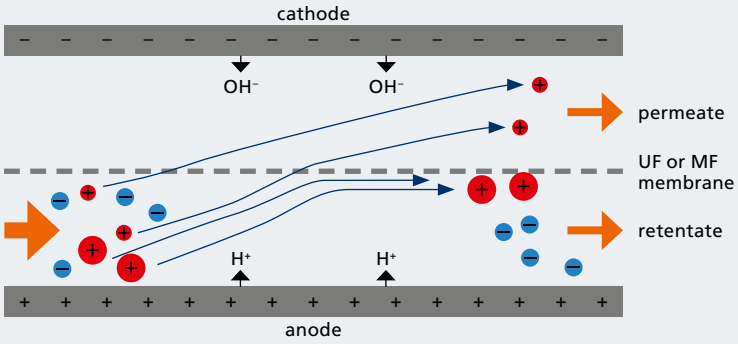
Uvasol Ltd, Leicester, UK | Meta Automation Ltd, Piräus, Greece | Jörg Heizmann Bauunternehmung GmbH, Osterburken, Germany | E.R.S. GmbH, Osterburken, Germany | Utingal S.L., Pontevedra, Spain | Sheffield Hallam University, Sheffield, UK

Further information

www.mcure-fp7.eu

1 *Bonding strength of MCure vs. normally cured repair at –5°C ambient temperature.*

2 *Overview of the MCure System.*



1

ENHANCED PROTEIN FRACTIONATION FOR USE IN FOOD APPLICATIONS

Ana Lucía Vásquez Caicedo, Carsten Pietzka, Fabiola Salguero del Valle, Salima Varona Iglesias

Food protein market trends

Consumers' awareness of health and wellness issues is increasing, thus driving market growth of food protein ingredients worldwide. Accordingly, whey proteins have attracted major attention for applications in infant formula, sports and clinical nutrition due to their health and nutritional benefits. Moreover, whey protein fractions have the potential to replace chemical additives in formulations due to their extraordinary technofunctional properties, including foaming, emulsifying, gelling and their water-binding potential. Whey is obtained in large quantities as a by-product in cheese manufacturing and is therefore available at low raw material costs.

In Europe, only 10 percent of liquid whey is currently transformed into food and human nutrition products. 60 percent of the whey produced is disposed of in municipal sewage systems, creating serious environmental problems. The main reason is the limited technological ability of dairies, specifically SMEs, to use this valuable resource appropriately.

Technological challenges

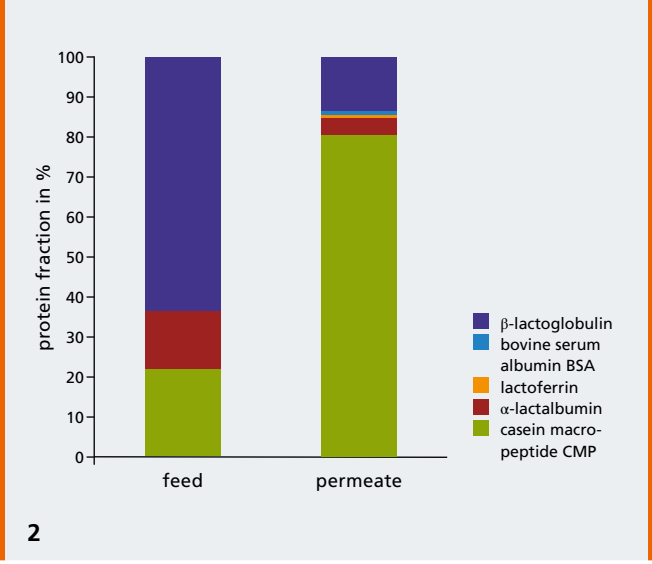
Current technologies for protein fractionation and concentration are still laborious and require several processing steps, the use of chemicals, large amounts of eluents or buffers or need huge cleaning efforts due to membrane fouling and have high membrane replacement costs (e.g. ultrafiltration). In addition, acids, alkalis and high temperatures are often needed to achieve separation, causing protein denaturation and diminishing product quality. In general, these technologies are difficult to up-scale and are associated with additional environmental problems due to disposal of chemicals and the large amounts of wastewater generated. An economic and sustainable solution for the valorization of whey is therefore urgently needed.

Electro-membrane filtration

The Whey2Food project aims to develop a highly efficient, selective, gentle and economically attractive electro-membrane filtration (EMF) technology to enhance separation and concentration of proteins and peptides from whey. This technique combines an electric field with mechanical membrane filtration. The driving gradient for the material transport across the membrane can be generated both by the transmembrane pressure and the electric field applied. This enables the separation both on the basis of the electric charge and the particle size (Fig. 1). Fraction purity and economic yields are increased due to the ability of EMF to increase the filtration flow rate and minimize membrane fouling, cleaning efforts and membrane replacement costs.

Transfer to an industrial scale

During this project, enriched whey protein fractions are obtained by selecting appropriate electrode material and cell configuration parameters, including placement of filtration membranes and electrode shielding membranes, electric field strength, pH, fluid temperature, fluid pressure gradient and membrane cut off (pore size). The aim is to obtain a full understanding of the EMF process and its interferences with whey and the compounds contained in it; also, to create a knowledge base that supports the development of an optimal system configuration at laboratory level and enables the scale-up of the process into a demonstration prototype suitable for use in an industrial relevant environment.



2

3

Optimized process for fractionation

The project focused on the enrichment of a whey protein suspension containing casein macropeptide (CMP), the hydrophilic fraction of κ-casein that remains in the whey. Separation of CMP from α-lactalbumin (α-La) and β-lactoglobulin (β-Lg) requires a fine adjustment and monitoring of parameters due to the narrow range in which their isoelectric points are found. The electric field applied is able to retain these substances at the retentate side while CMP is transmitted to the permeate under the influence of the transmembrane pressure. Commercial benchmark formulas report a CMP concentration ranging from 75 to 85 percent of total protein. Accordingly, our laboratory trials successfully enriched CMP to a concentration of 81 percent of total proteins transmitted to the permeate (Fig. 2), increasing over 10-fold the CMP/β-Lg ratio in a single step.

After process optimization at laboratory level, a pilot unit was developed. The core of this unit is an optimized EMF cell, which takes into account an optimum distribution of electric field, minimizes pH shifts and ensures the adjustment of the crossflow and transmembrane pressure to the required range. The unit operates in semi-batch mode (feed and bleed) with feed flow of 1000 L/h at optimum transmembrane pressure conditions (Fig. 3). Validation of the process up-scale is ongoing.

1 *Operation principle of electro-membrane filtration (EMF).*
2 *Enrichment of casein macropeptides via electro-membrane filtration.*
3 *Whey2Food pilot plant.*

Contact

Dr. rer. nat. Ana Lucía Vásquez Caicedo
Phone +49 711 970-3669
analucia.vasquez@igb.fraunhofer.de

Dr.-Ing. Carsten Pietzka
Phone +49 711 970-4115
carsten.pietzka@igb.fraunhofer.de

Literature

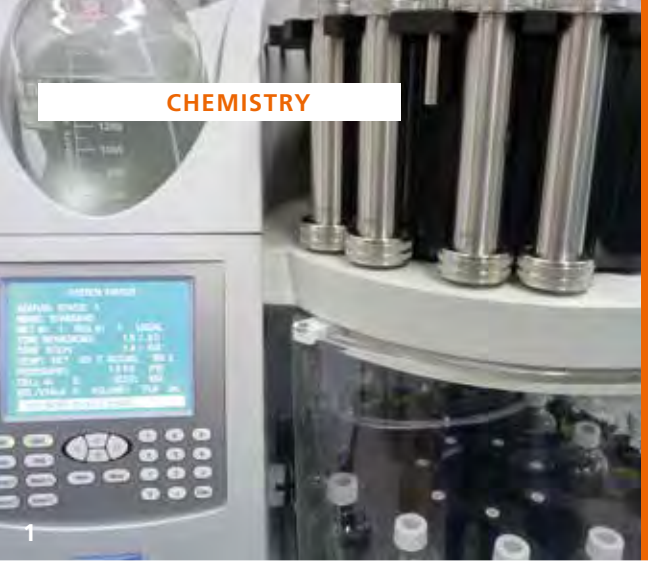
[1] European Whey Products Association. http://www.euromilk.org/ewpa/content_html (accessed on September 1, 2013)
[2] Electrofiltration of Biomaterials; Electrotechnologies for the extraction from foodplants and biomaterials (2008) Springer Science and Business Media, ISSN: 1571–0297
[3] Post, E. A.; Rapp, F.; Hinrichs, J. (2010) Separation of Caseinomacropeptide from whey by means of electrically enhancend cross-flow membran filtration. European Diary Magazine 3: 30–33.

