

BIOSTREAM

Technical
specifications

BioBench Twin

Microbial /Cell Culture



BIOSTREAM

Vision



We offer total solutions

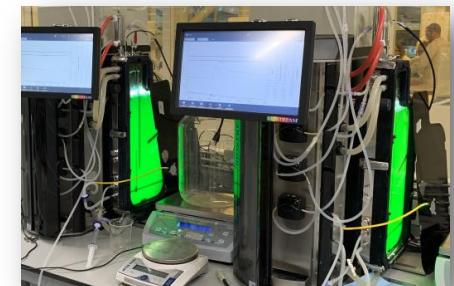
Open relation with the customer/
partner/suppliers and Employee's

Keep customer satisfied

Application fields



Food & Biobased



Algae



Cell culture

Type of Cells

All type of micro organisms
Fungi, yeast
Plant Cells
Solid state
Insect cells
Animal & human cells

Process Modes

Batch
Fed-batch
Continuous
Perfusion



Applications

Process development,
optimization and characterization
Scale-up and scale-down studies
Small scale production

Industries

Biopharmaceuticals
Vaccines
Cell therapies
Industrial biotechnology
Basic research
Education

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BioCompact multiple reactor



BioBench Twin



BioBench



BioPilot



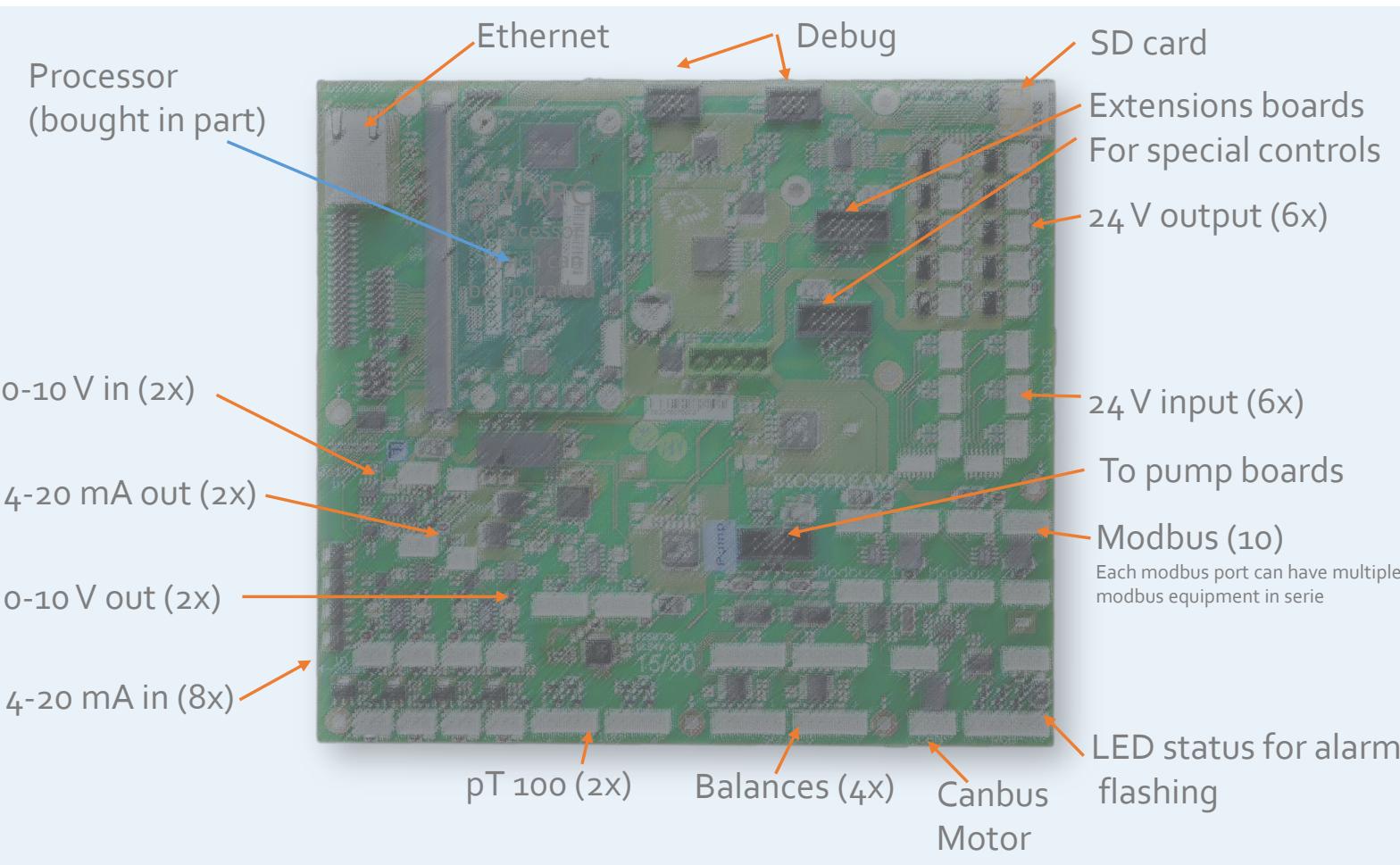
BioTwin
Single vessel



Bioproject

Range of Bioreactors

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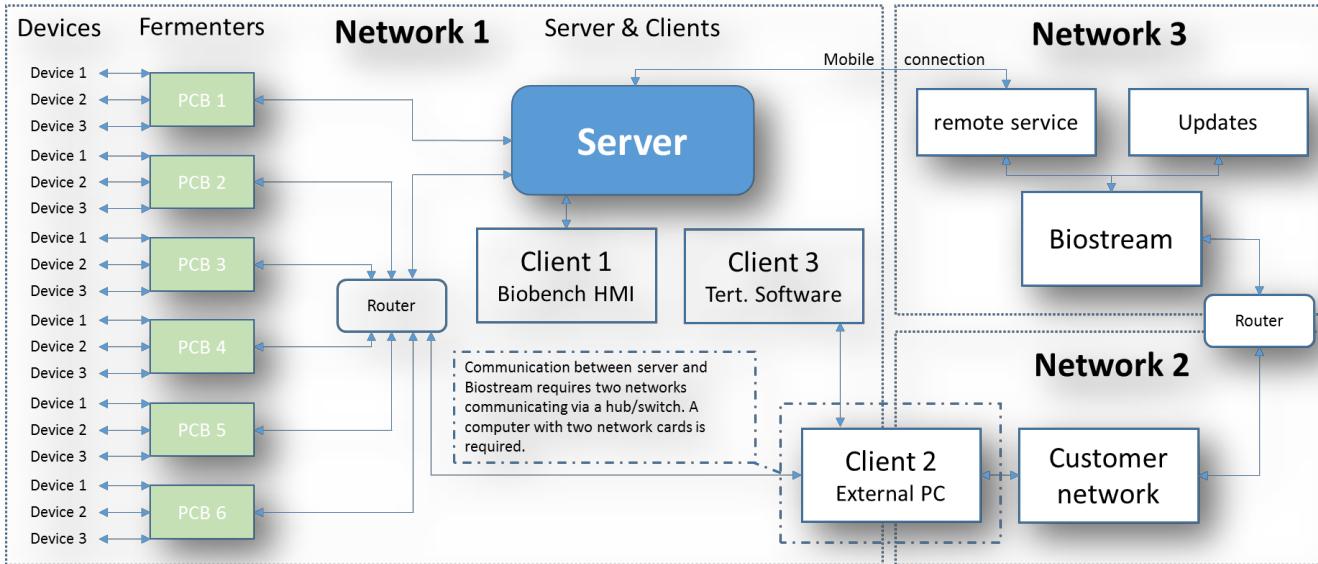
Basic control print

Extension board possibilities

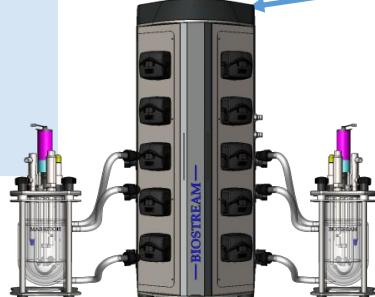
- Extra I/O channels
- Valve boards
- Connection of old equipment
- Custom made options



