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Bioflo 3000 Universal Fermentor: Versatile System for Fermentation & Cell Culture Research

The Universal Benchtop Fermentor/Bioreactor for Fermentation and Cell Culture

BioFlo 3000 is an advanced bioprocessing system designed to maximize yields in both fermentation and cell culture. Ideally suited to meet the changing needs of the research laboratory, this versatile fermentor/bioreactor is capable of producing high yields of biomass or secreted products from virtually any microbial, animal, insect and plant cell line. The stirred-tank system comes complete with everything needed for out-of-the-box fermentor start-up, and is offered with a variety of options for dedicated cell culture applications.

UNIQUE ADVANTAGES

- **Built-in Gas-Mixer Optimizes Dissolved Oxygen Levels For High-Density Culture.** **Two-Gas Mixing in Fermentation** provides automatic or manual blending of supplemental oxygen and air. Create air, oxygen, and agitation control cascades that respond to oxygen-demanding microbes, while limiting foam and shear.
- **Four-Gas Mixing in Cell Culture,** blends air, oxygen, carbon dioxide, and nitrogen for precise and gentle automatic control of both pH and dissolved oxygen
- **350 mM/L/Hr Oxygen Transfer Rate** obtained through powerful fermentation agitation motors and 6-bladed Rushton impellers
- **Choice of 12 Interchangeable Vessels.** Fermentation vessels offered with or without side ports, in four sizes from 1.6 through 14 liters. Glass-jacketed cell culture vessels, 2.2 through 14 liters total volume
- **Stainless-Steel Heat Exchanger** forms the rounded bottom of fermentation vessel assemblies. Allows the shortest autoclave time, with no impeding doubleinsulating glass to slow sterilization. Large-area high-conductivity steel surface provides superior temperature uniformity and the most efficient heat-transfer characteristics. The best

choice for fermentation, especially for high-density cultures and for temperature induction

- **Vessel Side Ports** support chemostat operation
- **Low Side Entry Ports** (optional)‡ two 19 mm ports in the stainless steel heat-exchanger support

additional probes, which enter the vessel below the impeller.

12 mm adapter available

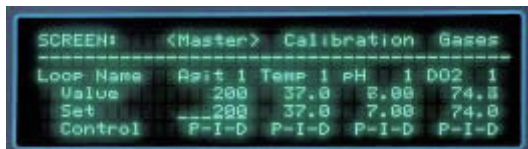
- **Patented Fibra-Cel® Packed Bed, and Cell-Lift Microcarrier Technologies**

maximize yields of animal cell products* (optional)

- **BioCommand® Software** (optional) automates data logging, centralized control and programmed process protocols with a powerful and easy-to-use program

OTHER ADVANTAGES

- **Integrated Vessel, Console, Controller and Pumps** conserve bench space and simplify connections
- **Choice of Thermal Mass Flow Meter or Thermal Mass Flow Controller** for accurate air flow monitoring and control
- **Choice of P-I or “Deadband” pH Control.** PI control provides maximum accuracy; Deadband minimizes addition of acid/base
- **Tunable P-I Values Optimize DO Control**
- **Five Assignable, Peristaltic Pumps** built in; with control included for optional sixth pump
- **Stainless-Steel Exhaust Condenser** minimizes media evaporation
- **Stainless-Steel Ring Sparger** provides uniform distribution of bubbles to impeller blades
- **Battery Back-Up** retains settings in the event of a power failure



The image shows a vacuum fluorescent alpha-numeric display with a green background and white text. The display is titled 'SCREEN: <Master> Calibration Gases'. Below the title, there is a table with columns for 'Loop Name', 'Posit', 'Temp', 'pH', 'DO2', and 'I'. The table contains data for 'Value', 'Set', and 'Control' for each loop.