Funding

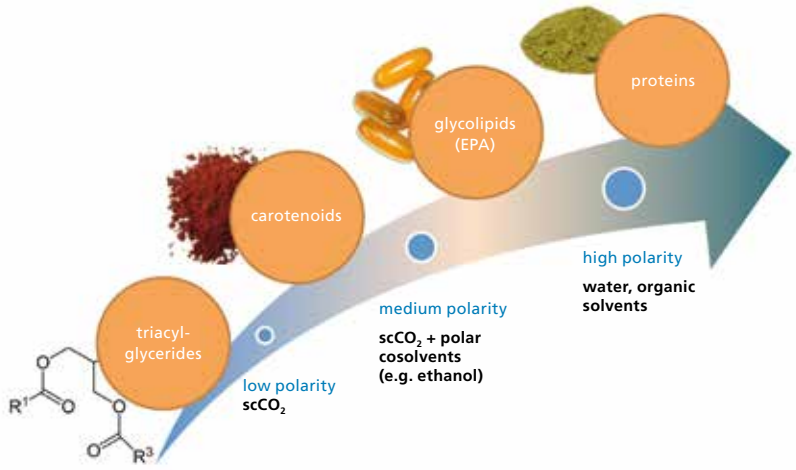
The project "Whey2Food – Enhanced protein fractionation from protein sources for their use in special food applications" has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 605807.

Further information and project partners

www.whey2food.eu



1



2

CASCADE USE OF MICROALGAE BIOMASS

Felix Derwenskus, Ulrike Schmid-Staiger

Microalgae – Integrated Use for Food and Feed

The fundamental idea of biorefinery concepts is the complete reutilization of biomass by means of fractionation and the extraction of various products. Microalgae can produce a large number of substances that are of interest to the food and feed sector. Depending on the species used and the cultivation conditions, they produce large quantities of fatty acids in the form of triacylglycerides (up to 70 percent of dry weight) or proteins (up to 50 percent of dry weight), polar membrane lipids with omega-3 fatty acids (up to 7 percent of dry weight) as well as various carotenoids and phytosterols. The aim is to use these fractions in food production while preserving their technofunctional, nutritional and physiological properties.

Due to the great diversity of ingredients and the different cell wall characteristics of various species of microalgae, it is necessary to carry out selective processing of the biomass in order to effectively extract the high-quality nutrients. The objective of the joint research network "Microalgae – Integrated Use for Food and Feed" in the Baden-Württemberg Bioeconomy Research Program is to utilize various fractions as completely as possible, in interconnected and cascade use, in order to develop sustainable processes for the bioeconomy.

Processing of algae constituents

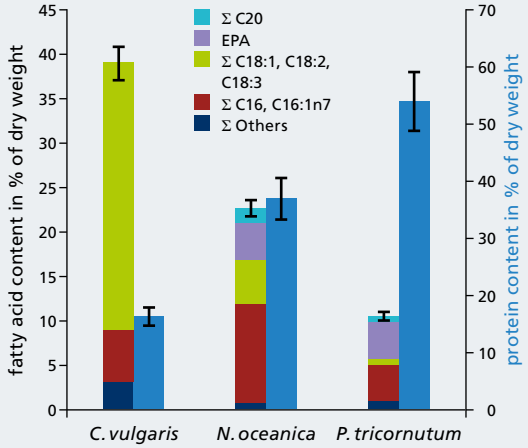
Special requirements apply to processing in the extraction of valuable compounds from algae biomass and the further use of the residual biomass, especially in cascade utilization. Basically the chemical character and the market specifications, for example the required degree of product purity, determine the processing technique. Further requirements are avoiding, as far as possible, an energy-intensive drying step as well as ensuring gentle extraction that both maintains the functionality and permits the extraction of further cell components.

Working together with the partners in the research network, three strains of microalgae (*Phaeodactylum tricornutum*, *Chlorella vulgaris* and *Nannochloropsis* spec.) were selected that differ fundamentally in cell size, formation of the cell wall and biomass composition. By combining successive extraction processes in various sequences, the objective is to obtain in particular the principal fractions consisting of proteins, polar membrane lipids with omega-3 fatty acids as well as nonpolar triglycerides sequentially from the microalgae biomass – in addition to the high-value components such as carotenoids.

Selective and targeted extraction

The technique called "Pressurized Liquid Extraction" is mainly employed here; this also permits extraction using wet biomass, as well as extraction by means of supercritical fluids (SCF). In order to increase the polarity of supercritical fluids, cosolvents such as ethanol can be employed. This results in a selective extraction of polar glycolipids containing eicosapentaenoic acid EPA; 20:5 ω-3. The different extraction behavior without and with a cosolvent was also used specifically for the sequential, selective extraction of nonpolar triglycerides, carotenoids and polar glycolipids. Currently the process parameters are being optimized with the aim of obtaining fractions that are then examined by the research partners in regard to an application in the food sector. After extraction of the lipophilic valuable compounds the aim is to separate the proteins from the residual biomass, so as to make them available for the production of novel foods by project partners. The residual biomass is suitable for animal feed production.

3



4

Outlook

The aim at the end of the project is to have a matrix of methods available for the processing of algae biomass that can be transferred to biomass of various algae species, with a different material composition in each case and with different target fractions. This would contribute a big step towards using microalgae holistically for nutritional purposes as well as an important step towards a biobased economy.

1 *Pressurized Liquid Extraction unit in laboratory scale (Dionex, ASE 350).*

2 *Utilizable algae ingredients with increasing polarity and the corresponding solvents used for extraction.*

3 *Extracts of microalgae biomass (from left to right): N. oceanica, P. tricornutum und C. vulgaris. The different color is caused by strain-specific carotenoids.*

4 *Fatty acid profile and protein content of algae biomass.*

Contact

Dr. rer. nat. Ulrike Schmid-Staiger
Phone +49 711 970-4111
ulrike.schmid-staiger@
igb.fraunhofer.de

Felix Derwenskus M. Eng.
Phone +49 711 970-4074
felix.derwenskus@igb.fraunhofer.de

Funding

The project is conducted at the Institute of Interfacial Process Engineering and Plasma Technology IGVP, Fraunhofer IGB's partner institute at the University of Stuttgart. We would like to thank the Baden-Württemberg Stiftung and the Ministry of Science, Research and the Arts of the State of Baden-Württemberg for funding the project "Microalgae – Integrated Use for Food and Feed. Partial Project: Development of Cell Disruption and Extraction Processes for the Cascade Utilization of Microalgae Biomass" (Mikroalgen – Integrierte Nutzung für die Ernährung. Teilprojekt Entwicklung von Zellaufschluss- und Extraktionsverfahren zur Kaskadennutzung von Mikroalgenbiomasse) in the Baden-Württemberg Bioeconomy research program, reference no. 7533-10-5-93.

Further information

www.bioeconomy-research-bw.de/mikroalgen

ENVIRONMENT

Against the backdrop of the global debate on global warming, resource scarcity and water pollution, resource and environmentally friendly economies are all the more important. In national and international projects with partners from research, industry and communities, the Fraunhofer IGB is developing innovative processes, reactors and apparatuses for a sustainable treatment of urban wastewater and industrial process water, exhaust air, contaminated soils and wastes. The environment business area thus stands for a variety of advanced technological developments that help to prevent a negative impact on the environment, and that combines economy with sustainability. Tasks and resolution approaches are, in many cases, linked with major topics in the business areas energy and chemistry.

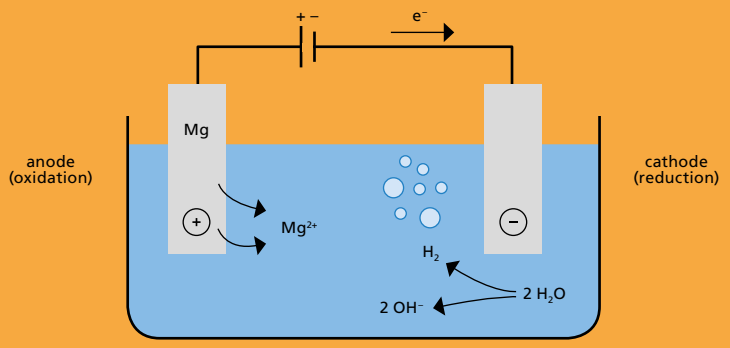
Recovery of secondary raw materials – Due to the finiteness of primary raw materials, we develop processes which enable recovery from production and waste streams for reuse as secondary raw materials – in a quality equivalent to that of primary raw materials and with a comparable process complexity. For inorganic raw materials (metals, rare earths), for example, we develop new reprocessing methods by which dissolved mixtures can be selectively separated on a molecular or atomic level. In the area of soil, we conceive of and realize methods for the recovery and processing of dissolved or organically bound phosphorus for use as high-quality fertilizers and soil conditioners.

Improving resource efficiency – In order to increase the efficiency of the raw materials used, our goal is to establish closed loop recycling systems as completely as possible. An example is the entire utilization of biogenic resources, where we combine a cascaded use of the material with energy recovery. In the regenerative production of algal biomass for material and energy use, an additional focus, the climate is saved through the fixation of carbon dioxide and high-value raw materials, such as for organic crop protection.

Wastewater treatment – Fraunhofer IGB offers innovative, infrastructural concepts as solutions, each of which is adapted to geographic, demographic and regional parameters, for an economical and ecological, semi-decentralized energy and water management. We use a variety of different technologies to prevent the emission of particulate or dissolved, persistent micro-pollutants. The recovery of components from agro-industrial process waters or from municipal wastewater treatment plants in the form of fertilizers combines wastewater purification with material value.

