VACCIXCELL
ADHERENT BIOPROCESSING SPECIALIST

Hybrid Bioreactor®

Changing Perspective from Discovery to Delivery

ESCO® Healthcare
"Discovery to Delivery"

Hybrid Bioreactor

Your Four in One Bioreactor

Hybrid Bioreactor

The VacciXcell Hybrid Bioreactor is a unique and multifunctional bioreactor system for your research and development. The control unit opens an innovative technology and robust flexibility suitable for your changing requirements. Whether adherent or suspension, choose your cultivation chamber from our range of multiple-use vessels:

- conventional stirred tank autoclavable vessels
- Tide-motion matrix vessel

Applications

- Research and Development
- Vaccine Development
- Vaccine Production
- Protein Production
- Antibody Development
- Antibody Production
- Cell Therapy
- Gene Therapy

Cells

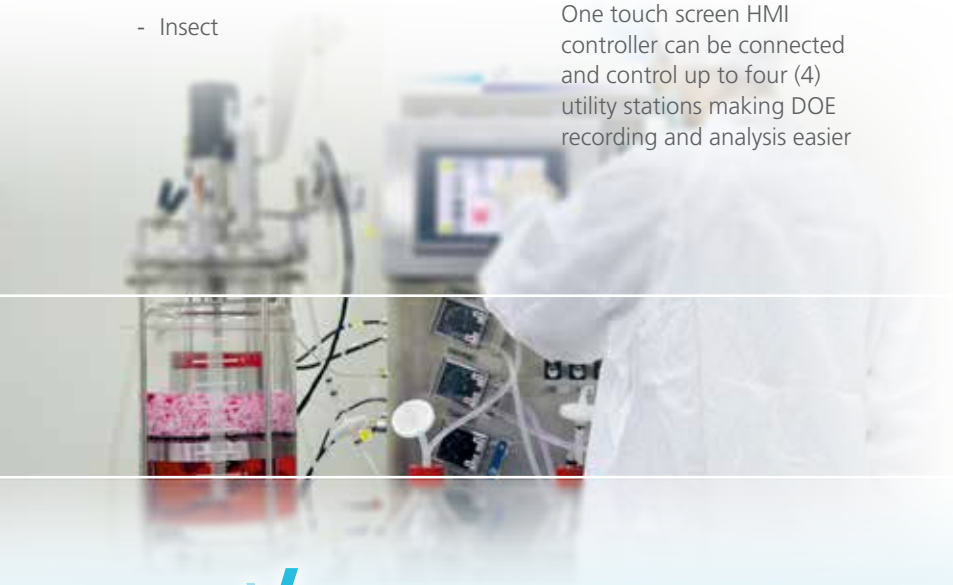
- Mammalian
- Microbial
- Yeast
- Fungi
- Insect

Process Modes

- Batch
- Fed-Batch
- Perfusion

Key Features

- Automated control of pH, DO, aeration, foaming, temperature, agitation, and level
- Glass water jacketed vessel heats to 37°C (±) 0.3 in just 30 minutes
- Inoculation and sampling in a closed system
- Working volume of up to 7 L
- Touch Screen HMI Controller. One touch screen HMI controller can be connected and control up to four (4) utility stations making DOE recording and analysis easier



VACCIXCELL
ADHERENT BIOPROCESSING SPECIALIST

Best Companion

Since the system can perform four (4) types of culture namely: adherent culture using macrocarriers, adherent culture using microcarriers, suspension culture and fermentation. Researchers can easily compare how one cell line performs or reacts to one type of culture method as compared to another.

Configurable Design

Esco VacciXcell offers configuration for your bioreactor to match your specific needs. Hybrid Bioreactor offers comfort and convenience for flexible and scalable options from 1L up to 50L stainless steel vessel for secreted biologics production and from 0.1L up tp 5,000L for adherent scale production.

Guaranteed World Class Quality

Esco VacciXcell Hybrid bioreactor is proven and tested for reliable quality. It is sold & serviced globally by Esco's 25 direct sales/service offices, factories and trained sales & service partners.

Hybrid Bioreactor Control Unit –

Hive of Activity

Tide-Motion Matrix Vessel

Our proven autoclavable borosilicate glass is available in both 1 Liter and 7 Liter suitable for your laboratory needs. The matrix vessel contains the carriers, BioNoc™ II, to which the cells adhere to and grow; it is oscillated up and down by air pressure to submerge and emerge the carriers in the nutrient medium.

