KIT Karlsruhe Institute of Technology

MAB PROCESS ENGINEERING IN LIFE SCIENCE

Themengebiete Abschlussarbeiten

Stand: Januar 2025

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 Rafaela Meutelet (rafaela.meutelet@kit.edu).

Giulia Polazzo

PhD project started 01.2025

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

Karlsruhe Institute of Technology

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

Background

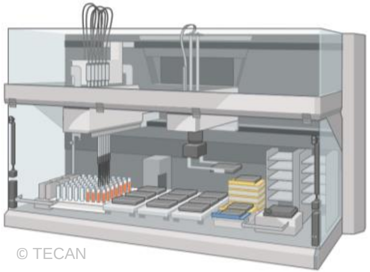
Adeno-associated virus (AAV) vectors are among the most promising gene delivery vehicles for therapeutic applications. Virus-like particles (VLPs) represent a valuable tool in AAV research, providing a non-infectious platform for studying vector assembly, stability, and purification. Previous research 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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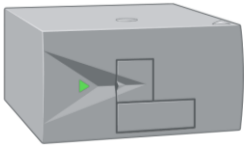

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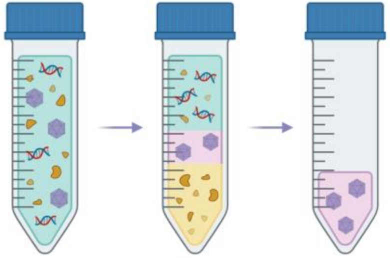


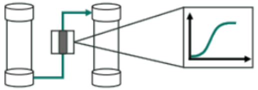
Jakob Müller

In-line PAT in DSP for in-silico model based process monitoring and control

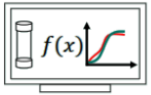
Background: The use of **process analytical technologies (PAT)** represents a central aspect of **biopharmaceutical process development**. Spectrometric and chromatographic analysis methods can be used for monitoring and controlling, for example, the purification of pharmaceutically active substances. Both the **optimization** of **production processes** and the improvement of **process robustness** are in the foreground. In addition, the data obtained can be used to create **mechanistic models**. These models allow the identification of relevant process parameters, the extrapolation beyond the experimental limits, as well as a facilitation of the technology transfer, with a simultaneous **reduction of the number of** often **cost- and time-intensive experiments** necessary for this. Thus, the **improvement** of a **process** can be achieved under **shortened development time.**

Small-scale model

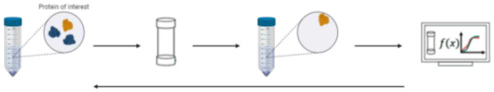
In-line PAT



Process modeling



Process digitization



Materials & Methods

- Selection and establishment of appropriate in-line process analytical technology for the detection of critical cQAs (e.g., aggregate content, aggregate size distribution).
- Development of a PAT-based soft sensor using the combination of in-silico model and the PAT used for monitoring relevant CQAs.

In lab:

- Chromatography (Prot.A, AIEX)
- Spectroscopy (UV/Vis, Raman, FTIR)
- Light scattering (MALS, RI, Zetasizer)
- Offline analytics (HPLC-SEC, ELISA)

Computational:

- Data management (Python)
- Process-/Analysisautomation (MATLAB)
- Mechanistic modeling (ChromX)

CHROM X

Institute of Process Engineering in Life Sciences
Section IV: Biomolecular Separation Engineering

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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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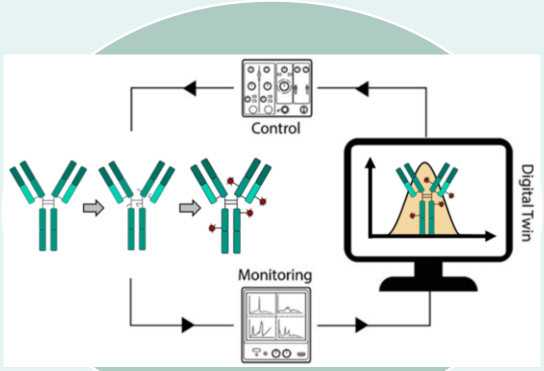


adapted from https://doi.org/10.1007/978-3-030-71660-8

Modelling

Projects:

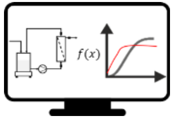
- Creation and optimization of mechanistic models for each step of the ADC manufacturing process.
- Combination of PAT sensors and mechanistic models to create a Digital Twin of the process

Methods:

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

© Python

© MATLAB



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Upcoming topics from:

- Doil Yun