For the inclusion of additional expertise, Fraunhofer IGB is engaged in the Fraunhofer Alliances Building Innovation, Cleaning Technology, Water Systems, Food Chain Management and Energy, the Fraunhofer System Research for "Morgenstadt" as well as in the national technology platform SusChem Deutschland, and is also excellently networked internationally, particularly within Europe.

1



2

ePhos® – ELECTROCHEMICAL RECOVERY OF PHOSPHORUS

Iosif Mariakakis, Uwe Claußnitzer, Jennifer Bilbao, Siegfried Egner

Recovery and recycling of phosphorus

The expansion of the bioeconomy coupled at the same time with the increasing demand for food worldwide is resulting in a growing demand for fertilizers, especially those containing phosphorus. However, the supply of phosphorus fertilizers is determined by the declining purity of the storage sites combined with a decrease in the phosphorus concentrations, so that the costs for both extraction and processing are rising. Likewise, the costs for the production of synthetic nitrogen fertilizers are increasing due to the high primary energy requirements. A way out of this situation in terms of sustainability is the recycling of the essential nutrient elements phosphorus (P), nitrogen (N) and potassium (K). These have to be recovered from material cycles in industrial production, the reutilization of foodstuffs, municipal wastewater and from the bioenergetic processing of waste.

Fraunhofer IGB is developing and implementing sustainable, cost-efficient technologies and strategies for the integrated management of resources. One of the key areas is the development of new technologies for recovering nutrients from wastewater and organic waste.

Electrochemical phosphate precipitation from wastewater

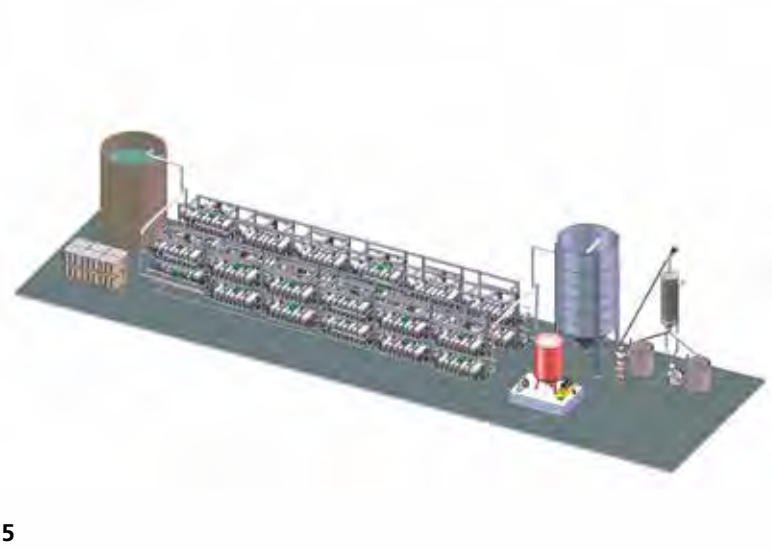
Fraunhofer IGB has developed the ePhos® process to recover ammonium (NH_4^+) and phosphate (PO_4^{3-}) from the filtrate water resulting from municipal wastewater treatment. The phosphate is precipitated electrochemically without any use of chemicals. During this process, phosphate precipitates as magnesium-ammonium-phosphate ($MgNH_4PO_4$*6 H_2O, MAP or struvite) (Fig. 1). The electrochemical phosphorus precipitation takes place in an electrolytic cell consisting of an inert cathode and a sacrificial anode of magnesium (Fig. 2). Water molecules are split by the cathodic reduction, forming OH^- ions that raise the pH-value. As a result, it is not necessary in the ePhos® process to adjust the pH value by dosing chemicals. Oxidation occurs at the anode: magnesium ions are released into the solution and react with the phosphorus and nitrogen in the water to form struvite.

Feasibility study in a pilot plant

In the course of a feasibility study the process was tested using a pilot plant (Fig. 3) with a flow rate of up to 1 m^3/h at a sewage treatment plant with biological phosphorus elimination in North Germany. We were able to demonstrate to the client that the phosphorus precipitation and recovery from the centrate water by means of the electrochemical ePhos® process can be carried out at the client's treatment plant, so that a full-scale plant would solve major operational problems caused by the fluctuating orthophosphate concentrations. All the trials were carried out successfully. The average phosphorus elimination rate from the centrate water of the digested sludge dewatering and the phosphorus conversion to struvite was more than 80 percent. The phosphorus concentration in the centrate water was reduced by an average of 180 mg/L to 20.8 mg/L. The phosphorus load that no longer has to be treated when the filtrate water is recirculated, decreases by 37 percent; this amounts to 9284 kilograms annually and results in a reduction of sludge production by 7 percent. The design of the process for the client's plant shows that the electrochemical phosphate precipitation would require approx. 10 tons of magnesium in the form of sacrificial electrodes per year. From this, approx. 73 tons of struvite per year would be

3

4



5

obtained which can then be used directly as a fertilizer. The total quantity of chemicals that would have to be used at the treatment plant would decrease by 40 tons or 20 percent per year.

Industrial-scale implementation with flat-panel reactors

With the results from the first pilot tests, in which tubular electrolytic cells were used (Fig. 3), the process was further developed with flat-panel reactors for industrial use (Fig. 4). At the WEFTEC (Water Environment Federation's Annual Technical Exhibition and Conference) in October 2015 we presented the process for market launch in the USA. Biological phosphorus elimination with subsequent stabilization of the biomass in anaerobic stages is being employed to an increasing extent at sewage treatment plants in North America. In this method of operation, phosphorus has to be specifically removed from the sewage treatment process to avoid uncontrolled precipitations in the filtrate water pipes and sludge dewatering equipment, which otherwise would cause enormous damage and operating costs.

Advantages and outlook

The ePhos® plant concept is based on the series connection of electrolytic cells in parallel (Fig. 5). As this is a purely electrochemical process, the cells or cell pathways can be switched on or off by a process control system depending on the demand. This beneficial mode of operation and the efficient, chemical-free operation represent unique selling propositions that insure competitiveness. License agreements for industrial use are at present being concluded with interested parties. The first industrial-scale plant in the USA is to be built and put into operation by the end of 2016. In the future, further process modules will be added to the ePhos® process in order to achieve sustained cycle management of the nutrients at sewage treatment plants.

Contact

Dr.-Ing. Iosif Mariakakis
Phone +49 711 970-4231
iosif.mariakakis@igb.fraunhofer.de

Dipl.-Ing. Siegfried Egner
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

Project partner
Ovivo LLC, Austin, USA

1 *Recovered struvite.*
2 *The basic principle of the ePhos® process.*
3 *The ePhos® pilot plant for electrochemical phosphorus precipitation with tubular reactors.*
4 *An enhanced ePhos® pilot testing with flat-panel reactors.*
5 *Planning study of an industrial-scale ePhos® plant for a sewage treatment plant with 70,000 PE to recover approx. 73 t/a struvite from 200 m³/d filtrate water with 250 mg/L orthophosphate.*

THE ULTRA-EFFICIENT FACTORY – PRODUCING WITHOUT LOSSES IN A LIVABLE ENVIRONMENT

Ursula Schließmann, Jan Iden

Initial situation

The project "The ultra-efficient factory – Resource-efficient production without emissions in urban areas" aims to create an optimally designed factory that does not cause any environmental impacts and where the resources being used are processed without any losses. As a result, the ultra-efficient factory can also manufacture in urban areas, without impacting negatively on its surroundings. Against this background three Fraunhofer Institutes have set themselves the goal of formulating a concept of how the ultra-efficient factory should be structured, and how existing companies can be evaluated and improved on the basis of this concept. The first phase of the project involved developing the concept of the ultra-efficient factory and establishing a comprehensive maturity model with a scaled indicator model for assessing ultra-efficient factories.

Tomorrow's production

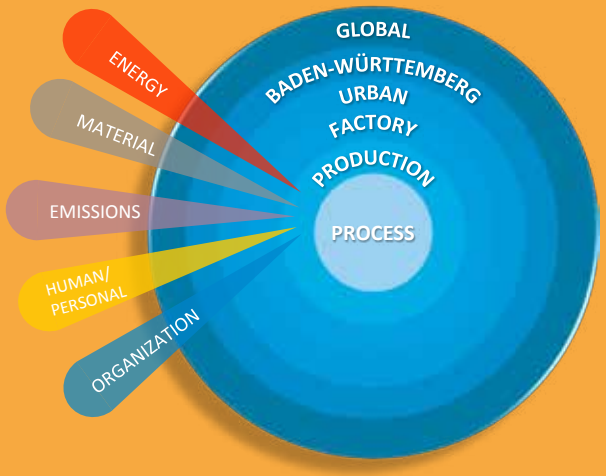
Producing efficiently and effectively to the highest technical standards, at the same time minimizing or avoiding environmental impact and resolving the conflicting aims – in brief, harmonizing future industrial production with urban life – is what lies behind the integrated (holistic) approach of the ultra-efficient factory. The ultra-efficient factory is an approach that reconciles efficiency (diminishing it as little as possible) and effectiveness (as ecologically compatible as possible), and further develops ultra-efficiency. Thus, the focus of attention is no longer on production alone; the whole manufacturing environment is integrated. In the ultra-efficient factory the action fields of energy, materials, emissions, people/personnel and the organization are examined at various levels (Fig. 1). All the topics and areas that are relevant for a company are dealt with and analyzed on the basis of this holistic approach.

