University of Natural Resources
and Applied Life Sciences, Vienna

Institute of Bioprocess Science and Engineering

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Annual Report 2019

March, 2020

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Introduction

In 2019 the Department of Biotechnology (DBT) changed the organizational structure and six institutes were defined and funded. The Institute of Bioprocess Science and Engineering (IBSE) included the Department research groups Hahn, Jungbauer/Dürauer, Marzban, Striedner and the BioIndustrial Pilot Plant. IBSE will still operate under the umbrella of the Department of Biotechnology, with intensive collaborations with the other institutes of the DBT. We understand IBSE as vital part of the DBT which is central representative for BOKUs competence field Biotechnology. I, Alois Jungbauer will serve as head of the institute and Gerald Striedner as the deputy for the next two years. Although we as IBSE are still in our infancy, we decided to write an annual report for 2019, because this helps us to shape our identity and provides a platform to demonstrate/represent our scientific activities and competences as well as our contribution to teaching and education at University level.

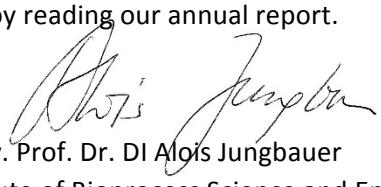
You will find highlights of our research and training work and a summary of our output in form of peer reviewed manuscripts, finished bachelor/master theses and doctoral theses, extra-curricular training activities as well as selected presentations at international conferences in this report. Besides individual research projects IBSE is strongly involved in a series of academia-industry research consortia and our strategic partner is the *austrian centre of industrial biotechnology* (acib).

We do not only want to look back, we want to look to the future, and we have ambitious plans. We want to strengthen our relationships to our academic and industrial partners. We will further intensify the research and training in the area of virtual bioprocessing and digitalization of bioprocesses, we want to actively go into processing of bionanoparticles to offer solutions to the combat against newly emerging infectious diseases. Process optimization and reduction of the environmental footprint of bioprocesses to offer solutions to the problems of climate change and to make bioprocesses more economic and sustainable. This is also important to lower the economic barrier for non-privileged countries to get access to modern therapies.

We have also started to do research in bioprocessing for a biobased industry and we are now involved in a research consortium, which tackles the problem of destruction of plastic waste. Our past research activities and built up of broad competencies together with our colleagues from the DBT, our national and international academic and industrial research partners will help us to conduct research at the forefront of bioprocess engineering. As a public university our main contributors are the Austrian taxpayers. I think we have well managed this taxpayer money and it is well invested.

I am proud to be the leader of this prosperous research institutions. I thank all our members for their input and enthusiasm to conduct excellent research and training.

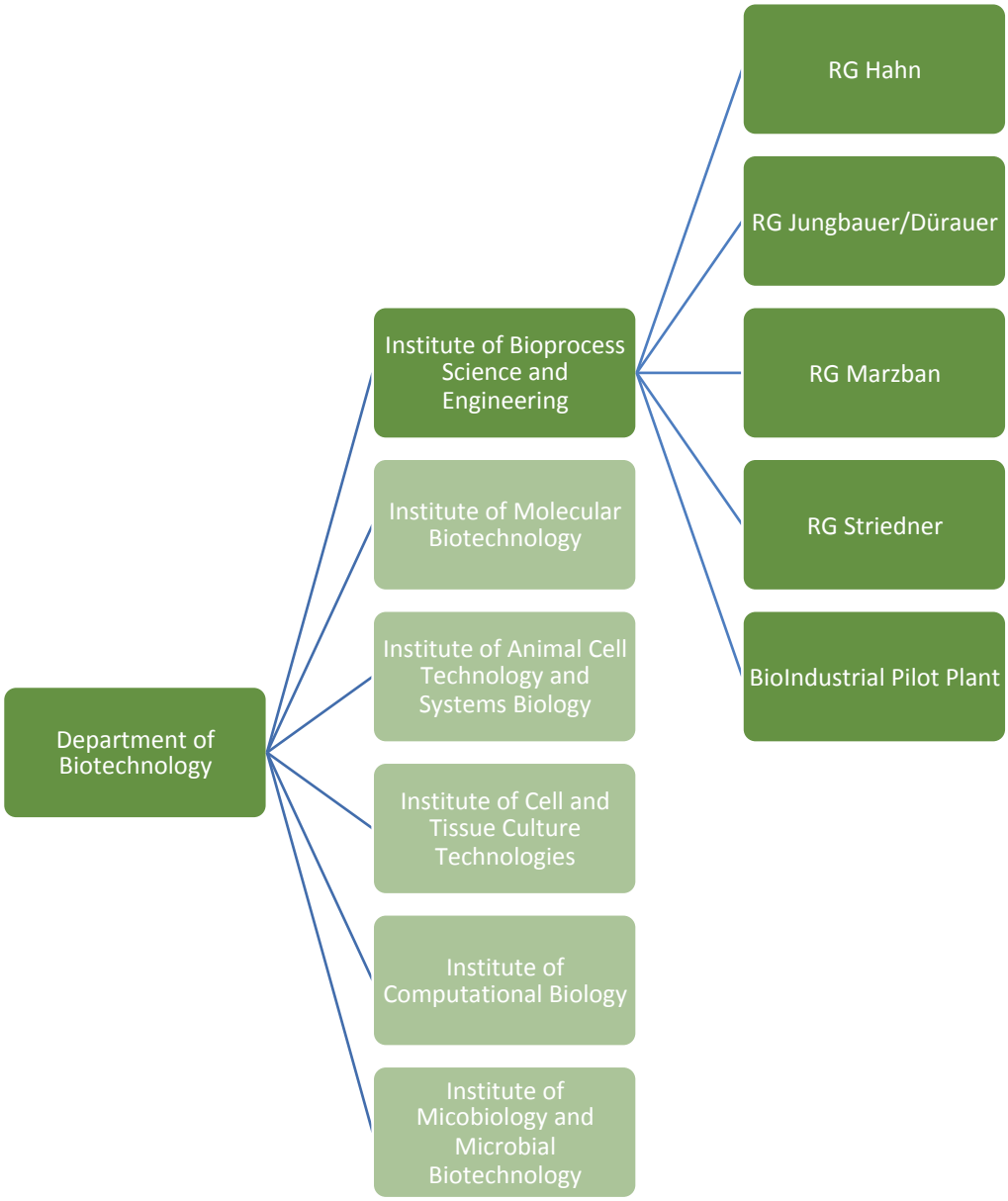
Enjoy reading our annual report.



Univ. Prof. Dr. DI Alois Jungbauer
Head of the Institute of Bioprocess Science and Engineering.

Structure of the *Institute of Bioprocess Science and Engineering*

Since January 2020 the Department of Biotechnology at BOKU is structured into 6 different independent institutes with research groups that deal with the main subject in the field of biotechnology. The institutes are sub-organizations of the Department of Biotechnology with their own specific orientation, to which the department's resources are allocated proportionally for administration and use after agreement with the department management.



Members of the Research Groups 2019

RG Hahn			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Rainer Hahn	Jürgen Beck Clemens Schimek	Markus Berg (MA) Alexander Jurjevec (MA) Matthias Müller Paola Orssini (IAESTE) David Scheich Negar Zaghi (IAESTE)	Matthias Kubek Alejandro Santiago Leon

RG Jungbauer/Dürauer			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Iara Bresolin (Guests) Igor Bresolin (Guests) Astrid Dürauer Alois Jungbauer Nico Lingg Peter Satzer Theresa Scharl-Hirsch Petra Steppert Ruper Tscheließnig Jelle de Vos (Guest) Christina Yassouridis	Patricia Pereira Aguilar Daniel Burgstaller Alessandro Cataldo Anna Christler Walpurga Krepper Gregory Dutra Hannah Engelmaier Stefan Hinterberger Leo Jakob Daniel Komuczki Maximilian Krippl Narges Lali Duarte Lima Martins Bettina Motycka Katrin Reiter Dominik Sauer Christian Schuster Tobias Schneider Jure Sencar Ignacio Montes Serrano	Lena Achleitner (MA) Teresa Brandtner (BA) Anna Frank (MA) Josef Hofer (MA) Gregor Stitz (BA) Ingnasi Bofarull Manzano (MA) Marcus Mozgocivz Patrícia Leong Rodrigues Viktoria Wetter (MA)	Eva Berger Edit Felföldi Andreas Fischer Jasmin Matzinger Magdalena Mosor

RG Marzban			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Gorji Marzban	Sonja Schürer-Waldheim		

RG Striedner			
Staff	**PhD student**	**BA/MA student, intern**	**Technician/ Student assistant**
Florian Bacher	Benjamin Bayer	Andreas Dietrich (MA)	Johanna Berein
Monika Cserjan	Natalia Danielewicz	Wanja Ehtreiber (BA)	Alexander Doleschal
Roger Dalmau Diaz	Mathias Fink	Lisa Fohler (BA)	Anna Hartmann
Mark Dürkop	Hana Hanaee	Emil Gerger (BA)	Katarina Kljajic
Esther Egger	Kulwant Kandra	Martin Gibisch (MA)	Veronika Költringer
Armin Khodaei	Florian Mayer	Christoph Köppl (MA)	Shirin Preinsperger
Julian Loibl	Artur Schuller	Anna Stock (BA)	Patrick Scheidl
Dieter Palmberger	Patrick Stargardt	Lina Vranitzky (MA)	Matthias Traninger
Magdalena Pappenreiter	Florian Strobl	Christian Zabik (MA)	
Natasa Saric	Sophie Vazulka		
Gerald Striedner			
Florian Weiß			

