Karlsruhe Institute of Technology

MAB
PROCESS ENGINEERING IN LIFE SCIENCE

Themengebiete Abschlussarbeiten

Stand: Oktober 2026

Allgemeines

- Die folgende Übersicht dient dazu, Interessenten von Studien- bzw. Abschlussarbeiten (BA, MA) einen Überblick über die Arbeitsgebiete am Institut für „Molekulare Aufarbeitung von Bioprodukten“ zu geben.
- Interessenten mit konkreten Themenwünschen können sich direkt bei den jeweiligen Doktoranden melden oder allgemein bei Raphael Nieß (raphael.niess@kit.edu).

Giulia Polazzo

PhD project started 01.2025

Starting from **May/June 2025**
Language spoken **English**

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Enrichment and separation of Adeno-Associated Virus-Like Particles using Aqueous Two-Phase Systems

Background

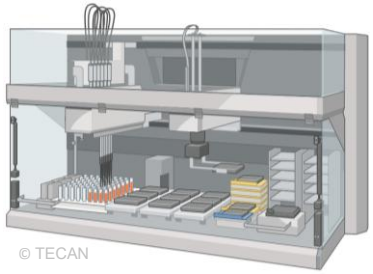
Adeno-associated virus (AAV) vectors are among the most promising gene delivery vehicles for therapeutic applications. Virus-like particles (VLPs) represent a valuable tool in AAV research, providing a non-infectious platform for studying vector assembly, stability, and purification. Previous research has demonstrated the potential of aqueous two-phase systems (ATPS) for enriching and separating recombinant AAV particles produced in HEK293 cells. However, further exploration is required to assess the efficiency of ATPS in purifying AAV-VLPs produced in *Escherichia coli*.

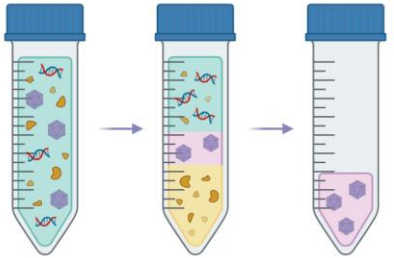
Research Objectives

- Evaluating the effectiveness of ATPS in enriching and purifying AAV-VLPs.
- Optimizing phase composition for maximum yield and purity of AAV-VLPs.
- Comparing the separation efficiency of different ATPS formulations.
- Assessing the impact of ATPS parameters (e.g., pH, polymer concentration, salt type) on VLP integrity and recovery.

Analytics and Tools

- Robotic liquid handling station (*Freedom EVO® 200*, Tecan Group Ltd.)
- Recombinant protein expression in *E. coli*
- SDS-PAGE electrophoresis system
- ELISA kit
- UV/Vis spectroscopy
- Dynamic Light Scattering





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Julian Gentes

Establishment of a Digital Twin for antibody-drug conjugate (ADC) manufacturing processes

Background: The development of **antibody-drug conjugate (ADC)** manufacturing processes typically requires extensive experimental efforts. In the current era of Industry 4.0, with the biopharmaceutical sector undergoing a digital transformation, new strategies are emerging to accelerate and reduce the cost of this development. These strategies include the integration of advanced **process analytical technologies (PAT)** sensors to monitor **critical quality attributes (CQAs)** in real time, alongside the development of **computational models** that can identify key process parameters through simulations. By merging these approaches, a **Digital Twin** of the manufacturing process can be created, which **updates the mechanistic model with real-time data**, enabling more precise prediction of process parameters and improving overall process control.

Experimental

Projects:
- Development of PAT sensors to monitor CQAs of ADC (e.g., aggregates, free drug, reduced species) in real-time.
- Determination of reaction kinetics to support the creation of mechanistic models.

Methods:
- Functionalization, conjugation, UF/DF,…
- Spectroscopy (Raman, FTIR, UV/Vis)
- Analytics (HPLC, CE-SDS,…)

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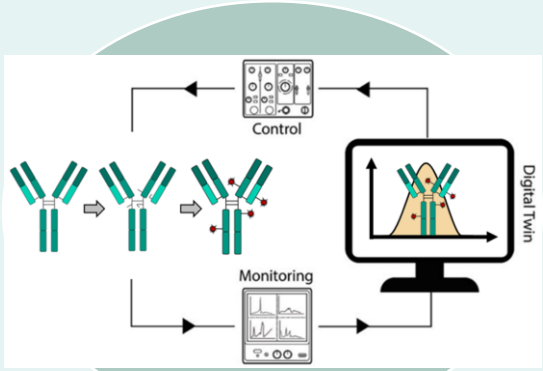

adapted from https://doi.org/10.1007/978-3-030-71660-8

Modelling

Projects:
- Creation and optimization of mechanistic models for each step of the ADC manufacturing process.
- Combination of PAT sensors and mechanistic models to create a Digital Twin of the process

