

# Mobius® Breez Microbioreactor

## A 2 mL Automated Perfusion Cell Culture Platform

The Mobius® Breez Microbioreactor is a 2 mL automated single-use perfusion cell culture platform designed to support gentle, adaptable, and reproducible cell culture processes. The system is capable of accelerating a range of applications such as cell line development, media screening and optimization, and early process development.

The Mobius® Breez Microbioreactor allows you to increase efficiency and reduce development timelines and costs over traditional technologies that require more material consumption. The platform comprises gamma-irradiated microbioreactor consumables with integrated fluid supply, four bioreactor controllers (PODs), accompanying hardware and intuitive software. Each POD provides closed loop control for pH, DO, temperature, and cell density via OD. With the Mobius® Breez Microbioreactor, readily run four experiments simultaneously and independently on your benchtop. Total control is at your fingertips to help support your development program and company goals, ensuring timely delivery of high quality data sets you can rely on.

### Benefits

- Enables perfusion processes to achieve high cell densities in 2 mL
- Run more experiments in parallel for higher efficiency
- Reliable run-to-run performance, obtain high-quality perfusate on demand
- Freedom from hands-on work with automated control and monitoring
- Operational flexibility allows you to save on development time and costs
- Easy to set up and use, allowing you to focus on your goals

### Modalities

- Monoclonal antibodies
- Recombinant proteins
- Cell therapy



## System Components

Perfusion is becoming a typical approach to achieving upstream process intensification. The ability to scale down these processes, however, has been limited due to a lack of appropriate technologies. Scientists have been forced to choose between small-volume cultures with no control capabilities and larger bioreactors with complete process control but at vastly increased costs and media volume requirements, limiting high throughput.

The Mobius® Breez Microbioreactor is designed to meet the needs of full control at a small working volume with high-throughput capabilities. The system comprises of a single-use, 2 mL microbioreactor consumable, four microbioreactor controllers, utility and communication hardware, and a laptop embedded with control software.



### Fully Automated Controller PODs

Each POD (pneumatic optical digital) controller operates independently and provides mixing and closed loop pH, DO, temperature, and cell density control



### Intuitive Software

Easy-to-use interface makes it simple to set up the experiment, monitor and control the PODs and microbioreactor consumable



### Gamma-Irradiated Microbioreactor Consumable

The single-use microbioreactor cassettes with fully integrated fluidics enable quick experiment setup and takedown with reduced contamination risk



### Microbioreactor Cassette

Fully integrated microfluidic bioreactor includes pH, O<sub>2</sub>, and OD sensors, as well as perfusion filter and pump