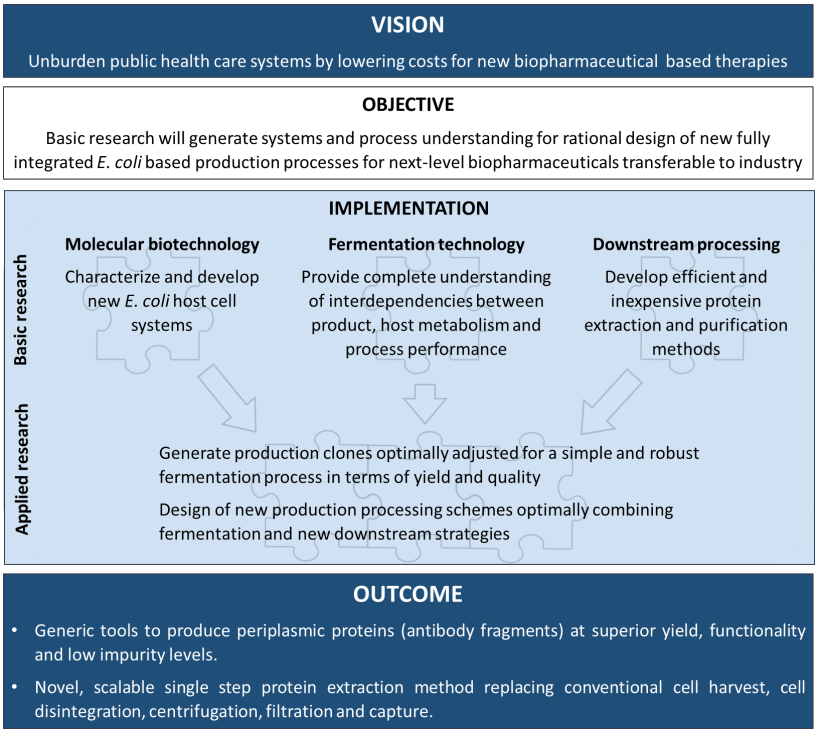
BioIndustrial Pilot Plant			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Markus Luchner	Dominik Jeschek (Co-supervisor-Biotop)	Stephan Gutmann	Martin Braunsteiner
Martin Voigtmann	Bernhard Sissolak	Raphael Große	Marco Kaupe
Karola Vorauer-Uhl	Ehsan Suleiman	Katarina Kljajic	Gabriele Lhota
		Elisabeth Lehner	Sabine Necina
		Philipp Lukas	
		Julia Mayer	
		Simon Netocny	

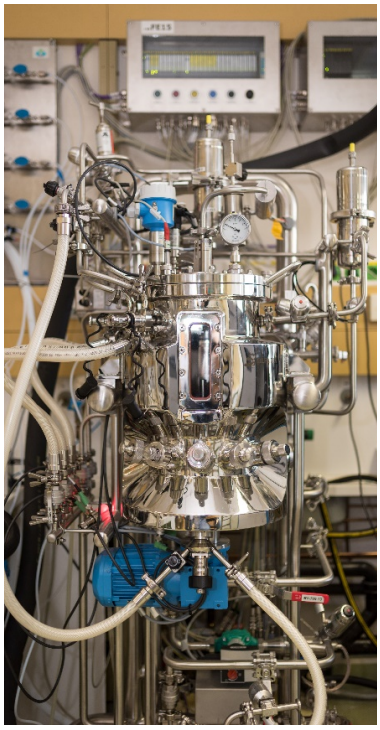
CD Laboratory for production of next-level biopharmaceuticals in *E. coli*

Boehringer Ingelheim

Christian Doppler Forschungsgesellschaft

The vision of the CD Laboratory is to make biopharmaceuticals affordable and accessible to the global patient community via new production and recovery technologies. We determine, develop, and deliver scientific fundamentals and solutions to efficiently produce functional protein scaffolds using *E. coli* as host organism. Based on the scientific competence of experts in molecular/cell biology, fermentation, downstream processing in university and our industrial partner Boehringer Ingelheim Regional Center Vienna (BI RCV), we intend to jointly elaborate pioneering concepts for integrated systems engineering.





The overall goal of our CD Laboratory is to overcome existing limitations in production of next-level biopharmaceuticals by the implementation of a holistic concept to process/systems design and optimization. The work on industrially relevant host strains, representative therapeutic protein classes and recovery technologies will provide the knowledge base and strategies for new and efficient biopharmaceutical production processes. We investigate the production of periplasmic antibody fragments as representatives of next-level biopharmaceuticals.

The first step towards improvement of these processes requires in-depth understanding of the overall process/systems at the fundamental level. In our CD Laboratory we emphasize the unity of the process and consider interactions between different unit operations to harmonize all the individual steps along the process chain and we develop a comprehensive system/process/product/analytical platform to identify bottlenecks. (M. Cserjan, R. Hahn, G. Striedner)

BioIndustrial Pilot Plant

Premises and Equipment

The "BioIndustrial Pilot Plant" at the Institute has been established as a semi-industrial facility for education, training and development of biotechnological processes.

In 2000 the Pilot Plant as a fermentation facility was adapted to full GMP compliance by Polymun Scientific, founded by Prof. Hermann Katinger. Until 2011 the Pilot Plant was continuously used under certain GMP regulations. With the relocation of Polymun Scientific to Klosterneuburg, the facility of 950 m^2 with installation costs of approx. € 4 Million was delivered to the BOKU/DBT.

The implementation and adaptation for teaching, training and research activities was enabled by significant funding of the Federal Ministry of Education, Science and Research of the Republic of Austria (BMBWF) by the so-called MINT-initiate (federal initiative to strengthen education in technical disciplines). With this funding the infrastructure was modernized to provide technical equipment for profound teaching and practical courses for our students in semi-industrial scale and additional capacity for industrial trainings for the industry and start-ups.

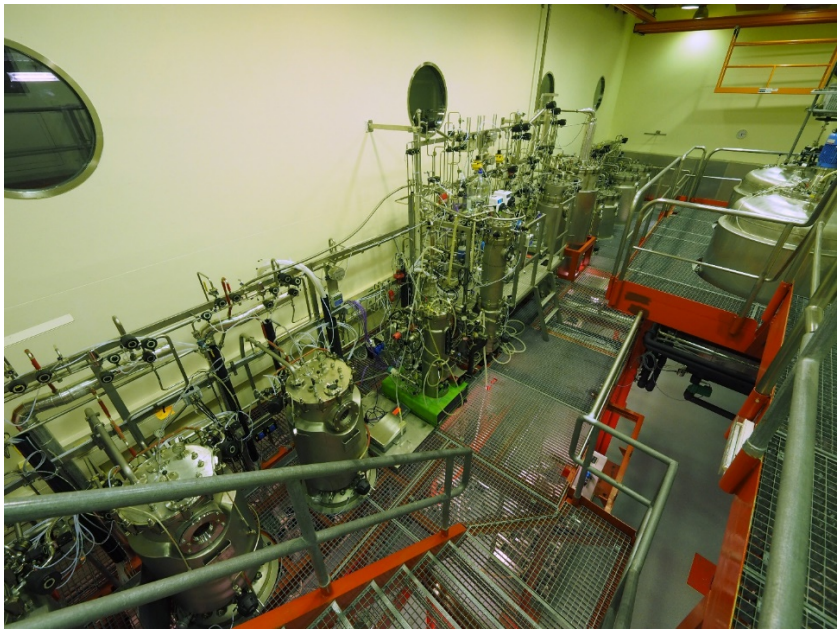
In 2013 the existing facility with its infrastructure – bioreactors and media vessels for microbials and mammalian cell culture in the scale from 30 to 1600 L - was modernized by upgrading to an industrial standard process control system (Siemens PCS7) as well as modern process sensors and analyzers. This GAMP 5 conform process control system allows flexibility in different process operation, feed strategies, cultivation strategies, and the batch program is based on the ISA-88 standard with an integrated audit trail system.

In 2016 the facility was expanded by two cell culture bioreactors, 15 and 100 L culture volume, as part of a research project together with a European company specialized in civil and industrial construction, engineering and services.

For primary recovery and downstream processing, the facility is equipped with a high-pressure homogenizer, ultra-and dia-filtration system, chromatographic system and filtration systems in pilot scale.

Process analytic of biomolecules complete the Pilot Plant portfolio. There are various HPLC devices with different detectors for the analysis of peptides and proteins, amino acids, nucleotides, carbohydrates, membrane components, and degradation products available. Furthermore, methods and devices for particle size measurement, homogeneity and surface charge of nanoparticles, biophysical characterization of nanoparticles, interaction and kinetics of biological fluids and samples are in place.

Approx. 650 m^2 of the entire facility with a total size of 950 m^2 are located in a monitored class D clean room, special labs are class C. The individual areas such as microbial fermentation, animal cell culture, downstream processing, inoculum preparation and filling as well as monitoring (both are class C clean rooms) are spatially separated from one another.
The plant has an independent water supply for high quality water, process air generation, pure steam generation and the inactivation of biological waste.



Activities

The University of Natural Resources and Life Sciences, Vienna (BOKU) started in 2019 the implementation of BOKU´s Core Facility Strategy with the focus to provide methodological and technological platforms for BOKU, other universities and research institutions as well as companies and organizations. The Department of Biotechnology was invited to participate to this initiative. In addition to the existing duties and functions, the Pilot Plant can partially provide capacities for defined services. In 2019 the planning phase, consolidation of the Core Facility Strategy of BOKU (CF) as well as the implementation, has been started.

During the planning phase general requirements, focus and tasks of the CF, organizational and administrative aspects, timelines, business conditions and general aspects of operational management need to be elaborated. According the timelines, realization of first work packages have been started:

I. Consolidation of the team: The BioIndustrial Pilot Plant is headed by Dr. Markus Luchner and provides expertise in fermentation technology, downstream processing and related analytics of biomolecules in a multi-purpose GMP-like facility and offers education and training courses in this field. Furthermore, to optimize our internal procedures the premises were rearranged and adapted for technical reasons, which should be finalized in 2020/2021.
II. In respect to organizational and operational management duties cost and activity accountings are in development to harmonize research, teaching and service activities. First procedures could be established.
III. General aspects, strategy and style for websites could be finalized and the individual homepages should be available in a medium-term.
IV. To improve the operational management of the BioIndustrial Pilot Plant, the implementation of ISO 45001, a data management system for Chemicals and other materials as well as the evaluation of an appropriate LIMS has been started.