Methods:
- Mechanistic modelling, Bayesian parameter estimation, Kalman filter,…
- Data Science (Python, MATLAB)

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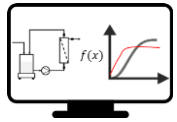

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Doil Yun

Master‘s theses are available on an ongoing basis.

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Integration of PAT and mechanistic/statistical modeling for automated process control

Background: Real-time quality assurance in pharmaceutical manufacturing processes requires precise **process control** strategies. Herein, **Process Analytical Technology (PAT)** tools provide valuable insights into process performance, by measuring **critical quality attributes (CQAs)**. The integration of PAT data with mathematical models, then allows for **predictive control** of the process, leading to improved product quality and operational efficiency. A hybrid modeling approach, combining **mechanistic and statistical models**, could provide increased process understanding and allow for proactive process adjustments. By establishing an **integrated framework**, consisting of the operating system, the PAT sensors and a model pipeline, advances can be made towards **automated** process control in real-time.

Experimental

Projects:
- Establishment of a PAT pipeline, capable of monitoring CQAs of Nanobodies

Methods:
- Chromatography, UF/DF
- Spectroscopy (UV/Vis, Raman, MIR,…)
- Analytics (HPLC-SEC, HPLC-IEX, HPLC-RP, CE-SDS,…)

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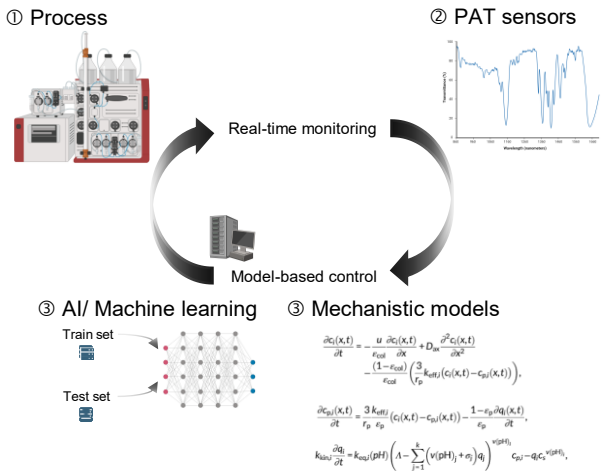

Computational

Projects:
- Mechanistic modeling of a chromatography unit operation
- Establishment of data-driven models for PAT sensors
- Model-based process control

Methods:
- Data Science (Python)
- Mechanistic modeling (CADET)
- Process Automation (MATLAB)

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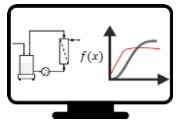

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Raphael Nieß

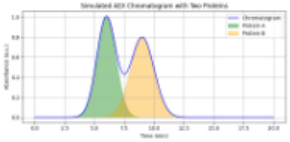
Development of Digital Twins for Process Monitoring and Control of Depth Filtration and Membrane-Based Ion Exchange Chromatography

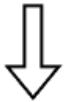
Background: This project aims to develop digital twins for two key unit operations in biopharmaceutical downstream processing: **depth filtration** and **membrane-based ion exchange chromatography**. Each process is modeled using a combination of **Process Analytical Technology (PAT)** and **mechanistic modeling**. PAT involves real-time, spectroscopic monitoring of critical quality attributes (CQAs), while mechanistic models utilize the underlying partial differential equations to predict process performance. By integrating both approaches, the digital twins enable automated, feedback-controlled operation with high robustness and predictive power.