The path to ultra-efficiency

Three checks were developed in the project: the Ultra-F-Check Basic, the Ultra-F-Check and the Ultra-F-Check Professional. These checks help companies to classify and upgrade themselves within the context of an ultra-efficient factory. The Ultra-F-Check Basic is an online-based test which gives enterprises an initial assessment – based on the holistic approach – of their status compared with other companies. The test provides a first compact overview of the efficiency of each company.

With the Ultra-F-Check the individual degree of ultra-efficiency is determined at on-site meetings and inspections. After evaluating this check, the potential for improvement can be shown at the various assessment levels of process, production and factory and also in the action fields of energy, materials, emissions, people/personnel and organization. The check provides companies with a comprehensive, integrated approach; they can then plan and implement specific measures for increasing effectiveness and efficiency.

The Ultra-F-Check Professional is a computer-aided detailed analysis of a company. By incorporating specific company indicators, the interactions between various parameters can be demonstrated and optimization measures and their effects can be represented in detail. Besides the interaction between the various parameters – such as the consumption of energy, the use of alternative raw materials and the occurance of residues or waste water – the economic impact of optimization measures is also clearly indicated.



1

2

In order to select suitable optimization measures a comprehensive best practice database was created for the period of the project; this helps the companies to identify the appropriate optimization possibilities to meet their needs. The model of the ultra-efficient factory includes performance indicators, degrees of maturity and examples of best practice to take into account "Supply and Recycling of Raw Materials".

Optimization by means of process technology

Several companies from various branches of industry have already been analyzed and optimized with the help of the Ultra-F-Checks, thus making it possible to try out and further optimize the implementation of the various Ultra-F-Checks. One of our customers discovered the need for optimization in the area of wastewater treatment by carrying out the Ultra-F-Check. As a direct measure Fraunhofer IGB is currently planning a new concept for the treatment of wastewater with sulfate content by means of physical/chemical treatment and subsequent biological purification. As a result of the process optimization, the prescribed threshold values can be complied with more easily and the result is a smaller volume of solids requiring disposal.

Within the scope of the project "The ultra-efficient factory – Resource-efficient production without emissions in urban areas" Fraunhofer IGB's expertise lies in the optimization of process technology in the field of water management, industrial wastewater treatment, environmental technology as well as the recovery of products from organic residues.

Contact

Dr.-Ing. Ursula Schließmann
Phone +49 711 970-4222
ursula.schliessmann@igb.fraunhofer.de

Jan Moritz Iden B. Sc
Phone +49 711 970-4030
jan.iden@igb.fraunhofer.de

Funding

We would like to thank the Ministry of the Environment, Climate Protection and the Energy Sector Baden-Württemberg for funding the project.

Project partners

Fraunhofer IPA, Stuttgart (Project Coordination), Germany | Fraunhofer IAO, Stuttgart, Germany

Further information

www.ultraeffizienzfabrik.de

1 *Action fields and assessment levels of the ultra-efficient factory.*
2 *Integrated approach to sustainable production.*

1

2

MORGENSTADT – CITY LAB TBILISI

Marius Mohr

System analysis for the sustainable city of the future

It was with good reason that the German Federal Ministry of Education and Research choose the motto "Year of Science: City of the Future" for the year 2015. Cities occupy a key role in the sustainable development of humankind. In 2012, the Fraunhofer-Gesellschaft launched the Morgenstadt Initiative with partners from science, municipalities and industry in order to give an impulse for the sustainable development of cities. One outcome was the City Lab – the development of a methodology for the system analysis of cities. The City Lab is based on Frederic Vester's model of sensitivity analysis [1] and the aim is to identify the principal action areas of a city for its future development.

Tbilisi becomes a City Lab

Financed within the framework of the cooperation with Georgia from funds of the German Federal Ministry for Economic Cooperation and Development and with a contribution provided by the City of Tbilisi itself, a City Lab in Tbilisi (Georgia) is being conducted under the leadership of Fraunhofer IGB from June 2015 to March 2016.

The aim of the City Lab is to create a sustainability profile and a roadmap for the sustainable development of a city. A total of 16 different sectors are being examined; taken together, these should provide an almost complete picture of the various action fields in a city. First of all, details of approximately 100 quantifiable indicators are collected and correlated with comparable cities. Then, approx. 80 action fields from the various sectors are assessed to find out to what extent the city in question is already active in each area. Finally, impact factors are determined that are particularly relevant for the city being analyzed and that could explain the developments which have taken place there. These factors may also have an impact on future developments.

On-site assessment shows the need for action

The crucial element in the City Lab is the on-site assessment. Over a period of two weeks the Morgenstadt city team carries out semistructured interviews, inspects important institutions and facilities and completes the collection of data. During the on-site-assessment in Tbilisi at the end of September/ beginning of October 2015 a total of 55 interviews were conducted with representatives of the municipal administration, universities, national ministries, non-government organizations (NGOs) and private enterprises. On October 9, 2015 an Innovation Workshop was held in Tbilisi in which eight initial project ideas were discussed with about 40 actors from Tbilisi.

Sustainability profile and concrete measures

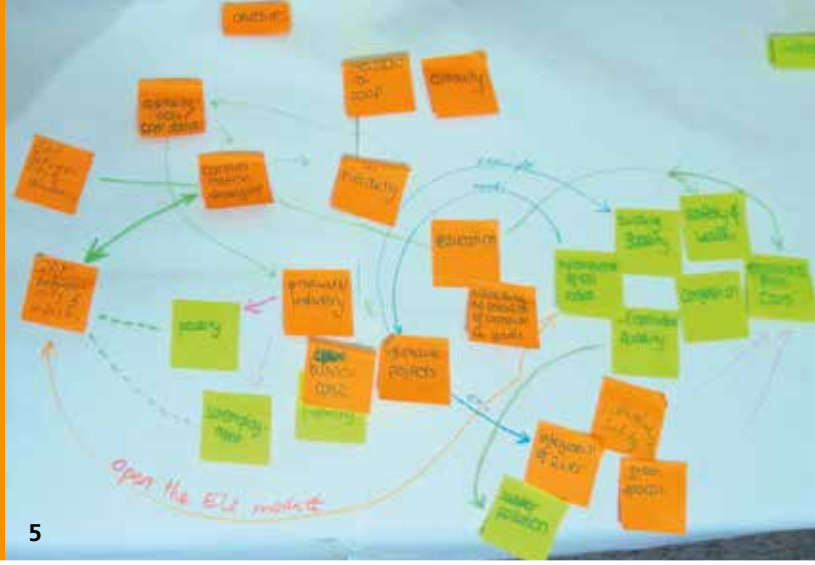
The sustainability profile of Tbilisi was drawn up on the basis of the on-site assessment. Parallel to this, in the course of creating the roadmap, a total of 19 project ideas were worked out from which the Tbilisi city administration selected eight that were further developed for the Project Development Workshop on January 29, 2016. This workshop planned and clearly defined the next steps for the selected projects. These measures are to be set in motion immediately after the final presentation of the roadmap for sustainable development in March 2016.

Results of the on-site assessment in Tbilisi

As the capital of Georgia at the interface between Europe and Asia, Tbilisi has a major influence on the development of this region in the Caucasus. On the one hand, the city, with its more than one million inhabitants, is characterized by an infrastructure dating back to the Soviet Union: housing developments with prefabricated panel buildings and a basic, but in many cases outdated infrastructure, for example the underground Metro system and the central water supply system.

3

4



5

On the other hand, since 1990 there has been a strong trend toward privatization and deregulation. For example, the water supply, sewage disposal, and also the power grid and gas supplies are currently privately owned. The biological stage of the central sewage treatment plant, originally designed for the mechanical-biological treatment of a million cubic meters of wastewater per day, is out of operation and the wastewater – now only treated mechanically – is discharged into the Mtkvari river. The green areas (parks and gardens), which until 1990 existed in many parts of the city as a result of the centralized planning, have since been greatly reduced by unregulated construction activity. During rush hours the traffic frequently comes to a standstill on roads that are mostly in a state of disrepair. Many manufacturing enterprises had to close down, so now there are quite a number of brownfield sites in the city. The emigration of many skilled and qualified people and the influx of low-skilled workers from the surrounding areas also represents a challenge.

However, as the undisputed center in Georgia, Tbilisi possesses a large number of universities and technical colleges. Tbilisi has interesting perspectives for the future because of its location between Russia, Iran and Turkey and because its surroundings are attractive to tourists. The city itself is also well worth seeing and tourism is growing. And last but not least, Georgia is, in addition to other aspects, a valuable trade partner of the EU and the USA due to the functioning democracy and a gas pipeline from Azerbaijan to the Black Sea.