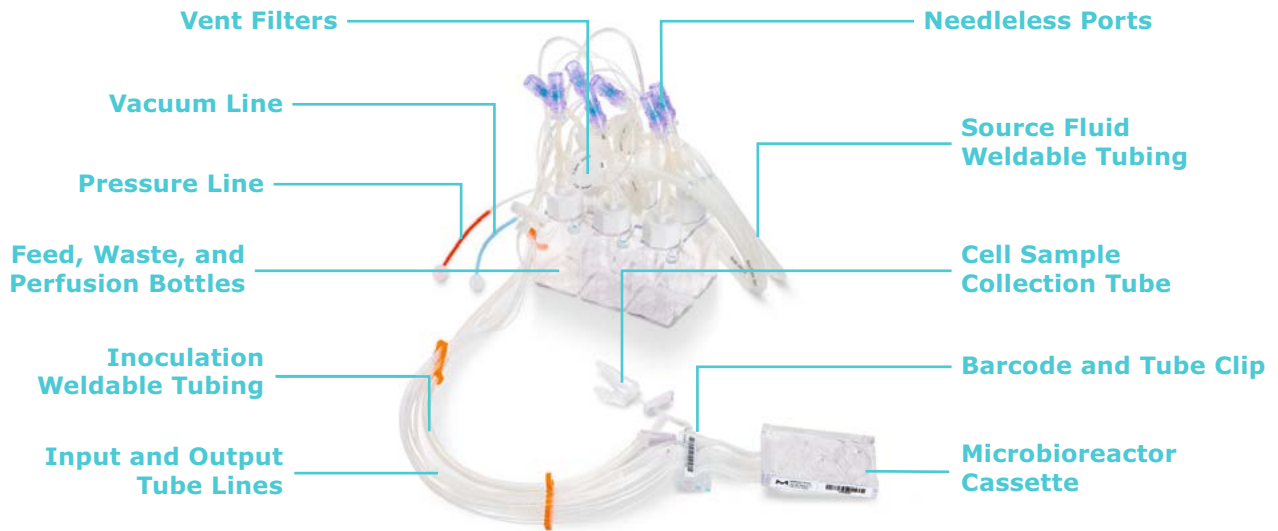


### Basestation Hub and CO<sub>2</sub> Sensor Box

The Basestation Hub and CO<sub>2</sub> Sensor Box supplies regulated gas pressure, electrical power, and communication to the PODs

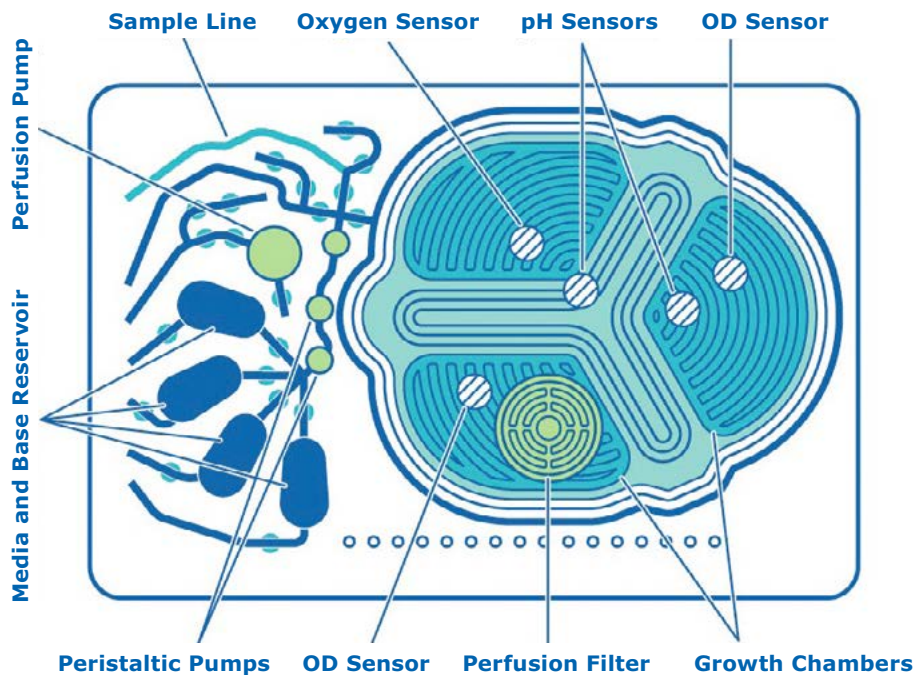
## Microbioreactor Consumable

Existing small-scale solutions consume time and labor during experiment preparation by requiring manual assembly of components and sterilization. The Mobius® Breez Microbioreactor is designed to help you set up perfusion cell culture experiments with ease and speed. It is a fully integrated assembly consisting of the microfluidic bioreactor cassette connected to a bottle rack that supplies fluids and collects perfusion harvest and waste. The microbioreactor consumable is single-use and gamma irradiated, enabling easy installation and quick take down while mitigating contamination risks. Media fill and inoculum transfer are possible in an open bench space through tube welding. Process sample is effortlessly delivered to a cell sample collection tube and harvest sample is accessible via needleless port of the perfusion bottle.



## Integrated Microfluidics and Sensing Controls

The 2 mL microbioreactor cassette integrates automated pumps, valves, optical sensors, and a cell retention filter. Four bioreactors can operate simultaneously, each with its own independent POD controller that provides closed loop control for pH, DO, temperature, and cell density via OD. Mixing and oxygenation supply is enabled through inflation/deflation of a gas permeable silicone membrane within the microbioreactor cassette layers. Precise fluid delivery is achieved via four feed inputs while three fluid outputs provide sample delivery, perfusion harvest, and waste removal.