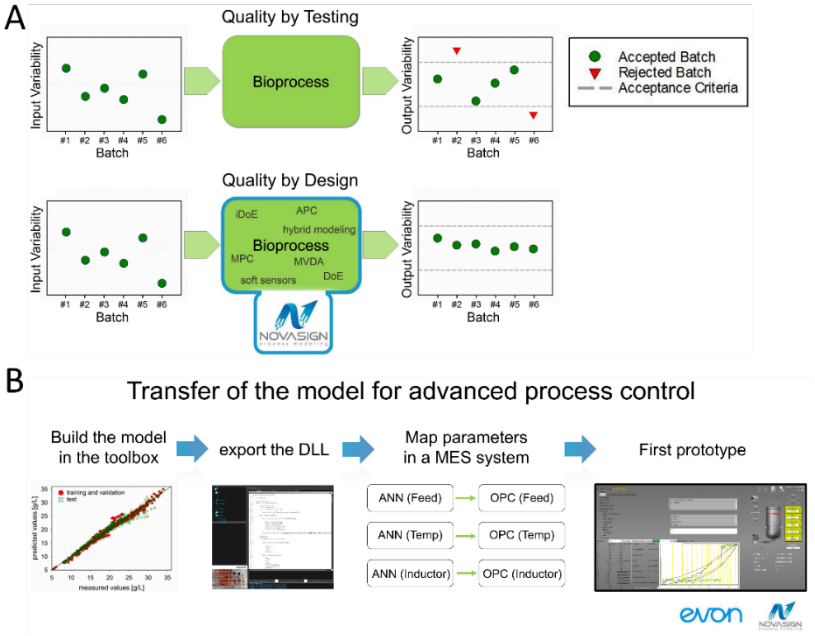
In addition to the time-consuming implementation procedure scheduled for the next following years, which has been started in 2019, several projects and services could be delivered:

I. Analytical method development, research and services for BOKU, ACIB, within industrial projects and special services for companies.
II. Upstream Projects and services for production of biomass and bio-molecules for industrial and academic partners.
III. Downstream focused projects for purification of proteins, enzymes, antibodies, and other bio-molecules.
IV. Technical Support and allocation of technical equipment for material testing, training, etc.
V. Installation of training courses for industrial partners
VI. Practical courses in the Bioprocess Engineering PhD Program

According to our engagement in education and training several master curricula courses (e.g. “Bioprocess Engineering Laboratory”, “Engineering of biotechnological production facilities”, “Automation of bioprocesses”) and importantly the course “Pilot plant BioproEng” in the doctoral program “Bioprocess Engineering” has been successfully implemented and already passed this year. Interested companies for industrial trainings have been conducted and first courses should be performed in 2020. Furthermore, in a collaboration with the Technical University Vienna and the FH CAMPUS Wien Bioengineering, additional courses were performed at the Pilot Plant. (M. Luchner, K. Vorauer-Uhl)

Project: Implementation of new quality concepts in biopharmaceutical production - solutions and strategies (FFG research studio "Novasign“)

Reducing time to market of new pharmaceutical treatments is of high interest for both patients, health insurances as well as for the pharmaceutical industry itself. Earlier market entry would extend both the timespan until a competitor can enter the market as well as consequently the return of invest. Therefore timelines for both clinical studies as and process development have to significantly decrease. With the strong background of process development and with new emerging machine learning tools in hands the research studio “Novasign” started in September 2017 with the aim to bring new machine learning solutions to significantly speed up biopharmaceutical process development. Further transferring these models from the development stage and deploying them on the shop floor for process control is one of the aims of the project. The project is supported by the FFG and BOKU with a total project sum of 1.6 m€ for 4 years. Due to the fast and promising development the Novasign GmbH was founded in 2019 offering unique process modeling solutions for both up and downstream processes. Currently Novasign hybrid model solutions mainly focuses on both upstream and tangential flow filtration processes. While in the upstream the approach of intensified design of experiments significantly reduces process characterisation times the TFF models for the downstream tackle both process control and continuo us manufacturing.



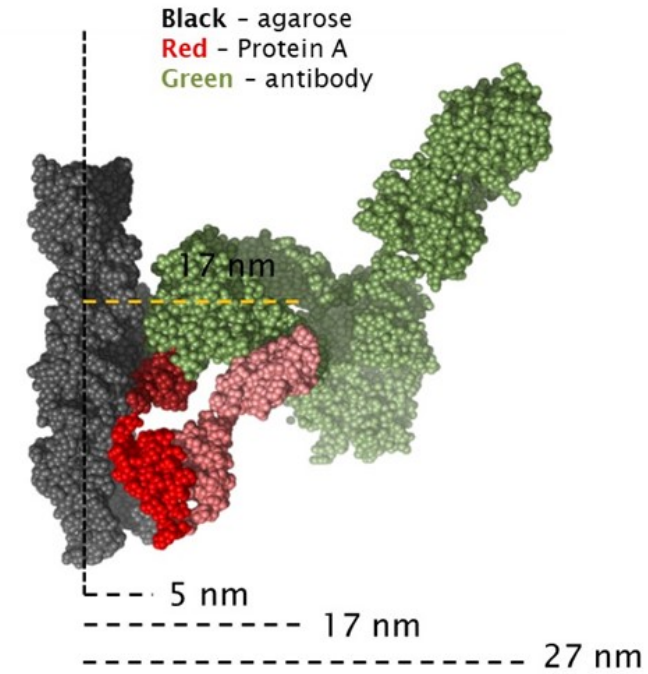
Implementation of Quality by Design approaches using advanced machine learning tools to generate soft sensors and advanced process control strategies to maintain product quality during production in a reduced development timeline. B: Simple workflow to implement a Soft-sensor or advanced process control on a supervisory control and data acquisition system: 1. Hybrid model building inside the Novasign Hybrid Model Toolbox, 2. Exporting a dynamic link library file, 3. Linking the modeling parameters with the corresponding open protocol communication 4. Real time tracking and control of critical quality attributes online in real time.

More Details: www.novasign.at

(M. Dürkop, G. Striedner)

Project: In-situ monitoring of adsorption

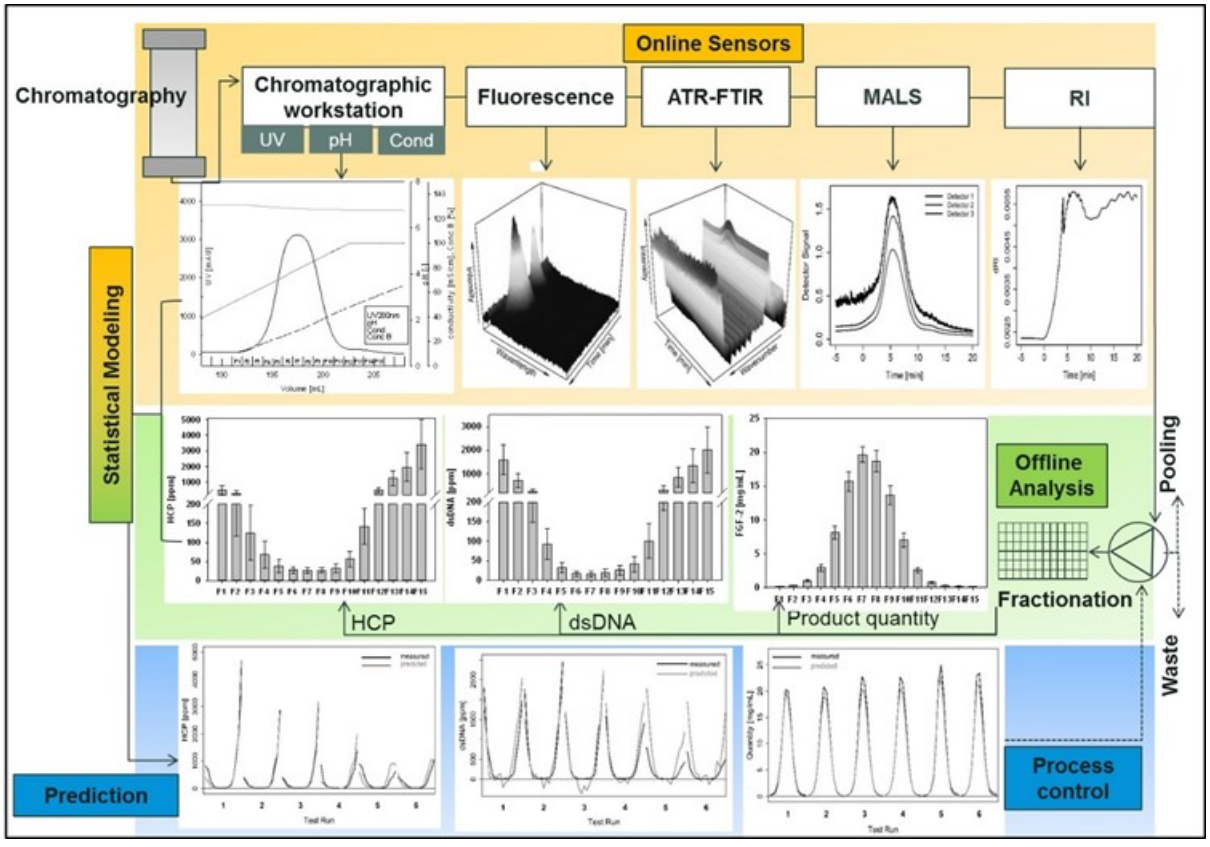
Elucidation of adsorption processes of proteins on a nanoscale level will lead to further innovation in respect to better design of materials for separation purposes, to better understanding of the underlying processes and eventually to new methods for *in-situ* monitoring of chromatography. Confocal scanning microscopy allows a closer look to adsorption processes of proteins in porous materials, but only provides information on µm scale le have. We have developed a methodology to get insight into the adsorption process on the nanoscale level. This allows us to measure the adsorption layer and to compare it to the macroscopic value of adsorption isotherms and hereby derive an explanation of adsorption isotherms on a molecular level. We conducted a highly interdisciplinary project joining complement research fields of physics, material science and bioprocessing. Key contributors were two PhDs Jacek Plewka, Goncalo Silva, Helga Lichtenegger, Harald Rennhofer (BOKU, Institute of Physics und Material Sciences), Alois Jungbauer and Rupert Tscheließnig (Institute of Bioprocess Science and Engineering). The scope was the development of a mechanistic model of the adsorption process of recombinant antibodies on protein A chromatography surfaces. Protein A affinity chromatography is an established platform technology for recombinant antibody purification. A 3D model of the antibody protein A complex on a chromatography surface was derived from SAXS measurements. For this purpose, the chromatography material was packed in a small quartz column, saturated with antibody and placed in the beam line. The SAXS measurements were performed in the beamlines Synchrotron Radiation Facility (Grenoble, France). Different binding conformations for different antibody to protein A ratios (1:1, 2:1) were obtained and the steric hinderance of the binding of more than two antibodies could be clearly demonstrated. This work will help us to understand adsorption, contribution of the backbone and optimal ligand arrangement on a nanoscale level. (A. Jungbauer, R. Tscheließnig)



*3D depiction of antibodies binding to a staphylococcal protein A ligand immobilized on agarose Adapted from L. Silva, et al (2019) Biotechnology and Bioengineering, **116**, 76-86.*

Project: Real Time monitoring of product quantity, purity and potency during downstream processing of biopharmaceuticals

Regulatory agencies have encouraged the implementation of process analytical technology (PAT) to enhance product quality and process robustness of pharmaceutical production. This combination of process understanding and process control by real-time monitoring of quality and performance attributes will also increase the process efficiency and productivity. However, while for conventional drug production this approach has been successfully implemented biopharmaceutical manufacturing is lagging behind. Currently, process performance in biopharma is monitored by laborious and time-delayed offline analysis after each process step. This conventional approach causes hold times and increases overall process duration as well as the risk for batch failure.



