



Single-use technologies

DynaDrive Single-Use Bioreactor (S.U.B.)

Dynamic cell culture performance
with right-sizing flexibility

Upstream bioproduction has experienced substantial movement toward single-use systems. This has been driven primarily by the need to reduce contamination risk and cleaning requirements when compared to stainless steel systems, and to allow for faster changeover of equipment between batches. At the same time, bioprocess manufacturing operations have matured significantly, and intensification of cell culture processes has pushed the limits of legacy single-use bioreactor systems.

With a continued focus on large-scale monoclonal antibody production, and tremendous growth of gene therapy and viral vector vaccines, companies are exploring how to scale manufacturing processes efficiently. The Thermo Scientific™ DynaDrive™ Single-Use Bioreactor (S.U.B.) is the latest advancement based on our history of proven innovation, offering superior performance to accommodate larger volumes as programs progress to commercialization.

Next-generation impeller drive train brings flexibility and economy of scale to single-use bioreactor technology

The DynaDrive S.U.B. can decrease the cost of production by 25% through a reduction in equipment, materials, consumables, and labor. The increased reactor size lowers the number of production batches required for a given volumetric demand. Beyond its value when compared to other single-use reactors, the DynaDrive S.U.B. expands the range for which single-use technologies (SUT) are a legitimate alternative to traditional stainless-steel bioreactor platforms.

Economic modeling has shown it provides both a lower average cost per gram and net present cost of investment up to scales of 4,200 kilograms per year of production. It is one of the largest single-use offerings in the market and is backed by the Thermo Fisher Scientific reputation for excellence. With a long history of maintaining a trusted bioreactor supply partnership measured by validation success, our technical professionals and continued support provide the reliability and flexibility needed to meet your needs, regardless of scale.

Meeting your needs of:

High performance that is predictable, flexible, and multipurpose

Through:

- A scalable design providing efficiency in manufacturing with the ability to transfer processes from 50 L up to 5,000 L
- Performance enhancements in mixing, power input per volume, and optimized $k_L a$ to accommodate high-density cell culture processes with 0.1 vvm flow
- Scalable and streamlined data flow, with digital scaling tools and robust data packages with integrated hardware and an automation solution: Thermo Scientific™ TruBio™ Bioprocess Control Software powered by the Emerson™ DeltaV™ Distributed Control Platform
- Hardware and Thermo Scientific™ BioProcess Container (BPC) design optimization for perfusion cell culture process capability

Cost-effective drug substance manufacturing

- Economies of scale with large-scale production, efficient labor usage, reduced vessel count, and optimized >10:1 seed train turndown, decrease the cost of production by 25%
- Leveraging higher in-vessel turndown ratios to run multiple stages in a single vessel, reducing the number of BPCs loaded and unloaded, as well as the number of vessels needed in the overall facility

Improved sustainability

- Reduced consumable waste by reducing waste per volume and vessel count

Reliability and risk reduction

- Robust and ergonomic BPC design for ease of loading with install assist hardware, and daily operations with reduced tubing connections required
- BPC film and components tested for leachable and extractable (L&E) evaluation according to BioPhorum Operations Group (BPOG) guidelines
- Hardware that is designed to meet 21 CFR 820 cGMP requirement

Greater productivity with increased flexibility

Efficient and fast

Leveraging higher in-vessel turndown ratios to run multiple stages in a single bioreactor can reduce the number of bags loaded and unloaded, as well as the number of bioreactors needed overall in the facility. With product sizing available up to 5,000 L, mass transfer and mixing allows for the use of the same technology over a larger range of facility networks, thus simplifying process transfers. This flexibility provides consistency from research and development to manufacturing phases. The DynaDrive S.U.B. provides:

- Optimal-precision load cells and standard sight-volume indicators allow you to keep your processes running efficiently
- Optional brushless DC motor includes encoder feedback for improved RPM accuracy and is ground-fault circuit interrupter (GFCI)-compatible
- 3/8 in. dimpled jacket improves flow rate through the water jacket for higher-performance temperature control
- Graduated sight-volume indicators accommodate visual volume references at a glance



Unsurpassed performance

Improved seed-train process

The DynaDrive S.U.B. brings a new level of performance to single-use bioprocessing. A >10:1 seed-train turndown ratio allows users to optimize the seed train, which helps reduce labor and risk, and improves facility space utilization.

The data in Figures 1 and 2 illustrate throughput for a full year with equivalent drug production yields, examining labor costs and facility footprint reduction. As shown in Figure 1, a 54% labor reduction is achieved by decreasing the amount of setup and takedown maintenance required by increasing the size, and thus limiting the number, of S.U.B. units needed to produce an equivalent production yield. Figure 2 highlights the reduction in facility footprint following the same principal of economies of scale. The larger the S.U.B. size and the higher the turndown ratio, the fewer units are required to produce an equivalent amount of drug.