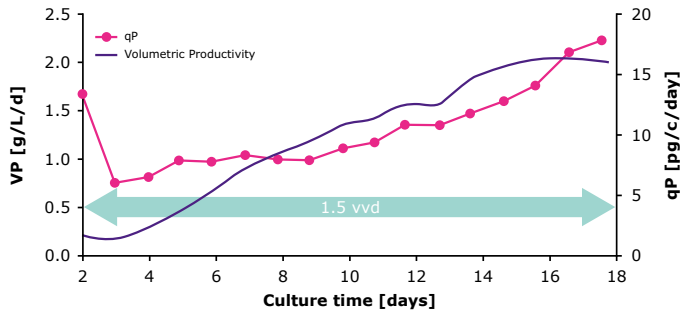
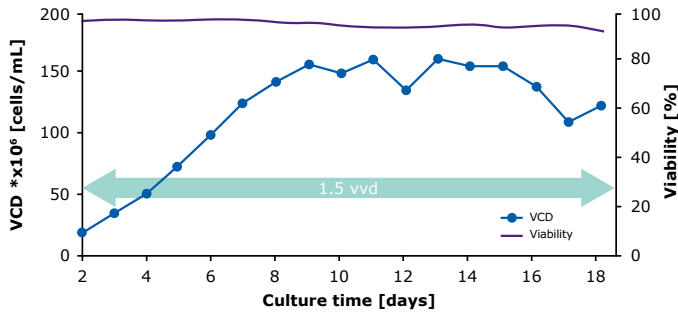


# Performance

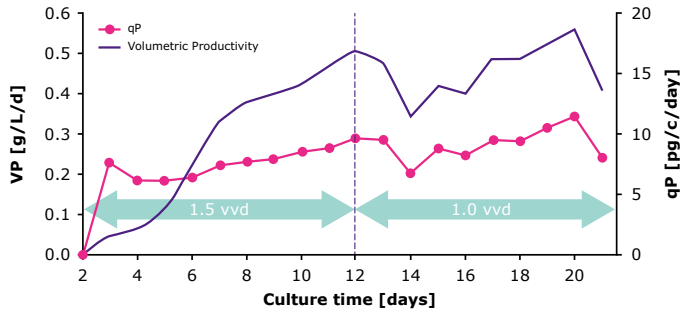
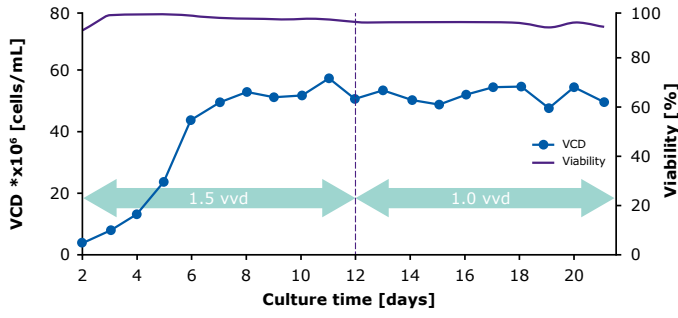
## Steady State and Dynamic Perfusion

To meet changing and demanding needs in process development, a small-scale cell culture platform must offer operational flexibility. Continuous cultures with the Mobius® Breez Microbioreactor are possible in both steady state and dynamically controlled conditions. In dynamic perfusion, the viable cell density (VCD) is allowed to get as high as possible without cell bleed control; in the steady state mode, VCD is maintained at a specified level by bleeding cells from the bioreactor.

