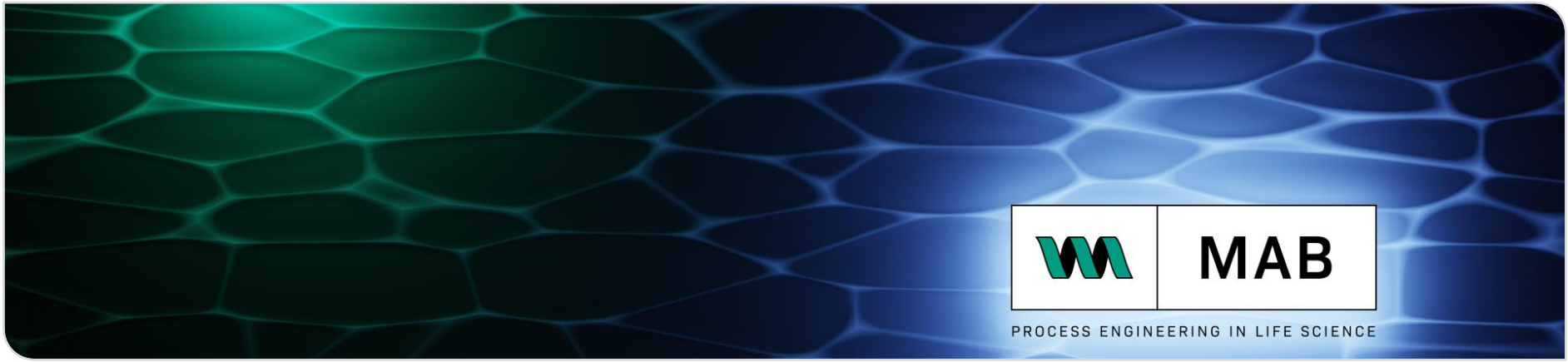
Karlsruhe Institute of Technology

MAB
PROCESS ENGINEERING IN LIFE SCIENCE

Themengebiete Abschlussarbeiten

Stand: Juli 2023



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).

Nicole Beckert

Drug compatibility in adherence technology

Background

Development of drug adherence technology is of major importance for efficient medication. To circumvent misapplication, user-friendly handling is inevitable. Self-administration of biopharmaceuticals requires the use of microfluidic devices like micropumps, for instance in patch pumps or pen injectors. However, it is necessary to validate the used micropump for its compatibility with the drug formulations. Of particular interest are the conformational as well as the colloidal stability of the pharmaceutical molecule. Excipients can be added to increase the stability of the molecule during storage and dosing.

Molecules

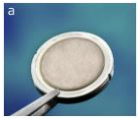
- Monoclonal antibody (mAb),
- Lipid nanoparticle (LNP)

Projects

- Process and analytical development for LNPs
  - Microfluidic mixing
  - Tangential-flow filtration
  - PAT
- (Re)Formulation of mAbs
- Stability studies
  - Pump studies
  - Freeze thaw studies

Analytics

- HPLC: SEC or RP, Detection: UV/Vis spectroscopy and CAD
- DLS
- Zetapotential
- …



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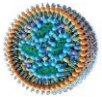
Annabelle Dietrich

Process development, analytical development and PAT implementation for various carrier systems with nucleic acid cargo

