

Pharmaceuticals • Chemical process

## ABEC

**Biopharmaceutical manufacturer uses Simcenter STAR-CCM+ to reduce blend time by 50 percent**

**Product**  
Simcenter

### Business challenges

Reduce time-to-market by accurately predicting and modifying bioreactor performance across a range of scales and platforms

Deliver product quality by creating a consistent formulation environment across scales and manufacturing platforms

### Keys to success

Use Simcenter STAR-CCM+ to rapidly determine best-performing designs

Validate high-fidelity CFD model using small-scale tests

Use validated CFD model to determine best designs for full-scale operations

Use high-fidelity simulation early in the scaleup process to understand hydrodynamic behavior

### Results

Cut blend time by 50 percent by using CFD simulation to determine better impeller designs

Reduced cost and time-to-market

Delivered bioreactor equipment that operates at predicted performance throughout the process

**Siemens Digital Industries Software solution helps ABEC to reduce risk, time-to-market and cost while delivering product quality**

### From lab scale to industrial scale

Every medicine ever developed started out in a lab, developed and tested in small batches until it was ready to be produced in large quantities. Although not unique to the pharmaceutical industry, the challenges of scaling up from lab-scale experiments to industrial-scale production are critical given the nature and intended use of the products. Scaleup is one of

challenges that ABEC has been dealing with since its inception over 45 years ago when it joined the marketplace as a supplier of bioreactors and fermenters. In many ways, the firm's timing couldn't have been better as major advances in cell culture and biotechnology were just emerging.

ABEC has been providing engineering, equipment and services to the biopharmaceutical industry throughout the world since 1974. Founded by Jack Wilson, ABEC provides custom-engineered solutions for the life sciences industry, supporting their efforts to create life-changing therapies. The company provides a range of engineering solutions for manufacturing therapeutics.





Since its inception, ABEC has enhanced its capabilities as technological advances became available. At the beginning, customer systems were being operated manually. ABEC initially helped its customers to automate their processes to achieve reproducible performance. Today it provides harvest, recovery and concentration capabilities, benefitting its customers by supporting the entire bioprocess. The company provides extensive aftermarket service and support, process consulting, equipment upgrades, maintenance services and customer training.

ABEC works with many of the world's pharmaceutical and biotech companies, and more than 3,000 of the company's systems are in use worldwide.

#### **Technology challenges in bioreactor modeling**

One of the main technology challenges facing ABEC customers is accurately predicting and modifying bioreactor performance across a wide range of scales and platforms. Each customer's needs and challenges determine the range of scales across which predictions need to be reproduced.

According to Paul Kubera, vice president of process technology at ABEC, "A typical scenario might involve a project that has moved from the laboratory bench at the tens-of-liters scale to process development, which may be operating on a few hundreds-of-liters scale. Another company on the verge of production might need to ramp up by thousands of liters in multiple units."

***“As an example, we demonstrated that we can cut blend time 50 percent by using laboratory tests to screen options and Simcenter STAR-CCM+ simulation to extend the results.”***

Paul Kubera  
Vice President, Process Technology  
ABEC





“Siemens provides us with the support we need to demonstrate to our customers this equipment can operate in a very predictable fashion immediately upon startup, reducing their time-to-market. Our relationship with Siemens Digital Industries Software helps us very capably provide that service.”

Paul Kubera  
Vice President, Process  
Technology  
ABEC

Platform incompatibilities present another potential obstacle. A company may be operating at one location with hardware that is different than that in use at a manufacturing location elsewhere. To solve this, ABEC assists the biopharmaceutical customer in bridging different platforms, from small to large, to ensure the same results are achieved. The challenge is to create a uniform environment that is consistent for each organism in a vessel at each of those scales across platforms.

According to Kubera, “In order to meet the requirements of the project, the growth of the organism must be supported – it needs food, a carbon source and to take in oxygen and give off carbon dioxide.

“It is critical to be able to deliver a known amount of oxygen in a given timeframe and remove carbon dioxide for all the organisms in the vessel. Depending on the customer objectives, a solution is tailored to meet their specific needs based on how tightly they need to constrain that solution regarding processes and validation of those processes.

“For instance, a customer may be heavily focused on geometric similarity and want uniformity as the equipment operates from a small scale to larger scale. Common practice uses two basic rules: maintain the same power per unit volume and keep everything the same geometrically.”

With this approach, performance parameters change as vessel size increases – for example, blending times increase, operating speed shifts and mixing forces get larger. All these changing parameters must be accounted for by the customer, who is growing the organisms. With ABEC’s use of predictive desktop calculations and simulations, customers have insight into the entire process

#### **Validating at small scale, executing at large scale**

ABEC employs a variety of approaches and methods to create solutions to these problems. These include calculations, lab models, testing of production equipment and computational fluid dynamics (CFD) modeling.

