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Accelerated bioprocess characterization by data enrichment in scale-down models

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[1] Christoph Herwig, "Assessment of data quality and Know-Why for a scalable QbD Approach." 2013. [2] M. von Stosch, S. Davy, K. Francois, V. Galvanauskas, J.-M. Hamelink, A. Luebbert, M. Mayer, R. Oliveira, R. O'Kennedy, P. Rice, and J. Glassey, "Hybrid modeling for quality by design and PAT-benefits and challenges of applications in biopharmaceutical industry," Biotechnology Journal, vol. 9, no. 6, pp. 719–726, Jun. 2014. [3] A. S. Rathore and R. Mhatre, Quality by Design for Biopharmaceuticals: Principles and Case Studies, Auflage: 1. Wiley-Interscience, 2011. [4] W. Zhou and A. Kantardjieff, Mammalian Cell Cultures for Biologics Manufacturing, 2014th ed. Heidelberg ; New York: Springer, 2014.

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Scale-down models are often used for the definition of operating ranges in process development and validation and therefore data exploitation is an important task. Usually, the experimental scientists have very tight timelines and consequentially may often only perform the required routine of cleaning and sorting the data without more sophisticated analyses, even though it might improve data quality. This problem is more exacerbated by the rise of fully automated, miniaturized high-throughput equipment in up- and downstream process development where data processing automation is not just optional but a must. However, cleaned, sorted and time-aligned data alone do not guarantee a sufficient representation of the process. Often, further data enrichment to extract relevant process parameters is required but omitted due to time constraints. The benefit of data enrichment is true process understanding [1]: the calculation of scalable rates and yields, minima, maxima, median or derivatives of measured online or offline signals and the categorization into clone, lot, feeding strategy, seed train fitness, feed or media can be easily used to explain variation in the current process. Multivariate regression methods such as partial least squares regression (PLS-R) or hybrid models [2] can then be used to explain the contribution and ranking of critical process parameters (CPPs) such as pH, pO2, temperature, metabolite concentrations or metabolic rates towards particular critical quality attributes (CQAs), for instance glycoform distribution, other product quality attributes or cell growth. The knowledge of these parameters can then feed directly into the generation of a statistically verified design space which may be then used for process scale-up and validation [3,4]. Summarizing this contribution, we present a methodology to automate data enrichment. Our suggested data enrichment concept is exemplified shown on upstream micro bioreactor data and comprise one of the necessary steps to characterize and ultimately qualify scale-down process models.

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