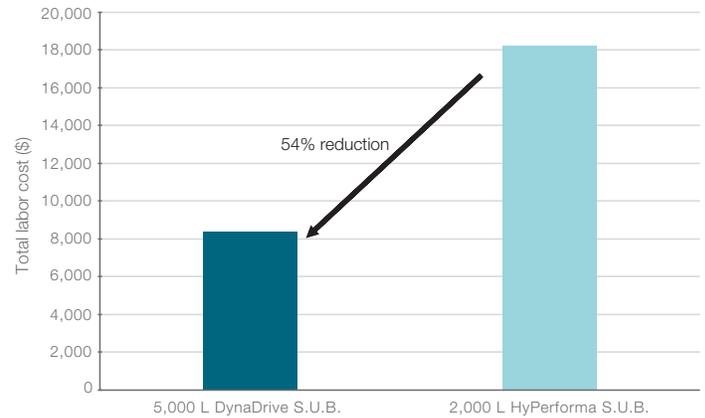


Figure 1. Evaluation of S.U.B. labor costs per year with matching production throughput.

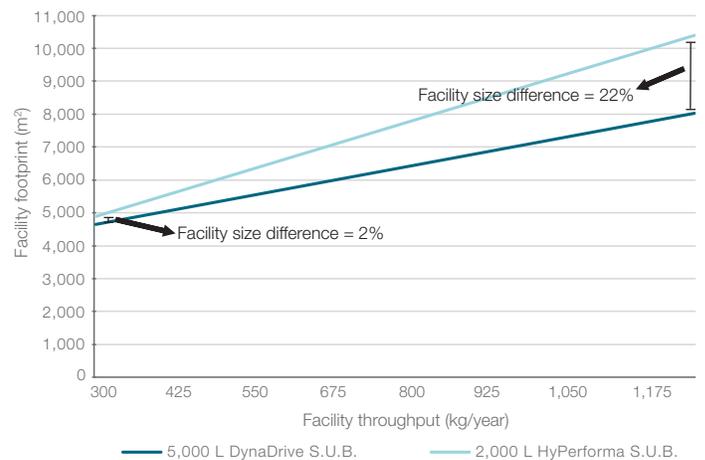


Figure 2. Comparing facility footprint reduction of the DynaDrive S.U.B. vs. legacy HyPerforma S.U.B.s.

Superior power input per volume and mixing times

Improved power input per volume (PIV) is critical to support the cell growth potential of modern cell lines and processes. PIV is normally enhanced by increasing either the RPM or the size of the impeller. Both of these changes can have detrimental effects, such as flooding of the impeller, or worse, cell shearing. Another way to increase PIV is to implement multiple impellers. For years, multiple impellers have been common in large stainless steel bioreactors. Some S.U.B.s also have multiple impellers, but they are ridged and difficult to maneuver, store, and deploy.

The DynaDrive S.U.B. has been designed specifically to increase PIV. The flexible drive train includes multiple impellers that provide more PIV while still maintaining reasonable RPM and tip speeds. The unique drive train is also flexible, which allows the BPC to be folded to minimize the size of packaging and improve BPC deployment and disassembly.

The increased number of impellers, location of the impellers, and cubical design of the reactor not only provide impressive PIV, but also improve mixing times of the bulk fluid. Mixing times have been confirmed to be less than 60 seconds at all scales, from 50 L to 5,000 L.

O₂ and CO₂ mass transfer ($k_L a$)

Thermo Scientific™ HyPerforma™ Single-Use Bioreactors (S.U.B.s) utilize a drilled hole sparge (DHS) for optimal $k_L a$ performance. The DHS used in the DynaDrive S.U.B. has been enhanced and specifically designed to optimize the $k_L a$ performance. The laser-cut holes in the DHS are smaller and the quantity has been increased so that bubble size is uniform and sized properly for O₂ delivery and CO₂ stripping.

The cubical design and impeller placement also increase the residence time of the bubbles in the reactor. As bulk-fluid

mixing occurs, the bubbles are pulled into and down the drive train, which optimizes the time needed for mass transfer. Results have shown that mass transfer $k_L a$ is better in the DynaDrive S.U.B. with 0.1 vvm flow than the standard HyPerforma S.U.B., allowing users to increase their cell culture performance by utilizing the improved $k_L a$. Therefore, the DynaDrive S.U.B. allows users to increase their cell culture performance by utilizing the better $k_L a$. Or, users can achieve the same $k_L a$ that they are used to but with a lower air-flow rate.