### Dynamic



### Steady-state

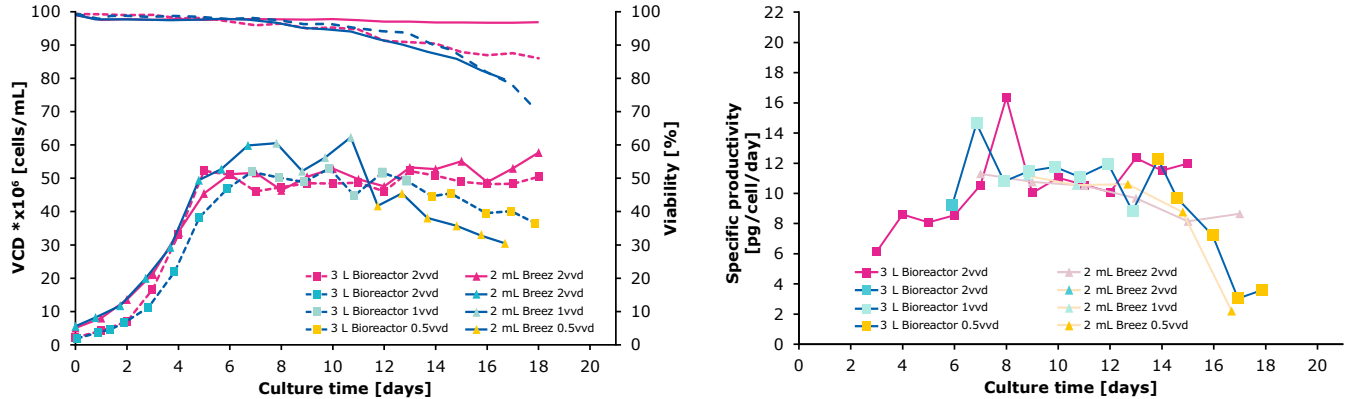


In dynamic perfusion, a high cell density of  $150 \times 10^6$  cells/mL at 1.0 VVD (CSPR of <10 pL/cell/day) was achieved, and both volumetric and cell specific productivities were increased over time. In steady state perfusion, target cell density of  $50 \times 10^6$  cells/mL was maintained at 1.5 and 1.0 VVD (CSPR of ~18–20 pL/cell/day), and both volumetric and cell specific productivities remained stable. Data were generated with CHOK1 in EX-CELL® Advanced HD Perfusion Medium using the 2 mL working volume microbioreactor at 37 °C, pH 7.0, and 40% DO.

## Perfusion Performance Predictability

Achieve high cell densities with integrated pH, DO, temperature and cell density control, and predict the performance of traditional stirred tank reactors at a much smaller volume scale, saving you media and associated costs.

The Mobius® Breez Microbioreactor is capable of replicating the performance of a 3 L bench-scale glass bioreactor in terms of viable cell density (VCD), cell viability, and harvest specific productivity. Experiments were performed using a CHOZN® GS cell line cultured in EX-CELL® Advanced HD perfusion medium. A steady state at  $50 \times 10^6$  cells/mL was achieved in both reactors, while cell viability in the Mobius® Breez cultures was higher compared to the 3 L bioreactor. Comparable trends were observed for harvest specific protein production with the CHOZN® GS cell line.



Overall, the data shows broad comparability between the Mobius® Breez Microbioreactor and the 3 L benchtop reactor, indicating Mobius® Breez is a suitable scale-down model for perfusion performance predictability. The data also showcases the benefits of running perfusion, which allows for several experiments to be performed in the same run, thus saving time. In this instance, the experiment shifted from 2.0 VVD to 1.0 VVD on day 8 and then to 0.5 VVD on day 12.