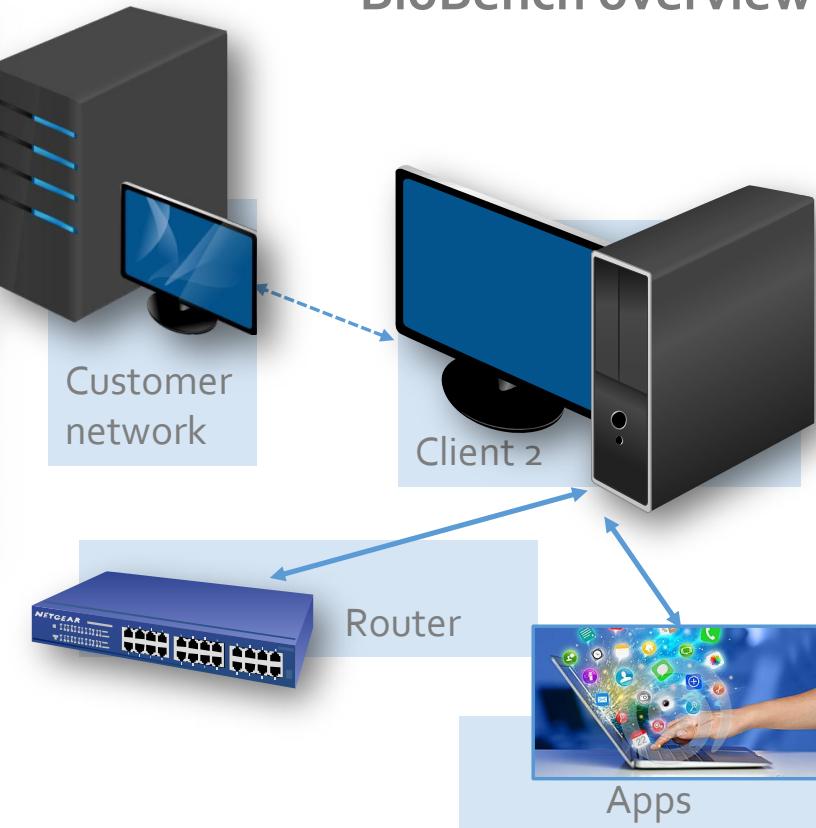
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Customer needs to give access to a VPN connection for Biostream if this is allowed
Possible to have Wi-Fi & Bluetooth connection or call in via mobile connection



BioBench overview



Expandable to 32 fermentors and more

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Connections of external equipment



Internal/
External pumps



Biomass/ OD



CO2/O2 Off gas



Mass flow controllers
& Gas mixers



CO2 in-line



Balances



pH and Do sensors
(disposable)



valves



All kind of motors
with adapter



Chillers

Example:
Adapter for Applikon vessel

Some Examples are shown in this overview

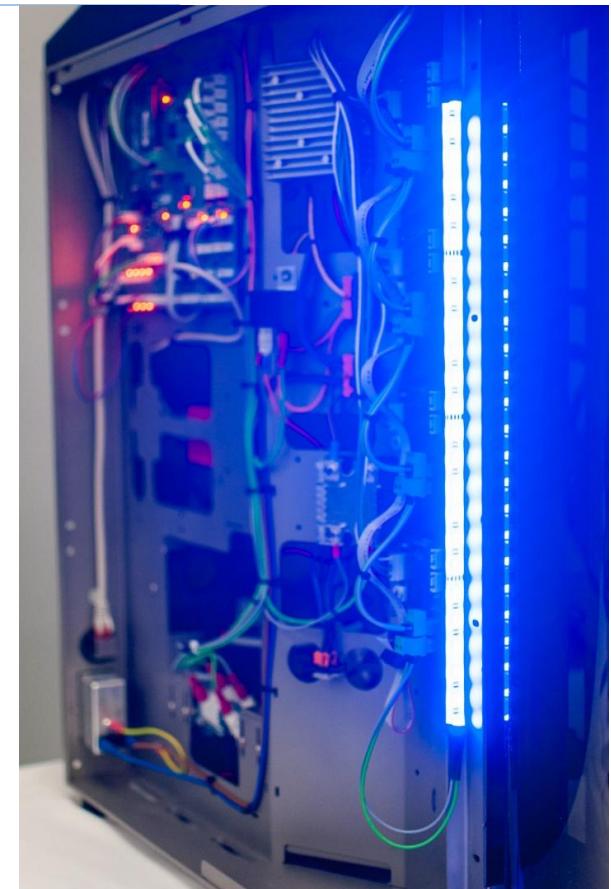
All measurement devices and actuators with
an in- or output can be connected

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Integration of Sensors, actuators and PID control loops in a standard BioBench

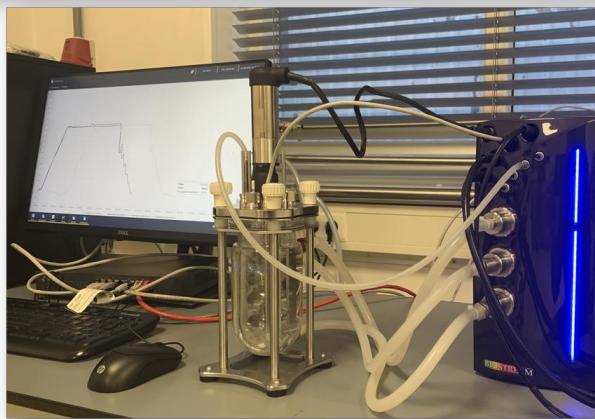
Setting	Number	Type of sensor&actuator
Modbus	64	For pO ₂ , pH, MFC, Off gas and other digital sensors
0-10 V Output	2	For pumps, LED, pressure, gasmix
0-10 V input	2	Redox-sensor, Gas-sensor, OD, Pressure, load cells and more
4-20 mA output	4	For pumps, LED, pressure, gasmix
4-20 mA Input	4	Redox-sensor, Gas-sensor, OD, Pressure, load cells and more
24 volt Output	10	Valves, solid state relais, pumps
24 volt Input	6	Others
CAN Bus	1	Digital motor control
RS-232	4	Balances
PT-100 config	2	pT100 sensor
Connection to pump boards	5	Only for integrated pumps in the Biobench
RGB option	1	For alarming and camera
Extension boards	2	

Extension boards can be used to get more I/O signals on the control board



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Fermentor A			No Alerts		Default User		08-me-2016 08:12:56	
Parameter	Value	Unit	Setpoint	Output	Gauge	Active	Settings	
Air_flow			not set			Off	Settings	
antifoam	0	V	10		0.0	Off	Settings	
Balance 1		kg	not set			Off	Settings	
Balance 2		kg	not set			On	Settings	
CO2_flow			not set			Off	Settings	
feed	0		not set		0.0	Off	Settings	
feed 2	0		not set		0.0	On	Settings	
internal temp		°C	100			Off	Settings	
O2_flow			0			Off	Settings	
pH	30		14		30.2	Off	Settings	
pO2			not set			Off	Settings	
stirrer	0		not set		0.0	Off	Settings	
temp	19	°C	not set		18.7	Off	Settings	



Selecting all the bioreactors or a specific one.
Easy addition of new bioreactors.
Adding new computers in the network where you can
Work the same as the local HMI.

BOS Controlling & Logging Software

Possible to use BOS software via Touch screen, tablet or via computer.

App available for Mobile phones.

Easy and free installation on PC.

Simple and intuitive use.

No license needed for more users.

Control via OPC UA/XML-DA.

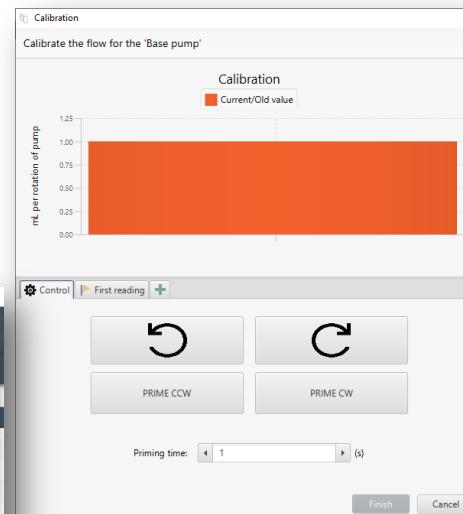
FREE upgrades of software. Each 2 months there is a release of new features. This can be downloaded and can be upgraded by yourself.