▶ Benefits

- Optimizes our patented tide-motion principle that is proven effective and linearly scalable up to 5,000 Liters
- 5.5g of BioNOC has enough surface area to culture up to 109 cells
- Ability to scale up for large scale production

▶ Main Applications

- Adherent culture (Insect, Plant and etc.)
- Research and Development
- Laboratory-scale production
- Process development, optimization and characterization

Stirred Tank Reactor Vessel

Our proven autoclavable borosilicate glass is available in both 1 Liter and 7 Liter suitable for your laboratory needs. The stirred tank reactor vessel is suitable for suspension culture. Easily switch from adherent to suspension by replacing the matrix vessel connected to the magnetic drive

▶ Benefits

- Equipped with CO_2 mass flow controller
- Proven scalable stirred tank design
- Extensive performance and simplifies suspension/fermentation culture with easy steps

▶ Main Applications

- Adherent culture (Insect, Plant and etc.)
- Research and Development
- Laboratory-scale production
- Process development, optimization and characterization

Tide Motion Technology Advantage

Total Nutrition

- ✓ Matrices are submerged into the culture medium
- ✓ Eliminates nutrient starvation

Total Aeration

- ✓ Direct exposure of matrices in the air
- ✓ Oxygen can penetrate the matrix bed

WHY TIDE MOTION TECHNOLOGY

The gentle vertical oscillation of the medium creates a dynamic interface between the air and the adherent cells in the culture medium. Tide motion provides the cells with an environment that has low shear stress, high aeration and nutrition levels, zero foaming, and no oxygen limitation. This efficient nutrient and oxygen transfer produces high cell density yield that is linearly scalable

VacciXcell's tide motion system is intended for the culture of adherent or anchorage-dependent cells to be used for various applications.

Benefits

- Large Surface Area (BioNOC™ II)
- High Productivity
- Low Downstream Processing Costs
- No Oxygen Limitation
- Low-shear Stress
- Zero Foaming
- Difficult Viruses
- Isolator Capability
- Continuous processing
- Immortal cell lines
- Linearly scalable from 1L up to 50L stainless steel for secreted biologics production and 0.1L up to 5,000L for adherent scale-up production

Main application

- cell banking
- cell culture-based vaccine production
- biologics production
- cell therapy
- gene therapy
- diagnostics

Hybrid Bioreactor

Exceeding your Expectations

Control Unit

The Hybrid bioreactor's control unit allows users to easily configure culture parameters while also allowing continuous data and result tracking. Culture parameters are embedded and can effortlessly switch to different culture modes.

Reactor Vessel

The double-jacketed reactor vessel is made of borosilicate glass that guarantees safety, quality, and durability. The head plate, sparger, shaft and impellers are made of stainless steel 316L making it rigid, heat-proof, acid-proof, and alkali-proof.

BioNOC™ II

VacciXcell's BioNOC™ II is a low fiber content macrocarrier that acts as the packed bed component of the tide motion system in the bioreactor. It is a 100% PET fibrous culture matrix with stability of up to 5 years that has enough surface area to culture up to 109 cells. BIONOC™ II macrocarriers are placed inside the matrix vessel of the hybrid bioreactor.

Connections for Sensors and Ports

All inlet and ports e.g. processed gases are located on the rear panel of the bioreactor's control unit. All connection are marked with the same names used in the reactor vessel for fast and efficient identification.

Connections for External Accessories

Hybrid bioreactor makes it easy for the user to attach all cables and supplies to the reactor vessel. The couplings are properly named to match the corresponding labels in the head plate.

Touch Screen HMI

8.4" touch screen HMI creates a comfortable working environment. The PLC-Base control structure increases performance, flexibility and reliability of the whole system. The main culture screen is a real time dynamic display that allows users to switch between automatic and manual control of parameters.

