STIRRED-TANK BIOREACTORS AND HOW THEY ARE USED IN THE DEVELOPMENT AND PRODUCTION OF COVID-19 VACCINES

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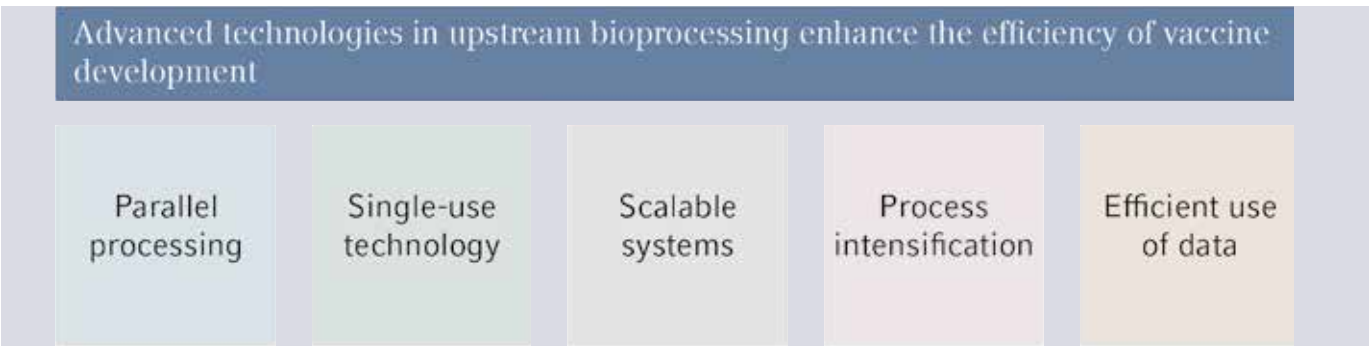
Increasing demands from governmental vaccination programmes and pandemic events such as the current COVID-19 outbreak require scientists to work under pressure to shorten the time-to-market of developed vaccines. The current global vaccine market valuation of approximately 50 Billion USD, with 80% of the market on human vaccines. Altogether, a need for new methods to increase speed and yield, and to produce new vaccines in a cost-effective manner in order to remain competitive is a constant concern for scientists. Although the competition on the vaccine market is high, a noteworthy effect of the current COVID-19 crisis is the fact that big vaccine manufacturers are forming and maintaining collaborations with comparably young companies, and former competitors are cooperating with each other in order to speed up vaccine development. And we see a trend towards collaboration in the biotechnology industry in order to accelerate the research, development and large-scale production of new vaccines.

Bottlenecks for production arise from the use of two-dimensional T-flasks and roller bottles. Therefore, a shift to stirred-tank biological control systems is essential in order to increase productivity. By enabling the parallel control of several bioreactors at the same time, monitored and controlled by powerful software solutions, vaccine development processes can be optimised in small scales and the parameters transferred in order to scale-up to large production volumes.

Parallel Processing – Learn from Failures and Optimise the Bioprocess

Process optimisation consumes time when experiments are running individually and sequentially. And these experiments are very costly. By utilising scale-down strategies and single-use bioreactors, the consumption of resources can be reduced. Parallel bioprocess control systems are well suited for scale-down approaches and offer the possibility to change individual parameters in several bioreactors at the same time, while monitoring and comparing the effect of the changes in parallel (Figure 1).



Single-use Solutions – A Step Ahead of Cross-contaminations

Process optimisation and development includes significant manual interactions, increasing the risk of contaminations. Traditional glass or stainless-steel bioreactors need to be carefully cleaned and sterilised after each run before they can be re-used. Especially nowadays, where time is crucial to find a cure against COVID-19, the use of single-use bioreactors offers the potential to speed up a bioprocess and prevent the loss of a whole run due to contamination.

Scalable Systems

Nearly five million people have been infected by the novel coronavirus so far. Due to its high infection rate, this number is expected to increase tremendously before a new vaccine will be available. In order to produce enough doses of vaccines to help develop immunity at a global scale, easy parameter and technology transfer is needed when scaling-up from bench to pilot and production. However, developing a scale-up strategy is time-consuming and cost-intensive. High titre, robustness of the process, constant product quality, fast turnaround times, and scalability are some of the success factors that need to be considered. It is important to work with bioreactors that are comparable at bench- and pilot- and production-sized bioreactors. Keeping in mind critical scalability-related engineering parameters like proportional vessel/impeller geometry, oxygen transfer rate (OTR), impeller power number (Np) and the impeller power consumption per volume (P/V) helps to optimise a scale-up strategy.

Experience the Power of Data

One of the major benefits of working with advanced bioreactor control systems is the use of powerful SCADA software. A powerful software suite, monitoring all critical parameters, automatically adapting feeding speed, gassing conditions, and many more parameters, is the heart of each process. With the help of software, limiting factors can be detected and eliminated to efficiently optimise a process. Thanks to the digitalisation, the global lockdown did not affect international collaboration of scientists and manufacturers. Like the scientists and manufacturers around the globe are communicating with each other, it is also important that the software is able to understand all the information delivered by the various sensors connected to a bioreactor. This is especially true when they are manufactured by different suppliers. Modern communication protocols such as OPC UA enable the seamless communication among devices, allowing the independent implementation into a process while being safe and stable.

Conclusion

Stirred-tank bioreactors are one of the key technologies needed on the journey of developing and producing a new vaccine (Figure 2). They are optimal tools during each step in upstream biology. Working with bioreactors enables the parallel control of several bioreactors, resulting in a more efficient and reproducible optimisation of various process parameters. The quality of the produced product greatly benefits from the possibility to program automated responses such as feeding cycles or pH control. And finally, large systems are available on the market that are suitable to operate in cGMP environments in order to produce vaccines.

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