Contact

Dr.-Ing. Marius Mohr
Phone +49 711 970-4216
marius.mohr@igb.fraunhofer.de

Dr.-Ing. Ursula Schließmann
Phone +49 711 970-4222
ursula.schliessmann@igb.fraunhofer.de

Literature

[1] Vester, F. (2002) Die Kunst vernetzt zu denken: Ideen und Werkzeuge für einen neuen Umgang mit Komplexität. Ein Bericht an den Club of Rome. dtv-Verlag, ISBN 3-423-33077-5

Funding

We would like to thank the German Federal Ministry for Economic Cooperation and Development for funding the project.

Project partners

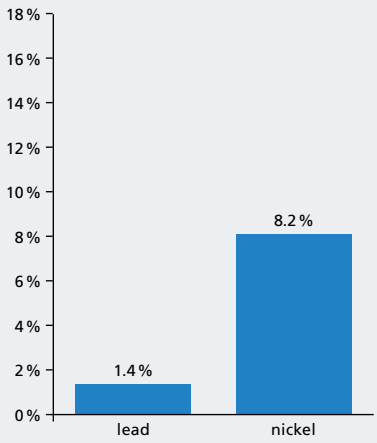
Fraunhofer IAO, Stuttgart, Germany | Drees & Sommer, Stuttgart, Germany

Further information

www.morgenstadt.de

1+2 *Tbilisi is a city well worth seeing.*
3+4 *Prefabricated panel buildings, brownfield sites and an ailing infrastructure are distinctive features of the city of Tbilisi.*
5 *City Lab: objectives and a roadmap for sustainable urban development.*

1



2

A WATER TEST FOR EVERY HOUSEHOLD

Gabriele Beck-Schwadorf, Susanne M. Bailer

Water – an important food product

Drinking water is tested very carefully in Germany. It complies with the legal prerequisites of the Drinking Water Ordinance, which ensure that communal water suppliers only supply water that is of the highest quality. However, there is also a significant number of self-sufficient households in Germany. In addition, external factors that are not controlled by the water supplier may also affect water quality. Fraunhofer IGB, in collaboration with an industrial partner, provides comprehensive water analysis for such cases. To date, this water quality check focused purely on chemical and physical properties. Bacteriological tests for germ load in the water samples have now been added.

Water that is low in nitrates (< 10 mg/L), for example, should be used for the production of baby food as nitrate increases the risk of cyanosis in babies. Water from wells that is used as drinking water or for watering vegetables and herbs must also be tested for heavy metals and nitrate, as well as pathogens.

The effect of plumbing and fittings

Drinking water must comply with both chemical and microbiological specifications. However, much can happen over the final meters of pipe that the drinking water passes through from the supplier to the faucet. Plumbing and fittings are a particularly critical area with reference to the supply of drinking water. Causes of adverse effects on water quality may be due, for example, to construction materials – lead pipes were often installed up to 1973. In addition, the fittings – independent of brand and price – may release metals like nickel or chromium into the water. Above all, pipes that are rarely used and filled with standing water may result in the accumulation of heavy metals and bacteria. Furthermore, in Germany, around one million people are self-sufficient, using wells as their water supply. These are not subject to any control and there are often no options for analyzing the water quality.

Recent analysis

A recent analysis of over 1500 water samples from German households revealed that almost every tenth sample exceeded the permissible threshold for nickel, as defined in the Drinking Water Ordinance. Intensive agricultural exploitation of land and soil may also pollute the groundwater, including with nitrates. Almost 16 percent of the water samples from household wells revealed elevated nitrate values.

3

Bacteria in water

Pathogens may colonize plumbing if contaminants enter into the pipes from the outside, e.g. due to construction or plumbing works, defective pipes or the proximity to agricultural facilities, especially in cases of household wells. An increase in the incidence of fecal or intestinal bacteria, such as *Escherichia coli* and coliform bacteria that can cause diarrhea, indicates hygiene deficiencies. *Pseudomonas aeruginosa* is a concern in relation to health, even at low bacterial counts, especially for the elderly and babies.

Chemical and physical tests

Using high-tech, quality-assured chemical and physical analytical methods, we test drinking water for metals and trace elements (lead, cadmium, nickel, copper, aluminum, iron, chromium, molybdenum, lithium), for cations (sodium, potassium, calcium, magnesium) and anions (chloride, fluoride, nitrate, phosphate, sulfate). In addition, tests are also carried out on sample sensory parameters such as odor and turbidity, water hardness and hydrogen carbonate content.

Microbiological tests

Classical microbiological culture methods are used for the analysis of microbiological parameters. Specific bacterial tests identify and quantify coliform bacteria, *Escherichia coli*, *Enterococci* and *Pseudomonas aeruginosa*. The test result is given as so-called colony-forming units (CFU) per 100 mL.

Contact

Staatl. gepr. LM-Chem. Gabriele Beck-Schwadorf
Phone +49 711 970-4035
gabriele.beck-schwadorf@igb.fraunhofer.de

Priv.-Doz. Dr. sc. nat. Susanne Bailer
Phone +49 711 970-4180
susanne.bailer@igb.fraunhofer.de

Project partner
AQA GmbH, Vienna, Austria

Further information
www.wassercheck.org

1 *External factors such as the quality of plumbing and fittings may also affect water quality.*
2 *Proportion of 1500 water samples analyzed by Fraunhofer IGB in which thresholds were exceeded.*
3 *Water analysis in the laboratory.*

E³-PRODUKTION

THE "E³-PRODUCTION" LIGHTHOUSE PROJECT – EFFICIENT, EMISSIONS-NEUTRAL, ERGONOMIC

Birgit Haller, Jan Iden, Ursula Schließmann

The future world of manufacturing

It is becoming increasingly important for manufacturing companies to efficiently utilize both alternative and renewable energy sources, and to retain materials in closed-loop systems. The role of the individual in an increasingly digitized and networked production environment must be considered as well. Against this backdrop, twelve Fraunhofer Institutes have set themselves the goal of changing the manufacturing world by applying new ways of thinking. The three E's of the E³ Lighthouse project stand for efficient engineering, efficient fabrication and efficient work. Put another way: maximal conservation of resources and minimal emissions while integrating and involving people. During the first two years of the project, promising solutions to challenges in planning, control, optimization and evaluation of production processes and facilities were developed within the consortium. These will now be amalgamated into an "E³ manufacturing world of tomorrow".

Sustainability and benefit assessment

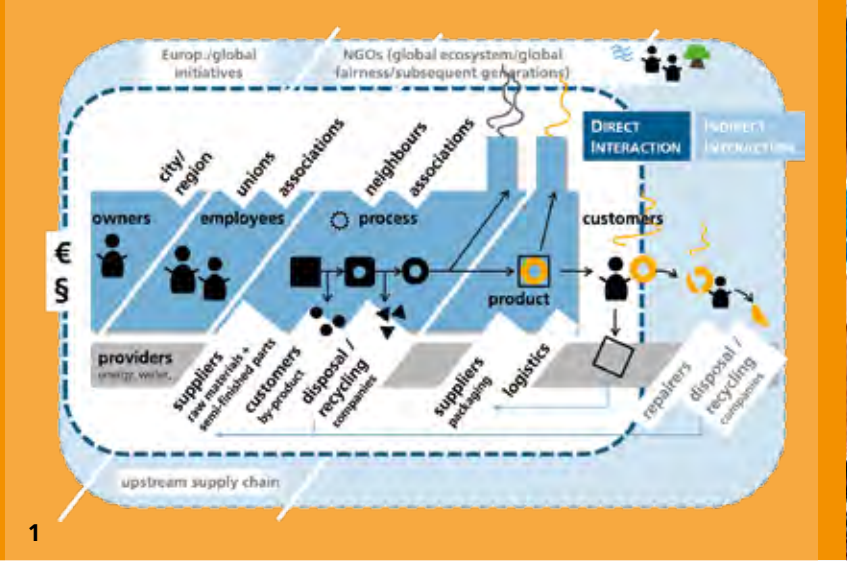
Involving all the participating parties in the planning process – well before the introduction of new industrial technology or construction of a new plant – becomes a critical factor for success of a manufacturing company, especially when production facilities and the urban environment are moving closer to one another. The focus of the sub-project "Sustainability and Benefit Analysis of Production for German Industry – SUSPROFIT" is the synergistic examination of the economic, social and ecological criteria in an efficient production sequence. A practical, industry-specific evaluation system is being developed under SUSPROFIT that categorizes the interests of affected parties in terms of sustainability and indicates options for action.

Stakeholder views broaden perspective

The goal is the evaluation of products and processes using a life-cycle approach that takes into account manufacturing, distribution, benefit, and waste management. The team of experts from Fraunhofer IGB and UMSICHT is able to call on its experience with sustainability management in large companies as well as from within its own organizations. Involving all stakeholders has long been a standard approach in these instances. The approach is tailored to examining production processes in small and medium-size operations in order to assist companies in responding more quickly to potential risks, achieving higher social acceptability and in the end being able to better withstand the challenges of the marketplace (Fig. 1). The interests of employees, investors, suppliers, clients and consumers, local residents, lawmakers and environmental organizations are analyzed in dialog with company representatives.

