Department of Mechanical Engineering
Technical University of Munich

150 Jahre
culture of
excellence

150 Years

Mechanical Engineering

Enabling Future

1868 – 2018

Annual Report 2018

Biochemical Engineering

Industrial biotechnology

■ *Industrial biotechnology ('white biotechnology') makes use of microorganisms 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 and CO_2 are the favored raw materials for industrial biotechnology. The Institute of Biochemical Engineering deals 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 isolation of bioproducts.*

Special microorganisms are able to produce chemicals with carbon dioxide as sole carbon source, but oxygen (air) is toxic to them. At the Institute of Biochemical Engineering these microorganisms are prepared in anaerobic (oxygen free) workbenches for reaction engineering studies in bioreactors. (photo: Tobias Hase, TUM)

Bioreactors

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 and digitalization.

Highlight

A new miniaturized laser-based sensor system has been established for parallel online measurement of optical densities as reference for microbial cell mass concentrations in 48 individual single-use stirred-tank bioreactors which are operated in a bioreactor unit on a shoe-box scale and automated with a lab robot.

Operation of a bioreactor unit with 48 parallel single-use stirred-tank bioreactors on a milliliter-scale (photo: Tobias Hase, TUM)

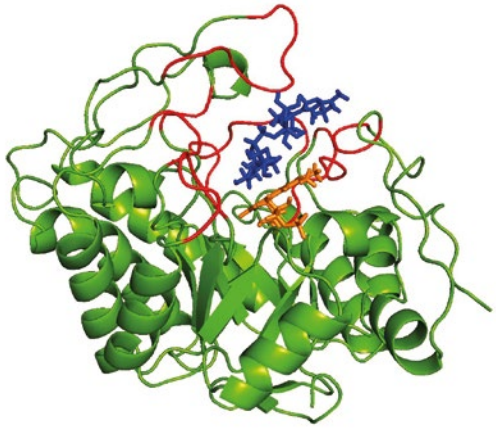
Projects

■ Multi-parameter analytics in parallel bioreactors

Biochemical Engineering

Biocatalysis

Great demands are placed on the optical purity of building-blocks for the production of pharmaceuticals. Due to the high natural selectivity of biocatalysts, biocatalysis appears to be a 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.



Model of an enzyme useful for the stereoselective reduction of alkenes which was improved by rational exchange of loop regions (colored in red) (copyright: Klermund, TUM)

Highlight

The activity of an industrially important enzyme isolated from a cyanobacterium which catalyzes the stereo-selective reduction of alkenes was improved by a factor of 6 by rational exchange of loop regions of the protein which are supposed to interact with the electron transport metabolite nicotinamide adenine dinucleotide (NADH).

Projects

- Polymeric nano-compartments for biocatalytic applications
- Membrane functionalization of nanoscale enzyme membrane reactors
- Surface functionalization of nano-scale enzyme membrane reactors
- Cellular envelopes for multi-enzyme synthesis
- Production of N-acetylneuraminic acid using epimerases from cyanobacteria
- Asymmetric syntheses with optimized ene-reductases

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

A new microbial production process was designed for the efficient production of up to 225 g L^{-1} L-erythrulose (tanning agent used in cosmetics) from *meso*-erythritol making use of a recombinant *Gluconobacter oxydans* provided by TUM Microbiology (Prof. Liebl).

Projects

- Population heterogeneity in industrial scale bioprocesses
- Metabolic analyses of recombinant microorganisms from production processes
- Production of single-stranded DNA with *Escherichia coli*
- Production of terpenoid glycosides by recombinant *Escherichia coli*
- Reaction engineering analysis of recombinant *Gluconobacter oxydans*

Pilot-scale fermentations were performed at the TUM Research Center for Industrial Biotechnology (photo: Tobias Hase, TUM)

Gas Fermentation

Special microorganisms are able to produce chemicals with carbon dioxide as sole carbon source. Electrons 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.

