In-silico Process Development for biopharmaceuticals

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The purification of biopharmaceuticals includes a sequence of different unit operations to capture, purify and polish the desired product. Though, finding the optimal purification sequence is challenging and in order to define that a comprehensive systematic approach is required (Hanke & Ottens, 2014). Model-based High Throughput Process Development (HTPD) allows to define the optimal purification process by combining miniaturized High Throughput Experimentation (HTE) in relation to process design with detailed mechanistic mathematical models.

The mechanistic mathematical models enable to rationally screen and select an 'optimal process', primarily determined by product quality requirements and cost-effectiveness, using mere *in-silico* simulations. The use of Artificial Neural Networks (ANN) in addition to mechanistic models enhances the optimization of certain purification steps and will be further developed during this project. Subsequently, process flowsheet optimization is performed by connecting the unit operation models and finding the optima of the overall purification process (Pirrung et al., 2019).

This project focuses on *in-silico* Process Development with an application in biopharmaceutical industry, including mechanistic mathematical modelling, Artificial Intelligence, database development and a full integrated process design.

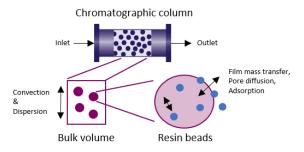


Figure 1. Overview of the transport and adsorption processes occurring in the chromatographic column.

References

Hanke, A. T., & Ottens, M. (2014). Purifying biopharmaceuticals: knowledge-based chromatographic process development. *Trends in Biotechnology*, 32(4), 210-220. doi:10.1016/j.tibtech.2014.02.001

Pirrung, S. M., Berends, C., Backx, A. H., van Beckhoven, R. F. W. C., Eppink, M. H. M., & Ottens, M. (2019). Model-based optimization of integrated purification sequences for biopharmaceuticals. *Chemical Engineering Science: X*, 3, 100025. doi:<u>https://doi.org/10.1016/j.cesx.2019.100025</u>