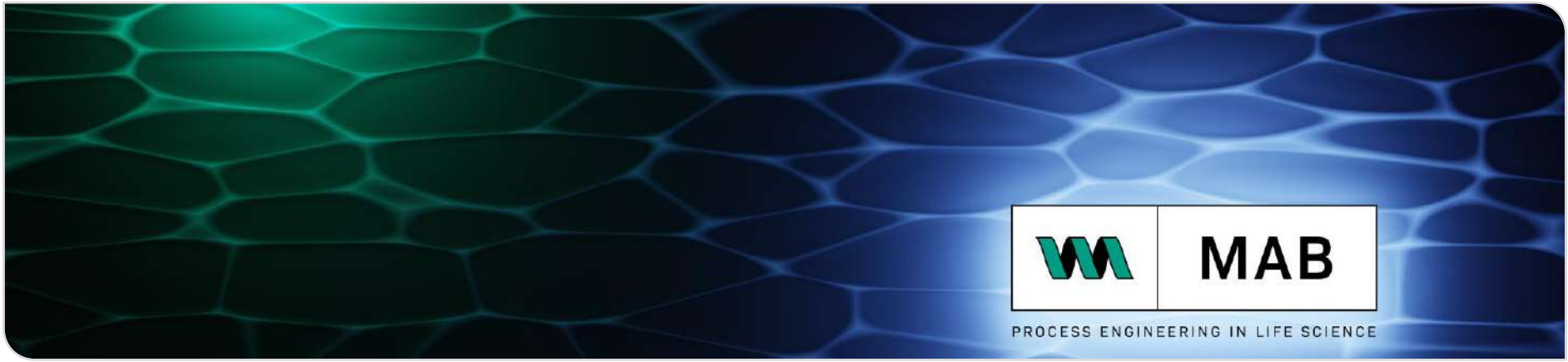
Karlsruhe Institute of Technology

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).

Supervision possible only until May/June 2025

Rafaela Meutelet

Development of an innovative process for the concentration and extraction of nucleic acids for tumor diagnostic (liquid biopsy)

Background

Liquid biopsy provides information about tumours which can help identify disease and guide treatment decisions. It is based on **biomarkers** found in various body fluids, mostly blood. One of these biomarkers is **circulating tumour DNA** (ctDNA), short fragments of DNA shed into the bloodstream by cancer cells in very small concentrations. In order to quantify and analyze the mutations of the ctDNA, it needs to be **extracted** from the plasma and **concentrated**.
The use of **aqueous two-phase systems** (ATPS) as an initial extraction step is being investigated.

Projects:

- **High Throughput Screening** of suitable ATPS components and system parameters for optimal DNA partitioning
- **Extraction and purification step** development and integration for further DNA concentration
- **Prototype** development for integrated extraction of ctDNA from blood plasma

Methods:

- Robotic liquid handling station, automated screenings
- UV/Vis spectroscopy
- Fluorescence assays
- PCR

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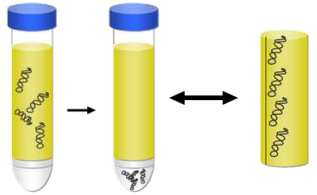

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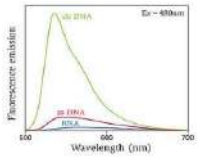

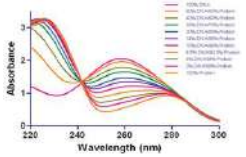

PhD project started 11/2021

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Section IV: Biomolecular Separation Engineering

Jakob Müller

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

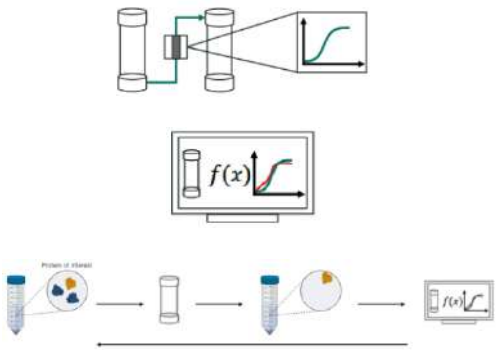
Background: The use of **process analytical technologies (PAT)** represents a central aspect of **biopharmaceutical process development**. Spectrometric and chromatographic analysis methods can be used for monitoring and controlling, for example, the purification of pharmaceutically active substances. 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)

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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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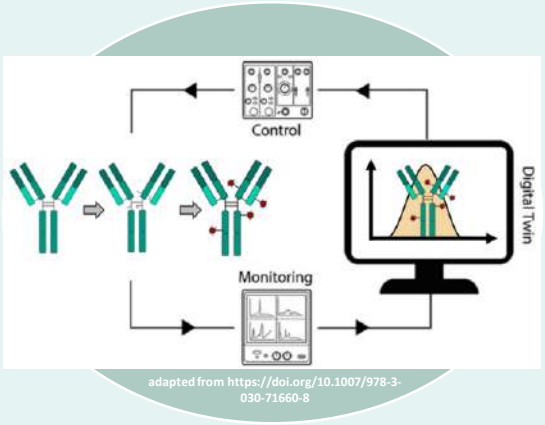

Modelling

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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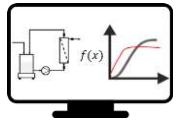
© MATLAB



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Upcoming topics from:

- Doil Yun
- Giulia Polazzo