simAbs

Application note 2

Continuous manufacturing outperforms traditional fed batch cultures

Thomas Geuens and Koen Dierckx

-40% CAPEX

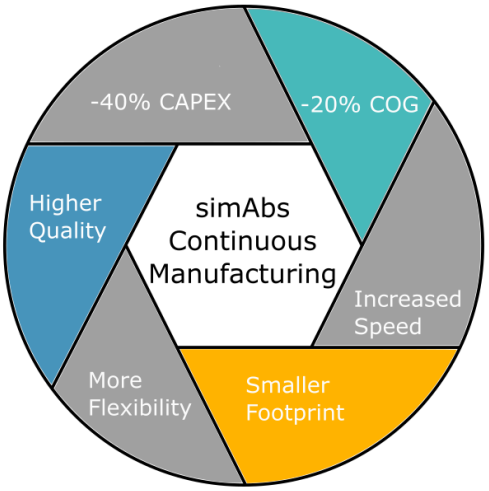
simAbs focusses on continuous manufacturing by coupling its perfusion bioreactor directly to a highly utilized purification train. This results in the need for smaller bioreactors as spent media, containing the produced monoclonal antibody (mAb), is constantly removed and replaced by fresh cell culture media. Our chromatography resins and equipment are traditionally smaller in volume and size as the harvested product is directly purified and polished without any hold steps. This results in significantly larger savings in capital expenses[2].

-20% COG

Our optimized perfusion process can proceed for many weeks to months. Such a long-term perfusion culture results in a 3- to 5-fold increase in productivity by maintaining very high viable cell densities in the bioreactor. The increased media cost that is typically associated with perfusion culture does not outweigh the high costs associated with chromatography resins used in batch processes. It is stated that continuous manufacturing results in savings in COG per gram mAb as it outperforms traditional (fed-) batch cultures because of its increased productivity[1].

Higher Quality

During perfusion there is a constant removal of the product. Therefore, it is not exposed to an increased presence of toxic waste products generated during cell culture. This avoids concerns about product degradation and stability[3]. In addition, perfusion culture results in a higher and more consistent product quality with regards to glycosylation patterns and avoids the production of undesired product variants[4].



Increased Speed

We have developed a continuous manufacturing platform based on the usage of disposables and single-use bioreactors. This reduces the downtime between production batches as we avoid extensive cleaning and validation events at the end and start of a production run. Our perfusion bioreactors range from 1 to 50L working volume enabling us to achieve in a very limited amount of time cell culture production phase.

More Flexibility

We can tailor the production process based on the amount needed by the client by simply shortening or lengthening the cell culture run. This decision can even be made during the production phase as our cells keep on producing when the culture run is continued in perfusion. Our production platform is easy to scale out which enables us to easily employ parallel production lines and thus multiproduct manufacturing.

Smaller Footprint

Continuous manufacturing offers, besides the potential of increased productivity, a significant smaller facility footprint compared to current (fed-) batch manufacturing sites. By employing a continuous usage of the purification train in combination with continuous perfusion bioreactors, the downstream and upstream capacities can be decreased in size. This is associated with a reduced buffer consumption which automatically decreases the usage of non-process water by ±30%[2].

About the author

Thomas Geuens obtained a PhD in Biochemistry and Biotechnology at the Flanders Institute for Biotechnology (VIB) in Antwerp, Belgium. After a 3-year post-doctoral stay abroad he joined simAbs NV as an Upstream Process Development Engineer. At this moment, he is fulfilling the role of Head of Research and Development and coordinates all research and process development activities.

Email: thomas.geuens@simabs.com

LinkedIn: https://www.linkedin.com/in/thomas-geuens-4b4816a/

References

1. Lundgren, B., Bösch, P. & Kaisermayer, C. *How to Construct a Monoclonal Antibody Factory: A Comparison of Production Costs in Fed Batch and Perfusion Culture with Microcarriers*. www.bioprocessingjournal.com.

2. Pollock, J., Ho, S. v. & Farid, S. S. Fed-batch and perfusion culture processes: Economic, environmental, and operational feasibility under uncertainty. *Biotechnology and Bioengineering* **110**, 206–219 (2013).

3. Bielser, J. M. *et al.* Perfusion cell culture for the production of conjugated recombinant fusion proteins reduces clipping and quality heterogeneity compared to batch-mode processes. *Journal of Biotechnology* **302**, 26–31 (2019).

4. Karst, D. J. *et al.* Modulation and modeling of monoclonal antibody N-linked glycosylation in mammalian cell perfusion reactors. *Biotechnology and Bioengineering* **114**, 1978–1990 (2017).