All fermentors		
	All fermentors	
	Bioreactor 1	Started
	Bioreactor 2	Preparing
	Bioreactor 3	Preparing

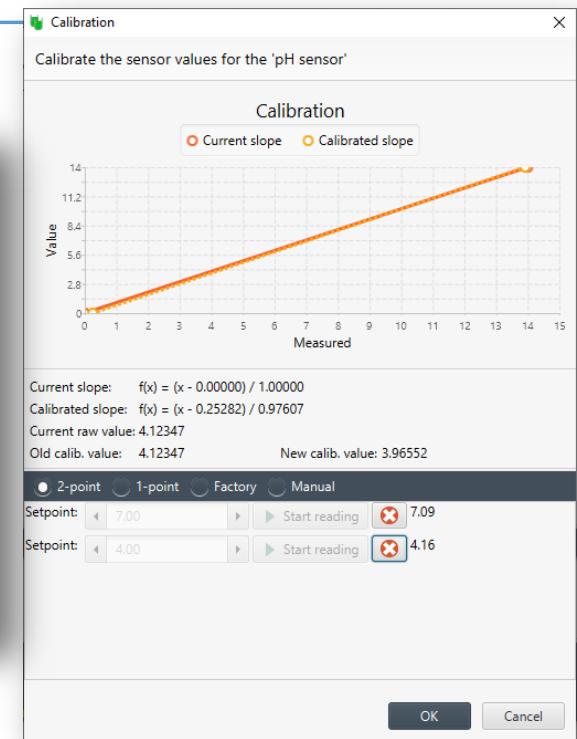
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BOS Controlling & Logging Software

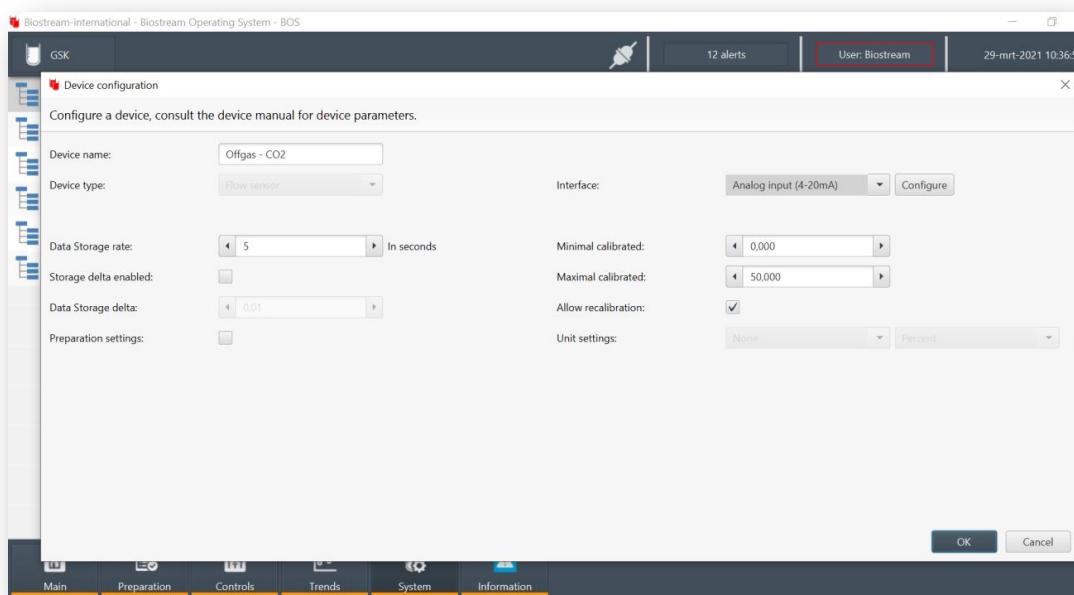
Easy one & two point calibration with graphical view and raw data for all sensors and pumps.
Multiple calibrations available for pumps to get a higher accuracy.
Maintenance information sensors.
Priming and control direction of the pumps.



Example: Pump calibration.



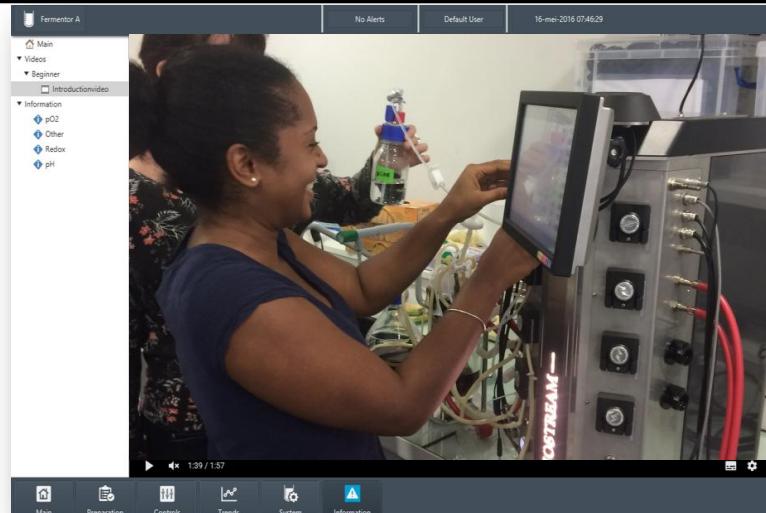
Example: Sensor calibration.



Adding external devices like sensors,
pumps and valves yourself.
Design your own parameter control
loops.

Parameters can be P&ID controlled

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Multimedia integration like movies from phone & tablets in the HMI.

K_A Measurements

Introduction
K_A values for the **Biobench** with different vessels were tested at different stirrer speeds with demi-water.

Setup
The **Biobench** vessels were connected to a controller unit and operated with the data logging and controlling software. Temperature was set to 30 °C. Pressurised air and nitrogen (grade 3.0) were used to flush the vessels. The oxygen sensors, Finesse TruDO 12mm D4 325mm³, were polarised and calibrated prior to measurements. The oxygen transfer rates were determined at different volumes (liter), agitation rates (rpm) and air flows (gas volume per liquid volume per minute) for each **Biobench** vessels as listed below. Also, the impeller type, size and relative location to the axis tip are listed below.

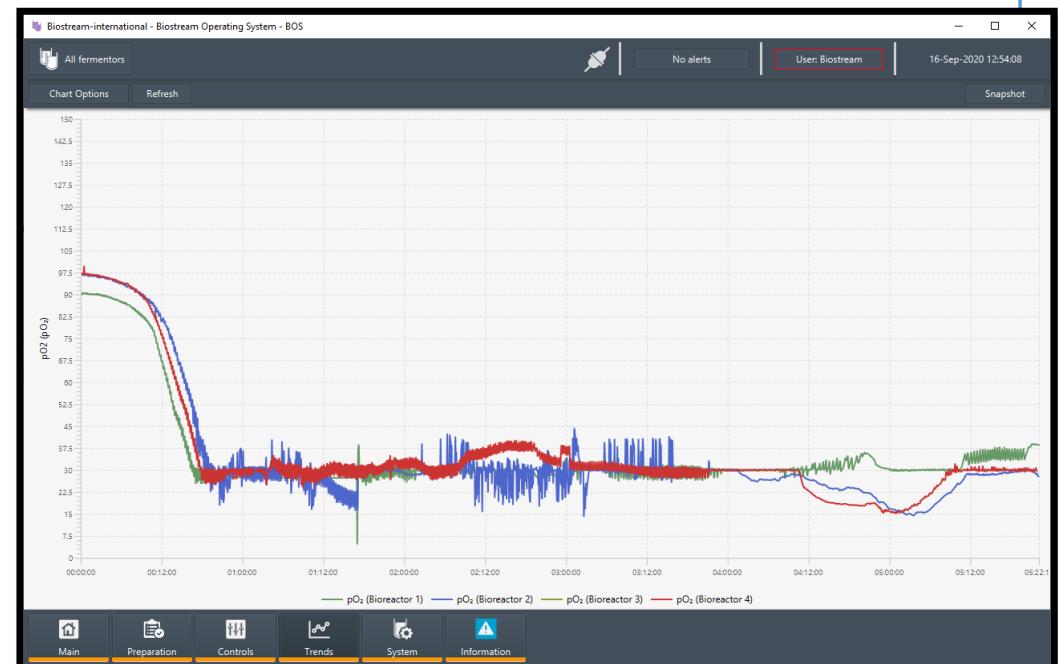
Volume vessel	2	3.6	7.5	7.5	13
Working volume	1, 1.5	2, 3	3.5	5	6, 10
Agitation (RPM)	200-1000	200-1000	250-1000	500-1000	200-1000
Impeller	2 Rushton 46mm	2 Rushton 46mm	2 Rushton 54mm	3 Rushton 54mm	2 Rushton 70mm
Impeller locations (mm)	0	50	110	0	139 20 117 216 10 145

The dissolved oxygen data were recorded, exported to Microsoft excel and plotted as $-\ln(C^* - C)$ versus time. (see Figure 1 as example) Where C^* is the maximum concentration (100%) and C is the measured dissolved oxygen concentration. The slope of a linear fit through these data points give the $-K_A$ (sec⁻¹). Multiply by -3600 to get the K_A (hours⁻¹).

