Xcellerex™ XDR-10 cell culture bioreactor system

CELL CULTURE

The single-use Xcellerex™ XDR-10 is a flexible, stirred-tank bioreactor system suitable for use in process development, small-scale production, and process troubleshooting (Fig 1). XDR-10 delivers accurate and predictable results that minimize the number of required runs, to save time, work, and costs. The system has a design based on the same technology platform as the larger Xcellerex™ bioreactors, allowing smooth scale-up from bench-top to pilot and full production scale in large bioreactor systems. The XDR-10 bioreactor system handles working volumes from 4.5 to 10 L and is available in single-, twin-, triple-, and quad-vessel configurations. The possibility of a multi-vessel configuration facilitates the use of design of experiment (DoE) strategies in, for example, process development.

XDR-10 bioreactor system offers the following benefits:

- Accurate and predictable performance for reliable process development and troubleshooting
- Multi-vessel configuration facilitates DoE strategies
- Flexible sparger options to suit a broad range of cell lines
- Industrial level process control and automation
- Convenient scale-up to larger reactors, in particular within the same technology platform

The XDR-10 bioreactor system is part of the Xcellerex™ XDR bioreactor product line spanning working volumes from 4.5 L to 2000 L (Fig 2). The product line offers the benefits of single-use technology and stirred-tank design in a modular, turnkey, bioreactor platform. Designed for scalability and robustness, the XDR bioreactor systems offer the performance and flexibility needed, from process development to large-scale biopharmaceutical manufacturing. All XDR bioreactor systems can be operated in batch, fed-batch, and perfusion modes.

System overview

The XDR-10 bioreactor system was developed to extend the Xcellerex™ portfolio and deliver true scalability, from process development to large-scale manufacturing, using the same platform technology. The XDR-10 is an excellent bench-top bioreactor tool for activities such as technology transfer from stainless steel to single-use vessels, process troubleshooting, and development for various applications.

Fig 1. XDR-10 bioreactor system with vessel frame, instrument tower, and single-use bag assembly.

Fig 2. The complete range of XDR bioreactor systems is available with maximum working volumes 10 L, 50 L, 200 L, 500 L, 1000 L, and 2000 L. Images are representative, some features and accessories may vary depending on the bioreactor configuration.

The XDR-10 design is based on the same principles as conventional bioreactors. Vessel geometry, gas transfer, and mixing are industry standard and chosen to mimic conditions in larger scale. Scaling is supported by traditional methodology, with measures such as shear, tip speed, power, and fluid velocity, just like the larger Xcellerex™ systems.

The XDR-10 bioreactor comprises three main parts: vessel frame, instrument tower, and disposable bioreactor bag assembly. The vessel shell and tubing manager are made of hard plastic with a convenient snap-lock system. The vessel frame and base are constructed of 304 stainless steel. The supporting instrument tower contains industry standard peristaltic pumps and pH and dissolved oxygen (DO) transmitters. Measurement and control are performed with an Allen-Bradley™ controller (Rockwell Automation Inc) and an AVEVA Solutions (formerly Wonderware™) user interface (AVEVA Group plc) via a PC laptop. The system is available in single-vessel or multi-vessel configuration, the latter with up to four parallel reactors to facilitate DoE.

System components

Vessel frame

The vessel frame supports the disposable bioreactor bag and contains a powerful, bottom, center-mounted magnetic drive that couples with the impeller in the bag. The brushless drive includes a sealed magnetic coupling, for years of trouble-free operation. The bag is easily inserted via a front opening double-door. After the bag is placed in the correct position, the doors are closed with a convenient snap-lock mechanism. Integrated tubing manager and exhaust filter holder facilitate set-up and bag handling. The temperature of the culture is accurately controlled with two heating pads, integral to the frame. The heating pads eliminate the need for heat-blanket adjustments. An exhaust gas filter heater is also included. The compact vessel frame, with a footprint (W × D) of 12.75" (32.4 cm) × 14" (35.6 cm), makes XDR-10 well-suited for bench-top use. The entire vessel subsystem may be placed on an optional bench scale for weight-based applications such as perfusion culturing.

Instrument tower

Each bioreactor vessel is supported by an XDR-10 instrument tower that contains peristaltic pumps, mass flow controllers (MFCs), and a transmitter for the pH and DO sensors. Standard gas and liquid management configurations cover most applications in cell culture.

Ethernet is used for communication between the instrument tower and the PC laptop. In a multi-vessel configuration, the instrument tower can be run in either master or slave configuration, depending on if the setup includes two, three, or four reactors in parallel. For more details on single- and multi-vessel configuration, see "Single- and multi-vessel configuration".

Liquid management

The instrument tower can be configured with up to four variable-speed peristaltic pumps with ranges to support liquid addition or removal. The peristaltic pumps can be configured for use with various control loops, including base addition for pH, substrate feeds, and level control.

Gas management

Up to six thermal mass flow controllers in combination with the different available sparger options offer multiple sparging regimes, overlay gas addition, and the ability of mimicking gas dynamics in larger scale.

Measurement of pH and DO

The pH and DO probes provide real-time data, monitored throughout the whole process using AVEVA Solutions (formerly Wonderware™) software. The pH probe relies on the well-known and industry-proven liquid chemistry technology. The DO probe is polarographic with a stainless steel construction. One dual-use transmitter is used as the interface between probe and instrument tower.