ABEC has found the most effective process includes desktop calculations, small-scale tests to generate data and validate CFD, full-scale CFD modeling and full-scale confirmation testing. ABEC relies on Siemens Simcenter STAR-CCM+ software for performing CFD simulations.

The desktop exercise tabulates information across the range of scales, including parameters for vessels and agitator details and size along with information on customer operation. Kubera observes, “We will look at consistent power per volume to start and see how various parameters like oxygen transfer or shear rate change. This comes out of the calculations and simulation.



“With Simcenter STAR-CCM+, we can run a computational simulation of the laboratory configuration and confirm the same results. We can then run a large-scale simulation and be confident that measured performance of the delivered equipment will track with expectations. As an example, we demonstrated that we can cut blend time 50 percent by using laboratory tests to screen options and Simcenter STAR-CCM+ simulation to extend the results.”

#### Demonstrating success

ABEC's expertise includes understanding process systems and simulation tools to support reactor design. It uses finite element analysis (FEA) for structural simulation, and CFD for fluid flow and process simulation. ABEC's investment in tools for process benchmarking and simulation have yielded a high return, allowing them to reduce their reliance on full-scale experimentation, ensure process stability across sites and platforms, increase the potential for enhanced production yield and reduce time-to-market.

One typical application of CFD in bioreactors is evaluating impeller blade designs for improving the blend time. As illustrated in figures 1 and 2, ABEC's approach is to validate the Simcenter STAR-CCM+ CFD model using results from small-scale experiments with different impeller designs, then use the validated CFD model to extrapolate the results to full scale.

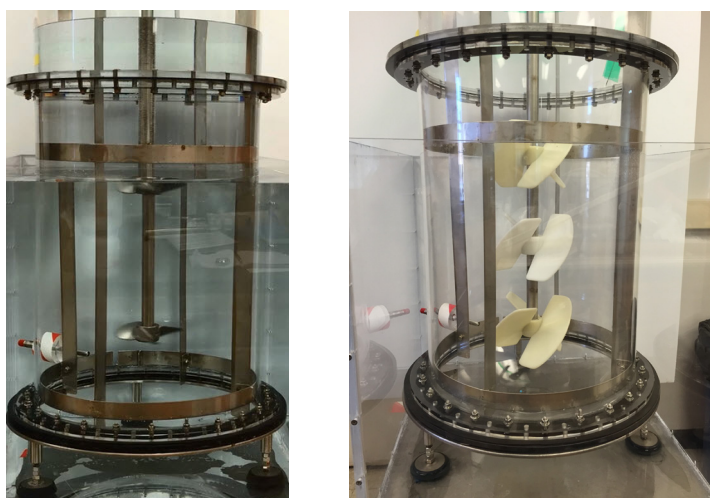


Figure 1. Experimental setups used for small-scale model testing of impeller configurations.

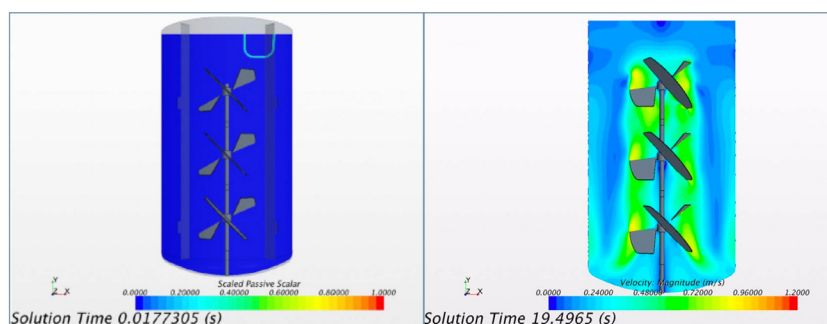


Figure 2. Shown are Simcenter STAR-CCM+ simulations of a triple low-shear impeller blender, which are used to simulate the operation of full-scale bioreactor units.