Integration of your own protocols (SOPs) in the HMI.

BOS Controlling & Logging Software

Own defined multiple graphs.
Comparison with on-line and historical data.
Change graph settings during the run.
Store different graphs per user.
Take a snap shots of graphs.
Running with one year of data
For each parameter can be set a logging rate and logging on a change of value



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Cascading and automation possibilities

Recipes

Independent automatic control of parameters and also simultaneously.
Unlimited numbers of programs.
All kinds of programming possible.

Recipes

Search...

Add View Start Stop

Name	Status	Sequence	Runtime
SAFETY: Headspace > 5% O ₂	Running	1: Wait for O ₂ > 5%	00:00:26
Level Control	Running	1: No Level	00:00:23
Feed up	Running	1: wait 5 min	00:00:20
Setpoint AF	Running	1: Check feed > 50%	00:00:17
Check Temp	Running	1: Temp > 20 C	00:00:10

Example: Different automation protocols

Cascading with P&ID

All kind of positive and negative cascades possible.
Selection of simple cascading or with P&ID.

pO₂

Active:

PID cascade:

Deadband: 0.000 pO₂

Deadband evaluation time: 1 Seconds

Example: Switch between normal and P&ID cascading



Recipe System

Name: Setpoint AF
Evaluation time (s): 1
After last sequence: Loop back to first sequence

Sequences

Seq.	Name	Action
1	Check feed > 50%	Wait for Condition
2	Setpoint AF = 4	Run for set time
3	Check feed < 50%	Wait for Condition
4	Setpoint AF = 2	Run for set time

OK Cancel

Example: Program block

Cascade

Configure a cascade.

Offgas analyzer

Offline Sample

Antifoam

pH

pO₂

Stirrer

Temperature

Feed 1

pH

pO₂

Stirrer

Drag here

Drag here

OK Cancel

Example: Drag and drop blocks for cascading possibilities

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BOS Controlling & Logging Software

Create your own simple check list for starting up a bioreactor

The screenshot shows a software interface with a dark header bar. Below it, a main window titled 'BioBench01' contains a 'Calibration' tab and a 'Checklist' tab. The 'Checklist' tab is active, displaying a list of items with checkboxes:

- Checklist Item 1 (checked)
- Calibrating the pH sensors (unchecked)
- Adding sulphate to the culture medium (checked)
- Checklist item 4 (unchecked)

Sample tracking

With possible volume correction on total
Volume to change feeding protocols

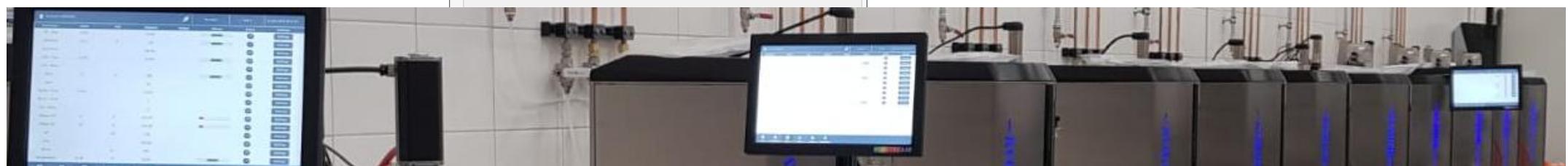
Sample overview		
Sample date	Description	mL
15-Sep-2020 09:29:38	Sample 1	23
15-Sep-2020 09:29:47	Sample 2	16

The screenshot shows a software interface with a dark header bar. The main window contains a table with columns: 'Parameter', 'Value', 'Unit', 'Setpoint', 'Output', and 'Alarms'. A row in the table is highlighted in grey, corresponding to the 'off line glucose' entry. To the right of the table, there is a form for inputting data:

- 'Add a sample value' button
- 'Select a sample:' dropdown menu
- 'Or set time directly:' date and time picker set to '29-3-2021 10:21:09'
- 'Selected insertion date/time:' text input set to '29-mrt-2021 10:21:09'
- 'Enter corresponding value:' numeric input set to '0,00000'

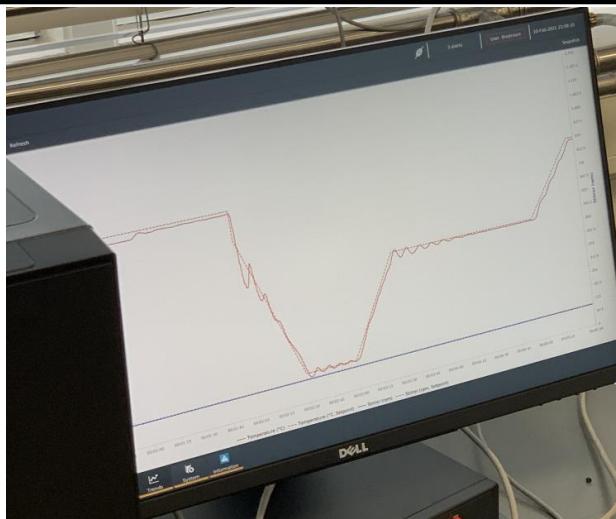
At the bottom right are 'OK' and 'Cancel' buttons.

Off-line measurement input



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BOS Controlling & Logging Software parallel functions



Biostream-international - Biostream Operating System - BOS

All fermentors

12

GSK

Parameter	Value	Unit	Setpoint	Output	Alarms
Gas Analyzer ...		%			
pH	pH		4.00		
pO2		%			
Stirrer	rpm		1200	100%	
Temperature	°C		20.00		

Merck

Parameter	Value	Unit	Setpoint	Output	Alarms
pO2					

CIP

Parameter	Value	Unit	Setpoint	Output	Alarms
pH	pH				
pO2		-			
Stirrer		rpm			
Temperature		°C			

DSM

Parameter	Value	Unit
Please select one or more parameters		

Main Preparation Controls Trends System Information

All fermentors

2 alerts

Log in

07-mrt-2021 16:24:08

#	Name	Status	Started	Inoculated	Stopped	Select
0	DTU Yellow	Stopped	18-nov-2020 12:10:34	-	-	<input type="checkbox"/>
1	DTU 7.5 liter	Stopped	18-nov-2020 12:10:34	-	18-nov-2020 12:57:09	<input type="checkbox"/>
2	CIP	Stopped	04-nov-2020 14:38:24	-	04-nov-2020 14:38:35	<input type="checkbox"/>
3	holiferm	Stopped	04-nov-2020 14:38:25	-	04-nov-2020 14:38:35	<input type="checkbox"/>
4	VIT (DEMO)	Started	19-nov-2020 11:29:03	-	-	<input type="checkbox"/>

Fill jackets Start Inoculate Stop selected Select All Select None Stop all

Main Preparation Controls Trends System Information

Select All Select None

Select	Name	Input/Raw	Old Slope	Old Offset	Old Value	First meas.	Sec. meas.	New Slope	New Offset	New Value
<input checked="" type="checkbox"/>	DTU	Invalid	1.00000	0.00000	Invalid	-	-	Invalid	Invalid	Invalid
<input checked="" type="checkbox"/>	GSK	Invalid	1.00000	0.00000	Invalid	-	-	Invalid	Invalid	Invalid
<input checked="" type="checkbox"/>	CIP	Invalid	1.00000	0.00000	Invalid	-	-	Invalid	Invalid	Invalid
<input checked="" type="checkbox"/>	Merck	Invalid	1.00000	0.00000	Invalid	-	-	Invalid	Invalid	Invalid

2-point 1-point Factory Manual

Setpoint: 100.00 Start reading

Setpoint: 100.00 Start reading

Parallel starting and inoculation
 Parallel calibration of pumps
 Overview control of bioreactors
 Parallel graphs with existing data and historical data.

