Technical University of Munich
Department of Mechanical Engineering

Annual Report 2016

Mechanical Engineering

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 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 isolation of bioproducts.

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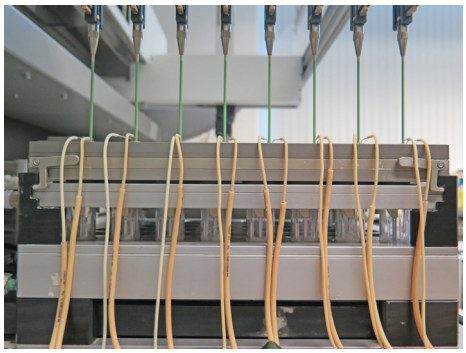
The new pilotscale photobioreactors of the Institute of Biochemical Engineering are operated in the TUM-Algae-Tech-Center at the Ludwig-Bölkow Campus in Ottobrunn using CO_2 as the carbon source (copyright: TUM)

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.



Continuous operation of a bioreactor unit with 48 parallel single-use stirred-tank bioreactors on a milliliter-scale (copyright: Schmideder, TUM)

Highlight

Continuous operation of the bioreactor unit with 48 parallel single-use stirred-tank bioreactors developed at the Institute of Biochemical Engineering enables the fast identification of microbial reaction kinetics within one set of parallel experiments.

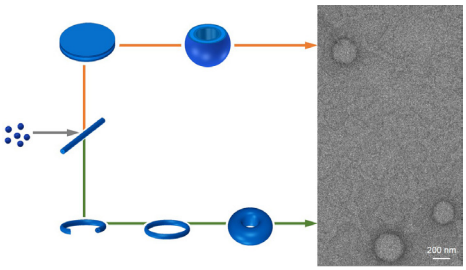
Projects

- Production of halophilic enzymes using *Haloferax volcanii* in stirred-tank bioreactors
- Continuous fermentations in miniaturized stirred-tank bioreactors
- Multi-parameter analytics in parallel bioreactors

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.

Highlight
A scalable process was designed for the mass production of polymeric nano-compartments and the formation mechanisms were elaborated. Various different enzymes were encapsulated within these nano-compartments, their membranes were functionalized by selective transport proteins and enzymes were immobilized on their surface resulting in 'enzyme-membrane reactors' on a nano-scale.



Scheme of the formation mechanism of polymeric nano-compartments in stirred-tank bioreactors and transmission electron microscopy (TEM) of the produced polymeric nano-compartments (copyright: Poschenrieder, TUM)

Projects
- Polymeric nano-compartments for biocatalytic applications
- Membrane functionalization of nano-scale 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

Pilot-scale membrane bioreactor fermentations for the production of microbial oils were performed at the TUM Research Center for Industrial Biotechnology (copyright: Sun, TUM)

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
Efficient production of microbial oils from diluted sugar mixtures usually derived from hydrolysis of (plant) biomass was enabled by application of a two-phase membrane bioreactor process with total cell retention. Microbial oils were produced with yeasts which accumulated up to 80% (w/w) lipid bodies inside the cells.

Projects
- Reaction engineering analysis of single stranded DNA production with bacteriophage M13
- Anodic respiration by *Pseudomonas putida* in stirred-tank bio-reactors
- Lipid production from diluted sugar mixtures with *Trichosporon oleaginosus*
- 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*

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

A standardized anaerobic batch process in continuously gassed stirred-tank bioreactors was designed and approved to characterize and compare the process performances of new syngas (CO_2, H_2, CO) converting microorganisms. *Sporumosa ovata* was revealed as particularly suitable for industrial applications. In appropriate reaction conditions for example, the autotrophic production of ethanol with *Sporomusa ovata* could be increased by two orders of magnitude.

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 of *Scenedesmus spec.* in flat-plate photobioreactors
- Comparative analysis of acetogenic bacteria for gas fermentation
- Gas fermentation with *Clostridium carboxidivorans*
- Gas fermentation with *Clostridium aceticum*
- Multi-purpose reactor for gas fermentations

Comparison of the process performances of new syngas converting microorganisms at standardized reaction conditions in continuously gassed stirred-tank bioreactors (photo: Tobias Hase)

Bioprocess Integration

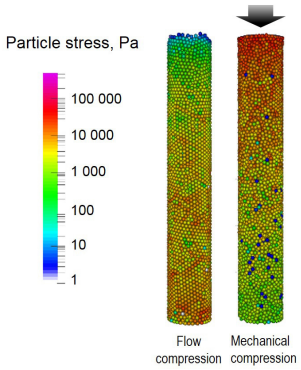
In many cases, downstream processing is by far the most cost-intensive step of a bioprocess. Often, multiple-step bioseparations are required yielding rather low product yields. Therefore, existing bioseparation processes should be improved and combined to reduce the number of process steps. The focus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



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

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 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