## Specifications

Consumable	
Materials of Construction (by component)	Cassette: Polycarbonate, Silicone, Polyethersulfone, PETG, Acrylic PSA, Silicone PSA Bottle set: C-Flex, Polycarbonate, Silicone, PETG, ETFE, PVDF, ABS, Polypropylene, HDPE, Polyurethane, PVC
Dimensions	Min Space Required (Bottle Set): 3.5" x 7" x 5" (W×H×D)
Tubing ID, OD, Lengths	For Tubing from Bottle to Cassette: Length Approx. 27" User connect tubing (C-Flex): Length Approx. 18", 1/4" OD, 1/8" ID User connect tubing (PVC): Length Approx. 18", 5/32" OD, 3/32" ID
Fluid Flow and Volume	
Microbioreactor working volume	2.155 mL
Number of Fluid Inputs	4 (one is reserved for DI water)
Number of Fluid Outputs	3 (sample, cell waste, perfusion harvest)
Flow Rate Range	0.1–10 VVD
Pump Accuracy, Resolution	±2%, 600 nL
Minimum Sampling Volume	50 µL
pH Measurement and Control	
Measurement Range	5.5–8.5
Measurement & Control Accuracy at pH 7	±0.1
Dissolved Oxygen	
Range	0–100% air sat
Measurement and Control Accuracy	±10%
kLa	Up to 40/hour
Temperature	
Measurement Accuracy	±0.5 °C
Control Range	Ambient +5 °C to 40 °C
Control Resolution	0.1 °C
Optical Density	
Linear Range (CHO)	0–50 M cells/mL
Usable Range (CHO)	0–200 M cells/mL
Auto cell bleed	±10% setpoint
Hardware	
Materials of Construction (by component)	Basestation: anodized aluminum, stainless steel, silicone, C-Flex, PVC, copolyester, polypropylene, vinyl CO <sub>2</sub> Box: anodized aluminum, vinyl, chrome/nickel plated brass, stainless steel POD: anodized aluminum, acetyl (Delrin), stainless steel, vinyl, silicone, C-Flex, solder mask, nickel plated copper, polycarbonate
Dimensions (W x H x D)	Minimum Space W (with laptop): 26 in. (66 cm) W (without laptop): 14 in. (36 cm) H: 16 in. (41 cm) D: 20 in. (51 cm)
Weight	As Installed (w/ Accessories): Approx. 60 lbs. (27 kg)
Power Supply	Base Station: Input — 90–264 VAC 50/60 Hz, Output — 24 VDC 6.25 A Max (150 W) CO <sub>2</sub> Box: Input — 90–264 VAC 50/60 Hz, Output — 24 VDC 0.8 A Max (19 W)
Languages supported	US English
Pressure range/accuracy	Minimum pressure input: 30 psi
List of inputs/outputs	Gas Input: Air, N <sub>2</sub> optional, O <sub>2</sub> , CO <sub>2</sub> Gas Output: Mixed gas (Air, N <sub>2</sub> , O <sub>2</sub> , and CO <sub>2</sub> ) Electrical input — 2× 24 VDC inputs
USB Interface	3× USB 2.0 connections for communication between computer and Mobius® Breez Microbioreactor system and barcode scanner. Additionally can be used to upload software updates.
Software	
Data logging	17 days of data logging on Mobius® Breez Microbioreactor. Long term data logging can be stored on computer and/or remote to system.
Back-up solution	Data from microbioreactor stored locally on PC, database backed up periodically onto local hard drive, can be configured for remote backup via 3 <sup>rd</sup> party applications
Network interface	Network optional via computer

## Mobius® Breez Microbioreactor Services

To support you as you navigate this challenging environment, we offer a wide range of services that can help save time and lower costs. All of our services are performed by global experts who have an intimate knowledge of our equipment backed by decades of experience, giving you peace of mind at every step.

### Setup and Installation

Integrating the Mobius® Breez Microbioreactor into your laboratory is seamless and quick. Our dedicated team ensures your equipment is properly installed and is functioning per your pre-defined requirements.

### Training Services

Appropriate training for users ensures your staff has the expertise to operate and manage the system as part of your process. Our training offering has been designed to make your staff more autonomous in managing your system and your process while saving time and money.

Our training services cover system use with interactive hands-on sessions, including:

- System setup and calibrations
- Bioreactor consumable installation
- Experiment initiation
- Process recommendations

These trainings can be delivered either at your site or in our M Lab™ Collaboration Centers. Please contact your local representative or email [ilearn@merckgroup.com](mailto:ilearn@merckgroup.com) to discuss our training offering.

### Repair Services

In the event your system experiences a problem, our worldwide engineering organization will provide on-site or repair center technical support to get you back up and running as quickly as possible.

### System Service Reliance Plans

To help you ensure optimum equipment uptime while mitigating risks, we have developed a wide range of services and support that allow you to select a coverage level that best fits your needs. Our System Service Reliance Plans, a complete range of services for your systems, offer priority access while ensuring your equipment is properly maintained. For additional details, please refer to the System Service Reliance Plans Data Sheet (MK\_DS7881EN), available at [sigmaaldrich.com/services-plans](http://sigmaaldrich.com/services-plans).