REQUEST a demo for testing

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BOS Controlling & Logging Software

On-line service and validation purpose

21 CFR part 11 compliance.

With user login and tracking user actions.

Logging of confirmed alarm overview by user.

Service tools for distance service and assisting.

Advanced options:

Filtering of parameters like OD raw value

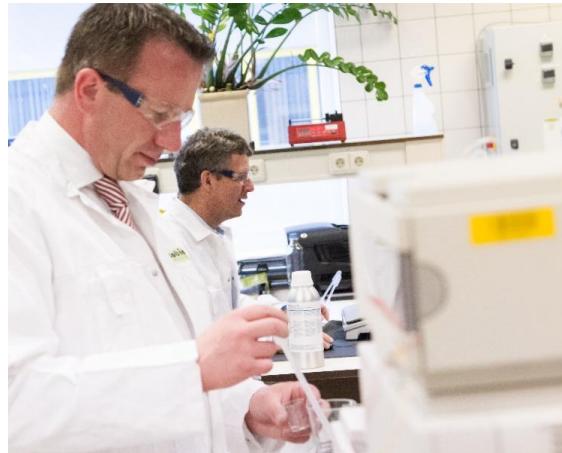
pH temperature correction

Confirmation to inform users before starting a run

Force check list for completion

Auto log on/off

Auto calibration of pumps



User actions

Biostream-international - Biostream Operating System - BOS

Actions

Date/Time	Fermentor	User	Action
16-Sep-2020 09:18:33	BioBench01	Biostream	The user "Biostream" set the recipe state of recipe "StabTest1" to: Started
16-Sep-2020 09:18:31	BioBench01	Biostream	The user "Biostream" set the recipe state of recipe "StabTest2" to: Started
16-Sep-2020 09:18:28	BioBench01	Biostream	The user "Biostream" set the recipe state of recipe "StabTest1" to: Started
16-Sep-2020 09:18:21	BioBench01	Biostream	The user "Biostream" set the fermentation state of the fermentor to: Started
16-Sep-2020 09:18:12	BioBench01	Biostream	The user "Biostream" set the fermentation state of the fermentor to: Started
15-Sep-2020 21:03:54	BioBench01	Biostream	The user "Biostream" set the fermentation state of the fermentor to: Started
15-Sep-2020 15:29:56	N/A	Biostream	The user "Biostream" changed the password of the user "Biostream". - The group was changed from "TestGroup" to "OpGroup". - The password was changed.
15-Sep-2020 15:28:06	N/A	Biostream	The user "Biostream" made changes to the user "Biostream". - The password was changed.
15-Sep-2020 13:02:45	BioBench01	Unknown	An unknown user set the recipe state of recipe "StabTest1" to: Started
15-Sep-2020 13:02:29	BioBench01	Unknown	An unknown user set the recipe state of recipe "StabTest2" to: Started
15-Sep-2020 13:01:56	BioBench01	Unknown	An unknown user set the fermentation state of the fermentor to: Started
14-Sep-2020 17:20:56	BioBench01	Biostream	The user "Biostream" set the fermentation state of the fermentor to: Started
14-Sep-2020 17:18:39	BioBench01	Biostream	The user "Biostream" changed the setpoint of the fermentor. - The Maximum Output was changed from 10.0 to 5.0.
14-Sep-2020 17:18:08	BioBench01	Biostream	The user "Biostream" changed the setpoint of the fermentor. - The Maximum Output was changed from 10.0 to 5.0.
14-Sep-2020 17:17:02	BioBench01	Biostream	The user "Biostream" changed the setpoint of the fermentor. - The Maximum Output was changed from 10.0 to 5.0.
14-Sep-2020 17:15:59	BioBench01	Biostream	The user "Biostream" made changes to the parameter "Maximum Output". - The Maximum Output was changed from 10.0 to 5.0.
14-Sep-2020 17:10:58	BioBench01	Biostream	The user "Biostream" made changes to the parameter "Maximum Output". - The Maximum Output was changed from 5.0 to 10.0.
14-Sep-2020 17:10:15	BioBench01	Biostream	The user "Biostream" made changes to the parameter "Maximum Output". - The Maximum Output was changed from 1.0 to 10.0.
14-Sep-2020 17:08:35	BioBench01	Biostream	The user "Biostream" made changes to the parameter "Maximum Output". - The Maximum Output was changed from 5.0 to 10.0.
14-Sep-2020 17:07:07	BioBench01	Biostream	The user "Biostream" made changes to the parameter "Maximum Output". - The Maximum Output was changed from 5.0 to 10.0.

Main Preparation Controls Trends System Information

Advanced options

Biostream-international - Biostream Operating System - BOS

Biostream System Settings

Sterilization settings

- Allow fermentation start after sterilization:
- Show sample valve sterilization:
- Show harvest valve sterilization:
- Show pressure test:

Custom confirmation messages (keep empty for no warning)

Waterjacket start: First watch movie

Fermentation start:

Inoculate:

Fermentation stop:

Sterilization start:

Sterilization stop:

Sample valve steril. start:

Harvest valve steril. start:

Start bioreactor not allowed before check list if finished

Sequence Runtime Inoculate

Checklist incomplete

Not all checklist items have been completed while required.

A total of 12 items still need to be completed before continuing.

OK Cancel

Checklist

Biostream-international - Biostream Operating System - BOS

GSK

Calibration Checklist

- Clean vessel with detergents
- Connect all the parts on the vessel
- Start pH calibration see procedure pH calibration
- Put pH sensor in the vessel and cover the head with aluminium foil
- Connect all addition bottles and clamp of the tubing between the vessel and bottle
- Cover filter on the bottle with Aluminium foil
- Put filter on the sparger and on the condenser
- Clamp tubing between filter and sparger

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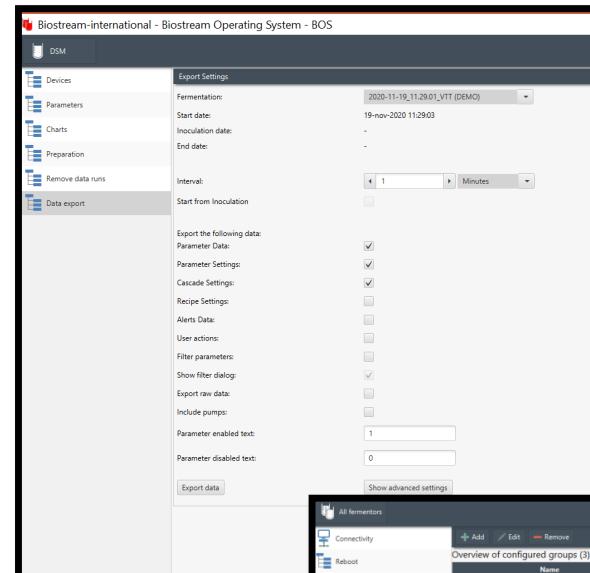
BOS Controlling & Logging Software

Export data and backup

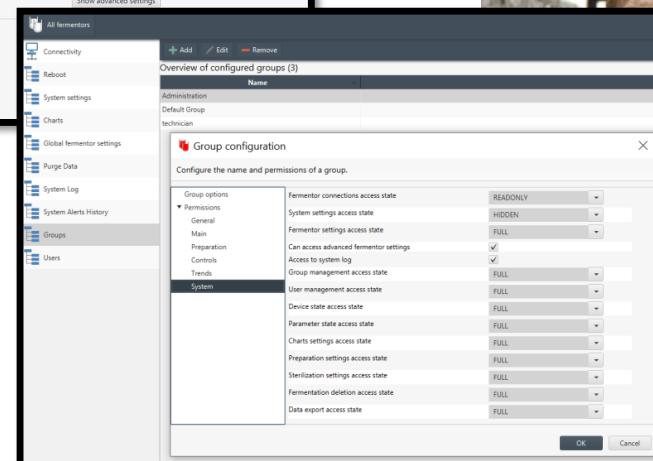
Data export function to excel or csv files
All the information which is stored can be exported

