

Advent Engineering Case Study

BioPharma Leader Scales Up Bioreactors Quickly and Cost-Effectively



A multinational company with a rich legacy of innovation was actively developing its biologics manufacturing capacity, with facilities under construction or expansion to allow the manufacture of greater quantities of new biopharmaceuticals. To enable this, the company needed to scale up the bioreactors it would use during the manufacturing process. The company engaged Advent Engineering to evaluate different design options and predict the performance of manufacturing-scale bioreactors under various operating conditions.



Challenge

A pharmaceutical corporation needed to predict the performance of manufacturing-scale bioreactors under various operating conditions and evaluate different design options to optimize production.



Solution

Trinity's Advent Engineering team partnered with the company to perform computational fluid dynamics (CFD) multiphase modeling.



Result

By using CFD to simulate the fluid dynamics and the working parts of the bioreactor, Advent was able to quickly and cost-effectively answer key questions related to the design and performance of the bioreactors.

Challenge

CFD multiphase modeling can reduce or eliminate the need to perform bioreactor scale-up studies by simulating full-scale manufacturing bioreactors to predict performance. Experimentation can be expensive and time-consuming, as it requires building a small-scale reactor, conducting small-scale experiments, analyzing results, then changing parameters. Such experiments must be repeated as needed to model different conditions, not all of which can be isolated.

CFD provides a faster, cost-effective alternative. It can be used to model bioreactor conditions at any scale by performing baseline simulations to predict large-scale performance, extracting detailed results, then updating the model and parameters as needed until arriving at an optimal design for large-scale fabrication. CFD modeling also provides detailed visual data that can complement or exceed experimental methods. This allows the pharmaceutical manufacturer to find a suitable operating match between the target bioprocess and the bioreactor, without having to undergo extensive experimentation.

Solution

Using CFD, the Advent team was able to simulate the fluid dynamics and the working parts of the bioreactor to simulate conditions that would normally be time-intensive or impractical on a manufacturing-scale bioreactor. Leveraging the team's extensive technical training, credentials, and real-world experience, Advent began by benchmarking a CFD model with one experiment, then testing how changing parameters in the CFD model impacted bioreactor performance. This saved significant time that would otherwise have been spent conducting time and resource consuming experiments.

Because the oxygen transfer rate, kLa , was the primary performance parameter of interest, the Advent team benchmarked a mesh-independent CFD model against an experimentally determined kLa . Advent then changed operating parameters (i.e., impeller speed and the gas sparge rate) on the mesh-independent model and compared the kLa prediction to experimental data. Good agreement provided confidence that the benchmarked bioreactor CFD model could be used to simulate various operating conditions to predict bioreactor performance.

Simulation models enabled the team to evaluate a variety of parameters, including:

- ▶ Velocity field for both gas and liquid phase
- ▶ Agitator fluid torque
- ▶ Fluid volumetric power
- ▶ Shear stress
- ▶ Overall hold-up
- ▶ Overall kLa value and distribution
- ▶ Gas phase volume fraction distribution
- ▶ Bubble residence time
- ▶ Bubble size group distribution
- ▶ Mean bubble diameter

By leveraging CFD as a predictive tool, the team delivered insight into different operating conditions and gas sparger designs.

Result

The CFD analysis enabled the team to answer key questions related to the design and performance of the bioreactors, including understanding, predicting, and explaining fluid problems; evaluating why a large-scale reactor might perform poorly compared to a smaller scale one; predicting when and where vortices form or local impellers flood; predicting levels of shear or the size of eddies throughout a bioreactor; and explaining anomalous behavior in a process.

Bioreactor performance is incredibly important to the manufacturing process; many companies end up trying to build bigger and bigger bioreactors or running multiple batches to arrive at the throughput needed, reducing efficiency and increasing costs. CFD simulation enabled the team to optimize the design of the bioreactors with results interpreted at a level often masked by natural variations in physical testing. The analysis also allowed the Advent team to optimize the design of the bioreactors before they were built, mitigating risk while improving speed to market.