University of Natural Resources
and Applied Life Sciences, Vienna

Institute of Bioprocess Science and Engineering

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Annual Report 2020

February, 2021

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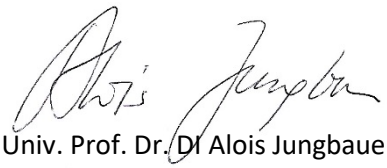
Introduction

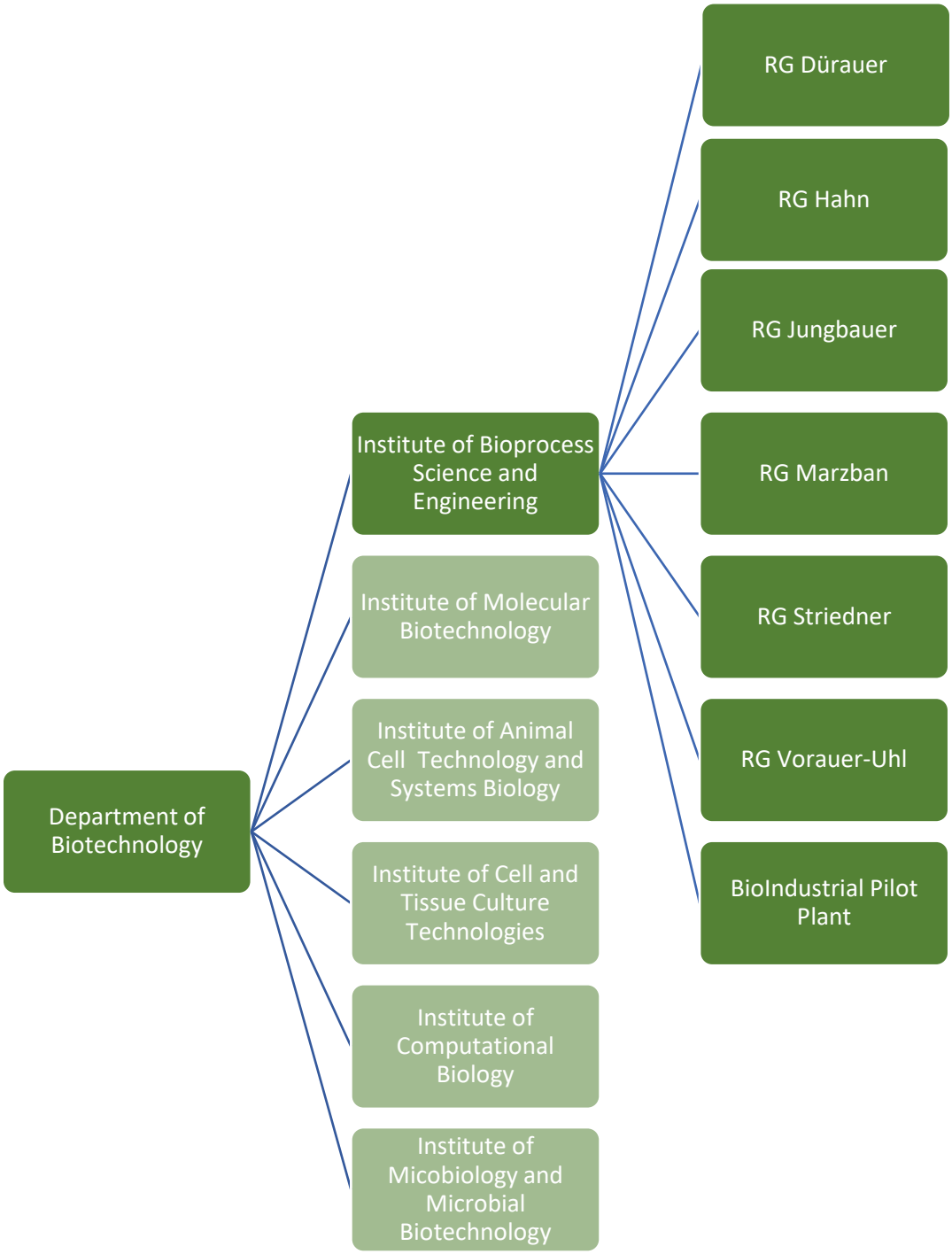
IBSE is not in its infancy anymore and has grown up. Founded in 2019, we have now successfully acted as a research and teaching institution for the second year. We have consolidated; new research groups were founded, and attractive research work was started alongside the already running programs. The pandemic made it challenging to keep up research and teaching operations. Fortunately, we had the privilege to contribute with existing research programs to contribute to an Austrian wide research consortium on Covid-19, led by Reingard Grabherr - the head of the Department of Biotechnology. Our expertise in upstream processing, downstream processing, in-process control and analytics was highly appreciated in the consortium and we were able to develop expression and production technologies for several SARS CoV-2 proteins, useful for research and diagnostic purposes. Thanks to a great donation, these proteins can be provided to the global research community and inquires can be made through the website (https://portal.boku-covid19.at/) which is handled by the IBSE spin off Novasign. I also want to express my gratitude to all who have contributed, and I am still impressed about the enthusiasm and the tireless dedication under these difficult circumstances. In March 2020 all of a sudden, the supply chain was interrupted and shipment of simple chemicals could take several months. We were well prepared, and it was at that time rewarding that we had a lot of auxiliary materials such as filters, chromatography columns, culture media and fine chemicals on stock. Otherwise, we would not have been able to conduct our research in such a short period of time, within 6 weeks from the design of the expression clone to the first batch of the purified proteins. In retrospect we also must reconsider radical solutions proposed by business economists who want to persuade us that we are old-fashioned and outdated when we have warehouses and material on stock. What we have experienced in our small universe of IBSE, may be true for our entire economy and society. Seamless supply chain, outsourcing and extreme specialization only works in fair weather and on sunny days. When the clouds gather, we will end up in a critical phase quickly. I do not want to propose an old-fashioned economy and running a research institution like in the last century, but we must learn from the recent year. It is too early to conclude which lessons we have learned. It seems trivial but a well-organized and structured institute with disciplined members is much better prepared to overcome unforeseen obstacles and global problems than an institution without any reserves. This is definitely a lesson learned, but must be emphasized, because the political debate and climate is not in favor of science and technology, despite the unprecedented success of life science and engineering in light of the ultra-fast development and production of Covid-19 vaccines. Government does not favor and support accumulation of assets at university institutes, although what we have learned last year that this would make us resilient. We should not complain, instead we should use our success as a best practice example and you are all invited to spread the success.

I highly appreciate the enthusiasm and dedication of all members of IBSE and want to thank our partners and colleagues at BOKU and outside for the excellent collaboration and I am fully convinced that physical meetings will be possible in near future and will we continue in a “hybrid” fashion, by exploiting the flexibility of virtual meetings and digital administration and therefore freeing up time for rewarding personal interaction.



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

Structure of the *Institute of Bioprocess Science and Engineering 2020*



Members of the Research Groups 2020

RG Dürauer			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Astrid Dürauer Rupert Tscheließnig Christina Yassouridis	Maximilian Krippl Ignacio Montes Serrano Bettina Motycka Valentina Ruocco	Tobias Kargl	Eva Berger

RG Hahn			
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RG Striedner			
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Roger Dalmau Diaz	Benjamin Bayer	Andreas Dietrich (MA)	Stephan Bunka
Mark Dürkop	Natalia Danielewicz	Wanja Ehtreiber (BA)	Alexander Doleschal
Armin Khodaei	Mathias Fink	Lisa Fohler (BA)	Christoph Köppl
Gerald Striedner	Martin Gibisch	Emil Gerger (BA)	Roman Liebhart
Peter Satzer	Stephan Gutmann	Anton Shpylovyi (MA)	Ignasi Bofarull Manzano
Birgit Wiltschi	Marco Klanschnig	Anna Stock (BA)	Shirin Preinsperger
	Christoph Köppl	Lina Vranitzky (MA)	Patrick Scheidl
	Claudia Lacombe		Johanna Trisko
	Florian Mayer		
	Tommaso de Santis		
	Artur Schuller		
	Patrick Stargardt		
	Florian Strobl		
	Sophie Vazulka		

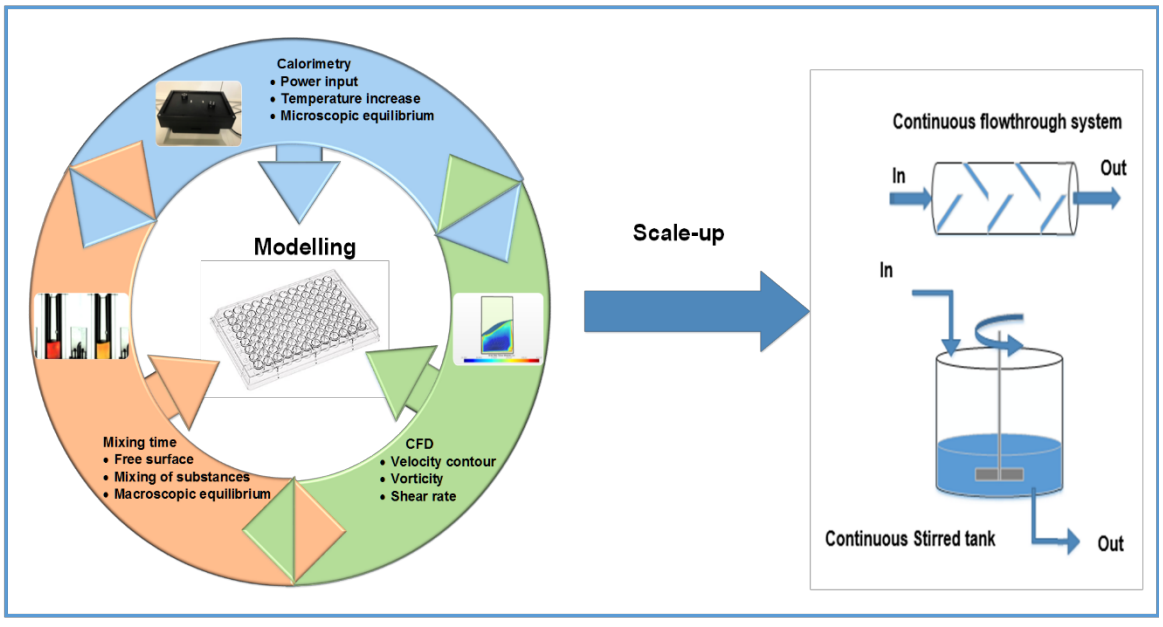
RG Vorauer-Uhl			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Karola Vorauer-Uhl	Dominik Jeschek (Co-supervisor-Biotop)	Konstanze Kastenhofer	Gabriele Lhota
Martin Voigtmann	Bernhard Sissolak	Alexandra Katholnig	
	Ehsan Suleiman	Magdalena Kößlbacher	
	Yuelang Yao	Elisabeth Lehner	
		Julia Mayer	
		Simon Nendwich	
		Simon Netocny	

BioIndustrial Pilot Plant			
Staff	**PhD student**	**BA/MA student, intern**	**Technician**
Markus Luchner		Alina Destinger (MA)	Martin Braunsteiner
			Marco Kaupe
			Matthias Müller
			Sabine Necina

