

SCALE-UP OF CELL CULTURE PROCESSES USING DIGITAL TWINS

Pranjul Mishra, Yokogawa Insilico Biotechnology Pte. Ltd.
P.Mishra@yokogawa.com
Kevin Schindler, Yokogawa Insilico Biotechnology GmbH
Pulkit Chhabra, Yokogawa Insilico Biotechnology Pte. Ltd.
Joachim Schmid, Yokogawa Insilico Biotechnology GmbH
Shilpa Nargund, Yokogawa Insilico Biotechnology Pte. Ltd.
Klaus Mauch, Yokogawa Insilico Biotechnology GmbH

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Background and novelty: Production of biologics requires operating cell culture bioreactors of greater than 1,000 liters, sometimes even up to 20,000 liters. However, a cell culture process is usually developed at 15 ml - 5-liter scale and needs to be scaled-up. Scaling-up cell culture processes is challenging as exact reproduction of growth conditions between scales is difficult due to different physicochemical conditions. In particular, the sensitivity of cells to oxygen availability and shear stress aggravates the usual challenges in scale-up of multiphase reactors. Several iterations of large-scale experiments are required to achieve the desired cell culture behavior at-scale. In this contribution, we show how the use of Digital Twins of bioreactors can minimize the engineering batches during scale-up and move your workflow to a right-first-time method.

Approach: The Insilico Digital Twin of a bioreactor is a hybrid model that combines mechanistic know-how with data-driven insights. It predicts the cell culture performance i.e., biomass, titer, lactate, ammonia etc. in a virtual experiment. With the Digital Twin, virtual experiments are performed by varying the scale-dependent parameters to minimize deviations in cellular performance from the reference state. The new methodology can be used for both scale-up and scale-down.

Results and discussion: In this presentation, we show how Digital Twins of bioreactors were used to scale-up or scale-down between 250 ml to 2,000 L.