Peristaltic pumps

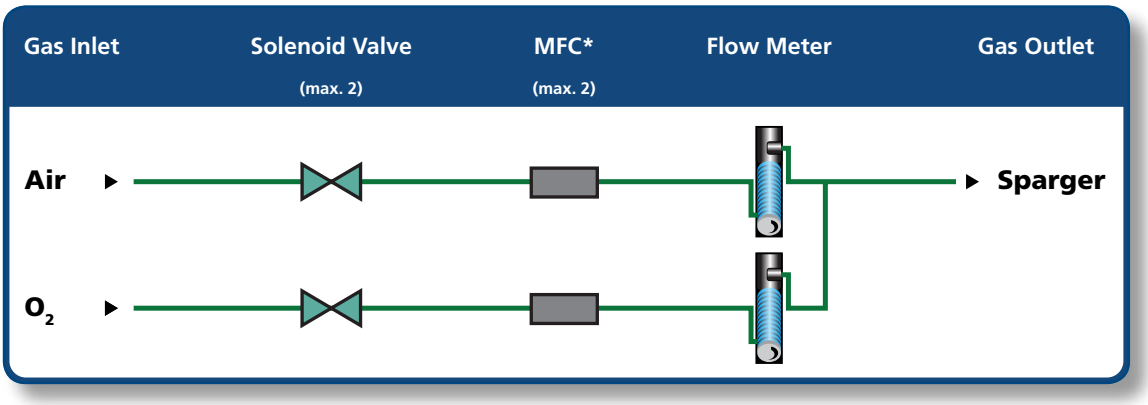
It is used to pump in liquids in the bioreactor. The hybrid bioreactor control unit has 4 function-assigned peristaltic pumps. Choose between pumps for feeding and harvesting of media or acid/base agents addition.

Aeration Strategies

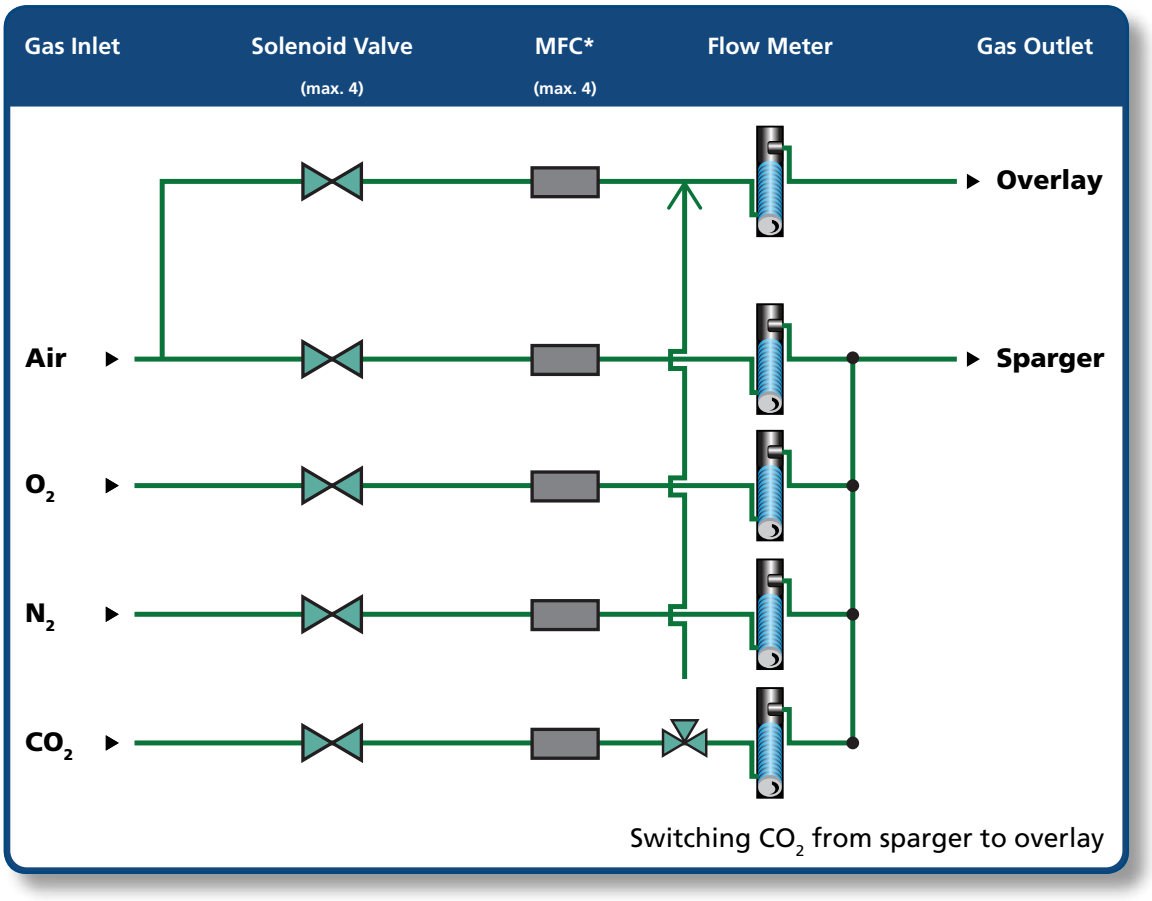
Microbial Applications in Suspension Reactor Vessel