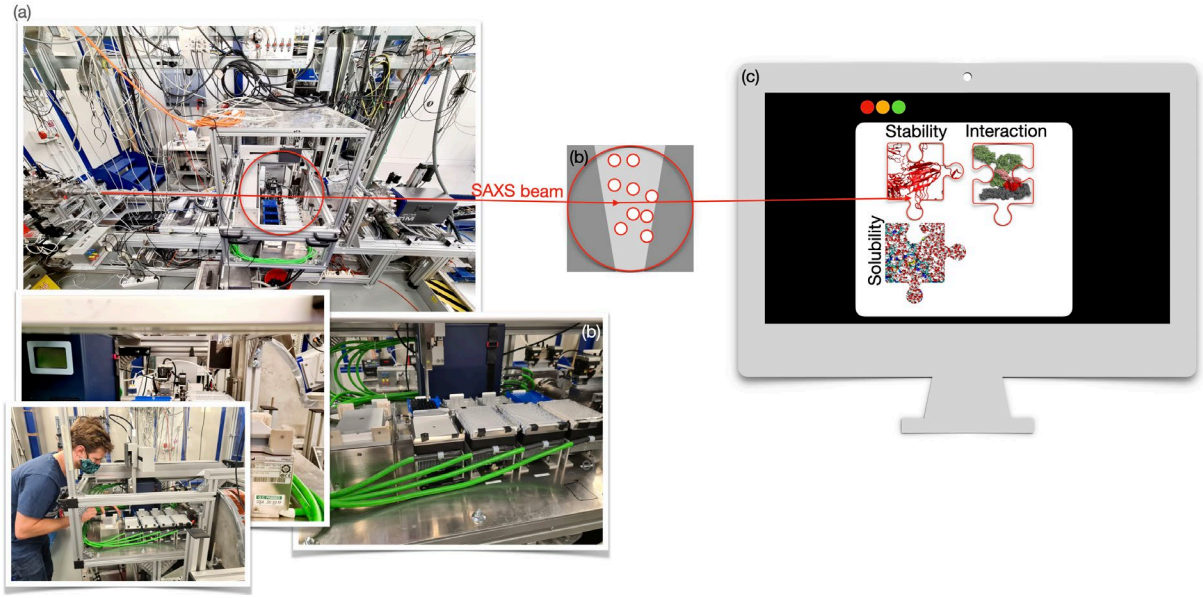
Project: Power input in microscale systems for continuous operations

ITN CODOBIO Continuous Downstream Processing of Biologics

The versatility offered by microtiter plates (MTPs) due to the possibility of changing conditions has given them an important position in plenty of laboratories as a tool for the development of downstream processes. On the downside, such development encounters a problem when it comes to the scale-up since the hydrodynamic behavior is altered due to an increase of volume and a change of the mixing mechanism from shaken to stirred or flow-through. Volumetric power input (VPI) allows for the determination of the hydrodynamics of the system and can be utilized as a scale-up variable. It is also linked to crucial variables in downstream processing such as shear stress or mixing time.
VPI can be determined and modelled in MTPs via the increase of temperature of the liquid as a consequence of the energy dissipation obtained from the motion. Such measurements need to be done under adiabatic conditions. Different types of microtiter plates with different inner diameters (96- 24- and 6-well) are placed inside a housing device, which is allocated on shakers with different orbital diameters, 3 and 25mm, under different shaking frequencies. The increase of temperature over time is recorded every ten seconds and then it is analyzed. In parallel, Computational Fluid Dynamics (CFD) are operated to study the motion of the media. CFD also allows to experiment with different impact factors such as viscosity, filling volume and a range of shaking frequencies, enabling a more detailed model for the scale-up. Current results have shown that, under the same shaking conditions, VPI decreases as the inner diameter increases. 74, 29 and 18W/m^3 were determined for 96-, 24- and 6-well, respectively at a shaking frequency of 800 rpm and 3 mm orbital shaking diameter, The simulated values of 70, 30 and 17W/m^3 for the respective conditions are in good accordance to the experimental results. The CFD simulations demonstrate a power trend of the volumetric power input as the shaking frequency increases. The established mathematical correlation follows a power trend that can be utilized as a proper scale-up tool for large scale mixing in batch or continuous model. (I. Montes Serrano, A. Dürauer)



Project: High throughput screening of protein surface interactions



a) The experimental setup at the Austrian SAXS beamline, Elettra (Trieste). MTS plates are manually transferred (red arrow). They can be shaken and tempered. Up to 4 MTPs can be loaded; a Tecan robot transfers samples to the (b) sample chamber. A sample chamber was designed, and 3D printed to keep resins in the X-ray beam line. c) Scattering data are collected and preprocessed on site. Later the data are analyzed by molecular modeling algorithms. By the now established workflow, we can optimize protein stability, protein-ligand interaction, and protein solubility.

We work for sustainable vaccine production. Among a plethora of factors: protein purification and protein storage are essential. We developed methodologies by that we can monitor protein stability, protein-protein interaction, protein-ligand interaction, and design protein solubility. The methodologies shall be applied online and in-situ, and design parameters shall be identified at the molecular level. We focus on microtiter plates (MTPs) in the established setup as we can easily change conditions and sample a vast arbitrary parameter space.

We deduce the impact of salt on protein form, protein-protein interactions, or protein surface interactions in any industrial relevant resin from in situ experimental data. Understanding the molecular mechanisms of protein adsorption and the molecular mechanisms of interactions are essential for protein purification or protein storage. Today, the only experimental setup capable of in situ access to the molecular mechanisms is small-angle X-ray or small-angle neutron scattering experiments combined with molecular modeling methods.

In a current BioTOP project, we analyzed kosmotropic and chaotropic salts' mixing and their impact on the excluded volume. We increased the binding capacity of dual salt systems in hydrophobic interaction chromatography. We immobilized different proteins at commercially available HIC resins. In an upcoming publication, we challenge the myth of protein Langmuir adsorption. In previous studies, we accessed the molecular mechanism of protein adsorption, i.e., binding and orientation of proteins at ligands and online analysis of the protein's layer thickness. Our experimental setup suffered from low throughput. To overcome this bottleneck, we opted for a Tecan pipetting robot at the SAXS beamline at the Elettra, Trieste. The setup enables in situ sample preparation and scans of vast numbers of samples. The sample cell (Figure b) is based on capillary forces for droplet formation.

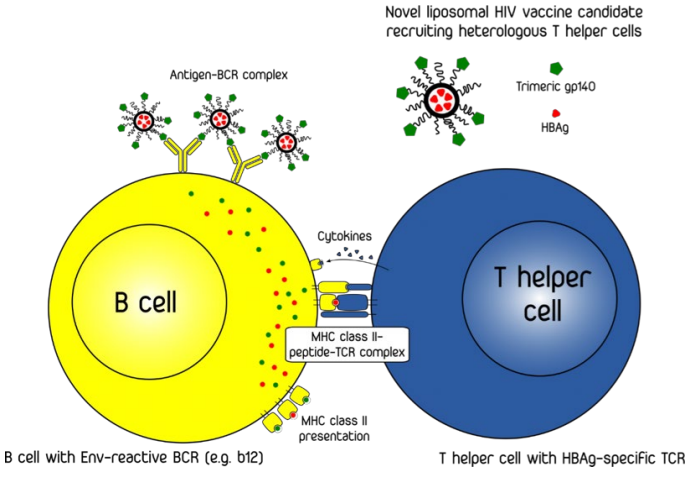
It was initially designed for in situ, high throughput screening of protein solutions. We challenged the setup by introducing resins. However, they counter played the capillary force concept. As resins settle in the drop, they accumulate at the bottom. The beam does not hit the resin but the supernatant. In creasing the resin, concentration led to 'viscus slurries and breaking of the drop. Resins are toxic for the drops surface tension.

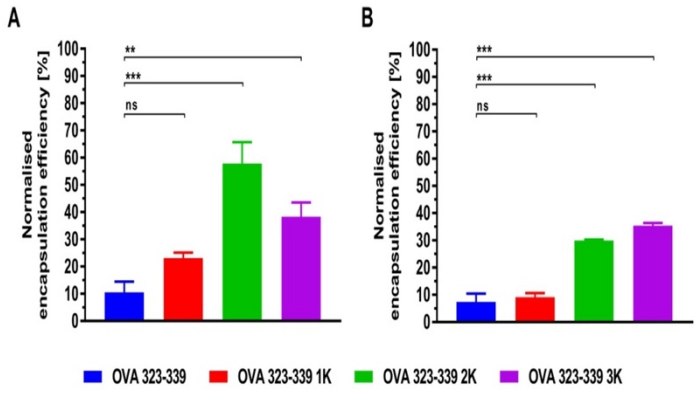
We adapted the experimental design in cooperation with the TU Graz, under the lead of Heinz Amenitsch. In close cooperation with his team, we designed 3D printed permeable stage. By its use and combination with the Tecan robot, now the molecular mechanism of protein surface interactions unfold, and high throughput screening of different resins are at hand. (L. Jakob, R. Tscheliessnig)

Project: Protein-liposome conjugates as novel HIV vaccine candidates

The aim of this project is the development, production and comprehensive characterization of a novel HIV vaccine utilizing the immunological phenomenon of infrastructural help.

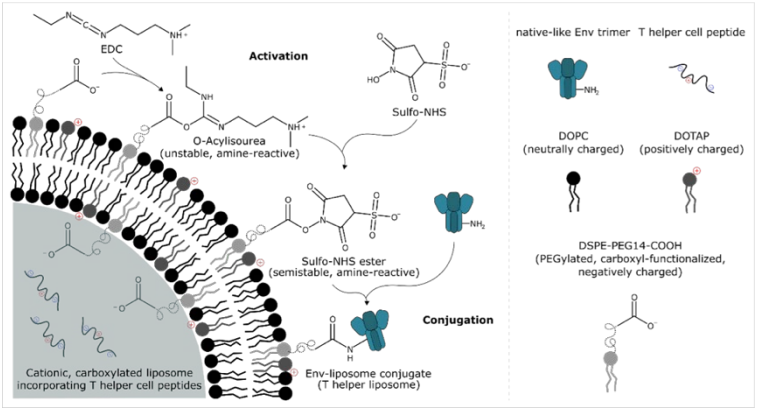
The development of reliable liposome formulations and the characterization of them are aimed thus they can be tested for their immunization capacity. Therefore, efficient encapsulation of immunodominant T helper cell epitopes was achieved by making use of the controllable electrostatic interactions of the peptides with the lipid bilayer of the liposomes. Human immunodeficiency virus envelope proteins ConSOSL.UFO.664, developed and produced by Polymun was used to decorate the peptide containing liposomes. This bioconjugation process is performed in a controlled manner with a particular emphasis on the preservation of the accessibility of epitopes relevant for the induction of broadly neutralizing antibodies. Since the first use of liposomes as carriers for antigens, much work has been done to elucidate the mechanisms involved in the encapsulation of vaccine-relevant biomolecules. However, only a few studies have specifically investigated the encapsulation of hydrophilic, non-conformational peptide epitopes. A plethora of peptide therapeutics and peptide vaccines, both prophylactic and therapeutic, have been evaluated in clinical trials. Nevertheless, the controlled and efficient encapsulation of peptides remains a demanding task, partly because peptides display a large diversity with regard to their aqueous solubility, hydropathicity and isoelectric point, i.e., net charge/pH profile. Here, we investigated the N- and C-terminal introduction of charged amino





acids in order to expand the physico-chemical conditions under which hydrophilic, non-conformational peptide epitopes can be efficiently encapsulated in an electrostatically driven manner. OVA 323-339, as a model peptide, was selected for the purpose of systematically investigating this approach in a model system comprising cationic peptides and anionic liposomes. Variants with elevated positive net charge were realized by bi-terminally extending the sequence with increasing numbers of lysine residues.

In agreement with theoretical considerations on the electrostatic binding of peptides to lipid membranes, experimental work on protein encapsulation has identified ionic strength, pH, the isoelectric point (pI) and the liposome composition (i.e., addition of charged membrane components), as the main determinants of a predominantly electrostatically driven encapsulation of hydrophilic proteins. [1]



Electrostatically driven encapsulation of cationic peptides into anionic liposomes. Peptide-loaded liposomes were prepared by (A) thin-film hydration with subsequent downsizing by means of extrusion or (B) microfluidic mixing of an ethanolic lipid solution with an aqueous T helper peptide solution . The second, essential step in this project, was the decoration of the T-helper peptide containing liposomes with functional, native-like human immunodeficiency virus type 1 envelope (HIV-1 Env). Known, non-covalent conjugates (in particular those that use NTA-functionalized lipids such as 1,2-dioleoyl-sn-glycero-3-[(N-(5-amino-1-carboxypentyl) iminodiacetic acid) succinyl] (nickel salt) (18:1 DGS-NTA(Ni))) readily dissociate in serum and are as such not suitable for any in vivo application or investigations under physiological conditions. To overcome this limitation, we have investigated N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide/ N-Hydroxysulfosuccinimide (EDC/Sulfo-NHS) chemistry for its potential to covalently conjugate tag-free, non-functionalized native-like Env trimers onto the surface of carboxyl-functionalized liposomes which is highly ionic strength- and pH-dependent. Overall, the close proximity between negatively charged Env trimers and positively charged liposomes established through electrostatic attraction seems to be one of the crucial factors for conjugation reactions to proceed [2].