Loop Name	Posit	Temp	pH	DO2	I
Value	200	37.0	8.00	74.0	
Set	200	37.0	7.00	74.0	
Control	P-I-D	P-I-D	P-I-D	P-I-D	

BioFlo 3000 data screen displays setpoints and process variables simultaneously. The vacuum fluorescent alpha-numeric display provides easy access to every phase of the process, including 13 control loops that simplify probe calibration, cell growth and process manipulation

OPERATING MODES AND ACCESSORIES

- **Microcarrier Cell Culture**
 - Optional dedicated cell culture vessel with Cell-Lift impeller. Optional decanting column or spin filter for perfusion
- **Batch Culture**
- **Fed-Batch Culture**

- **Continuous Culture**
 - Includes all required instrumentation as standard
- **Suspension Cell Culture**
 - Optional low-shear, pitched blade and marine blade impellers. Optional dedicated cell culture vessels.
 - Optional spin filter for perfusion
- **Packed-Bed Immobilized Cell Culture**
 - Optional dedicated cell culture vessel with packed-bed basket impeller for secreted products

PROCESS CONTROL SYSTEMS SUPPLIED

PARAMETER	CONTROL	SENSOR SUPPLIED
Temperature	PID	RTD
Agitation	PID	Photo-Optical Disk
pH	PID — Acid & Base Pump and 4-gas	Ingold or Broadley James
DO	PID Cascade to Agitation, Gas/Air Flow, & 2 or 4-Gas	Ingold or Broadley James
Foam/Level	Electronic Pump for AntiFoam, Nutrient or Harvest	Conductivity Probe
Gas/Air Flow	Electronic Monitoring (TMM) or Electronic Control (TMC)	Thermal Mass Flow Meter (TMM) or Thermal Mass Flow Controller (TMC)

High-Tech Fermentor Vessel Simplifies Operation FERMENTOR PENETRATIONS:

HEADPLATE

- Thermowell for platinum RTD Sensor*
- Ring Sparger
- Harvest Tube
- Sampler Assembly
- DO Electrode*
- pH Electrode*
- Acid Addition
- Base Addition
- Inoculation (Septum)
- Exhaust Gas Condenser
- Foam Level Detector*
- Anti-Foam Addition
- Spare Ports

SIDE WALL

- Four Process Ports
- Without Ports (optional)

HEAT EXCHANGER

- 2-Side-Entry Probe Ports (optional)

Vessel Description

BioFlo 3000 is equipped with a thick-walled glass tube fermentor vessel that provides superior resistance to rough handling and repeated autoclaving. This configuration allows for significant reduction in autoclaving time compared to glass-jacketed vessels. For precise temperature control the stainless-steel base has a dished bottom that is jacketed for the circulation of warm or cool water. The BioFlo 3000 provides a closed-loop temperature control system without the need for external water baths or circulators. The vessels are interchangeable and have working volumes of 1.25, 2.5, 5.0 and 10 liters. All seals are EPDM, silicone or Teflon. Easy handling, set-up, and installation are achieved by a detachable motor that readily couples to the agitator without tools, convenient quick-connects for jacket water circulation, and alignment pins that secure the vessel to the console without tools. In addition to eight fermentor vessels, four cell culture vessel assemblies can also be supplied with a choice of five low-shear impellers and a packed-bed basket accessory for immobilized cell culture. For details, please see our CelliGen Plus literature.

Greater Versatility in DO Control Than Ever Before

Dissolved Oxygen Control Strategies

Two operating modes accommodate fermentation and cell culture applications. In both modes the BioFlo 3000 controller features adjustable P-I values for those who want to customize DO response.

Fermentation Mode: More than a dozen built-in control cascades let you establish precise control of dissolved oxygen in the way best suited to your application. The Thermal Mass Flow Controller (TMC) equipped BioFlo 3000 can utilize agitation, oxygen enrichment, and air flow, together or in sequence, individually or in combination, to automatically maintain dissolved oxygen at the most productive levels. User-set agitation and gas flow limits let you avoid foaming, and ensure a uniform suspension under all conditions. The BioFlo 3000 has a guaranteed Oxygen Transfer Rate (OTR) of at least 350mM/L/hr at standard pressure using standard air, *before oxygen supplementation.*

Cell Culture Mode: DO and pH control are linked through the built-in 4-gas control system. Precisely metered air, oxygen, CO₂, and nitrogen are automatically blended to maintain DO and pH at desired levels. With the optional BioCommand® software, liquid base additions can be used in tandem with the 4-gas system.