Different controller and configurations within the system enable air circulation techniques utilizing air or oxygen or O2 enrichment of air.

The standard built-in solenoid valves located in the control unit, in combination with a rotameter (flow meter) ensures reliable gas supply for culture applications. Optional mass flow controllers automatically controls the gas flow rate to maintain stable flow which save both time and operational expense



Cell Culture Applications in Matrix Reactor Vessel



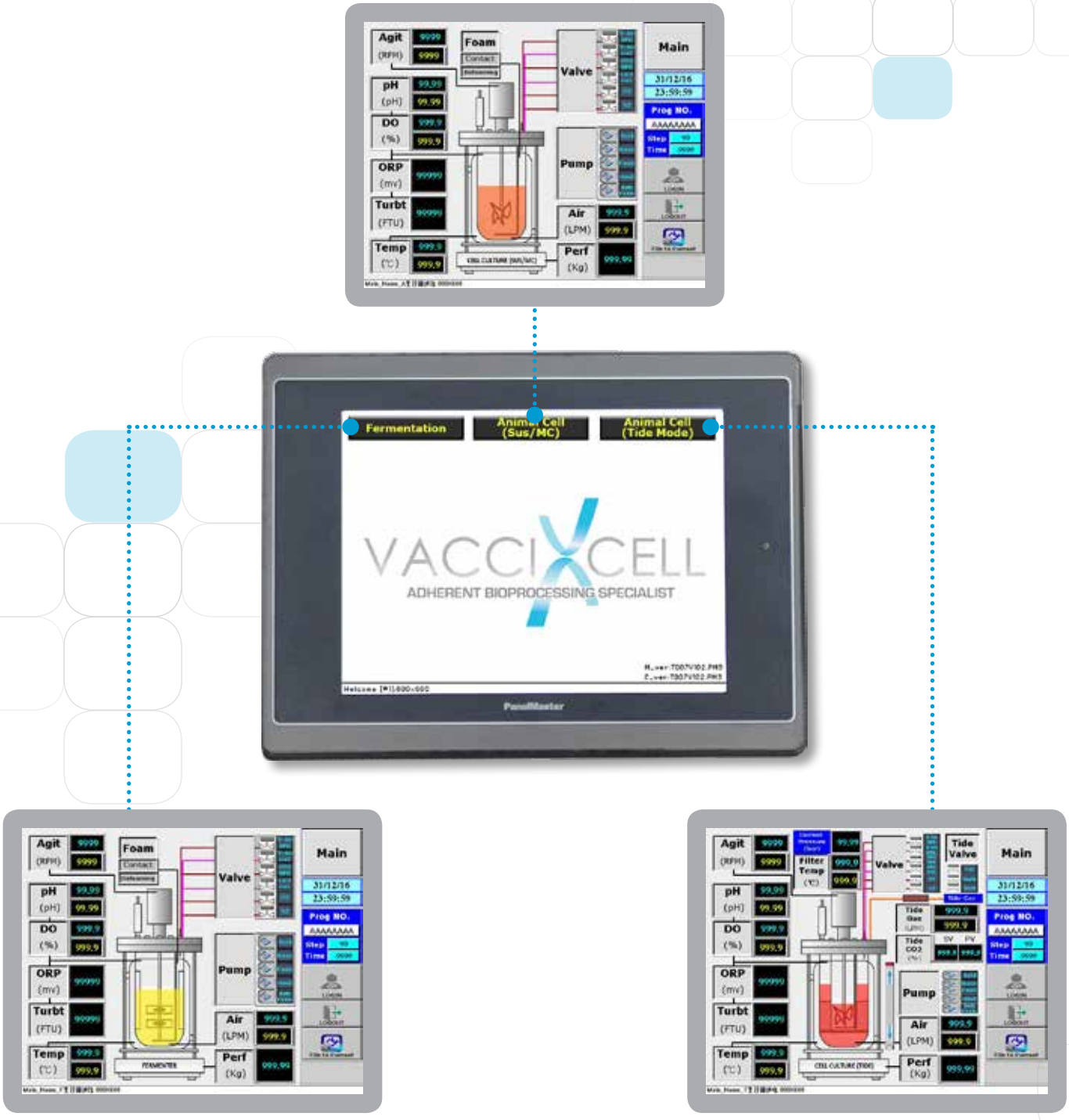
Gas lines are connected to its corresponding solenoid valves and|or optional mass flow controllers and rotameters deliver accurate and flexible control of gas flow.