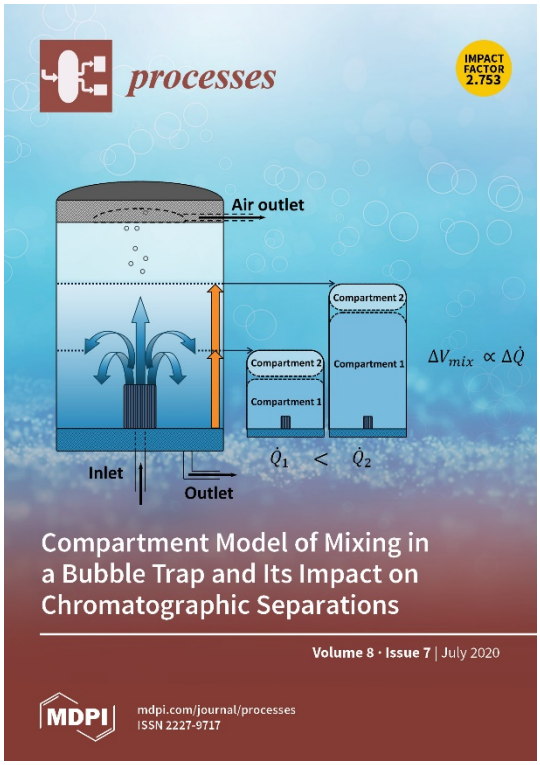
Thus, in conclusion, the systematic approach highlights the requirements and limitations of potentially scalable EDC/Sulfo-NHS-based approaches and represents a solid basis for further research into the controlled conjugation of tag-free, non-functionalized native-like Env trimers on the surface of liposomes, and other nanoparticles. (K. Vorauer-Uhl, E. Suleiman)

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No. 681137 (European AIDS Vaccine Initiative 2020). Ehsan Suleiman received funding from the PhD program "BioTop—Biomolecular Technology of Proteins" (Austrian Science Funds, Project number: FWF W1224).

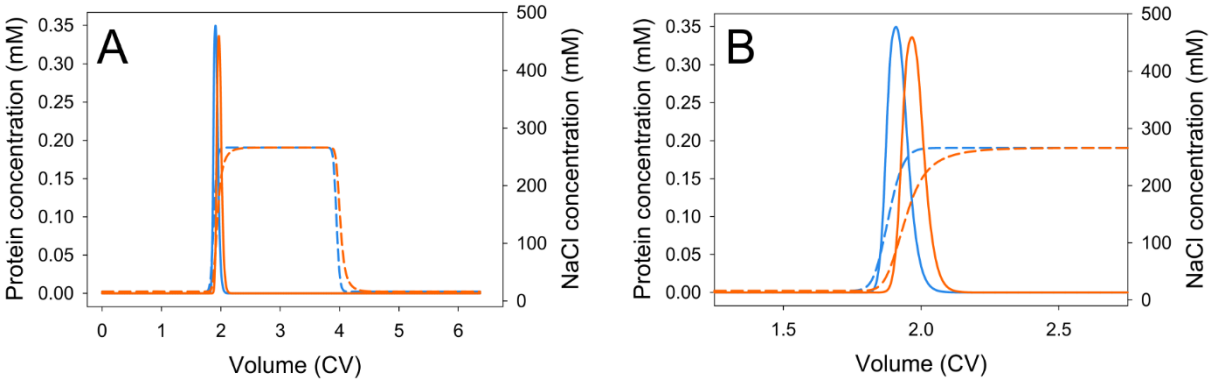
[1] Suleiman, E.; Damm, D.; Batzoni, M.; Temchura, V.; Wagner, A.; Überla, K.; Vorauer-Uhl, K. Electrostatically Driven Encapsulation of Hydrophilic, Non-Conformational Peptide Epitopes into Liposomes. *Pharmaceutics* **2019**, *11*, doi:10.3390/pharmaceutics11110619.

[2]Suleiman, E.; Mayer, J.; Lehner, E.; Kohlhauser, B.; Katholnig, A.; Batzoni, M.; Damm, D.; Temchura, V.; Wagner, A.; Überla, K.; and Karola Vorauer-Uhl Conjugation of Native-Like HIV-1 Envelope Trimers onto Liposomes Using EDC/Sulfo-NHS Chemistry: Requirements and Limitations. *Pharmaceutics* **2020**, *12*, doi:10.3390/pharmaceutics12100979.

Project: Chromatography modeling



Chromatography equipment includes hold-up volumes that are external to the packed bed and usually not considered in the development of chromatography models. These volumes can substantially contribute to band-broadening in the system and deteriorate the predicted performance. We selected a bubble trap of a pilot scale chromatography system as an example for a hold-up volume with a non-standard mixing behavior. In a worst-case scenario, the bubble trap is not properly flushed before elution, thus causing the significant band-broadening of the elution peak. We showed that the mixing of buffers with different densities in the bubble trap device can be accurately modeled using a simple compartment model. The model was calibrated at a wide range of flow rates and salt concentrations. The simulations were performed using the open-source software CADET, and all scripts and data are published with this manuscript. The results illustrate the importance of including external holdup volumes in chromatography modeling. The band-broadening effect of tubing, pumps, valves, detectors, frits, or any other zones with non-standard mixing behavior can be considered in very similar ways.

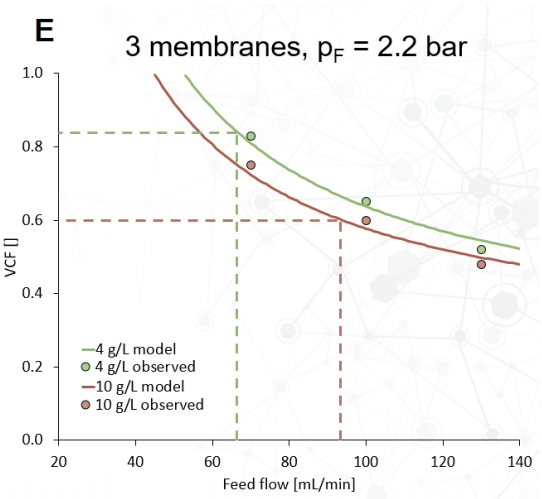


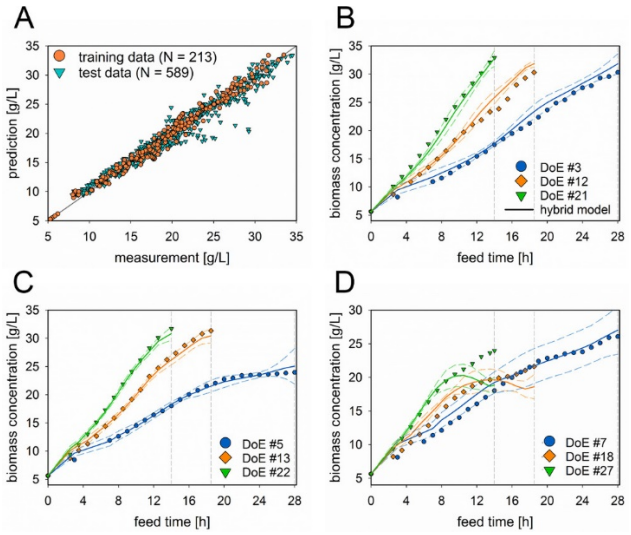
We could show that the inclusion of a bubble trap causes significant band-broadening during step elution procedures, as expected. Step changes and high flow rates result in longer residence time within the trap and larger effective mixing volumes. In contrast, a gradual change of the liquid as applied in linear gradient elution results in rapid mixing and transition through the trap and thus causes only slight shifts in retention time but not significant band-broadening. Our approach could be applied to model other challenging mixing problems with irregular residence time distributions. (J. Beck, R. Hahn)

Project: Research Studio Austria - NOVASIGN

The NOVASIGN project (funded by the FFG) started in September 2017 intending to speed up bioprocess development by applying advanced machine-learning algorithms. Currently, time to market of new pharmaceuticals is still in the range of 10-14 years. However, last year we saw SARS-CoV2 vaccines to enter the market within less than one year of development. Although high risk is put on the clinical evaluation process, the reduced timelines also test new standards. While bioprocess development and manufacturing speed was never considered a bottleneck, if significantly reduced times lines also want to be met for other life-saving medicines, industry behavior has to change.

The NOVASIGN project aims to reduce bioprocess development timelines significantly. The two showcases for better and faster process understanding were almost finalized within the last year, leading to 6 publications in 2020. Within the microbial upstream showcase, intensified Design of Experiments and hybrid modeling could save up to 66% of experimental effort, time, and resources. An innovative chosen experimental design fosters the in-silico prediction of different operational modes for tangential flow filtration representing the downstream showcase. We were able to identify ideal process conditions for batch-, fed-batch and single path tangential flow filtration (SPTFF) with a minimum set of experiments. The applied multi-step ahead prediction allows estimating process durations for defined process changes to enable a model predictive control approach. Finally, this project's hybrid modeling toolbox now entirely fits upstream cultivation and cross flow filtration usecases. Now, scientists and customers from pharma can smoothly progress from data to model with a minimum effort and modeling knowledge, increasing process understanding and experimental effort. (M. Dürkop, G. Striedner)

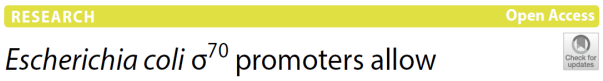




Two project highlights. A-D: A) Hybrid model built on nine intensified design of experiments runs with overall 213 samples to cover a 3x3 three-dimensional design space (orange dots). The hybrid model could predict the performance of 27 classic cultivations (A: green triangles and B-D: nine examples of ordinary DoE runs). This proves that iDoE together with hybrid modeling could save 66% of experimental effort! E) Hybrid model for a SPTFF trained on a minimum set of experiments. The model is used to predict conversion rates for different inputs (e.g. protein concentrations) enabling process control for continuous processes.

Success Stories: CD Laboratory of next-level production of biopharmaceuticals in *E. coli*

Advancement of genome-integrated *E. coli* expression systems


RESEARCH Open Access

Escherichia coli σ^{70} promoters allow expression rate control at the cellular level in genome-integrated expression systems

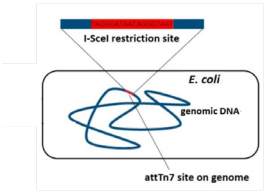
Artur Schuller[1], Monika Cserjan-Puschmann[1*], Christopher Tauer[1], Johanna Jarmer[2], Martin Wagenknecht[2], Daniela Reinisch[2], Reingard Grabherr[1] and Gerald Striedner[1]

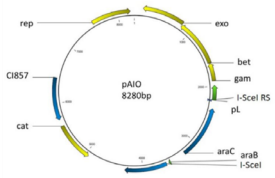
Christian Doppler Forschungsgesellschaft

Boehringer Ingelheim

Genome-integrated *E. coli* expression systems are a central component of the CD laboratory, as they are superior to conventional plasmid-based systems.These systems are ideally suited as model systems to answer fundamental scientific questions and due to their robustness they allow for more flexible process designs in recombinant protein production and even continuous production is possible. In this context further development of genome-integrated systems was on improvement of their suitability for continuous production.

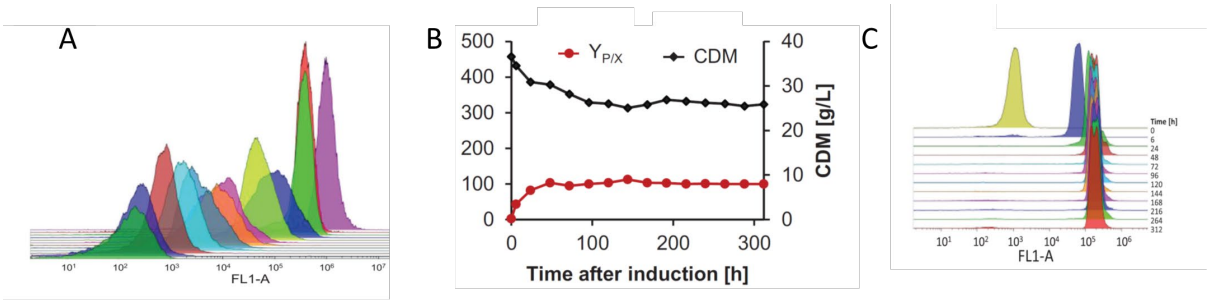
To improve our toolset for molecular modification we established the pAIO "**A**ll-**I**n-**O**ne" expression vector and we modified the host cell accordingly to allow for significantly accelerated and simplified site directed integration of genes of interest into the genome of *E. coli.*





Stepless control on product formation and full suppression of basal expression are prerequisites for continuous production. In addition to already existing T7 RNA based system, we developed a new genome-integrated host cell with a host-specific RNAP-dependent promoter (patent-pending) that delivers the descibed features.