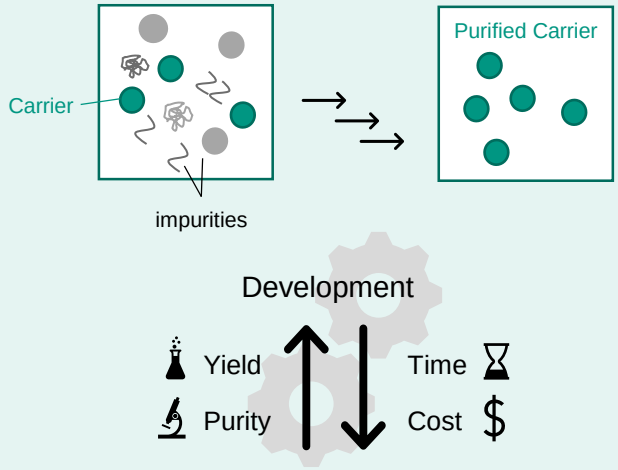
Background: Carrier systems with **nucleic acid cargo** are used for targeted delivery in the field of **gene therapy**. Specified process and analytical development is of key concern for different carrier systems to ensure their critical quality attributes (CQAs) such as composition, purity, yield, stability and nucleic acid content. CQAs are influenced by critical process parameters (CPPs). Therefore, **Process Analytical Technology** (PAT) can be applied to monitor process parameters by in-line, on-line or at-line measurements.

Experimental

Virus-like particle (VLP) production by cultivation in *E.coli* and purification by selective precipitation, UF/DF



Lipid-nanoparticle (LNP) production using microfluidics and purification/formulation by UF/DF



Analytics & Tools

- Spectroscopic methods (UV/Vis, Raman, FTIR)
- Light Scattering
- HT-CGE
- HPLC (RP-CAD, SEC-MALS)
- Fluorescence-based assays
- MATLAB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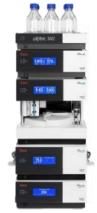
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Rafaela Meutelet

Development of an innovative process for the concentration and extraction of nucleic acids for tumour diagnostic (Liquid Biopsy)

Background

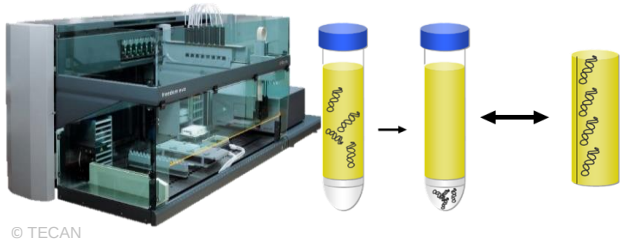
Liquid Biopsy provides information about tumours which can help identify disease and guide treatment decisions. It is based on **biomarkers** found in various body fluids, mostly blood. One of these biomarkers is **circulating tumour DNA** (ctDNA), short fragments of DNA shed into the bloodstream by cancer cells in very small concentrations. In order to quantify and analyse 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
- **Adsorption and desalting step** development and integration for further DNA concentration and purification
- **Reaction vessel prototype** development for integrated extraction of ctDNA from blood plasma

Methods:

- Robotic Liquid Handling Station, automated screenings
- UV/Vis Spectroscopy
- Fluorescence assays
- PCR
- 3D-printing …



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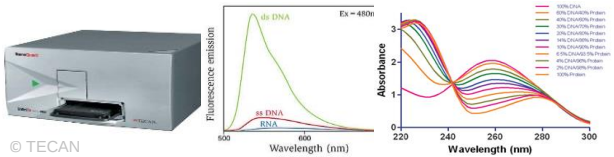

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PhD project started 11/2021

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Jakob Müller

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

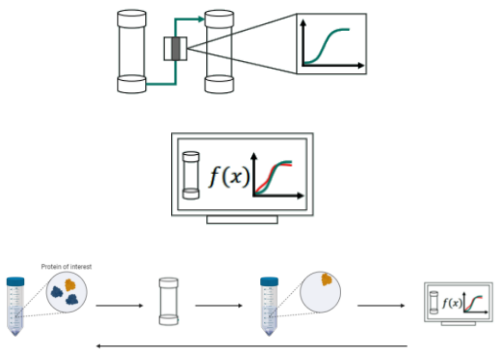
Background: The use of **process analytical technologies (PAT)** represents a central aspect of **biopharmaceutical process development**. Spectrometric and chromatographic analysis methods can be used for monitoring and controlling, for example, the purification of pharmaceutically active substances.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

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