Database back up can also be automatically done
On your network

Connection to tertiary programs.
like Lucullus, Matlab, python or even
mathematical & prediction software via OPC



Data export



User management

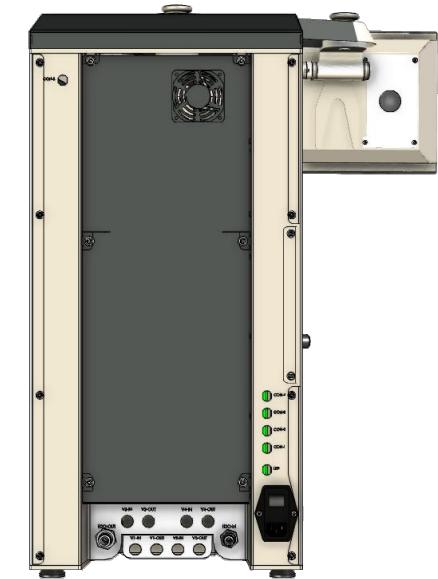


Integrations in the standard base unit

-  Motor holder
-  Gas mix
-  4 Mass flow controllers
-  3 rotameters
-  Network connections
-  Room for gas analyzers or other sensors
-  5 on/off or analog pumps



Internal room Biobench



Back plate can be dismantled

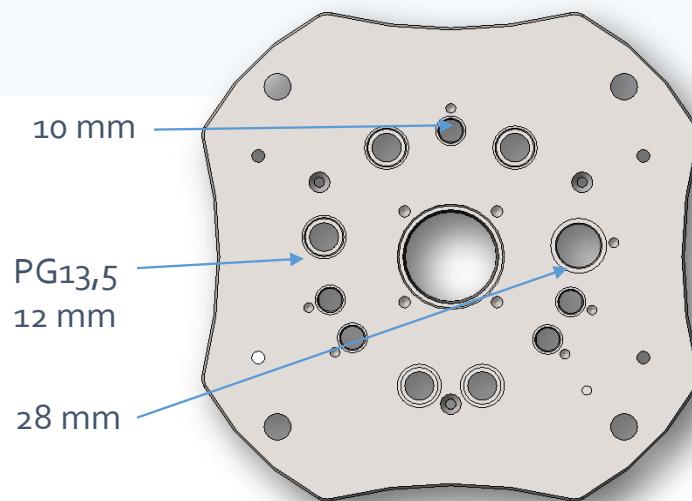
Vessel specifications

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Total Volume	250 ml	500 ml	750 ml	1.5L	2 L	3L	4L	5L	7.5L	13L	15L
Working volume	50-250ml	100-300ml	100-500ml	0,2-1L	0,4-1,5L	0,4-2L	0,5-3,4L	0,5-4L	0,5-5L	0,5-10L	0,5-13L
Head plate											
Type op ports (standard)											
8 mm	-	-	4	-	-	-	-	-	-	-	-
9 mm	8	9	-	4	-	-	-	-	-	-	-
10 mm	-	-	4	4	5	5	5	5	5	5	5
12 mm (PG13,5), 28 mm (for four way needle)	3	3	4	4	5	5	5	5	5	8	8
Half moon addition	-	-	-	-	1	1	1	1	1	1	1
Impellers Marine (0,5ID)	1	1	1	1	1	2	2	2	2	2	2
Vessel type:	Round bottom										



Pitched blade impeller

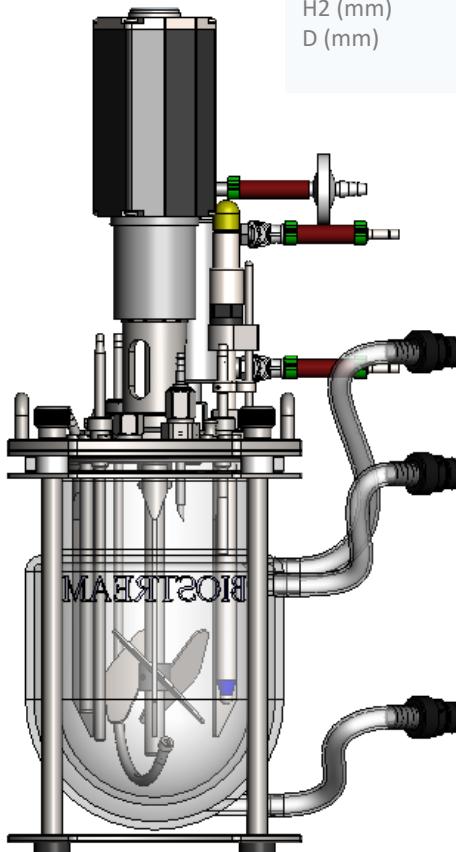


Vessel head plate from 2 to 7.5 L

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Universal water jacketed vessel

Total Volume	250 ml	500 ml	750 ml	1.5L	2 L	3L	4L	5L	7.5L	13L	15L
Dimensions											
H1 (mm)	199	242	269	373	254	345	309	309	496	605	715
H2 (mm)	307	351	378	482	377	467	434	434	660	666	859
D (mm)	158	158	158	174	208	201	194	194	169	290	290

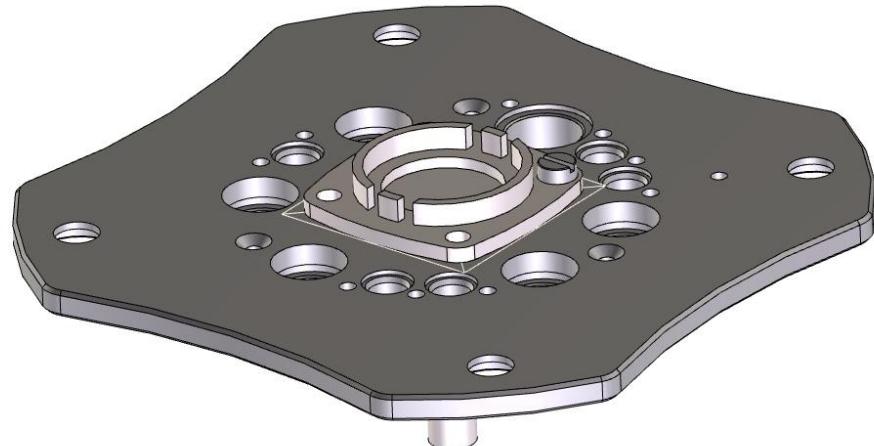


Linear scale up and down based on the same vessel dimensions.
Direct and magnetic drive systems.
Special designed for small autoclaves
Pitched blade, Marine, Spin filter, Cell lift or other mixing system
3D vessel will be available at delivery for easy finding parts



