ESTABLISHMENT OF AN N-1 PERFUSION/HIGH-SEED FED-BATCH TECHNOLOGY FOR THE INTENSIFICATION OF RECIMBINANT PROTEIN PRODUCTION PROCESSES: FROM AMBR250 TO 200 L STR

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Antibody production processes can be accelerated by considerably increasing the starting cell concentration in the production fed-batch bioreactor (high-seed FB). Combining a perfusion bioreactor at the n-1 stage, FB production bioreactors with initial cell concentrations of 10×10^6 cell/mL can be achieved. The resulting time-shortening at the production bioreactor (n stage) can potentially generate a 30 % increase in manufacturing capacity while yielding comparable product quality [1]. While this has been proven in 5 L benchtop bioreactors, a platform covering a broader range of scales can facilitate the process intensification activities from early stage process development up to manufacturing.

In this study, the production of a recombinant protein using a high-seed FB strategy was assessed in AMBR250, 2 L and 200 L bioreactor scales. An alternating tangential flow (ATF) perfusion system was used to expand the producer cells to target concentrations ≥ 60×10^6 cells/mL in the corresponding n-1 bioreactors. Production FB bioreactors were then inoculated with 10×10^6 cells/mL and operated up to 9 to 12 days using an automated feeding profile based on either at-line or on-line bio-volume measurements. Optimization of the feeding profile and rate led to comparable antibody productivities and quality throughout the different scales and with respect to the conventional 14-day FB process.

Overall, the application of a high-seed FB strategy allowed for a reduction of the processing time and proved the intended increase in the overall production capacity. Also, the assessment of the high-seed FB strategy throughout different scales set the base for the establishment of a robust technology that fulfills the requirements of different products during process intensification.

[1] Yang WC, Lu J, Kwiatkowski C, Yuan H, Kshirsagar R, Ryll T, et al. Perfusion seed cultures improve biopharmaceutical fed-batch production capacity and product quality. Biotechnol Prog. 2014;30:616-25.