### Spare Parts

Purchasing spare parts directly from us is the only way we can guarantee that you get the right parts every time, with the same level of performance as the original.

Learn more about our system services at [sigmaaldrich.com/services](http://sigmaaldrich.com/services)

## Related Products

When developing a monoclonal antibody with a world of potential, getting your upstream process development right the first time opens up exponential possibilities.

The decisions you make in upstream development have major impacts on your process performance. Wrong decisions are difficult to reverse or require significant backtracking and resources. Yet, all these critical decisions need to be made amid the race to market.

Our upstream ecosystem – comprised of cell line and media platforms, cell line development, product characterization services, bioreactors, single-use mixers, process development expertise and next generation processing programs – gets upstream process development right the first time. You save precious time, optimize performance, improve feasibility and sustainability, while laying the groundwork for downstream success.

### CHOZN® Expression Platform

The CHOZN® platform is a mammalian cell expression system based on CHO cells (Chinese Hamster Ovary) for fast and easy selection and scale up of stable clones producing high levels of recombinant proteins.

### EX-CELL® Advanced HD Perfusion Medium

Next generation perfusion processes require a new type of medium to facilitate high productivity at low perfusion rates. EX-CELL® Advanced HD Perfusion Medium was designed for CHO cells to reach and maintain high cell densities at low cell specific perfusion rates (CSPRs), while supporting high volumetric productivities of monoclonal antibodies and recombinant proteins in suspension culture.

### Mobius® Single-Use Bioreactors

Take full advantage of our fit-for-purpose perfusion systems. After screening and optimizing parameters at 2 mL scale, transition into late process development with the Mobius® 3 L Single-use Bioreactor to optimize and confirm scale-dependent variables at bench-scale with the predictability of a stirred tank design. Then, capture the advantages of perfusion at commercial scale from 50 to 2,000 L with the Mobius® iFlex Bioreactors, our next generation, high-performing and perfusion-ready bioreactors that support high cell densities.



## Ordering Information

Product Description	Catalogue Number	
<b>System</b>		
Mobius® Breez Microbioreactor System. Includes:		
<ul style="list-style-type: none"> <li>• Basestation Hub with CO<sub>2</sub> Box, 4 PODs, 4 Test Cassettes, Computer and Software</li> <li>• Vacuum Connection Kit</li> <li>• Media Characterization Kit</li> </ul>	BRZ01SYS	
<b>Power Supply</b>		
Australia	BRZC0RDAUS	
China	BRZC0RDCN	
Europe	BRZC0RDEU	
United Kingdom	BRZC0RDUK	
<b>Note: A North American power supply is included in the system (BRZ01SYS). Please order a local power cable in addition to the system.</b>		
<b>Consumables</b>	<b>Quantity 4</b>	<b>Quantity 1</b>
Mobius® Breez 2 mL Microbioreactor with C-Flex Tubing, Bioprocess Applications	BRZMBRCFLEX4	BRZMBRCFLEX
Mobius® Breez 2 mL Microbioreactor with PVC Tubing, Cell Therapy Applications	BRZMBRPVC4	BRZMBRPVC
Mobius® Breez Media Characterization Consumable for Media Calibration	N/A	BRZMCC
<b>Trial</b>		
Mobius® Breez Microbioreactor Trial for 4 weeks with initial system set up, training, and system access	BRZTRIAL	
<b>Installation</b>		
Mobius® Breez Microbioreactor – Installation	BRZSETUP	
<b>Training</b>		
Mobius® Breez Microbioreactor – Operator Training	OPTRBREEZCS1	
<b>Maintenance and Repair</b>		
Mobius® Breez Microbioreactor – Essential Service Reliance Plan	BRZESP001	
Mobius® Breez Microbioreactor – Advanced Service Reliance Plan	BRZESP001 + BRZADC001	
Mobius® Breez Microbioreactor – Total Service Reliance Plan	BRZESP001 + BRZT0C001	

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