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Mechanical drive system



To maximum 700 rpm

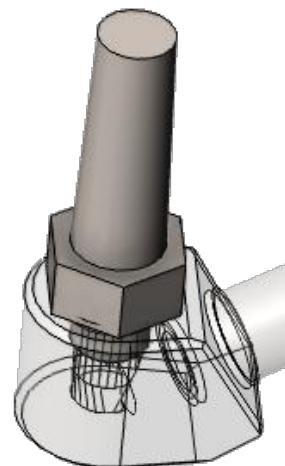


Sintered sparger

Sintered Sparger 5L Cell 15µm

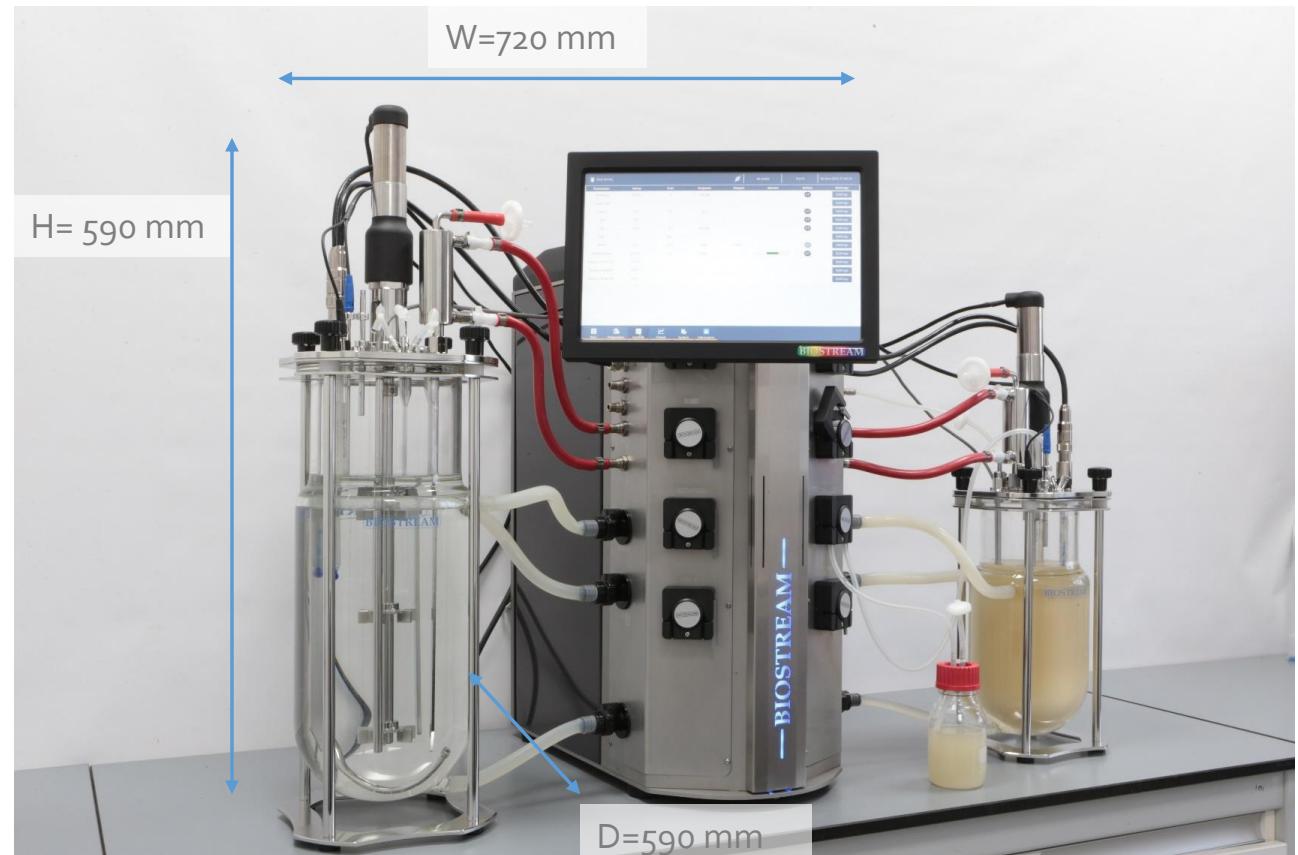
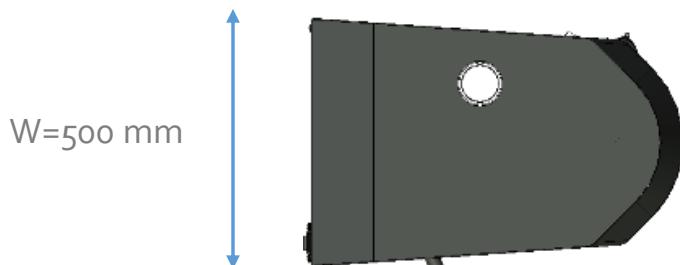
Specifications:

Tube OD/ID: 8 mm/ 4 mm



BIOSTREAM

Dimensions base unit





Pumps (also other pumps integration possible)

Free configurable for feed, base, acid, antifoam and more

Maximum 5 pumps in the cabinet. More pumps can be connected separate

Analog and On/off Pumps

Pump possibilities:

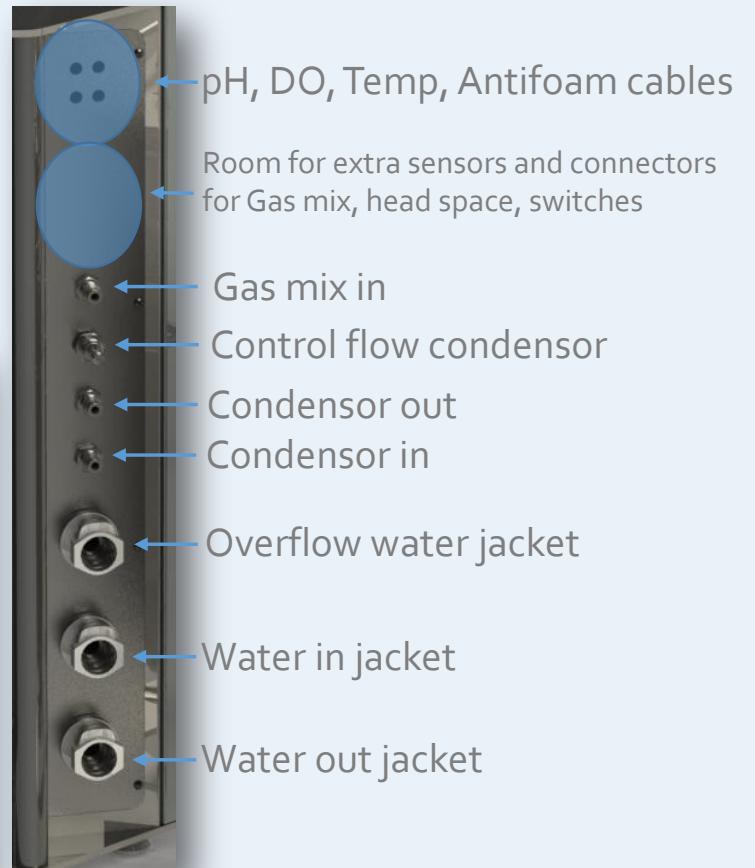
- Acid
- Base
- Foam & Level
- Feed 1
- Feed 2

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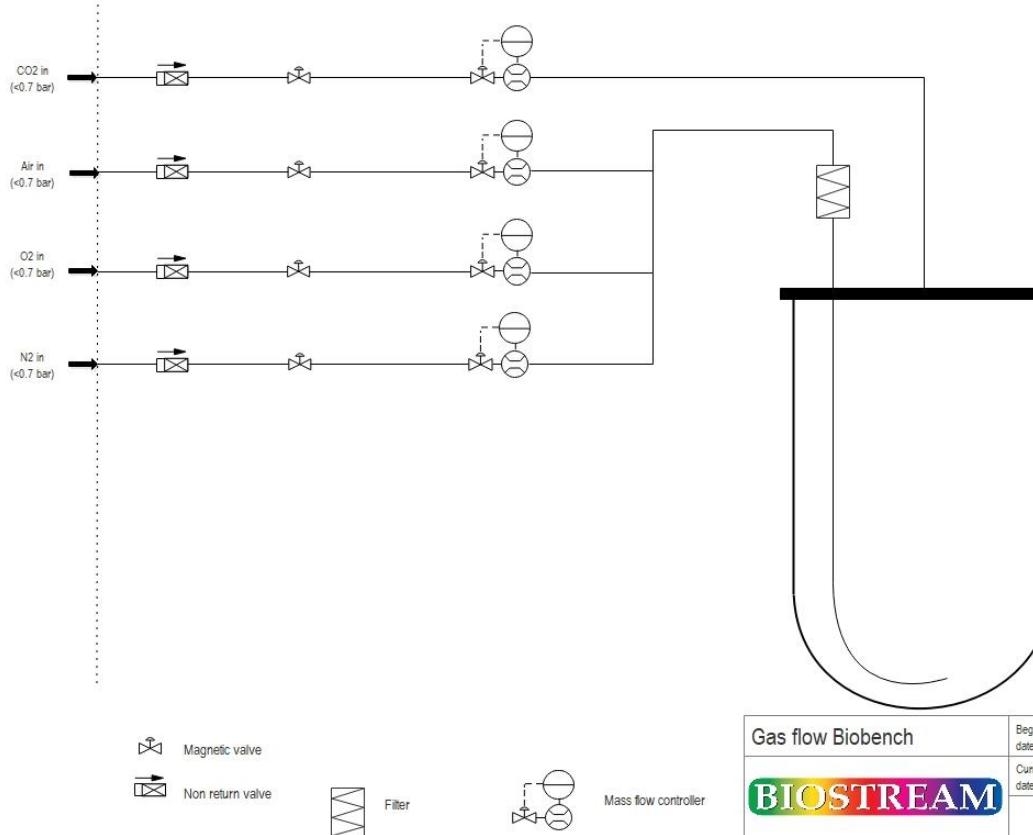
Connections to vessel