Subsequently, both variants were investigated with two different recombinant proteins in an adaptive evolution approach. The systems were subjected to high physiological stress through continuous product formation. In this approach, mutations in the genome led to an accumulation of cells with higher fitness, able to cope with the prevailing environmental conditions. These cell populations were then analyzed on genome level to identify the underlying mutations. In addition, they were then cultivated in long-term chemostat experiments and evaluated with respect to their performance in continuous production mode (M. Cserjan, G. Striedner).



A) Production clones with different expression levels separated in subsequent continuous µ-scale cultivations. B) Course of CDM and product in a chemostat cultivation of BQ<A1-GFP> wt the genome integrated system with the host RNAP dependend promotor and C) population homogeneity along the cultivition

Extraction of periplasmic proteins

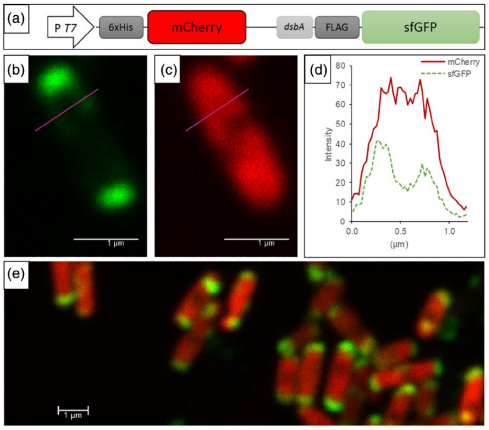
RESEARCH ARTICLE

BIOTECHNOLOGY PROGRESS

Extraction of recombinant periplasmic proteins under industrially relevant process conditions: Selectivity and yield strongly depend on protein titer and methodology

Clemens Schimek[1] | Esther Egger[1] | Christopher Tauer[1] | Gerald Striedner[1] | Cécile Brocard[2] | Monika Cserjan-Puschmann[1] | Rainer Hahn[1]

In this work, we attempted to identify a method for the selective extraction of periplasmic endogenously expressed proteins, which is applicable at an industrial scale. For this purpose, we used an expression model that allows co-expression of two fluorescent proteins, each of which is specifically targeted to either the cytoplasm or periplasm. We assessed a number of scalable lysis methods (high-pressure homogenization, osmotic shock procedures, extraction with EDTA, and extraction with deoxycholate) for the ability to selectively extract periplasmic proteins rather than cytoplasmic proteins. Our main conclusion was that although we identified industrially scalable lysis conditions that significantly increased the starting purity for further purification, none of the tested conditions were selective for periplasmic protein over cytoplasmic protein. Furthermore, we demonstrated that efficient extraction of the expressed recombinant proteins was largely dependent on the overall protein concentration in the cell. As a monitoring tool, we used chromoproteins as cytoplasmic and periplasmic markers. In contrast to other reports, we did not achieve true selectivity. We observed apparent selectivity for periplasmic extraction when applying nondestructive extraction methods with a relatively high target protein concentration. However, the same results were achieved with a cytoplasmic protein, as demonstrated with the cyto-GFPmut3.1 system. In addition to different action principles that lead to extraction, we clearly demonstrated that the target protein concentration was a major driving force of a method's efficiency. Besides extraction efficiency and purity of extracts, we also examined aspects relevant to the subsequent downstream processing. HPH caused full mechanical disruption, with consequently high levels of HCP, DNA, and endotoxins. The residual debris size was small, and applying HPH at lower pressure and with more passages did not yield relevant improvement in terms of impurity levels. EDTA treatment combined with heat resulted in large cell-like residual structures, thus simplifying centrifugation. The extracted target protein showed high purity, supported by the fact that heat treatment induced concurrent protein precipitation. However, this method is difficult to apply for temperature-sensitive proteins. Extraction with the detergent DOC was efficient, and is easy to apply and implement. Since no temperature increase is required, this method is also applicable for more sensitive proteins. Membrane solubilization resulted in relatively high protein impurity contents and smaller particle sizes. The OS method resulted in pure extracts; however, the POI was contained in two or three different fractions. Moreover, efficient extraction was associated with rather small particle sizes, and scaling up to an industrial scale seems challenging due to the stepwise procedure. Overall, depending on the target protein, our findings indicate that DOC extraction and EDTA/heat extraction are valuable alternatives to HPH as a release method for both cytoplasmic and periplasmic proteins. (R. Hahn)



Antibody fragment purification and characterization via 3-D-chromatography


Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Three-dimensional chromatography for purification and characterization of antibody fragments and related impurities from *Escherichia coli* crude extracts

Clemens Schimek[a,1], Matthias Kubek[a], David Scheich[a], Mathias Fink[a], Cécile Brocard[b], Gerald Striedner[a], Monika Cserjan-Puschmann[a], Rainer Hahn[a,*]

[a] Christian Doppler Laboratory for production of next-level biopharmaceuticals in E. coli, Department of Biotechnology, University of Natural Resources and Life Sciences, Muthgasse 18, A-1190 Vienna, Austria
[b] Biopharma Austria Process Science, Boehringer Ingelheim RCV GmbH & Co KG, Dr.-Boehringer-Gasse 5-11, A-1120 Wien

Christian Doppler Forschungsgesellschaft

Boehringer Ingelheim

Antibody fragments (Fab) are often produced by recombinant methods in Escherichia coli as no glycosylation is needed. Besides the correctly expressed Fab molecule, a multitude of host cell impurities and product related impurities are present in the crude sample. The identification and characterization of the product-related impurities, such as modified Fab-molecules or free light chain, are of utmost importance. The objective of this work was to design a purification strategy to isolate and characterize Fab and related impurities. A three-dimensional chromatography method was established, consisting of two affinity steps (Protein G and Protein L) and subsequent cation exchange chromatography, followed by mass spectrometry analysis of the purified samples. The procedure was automated by collecting the eluted target species in loops and directly loading the samples onto the high-resolution cation exchange chromatography column. As an example, four different Fab molecules are characterized. All four samples contained mainly the correct Fab, while only one showed extensive N-terminal pyroglutamate formation of the Fab. In another case, we found a light chain variant with uncleaved amino acids from the lead molecule, which was not used for the formation of whole Fab as only correct Fab was found in that sample. Impurities with lower molecular weights, which were bound on the Protein L column, were observed in all samples, and identified as fragments of the light chain. In conclusion, we have devised a platform for characterizing Fab and Fab-related impurities, which significantly facilitated strain selection and optimization of cultivation conditions. Besides providing a fast characterization of the fermentation product, further analysis could also be extended to samples drawn during the fermentation course. In contrast to HPLC methods, sample volumes can be very large, which is beneficial if titers are low. Within our research project, this type of analysis will be performed in the future. Additionally, we will investigate Fab expressed in different E. coli strains and with the use of different leader peptides. (R. Hahn)

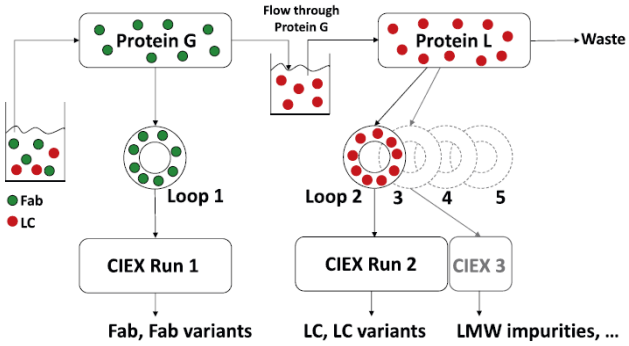
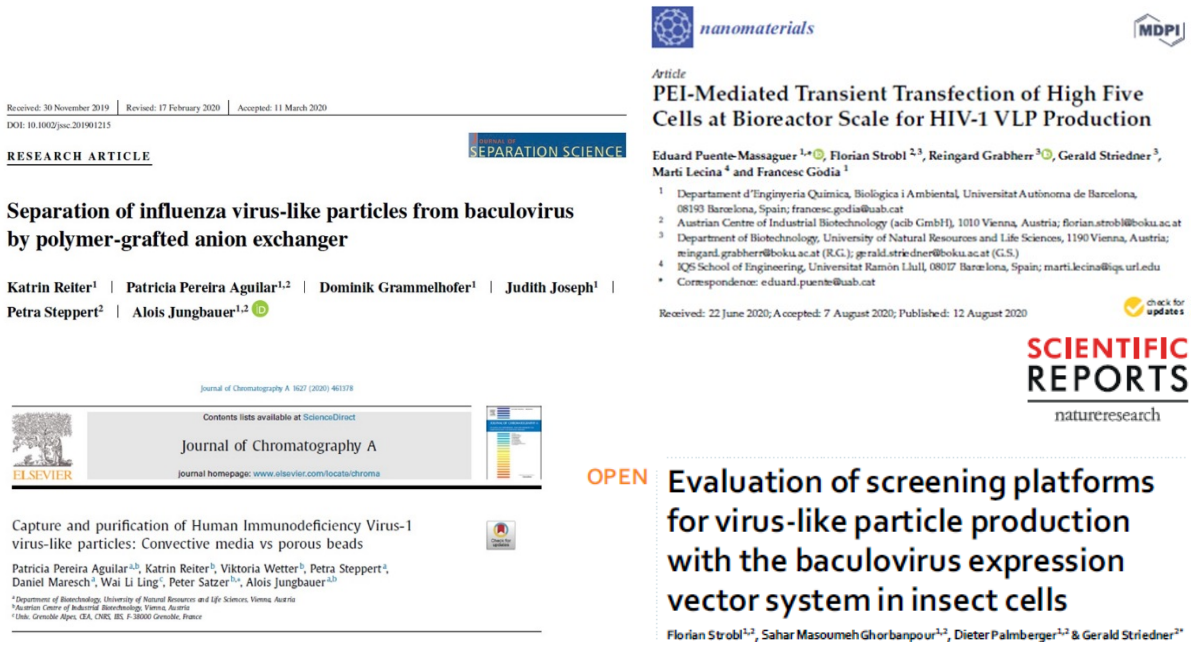


Fig. 3. 3D chromatography strategy for simultaneous purification of Fab and Fab-related impurities.

Success Story: Bionanoparticles



Received: 30 November 2019 | Revised: 17 February 2020 | Accepted: 11 March 2020
DOI: 10.1002/jssc.201901215
RESEARCH ARTICLE
SEPARATION SCIENCE
Separation of influenza virus-like particles from baculovirus by polymer-grafted anion exchanger
Katrin Reiter[1] | Patricia Pereira Aguilar[1,2] | Dominik Grammelhofer[1] | Judith Joseph[1] | Petra Steppert[2] | Alois Jungbauer[1,2]

nanomaterials
MDPI
Article
PEI-Mediated Transient Transfection of High Five Cells at Bioreactor Scale for HIV-1 VLP Production
Eduard Puente-Massaguer [1,*], Florian Strobl [2,3], Reingard Grabherr [3], Gerald Striedner [3], Marti Lecina [4] and Francesc Gòdia [1]
Received: 22 June 2020; Accepted: 7 August 2020; Published: 12 August 2020

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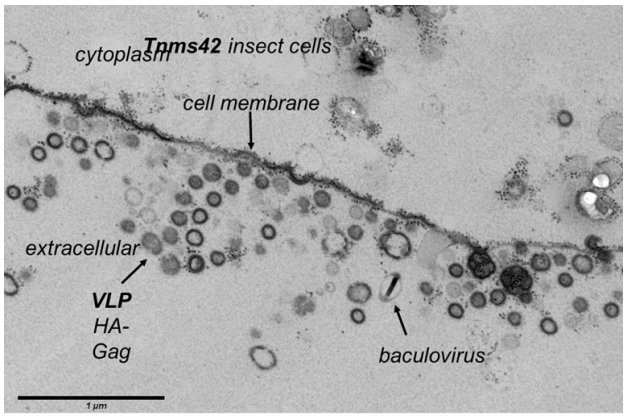
journal homepage: www.elsevier.com/locate/chroma
ELSEVIER
Capture and purification of Human Immunodeficiency Virus-1 virus-like particles: Convective media vs porous beads
Patricia Pereira Aguilar, Katrin Reiter, Viktoria Wetter, Petra Steppert, Daniel Maresch, Wai Li Ling, Peter Satzer, Alois Jungbauer