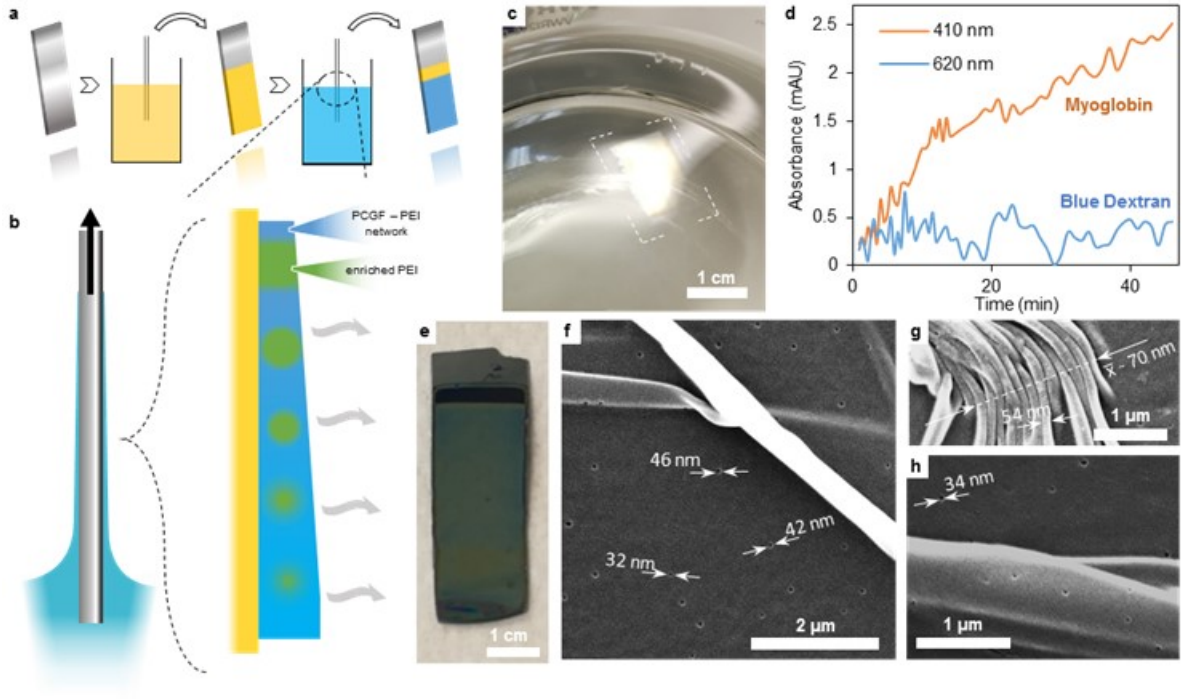
Work flow of development of a predictive model for prediction of purity, quantity and potency for a unit operation in downstream processing such a chromatography.

While for monitoring and controlling of production processes the feedback time required is in the range of minutes, real time monitoring of purifications steps relies on much faster response of sensors. We accepted this challenge and set up a system enabling the real time monitoring of product quantity, purity and potency in parallel during chromatographic purification and within a feedback time below 10 seconds. We equipped a commercial chromatographic workstation with additional online sensors based on multi-angle light scattering, refractive index, attenuated total reflection Fourier-transform infrared, and fluorescence spectroscopy. Online signals and

corresponding offline data for product quantity and co-eluting impurities such as high molecular weight impurities, HCP, dsDNA, endotoxin content, or product variants were analyzed by the statistical tools partial least square regression and boosted structured additive regression. These developed mathematical models were than applied to predict those quality criteria during capture, intermediate and polishing steps of a monoclonal antibody produced in CHO and for fibroblast growth factor 2 overexpressed in *E. coli*. Information on product quality and process performance attributes is received simultaneously from 13 different models during chromatographic purification within a feedback time below 1 sec. Elution pools collected based on such models were shown to be of the quality as if based on time delayed off line analytics but allow immediate further processing. These findings are fundamental for the successful implementation of continuous manufacturing and real-time release in biomanufacturing. (A. Dürauer, A. Jungbauer)

Project: Nanomembranes for bioseparation

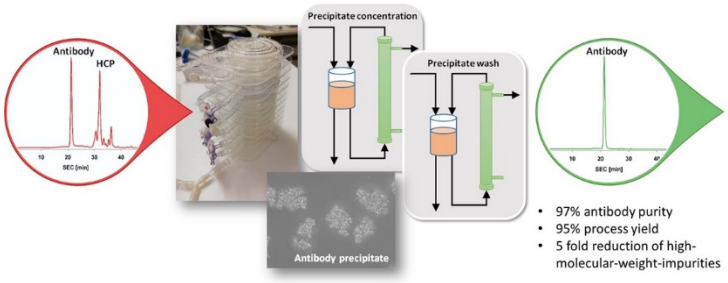
Introduction and advent of ultrathin separation layers enable new technologies in various different fields such as desalination, solvent nanofiltration, sensors and actuators, bioseparations, microfluidics and energy-related fields. Especially in bioseparations ultrathin films occupy a unique position as highly permeable and selective membranes which could revolutionize the industry but have yet to deliver on this potential at industrial scale.



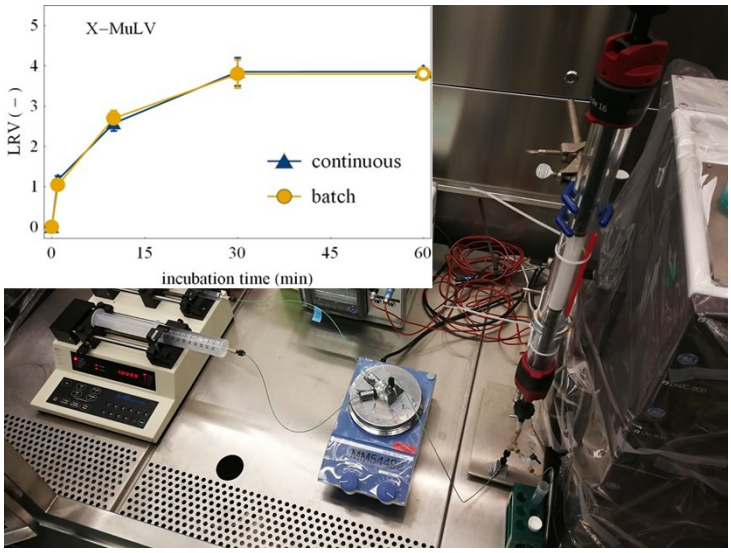
The dip-coating technique and characteristics of the corresponding nano-membranesmembranes. (a) Steps necessary for membrane casting starting with casting of the sacrificial layer, intermediate drying, coating of membrane polymer film and final drying. The following steps are identical to those of spin-coated membranes. (b) Schematic representation of the thin film formation (c) freestanding membrane piece floating on the water surface (d) Absorbance of the permeate side at the indicated wavelengths during a diffusion experiment with Myoglobin and Blue dextran. (e) Picture of a piece of silicon wafer dip-coated with a membrane on top of a sacrificial PSS layer. (f – h) SEM images of membranes supported on flat silicon.

A method has been developed to produce nanomembranes with a thickness of 75 nm and 40 nm pores with an epoxy resin suitable for large scale production. An ultrathin membrane with branched polyethylenimine is used to form a covalently crosslinked polymer membrane with pores that span the entire thickness. The pore formation relies on micro-phase separation of the curing agent during casting and the selective dissolution of the emergent nanodomains. The obtained membranes are hydrophilic and therefore suitable for applications in biotechnology. Proteins with a diameter of less than 12 nm can diffuse through the pores and permeation rates are pH dependent. The entire fabrication process has been transferred to a dip coating approach, which is more suitable for a potential large-scale production. (A. Jungbauer)

Project: Integrated continuous biomanufacturing



Schematic overview of the continuous capture of antibodies with non-interrupted mass flow of the product. HPLC size exclusion chromatograms show the purity before and after capture, adapted from Burgstaller, et. al. (2019) Biotechnol. Bioeng, ***116*** *(51053-1065).*

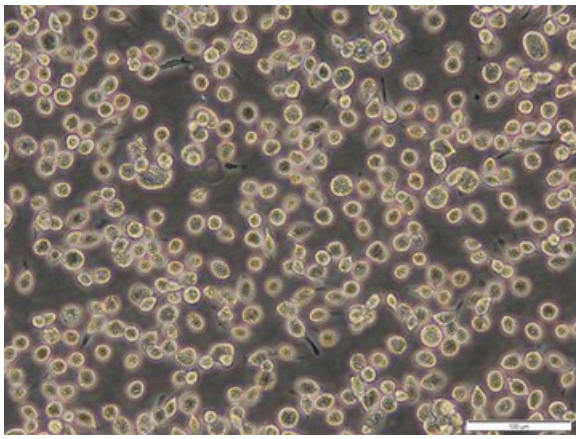


Laboratory set-up of continuous virus inactivation with packed bed reactor; top left: Virus inactivation kinetics of Murine Leukemia Virus for batch incubation in stirred tank rector and continuous inactivation, adapted from Martins et al. (2019) Biotechnology Journal, 14 art. no.

Currently, the majority of biopharmaceutical products are produced in fully batch wise manner, except for a handful licensed products where the upstream processing is conducted continuously in form of a perfusion culture or continuous stirred tank reactor. The fully integrated manufacturing is more efficient and has economic advantages. The questions how a manufacturing process can be converted into a fully integrated system is a strong focus of the IBSE. Precipitation is an alternative capture step to protein A affinity chromatography for purification of antibodies from a culture supernatant. It can be easily integrated into a continuous process by the use of a tubular reactors to achieve mixing and a certain hold time. An unsolved challenge was still the precipitate harvest. Centrifugation and dead-end filtration results in hardly soluble densely compressed precipitate pellets. The compression can be avoided by the use of tangential flow filtration. We developed a fully continuous two-stage TFF for precipitate concentration in the first stage and precipitate wash in the second stage. In this case we are able to generated a continuous capture process where the mass flow is not interrupted in contrast to capture with continuous counter current chromatography. We compared the economics and environmental impact of such process to batch operation and other continuous antibody manufacturing processes. The continuous downstream processing clearly showed and economic benefit in respect to cost of goods and reduction of environmental footprint. Another challenge in continuous integrated biomanufacturing is the continuous virus inactivation. When recombinant proteins are produced with Chine Hamster Ovarian Cells at least two dedicated virus inactivation steps are required, because the cell could be potential contaminated with a virus. We have developed a continuous virus inactivation procedure based on a backed bed reactor. The protein solution can be continuously mixed with the inactivation agent and the reactor is ensure the

necessary contact time in case of a continuous reactor the equivalent is the residence time. The reactor is a simple packed be with beads. The same inactivation kinetics could be shown for the continuous virus inactivation compared to a batch wise inactivation. The concept will be implemented in various integrated biomanufacturing processes and is considered as core piece for new continuous integrated manufacturing strategies. (A. Jungbauer)

Project: Bionanoparticle bioprocessing

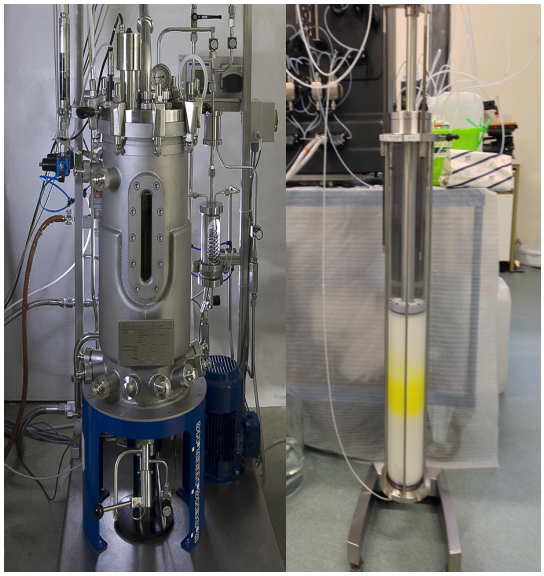


The Tmns42 insect cell line, a derivative of High Five cell line (Hi5) Trichoplusia ni (Lepidoptera: Noctuidae) cabbage looper (ovaries) adapted to serum-free medium in suspension culture.

Bionanoparticles such as viruses, virus-like particles, and extracellular vehicles are the next generation of therapeutics or vaccines for emerging viral diseases. We use enveloped virus-like particles as model or surrogate for bionanoparticle processing which can be produced in insect cells using the Baculovirus insect cell expression vector system. For this purpose we have developed a Noda-virus free Tnms42 insect cells, which is a versatile host for overexpression of proteins, VLPs and non-enveloped or enveloped viruses. Our virus-like particles have been produced in 10-liter bioreactors using suspension cell technology.

The major challenges for effective downstream processing of these virus-like particles with the Baculovirus expression vector systems is the co-expression of Baculoviruses and other extracellular vesicles. They share a lot of surface properties which and therefore separation is very difficult and can be only accomplished with high resolution methods. Immune response against Baculoviruses in humans have been observed therefore efficient removal is mandatory. A fast purification method for these VLPs by simple processing of the bioreactor broth and one chromatography step has been developed. A 4.2 log clearance of baculovirus from VLPs was reached. Absence of the Baculovirus specific proteins and electron microscopy in the VLP fractions also corroborated the clearance of Baculovirus. Strategies how to arrive at a process suited for a pandemic vaccine and how to scale up will are still a focus of IBSE and the Department of Biotechnology. (P. Aguilar, A. Jungbauer)

Project: Platform manufacturing process for recombinant proteins



Process development for recombinant protein production is a time consuming and expensive task. Scientists at acib developed a platform technology based on the expression of easy-to-be-purified fusion proteins in a combination with a proteolytic enzyme to cleave off the fusion-tag.

Biopharmaceuticals have enabled or improved the therapy of many diseases. Cancer, diabetes, auto-immune diseases, as well as many infectious diseases can be treated by recombinant proteins such as antibodies, hormones, cytokines and others. The production of most recombinant proteins, with the exception of monoclonal antibodies, requires a cost-intensive tailor-made process design for each protein including fermentation, recovery and purification. Especially the downstream process, i.e. the removal of harmful impurities while maintaining the native structure, can be immensely challenging, sometimes taking years to develop.

Scientists in molecular biology, upstream processing, downstream processing and molecular modelling at acib worked together to develop a new platform process for manufacturing of recombinant proteins in *Escherichia coli* that allows reduced time to market. Thereby, biopharmaceuticals can be made affordable and accessible to the global patient community.

The project objectives were the development of easy-to-be-purified fusion proteins including a specific purification-tag to economically capture the fusion protein using a generic downstream process and the efficient cleavage of the purification-tag. For this purpose, a human proteolytic enzyme was selected and modified to enable its production as an active monomer in *Escherichia coli*. Due to its involvement in a critical cellular pathway, the protease has a very high affinity for a specific recognition sequence. Via mutagenesis and molecular modelling in-silico a toolbox of several protease variants with the property to cleave the purification-tag before all amino acids was developed. This enables the manufacturing of any protein of interest with an authentic N-terminus.

This new platform technology is easily scalable from research- to industrial-scale and allows the cost-effective production at high amounts and purity. The process is now in use at the industrial partner Boehringer Ingelheim RCV and a patent was filed in August 2019. This work is performed in collaboration with Prof. Rainer Schneider (UIBK, University of Innsbruck, Austria) and Prof. Chris Oostenbrink (Institute of Molecular Modeling and Simulation, BOKU Vienna).

With our new platform process, the number of potential new biological drugs can be increased and the current focus on antibody-based therapies can be shifted. This enhances the prospect for new therapies for previously untreatable diseases. (M. Cserjan, N. Lingg, A. Jungbauer, G. Striedner)

Overview: final theses (finished and ongoing)

Habilitation (Venia Docendi)

Astrid Dürauer
Intensification of downstream processing for recombinant proteins
Field Bioprocess Engineering
Defense: June 2019

PhD projects

Finished

Hannah Engelmaier (acib project 25071)
Continuous downstream processing of proteins with focus on precipitation, solid-liquid separation and process analytics.
Supervisor: Alois Jungbauer, Rainer Hahn
Finished: July 2019

Stephan Hinterberger (acib project 25061)
INORGANIC FRACTAL STRUCTURES FOR BIOCHROMATOGRAPHY.
Supervisors: Alois Jungbauer, Rupert Tscheliessnig
Finished: Oktober 2019

Alexander Morokutti
DETERMINATION OF CROSS-REACTIVE NEUTRALIZING ANTIBODIES INDUCED BY A NOVEL REPLICATIONDEFICIENT LIVE INFLUENZA VIRUS VACCINE. DEVELOPMENT OF IMMUNOANALYTICAL GXP-COMPLIANT METHODS.
Supervisor: Alois Jungbauer
Finished: March 2019

Dominik Sauer (acib project 25011)
Real-time monitoring and model-based prediction of purity and quantity in a chromatographic step of a biopharmaceutical
Supervisors: Astrid Dürauer, Alois Jungbauer
Finished: June 2019 (with distinction)

Christian Schuster (acib project 25051)
CONDUCTIVE NANOMEMBRANES FOR ELECTRICALLY DRIVEN REACTIONS AND SEPARATIONS
Supervisors: Alois Jungbauer, Rupert Tscheliessnig
Finished: October 2019

On-Going

Patricia Pereira Aguilar (BioTop)
Downstream processing of enveloped virus-like particles by polymer grafted media
Supervisor: Alois Jungbauer
Start: 2016

Hanna Hanee Ahvaz (CD-Lab NLBP)
Development of Methods for in vivo quantification of proteolysis in E. coli expression systems
Supervisor: Gerald Striedner
Start: November 2019

Benjamin Bayer (FFG Research Studio Novasign)
Hybrid modeling and Quality by Design implementation in upstream processing
Supervisor: Gerald Striedner
Start: September 2017

Jürgen Beck
Impact of mass transfer mechanism on protein separation in two-component adsorption
Supervisor: Rainer Hahn
Start: November 2019

Anna Christler (acib project 25011)
Hybrid modeling approaches for preparative protein chromatography
Supervisors: Alois Jungbauer, Astrid Dürauer
Start: January 2017

Gregory Dutra (Marie Curie ITN A4B)
Continuous Separation of Recombinant Antibodies by non-chromatographic methods
Supervisor: Alois Jungbauer
Start: October 2018

Suleiman Ehsan
Protein-liposome conjugates as novel HIV vaccine candidates;
Supervisor: Karola Vorauer-Uhl
Start: 2016

Mathias Fink (CD-Lab NLBP)
Fab production in E. coli - an integrated approach for detailed systems and process characterization as basis for rational design
Supervisor: Gerald Striedner
Start: February 2017

Alexander Jurjevec (CD-Lab NLBP)
Polyethyleneimmine for protein extraction from bacteria
Supervisor: Rainer Hahn
Start: 2019

Daniel Komuzcki (Marie Curie ITN A4B)
Fully integrated continuous bioprocessing of recombinant proteins using mammalian cells
Supervisor: Alois Jungbauer
Start: May 2018

Maximilian Krippl (FFG Research Studio Novasign)
Hybrid-model approaches for crossflow filtration processes
Supervisor: Astrid Dürauer
Start: September 2018

Narges Lali (Horizon 2020 ITN CODOBIO)
Residence Time distribution of pseudo-continuous methods
Supervisor: Alois Jungbauer
Start: June 2019

Duarte Lima Martins (acib project 25011)
CONTINUOUS VIRAL INACTIVATION FOR BIOPHARMACEUTICALS
Supervisor: Alois Jungbauer
Start: January 2016

Florian Mayer (CD-Lab NLBP)
Influence of fermentation strategies and scale effects on Fab production in E. coli
Supervisor: Gerald Striedner
Start: July 2019

Bettina Motycka (BioTop)
Resolving dynamic protein conformations in multidomain enzymes with SAXS
Supervisors: Roland Ludwig, Rupert Tscheliessnig
Start: 2019

Karin Reiter (acib project 25041)
Separation of virus like particles and extracellular vesicles
Supervisor: Alois Jungbauer
Start: 2017

Clemens Schimek (CD-Lab NLBP)
Microparticles technology for extraction of periplasmic proteins
Supervisor: Rainer Hahn
Start: 2017

Sonja Schürer-Waldheim (BioTop)
Phosphoproteomics of antibody producing CHO cell lines
Supervisors: Renate Kunert, Gorji Marzban
Start: 2019

Artur Schuller (CD-Lab NLBP)
Advancements and further characterization of genome integrated systems
Supervisor: Gerald Striedner
Start: January 2017

Jure Sencar (acib project 25011)
Design of reactors for continuous purification of proteins
Supervisor: Alois Jungbauer
Start: January 2016

Ignacio Montes Serrano (Horizon 2020 ITN CODOBIO)
Determination of a mathematical model for the power input in shaken microtiter plates and correlation with larger size vessels
Supervisor: Astrid Dürauer
Start: May 2019

Bernhard Sissolak (FFG PAT Plant)
Development of an at- and offline analytical platform for characterization of product and cell related quality attributes as basis for advanced process design and control of cell culture processes
Supervisor: Karola Vorauer-Uhl
Start: September 2016

Patrick Stargardt (EU Project Rafts4Biotech/ extern Fa. enGenes GmbH)
Advancements and further characterization on growth devoupled protein expression using the phage T7 dervide GP2 protein
Supervisor: Gerald Striedner
Start: February 2018

Florian Strobl (acib project 25041)
Continuous production of biomolecules with insect cells
Supervisor: Gerald Striedner
Start: January 2016

Sophie Anna Vazulka (CD-Lab NLBP)
Host cell response to antibody fragment production in E. coli with special focus on transscriptome and translatome
Supervisor: Gerald Striedner
Start: January 2019

Master theses

Finished

Markus Berg (acib project 25011)
Purification of rh-TNF-α by chromatographic methods
Supervisor: Rainer Hahn, Astrid Dürauer
Finished: June 2019

Matthias Biechele
Retention characteristics of plasmid DNA on anion exchange resins.
Supervisor: Rainer Hahn
Finished: June 2019

Jacqueline Daume (FH Campus Wien)
Topische Produkte zur prophylaktischen und therapeutischen Anwendung bei UV-Exposition;
Co-Supervisor: Karola Vorauer-Uhl
Finished: January 2019

Benjamin Domanig
Purification process characterization and optimization of recombinant protein components of BM32, a grass pollen allergy vaccine.
Supervisor: Rainer Hahn
Finished: April 2019

Alexander Jurjevec (CD-Lab NLBP)
DNA and endotoxin removal from E. coli homogenate.
Supervisor: Rainer Hahn
Finished: February 2019

Maria Belen Davalos Krützfeldt
Online Monitoring of Protein Refolding from IBs overexpressed in E.coli.
Supervisor: Alois Jungbauer, Astrid Dürauer
Finished: March 2019

Anna Maria Lastin
Characterization of chromatographic resin material.
Supervisor: Alois Jungbauer
Finished: 2019

Philipp Lukas
GMP related qualification of a filtration system with respect to biological contaminants;
Supervisor: Karola Vorauer-Uhl
Finished: June 2019

Theresa Sophie Matuszek (FH Campus Wien)
Migration von Infektionskrankheiten – werden Tropenkrankheiten zur Gefahr in Mitteleuropa;
Co-Supervisor: Karola Vorauer-Uhl
Finished: June 2019

Florian Mayer (conducted at Linköping University)
State-of-the-art sensors for advancing bioprocess monitoring - Application to CHO cell cultivation
Supervisor: Gerald Striedner, Carl-Fredrik Mandenius
Finished: May 2019

Lisa Schlosser (FH Campus Wien)
Korrekte Anwendung von Desinfektionsmitteln in GMP und non-GMP Bereichen;
Co-Supervisor: Karola Vorauer-Uhl
Finished: September 2019

Doris Wolf (FH Campus Wien)
Internationale empirische Studie zum Berufsfeld der Pharmareferenten;
Co-Supervisor: Karola Vorauer-Uhl
Finished: September 2019

On-going

Andreas Dietrich (CD-Lab NLBP)
Influence of different fed-batch and induction strategies on cell growth, Fab production kinetics and downstream process performance in Escherichia coli lab-scale bioreactor cultivations.
Supervisor: Gerald Striedner, Monika Cserjan
Start: August 2019

Martin Gibisch (CD-Lab NLBP)
Influence of MicL co-expression on growth and Fab production kinetics in Escherichia coli lab-scale bioreactor cultivations
Supervisor: Gerald Striedner, Monika Cserjan
Start: August 2019

Stephan Gutmann (FH Bioengineering - Polymun/PP)
Design und Charakterisierung von Vorrichtungen zur Herstellung von Liposomen
Supervisor: Karola Vorauer-Uhl
Start: Juni 2019

Josef Horvath (acib project 25011)
2D simulation as tool for fast chromatography predictions
Supervisor: Astrid Dürauer
Start: May 2019

Christoph Köppl (CD-Lab NLBP)
Long-term response on chromosome-level of genome genome-integrated Escherichia. coli expression systems to recombinant gene expression
Supervisor: Gerald Striedner, Monika Cserjan
Start: April 2019

Christoph Sailer
Solids recovery modelling in centrifugal separations
Supervisor: Rainer Hahn
Start: March 2019

Alejandro Santiago-Leon (CD-Lab NLBP)
Chromatographic purification of Fab fragments
Supervisor: Rainer Hahn
Start: March 2019

Kathrin Seyrl
Inclusion body characterization and analytical method development for IB processing
Supervisor: Rainer Hahn
Start: May 2019

Matthias Müller
Optimization of filtrations steps for E. coli homogenates
Supervisor: Rainer Hahn
Start: March 2019

Ignasi Bofarull Manzano (Novasign)
Hybridmodeling for tangential flow filtration applied to multicomponent systems
Supervisor: Astrid Dürauer, Maximilian Krippl
Start: October 2019

Simon Netocny (MSD/PP)
Single-use process verification strategy-MSD Animal Health Krems
Supervisor: Karola Vorauer-Uhl
Start: Mai 2019

Lina Vranitzky (Novasign)
Intensification of the experimental design for Escherichia coli fed-batch fermentations
Supervisor: Gerald Striedner, Benjamin Bayer
Start: February 2019

Christian Zabik (PAT-Plant)
Feed on-demand glucose control for mammalian bioprocesses based on real-time oxygen uptake rate determination
Supervisor: Gerald Striedner, Wolfgang Sommeregger
Start: March 2019

Bachelor theses

Finished

Wanja Ehtreiber (acib project 25081)
Impact of a short Tag fused to recombinant model proteins – a characterisation in fed batch cultivation
Supervisor: Gerald Striedner, Monika Cserjan
Finished: January 2020

Lisa Fohler (CD-Lab NLBP)
Influence of N-terminal Flag-tag on periplasmic recombinant protein production in E. coli
Supervisor: Gerald Striedner, Monika Cserjan
Finished: March 2019

Emil Gerger (CD-Lab NLBP)
Influence of different Fab antibody fragments on growth and production kinetics in E. coli
Supervisor: Gerald Striedner, Monika Cserjan
Finished: February 2019

Katarina Kljajic (FFG PAT-plant)
Assessment of monoclonal antibody charge heterogeneity;
Supervisor: Karola Vorauer-Uhl
Finished: October 2019

Maria Toth (CD-Lab NLBP)
Evaluation of MicL co-expression in genome integrated E. coli production strains
Supervisor: Gerald Striedner, Monika Cserjan
Finished: June 2019

On-going

Teresa Brandtner (acib project 25011), Bachelor Thesis
Purification of antibody aggregates from CHO supernatants
Supervisor: Astrid Dürauer
Start: June 2019

Alexandra Katholnig (HIVVAC)
Optimization of N-terminal reductive alkylation of proteins for bioconjugation to liposomes;
Supervisor: Karola Vorauer-Uhl
Start: September 2019

Elisabeth Lehner (HIVVAC)
The influence of environmental conditions on EDC/Sulfo-NHS mediated conjugation of liposomes with an HIV protein
Supervisor: Karola Vorauer-Uhl
Start: Juni 2019

Anna Stock (CD-Lab NLBP)
Influence of different fermentation strategies on growth and Fab production kinetics in Escherichia coli lab-scale bioreactor cultivations
Supervisor: Gerald Striedner, Monika Cserjan
Start: July 2019

Scientific output

Scientific Publications in peer-reviewed journals

1. Beyer, B., Walch, N., Jungbauer, A. & Lingg, N. How Similar Is Biosimilar? A Comparison of Infliximab Therapeutics in Regard to Charge Variant Profile and Antigen Binding Affinity. *Biotechnology Journal* **14** (2019).
2. Burgstaller, D., Jungbauer, A. & Satzer, P. Continuous integrated antibody precipitation with two-stage tangential flow microfiltration enables constant mass flow. *Biotechnology and Bioengineering* **116**, 1053-1065 (2019).
3. Christler, A, Felföldi E, Mosor M, Sauer, D, Walch, N, Dürauer A, Jungbauer A. Semi-automation of process analytics reduces operator effect. *Bioprocess and Biosystems Engineering* (2019).
4. da Silva, G.F.L., Plewka J, Tscheließnig, R, Lichtenegger, H, Jungbauer, A, Dias-Cabral, A.C.M., Antibody Binding Heterogeneity of Protein A Resins. *Biotechnology Journal* **14** (2019).
5. Felfödi, E. , Scharl T, Melcher M, Dürauer A, Wright K, Jungbauer A. Osmolality is a predictor for model-based real time monitoring of concentration in protein chromatography. *Journal of Chemical Technology and Biotechnology* (2019).
6. Fink M, Vazulka S, Egger E, Jarmer J, Grabherr R, Cserjan-Puschmann M, et al. Microbioreactor Cultivations of Fab-Producing Escherichia coli Reveal Genome-Integrated Systems as Suitable for Prospective Studies on Direct Fab Expression Effects. Biotechnology Journal. 2019;14(11).
7. Iurashev, D., Schweiger, S., Jungbauer, A. & Zanghellini, J. Dissecting peak broadening in chromatography columns under non-binding conditions. *Journal of Chromatography A* **1599**, 55-65 (2019).
8. Janzen, N.H. et al. Implementation of a Fully Automated Microbial Cultivation Platform for Strain and Process Screening. *Biotechnology Journal* **14** (2019).
9. Jungbauer, A. Continuous Virus Inactivation: How to Generate a Plug Flow. *Biotechnology Journal* **14** (2019).
10. Krepper, W., Burgstaller, D., Jungbauer, A. & Satzer, P. Mid-manufacturing storage: Antibody stability after chromatography and precipitation based capture steps. *Biotechnology Progress* (2019).
11. L. Silva G, Plewka J, Lichtenegger H, Dias-Cabral AC, Jungbauer A, Tscheließnig R. The pearl necklace model in protein A chromatography: Molecular mechanisms at the resin interface. Biotechnology and Bioengineering. 2019;116(1):76-86.
12. Lemmerer, M., Maierhofer, J, Lepak A, Longus K, Hahn, R, Nidetzky, B,. Decoupling of recombinant protein production from Escherichia coli cell growth enhances functional expression of plant Leloir glycosyltransferases. *Biotechnology and Bioengineering* **116**, 1259-1268 (2019).
13. Martins DL, Sencar J, Hammerschmidt N, Tille B, Kinderman J, Kreil TR, et al. Continuous Solvent/Detergent Virus Inactivation Using a Packed-Bed Reactor. Biotechnology Journal. 2019;14(8).
14. Matlschweiger, A., Fuks, P., Carta, G. & Hahn, R. Hindered diffusion of proteins in mixture adsorption on porous anion exchangers and impact on flow-through purification of large proteins. *Journal of Chromatography A* **1585**, 121-130 (2019).
15. Pappenreiter, M., Sissolak, B., Sommeregger, W. & Striedner, G. Oxygen uptake rate soft-sensing via dynamic computation: Cell volume and metabolic transition prediction in mammalian bioprocesses. *Frontiers in Bioengineering and Biotechnology* **7** (2019).
16. Pereira Aguilar P, González-Domínguez I, Schneider TA, Gòdia F, Cervera L, Jungbauer A. At-line multi-angle light scattering detector for faster process development in enveloped virus-like particle purification. Journal of Separation Science. 2019;42(16):2640-9.
17. Pereira Aguilar P, Schneider TA, Wetter V, Maresch D, Ling WL, Tover A, et al. Polymer-grafted chromatography media for the purification of enveloped virus-like particles, exemplified with HIV-1 gag VLP. Vaccine. 2019;37(47):7070-80.

18. Reiter K, Aguilar PP, Wetter V, Steppert P, Tover A, Jungbauer A. Separation of virus-like particles and extracellular vesicles by flow-through and heparin affinity chromatography. Journal of Chromatography A. 2019;1588:77-84.
19. Rodler, A., Ueberbacher, R., Beyer, B. & Jungbauer, A. Calorimetry for studying the adsorption of proteins in hydrophobic interaction chromatography. *Preparative Biochemistry and Biotechnology* **49**, 1-20 (2019).
20. Satzer, P., Burgstaller, D., Krepper, W. & Jungbauer, A. Fractal dimension of antibody-PEG precipitate: Light microscopy for the reconstruction of 3D precipitate structures. *Engineering in Life Sciences* (2019).
21. Sauer DG, Melcher M, Mosor M, Walch N, Berkemeyer M, Scharl-Hirsch T, et al. Real-time monitoring and model-based prediction of purity and quantity during a chromatographic capture of fibroblast growth factor 2. Biotechnology and Bioengineering. 2019;116(8):1999-2009.
22. Sauer, D.G. Mosor, M, Frank, AC, Weiß, F, Christler, A, Walch, N, Jungbauer, A, Dürauer, A. A two-step process for capture and purification of human basic fibroblast growth factor from E. coli homogenate: Yield versus endotoxin clearance. *Protein Expression and Purification* **153**, 70-82 (2019).
23. Schuster, C., Matzinger, J. & Jungbauer, A. Micro-Phase Separation within Epoxy Resin Yields Ultrathin Mesoporous Membranes with Increased Scalability by Conversion from Spin- to Dip-Coating Process. *Macromolecular Materials and Engineering* **304** (2019).
24. Schweiger S, Berger E, Chan A, Peyser J, Gebski C, Jungbauer A. Packing quality, protein binding capacity and separation efficiency of pre-packed columns ranging from 1 mL laboratory to 57 L industrial scale. Journal of Chromatography A. 2019;1591:79-86.
25. Sissolak, B., Lingg, N., Sommeregger, W., Striedner, G. & Vorauer-Uhl, K. Impact of mammalian cell culture conditions on monoclonal antibody charge heterogeneity: an accessory monitoring tool for process development. *Journal of Industrial Microbiology and Biotechnology* **46**, 1167-1178 (2019).
26. Sissolak, B. et al. Application of the Bradford Assay for Cell Lysis Quantification: Residual Protein Content in Cell Culture Supernatants. *Biotechnology Journal* **14** (2019).
27. Suleiman E, Damm D, Batzoni M, Temchura V, Wagner A, Überla K, et al. Electrostatically driven encapsulation of hydrophilic, non-conformational peptide epitopes into liposomes. Pharmaceutics. 2019;11(11).
28. Vorauer-Uhl K, Lhota G. Assessing the quality of recombinant products made in yeast. Methods in Molecular Biology2019. p. 361-84.
29. Vorauer-Uhl K, Lhota G. Quantification of recombinant products in yeast. Methods in Molecular Biology2019. p. 385-428.
30. Walch N, Scharl T, Felföldi E, Sauer DG, Melcher M, Leisch F, et al. Prediction of the Quantity and Purity of an Antibody Capture Process in Real Time. Biotechnology Journal. 2019;14(7).
31. Wallner J, Sissolak B, Sommeregger W, Lingg N, Striedner G, Vorauer-Uhl K. Lectin bio-layer interferometry for assessing product quality of Fc- glycosylated immunoglobulin G. Biotechnology Progress. 2019;35(5).

Presentations

1. Christler, A, N. Walch, D. Sauer, A. Dürauer, A. Jungbauer (2019): Online monitoring and real-time prediction of product quantity, purity and potency during chromatographic purification processes, 15th International PhD Seminar on chromatographic separation Sciences, February 24-26, 2019, Quedlinburg, Germany
2. Duerkop, M.; Bayer, B.; Diaz, R.D.; Stosch, M.v.; Striedner,G. (2019): Intensified Design of Experiments – An Approach to Reduce Bioprocess Development and Characterization Times. Bioprocessing Summit , MAR 19-21,2019, Lissabon, Portugal
3. Felfödi, E, G. Dutra, K. Wright, A. Dürauer, A. Jungbauer (2019): Osmolality for control of downstream processing of recombinant antibodies, BPI Europe, April 2-5, 2019, Vienna, Austria

4. Hahn, R (2019): Multi-component adsorption as a challenge for process chromatography. Bioprocess Summit Europe, Mar 19-21, 2019, Lisbon
5. Hahn, R (2019): 3-D Chromatography For Fab Fragment Purification", 32st PREP Symposium, July 07-10, 2019, Baltimore, MD, USA.
6. Hahn, R (2019): Hindered diffusion of proteins in multicomponent adsorption on porous anion exchangers, 11th HIC/DSP Bioseparation conference, Feb 18.-21, 2019, Interlaken, CH.
7. Iurashev, D, A. Christler, J. Horvath, S. Schweiger, A. Dürauer, A. Jungbauer, J. Zanghellini (2019): Quantifying the importance of radial inhomogeneity in preparative chromatography columns, PREP Symposium 2019, July 7-10, 2019, Baltimore, USA
8. Kubek, M; Fink, M; Schimek, C; Brocard, C; Striedner, G; Cserjan, M; Hahn, R (2019): 3-D Chromatography For Fab Fragment Purification. 32st PREP Symposium, JUL 7-10, Baltimore
9. Kubek, M; Fink, M; Schimek, C; Brocard, C; Striedner, G; Cserjan, M; Hahn, R (2019): 3-D Chromatography For Fab Fragment Purification. 32st PREP Symposium, JUL 7-10, Baltimore
10. Mark Duerkop Benjamin Bayer Moritz von Stosch Roger Dalmau-Diaz Gerald Striedner (2019): The Virtual Bioprocess - to Speed up Bioprocess Development and ensuring constant manufacturing quality . European Summit of Industrial Biotechnology, NOV 15-18,2019, Graz
11. Mark Dürkop Benjamin Bayer Markus Luchner Moritz von Stosch Gerald Striedner (2019): Leaving behind Static Process Descriptions – Using Hybrid Modeling and Intensified Design of Experiments to Better Describe Bioprocesses. The Bioprocessing Summit, 12-16.08.2019, Boston
12. Mark Dürkop Benjamin Bayer Roger Dalmau-Diaz Moritz von Stosch Gerald Striedner (2019): Hybrid Modeling and Intensified DOE Enabling Faster Process Understanding and Model Predictive Control . Hybrid Modeling Summer School, SEP 25-27, 2019, Lissabon
13. Mark Dürkop Gerald Striedner Moritz von Stosch Benjamin Bayer (2019): Accurate Biomass Soft-Sensor Using 2-D Fluorescence and MARS Modeling. Bioprocess International, 09.-12.09.2019, Boston
14. Mark Dürkop Roger Dalmau-Diaz Benjamin Bayer Moritz von Stosch Gerald Striedner (2019): Hybrid Modeling and Intensified DOE Enabling Faster Process Understanding and Model Predictive Control. Bioprocess International, 09.-12.09.2019, Boston
15. Melcher, M, T. Scharl-Hirsch, d. Sauer, N. Walch, E. Felföldi, A. Christler, A. Jungbauer, A. Dürauer, F.Leisch (2019): Real-time prediction of protein quantity and purity in downstream processing, ECAB5, Sept 15-19th, 2019, Florence, Italy
16. Sauer, D, M. Melcher, N. Walch, T. Scharl-Hirsch, F. Leisch, A. Jungbauer, A. Dürauer (2019): Real-Time Monitoring and model-based Prediction of Purity and Quantity during chromatographic Purification of Biopharmaceuticals, BPP 2019, Nov 11-13, 2019, Sao Paulo, Brasil
17. Sauer, D, M. Mosor, M., A. Jungbauer, A. Dürauer (2019): Separation of fibroblast growth factor 2 variants and efficient depletion of host cell impurities by hydrophobic interaction chromatography, BPP 2019, Nov 11-13, 2019, Sao Paulo, Brasil
18. Sauer, D, M. Melcher, N. Walch, T. Scharl-Hirsch, F. Leisch, A. Jungbauer, A. Dürauer (2019): Real-Time Monitoring and model-based Prediction of Purity and Quantity during chromatographic Purification of Biopharmaceuticals, APCChE 2019, Sept 23-26, 2019, Sapporo, Japan
19. Sauer, D, M. Mosor, A.Jungbauer, and A. Dürauer (2019): Efficient depletion of a fibroblast growth factor 2 variant during polishing using hydrophobic interaction chromatography, ECAB5, Sept 15-19th, 2019, Florence, Italy
20. Sauer, D, M. Melcher, N. Walch, T. Scharl-Hirsch, F. Leisch, A. Jungbauer, A. Dürauer (2019): Real-time monitoring and model-based prediction of purity and quantity in a chromatographic step of a biopharmaceutical, PREP Symposium 2019, July 7-10, 2019, Baltimore, USA
21. Sauer, D, M. Mosor, A. Jungbauer, A. Dürauer (2019): Separation of fibroblast growth factor 2 variants and efficient depletion of host cell impurity by hydrophobic interaction chromatography, 11th HIC/DSP Bioseparation Conference, February 18-21, 2019, Interlaken, Switzerland