Techniques and Methods:

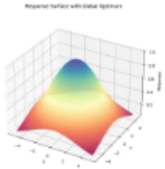
-	Data handling:	Python, Machine Learning
-	Mechanistic modelling:	Cadet, ChromX
-	Purification:	Depth filtration, AEX
-	Light scattering:	MALS, DLS
-	Specotroscopy:	Raman, IR, UV
-	Analytical methods:	HPLC, ELISA, Turbidity

Mechanistic Model





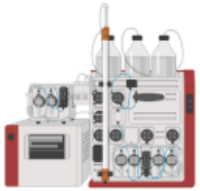
Prediction of optimal process parameters



Unit operations

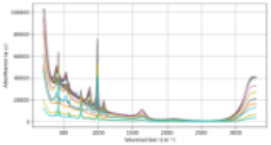
Depth filtration

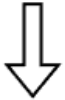
Membrane Anion Exchange Chromatography



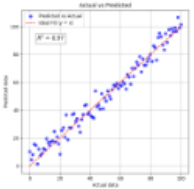
PAT approach

Spectral data (Raman, IR, UV)





Attribute prediction by regression (PLS, GPR)



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Loulotte Waling

Multisensory in-line PAT in downstream processing for *in silico* model-based process monitoring and control

In close collaboration with Giulia Polazzo as part of the EU funded CAARE consortium.

Background

Adeno-associated viruses (AAVs) are used as viral vectors for gene and drug delivery as well as for vaccine applications. Compared with recombinant AAVs, AAV virus-like particles (VLPs) offer key advantages such as improved safety and manufacturing flexibility, as they lack viral genetic material while retaining the native capsid structure. Within the CAARE consortium, Giulia and my work focuses on developing a robust downstream process for AAV VLPs. The aim of this project is to develop in-line process analytical technologies to monitor particle purity and integrity and to build a predictive model to understand how processing conditions affect particle stability. Finally, the objective is to integrate these tools into a digital twin to enable real-time process optimization of the VLP manufacturing process.

Techniques and methods

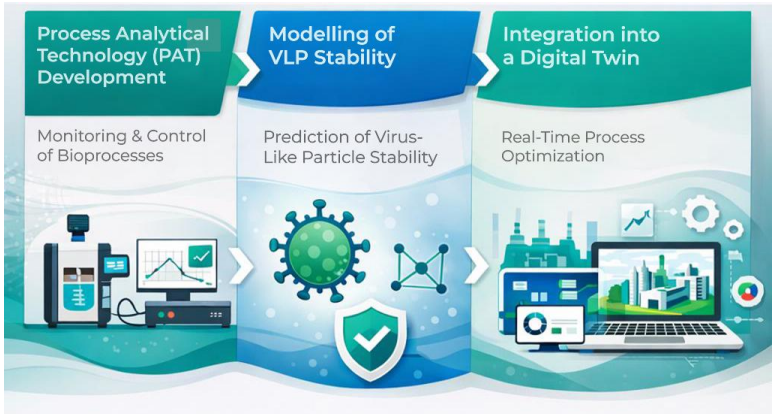
Analytical methods
- SEC-HPLC, CE SDS, …

Spectroscopy / light scattering
- Fluorescence, UV VIS, …
- DLS, MALS, …

Data & modeling
- Python, machine learning

Student projects

- PAT development for AAV PTM characterization with UV/VIS & MS data



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Christian Beyer

Bioprinting and Tissue Engineering with sustainable hydrogels using mono- and multidisperse microgel particle systems

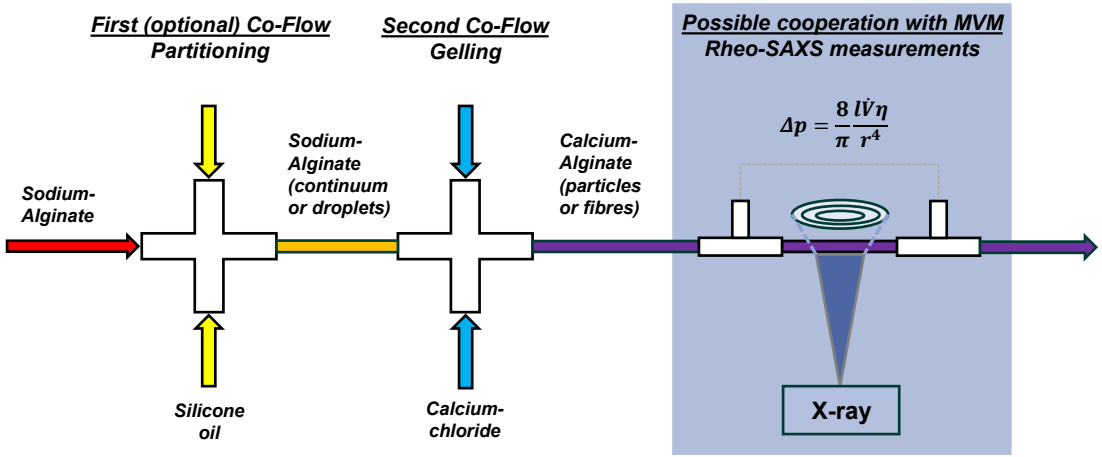
Background: This project is part of the DFG programme "SusGel: Additive manufacturing of polysaccharide gels", which aims to investigate and manipulate the macroscopic and microscopic properties of hydrogels made from sustainable raw materials.