SCIENTIFIC REPORTS
natureresearch
OPEN
Evaluation of screening platforms for virus-like particle production with the baculovirus expression vector system in insect cells
Florian Strobl[1,2], Sahar Masoumeh Ghorbanpour[1,2], Dieter Palmberger[1,2] & Gerald Striedner[2*]

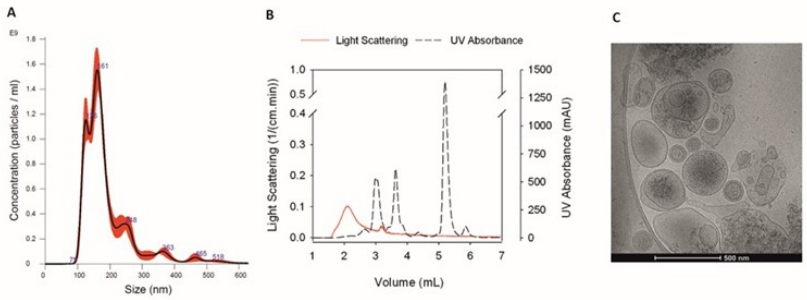
Bionanoparticles such as viruses, virus-like particles, exosomes and other extra cellular vesicles became very attracting entities for novel vaccines of emerging and re-emerging viral infections, cancer therapy as oncolytic viruses, delivery vehicles for drugs and as gene-therapy vectors. The size range of bionanoparticles is from approximately 30-600 nm in diameter and in general they are highly sensitive to mechanical/chemical stress which significantly impacts manufacturability especially on a larger scale. Many bionanoparticles for therapeutic purposes have a lipid bilayer as surface. In collaboration with the Boyce Thompson Institute (BTI) and acib we have developed our proprietary insect cell line, now used for the production of diverse virus, virus-like particles, exosomes and recombinant proteins, using the baculovirus systems designed at the Institute of Molecular Biotechnology (IMBT-BOKU). The cell line is meanwhile tested by several industrial partners.



Insect cell line Tnms42 developed together with BTI and acib, expressing influenza virus like particles

A cultivation process has been developed and scaled from the Biolector (~1-2 mL) to 20 L bioreactor. As model bionanoparticles, we used HIV-gag and influenza virus-like particles expressed in our cell line. The bioreactor harvest for bionanoparticle purification contains, besides the common host cell impurities (host cell protein and DNA), a lot of other impurities such as extra cellular vehicles, which are very similar to bionanoparticles in size, shape and surface properties. This is a big challenge and defines the purification and the characterization and quantification methodologies. The final purity criteria vary on

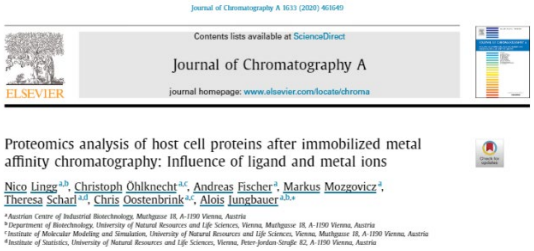
the application and changes from application as vaccines to chronical application for e.g. oncotherapy. To meet the purity requirements on the purification of bionanoparticles only a combination of several methods leads to the requested results. Each purification process starts with digestion of DNA but then rarely platform processes are available. For gene-therapy vectors such as Adeno-associated virus (AAV), the separation of empty and full particles may be a challenge whereas for enveloped bionanoparticles their large size is a challenge.



Comparison of nanoparticle tracking analysis, HPLC-SEC-MALS and high-resolution cryo-electron microscopy for detection and quantification of extra cellular vesicles and VLPs.

We have also put emphasis to develop scale-able platform processes for certain groups of bionanoparticles and orthogonal detection methods which consist of nanoparticle tracking analysis, HPLC-SEC combined with multi-angle light scattering (MALS) and high resolution cryo-electron microscopy. Currently we are able to offer methodologies for overexpression, purification, in-process control and analysis of enveloped virus and virus-like particles. (P. Aguilar, A. Jungbauer)

Success Story: CASPON technology – a generic manufacturing platform


Journal of Chromatography A 1633 (2020) 461649

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Proteomics analysis of host cell proteins after immobilized metal affinity chromatography: Influence of ligand and metal ions

Nico Lingg[a,b], Christoph Öhlknecht[a,c], Andreas Fischer[a], Markus Mozgovicz[a], Theresa Scharl[a,d], Chris Oostenbrink[a,c], Alois Jungbauer[a,b,*]


biomolecules

MDPI

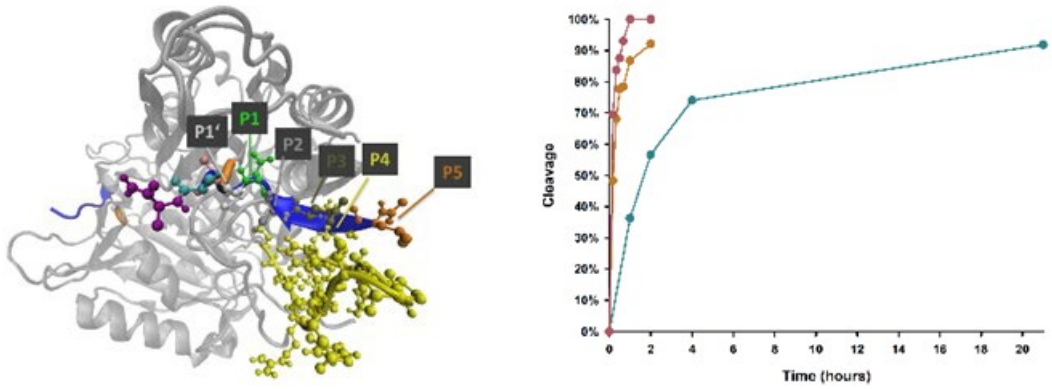
Article

Production of Circularly Permuted Caspase-2 for Affinity Fusion-Tag Removal: Cloning, Expression in *Escherichia coli*, Purification, and Characterization

Monika Cserjan-Puschmann [1,2,†], Nico Lingg [1,2,*,†], Petra Engele [1,3], Christina Kröß [1,3], Julian Loibl [1], Andreas Fischer [1], Florian Bacher [1], Anna-Carina Frank [1,2], Christoph Öhlknecht [1,4], Cécile Brocard [5], Chris Oostenbrink [1,4], Matthias Berkemeyer [5], Rainer Schneider [1,3], Gerald Striedner [1,2] and Alois Jungbauer [1,2,*]

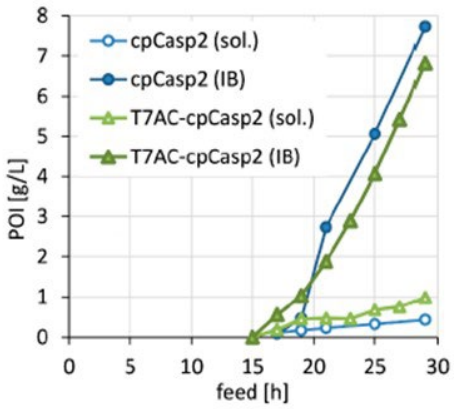
In a large consortium with the Institute of Biochemistry of the University of Innsbruck, the Institute of Molecular Simulation, and IBSE we have developed a generic manufacturing platform for production of recombinant proteins. This platform has been designed to enable therapeutic concepts which are based on non-mAb formats such as vaccines, enzymes, antibody fragments, peptides, cytokines and hormones. They suffer from slow developmentability and manufacturability and there is an urgent need for a generic manufacturing process. Affinity tags such as the commonly known six-His-tag can vastly simplify purification, but need to be removed for many applications such as biopharmaceuticals, when an authentic N-terminus is requested. Most proteases available for tag removal are too unspecific, too expensive or do not produce an authentic N-terminus.

We have developed an enzyme based on the human Caspase 2. This heterodimer is difficult to overexpress and therefore a circular permutation allow expression as a single strand.



3D structure of the circular permutated Caspase with its recognition sites and improvement of cleavage efficiency of a model protein by further mutation of the enzyme.

This enzyme has a high specificity for its five amino acid long recognition sequence and is independent of P1' site and therefore ideal for generation of native N-terminus of fusion proteins. The circular permutated enzyme has been further mutated and increased cleavage velocity was obtained by maintaining the recognition selectivity.



Production of the circular permuted caspase with and without solubility tag (sol. Soluble expression, IB portion of proteins expressed in inclusion bodies).

An additional advantage is high expression yield of the enzyme when overexpressed in *E. coli*. Expression of an enzyme with his tag allows simple removal of the enzyme by metal chelate chromatography. We have also studied the performance of metal chelate chromatography and have elucidated the effects of the metal and chelating ligand. We have successfully developed a protein production system, which has all elements for an industrial relevant production system. A highly specific processing enzyme, a high yield of the production of a protein of interest and a readily available and simple downstream processing. (A. Jungbauer, N. Lingg)

Success Story: Continuous integrated biomanufacturing

Received: 4 December 2019 | Revised: 18 February 2020 | Accepted: 5 March 2020
DOI: 10.1002/elsc.201900160
RESEARCH ARTICLE
Engineering in Life Sciences

Continuous capture of recombinant antibodies by $ZnCl_2$ precipitation without polyethylene glycol

Gregory Dutra[1] | Daniel Komuczki[1] | Alois Jungbauer[1,2] | Peter Satzer[1,2]

Received: 20 September 2019 | Revised: 16 December 2019 | Accepted: 2 February 2020
DOI: 10.1002/bit.27292
ARTICLE
BIOTECHNOLOGY BIOENGINEERING WILEY

Truly continuous low pH viral inactivation for biopharmaceutical process integration

Duarte L. Martins[1,2] | Jure Sencar[1,2] | Nikolaus Hammerschmidt[1,2] | Andreas Flicker[3] | Johanna Kindermann[3] | Thomas R. Kreil[3] | Alois Jungbauer[1,2]

Journal of Biotechnology 308 (2020) 87–95
Contents lists available at ScienceDirect
Journal of Biotechnology
journal homepage: www.elsevier.com/locate/jbiotec

Economics and ecology: Modelling of continuous primary recovery and capture scenarios for recombinant antibody production

A.L. Cataldo[a,b], D. Burgstaller[a,b], G. Hribar[c], A. Jungbauer[a,b,*], P. Satzer[a,c]

Received: 28 June 2019 | Revised: 16 October 2019 | Accepted: 24 October 2019
DOI: 10.1002/elsc.201900130
RESEARCH ARTICLE
Engineering in Life Sciences

Fractal dimension of antibody-PEG precipitate: Light microscopy for the reconstruction of 3D precipitate structures

Peter Satzer | Daniel Burgstaller | Walpurga Krepper | Alois Jungbauer

New BIOTECHNOLOGY 55 (2020) 98–107
Contents lists available at ScienceDirect
New BIOTECHNOLOGY
journal homepage: www.elsevier.com/locate/nbt

Full length Article

A narrow residence time incubation reactor for continuous virus inactivation based on packed beds

Jure Senčar[a], Nikolaus Hammerschmidt[a], Duarte L. Martins[a], Alois Jungbauer[a,b,*]

Contents lists available at ScienceDirect
Chemical Engineering Science: X
journal homepage: www.elsevier.com/locate/cesx

Water related impact of energy: Cost and carbon footprint analysis of water for biopharmaceuticals from tap to waste

Alessandro Luigi Cataldo[a,b], Bernhard Sissolak[c], Karl Metzger[b,d], Kristi Budzinski[a], Osamu Shirokizawa[f], Markus Luchner[a], Alois Jungbauer[a,b,*], Peter Satzer[a,b]

