RAMAN SPECTROSCOPY-BASED MONITORING AND CONTROL OF A HIGH CELL DENSITY CHO CULTURE

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Project description

The present PhD project is part of the industry-academia collaboration project called "Hands-free biotechnology: Biopharmaceutical process development for continuous manufacturing". This is a joint project between TU Delft (TUD) and Janssen Biologics (JBV) which is partly funded by Chemistry NL. The aim of this collaboration project is to develop an upstream (USP) and downstream (DSP) proof-of-concept that demonstrates a more efficient biopharmaceutical manufacturing process: a continuous process with higher productivity, higher product quality and automated monitoring & control [1]–[4]. This would allow to ensure patient affordability and industry competitiveness.

The upstream process of biopharmaceutical production faces some challenges for efficient manufacturing: how to cultivate an intensified and continuous CHO cell production bioreactor while ensuring efficient use of raw materials and high product quality? How to automate process monitoring and control? How can lab-scale developed cultures be effectively scaled-up to manufacturing scales? In order to answer these questions, this PhD project will rely on Process Analytical Technology (PAT), Raman spectroscopy coupled with chemometrics, and Computational Fluid Dynamics (CFD).

This PhD project will focus on the development of a "hands-free" proof-of-concept bioreactor. The ambition is that manual sampling for monitoring and manual operations for control during manufacturing will be eliminated by means of a PAT approach. Raman spectroscopy-based chemometric models will be developed and integrated for monitoring and control of a high cell density CHO culture producing monoclonal antibodies at lab-scale. In addition, CFD models will be used for the reduced-scale design and to evaluate the scale-up heterogeneity effects on the "hands-free" bioreactor performance.

References

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