Scaling up biotechnological and chemical processes

Use of renewable feedstock
Open development platform
to accelerate industrial implementation

The Fraunhofer Center for Chemical-Biotechnological Processes CBP focuses on the development, scaling and combination of biotechnological and chemical processes, and with its pilot scale technical equipment it closes the gap between the laboratory and industrial implementation. By providing the infrastructure and technical facilities as well as a staff of highly qualified experts it enables partners from research and industry to scale up biotechnological and chemical processes for the utilization of renewable raw materials to production-relevant dimensions, and also to accelerate process developments.

We enable innovations by closing the gap between laboratory and industrial scale along the entire process chain from the raw material to the product.
Fraunhofer CBP is a unique, modular platform for representing complete process chains – from processing raw materials followed by various conversion processes to product separation and purification. With this flexible concept raw materials such as plant oils, cellulose, lignocellulose, starch, sugar or CO₂ can be processed and converted into chemical products. The construction of Fraunhofer CBP was made possible by start-up financing provided by the Land of Saxony-Anhalt, project funding via the German Federal Ministry of Education and Research (BMBF), the German Federal Ministry of Food and Agriculture (BMEL) as well as the Fraunhofer-Gesellschaft.

The aim, according to the biorefinery principle, is the integrated and cascading material-energetic utilization of as many substances as possible obtained from plant biomass, as well as the establishment of novel process chains for the material utilization of CO₂.

A total of six pilot plants consisting of flexible unit operations are available for the smooth integration of laboratory protocols, the scale-up and further optimization. Supported by state-of-the-art analytical equipment and process simulation tools, the team of bioprocess engineers, chemists, engineers and technicians is pursuing the following key objectives across a wide range of projects:

- Maximum use of the carbon synthesis potential of nature
- Optimization of the energy and resource efficiency of the processes
- Robust process control and validation of parameters for plant design
- Minimization of waste streams
- Reduction of CO₂ emissions
- Use of raw materials that are unsuitable for food or feed production
- Integration of the newly developed processes into existing production networks
Fermentation plant for the cultivation of various microorganisms (cascade from 10 to 10,000 liters)
Range of services

From raw material to the purified product

To solve process-technical issues, Fraunhofer CBP provides modular process capacities of up to 10 m³ fermentation volume and continuous plants capable of high-pressure processing up to 20 kg per hour, plus a wide range of processing, treatment and reconditioning techniques and methods. This versatile “flexible biorefinery” facilitates the conversion of raw materials such as vegetable oils, cellulose, lignocellulose, starch or sugar into materials and chemical products.

With the available technical facilities and the combination of various types of process engineering expertise (biochemical, chemical, mechanical and thermal process engineering) an excellent, time-saving and cost-cutting way of scaling up new technologies is offered especially for small and medium-sized enterprises – with the aim of faster product development and market launch. Scientific and technical support also leads to significant risk minimization in engineering the design of demonstration or commercial plants.

The Fraunhofer CBP’s range of services
In the area of raw material processing, we are developing new technologies and innovative approaches for the processing of lignocellulosic raw materials and oilseeds in order to be able to use biomass as completely as possible and thus increase the value added. The focus is on wood pulping and fractionation processes, the processing of oilseeds using the mild EthaNa process, and their scaling up to pilot scale.

**Lignocellulose biorefinery**

One focus is on the pulping of lignocellulosic raw materials and their fractionation into their basic chemical components, lignin and sugar or fiber. For the research and development of processing and fractionation technologies, a specially developed integrated pilot plant is available that enables pulping with organic solvents under increased pressures and temperatures, the so-called Organosolv technology.

**Pilot plant for pulping of lignocellulose**

The plant reproduces a large number of individual process steps for the production of fibrous materials, concentrated sugar solutions and lignin. Up to 70 kg of wood or 20 kg of stalks can be processed per batch. The pilot plant includes a digester to separate the pulp from lignin and hemicellulose. The liquid phase is treated using a patented distillation process to precipitate the lignin. The Organosolv lignin obtained has high-grade properties, making it suitable for applications in pharmaceuticals or cosmetics, among others. The remaining hemicellulose solution can be further processed by hydrolysis and the resulting sugar solution concentrated by evaporation to be used in fermentation as a nutrient for microorganisms or as a raw material for biofuels. The plant was designed in such a way that the material and energy cycles can be closed and thus completely balanced.

**Oilseed biorefinery**

The oilseed biorefinery uses the mild EthaNa process for processing oilseeds, which is performed at ambient pressure and a maximum of 70°C to avoid protein denaturation and other quality-reducing reactions. In this way, the process enables a holistic utilization of the raw materials and provides product fractions with higher quality compared to conventional industrial processes. In addition to the extraction of high-quality vegetable oils, the processing of protein-rich fractions in particular contributes to the increase in added value. In addition, a pure hull fraction as well as other valuable molecules are obtained from the oilseeds, which can be used for a wide variety of applications.