RESEARCH ARTICLE
Biotechnology Journal
www.biotechnology-journal.com

Modeling the Residence Time Distribution of Integrated Continuous Bioprocesses

*Jure Sencar, Nikolaus Hammerschmidt, and Alois Jungbauer**

Research Article
SCI
(wileyonlinelibrary.com) DOI 10.1002/jctb.6648

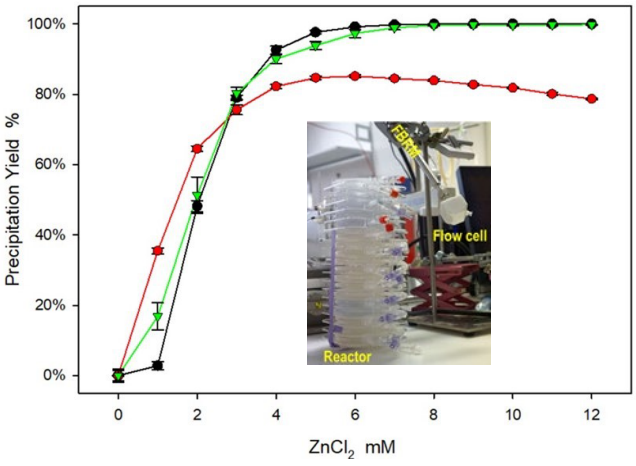
Impact of failure rates, lot definitions and scheduling of upstream processes on the productivity of continuous integrated bioprocesses

Peter Satzer,[a] Daniel Komuczki,[b] Magdalena Pappenreiter,[c] Alessandro Luigi Cataldo,[b] Bernhard Sissolak[c] and Alois Jungbauer[b]*

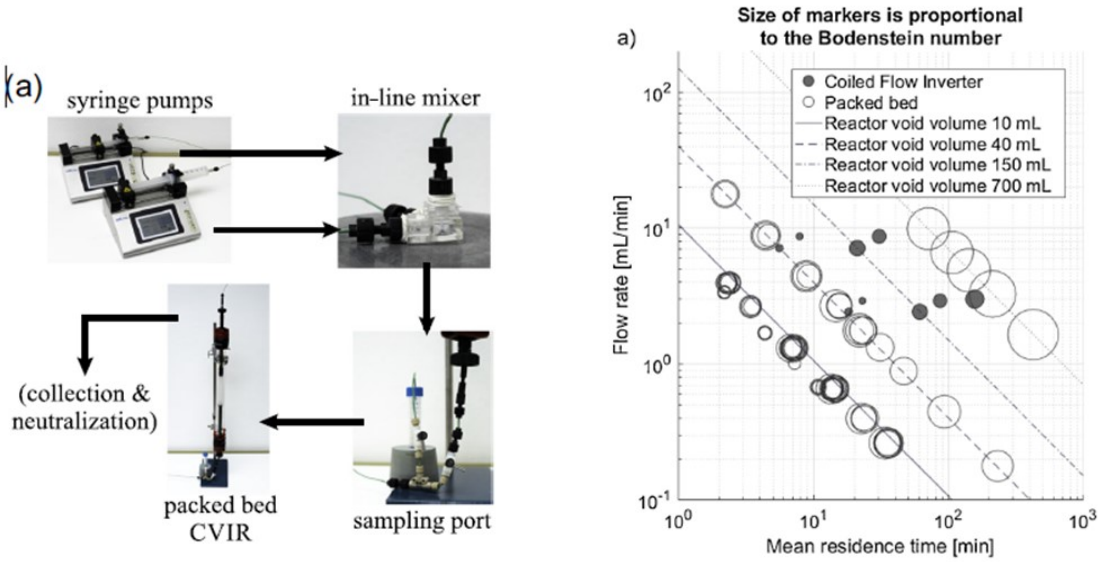
At IBSE several research projects are conducted in the field of continuous integrated biomanufacturing. The potential savings in investment costs, running costs and flexibility makes continuous integrated biomanufacturing very interesting and will be the next generation manufacturing technology for biopharmaceuticals. Compared with traditional batch-mode processes, the complexities of continuous processes are significantly increased with more operating parameters, dynamic variation, and integration of unit operations in a so called end-to-end functionally closed process. Therefore, the challenges for process design and optimization are also significantly increased, which needs novel scientific methods and approaches. We have developed new methods for precipitation of antibodies, conducted economic and environmental modeling to get an insight into benefits of continuous integrated biomanufacturing and developed models to understand the residence time distribution and the connected inertia of a continuous manufacturing system.

Traditional antibody production is based on a fed batch fermentation, bioreactor harvest using centrifugation and/or microfiltration, a capture step by protein A affinity chromatography, two dedicated virus inaction steps and several further purification, polishing and pre-formulation steps. To

render such a process into an end-to-end continuous process ends either in a pseudo continuous operation or new processes must be developed. Continuous precipitation is one possibility to establish a continuous process, where the mass flow of the product is not interrupted and a continuous inflow and outflow stream is guaranteed. The precipitant is continuously added, precipitate is formed and can be continuously harvested and dissolved. Recombinant antibodies can be captured from a culture supernatant by the sole addition of $ZnCl_2$ (Figure 1). This method is extremely cheap and has all the features necessary for large scale continuous manufacturing, like versatility, scalability, robustness, easy control schemes, and mechanistic model descriptions for the product behavior. Continuous precipitation can be conducted in simple tubular reactors with in-built static mixers with no special equipment needed.



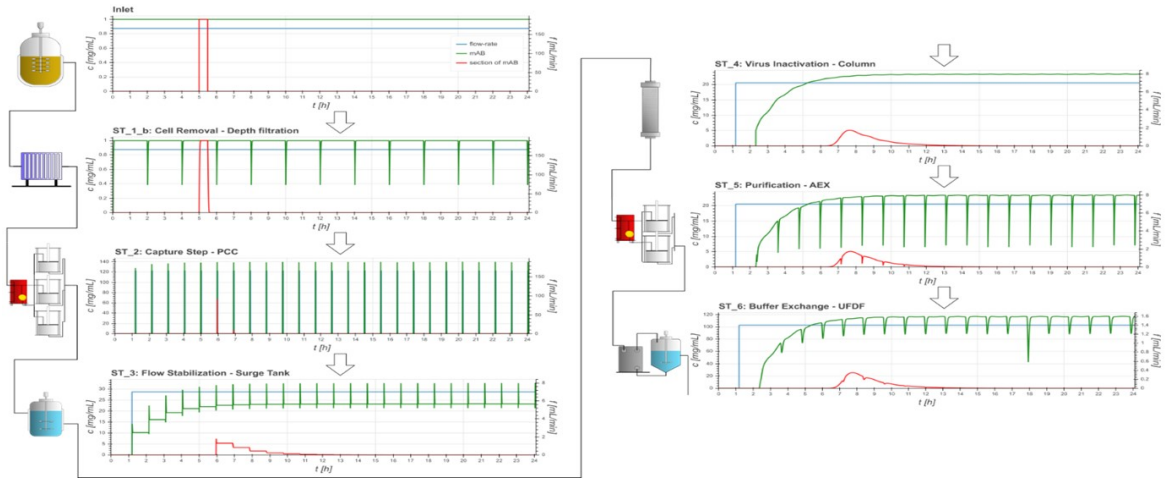
Precipitation of three different recombinant antibodies with Zn Cl2 (Dutra et al. 2020) and tubular reactor for continuous precipitation



(A) Experimental set up of laboratory scale system to test continuous virus inactivation from Martins et al. 2020 and (B) relationship between the flow rate, mean residence time and residence time distribution expressed as Bodenstein number. The larger the circle the narrower the residence time distribution.

Another challenge connected with continuous biomanufacturing is the continuous virus inactivation by low pH-incubation or addition of viricidal compounds. The incubation time is extremely critical to ensure the requested virus clearance, but overexposure may harm the product. Based on these constraints we have developed packed bed reactors for low-pH inactivation and solvent detergent virus inactivation and made theoretical studies how the residence time distribution of the system impacts virus inactivation. The performance packed bed reactors was also compared to other reactor types and the packed bed is favorable in respect to scalability, flexibility and residence time distribution (Figure 2). The Draft guidance of the US Food and Drug Administration FDA : Quality

considerations for continuous manufacturing suggest to have an understanding of process dynamics as a function of input material attributes (e.g., potency, material flow properties) and process conditions (e.g., mass flow rates). One common approach is characterization of the residence time distribution (RTD) for individual unit operations and the integrated system as a whole. A RTD is a probability distribution that describes the amount of time a mass or fluid element remains in a process, and can be measured through a tracer experiment, online process measurements of appropriate product attributes, and/or process modeling. This number is especially important when certain regulatory requirements for minimal treatment times for viral inactivation have to be met in a continuous system. We have developed a process model to calculated the RTD of a hypothetical continuous end-to end process for antibody purification.



RTD model of hypothetical continuous downstream processing of recombinant antibodies. The red rectangle at the beginning is a theoretical process deviation. By following the red tracer it can be observed how this deviation propagates throughout the process (Sencar et al. 2020).

The new process metrics

Recently the process mass intensity (PMI) was introduced to biopharmaceutical manufacturing. This metric counts the mass in kg which is required to produce one kg of product. Our analysis of continuous processes showed that the best combination in respect to process mass intensity is a combination of fed batch bioreactor and continuous downstream processing. The continuous perfusion consumes a lot of medium and this is reflected by a high PMI. The biggest reduction in PMI, and therefore saving resources was seen for chromatography and in particular through maximizing the dynamic binding capacity. This can lead to a lower productivity depending on the used technology but is a more efficient process in respect to used resources. A lower productivity is not the absolute measure for economics because other parameters must be considered as well, such as the required floor space and the associated consumption of energy for air filtration, cooling etc. The PMI is an interesting and very intuitive metric, but it does not reflect the whole environmental footprint of a process and is missing important factors such as energy consumption and CO_2 emission. Therefore, we have introduced a new metric called the WARIEN, the water related impact of energy. This metric takes into account the cost and carbon footprint for providing clean water and process water to produce biopharmaceuticals. High quality water production is a major contributor to energy consumption and therefore also the major cause for CO_2 emission for biopharmaceutical manufacturing.

In another work we have modelled the impact of failed batches for biopharmaceutical production. This is often neglected or not communicated by industry but has a severe impact on process economics and footprint. It is obvious that industry does not want to share this information with the public and their competitors. Due to these secrecy politics this issue was entirely overlooked (Satzer et.al. 2020). (A. Jungbauer)

Overview: final theses (finished and ongoing)

PhD projects

Finished

Patricia Pereira Aguilar (BioTop)
Downstream processing of enveloped virus-like particles by polymer grafted media
Supervisor: Alois Jungbauer
Finished: 2020

Benjamin Bayer (FFG Research Studio Novasign)
Hybrid modeling and Quality by Design implementation in upstream processing
Supervisor: Gerald Striedner
Finished: 2020

Dominik Jeschek
An in vitro assay to analyze the activity of membrane transport proteins.
Supervisor: Karola Vorauer-Uhl
Finished: 2020

Walpurga Krepper (H2020 Nextbiopharm)
Influence of capture step on critical quality attributes of monoclonal antibodies in biopharmaceutical production.
Supervision: Alois Jungbauer
Finished: 2020

Jure Sencar (acib project 25081)
Design of reactors for continuous purification of proteins
Supervisor: Alois Jungbauer
Finished: 2020

Clemens Schimek (CD-Lab NLBP)
Microparticles technology for extraction of periplasmic proteins
Supervisor: Rainer Hahn
Finished Dec. 2020, defensio Feb. 2021

Artur Schuller (CD-Lab NLBP)
Long-term stability of Escherichia Coli expression systems under production conditions
Supervision: Gerald Striedner
Finished: November 2020

Tobias Amadeus Schneider (acib project 25041)
Separation of HIV-1 gag H1 Virus-like Particles from Baculovirus expressed in insect cells.
Supervision: Alois Jungbauer
Finished: 2020

Bernhard Sissolak (Project-Part Analytical Platform for advanced Process monitoring: PAT-Plant Austrian Research Promotion Agency (FFG grant 840725) and Bilfinger Industrietechnik Salzburg;)
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: Vorauer-Uhl Karola; Striedner Gerald
Finished: April 2020

Duarte Lima Martins (acib project 25081)
CONTINUOUS VIRAL INACTIVATION FOR BIOPHARMACEUTICALS.
Supervisor: Alois Jungbauer
Finished: 2020

Karl Metzger
Advanced Bioprocess Engineering and Development of Escherichia coli based Recombinant Protein Production Processes.
Supervision: Alois Jungbauer
Finished: 2020