Toolbox for analyzing interaction

A modular kit of computer-aided analysis tools, a knowledge bank and evaluation methods provide the framework for a comprehensive systemization of factors that contribute to success and risk. The core element for stakeholder interaction analysis, as it is referred to, is the conversation with the company (Fig. 2). During this discussion, all relevant fields of activity, especially economic, ecological and social ones, are examined and investigated for their importance to key stakeholders. The form of the subsequent communication with stakeholder groups can be selected from various formats such as employee surveys or neighborhood dialogs. The company receives the following information from the focused amalgamation of analysis, research, dialogs and consultations:



1

2

Classification of the current state in terms of sustainability, indications of interest conflicts, hot spots, and feasibility of corrective measures as well as recommendations for action based on examples of good practice.

Actual test projects are currently running at two SMEs and an equipment manufacturer. During the remaining duration of the project, the interaction tool will be integrated into the E³-based demonstration platform for virtual product development in Berlin to enable people to see and experience the potential of the E³-Production system.

Contact

Dr.-Ing. Ursula Schließmann
Phone +49 711 970-4222
ursula.schliessmann@igb.fraunhofer.de

Dr. rer. nat. Birgit Haller
Phone +49 711 970-4083
birgit.haller@igb.fraunhofer.de

Funding

We would like to thank the Fraunhofer-Gesellschaft for funding the "E³-Production" Lighthouse project.

Project partners

Fraunhofer institutes FIT, IBP, ICT, IFF, ILT, IML, IPA, IPK, IPT, IWU, UMSICHT

Further information

www.e3-produktion.de

1 *Stakeholder Interaction Analysis model.*
2 *The core element of Stakeholder Interaction Analysis is the discussion held with the company.*

ENERGY

An energy supply based on the use of finite primary energy sources such as crude oil, natural gas and coal leads to a rapid rise in the concentration of CO_2 in the atmosphere – and thus to unpredictable climate changes. The transition to a sustainable, environmentally friendly yet reliable and economical source of energy supply – in view as well of the ambitious climate change targets – is therefore one of the major challenges Fraunhofer IGB meets in the use of electricity, heat, and chemical energy (fuels).

Sustainable energy conversion – The efficient production of biogas from organic waste, by-products of the food industry and agriculture, sewage sludge or wastewater by means of anaerobic technologies has been a key research area at IGB for decades. Increasingly, low mass flows from decentralized sources are gaining in importance. We make contributions to increase photosynthesis capacity by developing processes for cultivating microalgae. Their storage substances can be used either directly (lipids), after fermentative conversion to ethanol (starch), or after digestion to biogas (residual biomass) for energy. We also advance the exploitation of further regenerative energy sources by means of highly innovative membrane technology (gas separation, ethanol fuel cells, osmosis power plants).

Energy efficiency in engineering processes – Energy consumption in the process industry is substantial; savings are offered via optimizations such as through efficient separation processes as well as through the minimization of process steps. For the separation of high-purity methane from biogas as a basic chemical or fuel, we investigate absorption and membrane processes or ionic liquids that have a high capacity to bind CO_2. Noteworthy in this context are also energy-efficient drying processes with superheated steam at atmospheric pressure as well as methods for rapid energy input by means of microwave fields, e.g. as in pyrolysis processes. We have developed an anti-icing coating on film that makes it possible to operate wind turbines in freezing weather.

Energy storage – To achieve the climate objectives, waste heat that is generated in power plants and many other industrial processes, must be increasingly used. To make excess waste heat available for temporally and spatially decoupled heat requirements, the Fraunhofer IGB is developing thermo-chemical sorption systems for the long-term storage of heat. In addition, new techniques are being developed to utilize electrical energy by binding and converting CO_2 into chemical energy carriers, e.g. in the form of longer-chain hydrocarbons.

Integrated material flow and energy concepts for municipalities and regions are also to be tackled through approaches using state-of-the-art technologies – in order to replace historically evolved solutions. Therefore, the IGB is also involved with the Fraunhofer Alliances Energy, Construction, and Water Systems as well as with the Fraunhofer System Research for "Morgenstadt".

ETAMAX – BIOGAS FROM LOW-LIGNO-CELLULOSIC WASTE AND ALGAE RESIDUES

Brigitte Kempter-Regel, Ulrike Schmid-Staiger, Steffen Görner, Alexander Laug, Stephan Scherle, Christian Bringmann, Lukas Röhrenbach, Ronja Münkel, Ursula Schließmann

Bioenergy for mobility

In order to reduce dependence on dwindling oil resources and increasing carbon dioxide emissions at the same time, the use of renewable energies represents a sustainable alternative. Here, the use of plant biomass for the production of bioenergy – electricity, heat or fuel – plays a crucial role. Nevertheless, to date the potential of waste biomass to produce biogas as well as its use as fuel has been underexploited so far.

Efficient biogas production from biomass

Organic waste materials with very high proportion of water and low content of lignin and lignocellulose, for example waste from the food industry, wholesale market waste or algae residues, are perfectly suited for digestion.

Coordinated by Fraunhofer IGB, a project consortium has thus set itself the objective to obtain maximum energy generation by completely converting easily digestable, low-lignocellulosic wet biomass into biogas using an adapted high-load digestion process and closing all material cycles at the same time. In the project EtaMax the consortium is focusing in particular on cost-effective biowaste and algal biomass, both of which present no competition to food production. Local production and utilization of renewable methane from biogas represent the core of the project. Purified biomethane was used as a fuel to power CNG (Compressed Natural Gas) vehicles. Liquid, nutrient-rich digestates accruing during digestion were used to cultivate microalgae, since the residues contain a sufficient quantity of inorganic nutrients required for the growth of algae.

Conversion of wholesale market waste into biogas

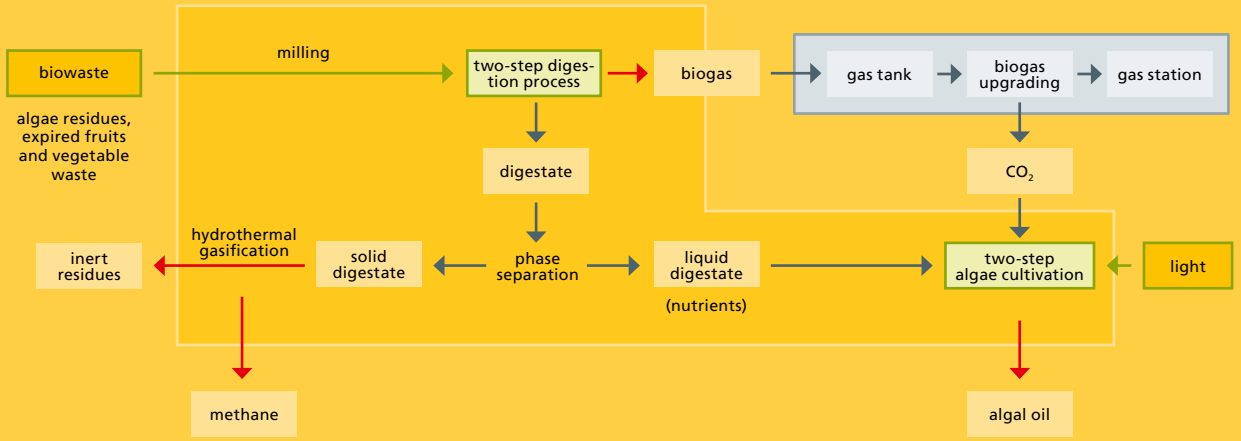
For the first time, expired fruit and vegetable waste from a wholesale market (Stuttgart wholesale market) was very efficiently converted into biogas using a two-stage process in two gas-lift reactors each with a capacity of 3.2 m^3. The high-load digestion process for this was developed at Fraunhofer IGB and has been technically realized for sewage sludge several times since 1994; the process was expanded and adapted for this substrate.

With an adjusted hydraulic retention time of 17 days per stage, the system could also be run by changing fruit and vegetable waste in a permanent and stable manner. Degradation levels of up to 95 percent could be reached with the largest part of degradation in stage 1. The biogas yield was between 840–920 norm liters of biogas per kilogram TVS (total volatile solids) added; the methane content was 55–60 percent.

Biogas production and algae cultivation as an efficient material cycle

For the energetic use of algal ingredients, Fraunhofer IGB developed a two-stage, fully automated process for the outdoor production of lipid-rich algal biomass in flat-panel airlift reactors (FPA) and transferred the process to pilot scale.

Closing the material cycles for nitrogen and phosphate between biogas production and algae cultivation was carried out using liquid digestate from biogas reactors as the medium component for the production of algal biomass. A mixed algae culture specifically adapted to this liquid digestate has been successfully cultivated with liquid digestate from the



4

fruit and vegetable waste digestion in 180 liter FPA reactors over a four month period. The ammonium concentration of approximately 800 mg/L contained in the liquid digestate was fully depleted. The biomass concentration in the FPA reactor was 2.5 g/L to 5.5 g/L between the times of harvest. The volumetric biomass productivity fluctuated between 0.1 and 0.35 g L^{-1} d^{-1} depending on the weather conditions.