The Hybrid Bioreactor HMI control page allows the user to switch amongst sparger and overlay for the CO_2 and Air (vent air for adherent culture) gas supply or pH control. Efficient gas exchange is achieved through the tide motion principle. Tide motion uses this upward and downward liquid flow to provide both oxygen and nutrients to the adherent cells being cultured. The gentle vertical oscillation of the culture medium creates a dynamic interface between air and culture medium on the surface of the cells, providing the cells with an environment that is of low shear stress, high aeration and nutrition levels, zero foaming, and no O_2 limitation.

Main Page

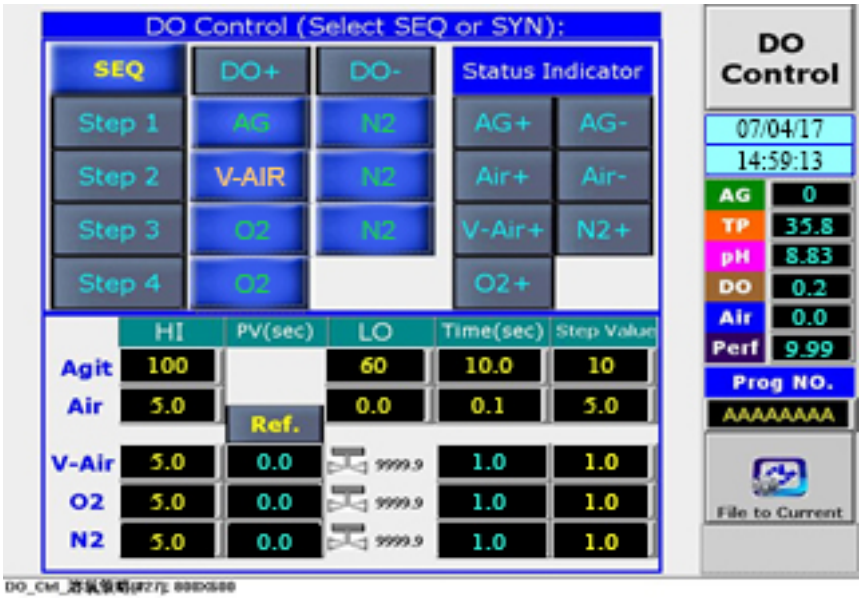
Easy Switch for Every Mode

The VacciXcell hybrid bioreactor gives its users exactly the option by being able to try out four (4) different types of culture namely: adherent culture using macrocarrier, adherent culture using microcarrier in a stirred tank environment, suspension culture and fermentation. By being able to do the design of experiment (DOE) using these four types of culture in one system, data gathering and analysis would be easier and more efficient, resulting in lower total cost and shorter process development period.



Perfusion Processing Control

The different peristaltic pumps of the hybrid bioreactor can be programmed to perform different functions such as acid/ base addition, feeding and harvesting. The hybrid can operate continuously for an extended periods of time at high cell density



Automatic DO Control

The DO Control Page contains parameters that can be set for advanced controlling of DO injected to the culture medium. Modifications on the parameter setting of DO from agitation rate to gases injected in the reactor vessel provides specific set point for control.

The sequence of the parameters are steps to be followed by the system to keep the gas flow rate constant. It shall operate until the preferred aeration strategy is reached. This gives the user a flexible configuration for better processing requirement.