On-Going

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

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

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

Suleiman Ehsan (European Union's Horizon 2020 research and innovation program94me under grant agreement No. 681137 (European AIDS Vaccine Initiative 2020). Ehsan Suleiman received funding from the PhD programme "BioTop—Biomolecular Technology of Proteins" (Austrian Science Funds, Project number: FWF W1224).
Protein-liposome conjugates as novel HIV vaccine candidates;
Supervisor: Vorauer-Uhl Karola
Start: 2016

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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: May 2019

Patrick Stargardt (EU Project Rafts4Biotech/ extern Fa. enGenes GmbH)
Advancements and further characterization on growth decoupled protein expression using the phage T7 deriede 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 transcriptome and translatome
Supervisor: Gerald Striedner
Start: January 2019

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

Master theses

Finished

Matthias Berger
Purification of Therapeutic Peptides Using the Fusion2O2O Platform Process.
Supervisor: Alois Jungbauer
Finished: 2020

Felix Dieringer
Application of Dynamic Light Scattering on Adeno-Associated Virus Particles.
Supervisor: Alois Jungbauer
Finished: 2020

Ines Melanie Donabaum
Purification and identification of an unidentified plasmid DNA isoform.
Supervisor: Alois Jungbauer
Finished: 2020

Edit Felföldi (FH Campus Wien)
Determination of multicomponent adsorption isotherm of IgG monomer and aggregate on an anion exchanger resin
Supervisor: Astrid Dürauer
Finished: October 2020

Josef Horvath (acib project 25011)
2D simulation as tool for fast chromatography predictions
Supervisor: Astrid Dürauer
Finished: 2020

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
Finished: December 2020

Stephan Gutmann (Polymun)
Design und Charakterisierung von Vorrichtungen zur Herstellung von Liposomen
Supervisor: Vorauer-Uhl Karola
Finished: April 2020

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
Finished: 2020

Matthias Müller
Optimization of filtrations steps for E. coli homogenates
Supervisor: Rainer Hahn
Finished Dec. 2020, defensio Jan. 2021

Simon Netocny (MSD)
Single-use process verification strategy MSD Animal Health Krems
Supervisor: Karola Vorauer-Uhl
Finished: June 2020

Alejandro Santiago-Leon (CD-Lab NLBP)
Chromatographic purification of Fab fragments
Supervisor: Rainer Hahn
Finished Nov. 2020, defensio Jan. 2021

Christoph Sailer (BI RCV)
Solids recovery modelling in centrifugal separations
Supervisor: Rainer Hahn
Finished Jan. 2020

Kathrin Seyrl (BI RCV)
Inclusion body characterization and analytical method development for IB processing
Supervisor: Rainer Hahn
Finished May 2020

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
Finished: 2020

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

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

Florian Kaiser
Increase of macroscopic understanding of protein refolding in batch and pilot scale manufacturing
Supervisor: Rainer Hahn
Start: Nov 2019

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

Konstanze Kastenhofer (AGES)
Brivaracetam – practical considerations for the development of a European Pharmacopoeia Monograph
Supervisor: Karola Vorauer-Uhl
Start: November 2020

Magdalena Kößlbacher (BI RCV)
Development of an analytical throughput cell disruption method
Supervisor: Karola Vorauer-Uhl
Start: September 2020

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

Alexander Mechtler
Investigations on solid diffusion mass transfer on anion exchange chromatography resins
Supervisor: Rainer Hahn
Start: July 2020

Matthias Medl (BI RCV)
Online Estimation of the Optical Density in a High-Throughput Fermentation Platform
Supervisor: Gerald Striedner
Start: July 2020

Franz Moisi (Valneva)
Evaluation of fermentation process parameters influencing the fatty acid composition of bacterial lipoprotein
Supervisor: Gerald Striedner
Start: July 2018

Markus Mozgovicz (acib project 91023)
Adsorption effects on thermal stability of proteins
Supervisor: Alois Jungbauer, Nico Lingg
Start: March 2020

Dominik Nendwich (Frontrunner)
Quality risk management process in an End-to-End process train for the production of bio-pharmaceutical products
Supervisor: Karola Vorauer-Uhl
Start: October 2020

Patrick Scheidl (acib project 94081)
Characterization of Circularly Permuted Caspase-2 and Screening of Buffer Conditions for Affinity Fusion-Tag Removal
Supervisor: Alois Jungbauer, Nico Lingg
Start: April 2020

Anton Shpylovyi (CD-Lab NLBP)
Fermentation scale effects on product related non-canonical amino acid misincorpoartion in different E. coli strains.
Supervisor: Gerald Striedner, Florian Mayer
Start: October 2020

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

Bachelor theses

Finished

Teresa Brandtner (acib project 25011)
Purification of antibody aggregates from CHO supernatants
Supervisor: Astrid Dürauer
Finished: 2020

Wanja Ehtreiber
Impact of a short Tag fused to recombinant model proteins – a characterisation in E. coli fed-batch cultivation
Supervisor: Monika Cserjan, Gerald Striedner
Finished: February 2020

Kerstin Holzer (acib project 94041)
Adsorption isotherms of fibroblast growth factor on cation exchange resins
Supervisor: Astrid Dürauer
Finished: October 2020

Elisabeth Lehner (HIV-Vaccine)
Can EDC/Sulfo-NHS mediated conjugation be influenced by environmental conditions? - A case study
Supervisor: Karola Vorauer-Uhl
Finished: January 2020

Julia Mayer (HIV-Vaccine)
Effects of using various EDC and Sulfo-NHS concentrations for covalent coupling of HIV-1 trimers to peptide encapsulating liposomes
Supervisor: Karola Vorauer-Uhl
Finished: July 2020

Gregor Stitz
Development of a HIC polishing step for purification of the spike protein of SARS-CoV-2
Supervisor: Alois Jungbauer, Nico Lingg
Finished: November 2020

Anna Stock
Influence of different fermentation strategies on growth and Fab production kinetics in Escherichia coli lab-scale bioreactor cultivations
Supervisor: Monika Cserjan, Gerald Striedner
Finished: June 2020

Yvonne Sorz (acib project 94041)
Risk analysis for biopharmaceutical processes
Supervisor: Astrid Dürauer
Finished: September 2020

On-going

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

Katharina Somogyi (acib project 94041)
Evaluation of commercial test systems for quantitative DNA analysis
Supervisor: Astrid Dürauer
Start: September 2020

Scientific output

Scientific Publications in peer-reviewed journals

1. Aguilar, PP; Reiter, K; Wetter, V; Steppert, P; Maresch, D; Ling, WL; Satzer, P; Jungbauer, A: Capture and purification of Human Immunodeficiency Virus-1 virus-like particles: Convective media vs porous beads. J CHROMATOGR A. 2020; 1627, 461378
2. Bayer, B; Sissolak, B; Duerkop, M; von Stosch, M; Striedner, G;: The shortcomings of accurate rate estimations in cultivation processes and a solution for precise and robust process modeling.. Bioprocess Biosyst Eng. 2020; 43(2):169-178
3. Bayer, B; Striedner, G; Duerkop, M: Hybrid Modeling and Intensified DoE: An Approach to Accelerate Upstream Process Characterization. BIOTECHNOL J. 2020; 15(9)
4. Bayer, B; von Stosch, M; Melcher, M; Duerkop, M; Striedner, G: Soft sensor based on 2D-fluorescence and process data enabling real-time estimation of biomass in Escherichia coli cultivations., ENG LIFE SCI. 2020; 20(1-2): 26-35.
5. Bayer, B; von Stosch, M; Striedner, G; Duerkop, MComparison of Modeling Methods for DoE-Based Holistic Upstream Process Characterization. BIOTECHNOL J. 2020; 15(5).
6. Beck, J; Heymann, W; von Lieres, E; Hahn, R: Compartment Model of Mixing in a Bubble Trap and Its Impact on Chromatographic Separations. PROCESSES. 2020; 8(7), 780
7. Cataldo, AL; Burgstaller, D; Hribar, G; Jungbauer, A; Satzer, P: Economics and ecology: Modelling of continuous primary recovery and capture scenarios for recombinant antibody production., J Biotechnol. 2020; 308: 87-95
8. Christler, A; Felföldi, E; Mosor, M; Sauer, D; Walch, N; Dürauer, A; Jungbauer, A; Semi-automation of process analytics reduces operator effect., Bioprocess Biosyst Eng. 2020; 43(5):753-764
9. Cserjan-Puschmann, M; Lingg, N; Engele, P; Krößl, C; Loibl, J; Fischer, A; Bacher, F; Frank, AC; Öhlknecht, C; Brocard, C; Oostenbrink, C; Berkemeyer, M; Schneider, R; Striedner, G; Jungbauer, A; Production of Circularly Permuted Caspase-2 for Affinity Fusion-Tag Removal: Cloning, Expression in Escherichia coli, Purification, and Characterization. Biomolecules. 2020; 10(12)
10. Dutra, G; Komuczki, D; Jungbauer, A; Satzer, P; Continuous capture of recombinant antibodies by ZnCl, Eng Life Sci. 2020; 20(7):265-274
11. Egger, E; Tauer, C; Cserjan-Puschmann, M; Grabherr, R; Striedner, G, Fast and antibiotic free genome integration into Escherichia coli chromosome. SCI REP-UK. 2020; 10(1)
12. Felfoeldi, E; Scharl, T; Melcher, M; Durauer, A; Wright, K; Jungbauer, A: Osmolality is a predictor for model-based real time monitoring of concentration in protein chromatography. J CHEM TECHNOL BIOT. 2020; 95(4): 1146-1152.
13. Heissenberger, C; Rollins, JA; Krammer, TL; Nagelreiter, F; Stocker, I; Wacheul, L; Shpylovyi, A; Tav, K; Snow, S; Grillari, J; Rogers, AN; Lafontaine, DLJ; Schosserer, M; The ribosomal RNA m. Elife. 2020;
14. Kołodzieja, M., Sauer, D. G., Beck, J., Mareka, W.K., Hahn, R., Jungbauer, A., Dürauer, A., Piątkowski, W. & Antos, D. Scale up of a chromatographic capture step for a clarified bacterial homogenate – influence of mass transport limitation and competitive adsorption of impurities. *Journal of Chromatography A* 1618 (2020) 460856
15. Komuczki, D; Lingg, N; Jungbauer, A; Satzer, P; (2020): In-situ gradient formation by direct solid addition of buffer components. J Chromatogr A. 2020;
16. Krepper, W; Burgstaller, D; Jungbauer, A; Satzer, P; Mid-manufacturing storage: Antibody stability after chromatography and precipitation based capture steps. Biotechnol Prog. 2020; 36(2)
17. Krippl, M; Durauer, A; Duerkop, M: Hybrid modeling of cross-flow filtration: Predicting the flux evolution and duration of ultrafiltration processes. SEP PURIF TECHNOL. 2020; 248