Outlook

For the first time, digestion of fruit and vegetable waste in changing composition could be carried out in a long-term operation under continuous conditions with a retention time of 17 days and in a stable manner with high degradation level and high biogas yield. The material cycles were closed by utilization of the biogas (not shown) and utilization of the digestate. The use of liquid digestate as a medium component for algae cultivation is one step towards decreased production costs for algal biomass. But the results also show a way to reduce the nitrogen and phosphate loads of liquid digestate and to produce phototrophic biomasses that can be used for material and energy recovery. This result is linked to a reduction of costs in both algae production and in wastewater treatment of biogas processes.

1 *Fruit and vegetable waste from the Stuttgart wholesale market.*
2 *Two-stage pilot plant for the digestion of fruit and vegetable waste.*
3 *Greenhouse facility with 180 liter flat-panel airlift reactors.*
4 *Procedure and value-added chain.*

Contact

Dr. rer. nat. Brigitte Kempter-Regel
Phone +49 711 970-4128
brigitte.kempter-regel@
igb.fraunhofer.de

Dr. rer. nat. Ulrike Schmid-Staiger
Phone +49 711 970-4111
ulrike.schmid-staiger@
igb.fraunhofer.de

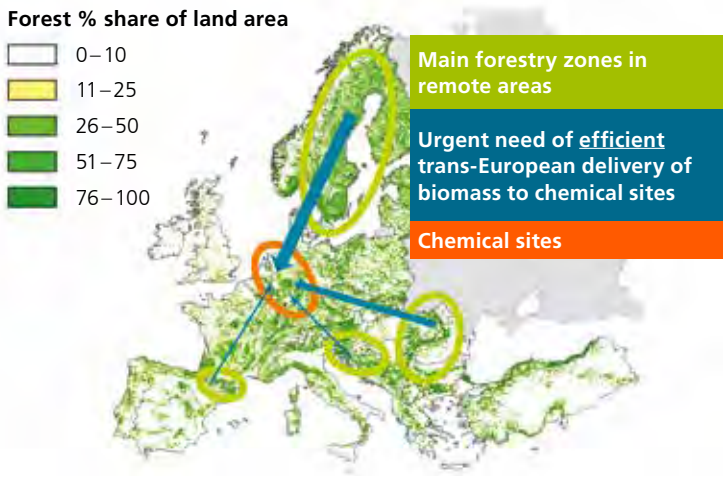
Funding

We would like to thank the German Federal Ministry of Education and Research for funding the project "EtaMax – Mehr Biogas aus lignocellulosearmen Abfall- und Mikroalgenreststoffen durch kombinierte Bio-/Hydrothermalvergasung", promotional reference 03SF0350A, in the "Bio-Energie 2021" program.

Project partners

Fraunhofer Institute for Process Engineering and Packaging IVV, Freising, Germany | Karlsruhe Institute of Technology (KIT), Germany | Paul Scherrer Institute PSI, Villigen, Switzerland | Daimler AG, Stuttgart, Germany | EnBW Energie Baden-Württemberg AG, Karlsruhe | FairEnergie GmbH, Reutlingen, Germany | Netzsch Mohnopumpen GmbH, Selb, Germany | Stulz Wasser- und Prozesstechnik GmbH, Grafenhausen, Germany | Subitec GmbH, Stuttgart, Germany | City of Stuttgart, Stuttgart, Germany

1



2

TORREFACTION TO CONDITION LIGNO-CELLULOSIC BIOMASS FOR TRANSPORTATION

Simone Mack, Sukhanes Laopeamthong, Siegfried Egner

The bioeconomy – an alternative source for the chemical industry

Due to the growth of inexpensive production in the emerging countries, the chemical industry throughout the EU is faced with the challenge of staying ahead of competitors by means of innovation and more efficient manufacturing. Currently, production in this branch of industry is largely based on the use of fossil fuels. More than 54 million tons of oil equivalent were consumed in 2010 [1]. These fuels do come primarily from competing or unstable regions outside the European Union. Additionally, consumer behavior has a growing influence on the chemical industry. To an ever greater extent consumers attach importance to environmentally friendly products, whose production and ingredients have no negative impact on the environment [1, 2]. As an alternative, by using biomass, industrial biorefineries have the potential to help ease the effects of climate change and to substitute the growing demand for energy, fuel, chemicals and materials [1].

SteamBio – Conditioning for economical transportation

The central priority is therefore to insure economical and sustainable supplies of biomass. Current research studies concentrate mainly on topics related to its use as energy or materials [3, 4]. So far, little attention has been paid to the long distances between the regions in Europe that can provide the necessary quantities of wood-based biomass (Scandinavia, Eastern Europe, etc.) and the few central industrial locations where the biomass is processed and used (Fig. 2). Therefore a concept for the decentralized preconditioning of the biomass is required to enable efficient transportation.

In order to make optimum use of the potential of the lignocellulose biomass resources, Fraunhofer IGB is developing a process that conditions lignocellulosic resources from forestry or agricultural residues using mobile plants locally in the region or on the site where they occur.

Torrefaction by drying with superheated steam

This is carried out by means of a flexible torrefaction process. Here, the biomass is heated in the inert atmosphere of pure steam for a certain process time. However, the process temperature lies below the value above which carbonization takes place, known as pyrolysis. The torrefaction process developed at IGB is based on its established process of drying by means of superheated steam at atmospheric pressure in the absence of air. This energy-efficient technology has already proven its worth in a very wide range of drying applications. In this project, we have demonstrated that woody biomass can be torrefied with superheated steam at below 300°C with minimum degradation of the lignocellulose.

The process of torrefaction results in a hydrophobic and very easily grindable solid. Volatile compounds that do also escape together with the moisture that is turned to excess steam are separated from the steam and recovered as highly valuable by-products.

Unlike with conventional torrefaction, in the clean atmosphere of the SteamBio reactor concept the torrefied biomass is not contaminated by exhaust gases. As a result, the volatile ingredients obtained are also of high purity and can be used as high quality products. A further advantage is the possibility of continuous process control. The key objective of the SteamBio

3

4

concept is to create a commercially utilizable platform. The flexible design of the process with a modular setup permits mobile operation, depending on seasonal fluctuations, with smaller throughputs and also use at fixed locations with high throughput rates.

One-year study with transportable demonstrator

Use of the SteamBio technology in a new marketplace also requires the development of new business models in order to establish the entire value creation chain. Within the framework of the project, a transportable demonstrator with a throughput of 500 kg lignocellulosic biomass per hour will be built. This will be operated and optimized at five locations in rural areas across Europe. A total of six different agricultural and forestry residues (e.g. coniferous wood, oak, straw, etc.) will be torrefied using the demonstrator.

Both the solid and the separated volatile components of the torrefied biomass can be used as a carbon-source in the chemical industry and as green fuel for bioenergy applications. The demonstration will extend over a whole year, so as to take into account the seasonal fluctuations of the raw material.

1 *Lignocellulosic biomass – the raw material for the torrefaction process.*
2 *Long distances between the main forestry areas and the European chemical industry.*
3 *Torrefaction plant for test trials.*
4 *Window to the process chamber with temperature measurement.*

Contact

Sukhanes Laopeamthong M. Sc.
Phone +49 711 970-3538
sukhanes.laopeamthong@
igb.fraunhofer.de

Dipl.-Ing. Siegfried Egner
Phone +49 711 970-3643
siegfried.egner@igb.fraunhofer.de

Literature

[1] Consumers identify with environmental issues: Environmental leader (1st September 2009)
[2] http://www.cosmeticsdesign-europe.com/Market-Trends/Consumer-demand-for-sustainability-leads-to-green-focus-for-chemical-industry (accessed on December 22, 2015)
[3] FP5 Project report VIEWLS
[4] Biomass potential and potential development: M. Pisarek 1st European Summer School on Renewable Motor Fuels (31st August 2005)

Funding

The research project "SteamBio" has received funding from the European Union's Eighth Framework Programme for Research and Innovation Horizon 2020 under grant agreement no. 636865.

Further information and project partners

www.steambio.eu

1

2

STORAGE OF RENEWABLE ENERGY IN CHEMICAL ENERGY MEDIA

Fabian Steffler, Lenard-Istvan Csepei, Tobias Gärtner, Volker Sieber

The challenge for renewable energy

The energy supply system in Germany is facing a huge challenge in converting to renewable forms of energy for electricity, heating, transportation, and industrial feed stocks in the long term. This conversion requires expanding the utilization of renewable energy sources on the one hand, and on the other accelerating the expansion of the power grid and setting up integrated high-capacity energy storage to level out energy fluctuations particularly from solar and wind sources. Linking the energy economy with manufacturing processes is critically important for this balance.