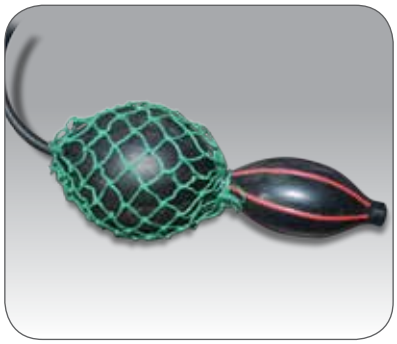
Automatic pH Control

pH requirement can be met through setting parameters. These parameters can be acid/base addition or by CO2 aeration and base addition. The hybrid bioreactor is equipped for setting parameters in different culture modes.

Seeding, Feeding and Harvesting

Seeding

Prepared seed for inoculation (1L volume)

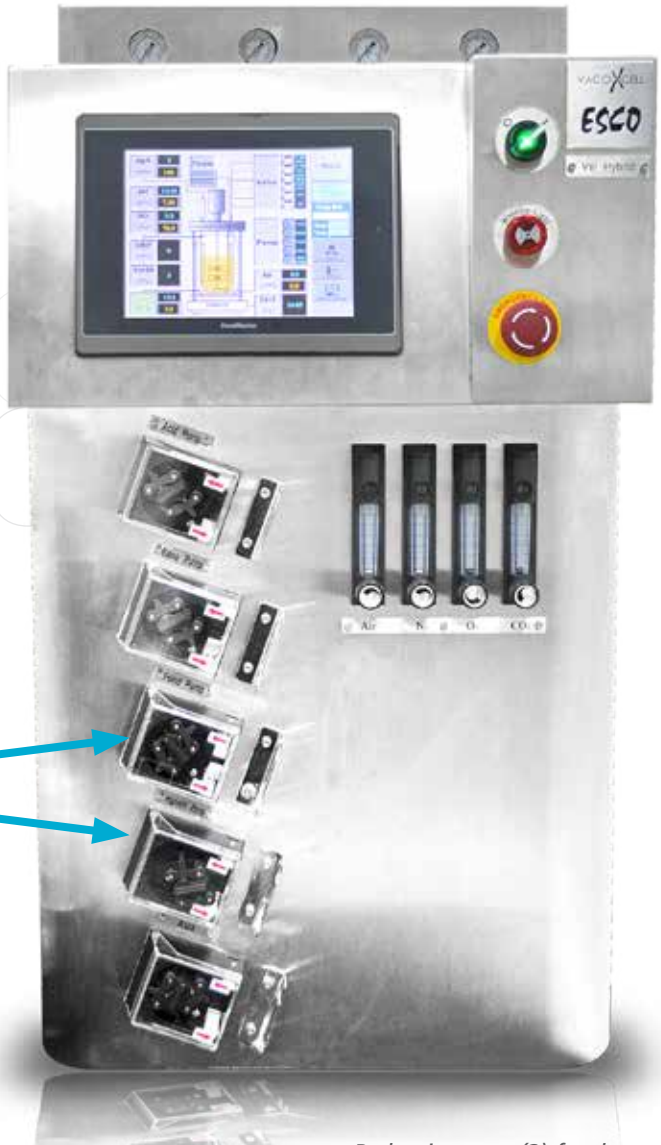


The inoculum from the seeding vessel is pumped through the bioreactor via balloon pump

Inoculum (seed) is pumped into the seeding port located inside the reactor vessel

Programmable Peristaltic Pump

The different peristaltic pumps of the hybrid bioreactor can be programmed to perform different functions such as acid/base addition, feeding and harvesting



Having programmable pumps allows hybrid to have:

- *one (1) feed and one (1) harvest pump or,*
- *two (2) feed pumps*

By having two (2) feed pumps, processes such as fed batch culture can be done with twice flow rate, giving more options to end users

▶ Feeding

- Feeding is the predetermined or controlled addition of nutrients into the bioreactor under culture operations
- Allows a degree of control on the process and operations of hybrid bioreactor. It can control the rate of growth of the microorganisms or the concentration of the biomass by controlling parameters such as frequency of feed and concentrations of feed

▶ Harvesting

- Harvesting is performed by separating the cell culture from the growing medium or harvesting secreted products in the bioreactor through the harvesting port

