Institute of Biochemical Engineering

Industrial biotechnology

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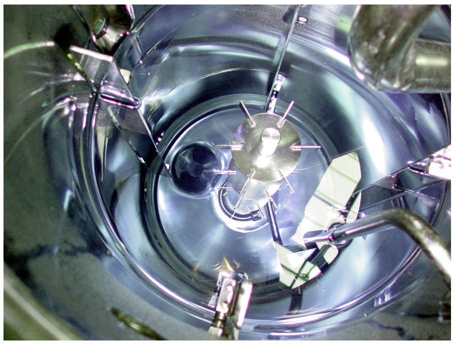
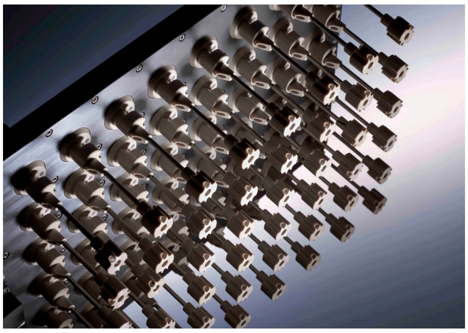
Industrial biotechnology ('white biotechnology') makes use of micro-organisms or enzymes for the industrial production of chemicals like special and fine chemicals, building blocks for agricultural or pharmaceutical products, additives for manufacturing as well as bulk chemicals and fuels. Renewable resources are the favored raw materials for industrial biotechnology.

The Institute of Biochemical Engineering is dealing with all aspects of the technical use of biochemical reactions for industrial biotechnology. The research focus is on bioreactors and biocatalysis, as well as on (gas-) fermentation and bioprocess integration.



View into a stirred-tank bioreactor at the Institute of Biochemical Engineering (copyright: Weuster-Botz, TUM)

Bioreactors



Gas-inducing stirrers for 48 parallel stirred-tank bioreactors (copyright: 2mag AG – www.2mag.de)

The effective generation of process information represents a major bottleneck in microbial production process development and optimization. An approach to overcome the necessity of a large number of time- and labor-consuming experiments in lab-scale bioreactors is miniaturization and parallelization of stirred-tank reactors along with automation of process management.

Highlight

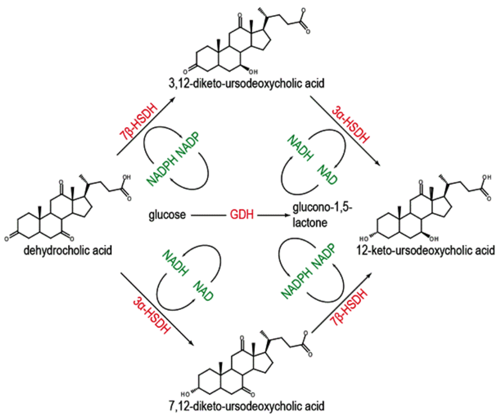
The license holder 2mag AG, Munich, Germany starts commercialization of the bioREACTOR48, a parallel stirred-tank bioreactor system developed at the Institute of Biochemical Engineering.

Projects

- High throughput reaction engineering analysis of halophilic microorganisms for enzyme production
- Continuous fermentations in miniaturized stirred-tank reactors
- Micro-dosing device and micro-sensors for pH control in parallel bioreactors
- Reaction engineering studies of butanol fermentation with Clostridium aceto-butylicum strains in parallel stirred-tank reactors

Biocatalysis

High demands are set upon the optical purity of building-blocks for the production of pharmaceuticals. Due to the high natural selectivity of biocatalysts, biocatalysis appears as favorable method for the purpose of chiral syntheses. Major research interests are the development of new reaction engineering methods and devices to intensify whole cell biotransformations of hydrophobic, unstable and/or toxic substrates up to the technical scale.



Scheme of the intracellular reactions established in E. coli for the production of the cholic acid derivative 12 keto-UDCA (copyright: Sun, TUM)

Highlight

The whole-cell biocatalytic process, developed at the Institute of Biochemical Engineering for the production of a cholic acid derivative (pharmaceutically used for the non-surgical dissolution of gallstones) was transferred to the industrial scale by the cooperation partner PharmaZell GmbH, Raubling, Germany.

Projects

- Polymeric nano-compartments for biocatalytic applications
- Membrane functionalisation of nano-scale enzyme membrane reactors
- Surface functionalisation of nano-scale enzyme membrane reactors
- Minimal cells for multi-enzyme synthesis
- Production of N-acetylneuraminic acid using epimerases from cyanobacteria
- Stereoselective multi-step reduction of dehydrocholic acid with hydroxysteroid dehydrogenases
- Asymmetric reductions using novel ene-reductases from cyanobacteria

Fermentation

Making use of microorganisms for the production of chemicals from renewable resources is the core of industrial biotechnology. Reaction engineering analyses of metabolically optimized producer strains and metabolic analyses of microorganisms in production processes are necessary for efficient bio-production on an industrial scale.