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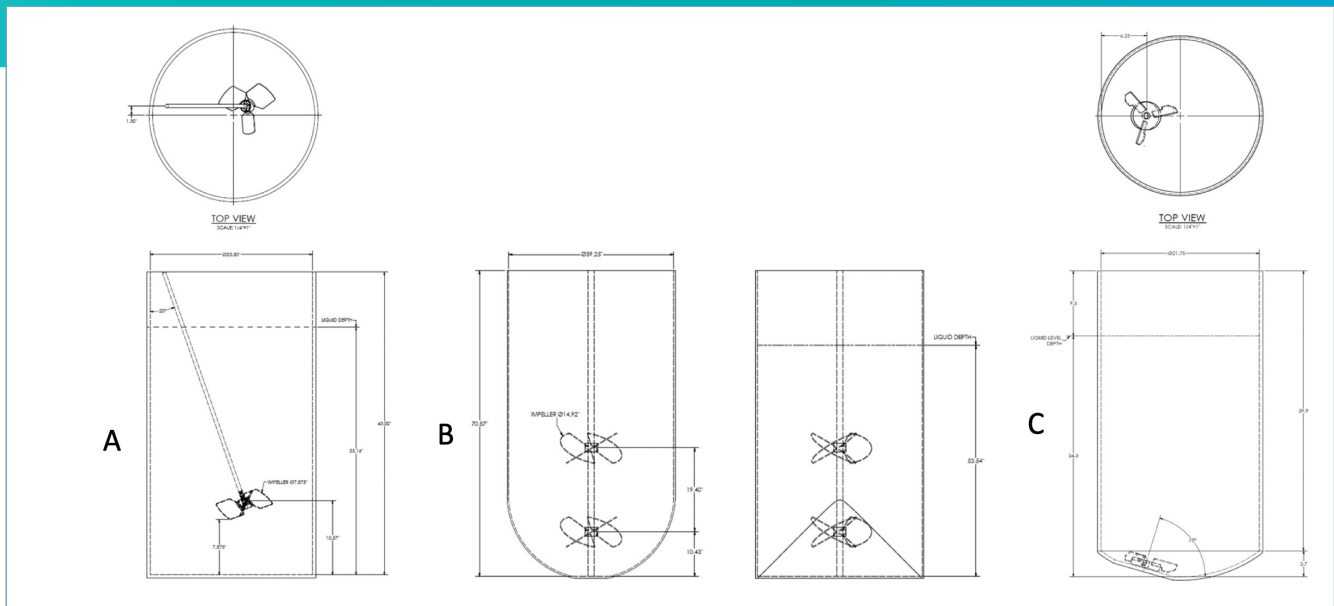


Figure 3. Platform options for bioreactor performance evaluation.

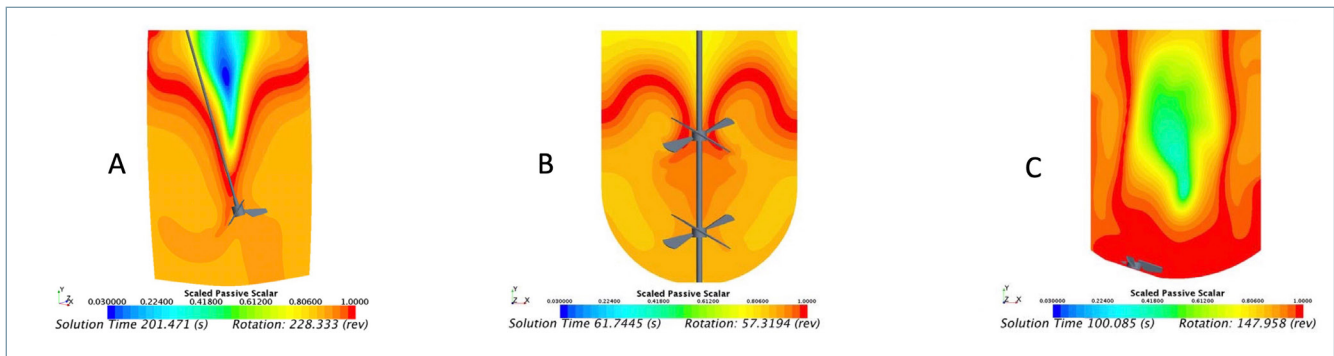


Figure 4. Comparing CFD simulations at full scale (at 95 percent volume uniformity) for each platform option, showing more homogeneous mixing in platform B.

Another typical application involves evaluating bioreactor production platforms for cell culture and bacterial fermentation – a critical first step in the production of biologicals. The goal is to assess the suitability of each platform for providing the same environment for each organism independent of scale. As illustrated in figures 3 and 4, ABEC uses Simcenter STAR-CCM+ simulations to guide the selection and determine which one best suits the customer's volume, geometry, environmental, production, schedule and economic constraints.