**Thermal processing of further raw materials through universal design**

Due to the universal design of the pilot plant, other pulping processes for lignocellulose can be optimized on a pilot scale in addition to the Organosolv process, e.g. aqueous hydrolysis and digestion using acid or the soda process. Extensive analytics are available for balancing the processes. By using individual process engineering units in the plant, questions in the area of thermal separation technology and extraction can also be dealt with. There is strong interaction here with the “Downstream processing” field of competence.
Ethana® pilot plant

Prior to the Ethana® pilot plant, there is a de-hulling pilot plant, in which the hulls are separated from the seeds. This fraction of hulls can, for instance, be used as a raw material for insulation material. At the same time, the proportion of hulls in the fractionated rapeseeds is reduced, which has a positive effect on their further processing.

In the Ethana® pilot plant, the rapeseeds are dispersed in ethanol and ground before the oil is separated from the rapeseeds with the help of a screw press. The obtained oil is separated from the ethanol phase. The remaining rapeseed is further ground and the remaining oil is separated from the solid phase in a multi-stage extraction process using a decanter. The obtained oil is already in pre-raffinate quality. The solid obtained in the decanter, the rapeseed concentrate, is rich in proteins. The product is dried in a tube bundle dryer and ethanol is recovered in the process.

Since the ethanol accumulates valuable dissolved molecules, there are research approaches to separate these dissolved molecules, such as sinapic acid or phospholipids, for their further use in cosmetics, pharmaceuticals or the agricultural industry. In addition to the processing of rapeseed, the raw material portfolio can thus be expanded together with partners.

Current R&D topics

- Development and optimization of pulping processes for lignocelluloses
- Recovery of ingredients from lignocellulose (extractives, hemicellulose, lignin, cellulose) with application-specific properties, e.g. for phenol-formaldehyde resins, polyurethanes or carbon fibers
- Production of cellulose and lignin by Organosolv pulping processes and correlation with required product properties, e.g. as biopolymers or carrier components in pharmaceutical products
- Processing of oils and protein-rich meals with the Ethana process for feed and food production
- Fractionation of by-product streams from the Ethana process, e.g. hulls or valuable molecules, for applications in construction, cosmetics or pharmaceuticals

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In Industrial Biotechnology we work on the material utilization of renewable raw materials by employing enzymatic synthesis or fermentative production of biobased chemicals, for example organic solvents and acids. We are also engaged in the recombinant production of proteins and enzymes for various applications.

**Range of services**

The team possesses broad bioprocess engineering expertise in the field of scale-up and process intensification. The processes developed on the laboratory scale are evaluated in the preliminary stages in terms of their transferability to industrially relevant equipment at scale and are optimized repetitively during transfer and scale-up. This includes, for example, the adjustment of process control strategies (batch, fed-batch, continuous) and integrated product purification to reduce the number of process steps or the reutilization of the deployed resources, e.g. by immobilization of biocatalysts on carrier materials.
Equipment

The facilities include a central microbiological laboratory, two module-based technical centers of the Biosafety Level 1, one of which can be operated under ATEX conditions.

Cultivation

- Fermentation reactor cascade with total volumes of 10, 100, 300, 1000 and 10,000 liters, equipped with four storage tanks each as well as comprehensive automation, measurement and control technology
- UHT plant for the continuous sterilization of fermentation media
- ATEX fermenter (total volume: 500 L) for conversion or production of highly flammable chemicals
- Continuous process control in fermentations by cell retention (sterilizable crossflow filtration plant with automatic feed level control)
- Online measurement of alcohol concentration in the reactor and of CO₂/O₂ in the fermentation exhaust gas

Product purification and finishing

- Harvest of the fermentation suspension as well as temporary storage of product solutions using stirred and temperature-controlled tanks (500 (mobile) / 2,000 / 5,000 and 10,000 L)
- Biomass separation (disk separators 0.5 – 2 m³/h, 0.5 – 1 m³/h, vacuum drum cell filter 0.5 m² and filter press 1.6 m²)
- Cell disruption (homogenizer 0.4 m³/h, 1,000 bar, optional with subsequent flow cooling)
- Membrane filtration (MF/UF) for desalination and product concentration processes; feeding up to 500 kg/h; flexible use of spiral wound modules (material, cut-off)
- Fine purification using liquid chromatography (35 L column volume, flow rate up to 180 L/h)
- Crystallizers (180 L, 800 L) with downstream vacuum filter dryer (0.5 m²) in ATEX version
- Spray (5 kg/h) and freeze drying (0.8 m²) for finishing the products