In the current project phase we are evaluating methods for microfluidic particle generation and bioink formulation for use in bioprinting and tissue engineering.

A hands-on Master's thesis could be in the fields of evaluation of different **microfluidic co-flow setups** for particle generation, **analyzing the size distribution** and further linking this to **rheological properties** of derived bioinks, like viscosity over shear stress and **shape fidelity** of 3D-printed objects.

Techniques and Methods:

- Microfluidics
- Image Analysis
- Rheometrics
- Extrusion-based bioprinting
- Rheo-SAXS possible (in cooperation with Augusto Palotti at MVM)



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Lea Bisch

PhD project started 05/2026

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Controlled Cargo Loading and Assembly of HBcAg Virus-Like Particles

From experimental self-assembly to model-supported process understanding

Background

HBcAg (Hepatitis B core antigen) proteins spontaneously self-assemble into highly ordered virus-like particles. Their reversible assembly behavior and arginine-rich C-terminal domain make them attractive platforms for cargo incorporation. However, reproducible loading and controlled assembly remain challenging due to interacting molecular and process-related factors.

Experimental investigation

Study how processing and cargo properties affect HBcAg disassembly, reassembly and the resulting particle populations.

Methods

- recombinant protein production
- chromatographic purification
- controlled disassembly / reassembly
- electrophoresis & HPLC
- particle, protein & cargo analytics

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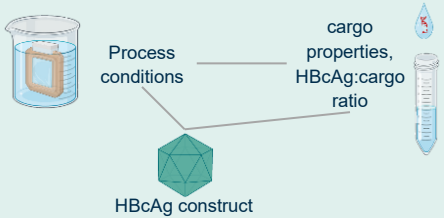
Research objective

Experimental data → Models
Model hypotheses → Targeted experiments

Understand how **process conditions, cargo properties and HBcAg properties** determine particle assembly, cargo incorporation and product quality.



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Model-supported investigation

Develop **quantitative descriptions** of assembly and **connect** experimental observations with underlying interactions and population dynamics.

Possible methods

- kinetic modeling
- population balance models
- data-driven modeling
- molecular dynamics / coarse-grained simulations
- parameter estimation and model validation

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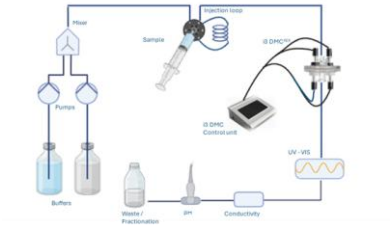
Dr.-Ing. Iris Perner-Nochta

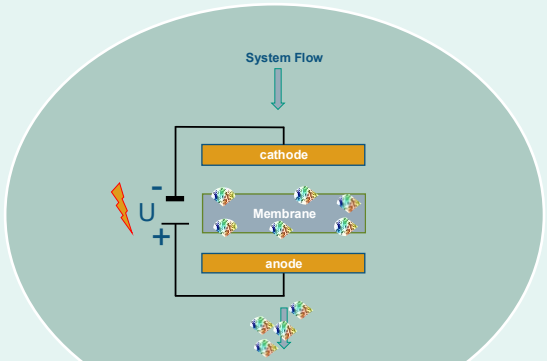
Modelling and Simulation of Protein Chromatography Induced by Electrical Stimulation

Background: Electrically switched membranes are suitable for the chromatographic processing of proteins. In this novel process, functionalized membranes are used for adsorption and electric fields for desorption. Mechanistic understanding of the processes taking place in an existing system can be deepened by modelling and simulation. Therefore, the system is modelled using COMSOL Multiphysics®. In addition to the fluid dynamic aspects, the electrochemical processes are considered. The work aims to improve the understanding of the mechanistic processes in order to fully exploit the potential of the procedure.

Experimental

Projects:
- Investigation of Protein Chromatography Induced by Electrical Stimulation





Modelling

Projects:
- Modelling and simulation of protein chromatography induced by electrical stimulation using COMSOL Multiphysics®.
- Simulation of fluid dynamics and the electrochemical processes within the system

Methods:
- geometry creation, meshing, model setup, and results unsing COMSOL Multiphysics®.

COMSOL

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