Technische Universität München
Department of Mechanical Engineering

Mechanical Engineering Annual Report 2015

Institute of Biochemical Engineering

Industrial biotechnology

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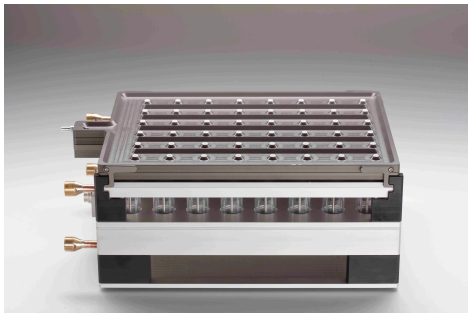
■ Industrial biotechnology ('white biotechnology') makes use of micro-organisms or enzymes for the industrial production of chemicals like special and fine chemicals, building blocks for agricultural or pharmaceutical products, additives for manufacturing as well as bulk chemicals and fuels. Renewable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

Pilot-scale bioreactors are used for the research at the Institute of Biochemical Engineering (copyright: TUM)

Bioreactors



Bioreactor unit with 48 parallel single-use stirred-tank bioreactors on a 'shoe-box scale' (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

New miniaturized fluorimetric pH sensors with a dynamic range of pH 4 - 7 are made available for the bioreactor unit with 48 parallel single-use stirred-tank bioreactors 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
- Multi-parameter analytics in parallel bioreactors

Biocatalysis

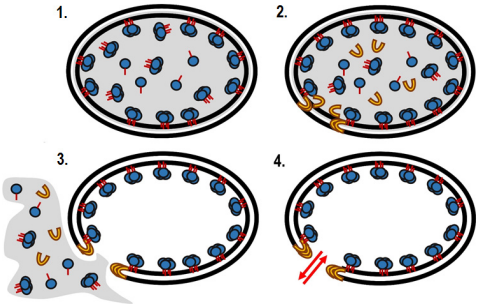
High demands are set upon the optical purity of building-blocks for the production of pharmaceuticals. Due to the high natural selectivity of biocatalysts, biocatalysis appears as favorable method for the purpose of chiral syntheses. Major research interests are the development of new reaction engineering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

Highlight

Production of enzymes with combined immobilization in one process step reduces the costs for biocatalyst preparation. Therefore, enzymes were first anchored to the inner membrane of *E. coli*. The cells were subsequently opened by expression of a lytic phage protein to obtain cellular envelopes with membrane anchored enzymes.

Projects

- Polymeric nano-compartments for biocatalytic applications
- Membrane functionalisation of nano-scale enzyme membrane reactors



Scheme of the novel one-step expression and immobilization method for the production of biocatalytic preparations: 1. Intracellular expression of enzymes with membrane anchors and in situ immobilization to the inner surface of the cell membrane; 2. Expression of a lytic phage protein; 3. Pore formation in the cell wall and release of the cytosol; 4. Cellular envelope with immobilized enzymes (copyright: Sührer, TUM)

- Surface functionalisation of nano-scale enzyme membrane reactors
- Minimal cells for multi-enzyme synthesis
- Production of N-acetylneuraminic acid using epimerases from cyanobacteria
- Asymmetric reductions using optimized 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

Metabolic control of the microbial L-phenylalanine production process with glycerol as carbon source was identified by applying short-term perturbation experiments of 20 minutes in stirred-tank bioreactors, metabolom and fluxom analyses and a kinetic network model.

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
- Production of terpenoid glycosides by recombinant *Escherichia coli*

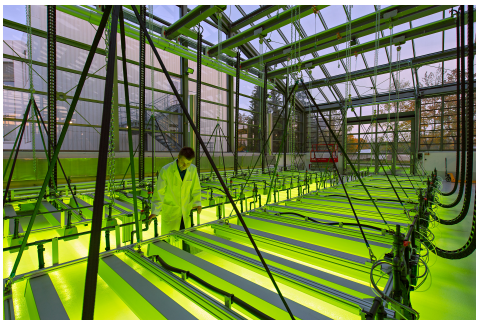
Pilot-scale fermentations were performed at the TUM-Research Center for Industrial Biotechnology (copyright: Sun, TUM)

Gas Fermentation

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
Phototrophic processes with micro-algea can now be studied on a pilot-scale making use of the new micro-algae pilot plant facilities with LED day light illumination at the Ludwig-Bölkow Campus in Ottobrunn. The climate simulation technology for the operation of new open algae bioreactors is unique in the world and was developed in close cooperation with the Institute of Biochemical Engineering.

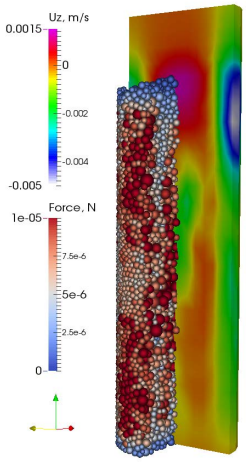
Projects
- Modeling of microalgae cultivation in open photobioreactors
- Characterization of new microalgae for open photobioreactors



Setting-up of operation of the newly developed LED day-light illumination at the micro-algae pilot plant facilities inaugurated in October 2015 (copyright: TUM)

- Mass production of microalgae in open photobioreactors
- Reaction engineering analysis of new microalgae
- Microbial production of chemicals from synthesis gas
- Gas fermentation with *Clostridium carboxidivorans*
- Hydrogenotrophic production of acetic acid
- Gas fermentation with *Clostridium aceticum*
- Multi-purpose reactor for gas fermentations

Bioprocess Integration



Simulation of chromatographic column packing behavior (copyright: Dorn,TUM)

In many cases, downstream processing is by far the most cost-intensive step of a bioprocess. Often, multiple-step bio-separations 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.

Highlight
A three-dimensional deterministic model applying Computational Fluid Dynamics (CFD) coupled with the Discrete Element Method (DEM) was developed and validated to simulate chromatographic column packing behavior during either flow or mechanical compression.

Projects
- Non-stationary hydrodynamics of chromatography columns
- Preparative purification of proteins via crystallization
- Preparative purification of proteins via extraction

Research Focus

- Micro-bioprocess engineering/bio-reactors
- 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 bio-products
- Practical training on biochemical engineering
- Practical training on bioprocess engineering

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Publications 2015

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Imprint

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