Measurement of dissolved carbon dioxide (CO_2)

Optional CO_2 measurement is available using a stand-alone bench-top CO_2 transmitter. Using an available analogue input, the CO_2 transmitter interfaces to the instrument tower. Conventional, reusable probe technology is used for monitoring dissolved CO_2. CO_2 measurement provides important insights during process development prior to scale-up.

Single-use bag assembly

The Xcellerex™ disposable bioreactor bag assembly (XDA) is an essential part of the process performance achieved with all XDR bioreactor systems. The XDR-10 bag is manufactured from a USP class VI-compliant flexible low-density polyethylene film and has a robust design to withstand demanding process conditions. The bag comes with an integrated, bottom- mounted magnetically coupled impeller/sparger assembly, which connects with the magnetic drive head in the vessel frame (Fig 3). The impeller is of M40e 40°, pitched-blade type with medical-grade ceramic bearings. The ceramic bearings were originally developed for aggressive mixing applications. The bearings meet the relevant industry requirements for leachables, extractables, and particulates according to the bag validation guide (for more information, please contact your sales representative).

Fig 3. Impeller/sparger assembly for XDR-10 with three pitched blades.

Up to four sparger elements are included in the impeller/sparger assembly and positioned below the impeller blades to maximize gas dispersion and dynamics. The impeller/sparger technology plays a major part in the performance of the XDR-10 bioreactor and provides a powerful and robust agitation system with minimal risk of seal leakage.

Additional XDA bag components include tubing with a combination of weldable sections and aseptic connectors for liquid addition/removal; a disposable pressure sensor; and filters for exhaust, sparge, and overlay/headspace gas. XDA bioreactor bags support insertion-type reusable probes. For details on probes, see "Measurement of pH and DO".

The XDR-10 bioreactor bags are available in Pro and ProPlus versions. Pro-type bags are available for all bioreactor systems and have validated sparger configurations, established based on customer feedback and our own biomanufacturing experience. ProPlus incorporates an additional centrally located diptube used particularly for perfusion or other subsurface, liquid addition or removal applications. To assist in efficient sampling, sample manifolds are available optionally.

Supervisory control

Supervisory control of the XDR-10 bioreactor can be performed via a PC laptop with AVEVA Solutions (formerly Wonderware™) software. Ethernet communication standards are included for equipment and local area network connectivity. The control system provides real-time data acquisition, enables accurate process control, and offers convenient, real-time trending.

Single-and multi-vessel configuration

The XDR-10 bioreactor system can be operated in single- or multi-vessel configurations, depending on the user needs. The single-vessel configuration with PC laptop is an excellent starting point if future needs may include additional vessels. A single-vessel setup is suitable for standalone experiments or when the available space is limited.

For more complex experimental setups and, for example, DoE strategies, a multi-vessel configuration is recommended (Fig 4). Multi-vessel configurations are available in twin, triple, and quad setups with two, three, or four parallel reactor vessels, respectively. The same software is used in management of the larger XDR bioreactor systems up to 2000 L scale, providing a universal platform that meets the requirements of both process development and manufacturing. Connectivity to legacy automated systems is supported by open platform communications (OPC). Each bioreactor vessel is supported by an instrument tower. The towers are run in master or slave configuration depending on the complete setup (Table 1).

Table 1. Instrument setup for single- and multi-vessel configuration

	Single	Dual	Triple	Quad
Vessels	1	2	3	4
Instrument towers in master configuration	1	1	2	2
Instrument towers in slave configuration	-	1	1	2
Instrument towers total	1	2	3	4
PC laptop	1	1	1	1

Fig 4. Multi-vessel configuration provides flexibility for process development.

Qualification support

The XDR-10 bioreactor system is designed for use in environments that require 21 CFR Part 11 and Good Automated Manufacturing Practice (GAMP™). The system is delivered with an operating manual, system specification, drawings, and major component documentation. Industry standard installation and operation qualification (IQ/OQ) packages are available as an option.

System specifications

System specifications are listed in Table 2.

Table 2. Specifications of XDR-10 cell culture bioreactor system

Specification	
Max working volume (L)	10
Min working volume (L)	4.5
Volume turn-down ratio	2.2:1
Vessel i.d. (in)	8
Aspect ratio (H/D)	1.5
Vessel	White acrylic
Filter heater assembly	1
Additional filter heater assemblies	0
Impeller, M40E pitched-blade type	3 blades at 40° pitch
Standard bag assembly	Pro: 29041068 ProPlus: 29041069
Process instrumentation	
pH probes	1
DO probes	1
MFC* (standard)	4
Additional MFC† (optional)	2
Internal pumps (standard)	3
Additional internal pumps (optional)	1
External pumps (optional)	2
Temperature control	2 heating pads
Weight measurement	Optional bench scale
Control options	PC laptop
Standards	Built to GAMP™ 5 standards/ 21 CFR Part 11 compliant
Automation hardware	Allen-Bradley™ (Rockwell)
Operator interface	AVEVA Solutions HMI* (AVEVA Group plc)
Data historian	AVEVA Solutions

* Human-machine interface
† Mass flow controllers

Note! For specifications of the larger XDR bioreactor systems, please see data file CY11759-10Aug20-DF.

Applications

XDR-10 bioreactor system has successfully been used to cultivate a wide range of organisms including CHO cells, HEK cells, insect cells, and hybridoma. The system can be operated in batch, fed-batch, and perfusion modes.

For more information on the XDR-10 bioreactor system, please contact your local sales representative.

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