New open thin-layer cascade photobioreactors operated in the TUM Algae TechCenter, Ottobrunn (photo: Tobias Hase, TUM)

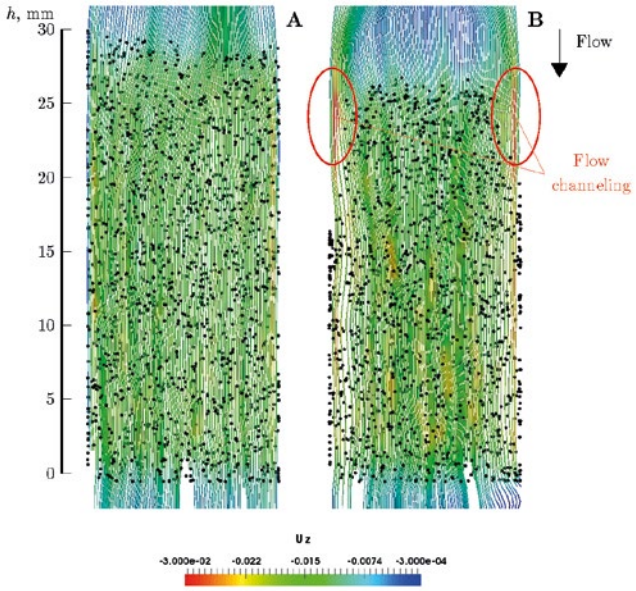
Highlight

New open thin-layer cascade photo-bioreactors made of pond liner were designed and operated up to pilot scale for the evaluation of new microalgae production processes at physically simulated dynamic climate conditions with respect to light (LED), temperature and air humidity (e.g. Mediterranean summer in Spain) in the TUM Algae TechCenter located at the Ludwig Bölkow Campus in Ottobrunn.

Projects

- Modeling of microalgae cultivation in open photobioreactors
- Characterization of new microalgae for open photobioreactors
- Mass production of microalgae in open photobioreactors
- Production of anti-oxidants with microalgae
- Light-dependent growth kinetics in flat-plate photobioreactors
- Microalgae processes in open photobioreactors with reduced water consumption
- Gas fermentation with *Clostridium carboxidivorans*
- Gas fermentation with *Clostridium aceticum*
- Multi-purpose reactor for gas fermentations

Bioprocess Integration



Simulated influence of particle migration on the fluid flow distribution in a chromatography column (copyright: Dorn, 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.

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
- Novel methods for packing of preparative chromatography columns
- Preparative purification of proteins via extraction
- Engineering of proteins for the control of crystallization processes
- Modeling and molecular dynamics simulation of protein crystals

Biochemical Engineering

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Research Focus
- Micro-bioprocess engineering
- Bioreactors
- Biocatalysis
- Fermentation
- Gasfermentation
- 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 workshop
- Analytical lab (LC-MS, flow cytometry, GC, LC, etc.)

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

Selected Publications 2017

- Praetorius F, Kick B, Behler KL, Honemann MN, Weuster-Botz D, Dietz H (2017): Biotechnological mass production of DNA origami. Nature 552: 84-87
- Koller A, Löwe H, Schmid V, Mundt S, Weuster-Botz D (2017): Model-supported phototrophic growth studies with Scenedesmus obtusiusculus in a flat-plate photobioreactor. Biotechnol Bioeng 114: 308-320
- Weiner M, Tröndle J, Albermann C, Sprenger GA, Weuster-Botz D (2017): Metabolic control analysis of L-phenylalanine production from glycerol with engineered E. coli using data from short-term steady-state perturbation experiments. Biochem Eng J 126: 86-100
- Apel AC, Pfaffinger CE, Basedahl N, Mittwollen N, Göbel J, Sauter J, Brück T, Weuster-Botz D (2017): Open thin-layer cascade reactors for saline microalgae production evaluated in a physically simulated Mediterranean summer climate. Algal Research 25 (2017) 381-390
- Dorn M, Eschbach F, Hekmat D, Weuster-Botz D (2017): Influence of different packing methods on the hydrodynamic stability of chromatography columns. J Chrom A 1516: 89-101

Imprint

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March 2018 (refering to data and events of the year 2017)