The extrema resulting from both the expansion of fluctuating renewable electrical energy sources and discontinuation of further conventional demand-follow power station operations could lead to reduced energy reliability and are already in evidence today. According to the "Agorameter" of the Agora Energy Transition initiative, power generation in Germany from renewable sources reached a temporary peak proportion of 75 percent of actual electricity consumption on May 11, 2014. In contrast, there was a minimum of only 12 percent on February 11, 2015 [1]. These extrema may bring increasing challenges, since they might encroach on the stability of a future power grid laid out based on distributed power generation.

Chemical energy storage

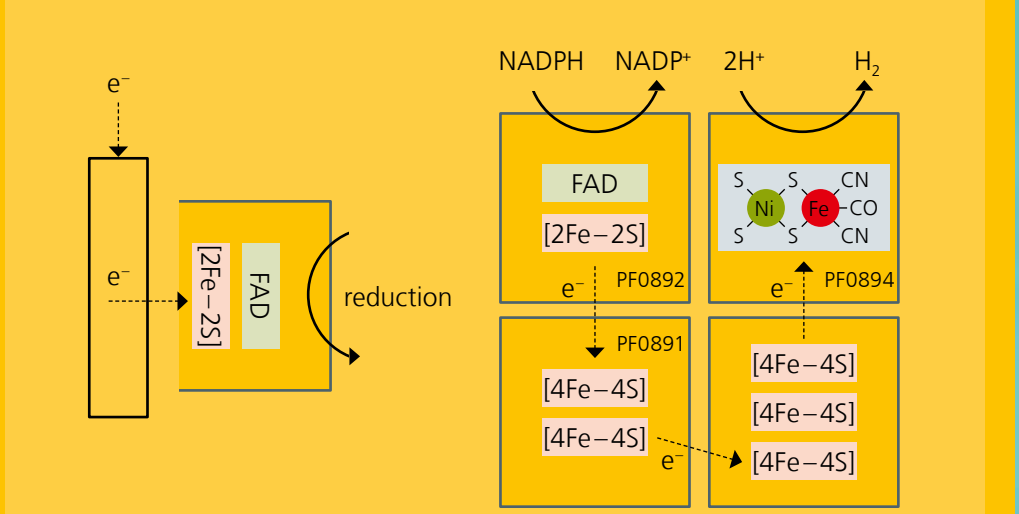
Chemical storage has the potential of usefully coupling the areas of electricity, heating, chemical production, and transportation. The development and implementation of new concepts and innovations are being promoted in all areas of technology with the goal of increasing storage efficiency, reducing costs, and making available suitable storage for each of these areas. Besides the principal approaches already available, such as power-to-gas for example [2], Fraunhofer IGB is involved with systematic development of the necessary storage technologies through its Center for Energy Storage set up in 2012. We develop implementations of applied technologies in the areas of biotechnological, chemical, and bioelectrocatalytic processes in order to store renewable energy in chemical energy media.

Fermentation processes

As biotechnological processes, fermentative synthesis pathways were investigated that facilitate the utilization of C1 compounds like CO_2, methane, and methanol using microorganisms. This involved applying a broad strain screening procedure to select suitable microorganisms capable of absorbing and utilizing these C1 compounds in their natural metabolisms. In a further step, the cultivation of the microorganisms and the formation of chemical energy storage compounds as reaction products, such as branched long-chain terpenes for example, were established, and optimization of the microorganisms with regard to substrate adsorption and product formation begun.

Chemical processes

The activities in the area of chemical processes have concentrated on topics including development of catalysts for methanol synthesis and development of new manufacturing processes. Various doped $Cu/ZnO/Al_2O_3$ catalysts were produced for manufacturing methanol that subsequently demonstrated excellent volumes in synthesizing methanol from CO_2 and H_2 in the gas phase reaction. Besides already familiar catalysts,



3

4

we were also able to study a completely new development for utilization of renewably generated hydrogen. This involves metallic catalysts where the substrate was produced by pyrolysing a deep eutectic solvent composed of urea and glucose.

Enzymes for electrode reactions

Various enzymes for electrode reactions were selected in the work on bio-electrocatalysts and molecular-biological methods developed for synthesizing these potential catalysts. In the further course of the work, we produced recombinant enzymes and optimized their preparation. Different methods for determining the activity of bio-electrocatalysts were developed with which the first biochemical reactions with CO_2 could be demonstrated.

Prospects

The conversions developed and in development at the Center for Energy Storage based on CO_2 and renewable energy create a sustainable link between the energy and chemistry sectors and acquire greater importance with the conclusion of the Paris Agreement on climate change. The work of Fraunhofer IGB through its BioCat branch in Straubing can make an important contribution to the success of the energy transition.

1 *Manufacture of biocatalysts.*
2 *Batch reactor for CO_2 conversion.*
3 *Schematic representation of an electro-biocatalyst reaction.*
4 *Target products are synthetic fuels, for example.*

Contact

Dr. rer. nat. Tobias Gärtner
Phone +49 9421 187-352
tobias.gaertner@igb.fraunhofer.de

Prof. Dr. rer. nat. Volker Sieber
Phone +49 9421 187-366
volker.sieber@igb.fraunhofer.de

Literature

[1] http://www.agora-energiewende.de/de/ (accessed in December 2015)

[2] http://www.powertogas.info/ (accessed in December 2015)

Funding

We would like to thank the Bavarian Ministry of Economic Affairs and Media, Energy and Technology for funding the project "Centrum für Energiespeicherung".

Project partner

Fraunhofer UMSICHT, Branch Sulzbach-Rosenberg, Germany

Further information

www.centrum-energiespeicherung.de

FURTHER DATA AND FACTS 2015

343 Publications

8 Book articles

109 Posters

100 Journal papers

126 Oral presentations

370 Applied patents in total

23 New patent applications

41 Patents granted in 2015

9 Inventions

19 Dissertations

28 Bachelor theses

110 Academic theses

19 Internship reports

39 Master theses

5 Diploma theses

47 Lectures

112 Teaching activities

1 Excursion

30 Practical courses, exercises

34 Seminars

25 Press releases and reseach news

1384 Followers on LinkedIn

507 Press clippings

1120 Followers on Twitter

78 Strategic cooperations

31 Trade fairs and events

150 Committee memberships

Detailed information
www.igb.fraunhofer.de/data2015

INFORMATION SERVICE

Would you like to receive further information?
We would be happy to inform you!

Please mark the relevant field on this page and
and send us per fax or post:

Periodicals

- ¬ Annual Report
- ¬ Online newsletter

Topic-specific brochures and product leaflets

- ¬ Medicine
- ¬ Pharmacy
- ¬ Chemistry
- ¬ Environment
- ¬ Energy

Sender

Name, First Name, Title

Company/Department

Street/P. O. Box

Postal code, City, Country

Phone

Fax

E-mail

Fraunhofer Institute
for Interfacial Engineering
and Biotechnology IGB
Press and Public Relations
Nobelstrasse 12
70569 Stuttgart | Germany

Phone +49 711 970-4150
Fax +49 711 970-4200
info@igb.fraunhofer.de
www.igb.fraunhofer.de

Visit our online ordering service and download area:
www.igb.fraunhofer.de/publications

EDITORIAL NOTES

EDITORIAL TEAM
Jan Müller M. A.,
Dipl.-Des. Thaya Schroeder (picture),
Dr. Claudia Vorbeck
and the scientists referred to as authors or contact persons.

LAYOUT AND PRODUCTION
Dipl.-Des. Thaya Schroeder

PRINTING
Fraunhofer Verlag, Mediendienstleistungen, Stuttgart | Germany

EDITORIAL ADDRESS
Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB
Dr. Claudia Vorbeck
Nobelstrasse 12 | 70569 Stuttgart | Germany

This annual report was printed climate neutral with mineral oil-free inks. The paper used is 100% recycled and FSC-certified, as well as awarded the EU Ecolabel AT/11/002 and the Blue Angel.

TRANSLATIONS, PROOFREADING
Dr. Stuart Amor, Stuttgart, Germany | Tim Ryan – In Your Best English, Hamburg, Germany and Victoria, Canada | Dr. Bhesham Sharma, Stuttgart, Germany Textworks Translations, Manchester, UK | Dr. Sabine Wacker – Wacker Translation, Aichwald, Germany

PHOTO ACKNOWLEDGMENTS
Altmann, Jürgen: page 7
Ausserhofer; David: page 31
Fogel, Walter: Cover, pages 5, 38, 39, 47, 54, 55, 60, 69
Fraunhofer UMSICHT: page 121
Fotolia: page 99
Krötz, Rafael: pages 12, 42, 58, 89
Loskill, Peter und Mathur, Anurag: page 25
MEV: page 129
Michalke, Norbert: pages 48, 49, 95
Müller, Bernd: pages 74, 110, 122
oe-werbung: page 49
Scheible, Wolfram: page 124
Shutterstock: pages 26, 50, 51, 66, 67, 93, 118, 119, 121, 126

Fraunhofer Institute
for Interfacial Engineering
and Biotechnology IGB
Nobelstrasse 12
70569 Stuttgart
Germany

Phone +49 711 970-4401
Fax +49 711 970-4200
info@igb.fraunhofer.de
www.igb.fraunhofer.de

Stay in contact: