Institute of Bioprocess Science and Engineering

Annual Report 2023

September 2024

Table of Content

Introduction

2023 was a challenging and very successful year for IBSE. Ongoing research projects have enabled us to expand the scientific expertise at the Institute, to present scientific results and to expand and consolidate our network in academia and industry. As you will see in the report, we achieved a high scientific output with many peer-reviewed publications and scientific presentations. We have also funded and supervised numerous Bachelor's, Master's and PhD theses, making a significant contribution to our educational mission.

Following the major changes of recent years, with the re-appointment of the Downstream Professorship, we have now entered a somewhat quieter phase at the Institute. Johannes Buyel has settled in very well, he has already successfully acquired projects and built up his research group accordingly. Two outstanding IBSE researchers, Nico Lingg and Birgit Wiltschi, have positioned themselves and will submit their habilitations at the beginning of next year.

Of course, the continuity and funding of our research can only be guaranteed by acquiring new research projects. In 2023, we were very active again in terms of project submissions and we submitted 3 EU, 2 WWTF,3 FWF, 1 NIH and 2 FFG research projects with 2 of them accepted, 6 rejected and for 2 projects decision is still pending. Last year, we worked very intensively on the extension application for the acib Comet Centre and, together with many scientists and companies involved, we achieved great success with the approval of the acib extension for another four years. Congratulations to our partners at acib and gratitude to our industry partners for great support and collaboration.

We are also happy to announce that Boehringer Ingelheim International GmbH will be the collaboration partner of the *Christian Doppler Laboratory for Knowledge-based Production of Gene Therapy Vectors from 2024*. With Boehringer Ingelheim we found a strongly committed partner ensuring the continuation of this important strategic project. Thanks to all colleagues – from industry and in house – for their support to make the “impossible” possible.

These successes are by no means a matter of course, especially in view of the global economic downturn, which has now also reached the biotechnology sector with a certain delay. It takes a great effort of all researchers to steadily and successfully present and communicate the scientific excellence of our research ideas and the economic benefits for industry that result from long-term research investments. In this context, I consider it particularly important to take the time to acknowledge and celebrate what we have achieved, as this can easily be forgotten in the rush of day-to-day work and the pursuit of new projects.

Finally, we would like to thank all colleagues and students of IBSE and all our partners in academia and industry for their commitment and willingness contributing to our common success We are happy to present the outcome of 2023 in some highlights and figures to you in this report We are confident that, as an IBSE team, we are well prepared to meet the challenges of 2024 with determination and motivation.

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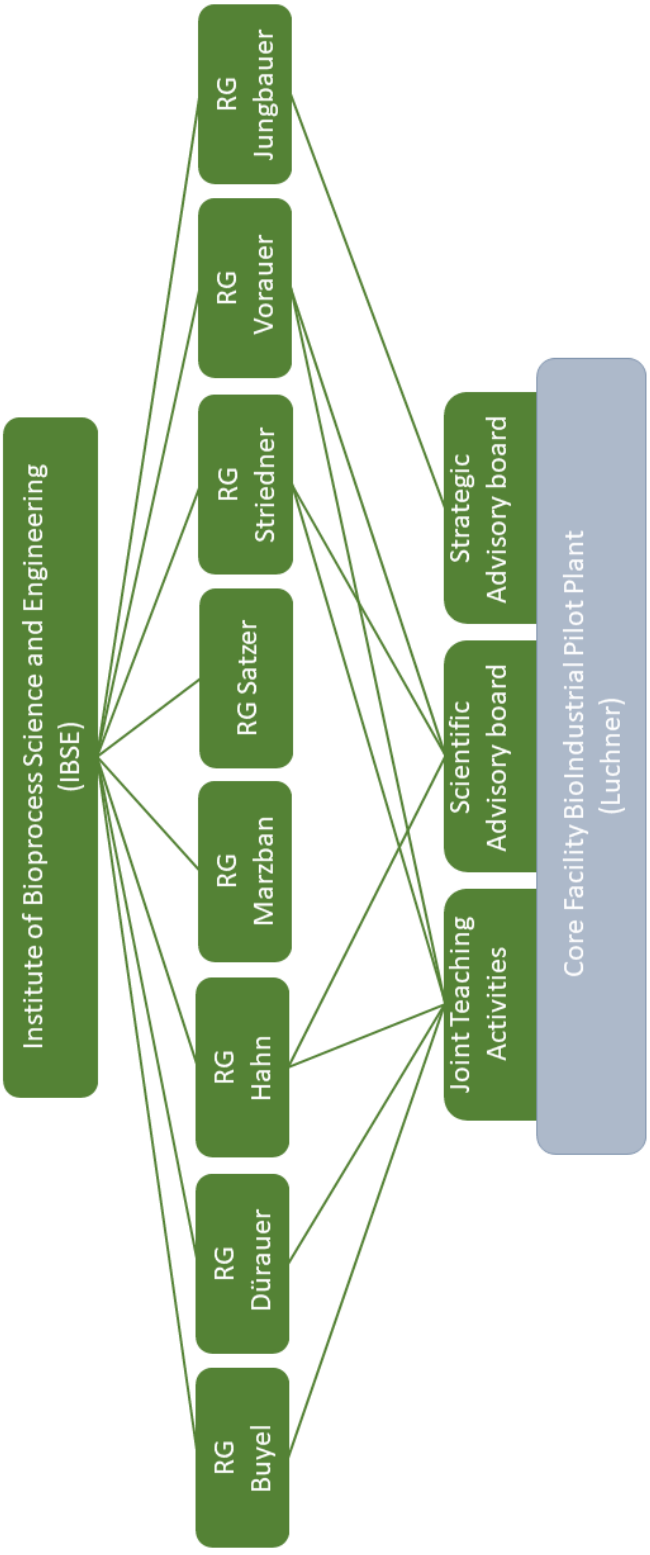
Gerald Striedner

Astrid Dürauer

Structure of the *Institute of Bioprocess Science and Engineering* 2023



Members of the Research Groups 2023

RG Buyel			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Janos Bindics Johannes Buyel			Ales Grundzi
RG Dürauer			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Astrid Dürauer Maral Rahimzadeh Nikolaus Virgolini	Sabrina Leigheb Ignacio Montes Serrano Bettina Motycka Valentina Ruocco Georg Smesnik Maria Toth Martina Winter	Verena Buchacher Tobias Kargl Catarina Sousa Neves Maia	Eva Berger Irfan Erdem Mahbod Mousavian Aida Tleuova
RG Hahn			
Staff	**PhD student**	**BA/MA student, intern**	**Technician/Student assistant**
Rainer Hahn Nico Lingg Daniel Komuczki	Jürgen Beck Markus Berg Anna Frank Nils Gehrmann Alexander Jurjevec Matthias Müller David Scheich	Georg Hochdaninger (MA) Gregor Stitz (MA)	Timon Kalchmayr
RG Jungbauer			
Staff	**PhD-student**	**BA/MA student, intern**	**Technician**
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	Magdalena Pappenreiter Carme Pons Royo Gabriele Recanati Alexander Zollner		
RG Marzban			
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Gorji Marzban	Sonja Schürer-Waldheim		
RG Satzer			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Peter Satzer	Lena Achleitner	Isabella Huber	
RG Striedner			
Staff	**PhD student**	**BA/MA student, intern**	**Technician/ Student assistant**
Monika Cserjan Mathias Fink Gerald Striedner Christopher Tauer Birgit Wiltschi Nora Bses	Natalia Danielewicz Tommaso de Santis Lisa Fohler Martin Gibisch Stefan Gutmann Hana Hanaee-Ahvaz Arasteh Kani Arshia Marco Klanschnig Christoph Köppl Claudia Lacombe Zana Marin Florian Mayer Sophie Vazulka Florian Simon	Johanna Berein (MA) Felix Faschingeder (MA) Brenner Helene (MA) Pawel Gorecki (MA) Lea Jusufagic (MA) Lukas Leibetseder (MA) Karoline Reznar (BA) Anton Shpylovyi (MA) Lina Vranizky (MA)	Alexander Doleschal Moritz Dielacher Lisa Letschnig Karoline Reznar Anton Shpylovyi Corinna Schödl
RG Vorauer-Uhl			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Karola Vorauer-Uhl	Sarah Übleis (Co-supervisor) Ehsan Suleiman Yuelang Yao	Konstanze Kastenhofer Magdalena Kößlbacher Jasmina Memic	Gabriele Lhota

		Simon Nendwich	
Core Facility: BioIndustrial Pilot Plant			
Staff	**PhD student**	**BA/MA student, intern**	**Technician/Student assistant**
Markus Luchner Mathias Fink		Elena Obetzhauser	Magdalena Hohlrieder Sabine Necina Philipp Peter Anita Zwanzleitner

Success Stories

A new period: Austrian Centre of Industrial Biotechnology (acib)

Rainer Hahn

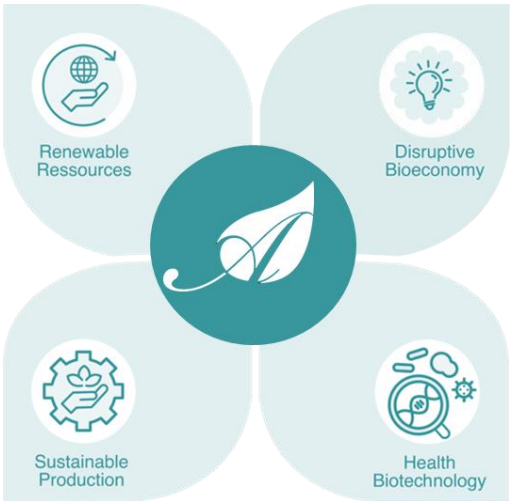
Scientists from IBSE played a pivotal role in expanding the COMET competence center acib, securing public funding of 24 million Euros from the federal government, including contributions from the Ministry of Climate Protection (BMK) and the Ministry of Labour and Economy (BMAW), as well as support from the federal states Styria (via the Styrian Business Promotion Agency, SFG), Vienna, Lower Austria, and Tyrol, along with the Austrian Research Promotion Agency (FFG). Over the next five years, a comprehensive project with a total volume of 53 million Euros will be undertaken, involving collaboration with more than 100 national and international industrial partners.

The COMET center is structured into four research areas, each addressing crucial challenges of our time with a focus on advancing solutions for a bio-based circular economy and enhancing health. Under the leadership of Johannes Buyel and Petra Heidinger (acib), the strategic area of Disruptive Bioeconomy lays the foundation for groundbreaking advancements in two high-risk thrusts, CO_2/H_2-based bioeconomy and the bioproduction of essential medicines in plant cells.

In the Health Biotechnology Area, led by Nico Lingg and Gerald Striedner, emphasis is placed on the development of production processes, molecular characterization of novel biopharmaceutical products, and identification of new active pharmaceutical ingredients (API). Additionally, the area is actively involved in the development of early diagnosis systems to facilitate a shift towards early prophylactic medical measures.

Led by Christiane Luley (acib) and Harald Pichler (TU Graz), the Renewable Resources Area targets key challenges in the industrial sectors of food, animal feed, and materials, aiming to address issues related to the circular economy and resource efficiency.

Led by Anita Emmerstorfer-Augustin (acib) and Brigitte Gasser (DBT), the Sustainable Production Area pioneers sustainable bioproduction through innovative strategies, employing next-gen microbial cell factories and advanced biocatalysis in environmentally friendly processes, addressing multiple aspects of eco-friendly biomanufacturing and green chemistry.

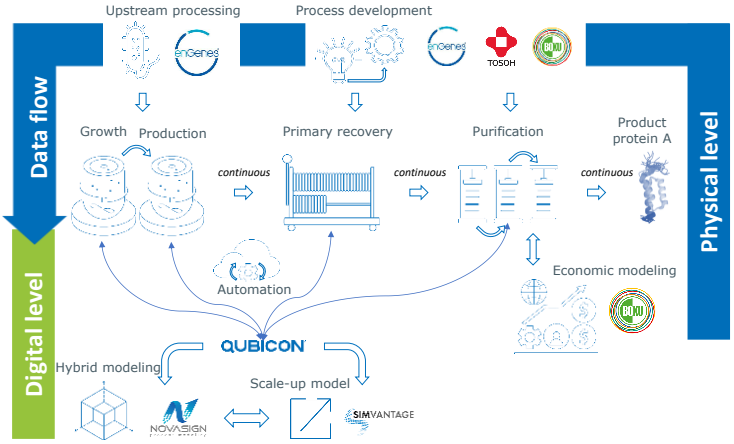


Project: E. conti

Rainer Hahn

A collaborative team, consisting of experts from IBSE—Alois Jungbauer, Rainer Hahn, and Gerald Striedner—in partnership with IBSE spin-off companies enGenes, Novasign, Qubicon, and other valuable collaborators, embarked on a groundbreaking 2-year FFG Flagship project commencing on March 1, 2023. The consortium also includes SimVantage, a TU Graz spin-off, and Tosoh Biosciences.

Under the leadership of Rainer Hahn, along with the dedicated efforts of Postdocs Markus Berg and Jürgen Beck, the project aims to pioneer the development of an advanced, fully automated continuous manufacturing prototype process for an *E. coli* expression system. This innovative system is designed to efficiently secrete recombinantly produced proteins into the supernatant. The developed system is highly modular and product agnostic, and allows for democratization of manufacturing capacity for new products.



Key focus areas within the project include:

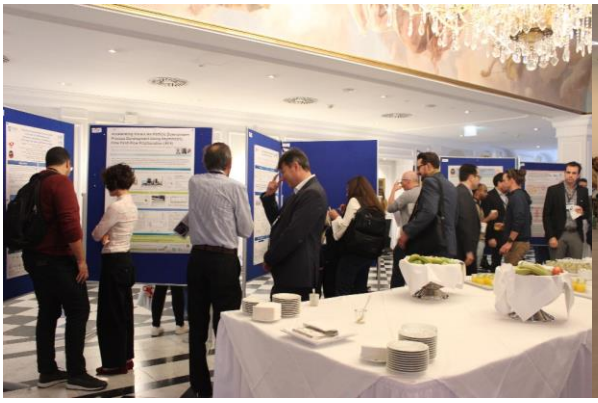
- Integration of the entire process chain into a seamless, continuous operation.
- Development of a primary recovery unit capable of handling low flux.
- Establishment of two-way communication between each device in the process.
- Optimization of each unit operation individually, culminating in a validated end-to-end model.
- Identification and validation of relevant scale-up parameters.
- Exploration of applicability of surrogate models between Novasign, SimVantage, and Qubicon.
- Implementation of model predictive control for each process step and entire process chain.
- Evaluation of the economic and ecological impact of the developed system.
- Pursuit of regulatory acceptance for the innovative manufacturing approach.

The project's ultimate goal is to usher in a new era of modular, flexible, and sustainable production processes, significantly contributing to the advancement of bioprocessing technologies.

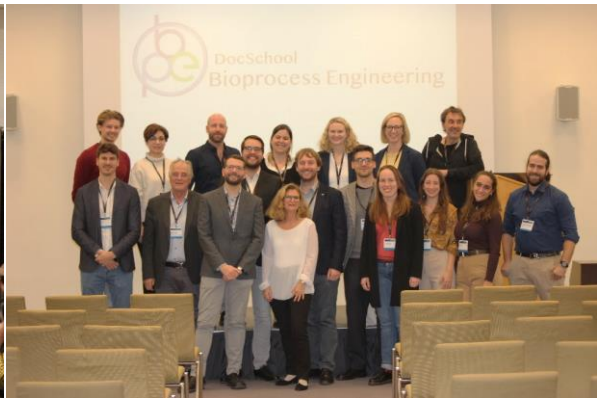
The 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP)

Rainer Hahn

The 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP) took place at Parkhotel Schönbrunn, Vienna, from November 5th to 8th, 2023, organized by Nico Lingg and Verena Beck (acib). The meeting was a full success with participants from 23 countries, with an exciting program featuring keynote speakers from Novo Nordisk, University College London and Leiden University Medical Center. The inclusion of mixed sessions featuring full talks and flash presentations, including a dedicated session to the BOKU DocSchool BioproEng, added a layer of diversity and depth to the event.



While the symposium delved into the traditional realms of protein, peptide, and polynucleotide purification, it also boldly ventured into the future with two groundbreaking sessions focused on analytics and the separation of various bionanoparticles. The invaluable contributions of researchers from IBSE extended beyond the presentation of their groundbreaking work; they also played pivotal roles as dedicated volunteers, ensuring the seamless execution of the conference. Their commitment to excellence and professionalism significantly contributed to the overall success of the event.



CD Laboratory for Knowledge-Based Production of Gene Therapy Vectors

Astrid Dürauer

With **January 2023** the Christian Doppler Laboratory for Knowledge-Based Production of Gene Therapy Vectors started. It is a collaboration between the Viral Therapeutic Center of Boehringer-Ingelheim in Biberach and BOKU. The head of this 9th CD laboratory at the Department of Biotechnology – out of over 22 at BOKU since 1995 – is Astrid Dürauer, deputy head of IBSE. Reingard Grabherr from the Institute of Molecular Biotechnology and Nicole Borth from the Institute of Animal Cell Technology and Systems Biotechnology as well as Theresa Scharl-Hirsch (Institute of Statistics), Patricia Aguilar (acib) and Peter Satzer (IBSE) are involved as PIs in the project.

Gene therapy offers the opportunity to treat or heal diseases which have their origin in defect or missing genes on DNA level. **Viral vector-based delivery of DNA** to the cell is the most promising strategy. Adeno associated viruses (AAVs) are frequently used for this purpose and are typically produced in mammalian cells. After the first approvals of recombinant AAV (rAAV) based gene therapeutics during the last decade, rAAV production now has to evolve into next generation manufacturing to efficiently provide these promising products.

We will establish **advanced analytics to thoroughly characterize rAAV** and impurities present. A high amount of empty rAAVs is one of the most crucial limitations of rAAV production. Therefore, analytics for the discrimination between full and empty rAAV and for their quantification is of utmost importance. These analytics will enable optimisation of both, cell lines and bioprocess conditions, to increase the percentage of high quality, full rAAV capsids.

Quality-by-testing with offline analysis as currently carried out for rAAV production is costly, requires holding times and does not allow process control as it only delivers retrospective information on product quality. Therefore, inline and at-line sensors will be investigated to **establish real time monitoring systems based soft sensors**, predictive models enabling process control during up and downstream processing of rAAV production. This approach will enhance safety and efficiency of rAAV production.

Different mammalian cell lines and their performance will be characterised to achieve a systematic understanding of critical parameters such as the virus construct, the length of the therapeutic gene, the co-transfection with required helper proteins and bioprocess conditions, as well as their interplay. For that purpose, **genome scale data on the cellular response to virus production** will be generated to provide a knowledge-base for subsequent engineering and optimisation design.

In the current production scheme typically three plasmids are co-transfected into mammalian cells. This requires a high cost and labour-intensive load of plasmids to be prepared for production. To address this problem, **cell lines that stably express proteins** needed for the viral vector production will be designed which are under control of inducible and/or tuneable promoters.

Bringing selected cell line and optimized production strategies to manufacturing scale is costly and time consuming as a multi-step process development from bench to production scale has to be carried out. As currently the smallest available process scale is a bench scale format, the number of experiments is limited due to high material consumption. A **miniaturized process development platform** integrating all steps from cell harvest to chromatographic polishing based on parallel mini reactors such will be established for rAAV process development. It will be used for evaluation of

upstream optimisation such as selected optimised cell lines and for establishment and optimisation of downstream processing.

The overall vision of this CD laboratory is the **transition of production** of gene therapy vectors from an empirically driven to knowledge-based and model predicted manufacturing. This CD laboratory will enable adequate and cost-effective supply of these important biopharmaceuticals. Enhanced understanding of the complex interplay between cell lines, gene of interest, bioprocess (up and downstream) conditions and product quality is needed for this transition.

Currently, the team tow Post Docs, four PhDs and tow technicians build the team of the CD laboratory. In 2023 already two Master thesis and one Bachelor thesis have been carried out in the laboratory. We are happy to have well-known experts in the field as scientific advisory board, Stefan Kochanek, University Ulm, Francesc Godia from Universitat de Barcelona and Jan Schöning from Boehringer-Ingeheim and we are looking forward to their perspective and advices for our research. In 2024 we expect our first scientific evaluation and we will be happy to update you on our progress in the upcoming annual reports.

ESBES Minisymposium High Throughput Screening and Process development HTPD2023

Astrid Dürauer

From April 12-14, 2023 the ESBES Minisymposium on High Throughput Screening and Process development HTPD2023 (https://www.acib.at/htpd2020/) took place in Muthgasse 11 at BOKU Vienna. The event was organized acib by Astrid Dürauer from IBSE and Marcel Ottens from TU Delft under the umbrella of ESBES and the Austrian Centre of Industrial Biotechnology.

Started as an event to dominantly introduce early stage researchers to the field and opportunities of HTPD it evolved to a get-together of well-known experts in the field delivering excellent talks addressing all important aspects of the topic. The two-days event started with two keynote lectures. The first given by *Jennifer Pollard* (Merck) who gave a great overview about the development of HTPD in industrial environment over the last decades and discussed the lessons learned for future developments. *Shuichi Yamomoto* (Yamaguchi University) critically examined the importance of HTPD and AI against the background of existing knowledge and understanding in mechanistic models for bioprocesses.

The first day of the symposium was focussing on *Engineering Fundamentals for Scaling* with talks given by *Johannes Buyel*, *Alois Jungbauer*, both from IBSE, and *Martina Micheletti* (UCL) discussing the challenges of scaling up from micro or nanoscale experiments to manufacturing scales for proteins and new formats of biopharmaceuticals. The presentations given by *Gerald Striedner* (IBSE), Daniel Fleischanderl (Boehringer-Ingelheim RCV) and *Peter Neubauer* (TU Berlin) focussed on the importance of HTPD for *Bioprocess Development* while the third session dealt with its impact in the field of Downstream Processing. Here, *Rainer Hahn* (IBSE) discussed the challenges of real-world chromatography facing multicomponent adsorption, *Cécile Brocard* (Boehringer-Ingelheim RCV) gave an insight in their inhouse process development platform for IB derived products and *Tim Schröder* (Repligen) presented results obtained for the separation of AAVs on prepacked microscale columns. After a series of excellent flash presentation, *Karol Lacki* (Repligen) guided us through his vast experience of 20 years HTPD and were he sees the future perspectives. The *round table discussion* of Cécile Brocard, Karol Lacki, Jennifer Pollard and Shuichi Yamamoto concluded that HTPD and modelling and AI in combination will be the future of process development but well-trained and experience engineers and scientist in the field of biochemical engineering are the fundament of the successful implementation. Vivid discussions were continued at the typical Viennese Heurigen later on.

The second day started with a *site visit at Boehringer-Ingelheim RCV* where the participants were introduced to the company's strategies and in house HTPD platform in the Process Science Division. AT this point we want to thank Boehringer-Ingelheim RCV, in particular Cécile Brocard, for the organisation of the site visit and the hospitality, as well as the contributions to the symposium.

After lunch we continued with a session on *Microfluidics* starting with *Marcel Ottens* giving an insight in nano-scale approaches for HTPD at TU Delft, followed by *Ana Azevedo* (IST Lisbon) showing how chromatography process development can be fastens by their microfluidic lab-on-the-chip platform.

Nicolas Szita and *Marco Marques* presented microfluidic approaches and flow biocatalysis for bioprocess development.

The last session of the event was dedicated to *Big Data and Modelling*, where ***R*** as important tool for the realization of statistical models in up and downstream processing was discussed by *Theresa Scharl-Hirsch*, who spontaneously stepped in for *Michael Melcher*. Thank you again! *Bernt Nilsson* (Lund University) showed us the beauty of mechanistic models, *Mark Dürkop* showed examples for the benefit of combining statistical and mechanistic models by hybrid modelling and *Cees Haringa* showed the potential of computational fluid dynamics to address challenges of scaling up bioprocesses.

Overall, with 80 participants, excellent presentation, vivid discussions and exchange the ESBES Minisymposium on High Throughput Screening and Process development HTPD2023 was a great success and it was a pleasure to organize and participate. We want to thank our sponsors *acib, cytiva, Repligen, Thermo Fisher and the BOKU DocSchool Bioprocess Engineering* for their financial support, all the participants for their contributions and especially *Petra Polak* for her never-ending effort to make this event with all its small and big challenges a great success.

Green initiatives

Peter Satzer

Peter Satzer (IBSE) and the PhD student *Lena Achleitner* (acib) have developed a sterile 3D printing process that enables the production of laboratory equipment from environmentally friendly and biodegradable plastic to combat single-use plastic waste in life science research. This new approach offers a sustainable alternative to single-use plastic saving 80% of CO_2 emissions associated with the use of single-use plastics in life science as a contribution to the Green Deal goals of 2030. The announcement gathered national interest (nationally featured by BOKU and acib on their respective channels, and picket up by Krone and Österreich Journal, and internationally featured by the online magazine 3Drintr and presented on various conferences)

As the first research group at BOKU, Peter Satzer joined the GreenLabs Austria Initiative, an initiative to identify and reduce the resource usage of life science laboratories, especially single-use plastic, energy, and water. Together with the company partner StoepselSammeln the first batch of collected single-use plastic could be recycled instead of going into the residual waste and being incinerated. IBSE is planning to expand this program in 2024 to more single-use items as well as more research groups to reduce the environmental footprint of life science research done at BOKU.

ISO 9001:2015 Certification of the Core Facility BioIndustrial Pilot Plant - Feasibility Study conducted by CF BiPP and IBSE

Markus Luchner, Karola Vorauer-Uhl, Michael Spitaler

BOKU´s Core Facilities were founded to bundle their large-scale equipment infrastructures and scientifically consistent method platforms. The Core Facilities are Department independent and contacted by an adequate management system and experts in the different fields. The Core Facility BioIndustrial Pilot Plant (CF BiPP) was established as a multi-purpose semi-industrial facility for education, training and development of biotechnological processes. For the continuous development and to improve the quality management system of CF BiPP, a feasibility study to evaluate the potential for an ISO certification was performed together with the management expertise of IBSE. The Feasibility Study was planned according to the principles of such studies and includes several assessment levels (figure 1).

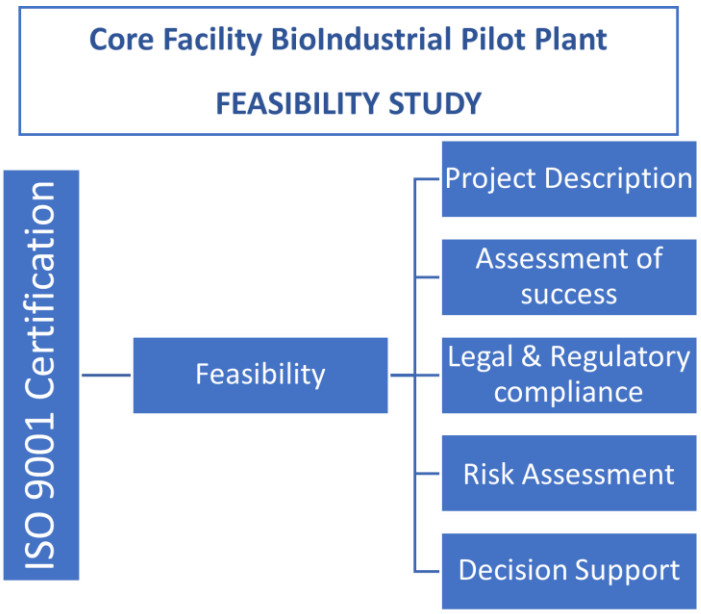


Figure 1: Structure of the feasibility study including the different process steps

The process was initiated with the project description, identifying the scope, the position of CF BiPP within BOKU and its tasks. These steps are essential to identify which ISO standard is applicable and how it can be managed. It became clear pretty quickly that although CF BiPP is a small entity of BOKU it could be certified by ISO 9001:2015 due to their distinct responsibilities as a service provider for different clients. As explained above these could be students, scientific institutions but also industrial customers. What they all have in common is that CF BiPP is providing different services in the field of Biotechnology.

As the next step the success of the project is evaluated for its practicality in order to determine whether it will be successful. Therefore, the established certification board consisting of the head of CF BiPP, Markus Luchner, and his deputy, Sabine Necina, and Karola Vorauer-Uhl from IBSE. They defined the required process steps and overview the project progress. To satisfy the high work load two master students were engaged to elaborate different defined tasks of this project. By this structure and intensive discussions, the high work load could be compensated and the time lines successfully reached.

To prove the legal and regulatory compliance, Michael Spitaler assessed the status quo of CF BiPP regarding the university laws and internal regulations affecting CF BiPP, the internal management concept of CF BiPP and finally identified specific tasks to meet the ISO 9001:2015 requirements. Based on these elements the first version of an ISO- Quality Manual could be successfully established and critical aspects could be identified. The existing management system was further developed in the second master thesis with main focus on management process documentation and adaption of the

existing document system. By an intensive knowledge exchange process between the certification board and Christian Pantazi, our master student, reorganization of the system and new, management required documents could be established.

Risk assessment was continuously applied at each process milestone as decision support for the next steps. Furthermore, it was applied for the assessment of the overall project success. In conclusion, we can assume that the process and the achievements will always be beneficial for the CF BiPP. If the certification by an accredited body is successful, CF BiPP will be able to improve the quality of the management system which increase the satisfaction of all clients. If the certification fails, the system is just as established and can be nonetheless successfully applied.

CF BiPP supported by IBSE and essentially, by the two master students is now in principle well prepared for the official contact with a selected certification body. Nevertheless, the final decision support from the rectorate of BOKU is mandatory due to several reasons. Certification requires additional support such as payments and organizational assistance. Besides that, it is essential that CF BiPP achieves the full commitment of BOKU to be a certified entity of BOKU. After the positive decision the certification process can be started (Fig.:2).

In summary it can be concluded that the feasibility study was scheduled for at least one year. Within the last year CF BiPP has established a convenient ISO 9001:2015 management system thus after the final decision of the rectorate the certification could be initiated. This process was informative for all participating people and the achievements are already beneficial for the CF BiPP to improve the quality assurance of the Core Facility. Basically, it can be noted that certification according to the ISO 9001 is very rarely seen at Austrian Universities however, the increased visibility which is achieved by a successful certification might be a significant benefit for entities such as Core Facilities and maybe motivate other Core Facilities to follow this process.

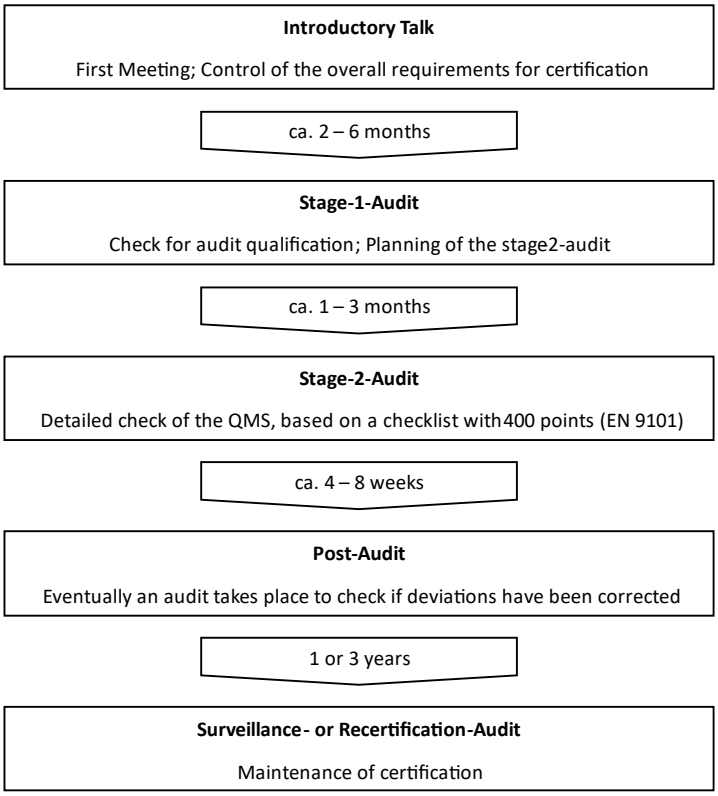
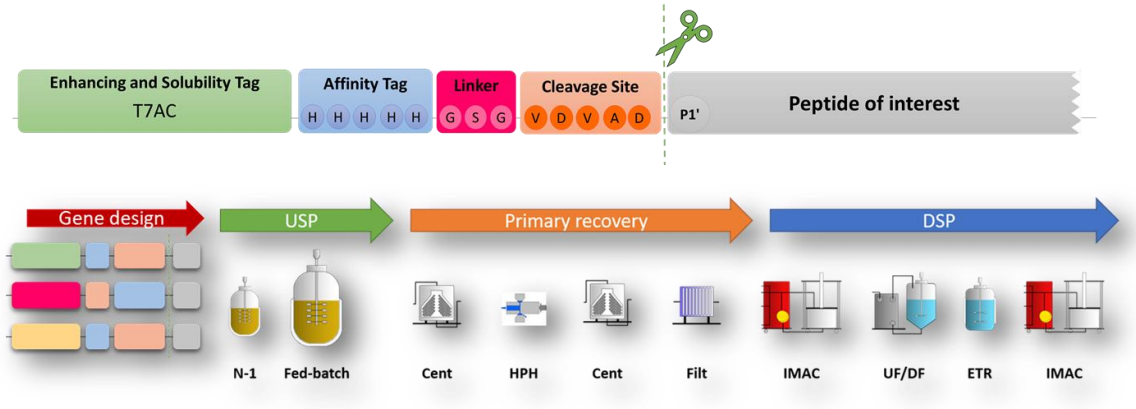


Figure 2: Certification steps; Adapted by Michael Spitaler; from (Hinsch, 2019)

CASPON™ Technology: Revolutionizing development timelines

Monika Cserjan

The landscape of protein-based biopharmaceuticals has long been challenged by issues of developability and manufacturability, impeding progress due to the absence of robust platform processes. In an eight-year long collaboration between BOKU IBSE, University of Innsbruck, acib and Boehringer Ingelheim, a new technology was developed that offers a solution to this problem. Building on a fusion-tag based process, the team developed a new protease based on human caspase-2 called CASPON™ enzyme. This enzyme combines several beneficial attributes that enable the use in industrial manufacturing as well as lab-scale applications. The enzyme itself can be produced in large quantities at moderate cost and is highly stable. Most importantly, its enzymatic activity allows for the tag removal before any N-terminal amino acid of a protein of interest in only a few hours. Furthermore, a CASPON™ tag has been developed that enhances solubility and expression and allows purification with affinity chromatography. The CASPON™ technology ensures a seamless process transfer from early stage research all the way to full scale commercial production.



The project resulted in over than 10 peer-reviewed publications and several patents. The technology is already at use at the company partner, but is also available for research purposes (casponrequest.vie@boehringer-ingelheim.com). A mini-symposium was held at Boehringer Ingelheim's Vienna campus to celebrate the successful conclusion of the project.

BOKU IBSE team members of the CASPON™ Technology project, from left to right: Gerald Striedner, Alois Jungbauer, Andreas Fischer, Christoph Köppl, Nico Lingg, Monika Cserjan.

Residence time distribution of continuous integrated processes:

Alois Jungbauer

Continuous integrated biomanufacturing is gradually being introduced for the production of biopharmaceuticals in order to reduce costs and the environmental footprint. An integrated process linking all steps together becomes very complex and difficult to characterize. In 2023, the US Food and Drug Administration (USFDA) and the European Medicines Agency (EMA) published a set of regulations with quality considerations for continuous manufacturing to guide the industry (ICH Q13). These guidelines recommend the "characterization of the process dynamics for the integrated system using a suitable scientific approach (e.g. RTD studies) and a material traceably strategy". In our research projects on continuous integrated biomanufacturing, we have developed strategies to characterize process steps and integrated processes. The RTD is a probability distribution function that describes the passage of a material part, e.g. a molecule, through a unit or process step. Its determination is particularly useful for understanding process performance during steady-state operation, but also for understanding the effects of transient events such as start-up and shut-down phases, process pauses or disturbances that could lead to product rejection.

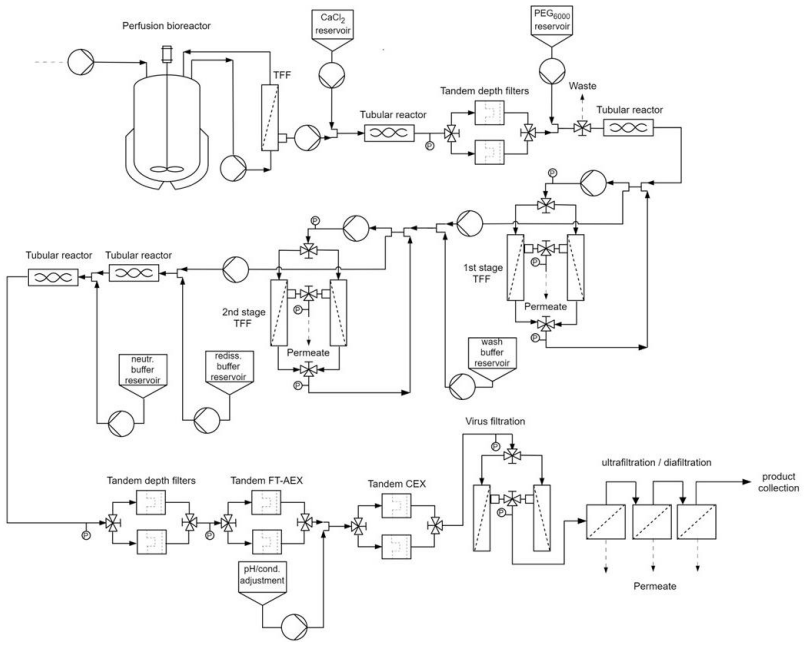


Figure 1: Schematic diagram of alternative integrated continuous process for production of antibodies

At BOKU together with the company Bilfinger Life Science we have developed and integrated process (Figure 1).

Using our simulation framework, we have validated our results and established a basis for further work on RTD determination for integrated continuous bioprocesses. In-silico scale-up (or scale-down) studies could be performed to explore different process scenarios and the effects of perturbations, while only step-input experiments are performed for the individual unit operations and the integrated system with either salts or precipitated proteins. Our simulation framework is also suitable for training and teaching students and employees in the biopharmaceutical industry.

Overview: final theses (finished and ongoing)

PhD projects

Finished

Jürgen Beck
Impact of mass transfer mechanism on protein separation in two-component adsorption
Supervisor: Rainer Hahn
Start: November 2019, Finished: October 2023

Markus Berg (acib project 94041)
Model based process development and scale up of primary recovery for biopharmaceutical production
Supervisor: Rainer Hahn, Astrid Dürauer
Start: January 2020, Finished: October 2023

Natalia Danielewicz (enGenes)
Process development for high yield fermentation of active recombinant lectins expressed in Escherichia coli
Supervisor: Gerald Striedner
Start: 2018, Finished: February 2023

Touraj Eslami (H2020 ITN CODOBIO, evon)
Online control of chromatographic steps using model predictive control (MPC) in continuous downstream processing
Supervisor: Gerald Ebner, Alois Jungbauer, Nico Lingg
Start: 2019, Finished 2023

Leo Jakob (BioTop)
Protein solubility in buffers with kosmotropic salts and polyols
Supervisor: Alois Jungbauer, Nico Lingg, Rupert Tscheließnig
Start: Juni 2019, Finished 2023

Narges Lali (H2020 ITN CODOBIO)
Residence Time distribution of pseudo-continuous methods
Supervisor: Alois Jungbauer, Peter Satzer
Start: June 2019, Finished 2023

Florian Mayer (CD-Lab NLBP)
Influence of fermentation strategies and scale effects on Fab production in E. coli
Supervisor: Gerald Striedner
Start: July 2019, Finished: January 2023

Ignacio Montes Serrano (H2020 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: 2019, Finished: May 2023

Bettina Motycka (BioTop)
Resolving dynamic protein conformations in multidomain enzymes with SAXS
Supervisors: Roland Ludwig, Rupert Tscheliessnig
Start: 2019, Finished 2023

Magdalena Pappenreiter (FFG Cubic)
Development of perfusion control concepts and integrated solutions in fully continuous and automated End-to-End biomanufacturing processes
Supervisor: Alois Jungbauer
Start: January 2020, Finished: May 2023

On-Going

Lena Achleitner (acib 94045)
Virus like particle production in insect cells and mammalian cells
Supervisor: Alois Jungbauer
Start: July 2021

Arasteh Kani Arshia (MISTER)
Metabolic incorporation of latent fast reacting thioesters
Supervisor: Birgit Wiltschi, Gerald Striedner
Start: May 2022

Sergio Araujo (FASEP)
Production of Zika surface protein in E. coli
Supervisor: Alois Jungbauer, Viviane Goncalves
Start: 2022

Johanna Bacher (acib 94045)
Fundamentals of fast virus quantification
Supervisor: Alois Jungbauer
Start: September 2022

Felix Dierlinger (Takeda)
Economic and envrionmetnal modelling of bioprocesses
Supervisor: Alois Jungbauer
Start: October 2021

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

Anna-Carina Frank (NextFlock)
Flocculants for improved monoclonal antibody purification.
Supervisor: Rainer Hahn, Peter Satzer
Start: June 2022

Lisa Fohler (ENZYCLE)

Fed-batch and continuous production of PET degrading enzymes in E. coli
Supervisor: Gerald Striedner
Start: July 2021

Nils Gehrmann (Sartorius)
An ultrafast antibody purification process based on membrane chromatography
Supervisor: Rainer Hahn
Start: October 2020

Martin Gibisch (CD-Lab NLBP)
Directed evolution using selective advantage for producing cells
Supervisor: Monika Cserjan, Gerald Striedner
Start: December 2020

Stephan Gutmann (CD-Lab NLBP)
Directed evolution using selective advantage for producing cells
Supervisor: Monika Cserjan, Reingard Grabherr, Gerald Striedner
Start: December 2020

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

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

Christoph Köppl (acib project 94081)
Fusion Tag design for generic CASPON platform
Supervisor: Monika Cserjan, Gerald Striedner
Start: Oktober 2020

Marco Kreß (Valneva)
Fast virus manufacturing
Supervisor: Alois Jungbauer
Start: June 2019

Claudia Lacombe (H2020 Fet Open PURE)
Production of ncAAs for spider silk protein modification
Supervisor: Birgit Wiltschi, Gerald Striedner
Start: November 2020

Sabrina Leigheb (CD Lab Gentherapy)
Analytics for Adeno-Associated-Viruses
Supervisor: Astrid Dürauer
Start: 2023

Zana Marin (synPPP)
Synthetic in Pichia pastoris

Supervisor: Birgit Wiltschi, Gerald Striedner
Start: January 2022

Victoria Mayer (acib)
Characterization of bionanoparticles by biophysical methods
Supervisor: Alois Jungbauer and Patricia Aguilar
Start: October 2020

Matthias Müller (CD-Lab NLBP)
Investigation on disulfide bridge formation in peptides produced by periplasmic expression in Escherichia coli
Supervisor: Rainer Hahn
Start: Februar 2021

Gabriele Recanati (FFG Cubic)
Modeling, optimization and automation of a continuous manufacturing process platform for biopharmaceuticals focused on downstream unit operations
Supervisor: Alois Jungbauer
Start: November 2020

Tommaso de Santis (ENZYCLE)
Economic modeling of enzyme based plastics degradation and recycling processes
Supervisor: Gerald Striedner
Start: December 2020

Mafalda dos Santos (acib 91201)
Nanomembranes for in-situ removal of products from fermentation broth
Supervisor: Alois Jungbauer
Start: November 2021

Florian Simon (E-Conti)
Process development of an integrated continous two-stage chemostrat manufacturing platform using growth-decoupled *Escherichia coli*
Supervisor: Gerald Striedner
Start: September 2023

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

Georg Smesnik (CD Lab Gene Therapy)
Genomic analysis of HEK cells used for AAV production
Supervisors: Nicole Borth, Astrid Dürauer
Start: 2023

Maria Toth (CD Lab Gene Therapy)
Development of inducible stable cell lined for AAV production
Supervisors: Astrid Dürauer, Reingard Grabherr
Start: 2023

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

Martina Winter (CD Lab Gene Therapy)
Online monitoring and modelling ofAAV downstream processing
Supervisor: Astrid Dürauer
Start: 2023

Yao Yuelang (Biotop Joint Project BOKU)
Effect of membrane organization on weak acid transport proteins;
Supervisor: Vorauer-Uhl Karola and Michael Sauer
Start: August 2020

Alexander Zollner (H2020 Fet Open PURE)
Functionalized non-woven nanofibers for the purification of virus-like particles
Supervisor: Alois Jungbauer
Start: September 2021

Master theses

Finished

Verena Buchacher (CD Lab Gene Therapy, FH Joanneum**)**
Characterization of (Bio)nanoparticle Size by Taylor Dispersion Analysis
Supervisor: Astrid Dürauer
Finished: September 2023

Florian Gisperg (Boehringer-Ingelheim)
On-line monitoring of process performance in a high-throughput automation platform using modeling strategies
Supervisor: Gerald Striedner
Finished: September 2023

Lukas Leibetseder (Enzycle)
Production of polyolefine degrading enzymes with E. coli expression systems and initial activity/degradation testing
Supervisor: Gerald Striedner
Finished: October 2023

Lea Jusufagic (CD-Lab NLBP)
CRISPRactivation mediating chaperon upregulation enhances recombinant polypeptide production in E. coli
Supervisor: Gerald Striedner, Monika Cserjan
Finished: September 2023

Catarina Sousa Neves Maia (CD Lab Gene Therapy, IST Tecnico Lisboa.**)**
Establishment of an Analytical Asymmetrical Flow Field Flow Fractionation (AF4) Method for Characterization and Quantification of Bionanoparticles
Supervisor: Astrid Dürauer
Finished: December 2023

Lea Milas (Takeda)
AAV purification by affinity chromatography
Supervisor: Astrid Dürauer
Start: September 2022

Franz Moisi (Valneva)
Evaluation of fermentation process parameters influencing the fatty acid composition of bacterial lipoprotein
Supervisor: Gerald Striedner
Finished: December 2023

Martina Christine Winter (research project)
Soft sensor for determining oxygen consumption rate and viable cell count
Supervisor: Satzer Peter, Gerald Striedner
Finished: 2023

On-going

Johanna Berein (enGenes GmbH)
Implementing growth-decoupled recombinant protein production in E. coli K-12 strains
Supervisor: Gerald Striedner, Jürgen Mairhofer
Start: December 2021

Nora Dürkop (BIOMIN)
Optimization of the drying process of a bacterial feed additive
Supervisor: Gerald Striedner
Start: July 2019

Felix Oliver Faschingeder (CD-Lab NLBP)
Recombinase mediated cassette exchange (RMCE) in E. coli
Supervisor: Gerald Striedner, Gutmann Stefan
Start: October 2022

Pawel Gorecki (CD-Lab NLBP)
Outer membrane permeabilization for extracellular recombinant peptide production in E. coli
Supervisor: Gerald Striedner, Monika Cserjan
Start: December 2022

Florian Wöls
Effect of column size and particle size on protein separation in small scale ion exchange chromatography
Supervisor: Rainer Hahn, Jürgen Beck
Start: Juni 2023

Georg Hochdaninger
Separation of two-component mixture of Conalbumin and Green Fluorescent Protein
Supervisor: Rainer Hahn
Start: May 2022

Marina Heine (Takeda)
Downscale model qualification on example of plasma-derived serine protease inhibitor purification process
Supervisor: Alois Jungbauer
Start: Mar 2020

Tobias Kargl (FFG Research Studio Novasign)
Predictive Hybrid Modeling of Single-Pass Tangential Flow Filtration
Supervisor: Astrid Dürauer
Start: 2020

Alexander Paul Karner (Boehringer-Ingelheim)
Towards a strategy for scientifically sound choice of depth filter in the clarification of soluble expressed proteins
Supervisors: Astrid Dürauer, Maria Weinberger (BI)
Start: 2023

Dieter Ratz
Downstream processing of a membrane bound Cytochrome P450 expressed in Pichia pastoris
Supervisor: Rainer Hahn, Diana Huber (Technical University Vienna)
Start: June 2022

Lukas Richter (Biomay)
Comparative Study of Chromatographic purification processes for mRNA manufacturing
Supervisor: Astrid Dürauer
Start 05/2022

Michaela Stadlmayr (Biomay)
Development of fast and robust purification process for plasmid DNA
Supervisor: Astrid Dürauer
Start 05/2022

Gregor Stitz
Advanced analytical characterisation of monoclonal antibody species
Supervisor: Rainer Hahn
Start June 2023

Ruben Stopper (Boehringer-Ingelheim RCV)
Continuous Centrifugation for Separation of ATPE phases after DNA purification
Supervisor: Astrid Dürauer, Thomas Mainka (BI)
Start: 2023

Michael Spitaler
ISO 9001:2015 Certification Project for the BOKU Core Facility "BioIndustrial Pilot Plant"
Supervisor: Karola Vorauer-Uhl, Markus Luchner (Co-Supervisor)
Start: 03/2023

Christian Pantazi
Optimization of a documentation management system for the BOKU Core Facility BioIndustrial Pilot Plant in preparation for the planned certification according to ISO 9001
Supervisor: Karola Vorauer-Uhl, Markus Luchner (Co-Supervisor)
Start: 10/2023

Bachelor theses

Finished

Dominik Kallinger
Bacterial Cell disruption in a Bench-top Bead Mill
Supervisor: Astrid Dürauer
Start: January 2022

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

Karoline Reznar (CD-Lab NLBP)
Downregulation of the periplasmic chaperon LolA by a synthetic small regulatory RNA strategy to increase cell permeability in Escherichia coli
Supervisor: Gerald Striedner, Monika Cserjan
Start: August 2021

On-going

Schnitzler Julia (Enzycle)
Enhancement of enzymatic activity through pre-treatment of E. coli fermentation suspension and supernatant
Supervisor: Gerald Striedner, Lisa Fohler
Start: August 2023

Schachinger Maximilian (CD Lab NLBP)
Decoupled expression of recombinant peptides and small sRNA MicL for downregulation of Lpp and peptide secretion in Escherichia coli
Start: October 2023

Scientific output

Scientific publications in peer-reviewed journals

Beck, J; Biechele, M; Repik, C; Gruber, P; Furtmüller, PG; Hahn, R. Desorption of plasmid DNA from anion exchangers: Salt concentration at elution is independent of plasmid size and load. J Sep Sci. 2023; 46(8):e2200943

Beck, J; Hochdaninger, G; Carta, G; Hahn, R. Resin structure impacts two-component protein adsorption and separation in anion exchange chromatography. J CHROMATOGR A. 2023; 1705, 464208

Berg M.C., Erdem I., Berger E., Martinetz M.C., Brocard C., Hammerschmidt N., Dürauer A., Hahn R. (2023): Genomic DNA causes membrane fouling during sterile filtration of cell lysates, Sep Purif Technol, 324, https://doi.org/10.1016/j.seppur.2023.124540

Berg, MC; Erdem, I; Berger, E; Martinetz, MC; Brocard, C; Hammerschmidt, N; Durauer, A; Hahn, R. Genomic DNA causes membrane fouling during sterile filtration of cell lysates. SEP PURIF TECHNOL. 2023; 324, 124540

Bernau, C. R.; Buyel, J. F. (2023): The use of antifoam agents to eliminate bubbles during biotechnological sample analysis. In: Discov Chem Eng 3 (1). DOI: 10.1007/s43938-023-00021-w.

Buyel, J. F. (2023): Product safety aspects of plant molecular farming. In: Front. Bioeng. Biotechnol. 11, Artikel 1238917, S. 1238917. DOI: 10.3389/fbioe.2023.1238917.

Csukovich, G; Kramer, N; Pratscher, B; Gotic, I; Freund, P; Hahn, R; Himmler, G; Brandt, S; Burgener, IA. Neutralising Effects of Different Antibodies on Clostridioides difficile Toxins TcdA and TcdB in a Translational Approach. INT J MOL SCI. 2023; 24(4), 386

Danielewicz, N., Rosato, F., Tomisch, J., Wiltschi, B., Striedner, G., Römer, W., Mairhofer, J. Clickable Shiga Toxin B Subunit for Drug Delivery in Cancer Therapy. ACS Omega, 2023, 8(17), pp. 15406–15421

Dürauer A., Jungbauer A., Scharl T. (2023): Sensors and chemometrics in downstream processing. Biotechnol Bioeng, https://doi.org/10.1002/bit.28499 (Review article)

Emonts, J.; Buyel, J. F. (2023): An overview of descriptors to capture protein properties - Tools and perspectives in the context of QSAR modeling. In: Computational and Structural Biotechnology Journal 21, S. 3234–3247. DOI: 10.1016/j.csbj.2023.05.022.

Guo Y, Kangwa M, Ali W, Mayer-Gall T, Gutmann J, Zenneck C, et al. Moving adsorption belt system for continuous bioproduct recovery utilizing composite fibrous adsorbents. Frontiers in Bioengineering and Biotechnology. 2023;11:-. doi:https://doi.org/10.3389/fbioe.2023.1135447

Hanaee-Ahvaz, H; Cserjan-Puschmann, M; Mayer, F; Tauer, C; Albrecht, B; Furtmüller, PG; Wiltschi, B; Hahn, R; Striedner, G. (2023): Antibody fragments functionalized with non-canonical amino acids preserving structure and functionality - A door opener for new biological and therapeutic applications. Heliyon. 2023; 9(12):e2246

Jakob L, Mesurado T, Jungbauer A, Lingg N. Increase in cysteine-mediated multimerization under attractive protein-protein interactions. Preparative Biochemistry & Biotechnology. 2023;53(8):891-905. doi:https://doi.org/10.1080/10826068.2022.2158471

Jakob, LA; Mesurado, T; Jungbauer, A; Lingg, N. Increase in cysteine-mediated multimerization under attractive protein-protein interactions. Prep Biochem Biotechnol. 2023; 53(8):891-905

Jurjevec, A; Brocard, C; Striedner, G; Cserjan-Puschmann, M; Hahn, R. Polyethyleneimine efficiently extracts recombinant cytoplasmatic green fluorescent protein produced in Escherichia coli with high purity. J BIOTECHNOL. 2023; 371: 41-49

Knödler, Matthias; Buyel, J. F. (2023): Extraction and purification of malaria vaccine candidate CLCT produced by transient expression in Nicotiana benthamiana plants. In: Discov Chem Eng 3 (1). DOI: 10.1007/s43938-023-00032-7.

Knödler, Matthias; Frank, Katharina; Kerpen, Lucy; Buyel, J. F. (2023a): Design, optimization, production and activity testing of recombinant immunotoxins expressed in plants and plant cells for the treatment of monocytic leukemia. In: Bioengineered 14 (1), S. 2244235. DOI: 10.1080/21655979.2023.2244235.

Knödler, Matthias; Opdensteinen, Patrick; Sankaranarayanan, Ramya Ambur; Morgenroth, Agnieszka; Buhl, Eva Miriam; Mottaghy, Felix M.; Buyel, J. F. (2023b): Simple plant-based production and purification of the assembled human ferritin heavy chain as a nanocarrier for tumor-targeted drug delivery and bioimaging in cancer therapy. In: Biotechnol Bioeng 120 (4), S. 1038–1054. DOI: 10.1002/bit.28312.

Knödler, Matthias; Reunious, Paul Winman; Buyel, J. F. (2023c): Risk assessment and bioburden evaluation of Agrobacterium tumefaciens-mediated transient protein expression in plants using the CaMV35S promoter. In: Bmc Biotechnol 23 (1), S. 14. DOI: 10.1186/s12896-023-00782-w.

Kopp, J., Bayer, B., Slouka, C., Striedner, G., Dürkop, M., Spadiut, O. Fundamental insights in early-stage inclusion body formation. Microbial Biotechnology, 2023, 16(5), pp. 893–900

Lingg N, Mozgovicz M, Schaufler T, Prokup A, Carruthers A, Boerema D, et al. Continuous cold ethanol precipitation of immunoglobulin G from human plasma. PROCESS BIOCHEMISTRY. 2023;132:121-9. doi:https://doi.org/10.1016/j.procbio.2023.07.013

Lingg, N; Mozgovicz, M; Schaufler, T; Prokup, A; Carruthers, A; Boerema, D; Keigher, L; Brinkman, N; Jungbauer, A. Continuous cold ethanol precipitation of immunoglobulin G from human plasma. PROCESS BIOCHEM. 2023; 132: 121-129.

Mayer, F; Cserjan-Puschmann, M; Haslinger, B; Shpylovyi, A; Sam, C; Soos, M; Hahn, R; Striedner, G. Computational fluid dynamics simulation improves the design and characterization of a plug-flow-type scale-down reactor for microbial cultivation processes. Biotechnol J. 2023; 18(1):e2200152

Mayer, F; Haslinger, B; Shpylovyi, A; Weber, A; Windberger, U; Albrecht, B; Hahn, R; Cserjan-Puschmann, M; Striedner, G. Scale-related process heterogeneities change properties of high-cell-density fermentation broths demonstrated with Escherichia coli B and K-12 strains. J CHEM TECHNOL BIOT. 2023; 98(6): 1443-1452

Medl M., Scharl T., Dürauer A., Leisch F. (2023): Explainable deep learning enhances robust and reliable real-time monitoring of a chromatographic protein A capture step, Biotechnol J, https://doi.org/10.1002/biot.202300554

Medl, M., Rajamanickam, V., Striedner, G., Newton, J. Development and Validation of an Artificial Neural-Network-Based Optical Density Soft Sensor for a High-Throughput Fermentation System. Processes, 2023, 11(1), 297

Montes-Serrano I., Komuczki D.P., Dürauer A. (2023): A modelling approach for volumetric power input in the microscale and its utilization for the scale-up of solid-liquid mixing systems, Chemical Engineering and Processing - Process Intensification, 184, art. no. 109303, https://doi.org/10.1016/j.cep.2023.109303

Mozgovicz M, Fischer A, Brocard C, Jungbauer A, Lingg N. L-Arginine sulfate reduces irreversible protein binding in immobilized metal affinity chromatography. Journal of Chromatography A. 2023;1706:-. doi:https://doi.org/10.1016/j.chroma.2023.464246

Mozgovicz, M; Fischer, A; Brocard, C; Jungbauer, A; Lingg, N. L-Arginine sulfate reduces irreversible protein binding in immobilized metal affinity chromatography. J CHROMATOGR A. 2023; 1706, 464246

Nausch, Henrik; Baldan, Marco; Teichert, Katrin; Lutz, Jannik; Claussen, Carsten; Bortz, Michael; Buyel, J. F. (2023): Simulation and optimization of nutrient uptake and biomass formation using a multi-parameter Monod-

type model of tobacco BY-2 cell suspension cultures in a stirred-tank bioreactor. In: Front. Plant Sci. 14, Artikel 1183254, S. 1183254. DOI: 10.3389/fpls.2023.1183254.

Opdensteinen, Patrick; Buyel, J. F. (2023): Zuverlässige Proteinquantifizierung durch Oberflächenplasmonenresonanzspektroskopie. In: Arnold Maria Raem und Peter Rauch (Hg.): Immunoassays. Berlin, Heidelberg: Springer Berlin Heidelberg, S. 231–249.

Pappenreiter M, Bayer B, Logarusic M, Sissolak B, Jungbauer A. Irreversible and reversible impact on cellular behavior upon intra-experimental process parameter shifts in a CHO semi-continuous perfusion process. Biochemical Engineering Journal. 2023;193:-. doi:https://doi.org/10.1016/j.bej.2023.108876

Pappenreiter M, Schwarz H, Sissolak B, Jungbauer A, Chotteau V. Product sieving of mAb and its high molecular weight species in different modes of ATF and TFF perfusion cell cultures. Journal of Chemical Technology and Biotechnology. 2023;98(7):1658-72. doi:https://doi.org/10.1002/jctb.7386

Recanati G, Pappenreiter M, Gstoettner C, Scheidl P, Vega E, Sissolak B, et al. Integration of a perfusion reactor and continuous precipitation in an entirely membrane-based process for antibody capture. Engineering in Life Sciences. 2023;23(10):e2300219-. doi:https://doi.org/10.1002/elsc.202300219

Ridgley, Laura A.; Falci Finardi, Nicole; Gengenbach, Benjamin B.; Opdensteinen, Patrick; Croxford, Zack; Ma, Julian K-C et al. (2023): Killer to cure: Expression and production costs calculation of tobacco plant-made cancer-immune checkpoint inhibitors. In: Plant Biotechnol J 21 (6), S. 1254–1269. DOI: 10.1111/pbi.14034.

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Santos M, Schuster C, Rennhofer H, Lichtenegger H, Peterlik H, Causon T, et al. Ultrathin membranes composed of branched polyethylenimine and poly [(o-cresyl glycidyl ether)-co-formaldehyde] for primary recovery of itaconic acid. Separation and Purification Technology. 2023;316:-. doi:https://doi.org/10.1016/j.seppur.2023.123738

Schütz, Anja; Bernhard, Frank; Berrow, Nick; Buyel, J. F.; Ferreira-da-Silva, Frederico; Haustraete, Jurgen et al. (2023): A concise guide to choosing suitable gene expression systems for recombinant protein production. In: STAR protocols 4 (4), S. 102572. DOI: 10.1016/j.xpro.2023.102572.

Spanov B, Olaleye O, Mesurado T, Govorukhina N, Jungbauer A, van de Merbel N, et al. Pertuzumab Charge Variant Analysis and Complementarity-Determining Region Stability Assessment to Deamidation. Analytical Chemistry. 2023;95(8):3951-8. doi:https://doi.org/10.1021/acs.analchem.2c03275

Spanov, B; Olaleye, O; Mesurado, T; Govorukhina, N; Jungbauer, A; van de Merbel, NC; Lingg, N; Bischoff, R. Pertuzumab Charge Variant Analysis and Complementarity-Determining Region Stability Assessment to Deamidation. Anal Chem. 2023; 95(8):3951-3958

Viktoria M, Anna-Carina F, Shirin P, Patrick C, Petra S, Alois J, et al. Removal of chromatin by salt-tolerant endonucleases for production of recombinant measles virus. Biotechnology Progress [Internet]. 2023;39:-. doi:10.1002/btpr.3342

Weber, A., Gibisch, M., Tyrakowski, D., Cserjan-Puschmann, M., Toca-Herrera, J.L., Striedner, G. Recombinant Peptide Production Softens Escherichia coli Cells and Increases Their Size during C-Limited Fed-Batch Cultivation. International Journal of Molecular Sciences, 2023, 24(3), 2641

Presentations and Posters

Oral Presentations

Achleitner L, Satzer P, Lingg N, Jungbauer A. Virus working stock production for large scale VLP production in insect cells. In: Austrian Proteomics and Metabolomics Association , editor. Book of Abstracts. 2023.

Berg M.C., I. Erdem, E. Berger, A. Dürauer, R. Hahn (2023): Genomic dsDNA induced membrane fouling during sterile filtration of cell lysates, Bioprocessing Summit Europe 2023, March 14 – 16, 2023, Barcelona, Spain

Buyel J. (2023) Digitalization in education. EFCE Working Party Education Business Meeting, April 28 2023, Athens, Greece

Buyel J. (2023) Yes you can – Protein expression screening in plants and plant cells. May 23rd 2023, 19th Annual P4EU Meeting, Trieste, Italy

Cserjan-Puschmann, M; Striedner, G; Recombinant protein production in E. coli - continuous vs. batch production. 4th Global Bioprocessing, Bioanalytics and ATMP Manufacturing Congress 2023

De Santis, T; Striedner, G. Economic and ecological evaluation of enzymatic plastic recycling, 9th International Conference on Engineering for Waste and Biomass Valorisation. 9th International Conference on Engineering for Waste and Biomass Valorisation 2023.

Dürauer, A. (2023): Multi-Dimensional Real Time Monitoring and Accelerated Process Development in DSP Based on Predictive Models, BPI West, Feb 27 - March 2, 2023, Invited Talk (hybrid), San Diego, US

Frank A.-C., Daniel Komuczki, Clara Hofmann, Natalie Deiringer, Felicitas Guth, Elisabeth Grünstein, Rainer Hahn, Peter Satzer. (2023): Cationic polymer assisted clarification. International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 05.-08.11.2023, Vienna

Gibisch M., Matthias Müller, Monika Cserjan-Puschmann, Rainer Hahn, Gerald Striedner. Extracellular recombinant peptide production in Escherichia coli. Himmelfahrtstagung 2023

Gibisch, M; Müller, M; Cserjan-Puschmann, M; Hahn, R; Striedner, G. Extracellular peptide production in Escherichia coli. 11th Conference on Recombinant protein production 2023.

Gibisch, M; Müller, M; Cserjan-Puschmann, M; Hahn, R; Striedner, G. Extracellular peptide production in Escherichia coli. ECAB/ECCE 2023

Hahn, R; Beck, J. (2023): Two-component protein adsorption and separation in anion exchange chromatography. 7th European Congress of Applied Biotechnology (ECAB 7), 17.09.2023-21.09.2023, Berlin, Germany

Jurjevec, A.; Brocard, C.; Striedner, G.; Cserjan-Puschmann, M.; Hahn, R. Polyethyleneimine efficiently extracts recombinant cytoplasmatic green fluorescent protein produced in Escherichia coli with high purity. International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP)

Jurjevec, A; Brocard, C; Striedner, G; Cserjan-Puschman, M; Hahn, R. Multicomponent Adsorption as a Hindrance of Fab Fragment Purification. Bioprocessing Summit Europe 2023

Klanschnig, M., Monika Cserjan-Puschmann, Gerald Striedner, Reingard Grabherr. CRISPRactivation-SMS, a message for PAM sequence independent gene up-regulation in Escherichia coli. Retreat UC Berkeley, Department of Molecular and Cell Biology (MCB); Division of Biochemistry, Biophysics and Structural Biology (BBS) 2023.

Köppl, C; Cserjan-Puschman, M; Lingg, N; Fischer, A; Kröß, C; Schneider, R; Jungbauer, A.,: Striedner, G. CASPON technology – a platform process for non-platform proteins using Escherichia coli. 11th Conference on Recombinant Protein Production

Köppl, C; Cserjan-Puschman, M; Lingg, N; Fischer, A; Krößß, C; Schneider, R; Jungbauer, A: Striedner, G;. CASPON technology – a platform process for non-platform proteins using Escherichia coli. Event: High Throughput Screening & Process Development – how small can we get? 2023.

Köppl, C; Cserjan-Puschmann, M; Lingg, N; Fischer, A; Krößß, C; Schneider, R; Jungbauer, A; Striedner, G. (2023): CASPON technology – a platform process for non-platform proteins using Escherichia coli. [Poster]. Bioprocessing Summit Europe, 14.03.2023 - 16.03.2023, Barcelona, SPAIN

Köppl, C; Gibisch, M; Cserjan-Puschman, M; Lingg, N; Fischer, A; Krößß, C; Schneider, R; Jungbauer, A: Striedner, G; CASPON technology – a platform process for non-platform proteins using Escherichia coli. Himmelfahrtstagung on Bioprocess Engineering 2023.

Lingg, N; Elsner, D. CASPON - a platform process for non-platform proteins. 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides – ISPPP 2023.

Lingg, N; Elsner, D; Brocard, C; Jungbauer, A. (2023): CASPON – a platform process for non-platform proteins. 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 5.11.2023-8.11.2023, Vienna, AUSTRIA

Lingg, N; Fischer, A; Mozgovicz, M; Jungbauer, A. (2023): Interactome of immobilized metal affinity chromatography. Affinity 2023 - 25th Meeting of the International Society for Molecular Recognition, 05.06.2023 - 07.06.2023, Lisbon, PORTUGAL

Lingg, N; Jungbauer, A; Pereira Aguilar, P; Grabheer, R. (2023): Baculovirus Expression Technology for the Production of Virus-Like Particles as Vaccine Candidates. ISBiotech 12th Spring Meeting, 20.03.2023 - 22.03.2023, Norfolk, USA

Medl, M. , T. Scharl, F.Leisch, A. Dürauer (2023): Uncovering the black-box of data-driven models in biotechnological process modelling, 42nd International Symposium on the Separation of Proteins, Peptides & Polynucleotides , Nov 5-8, 2023, Vienna, Austria

Müller M; Gibisch M; Brocard C; Cserjan-Puschmann M; Hahn R. Purification of recombinantly produced Somatostatin-28 comparing hydrochloric acid and polyethylenimine as E. coli extraction aids. 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 2023.

Santos M, Causon T, Bruggen B, Jungbauer A. Performance of ultrathin membranes for primary recovery of itaconic acid. In: Austrian Proteomics and Metabolomics Association , editor. Book of Abstracts. 2023.

Santos M, Causon T, Bruggen B, Jungbauer A. Ultrathin membranes for primary recovery of itaconic acid produced by fermentation. In: Austrian Proteomics and Metabolomics Association , editor. Book of Abstracts. 2023.

Scheich David, Diogo Ferreira-Faria, Rainer Hahn, Alois Jungbauer, Nico Lingg. (2023): Hindered diffusion of secretory immunoglobulin A in CaptureSelect IgA / IgA-CH1 resins. 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 05.11.-08.11.2023, Vienna, Austria

Scheich, David, Diogo Ferreira-Faria, Rainer Hahn, Alois Jungbauer, Nico Lingg. (2023): Hindered diffusion of secretory immunoglobulin A in CaptureSelect IgA / IgA-CH1 resins. 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 05.11.-08.11.2023, Vienna, Austria

Striedner, G. General considerations on scaling and high throughput aspects in upstream process development. High Throughput Screening & Process Development, Vienna 2023

Toth, M; Reithofer, M; Grabherr, R; Dürauer, A. (2023): The T7 inducible system for recombinant protein production in mammalian cells, 16th Conference of Protein Expression in Animal Cells (PEACe), Sep 24-28, 2023, Sitges, Spain

Poster Presentations

Beck, J; Schmölder, J; von Lieres, E; Hahn, R; (2023): Challenges in parameter estimation for two-component protein adsorption using batch and small-scale column adsorption. [Poster] 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides - ISPPP, 05.11.2023 - 08.11.2023, Vienna, AUSTRIA

Beck, J; Schmölder, J; von Lieres,E; Hahn, R (2023): Challenges in parameter estimation for two-component protein adsorption using batch and small-scale column adsorption. [Poster] 5th Modeling Workshop - Recovery of Biological Products Conference Series, 26.06.2023 - 27.06.2023, Hillerod, DENMARK

Berg, MC; Erdem, I; Berger, E; Dürauer, A; Hahn, R. (2023): Genomic dsDNA induced membrane fouling during sterile filtration of cell lysates, 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), Nov 5-8, 2023, Vienna, Austria

Berg, MC; Erdem, I; Berger, E; Dürauer, A; Hahn, R; (2023): Genomic dsDNA induced membrane fouling during sterile filtration of cell lysates. [Poster] Bioprocessing Summit Europe, 14.03.2023 - 16.03.2023, Barcelona, Spain

Jurjevec, A.; Brocard, C.; Striedner, G.; Cserjan-Puschmann, M.; Hahn, R. (2023): Polyethyleneimine efficiently extracts recombinant cytoplasmatic green fluorescent protein produced in Escherichia coli with high purity. [Poster] International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), 5.11.2023 - 8.11.2023, Vienna, AUSTRIA

Jurjevec, A; Brocard, C; Striedner, G; Cserjan-Puschman, M; Hahn, R (2023): Multicomponent Adsorption as a Hindrance of Fab Fragment Purification. [Poster] Bioprocessing Summit Europe , 14.03.2023 - 16.03.2023, Barcelona, Spain

Leigheb, S; Maia, C; Buchacher, V; Rahimzadeh, M; Virgolini, N; Aguilar, P; Dürauer, A; (2023): Asymmetric field flow fractionation and Taylor Dispersion Analysis for separation and characterization of Adeno Associated Viruses for gene therapy, 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), Nov 5-8, 2023, Vienna, Austria

Medl, M; Winter, M; Erdem, I; Dürauer, A; Scharl, T; (2023):Efficient identification of optimal process conditions with Gaussian processes, 42nd International Symposium on the Separation of Proteins, Peptides and Polynucleotides (ISPPP), Nov 5-8, 2023, Vienna, Austria

Müller, M; Gibisch, M; Brocard, Cecile; Cserjan-Puschmann, Monika; Hahn Rainer. (2023): Purification of recombinantly produced Somatostatin 28 comparing hydrochloric acid and polyethylenimine as E. coli extraction aids. [Poster] 14th European Congress of Chemical Engineering and 7th European Congress of Applied Biotechnology, 17.09.2023 - 21.09.2023, Berlin, GERMANY

Patrick Opdensteinen, Matthias Knödler, Johannes F. Buyel (2023): Producing enzymes for the removal of odorous substances in plants. [Poster] DECHEMA Himmelfahrtstagung 2023, Weimar, Germany

Smesnik, G; Virgolini, N; Dürauer, A; Borth, N. (2023): Assessing the underlying cellular response of HEK293 cells to evolutionary pressures, 30th Annual Congress of the European Society of Cell and Gene Therapy (ESGCT), October 24-28, Brussels, Belgium

Smesnik, G; Virgolini, N; Dürauer, A; Borth, N; (2023):Assessing the underlying cellular response of HEK293 cells to evolutionary pressures, 30th Annual Congress of the European Society of Cell and Gene Therapy (ESGCT), Oct 24-27,2023, Brussels, Begium

Smesnik, G; Virgolini, N; Dürauer, A; Borth, N;, (2023): Understanding cellular limitations of HEK293, Characterization of genetic and epigenetic state, 16th Conference of Protein Expression in Animal Cells (PEACe), Sep 24-28, 2023, Sitges, Spain

Other publications

Guest Editorial Activity

Multi--Omics of Extremophilic Organisms

Editorial: Gorji Marzban & Donatella Tesei

A special issue of Biology (ISSN 2079-7737). Special issue belongs to the section "Microbiology".**:**
Biology (MDPI)

https://www.mdpi.com/journal/biology/special_issues/6793MYHB39

Teaching activities

#	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
790434	IP-project management BioproEng (in Eng.)	DK BPE	0.5
790435	Scientific writing BioproEng (in Eng.)	DK BPE	0.5
790436	Interaction with biotech industry BioproEng (in Eng.)	DK BPE	1
790438	Biothermodynamics (in Eng.)	DK BPE	2
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,

Organization	Title	Program
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, Downstream Processing Labor UE, Gärungstechnisches Labor UE	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

Epilogue and outlook

The annual report presents some selected research highlights from 2023 and a general overview of our output in research and teaching. It is also an opportunity for us to make these data and figures accessible to a broader community. For an organization of our size the administrative tasks are very demanding. Even though there is great support from the Department Office and BOKU service units we always face bottlenecks. Only thanks to Petra Polak, our third party funded team assistant, who brings a high level of motivation and expertise, we are able to complete all tasks successfully, on time and with the necessary quality.

From a research perspective, 2024 will certainly be a very interesting year with a broad portfolio of 13 research projects already underway. Due to the new acib FFG COMET K2 program, four projects in the area of health biotechnology, two projects in the area of disruptive bioeconomy and one project in the area of sustainable production will be launched under the leadership of IBSE scientists. With Nico Lingg, Johannes Buyel and Gerald Striedner, colleagues of IBSE are the division heads of two out of four research areas in acib, health biotechnology and disruptive bioeconomy, respectively and will actively contribute to the successful implementation of the program.

We have just recently been informed by BOKU rectorate, that we will face major organizational changes in the coming years. As the number of departments will be reduced from 15 to 6. Our Department of Biotechnology will be merged with the Department of Food Science and Technology and the Department of Applied Genetics and Cell Biology. At IBSE we are looking forward to collaboration with the colleagues from our partner departments and the opportunity to improve workflows, break up outdated structures and leverage synergies in research and teaching activities.

Our tasks for 2024 are as varied and challenging as ever, and we are confident that we will master them with dedication, motivation and our scientific expertise.

Gerald Striedner Astrid Dürauer

On behalf of the entire IBSE Team

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