Highlight

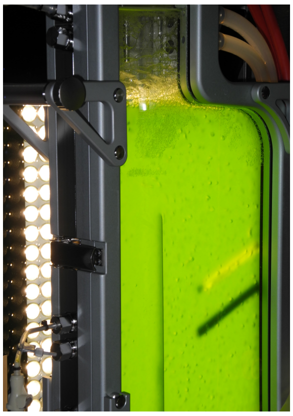
The fermentation process optimized at the Institute of Biochemical Engineering for the recombinant production of spider silk proteins with bacteria was transferred to the industrial scale (> 50 m^3) by the cooperation partner AMSilk GmbH, Planegg, Germany.

Projects

- Bioprocess development for the production of single-stranded DNA
- Microbial electrosynthesis for the production of chemicals
- Metabolic analyses of recombinant microorganisms from production processes
- Microbial production of lipids
- Metabolic control Analysis of microbial fed-batch production of L-phenylalanine
- Reaction engineering analysis of Escherichia coli for the production of a hydrophobic spider silk protein

Pilot-scale fermentations were performed at the TUM-Research Center for Industrial Biotechnology (copyright: TUM)

Gas Fermentation



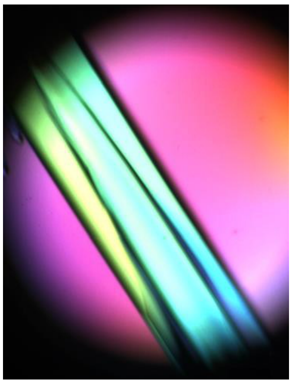
Flat-panel photo-bioreactor operated at the Institute of Biochemical Engineering (copyright: Weuster-Botz, TUM)

Special microorganisms are able to produce chemicals with carbon dioxide as sole carbon source. Energy may be supplied from sunlight or hydrogen gas. Bioprocess engineering is the key to make use of these energy sources for the microbial production of chemicals from carbon dioxide on an industrial scale.

Highlight
Reaction conditions were identified for the microbial production of acetate from CO_2 and H_2 with Acetobacterium woodii resulting in the highest product concentrations reported so far (> 60 g L^{-1}).

Projects
- Modeling of microalgae cultivation in open photobioreactors
- Characterization of new microalgae for open photobioreactors
- Mass production of microalgae in open photobioreactors
- Reaction engineering analysis of new microalgae
- Bioelectrosynthesis for the production of chemicals from carbon dioxide
- Microbial production of chemicals from synthesis gas
- Hydrogenotrophic production of acetic acid

Bioprocess Integration



Crystal of a therapeutic monoclonal antibody produced in a stirred crystallizer (copyright: Smejkal, TUM)

In many cases, downstream processing is by far the most cost-intensive step of a bioprocess. Often, multiple-step bioseparations are required yielding rather low product yields.
Therefore, existing bioseparation processes should be improved and combined to reduce the number of process steps.
The focus is on bioprocess integration of fermentation/biocatalysis and downstream processing (and follow-up chemistry).

Highlight
Process protein crystallization was shown to be an efficient, scalable, fast, and inexpensive alternative to key steps of a standard purification process for therapeutic antibodies.

Projects
- Non-stationary hydrodynamics of chromatography columns
- Preparative purification of proteins via crystallization
- Preparative purification of proteins via extraction
- Purification and formulation of a therapeutic antibody by crystallization
- Protein crystallization in stirred-tank reactors

Research Focus

- Micro-bioprocess engineering/bioreactors
- Biocatalysis
- Fermentation
- Gas fermentation
- Bioprocess integration

Competence

- Design and automation of bioreactor systems
- Bioprocess development and optimization
- Metabolic analysis of microbial reactions in bioreactors
- Metabolomics
- Downstream processing

Infrastructure

- Stirred-tank bioreactor systems up to a 100 L-scale
- Flat-panel photobioreactor systems with high-power LEDs
- Parallel bioreactor systems automated with lab-robots
- Anaerobic work benches/sterile laminar flow work benches
- Syngas labs (CO_2, CO, H_2)
- Phage lab
- Cooled lab (4° C)
- Electronic/mechanical work shop
- Analytical lab (LC-MS, flow cytometry, GC, LC, …)

Courses

- Biochemical Engineering Fundamentals
- Biochemical Engineering
- Bioprocesses
- Bioprocesses and Bioproduction
- Industrial Bioprocesses
- Bioreactors/Bioreaction Engineering
- Environmental and Biochemical Engineering
- Separation of macromolecular bioproducts
- Practical training on biochemical engineering
- Practical training on bioprocess engineering

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Publications 2013-14

- Albermann C, Weiner M, Tröndle J, Weuster-Botz D, Sprenger GA (2014): Utilization of organophosphate: phosphate antitransporter for isotope-labeling experiments in E. coli. FEMS Microbiol Lett 361: 52-61.
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