Technical Specifications

Hybrid Bioreactor Control Unit

Control Unit Weight	
Single	80 kg (177lbs)
Control Unit Dimensions	
Single	W460x D 637 x H 903 mm
Utility Connections	
Power Supply	220 volts, max power consumption 5A
Gases	4x6mm external tubing diameter Gas supply pressure, 10psi oil & moisture-free
Water	Water supply pressure- 1.5 M Flow rate up to 10-12 lpm Minimum temperature 13-14°C L/S 35 Silicone for tubing
Control Unit	
Housing	Stainless Steel, AISI 304
Display	HMI
Resolution	800x600
SCADA Communication	Ethernet
Safety valve gas pressure	10 psi for Matrix Reactor Vessel and Suspension Vessel
Water inlet pressure reduction	0.15bar, integrated pressure control
Motor Drive	
Direct Drive	Power: 400W

Reactor Vessel

Reactor Vessel Material	
1 Liter and 7 Liter vessel Total Volume: 1.5L and 8.2L	Borosilicate glass
14 Liter vessel	Borosilicate glass/Stainless Steel
25 Liter vessel	Stainless Steel
50 Liter vessel	Stainless Steel
Vessel Dimensions	
1 Liter	D 116 x H 148 mm
7 Liter	D 190 x H 320 mm
14 Liter	D 240 x H 450mm

Sensor | Measurement Range | Display Accuracy	Description	
Temperature	PT-100 class A ; Deviation: ±(0.15+0.00 |t|); 0°C-100°C	
Dissolved oxygen	**Measurement Principle**	Amperometric/ Polarographic
	Working Conditions	
	Pressure resistance measurement	0.2-6 bar absolute
		(2.9-87.0 psi absolute)
	Mechanical pressure resistance	max. 12 bar absolute
		(174.0 psi absolute)
	Measuring temperature range	0...80°C (32…176 °F)
	Temperature range	-5…140°C (23…284°F) (autoclavable)
	Construction	
	Temperature compensation	Automatic with built-in RTD
	Cable connection	VarioPin (IP 68) straight or angled K8S straight (digital ISM sensors)
	O-ring material	Silicone FDA and USPP VI approved
	Membrane material	PTFE/Silicone/PTFE (reinforced with steel mesh)
	Wetted metal parts	Stainless steel Special material on request
	Surface roughness of wetted metal parts (ISO 1320:1992)	N5 (< 0.4m [16in])
	Quick disconnect interior body	Standard
	Cathode	Pt
	Anode	Ag
	Guard ring	No
	Dimensions	
	Sensor diameter	12 or 25 mm (0.47" or 0.96")
	Immersion length (a) for 12 mm sensor	70, 120, 220, 320, 420 mm. (2.8, 4.7, 8.66, 12.6, 16.54")
	Immersion length (a) for 25 mm sensor	80, 160, 260, 360 mm (3.15, 6.3, 10.24, 10.17")
	Performances	
	Detection limit	6ppb
	Accuracy	≤ ±(1% + 6 ppb) of reading in liquids
	Response time at 25°C/77°F (air – N2)	98% of final value <90s
	Sensor signal in ambient air (25°C/ 77°F	50…110nA
	Residual signal in oxygen-free medium	<0.1% of the signal in ambient air
	Maximum flow error	≤ 5%

Sensor | Measurement Range | Display Accuracy	Description	
Dissolved oxygen (cont'd)	**Certification**	
	EHEDG, 3A	Yes
	3.1B (EN 10204.3/1.b)	Yes
	ATEX certificate	Yes
	FM Approval	Yes
	FDA/USP VI	Yes
	Quality control	Yes
pH	Measuring range	pH 0…14
	Temperature	0…80°C for operation 0…140°C for sterilization
	Pressure resistance	Up to overpressure of max. 6 bar (87psi)
	Reference system	Argenthal (Ag/AgCl)
	Reference electrolyte	Gel electrolyte
	Diaphragm	1 ceramic diaphragm
	Glass membrane	HA, high alkali glass quality
	Glass shaft	Ø12 mm
	Plug head	K8S, Pg 13.5 thread
Foam Control	Teflon insulated stainless steel	
Level	Teflon insulated stainless steel	
Turbidity	**Dimension**	W 270 x D 200 x H 300 mm
	Measuring principle	Backscatter, 1-fiber
	Sensor material	DIN 1.4435 (316L)
	Sensor diameter	12 mm
	Insertion length	120, 205, 297, or 407 mm
	Process connection	Pg 13.5
	Measuring range:	
	Formazin Turbidity Units	10…40000 FTU
	Suspended Solids (Diatomaceous earth as reference)	0…250 g/L
	Design:	
	Cable connectors	SMA
	Cable lengths	3m (10ft) optical
	Cable type	Duplex HCS fiber, fixed