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Publications 2016

- Strillinger E, Grötzinger SW, Allers T, Groll M, Eppinger J, Weuster-Botz D (2016): Production of halophilic proteins with Haloferax volcanii H1895 in a stirred tank bioreactor. Applied Microbiology and Biotechnology 100: 1183-1195.
- Schmideder A, Hensler S, Lang M, Stratmann A, Giesecke U, Weuster-Botz D (2016): High-cell-density cultivation and recombinant protein production with Komagataella pastoris in stirred-tank bioreactors from milliliter to cubic meter scale. Process Biochemistry 51: 177-184.
- Weiner M, Tröndle J, Albermann C, Sprenger GA, Weuster-Botz D (2016): Perturbation experiments: Approaches for metabolic pathway analysis in bioreactors. Advances in Biochemical Engineering/ Biotechnology 152: 91-136.
- Dorn M, Hekmat D (2016) Simulation of the dynamic packing behavior of preparative chromatography columns via discrete particle modeling. Biotechnology Progress 32: 363-371.
- Poschenrieder S, Wagner S, Castiglione K (2016) Efficient production of uniform nanometer-sized polymer vesicles in stirred-tank reactors. Journal of Applied Polymer Science 133: 43274.
- Kantzow C, Weuster-Botz D (2016): Effects of hydrogen partial pressure on autotrophic growth and product formation of Acetobacterium woodii. Bioprocess and Biosystems Engineering 39: 1325-1330.
- Klermund L, Riederer A, Hunger A, Castiglione K (2016): Protein engineering of a bacterial N-acyl-D-glucosamine 2-epimerase for improved stability under process conditions. Enzyme and Microbial Technology 87-88: 70-78.
- Groher A, Weuster-Botz D (2016): Comparative reaction engineering analysis of different acetogenic bacteria for gas fermentation. Journal of Biotechnology 228: 82-94.
- Schmideder A, Priebe X, Rubenbauer M, Hoffmann T, Huang F-C, Schwab W, Weuster-Botz D (2016): Non-water miscible ionic liquid improves biocatalytic production of geranyl glucoside with Escherichia coli overexpressing a glucosyl-transferase. Bioprocess and Biosystems Engineering 39:1409-1414.
- Klermund L, Poschenrieder ST, Castiglione K (2016): Simple surface functionalization of polymersomes using non-antibacterial peptide anchors. Journal of Nanobiotechnology 14: 48.
- Groher A, Weuster-Botz D (2016): General medium for the autotrophic cultivation of acetogens. Bioprocess and Biosystems Engineering 39: 1645-1650.
- Hintermayer S, Yu S, Kroemer JO, Weuster-Botz D (2016): Anodic respiration of Pseudomonas putida KT2440 in a stirred-tank bioreactor. Biochemical Engineering Journal 115: 1-13.
- Schmideder A, Cremer JH, Weuster-Botz D (2016): Parallel steady state studies on a milliliter scale accelerate fed-batch bioprocess design for recombinant protein production with Escherichia coli. Biotechnology Progress, DOI:10.1002/ btpr.2360.
- Pfaffinger CE, Schöne D, Trunz S, Löwe H, Weuster-Botz D (2016): Model-based optimization of microalgae areal productivity in flat-plate gas-lift photobioreactors. Algae Research 20: 153-163.
- Poschenrieder ST, Schiebel SK, Castiglione K (2016): Polymersomes for biotechnological applications: large-scale production of nano-scale vesicles. Engineering in Life Sciences, DOI 10.1002/ elsc.201600100.
- Koller A, Löwe H, Schmid V, Mundt S, Weuster-Botz D (2016) Model-supported phototrophic growth studies with Scenedesmus obtusiusculus in a flat-plate photobioreactor. Biotechnology and Bioengineering, DOI 10.1002/bit.26072.
- Kick B, Hensler S, Praetorius F, Dietz H, Weuster-Botz D (2016): Specific growth rate and multiplicity of infection affect high-cell density fermentation with bacteriophage M13 for ssDNA production. Biotechnology and Bioengineering, DOI 10.1002/bit.26200.
- Koller A, Wolf L, Weuster-Botz D (2016): Reaction engineering analysis of Scenedesmus ovalternus in a flat-plate gas-lift photobioreactor. Bioresource Technology, 10.1016/j.biortech.2016.11.025

Imprint

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Editor: Prof. Dr.-Ing. Nikolaus Adams
Sub-editor: Dr. Till v. Feilitzsch
Layout: Fa-Ro Marketing, Munich
Photo credits: Uli Benz, Matthias Bittner, Stephane Corvaja, Ingo Dumreicher, Astrid Eckert, Jan Greune, Tobias Hase, Andreas Heddergott, Christian Krempaszky, Jacob Lund/Getty Images, Jan-Fabian Meis, Rawpixel/Getty Images, Jan Musiol, Claas Olthoff, PeopleImages/Getty Images, Andreas Rücker, Albert Scharger and further illustrations provided by the institutes

March 2017