PC-Compatibility and Bioprocessing Software

BioFlo 3000's broad operating capabilities are extended even further by its PC compatibility and its optional advanced bioprocessing software. The computer facilitates yield optimization strategies as well as programmed data acquisition, data logging and real-time graphics.

Continuous Culture

In addition to routine batch and fed-batch fermentation procedures, the BioFlo 3000 is designed for operation as a chemostat. Nutrient is transferred from an accessory media reservoir into the fermentor via one of the panel-mounted pumps. Pump flow is calibrated to maintain the desired dilution rate, and is indicated on the data display screen. A vessel

overflow port is connected to an accessory product reservoir in order to maintain steady-state growth conditions in the fermentor.

THE NEW FERMENTATION TECHNOLOGIES

Microprocessor Control System (MCS)

An on-board control system has an extensive memory that helps simplify the entire operation, from probe calibration to cell growth and product recovery. The data control center displays over 75 setpoints and process variables in 13 control loops to help optimize fermentation parameters. The alpha-numeric display provides easy access to every phase of the operation, simplifying start-up, cell growth and product manipulation.

High Oxygen Transfer Rate Guaranteed

A permanent magnet motor is built for high-speed agitation of microbial fermentation as well as gentle stirring of shear sensitive cultures. The drive motor has high torque output and maintains speeds from 20 to 1,000 rpm via high-resolution optical sensor in a feedback control loop. The sensor can lock onto any setpoint with an accuracy of + 1 rpm. Vessel geometry combines with agitator power to achieve a high oxygen transfer rate of 350 mM O₂/L/Hr.

Electronic Air Flow Control

Both a Thermal Mass Flow Meter (TMM) and Thermal Mass Flow Controller (TMC) are offered. The TMM digitally displays air flow data on the fermentor's display panel, as well as exports the data to optional software for monitoring and archiving. The TMC not only offers display and export capability, but adds an electronically operated valve that allows the user to cascade air flow with other parameters, either via the built-in microprocessor or optional software. When utilizing optional BioCommand software, air flow can be associated with a time or event profile.

Built-In DO Control Strategies

Control strategies may be employed to optimize DO using agitation and/or pure oxygen to meet the desired DO concentration. If optimum DO is not reached in the first mode, the operator can switch to the second, third or fourth strategy until the DO setpoint is reached.

Pumping Versatility

Five built-in, programmable pumps can be assigned to more than seven different functions via the keypad. These include addition of acid, base, chemical defoamer and nutrients as well as the harvesting of culture, and pump actuation at three different liquid levels. Control capability is also provided for an optional sixth pump.

BioFlo 3000 Fermentor Specifications

VESSEL VOLUME

Total Capacity (L) 1.6 3.3 6.6 14.0
Working Maximum (L) 1.25 2.5 5.0 10.0
Working Minimum (L) 0.6 1.3 2.5 3.0

VESSEL DIMENSIONS for Autoclave2

Height 19" (48 cm) 22" (56 cm) 24.5" (62 cm) 27" (68 cm)

Diameter 9.5" (24 cm) 10" (25 cm) 10.5" (27 cm) 12" (31cm)

VESSEL DIMENSIONS

Height 11" (28 cm) 13" (34 cm) 16" (41 cm) 18" (46 cm)

with Slant Rack Diameter 11" (28 cm) 11" (28 cm) 11" (28 cm) 12" (31cm)

AGITATION

Drive Permanent magnet top-drive motor with high torque. Readily removable without tools.