Sensor | Measurement Range | Display Accuracy	Description	
Turbidity (cont'd)	**Wetted parts:**	
	Metals	DIN 1.4435 (316L)
	Plastic	None
	O-ring	Viton-FDA
	Sapphire spigot for fiber protection	None
	Sapphire window for fiber protection	None
	Working conditions:	
	Pressure range	0…6 bar (0…87psi)
Redox	**Dimension**	W 270 x D 170 x H 230 mm
	Measuring range	pH 0…12
	Temperature	0…100°C in operation 0…130°C for sterilization
	Pressure resistance	From vacuum up to a process pressure of max 2.5 bar (36psi)
	Reference system	Argenthal (Ag/AgCl)
	Reference electrolyte	Pressurized gel electrolyte
	Diaphragm	1 ceramic diaphragm
	Glass shaft	Ø12 mm
	Plug head	K8S, Pg 13.5 thread
RM load cells	Weight:100 kg Dimensions: (in mm) 330 X 330	

Vessel Sizing and Volume		
Model	**M-1000**	**M-5000**
Total Volume (L)	1.5	8.2
Maximum Working Volume (L) for Suspension Culture	0.6-1.1	4.5-7
Depth (mm)	116	190
Height (mm)	148	320
Recommended BioNOC II Matrix volume [ml]	180	1000
Recommended amount BioNOC II Matrix in grams	10	55
Aspect Ratio	1:2.5 (for suspension) 1:3 (for microbial culture)	

Temp depends on the chiller

Specifications* of VXL Hybrid Bioreactor	Adherent Cell Culture		Suspension Cell Culture		Fermentation		Microcarrier-Based Cell Culture	
Model	**M-1000**	**M-5000**	**M-1000**	**M-5000**	**M-1000**	**M-5000**	**M-1000**	**M-5000**
Vessel Material	Borosilicate Glass							
Temperature Range	20 °C-70 °C Precision: 0.1 °C	10 °C-70 °C Precision: 0.1 °C	20 °C-70 °C Precision: 0.1 °C	10 °C-70 °C Precision: 0.1 °C	20 °C-70 °C Precision: 0.1 °C	10 °C-70 °C Precision: 0.1 °C	20 °C-70 °C Precision: 0.1 °C	10 °C-70 °C Precision: 0.1 °C
Baffle	N/A		YES		YES		N/A	
Top Stirrer Motor	10-1200rpm							
Impeller speed	25-200rpm		50-1200 rpm		50-1200 rpm		25-400 rpm	
Impeller Design**	Small 6-Blade Rushton Turbine		3-Pitched-Blade Turbine and 3-Marine-Blade Propeller		Large 6-Blade Rushton Turbine		3-Pitched-Blade Turbine and 3-Marine-Blade Propeller	
Ventilation	Ring Sparger		Micro-Sparger		Ring Sparger		Ring Sparger	
Drive Method	Tide: KNF brushless motor with air pump, controlled by PID or constant voltage direct drive. Mixing: Top direct servo motor with PID/PWM control				Mixing: Top direct servo motor with PID/PWM control			
Condenser	Stainless steel condenser with 0.2 um disk type or cartridge type filter							
pH Range	pH 4-14 Precision: 0.01							
DO Range	0-100 % Precision: 0.01%							
Aeration	10L/min Precision: 2%							
Emerging Time	0-100mins		N/A					
Submerging Time	0-100mins		N/A					
Liquid Level Control	High Level Sensor		Electronic Scale					
Sampling	liquid: sampling bottle; matrix: sample port		liquid: sampling bottle					
Foaming Control	N/A		YES		YES		YES	
Control Unit	8.4" HMI							

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