Yet another application involves the detailed assessment of concentration vessel geometries – as product is concentrated in filtration applications, a stepped-volume configuration (illustrated in figure 5) is often used to manage batch geometry. When a new product or process suggests the use of a smaller sump volume, the question arises as to whether the sump volume should be modified rather than replacing the entire tank. Changing to a smaller sump leads to a smaller mixer, which affects blend time, vortex formation and short-circuiting (referring to the situation in which recirculated flow exits the tank quickly and is not well-blended with the sump contents).

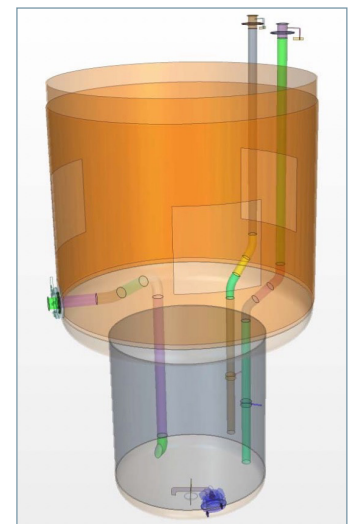


Figure 5. Stepped-volume configuration used to manage batch geometry as product is concentrated in filtration applications.



## Solutions/Services

Simcenter STAR-CCM+  
[plm.automation.siemens.com/global/en/products/simcenter/STAR-CCM.html](http://plm.automation.siemens.com/global/en/products/simcenter/STAR-CCM.html)

## Customer's primary business

Since 1974 ABEC has been a leader in delivering integrated process solutions and services for manufacturing in the biopharmaceutical industry. Many of the world's pharmaceutical and biotech companies are ABEC customers. Numerous leading therapies are manufactured by processes and equipment engineered, manufactured, installed and serviced by ABEC.  
[abec.com](http://abec.com)

## Customer location

Bethlehem, Pennsylvania  
United States

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ABEC uses Simcenter STAR-CCM+ simulations to generate detailed insights into the effects of geometry and mixer options for each of these behaviors. As illustrated in figures 6 and 7, simulations reveal details of the velocity vectors, flow streamlines, particle tracks and even the air-water interface, leading to insights about the level of mixing, vortex formation and air entrainment resulting from any given sump volume and mixer combination.

In each of these cases, robust, high-fidelity CFD simulations enable ABEC to refine its understanding, address questions and verify expected behavior at scale, which is especially critical in situations in which experimentation is not practical. Simulation also increases the potential for enhanced production yield by allowing detailed numerical experiments to be carried out on

the digital twin of any given bioreactor configuration to determine opportunities for process improvement.

As valuable a tool as Simcenter STAR-CCM+ is for ABEC, they are aware that it is capable of even more: "We don't perform enough CFD to take full advantage of all that it can do for us," says Kubera. "Siemens provides us with the support we need to demonstrate to our customers this equipment can operate in a very predictable fashion immediately upon startup, reducing their time-to-market. Our relationship with Siemens Digital Industries Software helps us very capably provide that service."

ABEC continues to innovate, recently introducing the 4,000-liter Custom Single Run™ bioreactor, effectively doubling the industry standard capacity for single-use bioreactors.

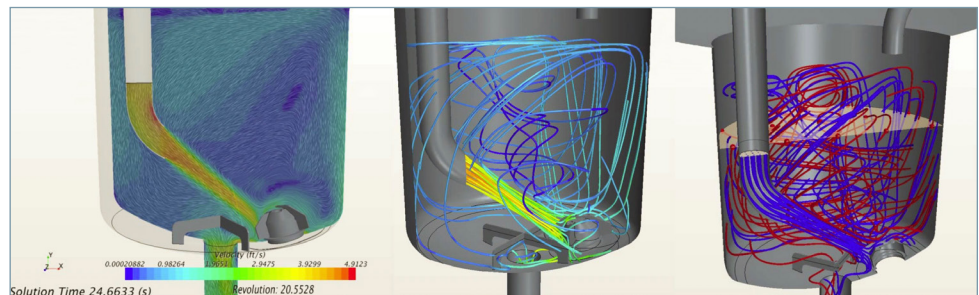


Figure 6. Simcenter STAR-CCM+ simulations showing velocity vectors, flow streamlines and particle tracks in the sump, indicating little short-circuiting and rapid dissipation of the recirculating flow by the impeller.

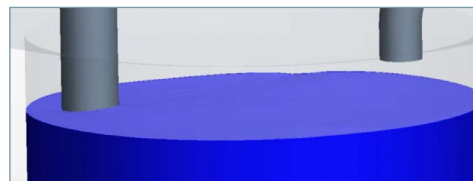


Figure 7. The air-water interface in the sump shows a low level of deformation, indicating no vortex formation or air entrainment.

## Siemens Digital Industries Software

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