Current R&D topics

- Fermentative production of
  - milk proteins and other food substitutes
  - organic acids (e.g. xylonic acid), solvents (e.g. butanol) and other bulk chemicals
  - fine and specialty chemicals (e.g. dyes)
  - technical and other enzymes
- Utilization of alternative carbon sources in fermentation (e.g. lignocellulosic hydrolysates or methanol)
- Scaling of enzymatic conversions and syntheses
- Scale-up and establishment of downstream processing strategies of fermentations and enzymatic reactions

Crystals of ferulic acid produced by fermentation

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This field of work focuses on the process-technological development of chemical processes to produce biobased basic, fine and platform chemicals for further processing in the chemical, pharmaceutical or food industries. In addition to new process concepts, the optimization of the resource and energy efficiency of existing processes also plays an important role here. Established processes can be adapted and optimized under ecological and economic aspects. In doing this, we not only consider biobased raw materials and carbon dioxide but also examine conventional processes for manufacturing petrochemical products.

Range of services

The range of services extends from representing the process parameters on the laboratory scale through to scaling processes up to pilot plant scale. Highly sophisticated reactions can be realized under high pressures (350 bar) and temperatures (up to 500°C) with the equipment and process technology installed. The following examples should be mentioned: gas phase reactions with hydrogen, oxygen or ammonia as well as reactions in the presence of flammable substances, in a strongly alkaline or acidic medium or in the near- and overcritical aqueous phase.

Together with our project partners and with the help of modern simulation software (ASPEN) the processes we develop are evaluated with regard to energy and resource efficiency; the further development of processes is therefore facilitated in an efficient way. The piloting of the processes also permits to synthesize relevant product quantities, for example for sampling purposes or the validation of the material flows for subsequent process steps.

Equipment

With the equipment available at Fraunhofer CBP we can represent a variety of established types of reactions and conversions in the gas or liquid phase, but we can also realize them with solids. Here the main emphasis is on catalytic reactions for the (de-)functionalization of biogenic raw materials. Before pilot testing, feasibility studies in the 0.1 – 10 liter scale can be carried out or the required synthesis stage can be modified accordingly.

Continuous and discontinuous reactors are used for scale up to the pilot scale in order to demonstrate conversions in the kilogram to
the metric tonne range. These reactors are designed in accordance with ATEX specifications (Zone 2).

Particularly noteworthy are:

- Stirred tank reactors for discontinuous reactions under atmospheric conditions with a capacity of 1, 10 and 100 liters
- Stirred tank reactors to represent pressure reactions up to 200 bar at 300°C with a capacity of 0.3, 1.2 and 50 liters, suitable for homogeneously and heterogeneously catalyzed reactions in the gas and liquid phase
- Flow tube reactors for high-pressure reactions on laboratory and pilot scale for the conversion of biogenic material flows, also in the gas phase

**Current R&D topics**

- Functionalization of lignin to aromatic molecule building blocks (e.g. by means of base-catalytic depolymerization or oxidation)
- Catalytic hydrogenation of biogenic substrates
- Continuous oligomerization of olefins
- Process technological development and scaling of chemical processes for the conversion of CO₂ and H₂ to basic chemicals as well as fuels

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The field of downstream processing includes the development of processes for separation and purification of product mixtures and is naturally closely interrelated with the other areas at Fraunhofer CBP. New tailor-made processing methods for the separation and purification are developed, scaled-up and evaluated to provide customized applications.

Range of services

Downstream processing and product conditioning are a decisive factor in the efficiency of the entire process chain and at Fraunhofer CBP these are integrated directly into the process development as unit operations. Our step-by-step approach covers the conception of suitable processes, the simulation and modeling of separation processes via ASPEN and their representation on the technical and pilot scale. At the same time the industrial practicability of the processes is already evaluated at the laboratory scale and then optimized. These trials enable us to make product samples available to our partners and customers for technical application tests. In parallel to the process, analytical methods are employed to evaluate the material composition of the product solutions.

Equipment

In addition to the above-mentioned process units Fraunhofer CBP has the following equipment for product purification and conditioning:

- Distillation columns for processing under atmospheric pressure and under vacuum with capacities of 1 L/h to 80 L/h
- Falling film, thin film and short path evaporators for distillation under vacuum up to 350°C and with throughputs of up to 60 L/h
Unit for liquid-liquid extraction with a maximum throughput of 85 kg/h
Unit for solid-liquid extraction with a capacity of 25 L
Unit for the high-pressure extraction in continuous and discontinuous operation with liquid propane and supercritical carbon dioxide for extraction rates up to 10 kg/h
Cross-flow membrane filtration plant for micro-, ultra- nanofiltration as well as reverse osmosis with max. 600 kg/h mass flow rate

The plants are mainly designed in accordance with ATEX specifications (Zone 2, high-pressure extraction Zone 1).