Custom made panels. No open holes



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Gas flow Biobench			
BIOSTREAM			
Begin date:		Drawer	
Current date:		Agreed	

3 MFCs with 1 MFC head space including gasmixing with valves

Gas mix can be adapted and you can use the gasses for head space and sparging

Define your own Gas mix

Option for more gas mixing strategies

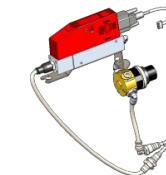


and more gasses

With flow meters:



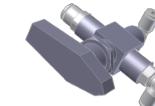
Rotameter



Mass flow controller



Manual switches for flexibility



BIOSTREAM

Controller specifications

1 Controller

Design	Multi touch 9 inch screen with advanced control or a separate PC Capable of communicating optimal with 6 utility stations Total 32 controllers possible.
Function	Monitoring (data storage) and control

2 Agitation

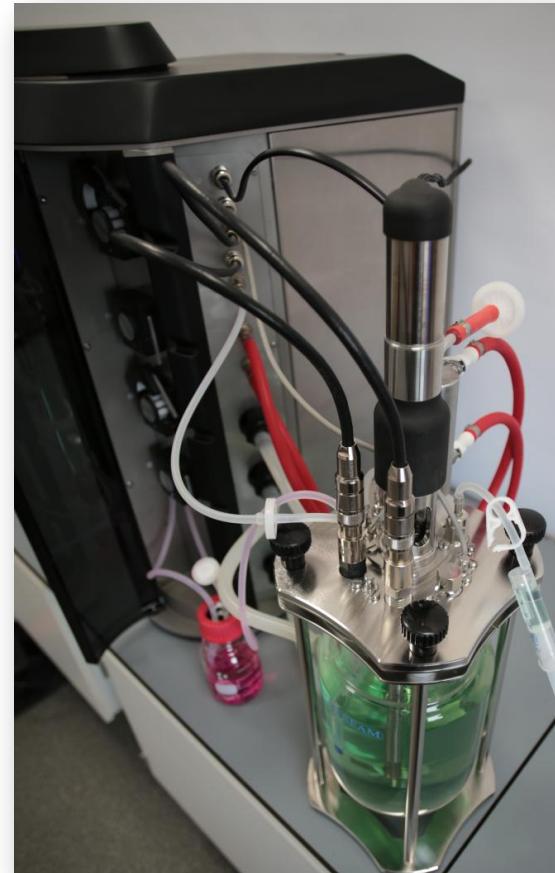
Drive	magnetic or mechanical
Stirrer speed	Speed is adjustable between up to 700 RPM.
Control	PID control.

3 Temperature:

Range	Water jacket vessel 5-8 °C above coolant (>0°C) from around 5°C above room temp to 85 °C.
Sensor	Pt-100 sensor (vessel and water system) Delta temperature control possible
Accuracy	+/- 0.1°C in range +10° to +60°C in fluids.
Control	PID control with cooling valve and water jacket heater
Temp. security	Automatic safety thermostat

4 pH

Range	2 - 14
Control	PID. Base and Acid (or CO2 gas) addition to control pH. Setting of dead band
Sensor	Intelligent pH probe with calibration data, runs and more (depends on brand)



BIOSTREAM

Controller specifications



DO

Range
Sensor

0 – 200 %
Intelligent DO probe with calibration data, runs and more (depends on brand)



Exhaust

Filter
Condenser

Standard 0,2 µm absolute filter (also other options available)
High condensation and can be dismantled completely.



Integrated Pumps

5 corrective reagent and Substrate pumps.
Standard 2 on/off (base, acid, foam) and 2 analog (feed in and out)
Easy adjustable from analog → digital
Additional integrated and external pumps possible.
Free configurable with a block at the back
Range from 0.001 to 347 ml/min with different tubings



Utilities

2 bar oil free gasses
0,5 - 3 bar water (normal tap water pressure)
The Biobench itself has pressure regulation internally for safety issues.



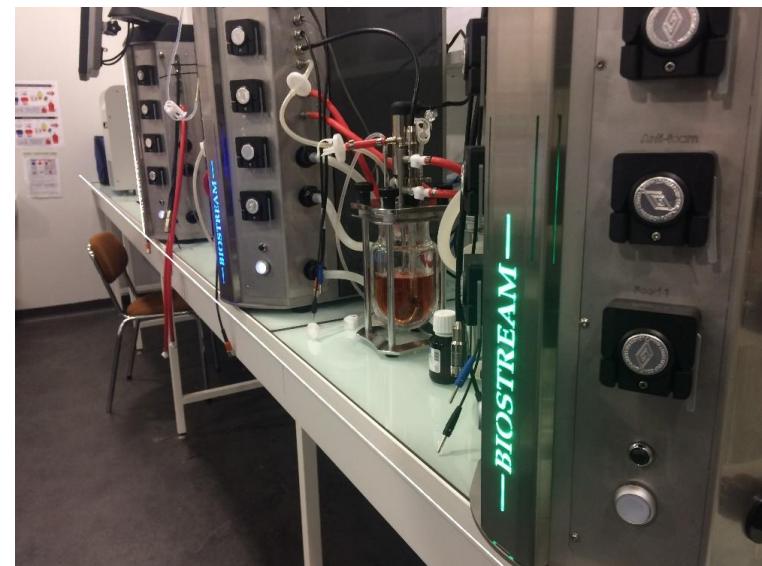
Aux. equipment

All kinds of external measurements can be integrated in the touch screen.



Electrical requir.

230V; 5 Amp (others also available)



Hamilton Digital DO sensor

DO Arc-sensor 12 mm

The VisiFerm DO Arc is the first optical oxygen sensor with integrated opto-electronics, having the full functionality of a measuring device with self diagnostics. It is steam sterilizable, autoclavable and CIP compatible. The VisiFerm requires less maintenance than a classical oxygen sensor as it does not have a mechanically sensitive membrane or a corrosive electrolyte.

Advantages:

- No electrolyte or polarization is necessary.
- Quality of the sensor
- Calibration data available
- Re-calibration of the sensor during the run.
- Cascade possibilities with Stirrer, Flow, Gasmix and O₂

a-length	120 mm
Accuracy at 25 °C	1 ± 0.05 %-vol; 21± 0.2 %-vol; 50 ± 0.5 %-vol
Analog Interface 1	4-20 mA for DO, programmable
Analog Interface 1 and 2	galvanically not isolated; pulse width modulation 3.5 kHz
ATEX Approval	No
Autoclavable	Yes
Baud Rate	4800, 9600, 19200, 38400, 57600, 115200 bd
Certificate	Yes, with parameter settings and materials used
CIP	Yes
Diameter	12 mm
Digital RS485 Interface:	Modbus RTU, max 31 addresses
Drift at Room Temp. under Constant Conditions	< 1 % per week
Electrical Connector	VP 8
Electrolyte	None



BIOSTREAM

Hamilton digital pH-sensor

The EasyFerm Plus sensors are designed to withstand demanding applications in pharmaceutical, biotechnology, and food & beverages industries. It is also suitable for harsh chemical processes. It withstands steam sterilization, autoclavation and cleaning in place (CIP). The electrolyte of the EasyFerm sensors is pre-pressurized to prevent the diffusion of sample into the sensor. The Everef-F reference cartridge ensures that the reference electrolyte remains free of silver and precipitation of proteins.

Advantages:

- Wide range of applications
- Ceramic diaphragm is an improved barrier of the electrode
- Highly reliable measurements after steam sterilization, autoclavation and CIP cleanings
- Drift-free measurement

EasyFerm Bio specifically designed for applications in Pharma and Biotechnology (EHEDG, Biocompatibility)

Pre-pressurized reference electrolyte ensures a clog-free diaphragm

Specifications

Measuring range	0 – 14 pH
Process temperature	0 – 140 °C (Arc: analog 0 – 110 °C, digital 0 – 140 °C)
Pressure range (relative to ambient)	0 – 6 bar (pressurized)
Hygienic aspects	Autoclavable, SIP, CIP
pH glass	PHI
Electrolyte	Phermlyte
Reference system	Everef-F
Diaphragm	HP Coatramic
Temperature sensor	Pt100 in VP version Pt1000 in LEVP version



BIOSTREAM

Option: Touch screen

- Touch screen computer
- Twistable arm and can be fixed in each position