22. Scharl -Hirsch, T, M. Melcher, E. Felföldi, D. Sauer, N. Walch, A. Jungbauer, A. Dürauer, F.Leisch (2019): Using large data for the prediction of quality attributes of an antibody capture process in real-time, ECAB5, Sept 15-19th, 2019, Florence, Italy
23. Striedner G., Von Stosch M., Duerkop M. (2019): Short Course: Saving Time in Process Development with Next-Generation Methods: PAT, Hybrid Modeling, Process Simulation, mDoe and iDoE. The Bioprocessing Summit, AUG 12 - 16, 2019, Boston
24. Striedner, G; Dürkop, M; (2019): Towards Model Predictive Control of Cell Culture Bioprocesses. Bioprocessing Summit Europe, MAR 19 -21, 2019, Lissabon
25. Striedner, G; Dürkop, M; Sommeregger, W; Sissolak, B; Dalmau-Diaz, R; (2019): Towards Model Predictive Control of Cell Culture Bioprocesses . Bioprocessing Summit Boston, AUG 12 - 16, 2019, Boston, USA

Poster Presentations

1. Christler, A, M. von Stosch, T. Scharl-Hirsch, M. Melcher, F. Leisch, A. Duerauer, A. Jungbauer (2019): Hybrid semi-parametric modeling of preparative protein chromatography for online monitoring and real-time process control, ECAB5, Sept 15-19th, 2019, Florence, Italy
2. Christler, A, D. Iurashev, S. Schweiger, J. Horvath, A. Dürauer, A. Jungbauer, J. Zanghellini (2019): Quantifying the importance of radial anisotropy in chromatography columns, PREP Symposium 2019, July 7-10, 2019, Baltimore, USA
3. Kandra, K; Sommeregger, W; Striedner, G; Melcher, M (2019): Online Bioprocess Monitoring based on 2D fluorescence spectroscopy. ESACT 2019, MAY 5-8, 2019, Copenhagen/Denmark
4. Schuller, A; Cserjan, M; Jarmer, J; Wagenknecht, M; Reinisch, D; Grabherr, R; Striedner; G (2019): Bioprocess control: Deeper insights into LacI autoregulation and how to exploit it. [National Meeting of the American-Chemical-Society (ACS), Orlando, FL, MAR 31-APR 04, 2019] ABSTR PAP AM CHEM S. 2019; 257
5. Schuller, A; Cserjan, M; Jarmer, J; Wagenknecht, M; Reinisch, D; Grabherr, R; Striedner; G (2019): Bioprocess control: Deeper insights into LacI autoregulation and how to exploit it.[RPP10 - 10th International Conference on Recombinant Protein Production, Crete, GREECE, APR 24 - 27, 2019] In: European Federation of Biotechnology (Ed.), RPP10 - 10th International Conference on Recombinant Protein Production
6. Vazulka, S; Fink, M; Jarmer, J; Cserjan, M; Striedner, G Production of antibody fragments with plasmid-based and genome integrated T7 E. coli expression systems - evaluation of systems performance in microtiter fed-batch like cultivations. [National Meeting of the American-Chemical-Society (ACS), Orlando, FL, MAR 31-APR 04, 2019] ABSTR PAP AM CHEM S. 2019; 257

Other Presentations

1. Tesei, D, Katja Sterflinger and Marzban G. 2019. “Global proteomics of Extremophilic Fungi: Mission accomplished?”, In Tiquia-Arashiro, SM; Grube, M; (Eds.), Fungi in Extreme Environments: Ecological Role and Biotechnological Significance. 44; Springer Nature AG 2019, Switzerland; ISBN 978-3-030-19030-9. https://doi.org/10.1007/978-3-030-19030-9_12 (Book Chapter).
2. Striedner G., Von Stosch M., Duerkop M. (2019): Short Course: Saving Time in Process Development with Next-Generation Methods: PAT, Hybrid Modeling, Process Simulation, mDoe and iDoE. The Bioprocessing Summit, AUG 12 - 16, 2019, Boston
3. Striedner, G; Dürkop, M; von Stosch, M; (2019): Short Course: At the heart of PAT lies the QbD approach. Bioprocessing Summit Europe, MAR 24-26, 2019, Lissabon

Teachings

#	Title	Programme	ECTS
166655	Integrated biopharmaceutical production in pilot scale	TU Vienna	6
772327	Biochemical and biotechnological methods (analytics design) (in Eng.)	BT	3
790044	Sicherheit am Arbeitsplatz	Bachelor´s FBT	2
790049	Masterseminar Angewandte Mikrobiologie (in Eng.)	Master´s FBT	2
790105	Practical course in applied microbiology	FBT	4
790107	Bachelor´s thesis seminar	Bachelor´s FBT	12
790120	Grundlagen der Bioverfahrenstechnik	Bachelor´s FBT	5.5
790321	Biotechnol. Praktikum	Master´s FBT	4.5
790350	Bioprocess engineering I (in Eng.)	BT	3
790353	Quality management in biotechnology (in Eng.)	BT	3
790358	Bioprocess engineering II (in Eng.)	BT	3
790359	Bioprocess engineering laboratory (in Eng.)	BT	5
790371	Automation of bioprocesses (in Eng.)	BT	2
790380	Engineering of biotechnological production facilities (in Eng.)	BT	2
790419	Journal club BioToP III (in Eng.)	DK BioToP	1.5
790423	Doctoral seminar BioToP III (in Eng.)	DK BioToP	1.5
790431	Pilot plant BioproEng (in Eng.)	DK BPE	8
790432	Doctoral Seminar BPE	DK BPE	0.5
790433	Journal Club BPE	DK BPE	0.5
790940	Dissertantenseminar aus Angewandte Mikrobiologie	BT	2
791432	Doctoral seminar BioproEng I (in Eng.)	DK BIOTOP	0.5
791433	Journal club BioproEng I (in Eng.)	DK BPE	3
791437	Automation and control in laboratory (in Eng.)	DK BPE	2
791438	Biothermodynamics (in Eng.)	DK BPE	2
894404	Basic course IV - bioinformatics and molecular modelling (in Eng.)	DK BIOTOP	3
894415	Instructional course IVA - molecular modelling (in Eng.)	DK BIOTOP	3

BT … Biotechnology, FBT … food and biotechnology, DK BPE … Doctoral School Bioprocess Engineering,

External Teachings and Courses

Organization	Title	Programme
BOKU, Novasign, ESBES	Hybrid Modeling Summer School 2019	Summer School
BOKU	Int. Protein Chromatography Course 2019	International Programme
FH-Bioengineering, Campus Wien	Qualitätskontrolle	Master Quality Management
FH-Bioengineering, Campus Wien	Qualitätskontrolle und Qualitätssicherung im Prüflaboratorium	Master Quality Management
FH-Bioengineering, Campus Wien	Downstream Processing, Protein VO	Bachelor Bioengineering
FH-Bioengineering, Campus Wien	Downstream Processing, Protein VO+UE	Master Biotechnology
IMC FH Krems	Process Control and Process Online Monitoring	Master Biotechnology
Montan Universität Leoben	Qualitätssicherung im chemischen Labor	University Course

Epilog and outlook

We have included highlights in our annual reports more information about IBSE, the Department of Biotechnology and BOKU can be found at the homepage of ISBE and the homepage of the individual faculties. We are strongly involved in industry-academia research collaborations and the industrial sponsor do not want to disclose results until the intellectual property is secured Thus more activities are going at IBSE as presented in the annual report. IBSE is highly connected with other institutes and departments at BOKU, with Austrian and international research institutions as well as the national and international Biotech industry.

What can expect from IBSE in the next years: We will develop a new teaching concept for bioprocess engineer which will emphasize the uniqueness of bioprocess engineering in the field of all engineering disciplines. In the bioprocess engineering we are still relying on laboratory experiments in the jargon of the simulation world wet lab experiments. It is an art and needs experience to find the right balance between experiments and computer simulation. Data from the nano scale work required for macro scale calculation still net a lot of these wet lab experiments. The ab initio models and the so-called mechanistic models are extremely important to guide us but they are not sufficiently developed to avoid experiments. This view and modern pedagogical approaches will direct new teach concepts.

You can expect from IBSE intensified work on hybrid and statistical model often circumscribed as artificial intelligence. This bridges the gap between the physical models and the complexity of a bioprocess. Definitely, we will contribute to the cyber physical depiction of a bioprocess.

In collaboration with acib other collaborators we will increase our knowledge and technology in the field of bionanoparticles to be able to offer trained researcher and engineers for production of therapeutics the new emerging infectious diseases. Will also expand our activities to be able to contribute to completely new avenues in bioprocessing such as ethical food production or reversing the carbon cycle.

We hope we can encourage the next generation of students to enter the field of bioprocessing, although it is challenging and demanding, we will offer interesting research that is helping to solve urgent problems in our society and a bright future in return.

The Institute of Bioprocess Science and Engineering

Contact

Post address (German/English)

Universität für Bodenkultur
Department für Biotechnologie
Muthgasse 18
1190 Wien
Österreich

University of Natural Resources and
Life Sciences, Vienna
Department of Biotechnology
Muthgasse 18
1190 Vienna,
Austria

Homepage

https://boku.ac.at/dbt/ibse

Head of the *Institute of Bioprocess Science and Engineering*

Univ.-Prof. DI Dr. Alois Jungbauer
alois.jungbauer@boku.ac.at
0043 1 47654-79083

Deputy of the *Institute of Bioprocess Science and Engineering*

Assoc. Prof. Dr. Gerald Striedner
gerald.striedner@boku.ac.at
0043 1 47654-79077

Administrative Assistant of the *Institute of Bioprocess Science and Engineering*

Petra Polak BA
petra.polak@boku.ac.at
0043 1 47654-79084