18. Lingg, N; Öhlknecht, C; Fischer, A; Mozgovicz, M; Scharl, T; Oostenbrink, C; Jungbauer, A; Proteomics analysis of host cell proteins after immobilized metal affinity chromatography: Influence of ligand and metal ions.. J Chromatogr A. 2020;
19. Martins, DL; Sencar, J; Hammerschmidt, N; Flicker, A; Kindermann, J; Kreil, TR; Jungbauer, A; Truly continuous low pH viral inactivation for biopharmaceutical process integration. BIOTECHNOL
20. Paumann-Page, M; Tscheliessnig, R; Sevcnikar, B; Katz, RS; Schwartz, I; Hofbauer, S; Pfanzagl, V; Furtmüller, PG; Obinger, C; Monomeric and homotrimeric solution structures of truncated human peroxidasin 1 variants. Biochim Biophys Acta Proteins Proteom. 2020; 1868(1)
21. Puente-Massaguer, E; Strobl, F; Grabherr, R; Striedner, G; Lecina, M; Godia, F: PEI-Mediated Transient Transfection of High Five Cells at Bioreactor Scale for HIV-1 VLP Production. NANOMATERIALS-BASEL. 2020; 10(8)
22. Reiter, K; Aguilar, PP; Grammelhofer, D; Joseph, J; Steppert, P; Jungbauer, A: Separation of influenza virus-like particles from baculovirus by polymer-grafted anion exchanger. J SEP SCI. 2020; 43(12): 2270-2278.
23. Roque, ACA; Pina, AS; Azevedo, AM; Aires-Barros, R; Jungbauer, A; Di Profio, G; Heng, JYY; Haigh, J; Ottens, M; Anything but Conventional Chromatography Approaches in Bioseparation. BIOTECHNOL J. 2020; 15(8).
24. Satzer, P; Burgstaller, D; Krepper, W; Jungbauer, A, Fractal dimension of antibody-PEG precipitate: Light microscopy for the reconstruction of 3D precipitate structures. ENG LIFE SCI. 2020; 20(3-4): 67-78.
25. Schimek, C., Egger, E., Tauer, C., Brocard, C., Cserjan, M., Striedner, G. & R. Hahn. Extraction of recombinant periplasmic proteins: Selectivity and yield strongly depend on protein titer and methodology. *Biotechnology Progress* 36 (2020) e2999
26. Schimek, C., Kubek, M., Scheich, D., Cserjan, M., Striedner, G., Brocard, C. & Hahn R. 3-D Chromatography for Purification, Quantification and Characterization of Antibody Fragments and related impurities from E. coli crude extracts. *Journal of Chromatography A* (2020) 1638 (2021) 461702
27. Schuller, A; Cserjan-Puschmann, M; Köppl, C; Grabherr, R; Wagenknecht, M; Schiavinato, M; Dohm, JC; Himmelbauer, H; Striedner, G;(2020): Adaptive Evolution in Producing Microtiter Cultivations Generates Genetically Stable Escherichia coli Production Hosts for Continuous Bioprocessing. Biotechnol J. 2020;
28. Sencar, J; Hammerschmidt, N; Jungbauer, A: Modeling the Residence Time Distribution of Integrated Continuous Bioprocesses. BIOTECHNOL J. 2020; 15(8)
29. Senčar, J; Hammerschmidt, N; Martins, DL; Jungbauer, A; A narrow residence time incubation reactor for continuous virus inactivation based on packed beds. N Biotechnol. 2020; 55:98-107
30. Stargardt, P; Feuchtenhofer, L; Cserjan-Puschmann, M; Striedner, G; Mairhofer, J: Bacteriophage Inspired Growth-Decoupled Recombinant Protein Production in Escherichia coli. ACS SYNTH BIOL. 2020; 9(6): 1336-1348.
31. Strobl, F; Ghorbanpour, SM; Palmberger, D; Striedner, G: Evaluation of screening platforms for virus-like particle production with the baculovirus expression vector system in insect cells. SCI REP-UK. 2020; 10(1)
32. Suleiman, E; Mayer, J; Lehner, E; Kohlhauser, B; Katholnig, A; Batzoni, M; Damm, D; Temchura, V; Wagner, A; Uberla, K; Vorauer-Uhl, K. Conjugation of Native-Like HIV-1 Envelope Trimers onto Liposomes Using EDC/Sulfo-NHS Chemistry: Requirements and Limitations. PHARMACEUTICS. 2020; 12(10), 979
33. Tran, T; Eskilson, O; Mayer, F; Gustavsson, R; Selegard, R; Lundstrom, I; Mandenius, CF; Martinsson, E; Aili, D; Real-Time Nanoplasmonic Sensor for IgG Monitoring in Bioproduction. PROCESSES. 2020; 8(10), 1302

Scientific publication for academic conferences

1. Jungbauer, A (2020): Virus and virus-like particles and extra cellular vesicles purification. [Webinar series of Universidade Federal de São Paulo (Unifesp), Sao Paulo, OCT, 8 2020] In: Universidade Federal de São Paulo (Unifesp), Webinar FullText
2. Manschadi, AM; Soltani, A; Fuchs, W; Ryall, SP; Koppensteiner, L; Eitzinger, J; Kaul H-P; Neubauer, T (2020): Integrating Crop Modelling in the Smart Farming Project Farm/IT in Austria: Achievements and Challenges. [iCROPM2020 - Crop Modelling for the Future, Montpellier,

FRANCE, FEB 3-5, 2020] In: Organising and Scientific Committees, Book of Abstracts - Second International Crop Modelling Symposium FullText

3. Motycka, B; Kracher, D; Ludwig, R; Tscheließnig, R (2020): Conformation of cellobiose dehydrogenase determined at different ambient conditions by small angle X-ray scattering (SAXS). [Poster] [FEBS3 + LS2 Annual Meeting 2020, Zurich, Switzerland, Feb 13-14, 2020] In: FEBS3, GMB, ÖGMBT, Meeting Booklet (FEBS3+LS2 Annual Meeting 2020)
4. Schiavinato, M; Bodrug, A; Marcet-Houben, M; Gabaldón, T; Dohm, JC; Himmelbauer, H (2020): Analysis of subgenome structure and evolution in allopolyploid plants. ["Digital Breeding". Internationales Symposium der Gesellschaft für Pflanzenzüchtung e.V. (GPZ), Tulln, AUSTRIA, FEB 11-13, 2020] In: Gesellschaft für Pflanzenzüchtung e.V. (GPZ), Digital Breeding - Book of Abstracts

Presentations

1. Duerauer, A.: Real Time Monitoring and Model-Based Prediction of Purity and Quantity during Chromatographic Purification of Biopharmaceuticals, Biologics World Nordics, Marc 19th, Copenhagen (ínvited talk), hybrid event
2. Duerkop, M; Bayer, B; Krippl, M; Duerauer, A; Striedner, G; (2020): Applications of hybrid models for up- and downstream enabling better process understanding, faster development and model predictive control . VIRTUAL ESBES, SEP 15-17, 2020, virtual
3. Duerkop, M; Bayer, B; Striedner, G; (2020): Hybrid Modeling and Intensified DoE Enabling Faster Process Understanding and Model Predictive Control. Bioprocessing Europe, Jul 21-23, 2020, Virtual
4. Duerkop, M; Bayer, B; Striedner, G; (2020): Hybrid Modelling and Intensified DoE Enabling Faster Process Understanding, Soft Sensors and Model Predictive Control.Bioprocess International, Jul 13-16, 2020, virtual
5. Duerkop, M; Benjamin, B; Krippl, M; Duerauer, A; Striedner, G; (2020): Hybrid Modeling and Intensified DoE Enabling Faster Process Development, Soft Sensors and Model Predictive Control. Bioprocessing Labroots, 08.04.2020, virtual
6. Duerkop, M; Klausberger, M; (2020): Development, assessment and commercialization of serological SARS CoV-2 tests - an interdisciplinary success story. Labroots - Coronavirus Virtual Event, Dez 3, 2020, virtual
7. Hahn, Rainer: Astonishing features of Protein A affinity chromatography resins. Bioprocessing Summit Europe Virtual, July 22-23, 2020 (invited lecture)
8. Jungbauer, A: Continuous Integrated Biomanufacturing: towards digital twins and process control at AIM-BIO Symposium, Raleigh, NC, USA, November 12-13, 2020, on-line, invited key note lecture
9. Jungbauer, A: Continuous Processing for Antibodies, at Bioprocessing Summit Europe, 21-23 July 2020, on-line, invited lecture
10. Jungbauer, A: Continuous Purification of Antibody with Precipitation, a Process with Non-Interrupted Mass Flow of the Product, PEGS, 09-12 November 2020, Barcelona, 09-12 November 2020, on-line, invited lecture
11. Jungbauer, A: Continuous Purification of Antibody with Precipitation, a Process with Non-Interrupted Mass Flow of the Product, at Peptalk, San Diego, CA, USA, January 20-24, 2020, invited lectureDuerkop, M, Klausberger, M; Cserjan, M; Gerner, W; Grebien, F; Binder, C; March,

L; (2020): Development, assessment and commercialization of serological SARS CoV-2 tests „made in Austria". ÖGMBT Anual Meeting, SEP 21, 2020, virtual

12. Jungbauer, A: Digital Twins of Continuous Integrated Biomanufacturing Processes, at ICBE Asia 2020 - 10th International Conference on Biomolecular Engineering, Singapore, January, 7-9, 2020 invited lecture
13. Jungbauer, A: Downstream processing of influenza virus-like particles, at Bioprocessing Summit Europe, 21-23 July 2020, on-line, invited lecture
14. Jungbauer, A: Modelling of propagation of process disturbances in continuous integration biomanufacturing, at Bioprocessing Summit, Boston, 24-25 August 2020, on-line, invited lecture
15. Jungbauer, A: Process intensification by parallel, flow though chromatography, and counter current chromatography, at Tosoh Bioseparation Forum, 01 October 2020, on-line, invited lecture
16. Jungbauer, A: Propagation of Process Disturbances in Continuous Integrated Biomanufacturing, Bioprocess International Europe, 13-17 July 2020, on-line, invited lecture
17. Jungbauer, A: Residence Time Modelling of Continuous Integration Biomanufacturing Processes, at 9th Annual Biologics Manufacturing Korea 2020, Incheon, South Korea, September 7-8, 2020, on-line, invited lecture
18. Jungbauer, A: Residence time modelling of continuous integration biomanufacturing processes, at 7th Annual Biologics Manufacturing Asia, 07 Jul - 08 Jul 2020, Singapore, on-line invited lecture
19. Jungbauer, A: Virus and virus-like particles and extra cellular vesicles purification, at seminar
20. Jungbauer, A: Virus-Like Particles and Other Extracellular Particles from Insect and Mammalian Cells, at Bioprocessing Summit, Boston, 24-25 August 2020, on-line, invited lecture
21. Striedner, Gerald: Advanced Control strategies in Upstream Processing. Bioprocessing Summit Europe 2020 Virtual, July 21-23, 2020
22. Striedner, Gerald: Microbial Enzymes for treatment of non-recycled plastic fractions. ENZYCLE Stakeholder Dialog biobased Industry, December 14, 2020
23. Striedner, Gerald; Continuous Production with E. coli USP Concepts and Strategies. PEGS Boston Virtual, September 1-4, 2020
24. Striedner, Gerald; Hybrid Modeling and Intensified DoE Enabling Faster Process Understanding, Soft Sensors and Model Predictive Control. Biologics Manufacturing Asia and Biologistics World Asia 2020 July 7, 2020
25. Striedner, Gerald; Rapid process development for production of SARS-CoV-2 proteins ESBES - Webinar Series - Bioprocess development challenges for fast manufacturing of SARS-CoV-2 proteins and vaccines. June 19, 2020

    Universidade Federal de São Paulo, October 8, 2020, on-line, invited lecture
26. Vazulka, Sophie; Fink, Mathias; Wagenknecht, Martin; Cserjan-Puschmann, Monika; Striedner, Gerald (2020): Aberrant ribosome stalling upon recombinant protein production: E. coli host strains activate different quality control systems. Microbial Stress 2020, 16.-18.11.2020, Online

Other Publications

Frontiers in Genetics, Omics Technologies Toward Systems Biology, Editorial by Fatemeh Maghuly, Gorji Marzban and Joanna Jankowicz-Cislac. Special issues guest editorial.
https://www.frontiersin.org/research-topics/13533/omics-technologies-toward-systems-biology

MDPI, Biology, Proteomics of extremophilic fungi, Editorial by Gorji Marzban and Donatella Tesei. Special issue guest editorial.
https://www.mdpi.com/journal/biology/special_issues/PEF

Mass Spectrometry in Food Analysis, Chapter 4. Food proteomics, by Gorji Marzban, CRC ress/Taylor & Francis Group. Book chapter.

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 2020

Organization	Title	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

Our intention to write an annual report is to get a sense of how an institution develops over time, to proudly show achievements and success stories to colleagues and the scientific community. An annual report also creates identity and helps form a community, a network and a brand. Therefore, the report is more inclined towards a report of research activities and it is intentionally not laid out with photos of testimonials and decorated with fancy art photographs.

At the end of the annual report, we want to look into the future and describe some activities and goals for the next year and beyond. We want to revamp our homepage and try to design it to be more attractive for students and our potential collaborators and partners. We also have started to plan research activities addressing the needs of a bio-based industry with zero emission. Additionally, we continue to plan research in the field of biopharmaceutical manufacturing with new production technologies and analytical methods.

The planning of research and teaching has changed since IBSE was found. We are impressed with how the mere naming of an institution influences the thinking of its members. Before founding IBSE we had an in-depth discussion about the name. Unequivocally we concluded to put Science into our institute name and this devotes us to beyond state-of-the-art engineering science. Our students and scientists learned pretty fast that our success and expertise will only grow by understanding engineering based on fundamental scientific principles. They have uncovered a lot of research questions by critically questioning engineering and design principles. Although this was lived also before IBSE was founded, but now it became a guidance for our research and teaching.

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