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## The perspective of digital twins in bioprocesses at different scales

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Scaling the production needs from CMC to flexible scale or large-scale fermentation-based production of APIs (like insulin) is a cumbersome endeavor. Even though key operational process parameters have been validated at development scale and common scale up methods have been applied, the variation in space, time, and yield can differ considerably from site to site. This presentation attempts to give examples of how a digital shadow of the process can help to decide on key parameters for understanding and design of the bioprocess at different scales.

Computational Fluid Dynamic methods are used to predict the inhomogeneities in mixing efficiencies in reactors. Kinetic models are coupled with the fluid dynamic models in order to understand and describe the performance of the process under those conditions. Ultimately such models will assist to develop small scale reactor systems for the experimental investigation of operational conditions. This contribution will include the underlying principle of mass transfer in chemical reactions, present the experimental and simulation results of a microbubble column-bioreactor ( $\mu$ BC)<sup>1</sup>, mixing at pilot scale<sup>2</sup>, reaction performance at full scale<sup>3</sup> and the practical considerations for digital twins applied to bioprocesses. Finally, some future opportunities for the application of digital twins will be discussed and the realistic, experimental constraints will be considered as well.

1. Lladó Maldonado, S. et al. Multiphase microreactors with intensification of oxygen mass transfer rate and mixing performance for bioprocess development. *Biochem Eng J* 139, 57–67 (2018).
2. Christian Bach, Jifeng Yang, Hilde Larsson, Stuart M. Stocks, Krist V. Gernaey, Mads O. Albaek & Ulrich Krühne, †. Evaluation of mixing and mass transfer in a stirred pilot scale bioreactor utilizing CFD. *Chem Eng Sci* 171, 19–26 (2017).
3. Wright, M. R., Bach, C., Gernaey, K. V & Krühne, U. Investigation of the effect of uncertain growth kinetics on a CFD based model for the growth of *S. cerevisiae* in an industrial bioreactor. *CHEMICAL ENGINEERING RESEARCH & DESIGN* 140, 12–22 (2018).

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