**Current R&D topics**

- Production of high-quality extractives from secondary and side streams of the renewable raw materials processing process industry by liquid-liquid extraction with organic solvents or at high pressures with liquid propane and supercritical carbon dioxide
- Downstream processing of fermentation solutions and extraction of fine chemicals
- Extraction of organic components from process streams through extraction/distillation, filtration
- Separation and purification of furan derivatives from lignocellulosic coupling streams
- Extraction of high-quality substances from algal biomass

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Reliable in-process analytics are essential for rapid evaluation and the associated successful establishment of new processes and the scaling of advanced procedures. A particular challenge here is the complex sample matrix of fermentation broths, lignocellulose or chemical reactor waters. Various are therefore available for analytical characterization, some of them online.

Thus utilization strategies can be represented along the entire process chain from raw material preparation via conversion through to product purification using mechanical and thermal separation processes.

**Range of services**

Our spectrum of services includes particularly process-accompanying analyses, but also the development and establishment of new analytical methods.

The focus is on:

- Quantification of the following substances:
  - Sugars from wood
  - Sugar degradation products
  - Organic solvents
  - Organic acids (simple carboxylic acids, diacids, fatty acids, aromatic acids)
  - Permanent gases
  - Aromatic compounds
- Screening of unknown ingredients
- Determination of enzyme activity
- Protein analysis
- NCHS and O determination
- Relative molar mass determination of lignin
- Determination of phenolic OH groups and carboxyl groups in lignin/oils

**Equipment**

Fraunhofer CBP is equipped with various devices for the instrumental analysis of different substance streams, which are partly also used online for reaction control:

- GC (gas chromatography)
- HPLC (high pressure liquid chromatography)
- GPC (gel permeation chromatography)
- MS (mass spectroscopy)
- Organic elemental analysis
- UV-VIS/IR spectroscopy
- Karl Fischer and potentiometric titration

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The Fraunhofer CBP’s networking activities

**Leading-edge BioEconomy Cluster**

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

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

**BioZ**

With more than 60 partners, BioZ is building a cross-sector innovation ecosystem along value chains with high innovation potentials in the agricultural, food and chemical industries. The innovation area lies in the biobased economy and is defined by the strengths and competencies available in the region. Fraunhofer CBP is involved both as a scientific coordinator and as an open scaling platform. The declared goal is the implementation of innovative ideas for the use of regionally generated material flows and thus the acceleration of structural change in the Central German region.

[www.bio-z.de](http://www.bio-z.de)

**Hydrogen Power Storage and Solutions East Germany (HYPOS)**

The central topic of the HYPOS network is the comprehensive use of electricity, in particular the temporary excess of electricity from wind, solar and biomass, for the economic production of hydrogen via electrolysis on an industrial scale. Hydrogen as a chemical energy source can thus be made available to the economy in many ways as a chemical base material, as a fuel for mobile applications, for heat generation and also for the generation of electric energy. Within HYPOS, Fraunhofer CBP acts as a research partner mainly for the use of regenerative hydrogen, e.g. in power-to-chemicals processes.

[www.hypos-eastgermany.de](http://www.hypos-eastgermany.de)

**Fraunhofer CBP – Leuna branch of Fraunhofer IGB**

The Fraunhofer Center for Chemical-Biotechnological Processes CBP in Leuna is a branch of the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB in Stuttgart. Processes for the production of bioeconomic products developed at the Stuttgart site or at the Straubing site (BioCat) are scaled up to industrial dimension at the CBP as well.

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

**4Chiral**

4Chiral is a network for fine chemicals in the Central German chemistry triangle, developing new products and technologies and transferring them into production. With its motto “Our core competence is fine organic synthesis” the network is conducting research and development projects in the field of chiral compounds, whereby the main focus is on pharmaceutical relevant enantiomers.

[www.4chiral.de](http://www.4chiral.de)

**High-Performance Center Chemical and Biosystems Technology**

The strategic goal of the High-Performance Center Chemical and Biosystems Technology is to investigate and optimize process chains in the plastic-processing, chemical, biotechnological and biomedical industries – from raw materials to the product – in the Halle-Leipzig region. To this end, the scientific institutions in greater Halle-Leipzig and the Martin Luther University Halle-Wittenberg will work even more intensively with companies in the area in order to decisively stimulate added value in the Halle-Leipzig region. The High-Performance Center will advance both excellence in research and sustainable regional development through the transfer of knowledge and technology.

[www.chemie-bio-systemtechnik.de](http://www.chemie-bio-systemtechnik.de)
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