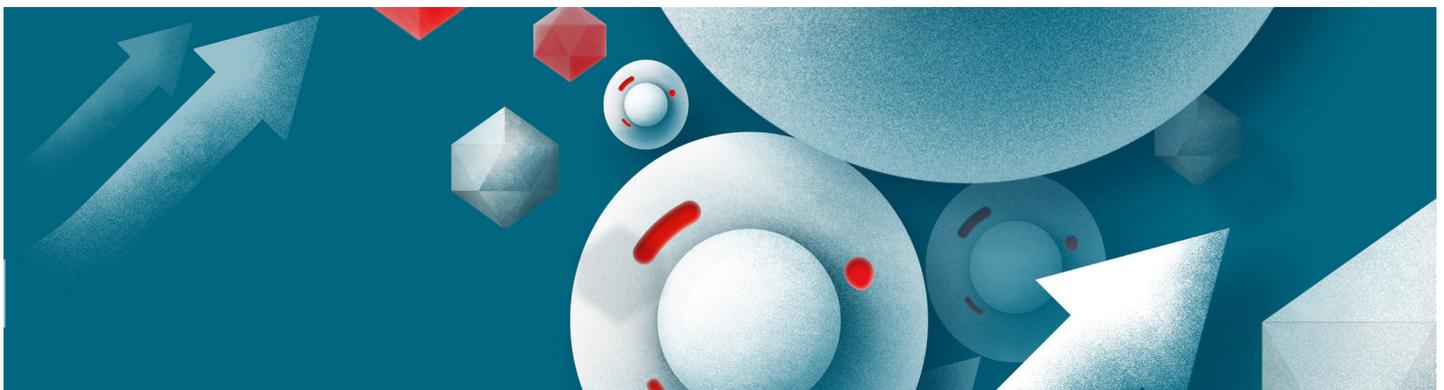
Volume flexibility within the reactor

Users often wish to multipurpose their reactor and run various processes within the same vessel. The DynaDrive S.U.B. provides that flexibility. High-density cell culture can be achieved and maintained at 4:1 turndown ratios. That means that the same 50 L reactor can be used as a 12–50 L terminal volume reactor, or the 500 L DynaDrive S.U.B. can be used as a 120–500 L reactor. Leveraging this flexibility means more of the same type and size of vessels can be used in a flexible-volume manufacturing or process development (PD) suite.

Consistent automation and control

Our automation has the ability to integrate with Thermo Scientific™ TruBio™ software, powered by the DeltaV Distributed Control Platform and the Thermo Scientific™ HyPerforma™ bioprocess controllers to provide unified and seamless data aggregation and quality control improving the user experience.

For specifications and more information on the Thermo Scientific™ HyPerforma™ G3Lite™ and G3Pro™ bioprocess controllers, refer to the appropriate product data sheet or contact your sales representative.



Innovative cubical geometry and ergonomic design

The DynaDrive S.U.B. is the latest advancement in our line of elegantly designed and highly functional S.U.B. hardware. It is designed to meet 21 CFR 820 cGMP requirements. All sizes of the DynaDrive S.U.B. include doors that provide ample space for BPC loading. The doors have been carefully designed so all probe ports and tubing line sets are positioned correctly and easily without the need to be put through constrained holes. The S.U.B. tank provides a small footprint and offers easy cleaning capabilities associated with an open-cart frame. We offer:

- Simple BPC loading with vertical access door on all sizes
- Efficiently sized hardware to help minimize vessel footprint
- Reduced hold-up volumes with smartly designed tank floor



BioProcess Containers

Quality and performance

The BPCs for the DynaDrive S.U.B. are available with our proprietary Thermo Scientific™ Aegis™5-14 film. Our film is widely used today by a large number of global biopharmaceutical companies for all bioprocessing steps.

We have completed the BPOG L&E testing guidelines for all components used in Thermo Scientific™ DynaDrive™ BioProcess Containers.

Single-use global network supply

We are committed to finding new solutions to optimize the way we deliver single-use products to our customers around the globe. These standardization efforts are designed with the goal of providing the shortest possible lead times while consistently meeting or exceeding industry quality standards, no matter where the single-use product is built.

The creation of the SUT manufacturing network is part of our global strategy to help provide our customers with a more responsive supply chain for our Thermo Scientific BPCs and fluid transfer assemblies (FTAs).

This SUT manufacturing network allows for more efficient capacity utilization through established manufacturing redundancies with the capability to transfer capabilities to meet demand across the network to meet complex customer needs. A core strength in the application of open architecture design principles to support customer-specific configurations is maintained but balanced with the option for standardized components and raw materials prequalified and stocked for use across our network.

Key benefits

We can address your specific application with either a standard or customized configuration. The standard designs are configured for a variety of applications, while the custom designs are for customer-specific applications.

The key benefits for our BPCs include:

- The latest sensor technology in single-use or autoclavable probes, including:
 - pH—electrochemical single-use or reusable probes, and optical single-use sensor
 - pO₂—optical single-use or reusable probes
 - Foam—single-use foam sensor built into the BPC
 - Capacitance—single-use sensor or reusable probe
 - Raman analysis—optical probe port built into the BPC
- Optional ports for alternating tangential flow (ATF) or tangential flow filtration (TFF)
- Built-in condenser system for 3,000 L and 5,000 L BPCs, which helps extend the life and reduce the quantity of exhaust filters needed
- Utilization of crossflow sparging technology to assure proper head-space gas mixing during low-volume seed or terminal cell cultures

Learn more at thermofisher.com/dynadrive

thermo scientific

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