Range 50 to 1000 rpm

Sensor Photo-optical encoder disk with a resolution of 1000 pulses/revolution

Control Microprocessor-based with PID

Impellers Six-bladed Rushton impellers standard. Other impellers optional

Indication Digital display in 1 rpm increments

OXYGEN TRANSFER RATE (OTR) 350 mM O₂/L/Hr or more, for fermentation applications only

TEMPERATURE

Range

From 5°C above coolant temperature to 80°C ± 0.1°C, or from + 4°C to 80°C with optional refrigeration system, ± 0.1°C. Rapid temperature shift of 1°C/minute (25°C-45°C)

Control PID with pulse-width modulation of heater and cooling water

Sensor Platinum RTD

AERATION

2-Gas Mode Air and O₂ metered to ring sparger in fermentation mode

4-Gas Mode Air, O₂, CO₂ and N₂ for interactive pH/DO control in cell culture mode or manual dosing of gasses for plant cell culture

Air Flow, Electronic Choice of Thermal Mass Flow Meter (TMM) or Thermal Mass Flow Controller (TMC)

Sparger Removable Ring Sparger

Inlet Filter 0.2 µm absolute filter cartridge interchangeable and repeatedly autoclavable

EXHAUST SYSTEM

Filter 0.2 µm absolute filter cartridge interchangeable and repeatedly autoclavable

Condenser Stainless steel water-cooled condenser mounted in headplate minimizes evaporation

pH

Setpoint/Display Range 2.00 to 12.00

Control Modes

Fermentation: PID control of liquid additions. **Cell Culture:** 4-gas interactive pH/DO control; and base addition with optional BioCommand software

Probe Select Ingold or Broadley James gel or Ingold liquid-filled probes

DO

Setpoint Range 0 to 100% \pm 0.1

Display Range 0 to 200% \pm 0.1

Control Modes

Fermentation: PID serial and parallel cascades to agitation and O₂ gas, (and to air flow with TMC only). **Cell Culture:** 4-gas interactive pH/DO

Probe Select Ingold or Broadley James probes

PUMPS

Control

5 assignable pumps provided for control of nutrient, acid, base, foam, harvest and 3 different levels 3. Control output for optional sixth pump also provided

Indication 0 to 100% of output

OVERALL DIMENSIONS

Width 25.5" (65 cm)

Front-to-back 24.75" (63 cm)

Height 30.0" (76 cm)

WEIGHT APPROXIMATE

Gross 372 lbs. (169 kg) 380 lbs. (172 kg) 390 lbs. (177 kg) 465 lbs. (211 kg)

Net 332 lbs. (150 kg) 340 lbs. (154 kg) 350 lbs. (159 kg) 405 lbs. (184 kg)

ELECTRICAL DATA

Fuse 12 Amps for 100V & 120V, 6.25 Amps for 220V & 240V

Power Accepts 100 - 240V 50 or 60 Hz service

DATA DISPLAY SCREEN

8" (20.3 cm) alpha-numeric vacuum-fluorescent screen displays multiple lines of data using 40 characters for up to 13 control loops

COMMUNICATIONS PORT

Compatible with both EIA-422A and 232C standards

RECORDER OUTPUT

4-channel output for pH, DO, temperature and agitation

- (1) For optional cell culture accessories and vessel dimensions, see our CelliGen Plus literature
- (2) Vessel dimensions shown are as set up for an autoclave, with the motor removed. Slant racks are available that reduce height requirements.
- (3) Different liquid levels may be employed to trigger pumps for delivery of antifoam and nutrient or for harvest of culture when liquid level reaches a pre-set volume.
- (4) Allowances should be made for additional space required for hose and electrical connections on both sides of the console, in addition to 4" (10 cm) of clearance required in rear of unit.
- (5) Agitation to 1,200 rpm maximum is possible. Consult with NBS.
- (6) Rapid temperature shifts applicable in vessels up to 5L working volume only. For 10L vessels, contact NBS.



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